A CLINICAL & HEALTH ECONOMIC EVALUATION OF THORACIC AORTIC ANEURYSM SURGERY

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor of Philosophy by

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DECLARATION

This thesis has been written exclusively by the PhD candidate Dr Mohamad Bashir and has not previously been submitted for a degree. All quotations have been distinguished by quotation marks and sources of information have been acknowledged. The Thesis is approximately 62,000 words in length.

DEDICATION

I lovingly dedicate this work to my beautiful wife Dalia and my beloved children Adam, Gabia, Eva, Roland and Oliver. I thank them for their time, patience, support and for giving me the reason to continue and for unburdening my journey. I also dedicate this work to my parents Mrs Nazmieh Yehya and Mr Ali Bashir, who without them I wouldn't have embarked on this beautiful journey of learning. I'm very grateful for their support and eternally thankful for their unparalleled giving.

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ABSTRACT

Thoracic aortic aneurysm is a life-threatening condition which affects different parts of the aorta. A significant proportion of patients present with incidental aneurysmal disease and are physically asymptomatic at the time of their first presentation. However, despite their asymptomatic nature the existence of an acute aortic syndrome represents a life threatening disease which is associated with a high mortality rate. Thus the effective and efficient diagnosis and treatment of such patients is essential in optimizing both their quality and quantity of life.

This thesis takes advantage of a range of structural and policy changes that have been undertaken at Liverpool Heart and Chest Hospital (LHCH) to evaluate the impact of such changes on the clinical and cost effectiveness of aortic surgery. Foremost amongst these changes was the reorganization of the aortic service in 2007 to concentrate treatment in the hands of a small number of specialists. This thesis examines subspecialisation and reorganisation of surgical expertise and activity for the treatment of aortic surgery patients at LHCH resulted in significantly improved patient outcomes which is being achieved with cost neutral changes in service delivery. The thesis will assess the impact of this subspecialisation on a range of outcome dimensions including patient outcomes and the efficiency of resource utilization within the aortic service at LHCH.

The focus of this study is in tune with increased sub-specialization in a wide range of therapeutic areas in hospitals throughout the UK. It is hoped that the methodology and findings of this study may contain lessons that may be applicable to specialisms outside aortic surgery throughout the NHS and assist in developing an evidence based health policy to inform the ever growing trend towards increased sub specialization. The improvements appeared to simply result from the natural enhancement of expertise that results from concentration of specialist surgery in fewer and hence more experienced hands. In this regard, centralization of thoracic aortic aneurysm service appears to enhance both survival. The generalizability of these findings and potential lessons for the provision of specialist surgery in other therapeutic areas await further investigation

CONTENTS

CHAPTER ONE

1. INTRODUCTION

1.1 Overview

Thoracic aortic aneurysm is a silent disease, which in the majority of cases is asymptomatic. The aneurysmal aorta grows slowly and remain indolent until it reaches a pivotal point, at which it could either dissects or ruptures—complications that are bound to produce futile outcomes unless prior intervention are taken to avert complications. Therefore, timely detection of patients at risk of developing a thoracic aneurysm is imperative. Such timely detection can be achieved by identifying and understanding risk factors, clinical conditions, and unequivocal development of screening tools such as biomarkers and genetic components.[1,2] In recent years conditions such as bicuspid aortic valve[3], intracranial aneurysm [4], and bovine aortic arch[5], as well as a strong family history of aortic disease have all been shown to be associated with thoracic aortic aneurysm and dissection and not only this but they have been proven to increase predilection to development of aortic aneurysm disease. Nevertheless, a large percentage of newly identified thoracic aortic aneurysms are incidental findings revealed during imaging studies (echocardiography, computed tomography, MRI) performed for unrelated reasons.

1 Elefteriades JA, Farkas EA. Thoracic aortic aneurysm clinically pertinent controversies and uncertainties. J Am Coll Cardiol. 2010; 55:841–857.
2 Davies RR, Kaple RK, Mandapati D, Gallo A, Botta DM Jr, Elefteriades JA, et al.. Natural history of ascending aortic aneurysms in the setting of an unreplaced bicuspid aortic valve. Ann Thorac Surg. 2007; 83:1338–1344
3 Kuzmik GA, Feldman M, Tranquilli M, Rizzo JA, Johnson M, Elefteriades JA. Concurrent intracranial and thoracic aortic aneurysms. J Am Coll Cardiol. 2010; 105:417–420
4 Hornick M, Moomiaie R, Mojibian H, Ziganshin B, Almuwaqqat Z, Lee ES, et al.. 'Bovine' aortic arch -a marker for thoracic aortic disease. Cardiology. 2012; 123:116–124.
5 lbornoz G, Coady MA, Roberts M, Davies RR, Tranquilli M, Rizzo JA, et al.. Familial thoracic aortic aneurysms and dissections–incidence, modes of inheritance, and phenotypic patterns. Ann Thorac Surg. 2006; 82:1400–1405.

Once a patient has been diagnosed with a thoracic aortic aneurysm, it is equally important to closely monitor the disease progression of the aneurysm until a critical size is attained, at which time surgical treatment would be considered appropriate if the patient was deemed suitable candidate for surgical intervention[6]. The estimated growth rate of thoracic aneurysms is approximately 0.1 to 0.15 cm/year.

If the aorta is rapidly increasing in size that will shift the paradigm and surgeons' will have to make an informed choice with patients and their families to intervene and avert potential complications. Surgery on the thoracic aortic arch has always posed equal challenges to the surgeons and patients. To the surgeon, aortic surgery challenges are:

1) This is a highly specialized procedure that require set of skills that are learned through apprenticeship and at high volume centers.

2) The surgeon performing the surgery should benchmark his/her intervention with standard high volume center outcomes and the intervention must attain cost-effectiveness.

To the patients, the challenges posed are the ability to retain a certain degree of quality of life after the surgical intervention and certainly survival for a long term. The surgical outcome for aortic arch aneurysm improved consistently; however, it remains associated with some morbidity and mortality despite the improved surgical technology and brain protection strategies.

The reported mortality in literature for an elective aortic arch operation ranges between 7-24%6. The required operation to repair an aneurysm and avert a devastating complication including aortic dissection or fatal rupture requires a multitude of understandings and specific set of skills.

6 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease. Circulation. 2010;121:e266-e369

The decision to intervene should be based on intricate understanding of aetiology and pathophysiology of the disease, an understanding of the natural history of aortic aneurysm, surgical indications and when to intervene and when not to intervene. The knowledge should also entail the provision of resources that could help in facilitating the decision and optimizing the management. The resources that could be utilized albeit an endovascular approach or an open surgical repair should be evidence based in terms of outcomes and survival.

In the UK, it has been suggested that volume-based referral strategies are most appropriate for operative interventions, which are relatively infrequent, technically complex and with challenging post-operative care. Surgery of the thoracic aorta would seem to be one area where such considerations might applicable.

The available technologies and resources of endovascular approach lead to a surge of such procedures to be done on the aorta. Although short-term morbidity appears to be reduced in hybrid repairs, it is not clear that early death is reduced. In addition to the uncertain long-term functionality and durability of endovascular devices, the substantial risk of stroke due to wire and device manipulation within the aortic aneurysm in particular the aortic arch is a drawback. Therefore, open aneurysm repair represents an option that can deliver quality outcomes and results. However, in order to achieve these goals; complex rearrangement in the way aortic service is provided needs to ensue across the country. Liverpool Heart & Chest Hospital (LHCH) developed a subspecialised scheme that further evolved to become an impact model for better aortic service provision in both elective and non-elective aortic surgeries. In 2007, the trust grouped a team of specialised experts to provide aortic surgery expertise to the widest catchment population of the Northwest of England and North of Wales which is estimated to be 2.8 million. LHCH became the first hospital to have a 24 hour on-call rota with a team on standby for aortic emergencies. This led to increase in surgical activity to around 180 aortic procedures performed each year at LHCH.

From a health economic evaluation perspective, an assessment of benefits derived from an intervention, are described as clinical outcomes and cost effectiveness. These are terms used to describe an improvement in the individual's health and wellbeing in terms of symptoms and functioning, and the way the individual values their particular state of health. Due to the complexity involved sub-specialisation aim to improve outcomes in all areas of aortic surgery in elective and non-elective workload.

The effect on costs is also of interest as it could potentially indicate whether the rearrangement in the service provision led to improved outcomes and can this coexist with reduced or neutral costs.

1.2 Hypothesis

1. The service rearrangement and the move from non-specialized to specialized aortic service at Liverpool Heart & Chest Hospital has improved clinical outcomes in both elective and non-elective aortic repair and was cost-effective?

2. The value of open surgical intervention was optimized through subspecialisation in elective and non-elective aortic aneurysm surgery?

1.3 Research Questions and Framework

1. **What is the natural history of operated and non-operated aneurysmal disease?**

Much has been known of natural history and its emphasis on the importance of the size of the aneurysm as an indication for surgical intervention. I will examine this question and assess whether this co-exist with other elements or factors that could potentially guide the surgeon and the patient.

2. **What is the UK volume-outcome relationship in acute type A aortic dissection?**

This question aims to illustrate the volume effect of ATAD per surgeon and per hospital and whether this correlates to the outcomes per se.

3. **What are the outcomes, survival and the factors that influence survival of aortic aneurysm elective and non-elective patients at LHCH? Does subspecialisation offer better results and could the volume-outcome relationship be applicable as a template of quality outcomes and survival benefit?**

Patients' at hospitals where a high number of procedures are performed (high-volume hospitals) have lower mortality rates than those at hospitals that are less experienced with the particular procedures or intervention. Hence, high-volume hospitals have access to broader range of resources and services including intensive care units, and other resources that are not available at smaller centres. By virtue, high-volume hospitals may be better equipped to deliver the complex perioperative care required for patients undergoing high-risk surgery. Such hospitals have concentration of experts that deliver a volume of case mix and at better outcomes.

Hence, LHCH stand out as a tertiary centre that provides expert opinion and surgical expertise in the field of cardiac, thoracic and aortic surgery. The effectiveness of the service provision and the quality of health care provided by measuring outcomes i.e the morbidity and mortality and survival will be demonstrated throughout this thesis.

The question of volume-outcomes relationship will be assessed utilizing LHCH dataset of aortic aneurysm patients. I will also evaluate whether the findings could prove to be a template of quality improvement.

4. **Is the concept of subspecialisation in aortic aneurysm surgery transferrable as an impact model in the NHS?**

In 2007, a specialised aortic service line was established at our LHCH in response to perceived poor outcomes from acute Type A aortic dissection repair. Prior to the change all elective and emergency aortic surgery were performed by general cardiac surgeons. Following the specialised team formation, the majority of elective aortic surgery and all emergency aortic surgery are currently being performed by 4 aortic surgeons.

The primary aim of the service rearrangement is to reduce operative mortality, morbidity and consequently to improve long term survival. This model of service provision is yet to be defined whether it's transferrable to other centres where concentration of expertise to provide aortic aneurysm surgery could ensue.

1.4 Study Setting

The study was conducted at Liverpool Heart & Chest Hospital (LHCH) formally known as The Cardiothoracic Centre in 1991 and which was later renamed to LHCH in 2008. The hospital is also known as Broadgreen since it located in that area and is attached to Broadgreen Hospital that offers different services to the wider community of Liverpool. LHCH is a specialist tertiary hospital and became a foundation trust in 2008. The specialism cover all kind of cardiological spectrum of healthcare including interventional state of the art services. The hospital also has state of the art cardiothoracic and aortic services. The first aortic operation done at LHCH was back in 1998.

Since then the activity has been increasing to meet the demand of wider population that LHCH covers. The estimated population is in the range of 2.8 million and areas covered are Merseyside, North West England, North Wales and the Isle of Man but also provides services for patients from all areas of the United Kingdom performing up to 1200 procedures a year.

Over a decade ago, Mr Abbas Rashid a retired consultant cardiac and aortic surgeon developed the thoracic aortic aneurysm service at Liverpool Heart & Chest Hospital. In the UK, the aortic team and service stands unique in that they perform all elective and non-elective aortic surgeries. This includes complex aortic procedures, endovascular repair of thoracic and thoracoabdominal aortic aneurysm (TEVAR),

hybrid repair of thoracic aortic aneurysms and minimal invasive aortic valve surgery.

Moreover, in 2007, the thoracic aortic service became the first in the UK to implement a subspecialized aortic on-call rota with dedicated 24 hours emergency on call service. The aortic team runs 4 dedicated aortic theatres a week and the work not only is limited to aortic surgery but we also perform conventional cardiac surgery as well. We run a multidisciplinary meeting to discuss complex cases with vascular surgeons, interventional cardiologists, interventional radiologists, intensivists and anaesthetists. This serves optimal quality decision making tailored to each and every individual patient.

For this particular study, we utilized a prospectively collected aortic database between October 1998 and August 2012.

1.5 Structure of the Thesis

The thesis lays the foundations for a decision support framework for healthcare professionals. The thesis fills important gaps between what is already known and what new knowledge is needed to make such a framework relevant. The first half of the thesis lays out and explores the theoretical foundations for such a framework, the second half goes on to explore the implications of putting such a framework into practice. Each chapter builds on previous chapters to develop a rational and logical structure to achieve the aims and objectives of the thesis. This process now moves into a comprehensive examination of aortic aneurysms – the clinical context in which our analysis is being undertaken**.**

CHAPTER ONE: Aimed at introduction, hypothesis, research questions and framework, thesis structure and study setting.

CHAPTER TWO: This chapter draws the aims Health Economic Evaluation requirements in thoracic aortic surgery. The chapter is also aimed at overviewing background of health economic evaluation tools.

CHAPTER THREE: This chapter is aimed at background and clinical overview from the evidence based literature on historical, clinical features pertinent to aortic aneurysm surgery and its modality of diagnosis and surgical indication perspectives.

CHAPTER FOUR: This chapter focuses on highlighting the clinical background literature of ATAD, its risk factors and modalities of diagnosis and management.

CHAPTER FIVE: This chapter signifies the importance of risk stratification in thoracic aortic aneurysm disease and demonstrates the development of risk prediction model based on common variables that alters surgical outcomes in thoracic aortic aneurysm disease.

CHAPTER SIX: This chapter reflects the comprehensive understanding of brain protection methods employed in open thoracic aortic aneurysm surgery in conjunction to the adjuncts used and ways of stroke avoidance.

CHAPTER SEVEN: Highlights the indications of when to operate upon thoracic aortic aneurysms. It also illustrates experiences upon open repair, endovascular and draws a comparative between the two modalities aforementioned.

CHAPTER EIGHT: This is the comparator when surgery is not employed and medical treatment is pursued. It also dwells onto the perspectives of natural history of thoracic aortic aneurysm disease in both operated and non-operated patients' cohort.

CHAPTER NINE: This chapter includes literature review of economic analysis and the concept of subspecialisation in aortic surgery. It marks the volume-outcome relationship and informs the economic evaluation and costing theoretical framework that aided in the development of analysis.

CHAPTER TEN: Is a constellation of the volume outcome effect nationally and internationally. It also highlights the need for subspecialisation and centralization of thoracic aortic services in the UK.

CHAPTER ELEVEN: This chapter describes the methodology utilized to validate the aortic database at LHCH and derive the clinical and economic analysis.

CHAPTER TWELVE: This entails the results attained from our analysis of clinical outcomes pertinent to the increased volume of aortic case mix. It demonstrates the outcomes of aortic arch aneurysm and acute Type A aortic dissection before and after subspecialisation. It will also include the cost-analysis made between two groups i.e. before and after subspecialisation.

CHAPTER THIRTEEN: This chapter thoroughly discuss the analysis that formed the backbone of the hypothesis and answers all the research questions raised during this study.

CHAPTER FOURTEEN: This chapter is aimed at conclusion and further recommendations. This will round up the salient points discussed and outline the strong points to be deduced as a take home message for further research.

CHAPTER TWO

2. HEALTH ECONOMIC EVALUATION IN THORACIC AORTIC ANEURYSM SURGERY

2.1 Introduction

"Economics is the science of scarcity. The application of health economics reflects a universal desire to obtain maximum value for money by ensuring not just the clinical effectiveness, but also the cost-effectiveness of health care provision" (Alan Haycox, April 2009)[7]

Economic evaluation in health economics is used as a tool to identify the optimal interventional option through a derived comparison between cost and benefits.[8] There are different applications to such tool and it has best been demonstrated by Ray Robinson[9] who published on the difference between economics tools, their settings and applications. The thesis aims to understand the assessment of cost-benefit analysis in elective and non-elective aortic aneurysm repair that typically carries dire results between centres and regions across the United Kingdom. It's not clear whether we could apply such economic tools to assess the volume-outcome relationship as clearly this has not been studied before. The volume-outcomes relationship has been clinically supported by different groups in their published work which states the higher the volume of caseloads the better the outcomes[185,].

7 Haycox, A., & Noble, E. (2003). What is health economics? Hayward Group. Retrieved 04/06/2015, from http://www.isciii.es/htdocs/pdf/WhatisHealthEcon.pdf.
8 National Institute for Health and Clinical Excellence. Guide to the methods of technology appraisal.
9 Economic evaluation and health care. What does it mean? BMJ. Sep 11, 1993; 307(6905): 670–673.

However, Kenneth Arrow, in his work on "product uncertainty" argues that the principles and implication of the standard demand paradigm do not apply to the current health market and resource utilization[10].

The vast difference in knowledge and application between the health care provider and the patient necessitate that there should be a tool through which patients reflect on their benefit gained from a particular intervention to alter their health status.

There is a general consensus among the aortic surgeons at Liverpool Heart & Chest Hospital that asymptomatic patients may harbour a significant health burden arising from becoming aware that they have an aneurysm that can dissect and rupture at any given point in time due to aneurysmal size increase.

The information given to patients on the day of consultation with members of the aortic team impact the overall patients' health related quality of life (HRQoL) and psychological wellbeing. Regardless of whether patients are aware that surgery will improve their chances of survival and precludes rupture and dissection their functional status is likely to initially deteriorate in relation to the prospect of surgical intervention, a situation which might normalize with time post-surgery. The quality of life trajectories for both symptomatic and asymptomatic patients have yet to be researched particularly in patients with thoracic aortic aneurysms. In addition, there is no evidence that surgical interventions will improve HRQoL and is cost-effective. Yet, there is a need to understand the psychological burden imposed upon patients' once they become aware of their diagnosis of aortic aneurysm and then establish how that has an impact on their health-related quality of life and explore the applicability of health-related quality of life tools in this type of surgery and their limitations.

10 The American Economic Review, UNCERTAINTY AND THE WELFARE ECONOMICS OF MEDICAL CARE Vol.3 , Number 5

In aortic aneurysm surgery, there is no one value-focused measure or termed "preference-based" to be able measures an individual's preference for a health state, as opposed to an individual's description of the state. As such, there exists a variety of methods for measuring preference-based health related quality of life (HRQOL).

The impact of any significant change in healthcare provision is akin to dropping a large stone into a millpond. The ripples associated with the change are greatest near the epicentre where the stone enters the water and gradually become less as the concentric waves move out. As such the clinical and cost effectiveness of any structure of clinical provision results from a vast and complex system of intrinsically interrelated components. Each element within the structure is related to every other element and, in large part, it is the quality of this 'meshing' of elements which delineates the quality of healthcare provision.

The fundamental issue, which neither clinicians or health economists to date have been able to address in an evidence based fashion is how a defined change in healthcare provision (sub-specialisation in aortic surgery) will impact upon the health of patients and the efficiency of the healthcare 'system' as a whole.

Economic Evaluation helps to provide information that can be utilized in decision making so we could make a better choice and informed decision among competing healthcare interventions. It allows us to evaluate and identify measurable values and input such as cost and its related output i.e. benefit. It aims to provide us with a source that can help in determining collectively there is any improvement in welfare of a particular individual with comparison to current trend and practices (Drummond, 1990).

2.2 Techniques of Economic Evaluation

Economic evaluation provides a systematic and objective framework for drawing up a balance sheet of costs and benefits which can assist decision-makers to make more informed choices. All economic evaluations have a common structure which involves explicit measurement of inputs ('costs') and outcomes ('benefits'). The four main methods of economic evaluation vary in terms of their evaluation of health outcomes. The appropriate analytical tool to choose in any given circumstance depends upon three main issues. First, what is the context in which the analysis is being undertaken? Second, what is the focus of the economic evaluation being undertaken? Third, what is the nature of the comparative outcome arising from the competing therapeutic options? Knowledge of these three issues will provide a guide to the appropriate economic tool to be employed for any particular analysis.

2.2.1 Cost-Minimisation Analysis

Cost-minimisation analysis is restricted to situations in which the health benefits of healthcare treatments have been proven to be identical. An example would be a decision to prescribe a generic drug instead of a brand- name drug, achieving the same outcome at less cost. Frequently, therefore, this technique is perceived as being the easiest to apply, but such a perception is misleading. Cost- minimisation analysis does not ignore health outcomes, but actually requires proof that outcomes are clinically equivalent to legitimise the use of this technique. This opens up a new and complex array of issues that need to be addressed prior to utilising this technique. What do we mean by 'clinical equivalence' and what evidence is required to support such equivalence (non-inferiority trials, equivalence trials or real-world audit data)? Such theoretical considerations need to be addressed if cost-minimisation analysis is to be appropriately employed as a valid technique of economic evaluation.

What is clear, however, is that it is highly inappropriate to simply assume clinical equivalence between competing therapies as a justification for the use of cost-minimisation analysis.

2.2.2 Cost-Effectiveness Analysis

The term 'cost-effectiveness analysis' properly refers to an evaluation where the outcomes are one-dimensional. Cost-effectiveness analysis is therefore used in health economics to compare the financial costs of therapies whose outcomes can be measured purely in terms of health effect (for example, years of life saved, ulcers healed). For instance, if we wanted to compare the use of a proton pump inhibitor to relieve severe reflux oesophagitis with the use of H2 blockers to achieve the same end, we could calculate the costs per patient relieved of symptoms for each therapy. Cost-effectiveness analysis is the most commonly applied form of economic analysis in the health economics literature, and is frequently used in drug therapy. However, it does not allow comparisons to be made between courses of action that have completely different therapeutic outcomes.

2.2.3 Cost–Utility Analysis

Cost–utility analysis is similar to cost- effectiveness analysis in that there is a defined outcome, and the cost to achieve that outcome is measured in money. However, in cost–utility analysis the outcome is measured in terms of survival and quality of Life. Since the endpoint may not be directly dependent on the disease state, cost–utility analysis can, in theory, compare courses of action in different areas of medicine. In practice, this is not so easy, since QALYs remain subject to much philosophical and technical criticism.

2.2.4 Cost–Benefit Analysis

In cost–benefit analysis the benefit is measured as the associated economic benefit of an intervention, and hence both costs and benefits are expressed in money.

Cost–benefit analysis may ignore many intangible but very important benefits that are difficult to measure in monetary terms (for example, relief of anxiety). It could also be seen to discriminate against those for whom a return to productive employment is unlikely (for example, the elderly or the unemployed).

However, the virtue of this analysis is that it enables comparisons to be made between schemes in very different areas of healthcare, and even with schemes outside the field of medicine. For example, using cost–benefit analysis, the costs and benefits of expanding university education (the benefits of improved education and hence productivity) can be compared with establishing a back pain service (enhancing productivity by returning patients to work). This approach is not widely accepted for use in health economics.

2.3 Evaluating Resource Use

2.3.1 Costing in the NHS

The NHS was founded in 1948 with a modest budget of 437 million pounds however since this date. The budget has been growing at a rate of approximately 4% per year [11](see figure 2.3.1).

11 Gateway reference: 9006/11400; Doh-NHS Costing Publications

The NHS was founded on the basis of providing equal access for equal need and is therefore funded from general taxation to enable the service to be provided free at the point of delivery hence moving the allocation of resources away from the willingness and ability to pay of the patient. As the NHS moves into the 21st century it faces an ever increasing demand for service delivery juxtaposed with an ever increasing constrain on available resources. As a consequence, the system requires each element of its service to generate the greatest possible outcome from the resources that it consumes.

The fundamental principle on which health economic evaluation is undertaken is that of 'opportunity cost'. This principle emphasizes that the true 'cost' of using resources in any particular manner is their subsequent unavailability for use in the provision of some alternative service. Hence the true cost of resources consumed in the provision of aortic surgery is the outcome that would have been generated (additional alternative cardiothoracic procedures) had the surgical expertise and resources been used in some alternative manner.

Whilst acknowledging the theoretical superiority of the concept of opportunity cost it is generally recognized to be an immensely difficult concept to operationalize in mainstream clinical practice. The alternative use of resources consumed in the provision of aortic surgery (either within cardiothoracic surgery or elsewhere) cannot be reliably ascertained. As such (and in line with the vast majority of resource analyses undertaken within the NHS) this study restricts any resource analysis to evaluating the physical amount of resources consumed and the associated cost imposed on the NHS. The manner in which this has been achieved and the sources of cost data utilized are outlined below.

2.3.2 NHS National Reference Costs

The UK Department of Health (DoH) is mandated to ensure efficient use of NHS resources. To achieve this, they developed a costing system which attempted to identify a nationally relevant cost of providing every type of procedure provided by the National Health Service. Each provider within the NHS is mandated to allocate their resource use and associated cost between each of the procedures that were carried out and submit this information to the DoH on an annual basis. Given the 'shared' nature of much NHS resource use such allocations were hugely difficult and, in large part, the final cost identified was largely dependent on the allocation procedure used to divide shared costs between individual procedures. Despite its limitations this process enabled DoH to identify average cost for various procedures across NHS organizations after eliminating outliers. This also helped hospitals to bench mark their cost against other providers in the sector.

The exercise provided also required a common structure of 'outputs' to be identified and this facilitated clear definitions of procedures known to be developed in the form of OPCS codes. Payment by result was introduced in England in 2005 which reimbursed provider organizations through national tariff only for completed spells for regular procedures carried out. High cost low volume specialist procedures (for example cancer interventions) are excluded from this model of reimbursement and continue to be based on demand, capacity and affordability. This new funding system created severe turbulence both on the part of providers and also of commissioners of care and, in extreme cases, caused severe financial problems for provider units[12].

12 Transparency and accountability: using better data to drive performance in the NHS. The Health and Social Care Information Centre

2.3.3 Activity Based Costing

Activity-based costing was first clearly defined in 1987 by Robert S. Kaplan and W. Bruns as a chapter in their book [13]. They initially focused on manufacturing industry where increasing technology and productivity improvements have reduced the relative proportion of the direct costs of labour and materials, but have increased relative proportion of indirect costs. For example, increased automation has reduced labour, which is a direct cost, but has increased depreciation, which is an indirect cost.

Like manufacturing industries, financial institutions have diverse products and customers, which can cause cross-product, cross-customer subsidies. Since personnel expenses represent the largest single component of non-interest expense in financial institutions, these costs must also be attributed more accurately to products and customers. Activity based costing, even though originally developed for manufacturing, may even be a more useful tool for doing this.

Activity-based costing was later explained in 1999 by Peter F. Drucker in the book Management Challenges of the 21st Century[14]. He states that traditional cost accounting focuses on what it costs to do something, for example, to cut a screw thread; activity-based costing also records the cost of not doing, such as the cost of waiting for a needed part. An activity-based costing record the costs that traditional cost accounting doesn't do. The overhead costs assigned to each activity comprise an activity cost pool.

13 Kaplan, Robert S. and Bruns, W. Accounting and Management: A Field Study Perspective (Harvard Business School Press, 1987)
14 Sapp, Richard, David Crawford and Steven Rebishcke. Journal of Bank Cost and Management Accounting (Volume 3, Number 2), 1990

2.4 Costing at Liverpool Heart and Chest Hospital

2.4.1 Patient-Level Information and Costing Systems (PLICS)

Patient-level information and costing systems (PLICS) represent a change in the costing methodology in the NHS from a predominantly "top down" allocation approach, based on averages and apportionments, to a more direct and sophisticated approach based on the actual interactions and events related to individual patients and the associated costs. Patient-level costing is defined by the ability to measure the resources consumed by individual patients. Patient-level costs are calculated by tracing resources actually used by a patient and the associated costs by using actual costs incurred by the organization in providing a service or event. Patient-level costing is the resourcing consequences of clinical activity and is primarily informed by the measurement of that clinical activity. Clinical validity is therefore underpinned by the accuracy and legitimacy of that core activity data. This necessitates the involvement of clinical staff in the definition, documentation and authentication[15, 16].

High cost treatments and procedures in specialty hospitals should also be allocated to individual patients on an activity basis. As far as is possible overheads should be allocated to these areas prior to allocation to patients, on the closest proxy to activity. It is not acceptable however to allocate any of the above resources as "overheads". In the event that data is missing proxy allocations must be created.

These might include standard costs (e.g. prosthesis by procedure) or service weights (i.e. data from other sources as substitutes). It is not sufficient to allocate ward costs by overall length of stay. Adjustments must be made for both the patients' admission and discharge days and for their acuity (i.e. severity, co-morbidities).[11,12,13,14,15]

15 Journal of Bank Cost and Management Accounting (Volume 4, Number 1), 1991
16 Drucker Peter F.Management Challenges of the 21st Century. New York: Harper Business, 1999.

PLICS in common with SLR is a change to traditional NHS costing methodology from top down to a bottom up approach. It captures costs at the level of individual patient activities.

The aim is to understand all the activities, and the associated costs, related to the care provided to an individual patient through the duration of the care episode. This will inevitably reflect the complexities of individual cases, and provide a very granular level of analysis.

The very nature of PLICS means that simply due to the volume of data to be considered, gaining meaningful insight into costs may be more complex. That is not to say that this is not a worthwhile aim, only that careful consideration must be given to how the data collected will be used. In simple terms, how it will be analysed and converted into useful information to inform decision making[14,17].

This thesis makes use of PLICS cost data from Liverpool Heart and Chest Hospital's service line reporting (SLR) system, enabling detailed micro-costing that is far superior to the use of NHS reference costs. SLR allows the trust to analyse cost and profitability at patient level of each service it provides rather than just overall profitability. Costs of resources that can be directly attributed to particular patient episode are 'traced', that is, they are allocated to the episode without any treatment or manipulation. Such costs include the likes of prostheses and consumables. The use of sophisticated consumables dispensing and supply tracking technologies assigns costs on the fly and allows precise tracing of resource use to the patient and episode on which they were used.

17 Kuzmik G a, Sang AX, Elefteriades J a. Natural history of thoracic aortic aneurysms. Journal of vascular surgery [Internet]. Elsevier Inc.; 2012 Aug [cited 2013 Jun 2];56(2):565–71.

This applies to drugs, and in surgery, where surgical consumables, valves, prostheses, anesthetic drugs etc. are all automatically attributed to the patient and procedure as they are used.

Staff time is allocated with reference to employment contracts and the proportion of the time that is to be dedicated to each duty. That is, the cost of a particular surgeon for a given procedure is a function of his salary, the proportion of his contract he is to operate, and the time the procedure takes. Similarly, the ward costs of clinician can be allocated in the same way.

These costs are then allocated based on the observed values of time for each patient episode. Indirect costs such as utilities and trust overheads are allocated/absorbed – although some of them are not directly attributable to any particular episode /service lines, they are divided up and shared amongst all episodes.

2.4.2 Service Line Reporting (SLR)/Resources and Activity

SLR is a statement of revenues and costs of clinical activities (and other key indicators in the form of a scorecard) to monitor and manage performance at service line level.

A resource is a source that performs activity. Typically, resources are materials or other assets including human resource that are transformed or used in the process of activity. Organizations expend money to hire or buy resources to perform activity which in turn bring revenue for the organization. Resources for inpatients should be measurable for each day or part day from the time of entry and admission to the hospital until the time of discharge. For outpatients and non-admitted A&E attendances, the consumption of resources will be on an occasion of service basis. Resources should be ascribed to patients on a clinically meaningful activity basis in accordance with the principles of activity based costing.

A minimum set of costs driven by activity should include: wards, pathology, imaging, pharmacy services and drugs, prostheses, therapies, critical care, operating theatres, special procedure suites, other diagnostics, emergency department and outpatient.

HRGs are standard groupings of clinically similar treatments which use common levels of healthcare resource. HRGs offer organisations the ability to understand their activity in terms of the types of patients they care for and the treatments they undertake. They enable the comparison of activity within and between different organisations and provide an opportunity to benchmark treatments and services to support trend analysis over time. HRGs are currently used as a means of determining fair and equitable reimbursement for care services delivered by providers. Their use as consistent 'units of currency' supports standardised healthcare commissioning across the service. They improve the flow of finances within - and sometimes beyond - the NHS. HRG4 has been in use for reference costs since April 2007 (for financial year 2006/7 onwards) and for Payment by Results (PbR) since April 2009 (for financial year 2009 onwards).

HRG4 was a major revision that introduced HRGs to new clinical areas, to support the Department of Health's policy of Payment by Results (PbR). It includes a portfolio of new and updated HRG groupings that accurately record patient treatment to reflect current practice and anticipated trends in healthcare [13,14,15]

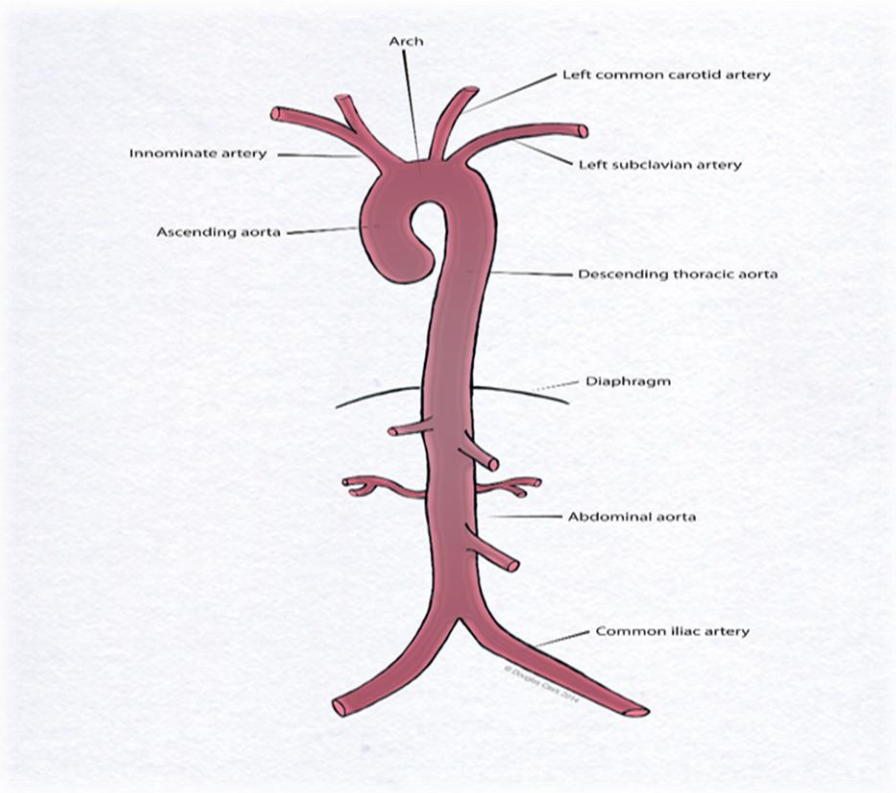
CHAPTER THREE

3. THORACIC AORTIC ANEURYSM DISEASE

3.1 Introduction

The aorta (Figure 3.1) is the main trunk of a series of vessels which convey the oxygenated blood to the tissues of the body for their nutrition.

Figure 3.1. The Aorta



It commences at the upper part of the left ventricle, where it is about 3 cm in diameter, and after ascending for a short distance, arches backward and to the left side, over the root of the left lung; it then descends within the thorax on the left side of the vertebral column, passes into the abdominal cavity through the aortic hiatus in the diaphragm, and ends, considerably diminished in size (about 1.75 cm in diameter), opposite the lower border of the fourth lumbar vertebra, by dividing into the right and left common iliac arteries. Hence it is described in several portions such as the root, the ascending aorta, the arch of the aorta, and the descending aorta, which last is again divided into the thoracic and abdominal aortae[18].

3.2 The History of Aortic Surgery

The word aneurysm is derived from the Greek words aneurusma and eurunein, meaning to dilate and to widen. (Figure 3.2)

Development for treatments of aortic aneurysms through the years has focused on abdominal aortic aneurysms. This is in part due to larger prevalence and ease of detection, particularly before the advent of radiological imaging. The principles underpinning surgical correction of thoracic aortic aneurysms are thus based mainly upon abdominal aortic aneurysms (AAA).

The initial treatments for aortic aneurysms were that of simple ligation, proximal to the aneurysm. A technique that had been first described for peripheral aneurysms by the Greek surgeon Antyllus, in the first half of the second century AD. [19,20] This technique was used with limited success, until 1899 when Keen operated on a ruptured AAA and reported a 48-day post-op survival, at which time the ligature eroded through the aorta despite the poor survival rates this practice continued.

18 Henry Gray (1821–1865). Anatomy of the Human Body.
19 DeBakey M. A surgical perspective. Ann. Surg. 1991;213:499–531
20 Cooley DA. Aortic Aneurysm Operations : Past, Present, and Future. Ann Thorac Surg 1999;67:1959–

Marin-Theodore Tuffier is credited as the first surgeon to attempt this technique in TAAs[21]. He used catgut to ligate both proximal and distal to the aneurysm. His endeavour in 1901 was unsuccessful, as were attempts on a subsequent three patients.

Renewed attempts to consolidate aneurysms, through the promotion of coagulation by means of the introduction of foreign material was tried in AAA (abdominal aortic aneurysm), again with limited success. Moore was the first surgeon to attempt this procedure on a TAA protruding from the right of the sternum in the second intercostal space in 1864[22].

Moore placed 26 yards of iron wire within the aneurysm; initially the patient did well but did not survive past day 4[22]. Surgeons attempted this technique with different metals, watch springs and other foreign objects, all without success. A small review of these practices in the 1900s revealed a 100% mortality in TAAs treated with the method described by Moore (n=8).

However, the review describes a modified method by Corradi, which involved passing a current through the wire inserted into the aneurysm to promote coagulation20. This method produced more favorable results, and of the 17 patients undergoing this procedure 24% recovered. The most successful development in these coagulation methods was in 1938 by Blackmore and King.

Their electro-thermic coagulation method gave a 27% survival rate 2-11 years post operatively, in a case series of 63 syphilitic aneurysms, with the majority symptom free. [22,23]

21 Tuffier T. Intervention chirurgicale directe pour un anevrisme de la crosse de l'aorte: ligature du sac. Press Med. 1902;10:267
22 Moore C, Murchison C. On a new method of procuring the consolidation of Fibrin in certain incurable Aneurisms with the Report of a case in which an Aneurism of the ascending Aorta was treated by the insertion of Wire. Med Chir Trans. 1864; 47:129–49.
23 Borrie J, Griffin SG. Twenty-seven cases of syphilitic aneurysms of the thoracic aorta and it branches. Thorax. 1950; 5:293–324.

A new advancement in aneurysm treatment occurred in 1943 when Harrison and Chandy described cellophane wrapping as a method to induce periarterial fibrosis in a subclavian aneurysm.[24] Reduction of the aneurysm was a long gradual process which in their case required 19 months. This method was tried in thoracic aortic aneurysms; however limited success was achieved with unpredictable results as reported by Poppe in 1948.

Interestingly, Albert Einstein, who suffered from an AAA was treated with this method, and survived a further 5 years before rupture.

It was not until 1951 that direct treatments for aneurysms evolved, rather than the indirect methods of ligation, wiring and cellophane wrapping. Charles Dubost, of France, resected an AAA, which was replaced with an allograft obtained from a young girl 3 weeks previous. In the same year Lam and Aram followed Dubost and resected a descending TAA with allograft replacement[25]. Lam's patient survived the operation but developed a mediastinal abscess ultimately leading to his death. Despite this the operation was replicated with success by other notable surgeons including DeBakey and Cooley20.

Furthermore, it led to the development of numerous allograft aortic banks worldwide in anticipation of a growing number of surgeries to the aorta. These methods were however introduced before the introduction of cardiopulmonary bypass and thus gave rise to a significant risk of paraplegia due to aortic ischaemia. It is at this time that important research to limit morbidity from the operation evolved including; hypothermia and shunts. Development of artificial aortic substitute were researched during this time, and DACRON was deemed to be the most suitable for graft implantation, first used by DeBakey in the 1950s, and still widely used in vascular surgery today.

24 Harrison PW, Chandy J. A Subclavain Aneurysm Cured by Cellophane Fibrosis Three Years Ago. Ann. Surg. 1941;118:478–81
25 Coselli JS, Green SY. A brief history of aortic surgery: insight into distal aortic repair. J Thorac Cardiovasc Surg. AATS; 2013;145:S123–5

Repair of ascending and aortic arch aneurysms still remained an unachievable goal through resection due to the unpreventable risk of cerebral ischaemia. This changed with the advent of cardiopulmonary bypass when Cooley and DeBakey were the first to successfully resect an ascending thoracic aortic aneurysm and replace it with an allograft. Repair of an aortic arch aneurysm came in 1957 with successful resection and replacement with a homograft, again by DeBakey19,20. These operations led to the widespread uptake in thoracic aortic aneurysm resection with either artificial DACRON or allograft replacement. In the recent past, endovascular repair began to excite the aortic world, particularly when Dake et al successfully repaired a thoracic aortic aneurysm in 1994[26]. However, with the first endovascular grafts being FDA approved in 2005 little long term data is available.

Currently, AAA is more commonly treated with an endovascular approach. With regards to thoracic aneurysms, endovascular repair remains a source of great debate, in terms of long term survival, long term durability of the grafts, and operative morbidity of paraplegia and stroke. Hybrid endovascular approaches to thoracic aortic aneurysm repair will undoubtedly remain at the forefront of modern research in these cases, however at present open repairs remain the standard treatment with more substantial data, and practice qualifying its use.

26 Dake M, Miller D, Semba C, Mitchel l R, Walker P, Liddell R. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. NEJM 1994;331:1792–34

3.3 Aetiology

There exists conflict surrounding the aetiology of TAAs in the literature. The prevailing consensus, reflected in the most recent guidelines for thoracic aortic disease, cites medial degeneration as the primary causative factor for the majority of TAAs6. Historically, atherosclerosis was credited as the main cause for aortic aneurysms, which was based upon findings from post mortems[27,28].

Although atherosclerotic lesions are commonly associated with thoracic aneurysms, typically they are preceded by medial degeneration[29,30]. This key point is still not conclusive proven. Patel et al wrote a detailed review discussing the pathogenesis of ascending and aortic arch aneurysms[30]. They describe three separate pathological aetiologies namely; degenerative, Marfans and other inherited connective tissue diseases, and syphilitic aneurysms. Degenerative aneurysms undergo a classical and specific pathological process. Post mortem examinations reveal greatly reduced elastin content within the ascending aorta, the media of the aneurysms displays a lack of smooth muscle cells [27]. Cystic medial degeneration can be observed in the media, which is described microscopically as fragmentation of elastin fibres. Although this process is widely regarded to be associated with aging, the recent analysis of the large Yale TAA database reveals a strong familial component[31]. Matrix metalloprotease (MMPs) are recognised to play a critical role in aneurysm formation[32,33].

27 Young R, Ostertag H. Incidence etiology and risk of rupture of aoritc aneursyms. An autopsy study. Dtsh Med Wschr. 1987;112(1253-6).
28 Kunz R. Aneurysms in 35,380 autopsies. Schweiz Med Wochenschr. 1980;110:142–8.
29 Bonser RS, Pagano D, Lewis ME, Rooney SJ, Guest P, Davies P, et al. Clinical and patho-anatomical factors affecting expansion of thoracic aortic aneurysms. Heart [Internet]. 2000 Sep;84(3):277–83.
30 Patel HJ, Deeb GM. Ascending and arch aorta: pathology, natural history, and treatment. Circulation. 2008;118:188–95
31 Coady M a, Davies RR, Roberts M, Goldstein LJ, Rogalski MJ, Rizzo J a, et al. Familial patterns of thoracic aortic aneurysms. Arch Surg. 1999;134:361–7.
32 Agarwal P, Chughtai A, Matzinger FR, Kazerooni EA. Multidetector CT of Thoracic Aortic Aneurysms. RG. 2009;29:537–53.
33 Elefteriades JA, Farkas E a. Thoracic Aortic Aneurysm Clinically Pertinent Controversies and Uncertainties. J Am Coll Cadiol. 2010;55(9):841–57.

MMPs are still being studied *in vitro* and *in vivo,* however it is known that MMPs significantly contribute to proteolysis of the aorta causing the aneurysm to expand. It is this observation that has developed a lot of interest lately in medical treatment of TAAs. In the past the majority of cases could be attributed to syphilitic infection, however with the modern era of screening and antibiotics it is now a rarity and is not discussed here. In the absence of connective tissue disease, current evidence points toward a strong inherited genetic phenotype of accelerated medial degeneration as the primary culprit for TAAs. However, there are many risk factors that contribute to formation of a TAA, which are discussed below.

Therefore, the likelihood that this is a multi-factorial disease, of genetics and lifestyle factors, is the consensus present and published in the literature.

3.4 Genetically Triggered Thoracic Aneurysm Syndromes

3.4.1 Marfan Syndrome

Classically, Marfan syndrome has been the most extensively studied connective tissue disorder in relation to thoracic aortic disease. Marfan syndrome is an autosomal dominant genetic disorder of the FBN1 gene encoding for fibrillin-1[34]. Usually fibrillin-1 is found in microfibrils located in the extracellular matrix. Microfibrils play a crucial role in maintaining the elastic fibres of connective tissues, and it is this that predisposes Marfans patients to TAAs[35,36]. It is a rare disease with

34 De Backer J. Cardiovascular characteristics in Marfan syndrome and their relation to the genotype. Verh K Acad Geneeskd Belg. 2009;71:335–71
35 Cury M, Zeidan F, Lobato A. Aortic disease in the young: genetic aneurysm syndromes, connective tissue disorders, and familial aortic aneurysms and dissections. Int J Vasc Med. 2013;2013:267215
36 Halme T, Savunen T, Aho H, Vihersaari T, Penttinen R. Elastin and collagen in the aortic wall: changes in the Marfan syndrome and annuloaortic ectasia. Exp Mol Pathol. 1985;43:1–12.

an incidence of approximately 1 in 5000, displaying a high penetrance and variable phenotype. Diagnosis is made using the 2010 revised Ghent Nosology, superseding diagnostic criteria primarily based on clinical features alone[37]. The revised criteria critically emphasize the presence of aortic root dilation or ectopic lentis (displacement or malposition of the eyes crystalline lens) in new patients without a family history, as a cardinal feature for a definitive diagnosis. A family history of Marfans syndrome, present in approximately 50% of patients, is more indicative of a diagnosis and thus requiring only one other factor of; an aortic root aneurysm, ectopic lentis, a pathogenic fibrillin-1 (FBN-1) mutation, or systemic features defined in the Ghent Nosology, to formulate a diagnosis.

It is well documented that approximately 50-90% of these patients will develop aortic root dilation. Because of this predictable progression, Marfan syndrome has previously been used to extrapolate clinical findings, practice and research, to TAAs of different aetiologies [38,39,40]. Currently, TAA guidelines segregate Marfans patients into a distinct subset of patients, preferentially indicating earlier surgical intervention for TAA. The evidence for this stems from numerous studies demonstrating a high association with an accelerated growth rate of the aortic root (0.2-0.3cm/year) [38,4041,].

The trend of using Marfan patients for research and extrapolating this to all aetiologies of TAAs has long discontinued. In part, this is due to the obvious differences in pathogenesis and varied clinical findings, and it is now realized substantial variation exists.

37 Loeys B, Dietz H, Braverman A, Callewaert B, De Backer J, Devereux R, et al. revised Ghent nosology for the Marfan syndrome. J Med Genet. 2010;47:476–85.
38 Van Karnebeek CD, Naeff MS, Mulder BJ, Hennekam RC, Offringa M. Natural history of cardiovascular manifestations in Marfan syndrome. Arch. Dis. Childh.. 2001;84:129–37
39 Glower DD. Indications for ascending aortic replacement size alone is not enough. Journal of the American College of Cardiology. 2011;58:585–6.
40 Brooke BS, Habashi J, Judge D, Patel N, Loeys B, Dietz III H. Angiotensin II Blockade and Aortic-Root Dilation in Marfan's Syndrome. NEJM. 2008;358:2787–95.
41 Cook JR, Nistala H, Ramirez F. Drug-Based Therapies for Vascular Disease in Marfan Syndrome : From Mouse Models to Human Patients. Mount Sinai Journal of Medicine. 2010;77:366–73

3.4.2 Familial Nonsyndromic Thoracic Aortic Aneurysm Syndromes

Familial Nonsyndromic Thoracic Aortic Aneurysm Syndromes are defined as patients who have a first degree relative that suffered an aortic aneurysm but are without a known associated genetic syndrome. Elefteriades et al have an extensive database of approximately 1200 patients who were diagnosed with TAA in Connecticut [33,1][31,]. Their analysis of this database identified 21% of this cohort who had a first degree relative with known or likely aortic aneurysm, in the absence of a connective tissue disorder. Within this subset of patients an autosomal dominant pattern with incomplete penetrance pattern was displayed. This observation has been made before, but due to the rarity and absence of large databases in previous years has not be studied extensively [31]. Elefteriades et al note that this percentage is likely to be higher as these results were based upon family interview and are subject to bias.

Because this observation is only recently being brought to light within the research world genetic identification of associated genes is still in its infancy. Currently, *ACTA 2*, *MYH11* and *TGFBR2* are implicated as the primary gene candidates associated with this syndrome. As genetic testing becomes more widely available and readily understood in the general public, ACTA 2 detection is recommended in suspected familial TAAs. In the future more genes may be tested but this requires further research and time.

3.4.3 Bicuspid Aortic Valve

A bicuspid aortic valve (BAV) is well recognized as an independent risk factor for aortic aneurysm[42,43,44.] This congenital cardiac malformation is reported to exist in the general population at a prevalence of 1-2%. In this subset of patients, one study found thoracic aortic dilation at a prevalence of 88% in those over the age of 80. It is known that BAVs can show an autosomal dominant inheritance in families, which is seen in approximately 9% of TAA cases [45].

Davies et al were the first to show that bicuspid aortic valves are associated with an increased aortic aneurysm growth rate [46]. Because the risk of TAA formation is so significant in these patients the latest TAA guidelines recommend intervening surgically earlier, when their aneurysms reach a size of 5.0cm. The pathogenesis remains a mystery. However, an aortic aneurysm associated with a BAV is histologically similar to that of Marfan patients chiefly; medial degeneration, increased metalloproteinase activity and decreased FBN-1 in the aortic wall. Combined this leads to increased aortic aneurysm growth rates with a propensity for rupture earlier than TAAs not associated with an inherited genetic condition [43]. Of note, coarctation of the aorta is highly suggestive of BAV (up to 50% of patients). Originally, the pathogenesis was linked to the common embryological development of the aortic valve and the ascending aorta[44]. This observation suggests that pathological changes are not isolated to the proximal aorta and may well involve the arch and the descending aorta.

42 Della Corte A, Bancone C, Quarto C, Dialetto G, Covino FE, Scardone M, et al. Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression. European journal of cardio-thoracic surgery : official journal of the European Association for Cardio-thoracic Surgery. 2007;31:397–404
43 Tadros TM, Klein MD, Shapira OM. Ascending aortic dilatation associated with bicuspid aortic valve: pathophysiology, molecular biology, and clinical implications. Circulation [Internet]. 2009;119:880–90
44 Fedak PWM. Clinical and Pathophysiological Implications of a Bicuspid Aortic Valve. Circulation . 2002;106:900–4
45 Loscalzo M, Goh D, Loeys B. Familial thoracic aortic dilation and bicommissural aortic valve: a prospective analysis of natural history and inheritance. Am J Med Genet A. 2007;143:1960–7
46 Davies R, Kaple R, Mandapat i D, Gallo A, Botta D, Elefteriades J, et al. Natural history of ascending aortic aneurysms in the setting of an unreplaced bicuspid aortic valve. Ann Thorac Surg. 2007;83:1338–44.

3.4.4 Vascular Ehlers-Danlos Syndrome

Also referred to as Ehlers-Danlos (ED) syndrome type IV, is another rare autosomal dominant disorder affecting the COL3A1 gene [35]. Typically, these patients have a distinctive facial appearance with an accompanying body habitus and a propensity to develop ecchymoses. It is described as a more serious form of ED syndrome in that blood vessels, particularly arterial vasculature, are prone to rupture. The syndrome causes a deficiency in the synthesis of type III collagen, the main component of connective tissue, the loss of which increases vessel fragility making surgical repair more difficult. These patients have a severely reduced life span approximated at 48 years.

3.4.5 Loeys-Dietz Syndrome

Loeys-Dietz (LD) syndrome is described as an autosomal dominant aortic aneurysm disorder with involvement of other systems [35,38]. The classical triads of features are arterial tortuousity and aneurysms, hypertelorism and bifid uvula or cleft palate, or a uvula with a wide base and prominent ridge. Diagnosis is made on mutational analysis in TGFBR1 or TGFBR2, which are genes recently discovered as the primary defect in LD syndrome[47]. Unlike VD syndrome surgical intervention is not complicated by vessel fragility; thus these patients can be managed aggressively in respects to aneurysm treatment. The majority of these patients have aneurysms of the aortic root (98%), rupture of which is reported to occur at smaller diameters than other genetic syndromes, thus the bar is further lowered to a diameter of 4.4-4.6cm in TAA as an indication for surgical repair[6].

47 Pezzin i A, Del Zotto E, Gioss i A, Volonghi I, Costa P, Padovani A. Transforming growth factor β signaling perturbation in the Loeys-Dietz syndrome. Curr Med Chem. 2012;19:454–60.

3.5 Risk Factors

The Whitehall study identified two major risk factors in the development of thoracic aneurysms, namely smoking and hypertension[48]. Of the 18,403 participants in the prospective cohort study, 99 patients suffered aortic aneurysms.

This extensive study is however subject to recall and measurement bias, as risk factors were assessed via questionnaire. Furthermore, the study was not particularly designed to look at TAAs. Smoking remains the highest modifiable risk factor for development of thoracic aneurysms in all studies[29,30]. Bonser et al evaluated TAA growth and used a univariate analysis to demonstrate; intramural thrombus, thrombus, previous stroke, smoking, and peripheral vascular disease as factors that statistically accelerate growth ($p<0.05$ in all cases)[29]. The study looked at 87 patients and used serial CT scans to identify aortic growth. It was limited by measurement bias, and referral bias, although this was improved by only one observer measuring aortic enlargement.

Non-modifiable risk factors include age, which reflects the most common aetiology of medial degeneration discussed above, male gender, genetics, connective tissue disorders, and high BMI[49]. The extensive database of TAA patients in Yale included data on patients totaling over 30001. Analysis of this database revealed a strong genetic link in approximately 20% of patients first degree relatives and was not associated with connective tissue genetic diseases, as noted previously. This striking observation has led to recommendations of earlier surgical intervention for aneurysm repair[93].

48 Strachan D. Predictors of death from aortic aneurysm among middle-aged men: The Whitehall study. BJS. 2005;78:401–4.
49 Elefteriades JA. Focused Review Thoracic Aortic Aneurysm : Current Approach to Surgical Timing. ACC 2002;1458(02):82–8

Trimarchi et al devised a study of 613 patients with type B TAAs. After statistical analysis they observed a number of independent risk factors for death in those with an aortic diameter less than 5.5cm which included; hypotension/shock (p=0.001), acute kidney injury (p=0.14), mesenteric infarction/ischaemia (p=0.012), and periaortic haematoma (p=0.19). The largest risk factor for progression to death, rupture or dissection was aortic size discussed below. These risk factors, except for acute kidney injury, have not been replicated in other high quality studies, but this may be due to the design of these studies.

Zierer et al used a multivariate analysis technique on 110 asymptomatic TAA patients undergoing elective TAA surgery. They identified predictors of late death as; thoracoabdominal aneurysms ($p < 0.004$), advanced age ($p < 0.03$), chronic renal failure ($p < 0.03$), and congestive heart failure ($p < 0.001$).

This data is hindered with a small number of patients and the main aim of the study was quality of life and not assessment of risk factors.

With the exception of connective tissue disorders, the pertinent risk factors which earlier active intervention is recommended are patients with bicuspid valves or familial TAA. Although other risk factors predispose to this condition, such as smoking, these factors have not been unified before to approximate risk stratification. Again this is because of small study numbers not being able to provide robust figures in risk.

3.6 Incidence of Thoracic & Thoracoabdominal Aortic Aneurysm in the UK

The incidence of thoracic and thoracoabdominal aneurysms specifically within the UK is difficult to estimate. Several international population- based studies have estimated the incidence rate of thoracoabdominal aneurysms at around six new aneurysms per 100,000 person years[50]. In the UK, we may use Hospital Episode Statistics (Hospital episode statistics [HES] data, www. hesonline) to get an indication of activity within the English National Health Service (NHS) (population 52 million) and National Statistics Service (www.ons.gov.uk) to get an indication of resulting mortality (England and Wales, population 55 million). HES 'Diagnostic' data suggest around 1000 admissions per year related to this disease ('Thoracic', 'Thoracoabdominal', 'with rupture', 'without rupture'). Cause of death data stated by Office of National Statistics suggest around 650 deaths per year ('Thoracic Aortic Aneurysm' [ICD 171.1/2] and 'Thoracoabdominal Aortic Aneurysm' [ICD 171.5/6], 'with rupture' and 'without rupture'). The data set suggests that in 2010 there were only nine deaths from 'ruptured thoracoabdominal aneurysms' nationally, clearly in gross error and likely reflecting diagnostic and coding errors. For comparison, this compares with 3593 deaths (2010) from abdominal aortic aneurysm with rupture (ICD 171.3). Although crude, these data help us understand the level of consumption of services within the NHS.

50 Bickerstaff LK, Pairolero PC, Hollier LH, et al. Thoracic aortic aneurysms: a population-based study. Surgery 1982;92:1103 – 8

3.7 Clinical Presentation of Thoracic Aneurysms

Most thoracic aneurysms are asymptomatic and are typically detected when imaging studies (chest x-rays, CT scans, MRI, etc) are being obtained for unrelated reasons. Intervention on this group of patients is not without caveats. The dilemma arises that asymptomatic patients are functionally able and clinically stable. However, the growth rate of an aneurysm dictates that this group of patients should undergo surgery to avert major complication and death. When aortic aneurysms reach larger sizes the symptoms are typically based on the location of the aneurysm[6]. A good percentage of aortic arch aneurysm patients are symptomatic (short of breath or chest pain) due to associated aortic valve dysfunction, heart failure, coronary disease or extreme size of aneurysm. These aneurysms can also result in a dull pain underneath the breastbone or radiating to the upper back. However, when large, these aneurysms can compress both the esophagus and the airway resulting in difficulty swallowing and hoarseness.

Descending thoracic aneurysms are mostly asymptomatic, but can occasionally cause back pain. In contrast, abdominal and thoracoabdominal aneurysms may cause a pulsating feeling in the upper abdomen. Abdominal and back pain may also be present if the aneurysm increases in size. Whereas, most of the symptoms of stable thoracic aneurysms are vague and non-specific, rupture or dissection of these aneurysms produces dramatic symptoms. A ripping sensation within the chest accompanied by severe pain in the back between the shoulder blades is the most typical complaint during thoracic aortic dissection or rupture. Dizziness, difficulty walking and speaking can all accompany this acute event.

3.8 Diagnosis and Imaging of Thoracic Aneurysms

Suggestions of a thoracic aneurysm can frequently be inferred from routine chest X-rays. However, thoracic aneurysms are most reliably diagnosed with a CT scan or MRI (Figure 3.8). Frequently, the diagnosis is made when one of these imaging studies is performed for symptoms unrelated to the aneurysm. Echocardiography is important for the evaluation of the aortic valve and also can be used to evaluate the size of the ascending aorta.

3.9 The Role of Biomarkers

The quest for the ideal biomarker to the detection and screening of aortic aneurysm and dissection continues. Trimarchi et al. summarized it at their best when they quoted **"*The utilization of biomarkers could lead to further improvements in diagnostic pathways in acute and chronic aortic diseases, highlighting potential targets for therapeutic intervention and establishing uniform, evidence-based follow-up programs."*[51].**

Currently, several biomarkers are being investigated as suitors for prediction, risk stratification and prognostic evaluation in TAA patients which include; D-dimer, Plasmin, Fibrinogen, Matrix metalloproteinases, Cytokines, CD4 + CD28- cells, C-reactive protein, Elastin peptide, Endothelin, Hepatocyte growth factor, Homocysteine, Ribonucleic acid signature. D-dimer has previously been identified as a potential biomarker in aortic dissection proving itself to have a sensitivity of 99%. Its downfall though is that elevated d-dimers are highly non-specific, particularly in diseases of the chest. This critical point negates its usefulness as a sole biomarker. The development of RNA signatures is yielding significant interest. These

51 Tsai TT, Trimarchi S, Nienaber CA. Acute aortic dissection: perspectives from the International Registry of Acute Aortic Dissection (IRAD). Eur J Vasc Endovasc Surg. 2009 Feb;37(2):149-59

biomarkers measure RNA regulation related to aortic aneurysms and potentially could be useful in dissection and rupture prediction.

So far, this RNA signature test, it has shown to be 80% accurate in determining whether a patient has an aneurysm, and potentially this may prove to be useful as a screening tool[52].

3.10 Medical Management

3.10.1 The Role of Pharmaco-Therapeutics

3.10.1.1 Beta Blockers

Medical therapy of TAAs has recently received a lot of attention. Historically all patients were prescribed a beta blocker on diagnosis of TAA, and this is still the case today. The basis of this was based on two reasons; small clinical trials of Marfan syndrome patients, and anecdotal evidence that lower blood pressures in the aorta would relieve the outward tension of an aneurysm meaning it would be less likely to rupture.

However, this belief has been challenged, firstly as Marfans patients make up a small proportion of TAA patients, secondly Marfans pathogenesis and degenerative TAA pathogenesis are two different entities and should be treated as such and thirdly recent evidence show limited benefit of beta blockers[53]. However, the current practice remains that once patients are diagnosed with an aneurysm of the thoracic aorta they tend to be placed on B-blockers. The 2010 guidelines on Thoracic aortic disease produced by *The American College of Cardiology Foundation* and *The*

52 Wang Y, Barbacioru CC, Shiffman D, Balasubramanian S, Iakoubova O, Tranquilli M, et al. Gene expression signature in peripheral blood detects thoracic aortic aneurysm. PLoS ONE. 2007;2:e1050
53 Andrew S. Chun, John A. Elefteriades, Sandip K. Mukherjee. Do Beta-Blockers Really Work for Prevention of Aortic Aneurysms? Time for Reassessment. AORTA, Vol.1, Issue 1

American Heart Association Task Force, state that: All patients should be receiving beta blockers after surgery or medically managed aortic dissection[6].

For patients with thoracic aortic aneurysm, it is reasonable to reduce blood pressure with beta blockers and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers to the lowest point patients can tolerate without adverse effects.

Beta blockers (β-blockers) are antagonists to sympathetic mediators for β-adrenoreceptors. Once bound, β-blockers diminish calcium currents and downplay the sarcoplasmic reticulum pump within cardiac myocytes. The result of this is a reduced contractile force, which, in turn, leads to a decrease in heart rate, cardiac output, and a lower blood pressure[54].

It is imperative that these patients' blood pressures are tightly regulated to maintain the surgical repair. The theory underpinning β-blocker therapy after TAA surgical repair is lower blood pressure produces less tension on the aorta, and subsequently, reduces the chances of the surgical repair failing. Evidence also suggests β-blocker therapy retards the diameter of aorta from expanding further; in a study comparing patients with Marfan's syndrome, those taking β-blockers were contrasted against the control group who were not taking any treatment. Overall, researchers concluded β-blockers reduce aortic dilation a reflection of the 2010 guidelines[55].

Similarly, Genoni et al also conclude that prolonged β-blocker use halts the further expansion of the aneurysm[56]; the incidence of an increase of aortic diameter was 12% amongst those taking β-blockers, compared to 40% in patients on other hypertensives. Furthermore, this adds weight to the decision to specifically name β-blockers above other hypertensives in the guidelines.

54 Levick JR. An Introduction to Cardiovascular Physiology. Fifth ed: Hodder Arnold, 2010
55 Shores J, Berger KR, Murphy EA, Pyeritz RE. Progression of aortic dilatation and the benefit of long-term β-adrenergic blockade in Marfan's syndrome. New England Journal of Medicine 1994;330(19):1335-41
56 Genoni M, Paul M, Jenni R, Graves K, Seifert B, Turina M. Chronic β-blocker therapy improves outcome and reduces treatment costs in chronic type B aortic dissection. European Journal of Cardio-thoracic Surgery 2001;19 (5):606-10

A recent meta-analysis concluded that beta-blocker therapy had no clinical benefit in Marfan patients[57]. Six studies were included, of which 5 were non-randomized follow-up studies and 1 was a prospective randomized trial, and totalled 802 patients. Using a random effects model, statistical significance was not reached for beta blocker therapy. The analysis is limited in that high quality randomized controlled trials are not available, furthermore, as it is standard practice to prescribe these patients beta blockers the control group in those not taking beta blockers is very small.

3.10.1.2 Angiotensin Converting Enzyme Inhibitors

Although ARBs and ACE inhibitors remain second-line choices for the treatment of hypertension in the absence of other compelling indications, drugs in these classes have been of particular interest as potential treatments for patients with Marfan syndrome (and Loeys-Dietz syndrome) because of their antagonism of TGF-β activity. In a signal study, mice heterozygous for a fibrillin-1 mutation (a model of Marfan syndrome) were treated with the ARB losartan and showed less elastin fiber fragmentation, less TGF-β signaling in aortic tissue, and slower aortic root growth rates than did placebo controls; the results in the losartan group were comparable to those of untreated wild-type mice and better than those of propranolol-treated mutant mice[55]. Investigators in Melbourne recently evaluated the effect of perindopril—an ACE inhibitor that effectively blocks angiotensin II receptors—in a small, randomized clinical trial[56].

Marfan patients who received a 24-week course of the study drug plus beta-blockers had less arterial stiffness, smaller aortic root diameters, and lower blood levels of TGF-β. MMP-2, and MMP-3 than patients receiving placebo plus beta-blockers; whether these short-term results will translate into long-term benefits is unknown

57 Thakur V, Rankin KN, Hartling L, Mackie AS. A systematic review of the pharmacological management of aortic root dilation in Marfan syndrome. Cardiol Young. 2013 Aug;23(4):568-81

and will need to be investigated in larger clinical trials. The National Heart, Lung, and Blood Institute is sponsoring a presently ongoing trial of losartan versus atenolol for Marfan syndrome patients aged 6 months to 25 years. The trial, which has an expected enrolment of 604 subjects, is designed to determine whether losartan is superior lo atenolol in reducing aortic root size (Z-score adjusted to body surface area) at 36-month follow-up [58]. However, recent evidence from Lacro et el. indicates that no benefit or superiority of losartan over the beta-blocker such as atenolol in respect to the rate of expansion of aortic-root dilatation in Marfan's syndrome patient population[59]. This study informs me that ARBs such as Losartan are as much effective as beta-blockers in the treatment of patients with Marfan's syndrome. A possible rhetorical idea would then emerge due to such interpretation to indicate that beta-blockers are an effective treatment option. This would happen to serve the thought mentioned in 2010 guidelines of the American College of Cardiology Foundation and the American Heart Association who recommended the use of beta-blockers, whereas the 2014 guidelines of the European Society of Cardiology did not [60]. Multicentre large clinical trials need to resolve this much debated topic on the efficacy of ARBs or ACE inhibitors over the standard beta-blockade therapy. This could result in significantly, shifting these Marfan patients' away from almost inevitable, high-risk surgery and present a new shift in the paradigm.

58 Habashi JP, Judge DP, Holm TM, et al. Losartan, an AT1 antagonist, prevents aortic aneurysm in a mouse model of Marfan syndrome. Science. 2006;312:117–21

59 Lacro RV, Dietz HC, Sleeper LA, Yetman AT, Bradley TJ, Colan SD, Atenolol versus losartan in children and young adults withMarfan's syndrome. N Engl J Med. 2014;371:2061-71

60 Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H,et al. ESC Committee for Practice Guidelines. 2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC). Eur Heart J. 2014 Nov 1;35(41):2873-926

CHAPTER FOUR

4. ACUTE AORTIC DISSECTION

4.1 Aetiology, Pathophysiology and Risks of Thoracic Acute Aortic Dissection

Aortic dissection is more common in males with a peak incidence at 50–70 yr of age. Aortic dissection can result either from a tear in the intima and propagation of blood into the media or from intramural haematoma formation in the media followed by perforation of intima. An intimal tear can occur in the regions of the aorta that are subjected to the greatest stress and pressure fluctuations. Because mechanical stress in the aortic wall is proportional to intramural pressure and vessel diameter, hypertension and aortic aneurysm are known risk factors for dissections. Most aortic dissections occur with an initial transverse tear along the greater curvature of the aorta, usually within 10 cm of the aortic valve. The aortic root motion has a direct impact on the mechanical stresses acting on the aorta[61]. Data from the International Registry of Aortic Dissection (IRAD) [62] showed the following risk factors in acute aortic dissections: male sex, age, a history of hypertension or atherosclerosis, prior cardiac surgery including aortic valve surgery, a history of bicuspid aortic valve, or a history of Marfan syndrome. The younger patients were more likely to have Marfan syndrome, bicuspid aortic valve, Ehlers-Danlos syndrome, Loeys-Dietz syndrome

61 The division of Cardiac Surgery at St. Luke's - Roosevelt Hospital. http://www.slrctsurgery.com/114 Diagnosis and management of aortic dissection. Contin Educ Anaesth Crit Care Pain (2009) 9 (1): 14-18.
62 Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL et al. The International Registry ofAcute Aortic Dissection (IRAD): new insights into an old disease. JAMA. 2000 Feb 16;283(7):897-903

and a history prior cardiac surgery. The average age for aortic dissection was 63.1 years. 65.3% of patients were male. 62.3% of the patients had type A dissection, 72.1% had a history of hypertension, and 4.9% had Marfan syndrome.

4.2 Clinical Presentation

The clinical presentation of dissection patients may be diverse. It has been described that the pain is as stabbing, tearing, or ripping in nature[63]. However, the most common characteristic of acute dissection presentation is acute pain localized to the chest, abdomen, and back and sudden collapse. Analysis of the International Registry of Acute Dissection (IRAD), noted that severe chest pain is more common with type A dissection, whereas back pain and abdominal pain are more common in type B dissection[62]. The IRAD reported that 95.5% of all AAD patients presented with pain. However, in previous reports it was revealed that between 5 and 17% of all dissection patients present with painless acute aortic dissections. As expected, atypical presentation can lead to a delay in diagnosis, which is associated with higher mortality[51]. Immediate adequate medical treatment is essential and has to include optimal blood pressure control in order to reduce shear stress and limit the propagation of the dissection. Therefore, it is important to recognize these patients at the earliest possible stage[62] .

The true incidence in the population is probably even higher, as an atypical presentation will likely result in a higher risk of death prior to the diagnosis. Physical examination may reveal tachycardia accompanied by hypertension from anxiety and pain. Tachycardia and hypotension result from aortic rupture, pericardial tamponade, acute aortic valve regurgitation, or even acute myocardial ischaemia with involvement of the coronary ostia. Differential or absent pulses in the extremities and a diastolic murmur of aortic regurgitation may also be present.

63 Klompas M. Does this patient have an acute thoracic aortic dissection? JAMA. 2002;287:2262–72

Syncope, stroke, and other neurological manifestations secondary to malperfusion syndrome may develop. A complete neurological examination is essential and findings should be documented.

4.3 Diagnosis

Accurate diagnosis of aortic dissection and a high index of suspicion are imperative especially in patients with predisposing risk factors such as hypertension, known and documented aneurysmal disease of the aorta, or a familial connective tissue disorders. However, not always we are presented with a full history and an all knowing patients of their medical status. This present a further challenge especially when patients are very moribund and their state of consciousness might not be pristine. What compounds the aforementioned is the delay in diagnosis. Approximately 4.4 million patients who present annually to the US emergency departments for chest pain, only about 2,000 have acute aortic dissection and as a result correctly diagnosed aortic dissection is only in 15%–43% of patients in the initial presentation[64, 65].

64 Trimarchi S, Jonker FHW, Hutchison S, Isselbacher EM, Pape L a, Patel HJ, et al. Descending aortic diameter of 5.5 cm or greater is not an accurate predictor of acute type B aortic dissection. J Thorac Cardiovasc Surg. 2001;142:e101–7

65 Mészáros I, Mórocz J, Szlávi J, Schmidt J, Tornóci L, Nagy L, et al.. Epidemiology and clinicopathology of aortic dissection. Chest. 2000; 117:1271–1278

4.4 Imaging

The choice for the diagnostic imaging depends on patient's stability, local expertise, and availability. Its use should be to expedite the assertion of aortic dissection, identify the type/extent and locate the intimal tears. It should confirm the presence of true/false lumen and whether a thrombus is present, assess any aortic side branch involvement, detect any aortic regurgitation or coronary artery dissection to certain extent, and aid in the identification of the dissection aftermath i.e. any extravasation within the pericardium, mediastinum or hemithorax [66,67,68].

Aortography has lost its place as the gold standard test due to a number of serious disadvantages, including the use of a heavy dose of IV contrast (1 mg/kg), the risks of an invasive procedure, and the extended time it takes to complete the procedure (up to 2+ hours).

On the contrary, in 2002 IRAD reported[69] that computed tomography angiography (CTA) is used in 63% of cases of suspected aortic dissection, followed transesophageal echocardiography (TEE) in 32%, aortography 4%, and magnetic resonance angiography (MRA) in 1%. Computed tomography angiography, TEE and MRA have similar pooled sensitivity (98%–100%) and specificity (95%–98%) although the pooled positive likelihood ratio appeared to be higher for MRA (positive likelihood ratio, 25.3; 95% confidence interval, 11.1–57.1) than for TEE (14.1; 6.0–33.2) or CTA (13.9; 4.2–46.0). CTA is widely available and relatively rapid, provides visualization of the entire aorta down to iliac arteries, and delineates the involvement of aortic side branches[6369,].

66 Imamura H, Sekiguchi Y, Iwashita T, Dohgomori H, Mochizuki K, Aizawa K, et al.. Painless acute aortic dissection. Diagnostic, prognostic and clinical implications. Circ J. 2011; 75:59–66
67 Braverman AC. Acute aortic dissection: clinician update. Circulation. 2010 Jul 13;122(2):184-8
68 Bashir, Mohamad; Fok, Matthew; Hammoud, Ibrahim; Rimmer, Lara; Shaw, Matthew; Field, Mark; Harrington, Debbie; Kuduvalli, Manoj; Oo, Aung. AORTA, Volume 1, Number 3, August 2013 , pp. 182-189(8)
69 Nallamothu BK, Mehta RH, Saint S, Eagle KA. Syncope in aortic dissection: diagnostic, prognostic, and clinical implications. J Am Coll Cardiol 2002; 39:241A.

The use of ECG-Gated CT offered the option instead of selecting scan data acquired in exactly the same phase of the cardiac cycle for each image as in standard ECG-gated reconstruction techniques, the patient's ECG signal is used to omit scan data acquired during the systolic phase of highest cardiac motion. With this approach cardiac pulsation artefacts in CT studies of the aorta, of paracardiac lung segments, and of coronary bypass grafts can be effectively reduced. Again the culprit of CTA being the first definitive choice include the requirement that patients be transported to the CTA suite, the use of potentially nephrotoxic contrast, and the inability to assess aortic insufficiency.

MRA is highly accurate and does not require the use of a contrast dye. It is, however, usually not available on an emergency basis and requires patients to be in MRA suite for an extended period of time. Other issues such as claustrophobia, the use of ventilator, and patient's use of metal devices (pacemakers, aneurysmal clips) may further complicate its routine use[69].

TEE is a viable alternative in patients who are critically ill and/or hemodynamically unstable. The main advantages of a TEE include speed, good sensitivity and specificity, and the fact that it can be performed at the patient's bedside in the ED. Its main limitations are lack of widespread expertise and subjective reporting which necessitates high level of expertise to avoid false positive reports. An aortic dissection is a tear in the inner layer of the aortic wall, which allows blood to enter into the wall of the aorta, creating a new passage for blood, known as the "false lumen." Blood flow into the false lumen can cause several problems: It can rob crucial blood from the rest of the body, it can cause the dissection to spread and affect other arteries, and it can block blood flow in the true aortic channel ("true lumen"). These problems may cause decreased blood flow to vital organs. Aortic dissection also weakens the aortic wall and may lead to rupture, which may be fatal, or to formation of a balloon-like expansion of the aorta, known as an aneurysm. Aortic dissections are uncommon, yet they are highly lethal.

If untreated, an aortic dissection can be fatal within the first 24 to 48 hours. Several risk factors are associated with aortic dissections, such as high blood pressure (hypertension), genetic disorders affecting the blood vessel wall, atherosclerosis, cocaine use, and trauma.

4.5 Management of Thoracic Acute Aortic Dissection

Immediate management of aortic dissection includes stabilizing the patient with prompt attention to blood pressure reduction. B-Blockers are the first drugs of choice because of their mechanism of lowering the rate of rise of ventricular force (dP/dt) and stress on the aorta. Intravenous agents are chosen for rapid onset. In many instances, multiple blood pressure agents are required. In patients in whom refractory hypertension exists, renovascular hypertension related to the dissection flap must be considered. All patients with acute aortic dissection should undergo multidisciplinary evaluation that includes cardiothoracic and/or vascular surgical consultation.

Emergency surgery is recommended for acute type A dissection, in the International Registry of Acute Aortic Dissection, the mortality rate of patients undergoing surgery for type A dissection was 26% and for those treated medically was 58%. Patients with low-risk features have a significantly lower mortality rate than those with malperfusion, shock, or cardiac tamponade.

Surgical management of type A dissection involves excision of the intimal tear when possible, obliteration of entry into the false lumen proximally and distally, and interposition graft replacement of the ascending aorta. The aortic valve may need to be replaced, depending on the underlying pathology of the valve and aortic root[70] .

70 McCaig LF, Nawar EW. National Hospital Ambulatory Medical Care Survey: 2004 emergency department summary. Adv Data. 2006; 372:1–29.Sullivan PR, Wolfson AB, Leckey RD, et al. Diagnosis of acute thoracic aortic dissection in the emergency department. Am J Emerg Med. 2000;18:46–50

CHAPTER FIVE

5. RISK STRATIFICATION OF THORACIC AORTIC ANEURYSMS

5.1 Introduction

Risk stratification for the individual patient is a pertinent goal that has received much attention for many years. Historically this has been guided by personal clinical prowess and anecdotal evidence as noted by the Yale group. Retrospective analysis of data from large databases has shown insight into risk of rupture, dissection and death from absolute aortic size as mentioned above. This cumulated to the 5.5cm guideline as an operative indicator for asymptomatic TAA's[6]. There are now more risk scores being developed that may be able to provide better insight into TAA complications and better guide clinical decisions.

5.2 Seeking the Ideal Risk Prediction Model

The Yale group were the first to publish data on relative aortic size in comparison to body surface area[71]. They retrospectively analysed data from 410 patients on their extensive TAA database. The study demonstrated a lower body surface area was

71 Elefteriades J. Thoracic aortic Aneurysms: Reading the enemies playbook. Curr Probl Cardiol. 2008 May;33(5):203-77.

associated with a higher incidence of dissection, rupture and death. This data was extrapolated to make a measure of relative aortic size (ASI) and in this study ASI was a better predictor of negative outcomes than maximal aortic diameter. Statistical analysis was able to group patients into three stratified groups, according to aortic size index, that gave the patient a probability of rupture, dissection or death ($p<0.00001$). Namely; low risk (ASI 2.75cm/m2) as less than 4%/year, moderate risk (ASI 2.75-4.24cm/m2) as approximately 8%/year and high risk (ASI <4.25cm/m2) as approximately 20%-25%/year. The data is consistent with the guidelines that surgery should be performed before an aneurysm is able to grow to 6cm or greater.

Furthermore, ASI proves to be a useful tool to guide patient decision regarding clinical decisions. The data provides a new insight in that it may be beneficial in a selected subgroup of patients, who have a small aortic aneurysm size, but with a high ASI, operative intervention maybe indicated before the aorta reaches 5.5cms as recommended in the guidelines.

The author acknowledges that there are limitations to the data; measurement bias in so far as height and weight recorded in the emergency room is inaccurate, rupture rate is not accurately represented in all these patients as elective operative management eliminates the risk of rupture. Shimada et al used mathematical modelling to describe a formula that would predict thoracic aneurysm growth in their cohort of 88 patients [72]. This formula used the difference between their initial diameter of their aneurysm, their current diameter, the time between the two measurements and a constant. Their formula derived an r value of 0.617, furthermore similar formulae from the Yale group, Mt Sinai and Osaka group applied to the data from this cohort of patient revealed very similar results. The authors concluded that because of this similarity TAA expansion is similar in different sample populations worldwide.

72 Shimada I, Rooney SJ, Pagano D, Farneti PA, Guest PJ, Bonser RS, et al. Prediction of Thoracic Aortic Aneurysm Expansion : Validation of Formulae Describing Growth. Ann Thorac Surg. 1999;67:1968–70

The study is limited is the small nature of the number of patients, and subject to measurement bias. It does not reliably predict TAA growth, but it can give a rough estimate for patients as to when they may likely be required to have surgery.

5.3 Importance of Risk Prediction Models in Thoracic Aortic Aneurysms

Risk prediction models can be used to provide important information to both patients and clinicians about the risks of surgery. They may even be used to decide between different treatment options. Risk prediction models also have a vital role to play in clinical governance analyses. Currently generic cardiac surgery risk prediction models are used for proximal aortic surgery.

As these models were specifically developed for proximal aortic surgery they may be more accurate than generic models for informing patients and clinicians about the risks of in-hospital mortality following surgery on the aortic root, ascending aorta or aortic arch, and for risk-adjusting proximal aortic surgery outcomes analyses.

5.4 Developing a Thoracic Aortic Risk Prediction Model

For the sake of this thesis, separate models for elective and non-elective surgery were developed as it has previously been demonstrated that cardiac surgery models that have been developed for both elective and non-elective surgery can perform poorly in emergency surgery.

Although surgical activity in proximal aortic cases is relatively low compared to cardiac bypass graft or valvular surgery, the procedure itself carries a greater risk of mortality. Consequently, a number of studies have previously attempted to quantify the risks involved. Williams et al [18] presented risk factor results of proximal aortic surgery based on the Society of Thoracic Surgeons (STS) Dataset for both in-hospital mortality and mortality plus major morbidity, in overall and elective cohorts. The predictive power of their elective mortality model had an AUC of 0.77. As this study contained four separate models and was part of a wider review of North American outcomes an extended description of the model coefficients was not available.

Other work by Huijskes [24] and Nishida [25] incorporate the widely used EuroSCORE and EuroSCORE II algorithms [26, 27, 28] in order to make comparisons with local models and to ascertain how the model performs in aortic surgery cohorts.

CHAPTER SIX

6. BRAIN PROTECTION DURING OPEN THORACIC AORTIC SURGICAL REPAIR

6.1 Historical Perspective of Deep Hypothermic Circulatory Arrest (DHCA)

The first reported use of hypothermia as a therapeutic intervention dates to the Hippocratic era, from the Hippocratic School of Medicine, where it was described as a treatment for tetanus[73]. Hippocrates himself promoted the use of snow and ice packed around the injured soldier to promote healing[74]. In 1812, Dominique Larrey, surgeon to famous military leader Napoleon, used ice to alleviate injured soldiers' pain during amputations[75]. Despite a history of well over two thousand years, hypothermia did not gain popularity until the 21st century. In modern medicine, mild therapeutic hypothermia is widely used post cardiac arrest with return of spontaneous circulation in an effort to reduce the incidence of neurological

73 Adams F. The Genuine Works of Hippocrates. New York: William Wood. 1929
74 Lloyd G (editor), Chadwick J (trans), Mann N. Hippocratic Writings. London Penguin Books. 1983;223.
75 Naef a P. The mid-century revolution in thoracic and cardiovascular surgery: part 4. Interact CardioVasc Thorac Surg. 2004;3:535-541

damage[76]. DHCA is, however, reserved for aortic surgery and cerebrovascular surgery as a method of cerebral protection[77].

The birth of hypothermic cooling techniques for use in cardiac surgery began in earnest with the work of William Bigelow[78]. Today, Bigelow is famous for writing two books, including one called "Cold Hearts". He is further recognized for his role in the development of the pacemaker. He was awarded the title of Officer of the Order of Canada, the second highest honor of merit awarded by the Queen to civilians, and he was inducted into the Canadian Medical Hall of Fame in 1997.

In 1950, a research team in Toronto led by Bigelow published their two years' work on oxygen uptake and expenditure in canines at temperatures considered hypothermic[78].

They hypothesized that a reduced body oxygen requirement could be achieved through a reduced metabolic drive secondary to hypothermia. This in turn would enable the heart to be excluded from circulation and allow the possibility of cardiac surgery. Their work was published before the invention of cardiopulmonary bypass by John Gibbons, who began clinical application of his heart-lung machine in 1952[79]. Bigelow's experiments encompassed 176 dogs, who were cooled with the by muscle relaxants to control homeostatic temperature regulation resulting in severe shivering, venesection as a method of reducing pressure within the venous system, and phrenic nerve stimulation to induce artificial respiration. Bigelow was able to successfully exclude the heart from circulation without arrest at a core temperature of 20˚C in 39 of his dogs. Of these 39, 51% of dogs were successfully revived.

76 Mikkelsen M, Christie J, Abella B, Kerlin M, Fuchs B, Schweickert W. American Heart Association's Get With the Guidelines- Resuscitation Investigators. Use of therapeutic hypothermia after in-hospital cardiac arrest. Critical Care Med. 2013;41:1385–95
77 Chau KH, Friedman T, Tranquilli M, Elefteriades JA. Deep hypothermic circulatory arrest effectively preserves neurocognitive function. Ann Thorac Surg. 2013;96:1553-9
78 Bigelow WG, Callaghan IJC, Hoppst JA. General hypothermia for experimental intracardiac surgery. Ann Surg. 1950;531–7
79 Stoney WS. Evolution of cardiopulmonary bypass. Circulation. 2009 ;119:2844–53

Cardiac arrhythmias, particularly ventricular fibrillation, was the major hindrance in the dogs who were successfully revived[78].

In these early experiments, a common theme was to avoid ventricular fibrillation or at least to correct it as soon as it developed. We must remember this, as in the current era of cardiopulmonary bypass, we are immune to the impact of ventricular fibrillation, which is expected as part-and-parcel of deep hypothermia.

Despite these promising advances, the team continued to search for better methods of cooling. They knew that a hibernating mammal, such as the groundhog, could survive a temperature of 3˚C. They wished to reduce the current limit of 20˚C [7880]. The team performed further research on *Macacus Rhesus* monkeys, once again using cooling blankets, this time to below 20˚C. 11 of 12 monkeys cooled to temperatures between 16 to 19˚C survived between 15 to 24 minutes. Whereas in previous experiments on dogs, at which their respirations ceased around 24˚C, monkeys continued to respire at 8 per minute at 20˚C.

Similarly, Bigelow *et al.* used groundhogs cooled below 5˚C (as in their natural hibernating state), operated and successfully revived 5 out of 6 of the animals[81].

A physiologist named Frank Gollan worked in the 1950s using hypothermia and an oxygenator of his own invention, and presented his work in 1955[81,82,83]. Gollan made an important step in that his bubble oxygenator included a heat exchange device, whereby he could induce hypothermia as well as carryng out rewarming[84]. He was able to achieve measured core temperatures of 4^0C and published revival of the animals.

80 Bigelow WG, Mcbirnie JE. Further experiences with hypothermia for intracardiac surgery in monkeys and groundhogs. Annals of surgery. 1953;137:361–5
81 Clark L, Gollan F, Gupta V. The oxygenation of blood by gas dispersion. Science. 1950; 111:85-87.
82 Clark Lc, Gupta Vb, Gollan F. Dispersion Oxygenation For Effecting Survival Of Dogs Breathing Pure Nitrogen For Prolonged Periods. Proc Soc Exp Biol Med. 1950;74:268-71
83 Gollan F, Clark Lc Jr, Gupta Vb. The Prevention Of Acute Anoxic Anoxia By Means Of Dispersion Oxygenation Of Blood. Am J Med Sci. 1951;222:76-81
84 Gollan F, Blos P, Schuman H. Studies On Hypothermia By Means Of Pump-Oxygenator. Am J Physiol. 1952;171:331-4

Despite this, his research was not widely recognized and was largely ignored amongst the surgeons at the American Association for Thoracic Surgery[85]. In Sweden, Juvenelle *et al.* were also coming to similar conclusions to Gollan—specifically that the use of a pump-oxygenator and hypothermia of 12˚C would decrease oxygen requirements of the body to allow open cardiac operating times of up to 2 hours without adverse consequences[86]. However, Juvenelle's method produced little in the way of long term survival[85].

The first successful human operation utilizing a period of hypothermia was performed in 1952 at the University of Minnesota by Dr. John F. Lewis[87]. Armed with knowledge of William Bigelow's experiments on hypothermia, and his own extensive experiments involving several hundred canines, he was successful in closing a secundum atrial septal defect in a 5-year-old girl. For two hours he wrapped the anaesthetized patient in refrigerated blankets until her rectal temperature had fallen to below 28˚C. Lewis describes the operation in his landmark paper[87]. "The chest is opened with a transverse, sternal splitting incision through the 4 interspaces, the heart is explored digitally through the right auricular appendage. Cardiac inflow and outflow are occluded and the right atrium is opened widely to allow repair. The left and right heart are filled with saline and atrium closed". Following the operation, the patient was placed in hot water at 45˚C to increase her rectal temperature to 36˚C. This operation is heralded in cardiac history as the first ever successful operation within the open human heart under direct vision.

Subsequently, Lewis used this technique on 29 more patients, with only three deaths[88]. Without cardiopulmonary bypass, hypothermia still carried an inherent risk of ventricular fibrillation, which remained a significant danger of hypothermia,

85 Dobell a R, Bailey JS. Charles Drew and the origins of deep hypothermic circulatory arrest. The Annals of thoracic surgery. 1997;63:1193–9.
86 Juvenelle A, Lind J, Wegelius C. Quelques possibilites offertes par l'hypothermie generale profonde provoquee (Une etude experimentale chez le chien). Presse Med. 1952;60:973–978
87 Lewis Fj, Taufic M. Closure Of Atrial Septal Defects With The Aid Of Hypothermia; Experimental Accomplishments And The Report Of One Successful Case. Surgery. 1953;33:52-9
88 Lewis Fj, Taufic M, Varco Rl, Niazi S. The Surgical Anatomy Of Atrial Septal Defects: Experiences With Repair Under Direct Vision. Ann Surg. 1955;142:401-15

previously noted by Bigelow *et al and* Lewis *et al* who used cardiac massage, intra-cardiac adrenalin and electrical shock successfully in over ninety percent of patients for restoration to normal sinus rhythm[80,88]. The success of Lewis's operations gained worldwide medical recognition, and they represent a major milestone in cardiac surgical history. However, with the introduction of the cardiopulmonary bypass machine, the sole use of hypothermia as a technique to allow intra-cardiac operations was short lived, in view of the limited operating time this technique provided and the associated complications it carried.

1953 came Henry Swan, who had repeated the work of Bigelow to investigate impact on the variables of pH, serum sodium, chloride, potassium, phosphorus, plasma protein and haematocrit under the influence of hypothermia, with particular interest in prevention of the well documented complication of ventricular fibrillation. On February 19th of the same year, Swan carried out open-heart surgery, a pulmonary valvulectomy, using hypothermia for the first time[89,]. Swan then applied these findings in a surgical setting, prior to the use of cardiopulmonary bypass, using 26-28˚C hypothermia on hundreds of patients, with a low mortality rate[75]. As such, Swan was considered to have the most surgical experience using hypothermia.

The renowned surgeon Dr Denton Cooley employed hypothermia for cerebral protection during his first attempt at total resection and replacement of the aortic arch in 1955[90,91]. The 49-year-old gentleman was suffering from a syphilitic aneurysm involving the arch and a further aneurysm affecting the descending aorta. Cooley used surface cooling to achieve 33˚C, and temporary shunts were placed to provide blood to the carotids and distal aorta. In this case, the patient went on to suffer a stroke and then death, although this was attributed to an 8-minute occlusion of the right carotid shunt. This case not only represented the first ever aortic arch

89 Swan H, Zeavin I, Holmes Jh, Montgomery V. Cessation of Circulation in General Hypothermia. I. Physiologic Changes and Their Control. Ann Surg. 1953;138:360-7
90 Cooley DA. Milestones in the Treatment of Aortic Aneurysm. Tex Heart Inst J. 2005; 32: 130–134.
91 Cooley D, Mahaffey D, Bakey M. Total excision of the aortic arch for aneurysm. Surg Gynecol Obstet. 1955; 101:667–72.

resection and replacement but exploited the use of hypothermia as an adjunct in aortic arch surgery, as it is still used today.

Further, important developments in 1955 were introduced by Lillehei and Kirklin who used the pump-oxygenator for intra-cardiac surgery[85]. During their operations, it was noticed that body temperature would often cool spontaneously, as early oxygenators lacked heat exchangers. In this way it was noted that allowing spontaneous cooling alongside pump-oxygenators could produce better outcomes. Lillehei and Kirklin published their successful work, and their techniques became fashionable. [85]

Sealy *et al.* fronted this development throughout the late 1950s, and in 1959 and was the first to add a heat exchanger alongside a DeWall oxygenator[85]. This allowed rapid active cooling and rewarming to patients to a temperature 32˚C. They confirmed the compatibility of using hypothermia alongside oxygenator. He reported this technique for 95 patients in a variety of open cardiac surgeries including; tetralogy of fallot, compete transposition, valvular disease, septal defects, and reported a mortality rate of 17%[85].

From 1959 onwards, Charles Drew, a surgeon at the London Westminister Hospital, began developing his own methods for intracardiac surgery after disappointing results using other popularized methods[85]. Drew first used his technique, developed through experimentation on dogs, on a 1-year-old child with Down's syndrome in congestive heart failure from an endocardial cushion defect, although the child later died after recovery.

He successfully repaired his following two patients, who underwent VSD closure, and they recovered without complications in 1959[85]. His technique involved a circulatory support system to cool patients to 15^{o}C. His cynicism towards oxygenators led to using the patient's own lungs for oxygenation. This technique was gradually advanced to children and adults across a career of 22 years, with varying degrees of success. But, eventually this technique lost ground.

Drew's work represented a cardinal contribution to today's knowledge of hypothermia, and this was recognised in 1961, when Drew was invited to present the renowned Hunterian lecture at the Royal College of Surgeons.

In Siberia, Professor E. N. Meshalkin, who is credited as the pioneer of Soviet cardiac surgery, used hypothermia during the 1960s on a variety of patients. He was notorious for operating on congenital defects without cardiopulmonary bypass with only mild hypothermia[77]. It is documented that Prof. Meshalkin's method of cooling was the utilization of the abundance of snow and ice available in Siberia for surface cooling[92].

Meanwhile, methods of cooling were being advanced by Delorme and Bruce via the insertion of a cannula into the femoral artery of canines, passing the blood through an extracorporeal coil immersed within an ice bath, and returning the cooled blood through the femoral vein[93]. They were both able to cool canines to 22 to 26^{o}C without causing fibrillation, a dreaded complication of surface cooling (except in 1 dog). Delorme concluded that, armed with this knowledge, operating on a bloodless field would become possible in cardiac surgery. However, arteriovenous cooling was subject to complications, including fistula formation and thrombosis. Furthermore, the technique required initiation before surgery.

Mr. Donald Ross, well known for leading the team that performed the first cardiac transplant in the United Kingdom, is further credited with popularizing veno-venous cooling, a method he had devised in canine experimentation by cannulating the external jugular vein for blood drainage and providing return through the superior vena cava[94].

92 Karaskov A, Litasova E, Vlasov Y. A documentary on the life and work of Eugenij Nikolaevich Meshalkin. Circ Pathol Cardiac Surg. 1999;4-11
93 Bruce C. Discussion on the application of hypothermia to surgical procedures. Royal Society of Medicine. 1956; 49:345–54.
94 Ross D. Report of a heart transplantation operation. Am J Cardiol. 1968;

He reported improved success using veno-venous cooling over surface cooling due to the greater control over the stages of cooling, preventing core temperatures to drop too low, or too rapid reducing the risk of cardiac irregularities. The recognized detrimental effect of ventricular fibrillation from rapid cooling was still a very real risk. Ross did not commence cooling until the chest was open, and thus able to observe the heart and deal with any irregularities.

In 1959, Ross and Sir Russel Brock, from Guy's Hospital London, declared "deep hypothermia by means of a heart lung bypass machine or a differential cooling technique holds promise of longer safe periods of safe intra cardiac surgery in the future"[95]. Following this pronouncement, there was a wave of experiments in the use of cardiopulmonary bypass with hypothermia.

World renowned Dr Christiaan Neethling Barnard and Velva Schrire in 1963 were the first to use deep hypothermic circulatory arrest and cardiopulmonary bypass simultaneously, on two patients with aortic aneurysm involving the ascending aorta and arch. They cooled the patients to a temperature of approximately 10^{o}C measured in the oesophagus[77]. They were successful in one of their patients. Following this, multiple renowned surgeons began reporting success with combinations of hypothermia and cardiopulmonary bypass, including Borst and Lilliehei.

In 1975, Professor Randall Griepp published a series of four patient operations for aortic arch aneurysms using hypothermia via a combination of surface cooling and cardiopulmonary bypass[96]. He published successful resection of aneurysms in all four patients. Griepp *et al*. would later report (1991) the limitations of using

95 BROCK R, ROSS DN. Hypothermia. III. The clinical application of hypothermic techniques. Guys Hosp Rep. 1955;104:99-113.
96 Griepp RB. Cerebral protection during aortic arch surgery. J Thorac Cardiovasc Surg 2001;121:425-7.

hypothermic circulatory arrest alone for cerebral protection, noting a relationship between duration of hypothermic arrest and mortality[9697,98,99].

These concerns were echoed by Haldenwang *et al.*, who noted that temporary or permanent neurologic dysfunction incidence rose when HCA exceeded 40 minutes and mortality rates increased above 60 minutes of HCA[100]. It was this observation that led to the development of further techniques: antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP), which are used in combination with DHCA today.

6.2. Deep Hypothermic Circulatory Arrest (DHCA)

DHCA has been in clinical practice for over 30 years and allows the surgeon to excise the distal clamp site, completely view the aortic anatomy in a bloodless field and perform a distal anastomosis without leaving any clamp-compromised tissue[101102]. The reasoning behind this technique is to reduce the brain's activity and energy demand to a minimum.

97 ROSS DN. Venous cooling: a new method of cooling the blood-stream. Lancet. 1954;266:1108-9
98 Barnard CN, Schrire V. The surgical treatment of Acquired aneurysm of the thoracic aorta. Thorax.1963;18:101-15
99 Griepp RB, Ergin MA, Lansman SL, Galla JD, Pogo G. The physiology of hypothermic circulatory arrest. Semin Thorac Cardiovasc Surg. 1991;3:188-93
100 Haldenwang PL, Bechtel M, Moustafine V, Buchwald D, Wippermann J, Wahlers T, Strauch JT. State of the art in neuroprotection during acute type A aortic dissection repair. Perfusion. 2012 Mar;27(2):119-26
101 Reich DL, Uysal S, Sliwinski M, et al. Neuropsychologic outcome after deep hypothermic circulatory arrest in adults. J Thorac Cardiovasc Surg 1999;117:156-63
102 Svensson LG, Crawford ES, Hess KR, et al. Deep hypothermia with circulatory arrest. Determinants of stroke and early mortality in 656 patients. J Thorac Cardiovasc Surg 1993;106:19-28; discussion 28-31.

There are two specific concerns about the use of DHCA:

1) What temperature should be achieved before the extracorporeal circulation can be stopped?

2) What is the anticipated 'safe' interval for a repair without neurological complications?

Most clinicians consider 35-40 mins of HCA at 20 °C as relatively safe, but there is increasing evidence that the interval could be a lot shorter. The most common complications of this approach are post-ischemic hypothermia, impaired autoregulatory mechanisms, and the abolishment of the brain protective barriers manifested by the increase in the cerebrovascular resistance that is initiated during the rewarming part of the procedure. To counteract these untoward effects, reperfusion and rewarming are established gradually and slowly. Additionally, the gradient temperature between the perfusate temperature and the core temperature should never exceed 10 °C. The metabolic management during this crucial phase also plays a pivotal part, supplemented with pharmacological adjunct such as Mannitol, which aids in the prevention of cerebral oedema and increased intracranial pressure, and also act as a free radical scavenger[103].

The advantages of DHCA include:

- A bloodless and motionless operative field;
- Avoidance of clamping and manipulation of the aorta with reduced risk for brain embolism;
- Simplicity and no need for additional perfusion equipment.

103 Hagl C, Khaladj N, Karck M, et al. Hypothermic circulatory arrest during ascending and aortic arch surgery: the theoretical impact of different cerebral perfusion techniques and other methods of cerebral protection. Eur J Cardiothorac Surg 2003;24:371-8

The disadvantages of DHCA include:

- Limited safe time of circulatory arrest;
- Prolonged cardiopulmonary bypass (CPB) time required to cool down and rewarm patients, which may result in an increased occurrence of pulmonary, renal, cardiac and endothelial dysfunction;
- Reperfusion injury;
- Clotting complications[104]

Svensson *et al*. [102] reported in a series of 616 patients an overall stroke rate and early mortality rate of 7% and 10%, respectively (median DHCA time: 31 mins; range, 7-120 mins).

On univariate analysis, periods of circulatory arrest greater than 45 and 60 mins emerged as independent predictors of stroke and early mortality respectively. However, more recently, McCullogh *et al*. [105] demonstrated that the human cerebral metabolic rate is still 17% of baseline at 15 °C and that at this temperature the safe duration of circulatory arrest is no longer than 29 mins. Similarly, Reich *et al*.[101], Di Eusanio *et al*.[106] and Sakamoto *et al*. [107] have indicated that a duration of circulatory arrest of 25 mins is associated with an increased risk of transient neurological, memory and fine motor deficits.

104 Di Bartolomeo R, Pilato E, Pacini D, et al. Cerebral protection during surgery of the aortic arch. MMCTS 2011;2010:004457
105 McCullough JN, Zhang N, Reich DL, et al. Cerebral metabolic suppression during hypothermic circulatory arrest in humans. Ann Thorac Surg 1999;67:1895-9; discussion 1919-21
106 Di Eusanio M, Wesselink RM, Morshuis WJ, et al. Deep hypothermic circulatory arrest and antegrade selective cerebral perfusion during ascending aorta-hemiarch replacement: a retrospective comparative study. J Thorac Cardiovasc Surg 2003;125:849-54
107 Sakamoto T, Zurakowski D, Duebener LF, et al. Combination of alpha-stat strategy and hemodilution exacerbates neurologic injury in a survival piglet model with deep hypothermic circulatory arrest. Ann Thorac Surg 2002;73:180-9; discussion 189-90

For these reasons, the employment of DHCA seems to be rational only in patients requiring aortic arch repair with an anticipated duration of circulatory arrest shorter than 30 mins.

6.3 Retrograde Cerebral Perfusion (RCP)

The use of RCP was originally reported by Mills and Ochsner[108] for the management of massive arterial air embolism during cardiopulmonary bypass in 1980. In 1982 Lemole and colleagues[109], described intermittent RCP as a method of facilitating intraluminal graft placement in the aorta. In 1990, Ueda and associates[110] first described the routine use of continuous RCP in thoracic aortic surgery for the purpose of cerebral protection during the period of obligatory interruption of anterograde cerebral flow.

There is compelling evidence that RCP may accomplish neuro-protection through providing cerebral metabolic support, expelling atheromatous and gaseous emboli from the cerebral vasculature, and maintaining cerebral hypothermia.

The disadvantages in the use of RCP include cerebral oedema and the concern that very little of the perfusate actually reaches the brain to provide adequate neuroprotection.

The Safi group from Houston reported on the concept of an "opening" pressure that was required to observe a reversal flow in the middle cerebral arteries. 31 mmHg

108 Mills NL, Ochsner JL. Massive air embolism during cardiopulmonary bypass. Causes, prevention, and management. J Thorac Cardiovasc Surg 1980;80:708-17
109 Lemole GM, Strong MD, Spagna PM, et al. Improved results for dissecting aneurysms. Intraluminal sutureless prosthesis. J Thorac Cardiovasc Surg 1982;83:249-
110 Ueda Y, Miki S, Kusuhara K, et al. Surgical treatment of aneurysm or dissection involving the ascending aorta and aortic arch, utilizing circulatory arrest and retrograde cerebral perfusion. J Cardiovasc Surg (Torino) 1990;31:553-8

was required to open the venous capacitance vessels and overcome the jugular venous valves. This yielded acceptable results in terms of stroke[111].

The relationship between use of RCP and clinical outcome is also unclear. Some authors reported RCP duration to be a predictor of death and adverse neurological outcome[112,113], whereas others did not[114,115116].

Current practice for RCP deployment is through a superior vena cava cannula with snaring of the caval cannula to prevent cardiac distention. The mode of application of RCP is uniformly accepted based on clinical observations, and anatomic and experimental data that support RCP with a pressurized entire venous system. Some centers limit the use of RCP to the prevention of neurologic injury in patients at high risk of embolic strokes. RCP could also be used in brief cycles to flush out the debris prior to the commencement of antegrade flow and reperfusion.

In summary, based on human and laboratory investigations, RCP neuro-protective mechanisms still remain controversial. When compared to SACP, RCP seems to be less effective whilst still providing some adjunctive brain protection compared to DHCA alone, due to continued cerebral cooling via the veno-arterial and veno-venous collateral circulations.

111 Lee TY, Safi HJ, Estrera AL. Cerebral perfusion in aortic arch surgery: antegrade, retrograde, or both? Tex Heart Inst J 2011;38:674-7.
112 Sasaguri S, Yamamoto S, Hosoda Y. What is the safe time limit for retrograde cerebral perfusion with hypothermic circulatory arrest in aortic surgery? J Cardiovasc Surg (Torino) 1996;37:441-4.
113 Deeb GM, Williams DM, Quint LE, et al. Risk analysis for aortic surgery using hypothermic circulatory arrest with retrograde cerebral perfusion. Ann Thorac Surg 1999;67:1883-6; discussion 1891-4.
114 Okita Y, Takamoto S, Ando M, et al. Mortality and cerebral outcome in patients who underwent aortic arch operations using deep hypothermic circulatory arrest with retrograde cerebral perfusion: no relation of early death, stroke, and delirium to the duration of circulatory arrest. J Thorac Cardiovasc Surg 1998;115:129-38
115 Wong CH, Bonser RS. Does retrograde cerebral perfusion affect risk factors for stroke and mortality after hypothermic circulatory arrest? Ann Thorac Surg 1999;67:1900-3; discussion 1919-21
116 Ueda Y, Okita Y, Aomi S, et al. Retrograde cerebral perfusion for aortic arch surgery: analysis of risk factors. Ann Thorac Surg 1999;67:1879-82; discussion 1891-4.

6.4 Selective Antegrade Cerebral Perfusion (SACP)

The first attempt to repair the aortic arch relied on complex methods of antegrade cerebral perfusion. In 1957, DeBakey reported a successful resection of an aortic arch aneurysm using normothermic CPB and cannulation of both subclavian and carotid arteries by means of several pumps[117]. However, after early attempts, antegrade cerebral perfusion was abandoned due to unsatisfactory results and growing utilization of DHCA. SACP was then re-introduced by Frist *et al*.[118], Bachet *et al*.[119] and then popularized by Kazui *et al*.[120] They employed two separate pump heads for cerebral and systemic circulations and, in an elegant experimental study, indicated optimal cerebral flow rate (10 mL/kg/min) and perfusion pressure (40-70 mmHg) at 22 °C.

SACP provides several advantages: (I) the circulatory arrest time can safely be extended up to 90 minutes allowing more complex aortic repairs to be performed, (II) moderate (nasopharyngeal, 25 °C) instead of profound hypothermia can be used with reduced coagulative and systemic complications. Criticisms against SACP include technical complexity, reduced surgical visibility, and manipulation of the aortic arch and arch vessels especially in cases of acute dissections or severely atherosclerotic aortic arch aneurysms[106121,122].

117 DeBakey M, Crawford ES, Cooley DA, et al. Successful resection of fusiform aneurysm of aortic arch with replacement by homograft. Surg Gynecol Obstet 1957;105:657-64
118 Frist WH, Baldwin JC, Starnes VA, et al. A reconsideration of cerebral perfusion in aortic arch replacement. Ann Thorac Surg 1986;42:273-81
119 Bachet J, Guilmet D, Goudot B, et al. Cold cerebroplegia. A new technique of cerebral protection during operations on the transverse aortic arch. J Thorac Cardiovasc Surg 1991;102:85-93; discussion 93-4
120 Kazui T, Inoue N, Yamada O, et al. Selective cerebral perfusion during operation for aneurysms of the aortic arch: a reassessment. Ann Thorac Surg 1992;53:109-14
121 Okita Y, Minatoya K, Tagusari O, et al. Prospective comparative study of brain protection in total aortic arch replacement: deep hypothermic circulatory arrest with retrograde cerebral perfusion or selective antegrade cerebral perfusion. Ann Thorac Surg 2001;72:72-9
122 Tanoue Y, Tominaga R, Ochiai Y, et al. Comparative study of retrograde and selective cerebral perfusion with transcranial Doppler. Ann Thorac Surg 1999;67:672-5

Although many experimental animal and patient cohort studies have been performed with SACP, only three prospective randomized controlled trials have compared SACP with RCP. Okita and associates [114] studied a total of 60 patients (30 with SACP and 30 with RCP) and found a decreased rate of total neurologic deficit in the SACP group (33% *vs*. 13%, P<0.05) but found no difference between groups in rates of death, stroke, or neurocognitive deficit. In an earlier report, Tanoue and colleagues[122] used transcranial Doppler ultrasonography to verify cerebral blood flow in 32 patients (15 with RCP and 17 with SACP). This study found improved cerebral blood flow in the SACP group. Only 3 patients in the RCP group showed evidence of reversal of cerebral blood. This low incidence of identification of flow reversal can be attributed to the technique of RCP used in the study: the superior vena cava pressure was only 15 to 25 mmHg. In addition, the cerebral perfusion time was 71 minutes in the SACP group, but only 38 minutes in the RCP group (P=0.0047). No differences in clinical outcomes were noted. Recent studies with SACP have reported excellent clinical outcomes, but variations in technique make it difficult to determine if SACP alone was responsible. The limitations, in common with most of such clinical studies, included differences in cannulation, delivery of perfusate (unilateral *vs*. bilateral), amount of perfusate and temperature of perfusate.

6.5 Neuromonitoring and Avoidance of Stroke

Neurologic complications following aortic surgery impose a negative impact and burden on patients' quality of life. Several mechanisms are implicated, including cerebral embolism, cerebral hypo-perfusion and inflammatory reactions. All of these mechanisms cause an imbalance between oxygen delivery and oxygen consumption in the brain. Neuromonitoring during aortic surgery may help to prevent injurious events or even detect them in a stage early enough to employ strategies to minimize secondary cerebral damage.

While there are many modalities that can be used to demonstrate specific or regional brain oxygen deprivation during aortic surgery, all of these modalities have limitations.

Near infrared spectroscopy (NIRS) can be used to measure the cerebral tissue oxygen saturation of the bifrontal cortical regions.

This method is non-invasive and works by emission of near infrared light and measurement of the absorption characteristics of oxy- and deoxyhemoglobin.

Furthermore, transcranial Doppler (TCD) presents a non-invasive technique to monitor not only cerebral blood flow velocity, but also to detect cerebral emboli.

Finally, epi-aortic echocardiography is an important tool to help avoid or minimise cerebral injury during cardiac and aortic surgery. Even though this technique does not monitor the brain directly, it can be considered as a neuromonitoring technique in the broader sense.

Furthermore, the best manoeuvre to avoid stroke during complex aortic surgery is not only related to the sophisticated modality for neuromonitoring but also to the manoeuvres that are employed when a regional drop in oxygen is detected. This includes checking the patient's head position to ensure that it is not rotated, increasing the $PaCO_2$ to above 40 mmHg, increasing the mean arterial pressure to above 60 mmHg, increasing the pump flow to 2.5 $L/m^2/min$, raising the haematocrit above 20%, lowering the central venous pressure below 10 mmHg, increasing the inspiratory oxygen concentration, and deepening anaesthesia[123]. In addition to this, scrupulous avoidance of manipulation of the diseased arch and cerebral vessels except during HCA is absolutely mandatory, as is careful, repeated aspiration of the

123 Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. Anesth Analg 2007;104:51-8

cerebral vessels after circulatory arrest and before institution of antegrade flow[96,124].

124 Hagl C, Ergin MA, Galla JD, et al. Neurologic outcome after ascending aorta-aortic arch operations: effect of brain protection technique in high-risk patients. J Thorac Cardiovasc Surg 2001;121:1107-21

CHAPTER SEVEN

7. THE ROLE OF SURGERY IN THORACIC AORTIC ANEURYSM

7.1 When Is Surgery Indicated?

Once a thoracic aneurysm is diagnosed, routine, scheduled follow-up is necessary by an aortic specialist. Aneurysm size needs to be followed closely and surgery is warranted if there is rapid growth over a short period of time or if a critical size is reached. Follow-up typically includes CT scans or MRI's every 6-12 months. The ascending aorta grows at a rate of 0.10 cm per year and the descending aorta at a rate of 0.20 cm per year. Should an aneurysm increase in size by 0.4cm in any one year then surgery should be performed6.

Decisions regarding surgery can be made if the risk of death, dissection or rupture is known for any particular aneurysm size. This risk can then be compared to the risk of surgery. The mortality for aortic arch surgery increases to 5-8% and the mortality for descending thoracic aneurysm surgery is 5.5%. Below is listed the yearly risk of complications based on aortic aneurysm size (Table 7.1)

Given these statistics it is recommended that asymptomatic ascending aortic aneurysms be resected at a size of 5.0-5.5 cm. If severe aortic insufficiency is present in the setting of a bicuspid valve, the ascending aorta should be resected when it is 4.5 cm in diameter. Descending thoracic and aortic arch aneurysms typically are resected when they exceed 6.0 cm in diameter.

A patient with Marfan syndrome typically warrants earlier intervention. Symptomatic aneurysms should be resected regardless of size6.

7.2 Operative Techniques

To allow an understanding of the extent of resection and reconstruction, we have defined the following terms:

1) Hemiarch Surgery

Hemiarch surgery or proximal arch surgery is performed as either a "simple" hemiarch or a "deep" hemiarch. In simple hemiarch surgery, under deep hypothermic circulatory arrest, the arch is resected in a line from the origin of the brachiocephalic artery to the apex of the underside of the arch opposite the left subclavian artery. In deep hemiarch surgery, the entire anterior and posterior wall of the arch is removed leaving an effective Carrel patch of arch vessels connected via a "bridge" of aorta to the descending thoracic aorta. In this study, these two groups have been amalgamated as historical records do not make this distinction. Simple open distal anastomosis under deep hypothermic circulatory arrest has been excluded. Patients undergoing simple open distal anastomosis for acute Type A repair (137 additional cases during this period) have been excluded.

2) Total Arch Surgery

We have defined total arch surgery as that occurring under deep hypothermic circulatory arrest and involving resection of the arch such that at least one of the great vessels requires reimplantation. Arch vessels were anastomosed either separately or as a Carrel patch. This simple definition was chosen to avoid subclassification of the myriad of permutations of aortic arch surgery. A number of patients who underwent total aortic arch replacement also underwent placement of

a conventional elephant trunk using an 8 cm graft in preparation for possible second stage procedures. In addition, in the latter half of the series, a number of patients underwent placement of a "frozen elephant trunk" using either an EVITA Open Plus Hybrid Stent Graft (Jotec, GmbH, Hechingen, Germany) or a Thoraflex device (Vascutek Terumo Thoraflex Hybrid Stent Graft; Vascutek, Renfrewshire, UK). These devices were only deployed in aneurysms in which there was no chronic dissection or evidence of connective tissue disorder. In addition, they were only deployed in patients who had proximal descending thoracic aneurysms with suitable distal landing zones. Our operative techniques have evolved through the study period as technology and experience have shaped our approach. Below is a general approach to our operations.

It is relevant to say that between 1999 and 2007, operations were performed by all surgeons within the center, but principal activity was by a single subspecialized surgeon (Mr Abbas Rashid). After 2007, this same principal surgeon and 4 others subspecialized in aortic surgery (D.H., M.F., M.K., and A.O.) performed the operations.

3) Conventional Elephant Trunk

A conventional elephant trunk is defined as placement of a redundant extension of the arch graft into the descending thoracic aorta for use in subsequent second stage procedures. This may be placed proximal or distal to the left subclavian artery. Typically, these are no longer than 8cm in length.

4) Prophylactic Elephant Trunks

These are elephant trunks placed at the time of Stage I or Stage II but with no indication for an immediate subsequent stage.

5) Frozen Elephant Trunk

Frozen elephant trunks are hybrid stent grafts which is this series were entirely Jotec E-Vita prostheses. They allow for endovascular stenting of distal arch/proximal descending thoracic aneurysms, with open deployment at the time of surgery on the aortic arch. The attached surgical graft allows for concurrent reconstruction of the aortic arch.

6) Reverse Elephant Trunk

Reverse elephant trunks are invaginated, redundant, surgical graft tissue placed at the time of construction of the proximal anastomosis at the level of the left subclavian artery during surgery on the descending thoracic aorta. This aide reconstruction of the arch during second stage operations through a median sternotomy. These are typically short and 3cm in length and may also be "prophylactic".

7.3 Mortality Following Surgery

Operative mortality has drastically improved over the last century when thoracic aortic aneurysm repair was not survivable. Significant advances have been seen in Mortality following thoracic aortic aneurysm repair is dependent on many variables, the main ones being; extent and size of aneurysm, patient co-morbidities present, operation underdone on an elective or emergent basis, and recent evidence from the US showing better outcomes in centers who undergo higher volume of cases.

The current 2010 guidelines for thoracic aortic disease describe death following composite valve graft as unusual and the risk is between 1 and 5%6. This risk is however center dependent.

Many centers have reported learning curves in all aspects of thoracic aortic surgery which improvements over time in terms of mortality, which adds to the argument that volume is an important factor in operative mortality[125].

In 2007, Kalkat et al from Birmingham, UK, interrogated the UK heart valve registry which contained data on 1962 patients undergoing first time composite valve graft replacement and report a 30-day mortality as 10.7%[126]. These results include patients operated on an emergency basis as with those with genetic conditions, which may explain the reported higher incidence of mortality compared to that of the 2010 guidelines.

In consideration of patients with genetic conditions, Karck et al from Germany, describe postoperative mortality in Marfan patients as high as 6.8% in those undergoing composite valve grafts in a retrospective group of 119 patients (Figure 7.3a)[127]. A further paper in 2010 by Bernhradt et al describes a 30 day mortality in Marfans patients undergoing composite graft replacement as 0%, however this rose to 10% at follow up. Patel et al also describe a 10% mortality following Bentall procedure in Marfan patients at 8 year follow up[128]. Other papers describing other genetic syndromes, such as Loeys-Dietz, and composite graft replacement report series too small to draw any relevant conclusions[129]. BAV and ascending aorta repair is now a commonly recognized procedure. El Khoury et al report no hospital mortality following repair of a regurgitant bicuspid aortic valve with aortic root

125 Gazoni LM, Speir AM, Kron IL, Fonner E, Crosby IK. Elective thoracic aortic aneurysm surgery: better outcomes from high-volume centers. J Am Coll Surg. 2010;210:855-9
126 Kalkat MS, Edwards MB, Taylor KM, Bonser RS. Composite aortic valve graft replacement: mortality outcomes in a national registry. Circulation. 2007. 11;116:I301-6
127 Karck M, Kallenbach K, Hagl C, Rhein C, Leyh R, Haverich A. Aortic root surgery in Marfan syndrome: Comparison of aortic valve-sparing reimplantation versus composite grafting. J Thorac Cardiovasc Surg. 2004;127:391-8
128 Patel ND, Weiss ES, Alejo DE, Nwakanma LU, Williams JA, Dietz HC, Spevak PJ, Gott VL, Vricella LA, Cameron DE. Aortic root operations for Marfan syndrome: a comparison of the Bentall and valve-sparing procedures. Ann Thorac Surg. 2008;85:2003-10
129 Williams JA, Loeys BL, Nwakanma LU, Dietz HC, Spevak PJ, Patel ND, François K, DeBacker J, Gott VL, Vricella LA, Cameron DE. Early surgical experience with Loeys-Dietz: a new syndrome of aggressive thoracic aortic aneurysm disease. Ann Thorac Surg. 2007;83:S757-63

replacement[130]. A BAV does not significantly increase the risk of mortality following operation compared to those with a tricuspid valve.

Aortic arch operations carry a pre-requisite of cerebral protection due to the nature of the procedure. This opens patients to higher risk of mortality, relating to reduced cerebral perfusion, time of operation, cardiopulmonary bypass time, aortic cross clamp times and periods of deep hypothermic circulatory arrest.

The 2010 thoracic aortic guidelines quote a 2 to 6% risk of death in patients undergoing these types of operations. Leshnower et al report their center experience between 2004 and 2009 encompassing 412 patients and report and operative mortality of 7.0%, this included patients undergoing emergency operations[131].

The Mayo clinic reports 9 years of results from 2001 to 2010 of 209 patients and report a procedure specific mortality of 5.5% and 1.0% in total arch and hemiarch procedures respectively**256**. Furthermore, the same paper describes how even over 9 years they have seen decreases in rates of mortality from the first half of their study period compared to their second half (7.9% vs 4.5% respectively). Other centers have reported similar decreases in mortality over short spans of time including Mount Sinai[132,133].

130 El Khoury G, Vanoverschelde JL, Glineur D, Pierard F, Verhelst RR, Rubay J, Funken JC, Watremez C, Astarci P, Lacroix V, Poncelet A, Noirhomme P. Repair of bicuspid aortic valves in patients with aortic regurgitation. Circulation. 2006.4;114:I610-6

131 Leshnower BG, Myung RJ, Kilgo PD, Vassiliades TA, Vega JD, Thourani VH, Puskas JD, Guyton RA, Chen EP. Moderate hypothermia and unilateral selective antegrade cerebral perfusion: a contemporary cerebral protection strategy for aortic arch surgery. Ann Thorac Surg. 2010;90:547-54

132 K. Minatoya, H. Ogino, H. Matsuda, H. Sasaki, H. Tanaka, J. Kobayashi et al. Is conventional aortic arch surgery justifiable in octogenarians? J Thorac Cardiovasc Surg, 2010;139:641–645

133 Strauch JT, Spielvogel D, Lauten A, Galla JD, Lansman SL, McMurtry K, et al. Technical advances in total aortic arch replacement. Ann Thorac Surg. 2004;77:581-89

Gega et al from Yale published results in 2007 using deep hypothermic circulatory arrest as the sole means of cerebral protection[134]. In their study of 394 patients over 10 years they report a mortality rate of 3.6% in elective cases.

Such rapid advancements in aortic arch surgery have led to different techniques being used by different centers worldwide. This adds a further variable that should be considered when studying mortality rates. Although mortality rates vary worldwide, in general mortality rates reported are in the single digits, particularly so in elective repair and modern day aortic arch surgery is performed with low risk of mortality.

Thoracoabdominal aortic aneurysm surgery represents the most challenging operation that can be undertaken on the aorta. The 2010 guidelines describe an approximate mortality of 10% in patients undergoing type II thoracoabdominal repair, again this is center dependent and furthermore this is recognized in the guidelines. Wong et al, describe 305 patients undergoing TAAA repair of which operative survival following elective repair is 6.2% (Figure 7.3b)[135]. In 2007, Coseli et al report their entire open thoracoabdominal aneurysm repair encompassing a total of 2286 patients and report 30-day survival rate of 95.0% [136]. Coseli et al have also reported their experience of TAAA surgery in patients with Marfans syndrome, which totally 50 patients between 1986 and 1996. 30-day survival in these patients was 96%. Cambria et al from Havard, performed 337 operations on the thoracoabdominal aorta, and reported operative mortality of 8.3% [137]. This mortality rate included patients undergoing operations in a non-elective setting and all types of TAAA repair. Endovascular interventions are becoming ever popular in

134 Gega A, Rizzo JA, Johnson MH, Tranquilli M, Farkas EA, Elefteriades JA. Straight deep hypothermic arrest: experience in 394 patients supports its effectiveness as a sole means of brain preservation. Ann Thorac Surg. 2007;84:759-66

135 Wong DR, Parenti JL, Green SY, Chowdhary V, Liao JM, Zarda S, Huh J, LeMaire SA, Coselli JS. Open repair of thoracoabdominal aortic aneurysm in the modern surgical era: contemporary outcomes in 509 patients. J Am Coll Surg. 2011;212:569-79

136 Coselli JS, Bozinovski J, LeMaire SA. Open surgical repair of 2286 thoracoabdominal aortic aneurysms. Ann Thorac Surg. 2007;83:S862-4

137 Cambria RP, Clouse WD, Davison JK, Dunn PF, Corey M, Dorer D. Thoracoabdominal aneurysm repair: results with 337 operations performed over a 15-year interval. Ann Surg. 2002;236:471-9

TAAA repair, particularly as hybrid techniques are being developed. However, these are still very much in their infancy. Although there are some published literatures on long term data it still represents an area that is currently under close investigation.

Survival rates still rank highly in TAA research, as it should in all diseases as we strive to improve patient care. The majority of survival rates in TAA are subdivided according to; TAA size or growth, type of aneurysm, location of aneurysm, and ASI[138].

A paper published by Clouse et al statistically showed that over the past 15 years (from 1998) the prognosis of patients diagnosed with TAA has improved[139]. This retrospective review used 133 patients who were with a diagnosis of degenerative TAA from 1980 to 1994 were compared against a similar cohort of patients from 1951-1980. Overall 5-year survival improved from 19% to 56% in the two different time points. The median survival time was 6.6 years with the most common cause of death cited as rupture of the thoracic aneurysm accounting for 30%, other causes included cardiac events (25%), pulmonary causes (15%), cancer (10%), stroke (4%), other (16%). This study was performed in 1998 and included a small number of patients over many years. This report is subject to reporting and measurement bias. Trimarchi et al studied 613 patients with type B TAA only revealing an in hospital mortality rate of 6.6% and 23.0% for TAA's or less than 5.5cm and greater than 5.5cms respectively ($p<0.001$).

This study looks only at patients with type B TAA, and is subjected to measurement bias. These figure further enforce the surgical indications of 5.5cm in TAAs.

138 B Patterson, P Holt, C Nienaber - Journal of Vascular …, 2013 - elsevier-usairforce.com Journal of Vascular Surgery, Volume 57, Issue 5, Pages 1449, May 2013, Authors:B. Patterson; P. Holt; C. Nienaber

139 Improved Prognosis of Thoracic Aortic Aneurysms. A Population-Based Study William Darrin Clouse, MD; John W. Hallett, Jr, MD; Hartzell V. Schaff, MD; Michelle M. Gayari, BS; Duane M. Ilstrup, MS; L. Joseph Melton III, MD. JAMA. 1998; 280(22):1926-1929. doi:10.1001/jama.280.22.1926

Zierer et al[140] retrospectively analysed 110 asymptomatic patients who underwent elective TAA repair. Overall survival at 2 and 4 years was 79% and 70% respectively. This study included all types of TAA's and did not differentiate between them. It is worth mentioning that this study is the first of its kind to look at quality of life and functional status following thoracic aneurysm operations. Age and procedure did not significantly impede return to normal function ($p>0.59$ and $p>0.18$ respectively). Older patients (greater than 70 years) had an improved psychological quality of life. Thus the authors concluded that age should not be a determinant factor alone to perform elective TAA surgery.

The Yale TAA database is likely to hold the largest sets of data on these specific subsets of patients2. They analysed 1600 patients, which included a total of 3000 images. They were then able to provide statistical analysis to give calculations of death based entirely on aortic size. The yearly risk for aortic size; 3.5cm – 3.9cm is 5.9%, 4.0 – 5.0cm is 4.6%, 5.0 – 6.0cm 4.8%, and greater than 6cm as 10.8%. This correlates with previous studies mentioned above that mortality increases with increasing aortic aneurysm size. The Yale group used their new stratification system based on aortic size index to further divide patients into groups to relate a mortality risk to. Five-year survival in patients with; the highest ASI was 44.4%, compared to a low ASI was 94.7% ($p<0.0001$). These figures are likely to be skewed as it included patients who underwent operative repair.

Davies et al used the data from 721 to show a 5-year survival for patients with TAA not operated on as 54%2. Furthermore, in this cohort of patients TAA with a size greater than 6cm gave a yearly mortality rate of 11.8%. They found that elective surgery to prevent TAA's reaching the critical 6cm point restored patient survival rate to near normal.

140 Zierer A, Melby SJ, Lubahn JG, Sicard G a, Damiano RJ, Moon MR. Elective surgery for thoracic aortic aneurysms: late functional status and quality of life. Ann Thorac Surg [Internet] 2006 [cited 2013 Mar 12];82(2):573–8

The authors strongly advocate the need for regular monitoring in TAA patients, stress that TAA is a lethal disease and increasing size is strongly related to increased morbidity and mortality.

Although there is a tendency to report mid-term and late out comes amongst the endovascular aortic arch repair; there remain a subtlety in these report on the re-intervention rate. It's the case that endovascular procedures, patients need to be fully informed that they will require a lifetime of careful follow-up and that in those patients who have a life expectancy of more than 5 to 10 years; it is likely they will require multiple repeat procedures. Indeed, in an independent audit of stented patients in France, 45% of patients had an event in the first year, excluding deaths. There is no doubt that future work is needed to identify TEVAR candidates unlikely to benefit from repair.

7.4 Aortic Intervention in the UK

Current intervention on thoracic and thoracoabdominal aneurysms within the UK is not well documented. It is performed by cardiac surgeons, vascular surgeons, interventional radiologists and a few cardiologists and varies by region and local historically based arrangements. There is no single regulatory body and no single registry. Data are stored by the Society for Cardiothoracic Surgery, the Vascular Society and Commercial Companies including the UK Registry for Thoracic Stent Grafts. In addition, some registries are pan-European making it difficult to extract UK-specific data. Although these figures also include intervention on ascending and arch thoracic aortic aneurysms they give an interesting representation of the total activity and distribution of thoracic aortic activity with centres in England (Figure 7.4).

For open surgical approaches, data from St Mary's published in 1995[141] and 1999 [142] have influenced approaches within the UK. Results in this study suggested very poor outcomes from an open approach. However, these data should be judged in their historical context with no or little use of perfusion, cell salvage or clotting products. More contemporary results presented by Thoracic Aortic Aneurysm Service at the Liverpool Aortic Symposium (2011) (www.aorticaneurysm) suggest results comparable with any international institution are achievable within the UK.

In a series of 80 elective open repairs (60% Extent I and II [left subclavian to either visceral vessels or aortic bifurcation]), 30-day mortality was 6.25% and in-hospital mortality was 11.2%, with a permanent paraplegia rate of 2.5%. Interestingly, within Scotland, the National Services Advisory Group nominated the Royal Infirmary of Edinburgh the sole national provider of thoracoabdominal aortic aneurysm intervention in April 2001 (www.nsd.scot.nhs.uk). The group has published outcomes for Type IV (abdominal) and what they describe as supra-coeliac aneurysms, via a totally abdominal approach with a 30-day mortality of 6% (3/53). Their Government Review in 2007 (www.nsd. scot.nhs.uk) does suggest a practice dominated by this group of patients (Extent IV, 60%), with patients undergoing Extent II repairs (left subclavian to aortic bifurcation) only 14%, respectively.

This together with the lack of provision for cardiopulmonary bypass presumably reflects the lack of involvement of cardiac surgical services. Certainly, their outcomes for this particular extent are comparable with any international centre. However, the poor early outcomes from open surgery in the UK undoubtedly have driven attempts at total endovascular solutions and hybrid approaches reflecting some inter- national practices.

141 Gilling-Smith G, Worswick L, Knight P, Wolfe J, Mansfield. Surgical repair of thoracoabdominal aortic aneurysm: 10 years' experience. Br J Surg 1995;82:624 –
142 Bradbury A, Bulstrode N, Gilling-Smith G, Stansby G, Mansfield A, Wolfe J. Repair of ruptured thoracoabdominal aortic aneurysm is worthwhile in selected cases. Eur J Vasc Endovasc Surg 1999;17:160 – 5

Results from the Royal Liverpool University Hospital suggest acceptable early results from Extent II branched stent grafting[143] and other less complex pathologies published from London[144,145]. However, UK Commissioners have increasingly questioned the clinical and cost- effectiveness of endovascular approaches as international studies have shown mixed outcomes from this approach. Certainly, in our Institution, we are required to request funding for endovascular approaches on a case-by-case basis but require no such scrutiny for open surgical intervention. Hybrid approaches with staged extra-anatomical bypass and endovascular stenting have been trialed in an attempt to reduce morbidity, mortality and cost[146,147]. However, results have also been mixed and this approach has not provided the expected solution. The Society of Cardiothoracic Surgeons has published limited data on out- comes from intervention on the descending thoracic aorta and thoracoabdominal aneurysms; however, the data are rudimentary and few conclusions can be drawn. [148]

7.5 Open Aortic Arch Aneurysm Surgery in the UK

Within the United Kingdom thoracic aortic surgery is performed to some degree by all cardiac surgery units and this is principally open intervention. It is difficult to get an accurate picture of the activity, extent of service and outcomes from published

143 Scurr J, McWilliams RG. Aorta and Great Vessels: Fenestrated Aortic Stent Grafts. Semin intervent radiol. 2007;24:211-220
144 Thompson M, Avaz S, Cheshire N, et al. Early results of endovascular treatment of the thoracic aorta using the valiant endograft. Cardiovasc Intervent Radiol 2007;30:1130 – 8
145 Clough R, Mani K, Lyons O, et al. Endovascular treatment of acute aortic syndrome. J Vasc Surg 2011
146 Choong A, Clough R, Bicknell C, et al. Recent advances in thoraco-abdominal aortic aneurysm repair. The Surgeon Royal College of Surgeons Edinburgh and Ireland 2010;8:28 – 38
147 Biasi L, Ali T, Loosemore T, Morgan R, Loftus I, Thompson M. Hybrid repair of complex thoracoabdominal aortic aneurysms using applied endovascular strategies combined with visceral and renal revascularisation. J Thoracic Cardiovasc Surg 2009;138:1331 – 8
148 The Fifth National Adult Cardiac Surgical Database Report 2003. The Society of Cardiothoracic Surgery in Great Britain and Ireland. Dendrite Clinical Systems Ltd

date which in the case of cardiac surgery is the Society for cardiothoracic surgeons' Blue book (www.scts.org).

Very few cardiac centres have high volume activity and outcomes and even fewer have published their results, with the noticeable exceptions of Birmingham and Bristol. Undoubtedly, this has given an impression that open aortic arch surgery is not widely available and comes at high risk of stroke and death.

In order to circumvent this issue and offer treatment options for this group of patients there has been much innovation in endovascular technology principally driven by Vascular Surgery and Interventional Radiology. Within the Northwest the thoracic aortic aneurysm service at the Liverpool Heart and Chest Hospital (LHCH) has increasingly specialized in thoracic and thoracoabdominal intervention. This service has not been formally commissioned but has been supported by the LHCH NHS Trust Board with the appointment of 4 cardiac surgeons with a specialized interest in thoracic aortic surgery.

Bristol published an analysis of their results for ascending/arch surgery in 2004[149]. The objective of the work was to compare outcomes within the unit between a single high volume operator and a group of other more general operators performing aortic surgery on a more ad hoc basis. The study had a high percentage of urgent/emergency cases. Although there was no mortality difference between the two groups there was a significant difference in morbidity. A detailed breakdown of the extent of arch surgery is not available but we know 291 patients underwent surgery on the ascending aorta/aortic arch. Overall mortality was 12.5%; 10.8% in high volume group and 13.9% in low volume group. Only 16.9% of cases by the higher volume surgeon and 5.4% in the lower surgeons group were labelled as involving the aortic arch. Neurological complications were noted in 7.7% and 7.8% in the two groups respectively.

149 Early and midterm outcome of surgery of the ascending aorta/arch: is there a relationship with caseload?. / Narayan, P; Caputo, M; Rogers, CA; Alwair, H; Mahesh, B; Angelini, GD; Bryan, AJ. European Journal of Cardiothoracic Surgery, Vol. 25, 05.2004, p. 676 - 682

A second paper by the Bristol group[150] compared surgery on the ascending aorta +/- arch examining the impact of redo operations. The overall mortality was 13.8% (4/29) versus 12.4% (33/267) for primary operations. Mortality in redo elective surgery was 5.9% versus 25% for emergencies. However, this was a mixed group of patients with only 49% elective and 55% of redo patients requiring circulatory arrest. Only 10% of first time and 14% of repeat procedures were labelled as arch replacements. Neurological complications were seen in 7% of first time procedures and 7% of repeat procedures.

In a third analysis of the Bristol data set[151] this group looked at the influence of coronary artery bypass surgery on surgery of the ascending aorta/arch. Of the 296 patients analysed, addition of CABG to this group changed the mortality from 11% to 21.4%. However, again this is a heterogeneous group with a high proportion of emergencies and only 10.2% involving arch surgery in the "no CABG" group and 11.9% in the "added CABG" group.

Within the context of two randomized controlled trials investigating methods of neuro-protection during deep hypothermic circulatory arrest, the Birmingham group have documented their mortality and morbidity outcomes for open aortic arch surgery. In a study by Harrington et al[152] looking at neuropsychometric outcomes from deep hypothermic circulatory arrest with and without retrograde cerebral protection in patients undergoing hemiarch and total arch replacement there were 2 deaths in 38 (5.25) and one permanent stroke.

150 Ascending aorta or arch surgery: is previous cardiac surgery a risk factor? Narayan, P; Rogers, CA; Caputo, M; Angelini, GD; Bryan, AJ. Asian Cardiovascular and Thoracic Annals, Vol. 14 (1), 02.2006, p. 14 - 19
151 Influence of concomitant coronary artery bypass graft on outcome of surgery of the ascending aorta/arch. Narayan, P., Rogers, C. A., Caputo, M., Angelini, G. & Bryan, A. J. Feb 2007 Heart. 93(2), p. 232 - 237 6 p
152 Selective antgegrade cerebral perfusion attenuates brain metabolic deficit in aortic arch surgery: a prospective randomized trial, Circulation 14/9/2004. Harrington, Deborah | Walker, Anne | Kaukuntla, Hemanth | Bracewell, Robert | Clutton-Brock, Thomas | Faroqui, Muzaffar | Bonser, Robert | Pagano, Domenic

A second study by Harrington et al [153] examined the effect of selective anterograde cerebral perfusion on brain metabolic deficit during deep hypothermic circulatory arrest and aortic arch surgery. 42 patients underwent aortic arch surgery with 3 deaths (7.1%). Two patients experience stroke and 6 had transient neurological deficit. Certainly the publication of detailed open outcomes in the UK has been limited by heterogeneity of datasets and limited by the context of randomized trials.

There is a lack of published data on a large consecutive group of patients, principally undergoing arch surgery, with detailed information on extent of resection, outcomes and survival. The Society for Cardiothoracic Surgeons four yearly publication of outcomes ("Blue book") does not document in sufficient detail outcomes from aortic arch surgery.

7.6 Endovascular Intervention in the UK

Both the St Mary's unit and the St George's unit in London have published outcomes for endovascular intervention on the aortic arch. Holt et al [154] from St George's group, published on outcomes of the endovascular management of aortic arch aneurysm, in particular focusing on the management of the left subclavian artery. The series involved non-fenestrated grafts and extra-anatomic reconstruction. Over an 8-year period, 78 patients were treated. Overall mortality and stroke rate was 14.3% and 14.3% for emergency treatment versus 4% and 2% for elective patients. Three patients (3.85%) sustained paraplegia. Re-intervention was required in 9 of 68 patients (13%) with 1 year of follow-up. Long term survival data and re-intervention rates are missing.

153 Non-neurological morbidity and profound hypothermia in aortic surgery, The Annals of thoracic surgery 1/1/2003. Harrington, Deborah | Rooney, SJ | Lilley, JP | Bonser, Robert

154 Holt PJ, Karthikesalingam A, Patterson BO, Ghatwary T, Hinchliffe RJ, Loftus IM, Thompson MM. Aortic rupture and sac expansion after endovascular repair of abdominal aortic aneurysm. Br J Surg. 2012 Dec;99(12):1657-64

Antoniou et al [155] from Nick Cheshire's group at St Mary's have published a series of 33 patients over 6 years who underwent similar hybrid repair of arch aneurysms with endovascular intervention and extra-anatomic bypass.

Elective 30-day mortality was given as 13% and 35% for elective and urgent/emergency respectively. However, when divided into complete arch repair verses partial arch the 30-day mortality was 44% versus 13% (P<0.046). When this was further subdivided into just elective patients the 30-day mortality was 29% versus 6% (P<0.144). Late endoleak rate was 35%. Stroke rate was 12% and paraplegia rate was 6%. Certainly endovascular intervention on the aortic arch is in its infancy but with acceptable outcomes. Undoubtedly, outcomes will improve further with current innovations in fenestrated and branched stent grafts. However, as with most comparisons of stent versus surgery for thoracic aortic intervention, the patient groups are not comparable and interpretation of superiority is not possible. Certainly in our practice, endovascular intervention on the aortic arch is limited to those too old and frail for surgery and blunt traumatic aortic rupture.

7.7 Open Aortic Arch Surgery Vs Endovascular Repair

To date, there has been no prospective, randomized trial that has compared open aortic arch surgical repair versus endovascular stenting approaches. The current published reports are not without significant limitations due to essentially the ambiguity and lack of consensus of the understanding of the natural history of aortic arch disease. In a recent review by Abraha et al[156] they found no published or unpublished evidence to assess the efficacy of TEVAR over conventional aortic surgical repair. The authors concluded that there is a need to carry out a quality

155 Hybrid Repair of the Aortic Arch in Patients with Extensive Aortic Disease European Journal of Vascular & Endovascular Surgery Volume 40, Issue 6 , Pages 715-721, December 2010

156 Abraha I, Romagnoli C, Montedori A, Cirocchi R. Thoracic stent graft versus surgery for thoracic aneurysm. Cochrane Database Syst Rev. 2013 Sep11;9:CD006796

randomized control trail to assess TEVAR and open repair. The trials should have adequate follow up and be enough to evaluate the durability of endovascular treatment in terms of endoleak rate, re-intervention rate, open-conversion rate, and rupture-free survival. In addition to clinically relevant outcomes including early and late mortality, major complications, and hospital and intensive care unit stay must be considered. Despite the aforementioned, studies by Orandi et al and by Walsh et al suggested that endovascular techniques are considered safer and less invasive with mortality and morbidity that are similar to conventional open aortic surgical repair. Orandi et al[157] found that among a total of 1030 patients who underwent open TAA repair and 267 who underwent TEVAR, there was no significant difference in mortality between open aortic repair and TEVAR. They also added that although open repair patients were more likely to have cardiac, respiratory, and hemorrhagic complications, patients undergoing TEVAR were more likely to be discharged to home and had a decreased length of hospital stay. On the other hand, Walsh et al[158] based their conclusion on series of comparative studies that solely looked at stent grafting to the descending aortic aneurysm without any reference to the ascending and aortic arch aneurysms and the surgical management of this entity.

The Gore TAG trial compared the TAG endograft patients (n=140) with standard open surgical controls (n=94) with enrollment from September of 1999 to May of 2001[159]. At 5 years, aneurysm-related mortality was lower for TAG patients at 2.8% compared with open controls at 11.7% (P=0 .008). No differences in all-cause mortality were noted, with 68% of TAG patients and 67% of open controls surviving to 5 years (P=0.43). Major adverse events at 5 years were significantly reduced in the TAG group; 57.9% vs 78.7% (P=0.001). Endoleaks in the TAG group decreased from 8.1% at 1 month to 4.3% at 5 years. Five TAG patients have undergone major

157 Orandi BJ, Dimick JB, Deeb GM, Patel HJ, Upchurch GR Jr. A population-based analysis ofendovascular versus open thoracic aortic aneurysm repair. J Vasc Surg. 2009 May;49(5):1112-6
158 Walsh SR, Tang TY, Sadat U, Naik J, Gaunt ME, Boyle JR, Hayes PD, Varty K.Endovascular stenting versus open surgery for thoracic aortic disease: systematic review and meta-analysis of perioperative results. J Vasc Surg. 2008.May;47(5):1094-1098
159 Makaroun MS, Dillavou ED, Kee ST, Sicard G, Chaikof E, Bavaria J, Williams D,Cambria RP, Mitchell RS. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. J Vasc Surg. 2005 Jan;41(1):1-9

aneurysm-related re-interventions at 5 years (3.6%), including one arch aneurysm repair for type1 endoleak and migration, one open conversion and five endovascular procedures for endoleaks in three patients. At 5 years, there have been no ruptures, one migration, no collapse, and 20 instances of fracture in 19 patients, all before the revision of the TAG graft. A study by Goodney et al looked at survival among the open aortic arch repair and endovascular groups[160]. Their conclusion was that although perioperative mortality is lower with TEVAR, Medicare patients selected for TEVAR have worse long-term survival than patients selected for open repair. The results of this observational study suggest that higher-risk patients are being offered TEVAR and that some do not benefit on the basis of long-term survival. Evolution of surgical techniques and perioperative care has significantly improved morbidity and mortality rates for patients undergoing aortic arch surgery and acute aortic dissections cohort[161]. Whereas early surgical series reported mortality rates that would be prohibitive today, recent studies have published rates largely in single figures [1,2,3,4]. A number of studies have also published rudimentary survival data demonstrating a beneficial effect of surgery compared to estimated natural history of patients with aortic arch aneurysms [8,9,13].

The objectives of this study were to:

1) Report, compare, and analyse our morbidity and mortality outcomes for hemiarch and total aortic arch surgery;

2) Examine the survival benefit of hemiarch and total aortic arch surgery compared to age- and sex-matched controls;

3) Define factors which influence survival in these two groups and, in particular, identify those that are modifiable and potentially actionable and

160 Goodney PP, Travis L, Lucas FL, Fillinger MF, Goodman DC, Cronenwett JL, Stone DH. Survival after open versus endovascular thoracic aortic aneurysm repair in an observational study of the Medicare population. Circulation. 2011 Dec 13;124(24):2661-9

161 BioMed Research International Volume 2014 (2014), Article ID 736298, 10 pages

4) Compare outcomes within the unit between high volume operators and a group of other more general operators performing aortic surgery on a more ad hoc basis.

This is clearly reflected under the general term of subspecialisation in aortic surgery.

7.8 Long Term

The rapid and evolving nature of thoracic aortic surgery means long term survival is hard to assess. Many centres have reported "learning curves" that show even over a ten-year period their mortality rates can be reduced by half. Such advancements are not limited to the surgery itself but also to anaesthetic, pre and post-operative management of these patients.

Higgins et al analysed a database containing data on all adult patients who had undergone thoracic aortic aneurysm repair in British Columbia which totalled 1960 patients (Figure 7.8a) [162]. Long-term survival was 77.7%, 59.6%, and 44.7% at 5, 10, and 15 years, respectively. Survival in the first half of the study was significantly less compared to the second half of the study 74.3% (95% CI, 70.6-77.7) versus 60.4% (95% CI, 56.6-63.9) respectively. Crawford et al report a similar experience of 605 patients in 1986 and report a 5-year survival of 60% [163].

Mount Sinai published long term data in 2010 after aortic arch replacement in 206 patients between 1999 and 2009 (Figure 7.8b)[164]. Bischoff et al describe at 6 years, 75% of patients were still alive, compared with 92% in a matched New York State

162 Higgins J, Lee MK, Co C, Janusz MT. Long-term outcomes after thoracic aortic surgery: A population-based study. J Thorac Cardiovasc Surg. 2013. pii: S0022-5223(13)00805-2
163 Crawford ES, Crawford JL, Safi HJ, Coselli JS, Hess KR, Brooks B, et al. Thoracoabdominal aortic aneurysms: preoperative and intraoperative factors determining immediate and long-term results of operations in 605 patients. J Vasc Surg. 1986;3:389-40
164 Bischoff M, Brenner R, Scheumann J, Bodian CA, Griepp R, Lansman S, et al. Long-term outcome after aortic arch replacement with a trifurcated graft. J Thorac Cardiovasc Surg. 2010;140;s86-91

control population (P < .001). In Japan, Minakawa et al analyzed data from 122 patients who underwent total aortic arch replacement.

Overall long-term survival was 80.4% at 5 years and 58.9% at 10 years. Estrera et al have published results in 2002 relating to long term survival in aortic arch patients[165], with long term survival rates 72% at 5 years and 71% at 10 years after surgery.

Cambria et al from Havard Medical School reported their 15-year experience of 337 TAAA repairs survival rates at 2 and 5 years were 81.2 +/- 3% and 67.2 +/- 5%, which in their study is comparable to routine aortic abdominal repair. Fehrenbacher et al reviewed 343 patients in their center undergoing TAAA repair or descending aortic aneurysm repair and report The 1, 5, and 10-year survival rates were 90%, 69%, and 54%, respectively. Kouchokos et al looked at survival following TAAA using hypothermic circulatory arrest in 243 patients between 1986 and 2012[166]. They reported a 5-year survival rate of 55%.

Long term survival is hard to assess particularly considering many centers report significant reductions in mortality in as short a time as ten years. This can be attributed to major advances made in this subspecialty, as well as improved anaesthetic, pre and post-operative management.

The wealth of techniques and devices available for use also add to variables that can potentially affect long term survival. However, the amount of data available to assess best practice is still in its infancy. It is because of this; thoracic aortic surgery is a rapidly advancing subspecialty which is exciting to see what developments are made in the near future.

165 Estrera AL, Miller CC 3rd, Huynh TT, Porat EE, Safi HJ. Replacement of the ascending and transverse aortic arch: determinants of long-term survival. Ann Thorac Surg. 2002;74:1058-64
166 Kouchoukos NT, Kulik A, Castner CF. Outcomes after thoracoabdominal aortic aneurysm repair using hypothermic circulatory arrest. J Thorac Cardiovasc Surg. 2013;145:S139-41

7.9 Reoperation

All operations carried out on the thoracic aorta carry a risk of reoperation. It is thought that this risk is reduced with the use of beta blockers. Theoretically, with reduction of the heart rate the blood pressure is subsequently reduced and in turn relieves the pressure that the repair is subjected to from the heart. Beta blockers are also thought to reduce the expansion rate of thoracic aortic aneurysms before operation; however, the use of beta blockers before and after operation is highly debated. To date though, the 2010 guidelines still recommend the use of beta blockers lifelong following diagnosis of aneurysm[6].

It is well described that reoperation is significantly increased in patients with Marfan syndrome. Geisbuesch et al describe that almost half of the Marfan's patients who undergo surgical repair will require reoperation[167]. This is well described in centers that deal with high volumes of patients and come across a higher number of Marfan patients[168]. In comparison, Osslen et al report analysis of the Swedish national healthcare register of patients with thoracic aortic disease, incorporating over 14000 patients[169]. In this paper, Osslen describes a reoperation rate of 7.8%.

However, survival following reoperation in all aetiologies can be described as low. The 2010 guidelines describe the risk of death following reoperation as between 2 and 6%. This is also described in a similar report on Marfan patients by Geisbuesch who describe reoperative hospital mortality between 0 to 1.6%[167].

Although more common in Marfan patients' reoperation is considered a procedure that when undertaken electively can be done with a low mortality rate.

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167 Geisbuesch S, Schray D, Bischoff MS, Lin HM, Di Luozzo G, Griepp RB. Frequency of reoperations in patients with Marfan syndrome. Ann Thorac Surg. 2012;93:1496-501

168 Lombardi JV, Carpenter JP, Pochettino A, Sonnad SS, Bavaria JE. Thoracoabdominal aortic aneurysm repair after prior aortic surgery. J Vasc Surg. 2003;38:1185-90

169 Olsson C, Thelin S, Ståhle E, Ekbom A, Granath F. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation. 2006. 12;114:2611-8

Modern day thoracic aortic aneurysm surgery is a relatively new specialty, but has roots deeply embedded in history. Mortality rates have remained high until the advent of specialty has progressed at a rapid rate. In general, mortality is higher in patients with a larger extent of aneurysm and those associated with a genetic syndrome. However, TAA surgery can be carried out on an elective basis with excellent results, in terms of post-operative mortality and reoperation. It is of vital importance to understand how operation affects TAAs so we can confer this knowledge to the patient and to be able to improve on our current results. Genetic syndromes represent a rare subset of patients who suffer from aortic aneurysms and they represent an area of medicine for which there remains many unanswered questions. Undoubtedly, considering the pace of discoveries and developments within this specialty in such a short amount of time, we will see research become more focused towards a personalized approach.

CHAPTER EIGHT

8. THE COMPARATOR: WHAT WOULD HAPPEN TO PATIENTS IN THE ABSENCE OF SURGERY?

8.1 A Perspective on the Natural History and Survival in Non-Operated Thoracic Aortic Patients

8.1.1 Introduction

Thoracic aortic aneurysm (TAA) represents an important component of vascular disease due to the particularly lethal nature of this disease[138]. It is widely accepted that without intervention, medical or surgical, TAA carries a poor prognosis. The bleak long-term prognosis of TAA underpins the critical importance of understanding precisely the natural history of the disease. Such understanding is crucial to making precise diagnostic, management, and prevention plans. Furthermore, such understanding is imperative, as it needs to be imparted on patients, allowing them to make a well-informed decision and provide consent regarding their management plan. Knowledge of the natural history is critical when planning elective surgery in order to weigh the significant risk of major surgery against the risk of aneurysm progression. This is particularly pertinent considering that, after surgical aneurysm repair, survival rates comparable to that of a matched general population can be achieved[50].

8.1.2 Methods

8.1.2.1 Literature Search Strategy

Electronic searches were performed on PubMed and Cochrane databases with no limits placed on dates. Search terms included natural history, thoracic aortic aneurysms, aneurysm size, risk factors, survival rates, medical therapy, aneurysm growth, dissection, rupture, and mortality. Search terms were charted to MeSH terms and combined using Boolean operations, and also used as key words.

Papers were selected on the basis of title and abstract. The reference lists of selected papers were reviewed to identify any relevant papers that might be suitable for inclusion in the study.

8.1.2.2 Selection Criteria

Research papers were not excluded based on study design except for case reports. Comments, opinions, or editorials were not included in our selection, so as to provide an unbiased view. Papers were selected based on providing primary end points of death, rupture, or dissection and/or information regarding aortic aneurysm growth. Papers were not excluded based on patient population age.

8.1.3 Survival

There is unarguable evidence that a diagnosis of TAA carries with it a dismal prognosis. This is well described by Crawford [170]in an observational study of

170 Crawford S, Denatale R. Thoracoabdominal aortic aneurysm: observations regarding the natural course of the disease. Journal of vascular surgery1. 1986;3:578–82.

unoperated thoraco-abdominal aneurysm patients published in 1986. This observation has since been repeated in much larger cohorts that also include TAAs of the ascending and descending portions of the aorta. This is visibly demonstrated in Figure 8.1.3, a Kaplan-Meier plot displaying the starkly poor 10-year survival in a group of 170 patients from 1984 to 1993 [144], which compares TAAs, thoraco-abdominal aneurysms, and abdominal aortic aneurysms. A report of 107 patients with TAAs attending the Mayo Clinic between 1945 and 1955 describes 1- and 5-year survival rates of 87% and 50%, respectively[145]. It is pertinent to consider that these observations were reported more than 5 decades ago, and advances in conservative management may have improved prognosis, although even this is currently debated. The advent of large databases, specifically designed for thoracic aortic aneurysms, has allowed for more recent estimates of survival.

Coady et al [78] report overall survival in 230 patients at 1 and 5 years from diagnosis to be 85% and 64% respectively, during the period 1985 to 1996. To date, this database has now recruited 721 patients and reports that 5-year survival in medically treated patients is approximately 66%.

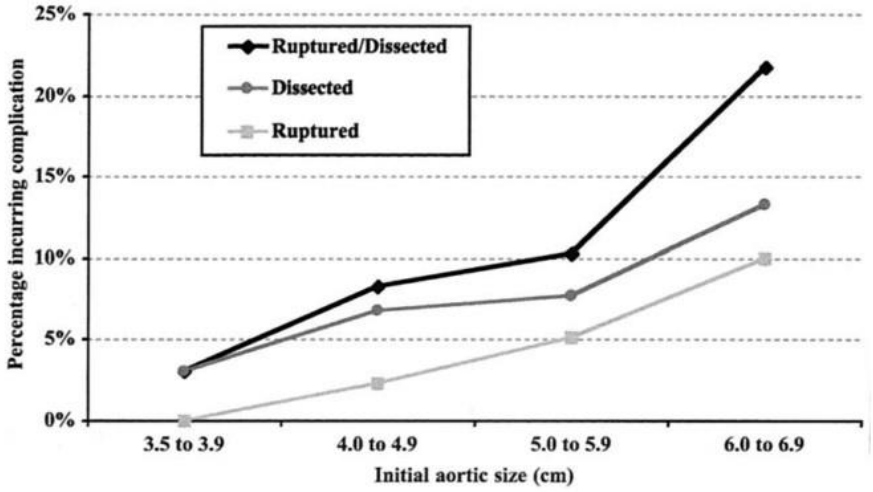
8.1.4 Size of Aneurysm

TAA size is currently utilized as the primary marker for surgical indication in asymptomatic patients. The Yale group was amongst the first to provide evidence-based data supporting aortic size as a predictor of rupture and mortality[171]. Their initial work encompassed clinical and radiological data of 370 patients with TAAs from 1985 to 1997.

171 Coady MA, Rizzo JA, Hammond GL, Mandapati D, Darr U, Kopf GS, et al. What is the appropriate size criterion for resection of thoracic aortic aneurysms? J Thorac Cardiovasc Surg. 1997;113:476–91

This produced a striking graph depicting how survival significantly decreases over time with increasing aortic aneurysm diameter (Figure 8.1.4a.) please note that small aneurysms take years to produce mortality: this is a virulent but indolent disease. Furthermore, the incidence of rupture and dissection as a function of initial aneurysm size increases with greater aneurysm diameter (Figure 8.1.4b.).

Figure 8.1.4b. Cumulative Incidence of Rupture and/or Dissection displayed as a function of initial aortic size.



From Davies et al.

Statistical analysis reveals odds of rupture or dissection to be 8.84 times greater for an aneurysm of 6-6.9 than that of an aneurysm of 4.0-4.9 cm. This paper demonstrates how aneurysm size significantly relates to probability of rupture, dissection, and death. These data have since been the foundation of current recommended guidelines for surgical intervention based on size, and these evidence-based paradigms are used internationally6 Other groups as well have published results pertaining to aneurysm size, morbidity, and mortality which show similar results, strengthening the evidence in favour of using size as a predictor of

rupture or dissection[172,173] . Perko et al.[173] report a 5-fold increase in cumulative hazard of rupture in aneurysms greater than 6 cm compared to those below this threshold, and a 66% probability of rupture.

Further analysis of size, from the Yale group, reveals a statistically significant increase in the incidence of rupture, mortality, and dissection with increasing size.2

Certainly, there is powerful evidence that initial measured aortic size accurately predicts prognosis with regard to mortality, rupture, and dissection. Furthermore, documented analysis shows these risks increase with increasing aortic size, and maximal risk is realized in aneurysms > 6 cm. Analysis from the Yale database in 2002, that includes data prospectively collected from 1600 patients, demonstrates that even in aneurysms categorized to the smallest diameter (3.5 cm-3.9 cm) have a yearly risk of rupture, dissection, or death of 7.2% (Figure 8.1.4c.)[174] the majority representing dissection rather than rupture. Rupture is reported at a 0% rate in aortic sizes of 3.5-4.0 cm.

However, size as a model of prediction of the natural history is not perfect. It could be argued that information derived from large groups and data sets do not accurately predict the behaviour of the individual patients. The ideal would be a move toward a personalized medical model, however to achieve this, the complete understanding of the natural history of the disease is a necessity.

172 Joyce JW, Fairbairn JF, Kincaid OW, Juergens JL. Aneurysms of the Thoracic Aorta: A Clinical Study with Special Reference to Prognosis. Circulation. 1964;29: 176–81.
173 Perko MJ, Nørgaard M, Herzog TM, Olsen PS, Schroeder TV, Pettersson G. Unoperated aortic aneurysm: A survey of 170 patients. Ann Thorac Surg. 1995;59:1204–9
174 Elefteriades JA. Natural History of Thoracic Aortic Aneurysms : Indications for Surgery, and Surgical Versus Nonsurgical Risks. Ann Thorac Surg. 2002;74:S1877–80

8.1.5 Location

The thoracic aorta is a complicated structure that has been shown in mechanical ex vivo modelling to display different characteristics on both a macro- and microscopic level in different anatomical locations along the aorta [175,176].

Clinically, aneurysms located in the ascending, descending and thoraco-abdominal aorta vary in terms of prevalence, management, and prognosis. Elfeteriades differentiates two different diseases, separated at the ligamentum arteriosum[33].

Ascending aortic aneurysms are rarely calcified, almost never contain thrombus, and are not as strongly correlated with traditional arteriosclerotic risk factors. On the other hand, descending and thoracoabdominal aneurysms are almost invariably calcified, contain generous thrombus, and correlate well with traditional arteriosclerotic risk factors.

It is recognized that descending aneurysms are less prevalent than ascending aneurysms, but are associated with a poorer prognosis, starkly demonstrated in Figure 8.1.5a. [171]. The Yale group report 5-year survival in ascending and descending aneurysms as 77% and 39% respectively, in a cohort of 153 patients. In this study the prevalence of ascending and descending aortic aneurysms were 64% and 24% respectively. Other groups report similar figures and a similar difference in survival amongst ascending and descending aortic aneurysms [177]. The postulated reasons why descending aneurysms are more deadly than ascending aneurysms are speculative and not conclusively proven.

175 Haskett D, Johnson G, Zhou A, Utzinger U, Vande Geest J. Microstructural and biomechanical alterations of the human aorta as a function of age and location. Biomech Model Mechanobiol. 2010;9(6):725–36.
176 Koullias G, Modak R, Tranquilli M, Korkolis DP, Barash P, Elefteriades JA. Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta. J Thorac Cardiovasc Surg. 2005;130:677–83.
177 Clouse WD, Hallett JW, Schaff H V, Gayari MM, Ilstrup DM, Melton LJ 3rd. Improved Prognosis of Thoracic Aortic Aneurysms. JAMA. 1998;280:1926–9.

A further critical observation of aneurysm location regards the mean aortic diameter for rupture. Coady et al report significantly different probabilities in the complications from aneurysms with similar aortic sizes, in the ascending and descending aorta[171] . They describe these sizes where the risk dramatically increases as “hinge points”, which are 6 cm and 7 cm in the ascending and descending aorta respectively (Figures 8.1.5b and 8.1.5c). This observation has influenced recent aortic aneurysm surgical guidelines in so far that it is recommended to operate on ascending and descending aneurysms at different sizes6.

Thus, location of an aortic aneurysm plays a decisive role in the natural history of the disease. There is a significant difference in the prognosis of ascending and descending aortic aneurysms. Furthermore, the ascending aorta has a susceptibility to rupture at smaller diameters in comparison to the descending aorta. However, it is pertinent to consider aortic arch involvement, which has not yet been discussed.

Involvement of the arch is not uncommon in TAA disease, and considering its added complexity, it is natural to question whether aortic arch involvement can influence the natural history of the disease. This is a question that has not been thoroughly investigated, and our future research will address this.

8.1.6 Growth Rate

TAAs growth rate is an important factor to consider in the natural history of the disease. Graph 3 demonstrates that with increasing aortic size, the risk of rupture, dissection or death is increased. Accurate predictions of aneurysm growth would significantly add to the surgeon's armamentarium to predict the opportune time for surgical intervention. Such ability would enhance decision making, which is currently based on current indications of aneurysm size6.

Calculation of growth rate exhibits controversy in the aortic world[178]. In particular, many studies ignore the fact that measurements vary about a mean, and that specific aortic measurements may be *lower* than a prior measurement in the same patient. To discard such measurements leads to an erroneously high calculated rate of growth. Accordingly, some experts argue that such measurements not be discarded. Such issues contribute to much varied reported aneurysm growth rates in different centre,[238].

Bonser et al described a mean aneurysm expansion rate of 1.43 mm/year[31]. This expansion rate was significantly different by anatomical location of the aneurysm and aneurysm size. The ascending aorta experienced the lowest expansion rate, with the highest rate of expansion observed in the mid-portion of the descending. In all segments, increasing aortic size was associated with increasing rate of aneurysm expansion. Aneurysm growth was not affected by presence of a dissection in this study.

178 Rizzo JA, Coady MA, Elefteriades JA. Procedures for estimating growth rates in thoracic aortic aneurysms. Journal of clinical epidemiology. 1998;51:747–54.

Nishimura et al in Japan, observed in a case series of 82 TAAs, aneurysms of the arch grew at the faster rate than any other location (0.56cm/year, n = 34)[179]. Other quoted rates of aneurysm growth vary between 0.07 to 2.0cm per year, but on average are about 1mm per year.[178]

TAA growth rate is often described as indolent, and thus it is recommended that asymptomatic TAA that have yet to reach the appropriate size for intervention be imaged yearly (or even less frequently). However, it is generally accepted that rapid expansion of TAAs is a criterion for surgical intervention. Clinical practice tells us that these patients are likely to suffer an acute aortic dissection or rupture, although documented evidence behind this is limited though[180].

179 Hirose Y, Hamada S, Takamiya M, Imakita S, Naito H, Nishimura T. Aortic aneurysms: growth rates measured with CT. Radiology. 1992;185:249–52.
180 Gallo A, Davies RR, Coe MP, Elefteriades JA, Coady MA. Indications, timing, and prognosis of operative repair of aortic dissections. Semin Thorac Cardiovasc Surg. 2005;17:224–35.

CHAPTER NINE

9. NATIONAL TARIFF REIMBURSEMENT IN THORACIC AND THORACOABDOMINAL AORTIC ANEURYSM SURGERY

9.1 Introduction

Currently thoracic aortic surgery is performed on patients in a few large cardiothoracic centres within the UK. The outcomes for patients are improving as the skills/competencies within the MDT's at these centres increases. There is however a significant financial risk associated with delivery of this service and that relates to the national tariff reimbursing this activity, in that the HRGs are not adequately supporting the current range of surgical procedures involved in aortic surgery.

Since the formation of the current set of HRGs, aortic surgical procedures and techniques have developed significantly, allowing interventionists (cardiac surgeons, vascular surgeons and interventional radiologists) to perform a larger variety of operations on the aortic root, ascending thoracic aorta, aortic arch, descending thoracic aorta and abdominal aorta and their combinations. These operations are currently being performed as either elective or emergency procedures, and include replacement of a part of the aorta or a combination of both.

Consequently, in large cardiothoracic centres, aortic surgery has become a subspecialisation within cardiac surgery requiring interventionists and other staff to dedicate the majority, or all, of their time to this sub-speciality, in order to deal with the increasing complexity of the procedures.

9.2 Developing a Homogeneous Coding of Procedures

OPCS developed a coding system to classify interventions and procedures in health care. In UK health care, OPCS Classification of Interventions and Procedures (OPCS-4) is a procedural classification for the coding of operations, procedures and interventions performed during in-patient stays, day case surgery and some out-patient attendances in the National Health Service (NHS). Responsibility for revision and maintenance is currently with NHS Connecting for Health (NHS CFH). Though the code structure is different, as a code set, OPCS-4 is comparable to the American Medical Association's Current Procedural Terminology. This coding system is generally understood by clinicians and the HRGs are developed around OPCS codes. On the other hand, quality demand and advances in technology were growing requiring additional expenditure. In addition to the above, global financial crunch in 2008 has forced DoH to freeze NHS funding at the levels of 2010 necessitating the NHS to find 20 billion pounds recurrently in order to fund expansion and development. Suddenly every provider realized that they had to do more for less. Traditional financial information and management techniques were not providing enough information to effectively understand and manage the behavioural pattern of costs. Monitor that was established in 2004 to authorize and regulate NHS foundation trusts, recommended as part of their process of awarding foundation status to implement service line reporting (SLR). It is broadly accepted that clinical engagement is essential to deliver a healthcare change programmed at all stages from developing the vision through to the implementation and embedding of a policy[13].

9.3 Current Issues of Reimbursement

The complexity of aortic surgery and the current level of clinical expertise required to manage this complexity have outstripped the scope of the existing HRGs assigned to the area.

Two particular aspects of complex thoracic aortic surgery which characterise the involvement of cardiac surgeons, and underpins their ability to intervene on previously inoperable disease, is that of: perfusionists and cardiopulmonary bypass. This is not reflected in the tariff of "vascular surgery" performed by vascular surgeons without bypass;

More recently the introduction of highly skilled technicians to support the use of Spinal drains /monitoring in the intra and post-operative stages following complex thoracic aortic surgery

New HRGs need to be developed to appropriately reflect the specialist developments in this area of cardiothoracic surgery. The revision should also reflect the procedure times as well as the perioperative and post-operative needs of the patients. Neither of these issues are reflected in existing tariff adding to the significant financial risk in those centres delivering the service. The current reimbursement supports 1 session in the theatre complex, these procedures take much longer.

One particular aspect of complex thoracic aortic surgery which characterises the involvement of cardiac surgeons, and underpins their ability to intervene on previously inoperable disease, is that of perfusionists and cardiopulmonary bypass. This is not reflected in the tariff of "vascular surgery" performed by vascular surgeons without bypass. A new HRGs need to be created that appropriately reflect the specialist developments in this area of cardiothoracic surgery as well as the extended length of the procedures and the need to support these patients

peri-operatively. The attached table 9.3 highlights the current difficulty within the existing HRG structure. The structure needs to be modified to both reflect the specialist nature of the work being done and also to allow for the financial reimbursement of these new complex procedures. This paper is the collaborative work of the three hospitals that comprise 2 of the UK's specialist centres currently performing the specialist thoracic and thoracic-abdominal aortic surgical procedures - Liverpool Heart and Chest Hospital NHS FT and Royal Brompton and Harefield NHS FT. We have reviewed and compared the coding of these procedures in both Trusts (as presented in the table 9.3), and conducted analysis of HRGs, procedure costs and income.

9.4 Proposition of Reimbursement

Our main observation as evident from table 9.3 is that at present HRGs do not capture or reflect the complexity of the specialist aortic surgery (or the pre and post-operative care), where often multiple surgical procedures occur within one single case / episode. Consequently, we would like to propose firstly that the current HRGs are split into separate bandings that cover groups of procedures of differing complexity; and secondly that some new HRGs are created to cover some of the more specialist procedures that do not readily fit within these bandings.

We also would like to share with the NHS Information Authority team some additional observations and suggestions which might help development and fine-tuning of those HRGs:

1. We believe that in the next 3-5 years there will be:

a. Growth in hybrid and endovascular procedures, particularly involving aortic arch: this currently is not set up as a separate OPCS group of codes. This will require procedures to be carried out in a hybrid theatre environment;

b. Increase in stenting of the thoracic aorta: this will require more expensive surgical set up (again the hybrid theatre) plus more sophisticated higher value devices and stents. This procedure will lead to shorter lengths of stay, and will enable a wider range of patients to be operated upon. Again the OPCS codes have not been developed for this likely growth area.

2. In addition to the standard list of comorbidities and complications leading to increased medical dependency, longer recovery and higher complexity which applies to cardiac surgical procedures, specialist aortic surgery has additional significant complications that need to be taken account of as HRG modifiers.

3. The main additional complications include: stroke, paraplegia (particularly when operating on the descending thoracic aorta), damage to the recurrent laryngeal nerve, damage to the lungs (resulting in the need for prolonged ventilation), renal impairment, infections (more commonly in the lungs).

Any of the above complications, as well as the standard complications and comorbidities affecting the HRGs in cardiac surgery, will have a very significant effect on the complexity of the procedure, speed of recovery and the degree of the medical dependency. We believe therefore that each of the HRGs for specialist aortic surgery needs to reflect these significant comorbidities and complications.

Many of the aortic surgical procedures need to be performed with full circulatory arrest and body cooling - both will increase the complexity and the duration of the surgery.

4. For many but not for all of the procedures the theatre time was a good indicator of complexity of the procedure, recovery time and the overall cost. The longest average theatre times were for the following groups of procedures:

- Other aortic aneurism procedures (proposed Group C)- 20 hours of theatre time per elective patient and 23 hours per emergency procedure on average;
- Aortic surgery plus other simultaneous procedures such as CABG, MVR, TVR etc. (group D) – 15 hours of the theatre time;
- Root plus AAo+ AVR, hemiarch, total arch, or and ET (Group B2) – 11 hours;

5. In addition to the theatre time as described above the other indicators of the complexity of the procedure and the total cost were: lengths of stay on the ward, involvement of second surgeon/anaesthetist.

The cost of valves is also currently not separately reimbursed so any procedure requiring a valve has a higher degree of mismatch between the procedure cost and income.

6. The TAAA (thoracoabdominal aortic aneurysm) is a very complex group of patients. They are either managed medically with drugs, use of complex endovascular stents of with surgery. The surgical procedure is either done on left heart bypass or on cardiopulmonary bypass and circulatory arrest. They could be divided into 2 main groups in terms of extent of their aneurism: either isolated thoracic aortic aneurysms or thoracoabominal aortic aneurysms.

9.5 Reflection of 2012/2013 Tariff to Existing Cost Analysis for Aortic Arch Surgery

Table 9.5 shows a breakdown of the cost per aortic arch surgery based on tariff obtained from the department of health 2012/2013. The table is split in between revenue and actual cost, per procedure (hemi arch and total arch). The total median revenue for hemi arch is £26,035 whereas for total arch is £27,246. The actual median cost per hemi arch is £24,152, and for total arch is £32,515. It is observed the median loss and surplus per case were as follow, for hemi arch there is a surplus of £1883 where as there is a median loss for total arch of £5269.

Table 9.5. Cost Analysis for Aortic Arch Surgery Based On 2012/2013 Tariff

Cost Analysis for Aortic Arch Surgery based on 12/13 Tariff			
		Hemi Arch	**Total Arch**
Revenue	BASE TARIFF	16,489	10,822
	CRITICAL CARE FUNDING	4,540	9,359
	DEVICE EXCLUSION FUNDING	4,836	4,836
	DRUGS EXCL. - TISSEEL ETC. ETC	169	463
	EXCESS BED DAYS	0	1,766
	Total median Revenue	**26,035**	**27,246**
Cost			
	Critical Care	3,722	7,319
	Departmental overheads	384	447
	Drug costs	601	1,201
	Imaging	249	627
	Medical staffing	2,197	2,290
	Other Clinical Supplies and services	3,089	3,373
	Other Diagnostics	121	130
	Pathology	376	588
	Pharmacy Services	202	324
	Prostheses / Implants / Devices	2,520	2,600
	Theatres & Cath Labs	6,351	7,449
	Therapies	194	398
	Trust Overheads	1,701	2,319
	Ward and Other Settings	2,445	3,449
	Total median cost	**24,152**	**32,515**
Median loss / (Surplus) per case		**(1,883)**	**5,269**

CHAPTER TEN

10.VOLUME OUTCOME RELATIONSHIP AND SUB-SPECIALIZATION IN THORACIC AORTIC ANEURYSM AND DISSECTION SURGERY

10.1 Volume-Outcome Relationships in Thoracic Aortic Surgery

It is generally anticipated that in undertaking any activity the greater the level of experience/practice that any individual has access to then the better the performance and hence the outcome of the service being performed. In the clinical context this volume outcome relationship is a longitudinal process where an increase in the volume of a particular procedure performed by a surgeon is anticipated to lead to improved patient outcomes (mortality, hospital length of stay and survival)[181]. This is referred to as subspecialised practice and ability to perform caseload of interventions that are highly specific-procedure to one organ system.

In order for subspecialisation to be effective, utilising procedure-specific resources must be applicable. This study provided an insight into the specificity of procedure volume–outcome associations and its inverse effect in a service that deliver aortic

181 Hannan EL, Radzyner M, Rubin D, Dougherty J, Brennan MF. The influence of hospital and surgeon volume on in-hospital mortality for colectomy, gastrectomy, and lung lobectomy in patients with cancer. Surgery 2002;131:6-15

aneurysm surgery. It certainly suggests that the benefits of high volume are restricted to the specific procedure for specific disease and not for the generality of cardiac surgical interventions. There exist different structural components of service delivery and care that contributed to this mechanism to be most effective and efficiently executed. The most effective component is the uniformity of the surgical techniques among the team. The aortic team at Liverpool Heart and Chest Hospital efficiently perform aortic aneurysm surgical repair declaring not only unique surgical skills but also the application and methods of such skills that have been transformed and passed on from trainer to apprentice over multitude of case work.

Hence, the examined effect was proven to be effective and is translated in the improvement of clinical outcomes among the examined group performing elective and non-elective aortic aneurysm repair.

Surgical outcomes are increasingly being scrutinised through national audit and publication of unadjusted practice and surgical intervention. The volume outcome relationship is not unique to aortic surgery and has been the centre of debate and discussion amongst other disciplines including arterial and hepato-pancreato-biliary surgery, have focused on the relation between hospital annual workload (volume) and outcome[182]. Their reported results show that units doing a higher volume of work produce significantly better outcomes. This association must be acknowledged when services are commissioned, and complex surgery should not be performed in low volume centres. However, the aforementioned is not applicable for aortic surgery in the UK since there isn't one centralised centre that only perform complex aortic surgery. This point brings us to the current climate of operating on aortic aneurysm in the UK, which doesn't follow selective referral and surely is a mix and match between "practice makes perfect" and low volume centres.

182 Boudourakis LD, Wang TS, Roman SA, Desai R, Sosa JA. Evolution of the surgeon-volume, patient-outcome relationship. Ann Surg. 2009 Jul;250(1):159-65

The low volume centres are often unable to provide evidence of improved outcomes not only due to their low case volume but also due to consequent lack of statistical power that could potentially provide meaningful analysis.

Therefore, not only are low volume centres associated with a worse outcome, but the appropriateness of performing high risk surgery in such centres is questionable because outcomes cannot be assessed in terms of safety.[183,184,185].

Analyses of national data have an important role in planning the delivery of services and in comparing peers. Local data must be used to understand individual unit outcomes, identify areas for improvement, quality assurance and guide local commissioning.

This has been the initiative followed by the aortic service at Liverpool Heart & Chest Hospital. The essence of aortic subspecialisation was a pair between local expertise and interest of individual surgeons who wanted to perform aortic surgery. Needless to say, the divergent results of poor aortic surgery outcomes were at the centre that evoked subspecialisation and mandated the change in the trend of surgical delivery at LHCH. The analyses of aortic local data revealed to be of interest to healthcare commissioners that supported the scheme of rearrangement of services.

Aortic aneurysm surgery remains a priority at local institutions but not at national levels. National data unfortunately doesn't follow pursuit and clinical input a high enough standard to provide evidence to facilitate service reconfiguration nationally is still controversial.

183 Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. JAMA 1998;280:1747-1751
184 Dudley RA, Johansen KL, Brand R, Rennie DJ, Milstein A. Selective referral to high-volume hospitals: estimating potentially avoidable deaths. JAMA 2000;283:1159-1166
185 Halm EA, Lee C, Chassin MR. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med 2002;137:511-520

The initiative to improve aortic outcomes in elective and non-elective work drove the aortic team at Liverpool Heart and Chest to rearrange the service because it warranted immediate attention. This was followed by investigation on how to change and rearrange the service promptly.

10.2 Subspecialisation, Centralization and Concentration of Aortic Expertise in the UK

Since the 70s of last century, surgical specialties such as Urology, ENT, and orthopaedics have followed pursuit of subspecialty and came off the general surgery rooster. This has led to restructure of training programs and final speciality exit exams that met the development of alternative tracks or pathways to provide earlier or increased exposure to subspecialties. In current climate there is certainly an interest and place for specialization in the different disciplines of surgical practice.

This serves well the increasing and demanding well-informed public interest that frequently seeks advanced and specialized care for their healthcare. In many healthcare systems and in particular in surgery, sub-specialty and subspecialisation has developed and evolved from the generality of surgery. For instance, vascular surgery that has been widely practiced amongst general surgery has been recently devolved from this non-yielding linkage and is now considered as a standalone speciality.

This similarly was the case demonstrated in cardiothoracic surgery and hepato-pancreatobiliary surgery. Due to the increase in hospital workload and surgeons' case mix of volume and the need to report outcomes, many specialities are seeking to centralize their service and care provision. Hence, many healthcare systems have embraced a move to specialization in surgical practice and regionalization of complex services. Not to forget the patient choice policy that utterly relies on the

patient having the freedom of choice of care provider and access to the public reporting of outcome data for surgical procedures. In this context, quality became an important barometer of service measurable outcomes which in turn is imperative to concentrate the expertise of experts in a complex and regional centres.

The volume and outcome relationship has not been supported by evidence extensively in thoracic aortic aneurysm repair. Hence, further research is required to define the correlation and existing nature of this relationship. There is no clear cut evidence to suggest that certain volume of cases is required for subspecialisation to be attained. Many factors have been shown to underlie the relationship between volume and outcome in a subspecialised unit. Such could be attributed to specialised anaesthetists, along with advanced intensive care facilities, that would support the transformation of service not only around the surgeon but also to other disciplines.

The UK is quite different to USA and Europe with training in Cardiac Surgery unlinked to Vascular Surgery. Vascular surgery is a separate specialty with its roots in General Surgery with significant involvement in interventional radiology. Thus, training and service provision have influenced the development of services for intervention on the thoracoabdominal aorta.

Effectively, this has led to a dependence on collaboration between specialties with a reliance on cardiac surgeons to provide adjuncts such as cardiopulmonary bypass and on vascular surgeons and radiologists to provide guide wire skills and endo-vascular options. In some centres, collaboration has flourished to the benefit of patients; however, in other centres treatment has been concentrated to one form of intervention such as surgery or endovascular approaches. The benefits of this arrangement are in the fact that skills are highly developed in respective specialties and where collaboration occurs the treatment options are impressive and outcomes are comparable with any international centre.

There is good evidence from the literature on the relationship between hospital volume and mortality risk for many surgical procedures including heart valve replacement and aortic root replacement. Recently published data from the US Nationwide Inpatient Sample has confirmed that this is also true of acute type A aortic dissection. Hence, the evidence indicates that complex operations performed by specialized, high-volume surgeons have better outcome.

In terms of resource utilisation two contradictory influences affect total hospital costs. If subspecialisation reduces in-hospital mortality, the average length of stay could easily increase, since a patient who dies in hospital has their stay curtailed while a patient who is sent home does so only when they have a sufficient recovery in hospital. On the other hand, higher quality surgery and a reduction in adverse events could mean that patients recover more quickly and avoid the very long ICU and ward stays that result from complications. The same is also true for the costs of the surgeries themselves; a successful surgery may take longer than one in which the patient dies before it is completed, but a more experienced surgeon may complete the surgery with fewer complications and in less time than one who is less skilled[186].

10.3 Existing Outcomes and Volume Effect Nationally

Within the United Kingdom, few cardiac centres have established high volume activity in aortic arch and acute type A dissection surgery and even fewer have published their outcomes.

Currently two formally published historical series of open repair exist from Birmingham and Bristol aortic services.

186 An Economic Analysis of Aortic Surgery- University of York

No meaningful data on open aortic arch repair has been published in The Society for Cardiothoracic Surgeons "Blue book" (National Adult Cardiac Surgical Database Report).

The lack of nationwide service provision for open intervention and perceived high risk nature of this surgery has led to regional centres developing local endovascular strategies to treat these patients principally led by Vascular Surgeons and Interventional Radiologists. Several groups have published UK outcomes for endovascular intervention on the arch however activity is limited.

10.4 UK Data on Aortic Arch Intervention

Several sources of data exist, some from pier reviewed journals and some from less reliable sources such as government statistics (HES and ONS) and from national societies and registries (Society for Cardiothoracic Surgeons and The Vascular Society).

10.5 Existing Outcomes and Volume Effect Internationally

Thoracic aortic aneurysm is a fatal condition with dire prognosis unless surgical intervention is performed. Open aneurysm repair has traditionally been associated with high operative morbidity and mortality Table 10.5. The International Registry of Acute Dissection (IRAD) has published outcomes from multiple centres worldwide with an average mortality of 25.1% in 2005[187].

187 Tsai TT, Evangelista A, Nienaber C, Sechtem U, Fattori R, Myrmel T, Llovet A, Cooper JV, Fang J, Isselbacher E, Eagle KA. Long-term survival in patients presenting with type A aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2005; 112:534-535

European registries in the United Kingdom and Germany have published operative mortalities of 23.1% and 17% respectively[188].

A recent publication from Mount Sinai Medical Centre, using the Nationwide Inpatient Sample database of 24,777 patients between 1998 and 2008, showed average operative mortality of 21.6%[189]. Further analysis of this data set demonstrated mortality was related to surgeon volume (odd ratio 1.78) and centre volume.

Anderson et al. from the Duke Group published their results pertaining to the impact model of multi-disciplinary team approach[190]. They reported operative mortality before multi-disciplinary implementation was 33.9% and was statistically equivalent to the expected operative mortality rate of 26.0% (observed-to-expected mortality ratio 1.30; p = 0.54). Operative mortality after multi-disciplinary implementation fell to 2.8% and was statistically improved compared with the expected operative mortality rate of 18.2% (observed-to-expected mortality ratio 0.15; p = 0.005). Clearly, the United States has established aortic supercentres, which have demonstrated clear improvements in the short-term and long-term outcomes after surgery on the thoracic aorta. This model of care does not exist in the United Kingdom.

In aortic dissection, 3 patients with acute Type A aortic dissection are diagnosed out of every 1,000 emergency department patients presenting with acute back, chest, or abdominal pain6. Mortality in untreated patients is estimated at more than 1% per hour after onset of symptoms, whereas 30-day survival for appropriately treated and early diagnosed patients approaches 80%.

188 Conzelmann LO, Krüger T, Hoffmann I, Rylski B, Easo J, Oezkur M, Kallenbach K, Dapunt O, Karck M, Weigang E; Teilnehmenden GERAADA-Zentren. [German Registry for Acute Aortic Dissection Type A (GERAADA): initial results]. Herz. 2011 Sep;36(6):513-24

189 Chikwe J, Cavallaro P, Itagaki S, Seigerman M, Diluozzo G, Adams DH. National outcomes in acute aortic dissection: influence of surgeon and institutional volume on operative mortality. Ann Thorac Surg. 2013 May;95(5):1563-9

190 Andersen ND, Ganapathi AM, Hanna JM, Williams JB, Gaca JG, Hughes GC. Outcomes of acute type a dissection repair before and after implementation of a multidisciplinary thoracic aortic surgery program. J Am Coll Cardiol. 2014 May 6;63(17):1796-803

The International Registry for Acute Dissection and the Society for Cardiothoracic Surgery still publish mortality rates of 26.6% and 25% respectively. The timely diagnosis and rapid surgical management of acute Type A aortic dissection are of paramount importance for better outcomes and survival. Once diagnosed the key to a successful outcome is rapid referral to a cardiac surgery centre and immediate surgical intervention. Surgical outcomes are highly variable from centre to centre (Table 10.5).

A significant amount of literature exists relating outcome to volume of activity by surgeon and hospital in the related specialty of Vascular Surgery. Outcomes from the USA show a very clear relationship between activity and outcome from abdominal aortic aneurysm repair and this has led to a major review in the UK and rearrangement of services to address these issues and improve outcomes. Bristol published an analysis of their results for ascending/arch surgery in 2004. Although there was no mortality difference between the two groups there was a significant difference in morbidity.

CHAPTER ELEVEN

11. METHODS

11.1 Ethics in Research

The Hippocratic oath that clinicians take and build on their code of conduct and practice is centered around "First of all, do no harm". This reflects the certain degree of norm that allows us to distinguish between the acceptable and the non-acceptable which very much coincide with the bylaws of a civil society. The society we serve expect an unremitted honesty and confidentiality that bounds the very things that we do to the norms accepted by the social welfare of the society and the community at large. As such, the development and adherence to the social norms in clinical practice is not very different from ethical application on the research front. The latter provides a degree of clinical knowledge to be attained that will reciprocate its benefit in clinical settings. Accepting to conduct research on clinical grounds and providing an ethical approval allows the clinical researcher to avoid commitments of error, fabricating, falsifying, or misrepresenting research data interpretability of results and perception of proper judgments. Clinical research often involves interactivity, cooperation and coordination amongst different researchers of various disciplines. This collaborative work is centered on mutual trust, accountability and mutual respect. It's from these fundamental understanding guidelines reflecting authorship, copyright and patenting policies, data sharing policies, and confidentiality rules exist in peer review process to protect the intellectual property of the research team, individuals and the institution.

Liverpool Heart & Chest Hospital, collects important data and demographics about patients for the purposes of governance and research output. This is done through rigorous steps that the trust maintains including: Accessing health records and personal information, Patient confidentiality, Data Protection Act 1998 and Caldecott Principles - the principles covering the safe handling of patient identifiable information. These steps are overseen by Information Governance to provide and reciprocate safe healthcare provision for patients and for provider in equal manner.

For this particular research, I have attained local institutional approval from governing committee that scrutinized the application process maintaining that patients' identifiers information is not to be disclosed and confidentiality not to be breached. Strictly speaking, the committee commission its decisions according to the Caldecott Principles in that the review process of my research data acquisition application was to ensure that patient-identifiable information was only shared for justified purposes and that only the minimum necessary information was used. The Committee also advised on actions to minimize risks to confidentiality. Hence, upon a stringent process the aortic data from a wide range of cardiac database was filtered that supported the foundation of analysis this thesis was built on.

11.2 Research Bias

Its endurably valid to state that this thesis is built around the motion of validity of the construct and in this case the impact model that the aortic service represent not only in aortic surgery nationally but also in the domain of public health sector. The motion of validity of the construct provided me as a researcher with available resources in a utilitarian manner to conduct an analysis on aortic surgery performance knowingly that I belong to that aortic surgery team and service.

The performance bias is rather applicable, however, researchers are fallible. We do the mistakes and learn from the very experience of that mistake but also we provide the solution knowingly that there is no paradigm solution to the elimination of error and bias. In that sense, considerable consideration was needed to be able to draw the focus of my intention to analyze a team and their results in a rather objective and not subjective manner. This dwells on the facts that as a sceptic who genuinely understand the process of skepticism, I have given this step a personal and clinical strategy so that its addressed adequately.

The realization of the aforementioned limitation in this thesis enforced the commitment and detachment from the aortic service and team. This required intense concentration and efforts so that my research attitude and approach remain open non-framed in intellectuality and concept.

This helped in allowing me to attain a degree of foreclosure and to source out measures to prevent imminent favoritism that will falsify prudent judgment. These measures included obsolete detachment from oneself as part of the service and the willingness to look at the influences that might cause hind-sight representation of the quality of data and reports. A very exact approach was to present the data at various national and international platforms allowing for a degree of criticism in addition to being rounded by self-criticism in a constructive manner.

For this thesis to qualify as not built on cognitive bias, the utilization of critical thinking was paramount. This confined certain elements that were required in the analysis and avoided the prospect of cognitive flaws. Hence, this step aimed to promote a sense of logic reasoning and empiricism. I always apply such tactics in the field of surgery and I refer for them as prediction and definitive diagnosis. The elements of definitive diagnosis are concentrated on utilization of multiple resources available that will help in drawing up judgement and conclusion and aim to avoid prediction in most settings.

Applying such concept in dealing with the confounding bias of me as a researcher belonging to a team to be researched allowed for the analysis to be made in conjunction with approaches such as positivism and avoiding the effect of the interpretivist. As a positivist, the data were compiled, validated thoroughly and analyzed using appropriate scientific methodology. This was done avoiding the bias of the interpretivist who happens to be in this case the surgeon and the team. Having been equipped with this fundamental evaluation allowed the biases to be controlled yielding the following thesis.

11.3 Liverpool Heart & Chest Cardiac Database

The cardiac database at Liverpool Heart and Chest Hospital is used to collect data for every cardiac surgical operation performed; pre-operative data is collected about the clinical condition of the patient (demographics such as age, gender, Body Mass Index, etc along with potential risk factors such as diabetes, renal insufficiency, previous cardiac operations, etc), the operation itself (details such as bypass strategy, time on bypass, aortic cross-clamp time, graft or valve details and so on), and post-operative outcomes (including mortality, morbidity, critical care information and any reoperation information).

The cardiac database is recognised as being an integral component of delivering high quality clinical information to the trust; it has been specifically designed along with input from cardiac consultants to facilitate the process of data entry and data reporting. Cardiac data is used within the hospital for measuring and managing cardiac surgical performance at a unit and an individual consultant level (using risk adjusted models which typically assess expected levels of mortality based on the EuroSCORE risk model 1, 2).

Liverpool Heart and Chest Hospital participate in the UK National Adult Cardiac Surgery Audit via the National Institute for Cardiovascular Outcomes Research (NICOR: http://www.ucl.ac.uk/nicor). The aim of this audit is to collect information about all major heart operations carried out in the UK and through that to improve the quality of patient care. The audit allows appropriate comparison of clinical performance with national and international standards, and provides useful data on changing trends within the specialty.

11.4 Liverpool Heart and Chest Aortic Database Validation

The initial phase of my thesis mandated that I validate and verify the entry of variables into the database. To enhance this method, I followed the literature on the validation of database and its appropriate application. Below are the steps that I used to validate and verify the aortic arch and acute type A dissection:

1) **Character checks:** to ascertain that characters are present across all the data set and fields. When a missing record is identified, I utilized the case notes of that particular patient to verify and record the missing field. When the case notes happened to be off-site i.e. stored in secured storage place, I would request the case notes to be delivered back to the hospital for validation. In order to facilitate this process, the request case notes were ordered in batches. Request were made to Health Record Department at LHCH.

2) **Cardinality & Format:** This would allow me to ascertain a valid number of related records. Unfortunately, some of the historical data that goes as far as 1998, contained missing cardinal notes on patient hospital number and

identifiers. To overcome this step, I crossed check their other identifiers (date of birth, address, hospital admission and discharge and consultant in charge) with other possible databases. This would then flag out the patient and the patient would then be given an appropriate identifier. Format of entered data is also checked and formatted data are all placed in a specified format (template) to allow accurate analysis and avoidance of missing data.

3) **Consistency:** This was utilized to ensure data in different fields corresponds with patient clinical data, demographics ad characteristic. Incorporated in this check was the cross-system consistency check that enabled me to compares data in different systems and databases to ensure it is consistent, present and usable for analytical basis.

4) **Quality:** The data quality is universal and in essence, all relevant clinical data were collected prospectively and entered into our local hospital database from which, periodically, core datasets were validated and submitted to The Society for Cardiothoracic Surgery (UK). In brief, for each operation, a dataset was collected that included relevant demographics, indicators of disease severity, acuity, comorbidities, and procedural details, along with all relevant in-hospital outcomes. Outcomes evaluated for the purposes of this study include neurological and renal complications, postoperative ventilation times, and both in-hospital and follow-up mortality. This section also included spelling and grammar check to look for spelling and grammatical errors that could refrain and limit the analysis and its accuracy.

5) **Logic check** was also followed to attain a logical input in data entered that should correspond with the surgical intervention on patient. This would allow to avert duplication and conflicting data.

11.5 National Institute of Cardiovascular Outcomes Research Database

Prospectively collected data were extracted from the National Institute for Cardiovascular Outcomes Research (NICOR) National Adult Cardiac Surgery Audit (NACSA) registry (version 4.1.2) on 20th November 2014 for all adult cardiac surgery procedures performed in the UK. As described elsewhere, reproducible cleaning algorithms were applied to the database[191]. Briefly, duplicate records and non-adult cardiac surgery entries [including transcatheter aortic valve implantations (TAVIs)] were removed, transcriptional discrepancies harmonised and clinical and temporal conflicts and extreme values corrected or removed. Data summaries are returned regularly to each unit for local validation as part of the NACSA in the UK.

11.6 Variables Documented and Definitions

11.6.1 Variables

Preoperative variables

a) *Current smoker:* Smoking within six weeks of the operation.

b) *Diabetes:* Diagnosis of diet, tablet or insulin controlled diabetes.

191 Hickey GL, Grant SW, Cosgriff R, Dimarakis I, Pagano D, Kappetein AP et al. Clinical registries: governance, management, analysis and applications. Eur J Cardiothorac Surg 2013;44:605–14

c) *Hypercholesterolemia:* Diagnosed with cholesterol over 5.0 mmol/L or on drug treatment.

d) *Hypertension:* Diagnosed with hypertension (blood pressure > 139/89 mmHg) or on antihypertensive treatment.

e) *Cerebrovascular disease:* The presence of carotid artery disease, chronic neurological injury, or a history of transient ischemic attack (TIA) or cerebrovascular accident (CVA).

f) *Respiratory disease:* Diagnosed with a respiratory disease (i.e., asthma, emphysema, bronchiectasis, chronic obstructive pulmonary disease), on treatment (i.e., inhalers) or impaired pulmonary function tests.

g) *Peripheral vascular disease:* Diagnosed with peripheral vascular disease on the basis of symptoms (claudication), previous intervention, or evidence of stenotic disease.

h) *Renal dysfunction:* The definition of renal failure has changed over time. Over the last 3 years we have recorded eGFR (estimated glomerular filtration rate) as well as the presence of established renal failure and dialysis. An eGFR < 89 mL/min/1.73 m^2 is considered as renal dysfunction (Chronic Kidney Disease). Prior to this, we recorded renal dysfunction as a creatinine value greater than 200 μmol/L and as established renal failure with dialysis.

i) *Previous cardiac surgery:* Previous sternotomy for any reason.

Postoperative variables

- *Intubation time (hours):* Presence of endotracheal tube with supported respiratory effort.

- *Intensive Therapy Unit (ITU) stay (days):* Care within our Critical Care Area which includes 1:1 nursing care as "intensive care" or 2:1 nursing as "high dependency care."

- *Postoperative stay (days):* Number of days within the hospital setting from the day after surgery.

- *Acute renal failure:* Postoperative requirement for hemofiltration.

- *Deep sternal wound infection:* This is defined as wound dehiscence to the sternal plate with a positive wound culture. It excludes simple superficial wound infections and aseptic mechanical dehiscence.

- *Reexploration for bleeding:* This is defined as resternotomy and exploration in the acute postoperative period for bleeding and/or evidence of tamponade.

All stroke:

- CVA, diagnosed clinically or on imaging.

- TIA, diagnosed as clinical evidence of neurological impairment with return of function within 24 hours.

- *Confusion:* Acute confusional state diagnosed clinically.

11.6.2 Surgical Definitions

1) *Incisions*. All elective operations were performed through a midline and full sternotomy. In a very small number of emergencies we used either a clamshellor lateral extension to a sternotomy incision.

2) *Cannulation options*. A myriad of cannulation techniques were used depending on the anatomy, pathology and available imaging.

3) *Arterial cannulation*. Arterial cannulation of either the ascending aorta, arch of the aorta, femoral artery, or axillary arteries was performed. In a limited number of emergency operations, the left ventricular apex was cannulated. All cannulations via the axillary artery were through an anastomosed 8 mm graft.

4) *Venous cannulation*. Venous drainage was achieved via the right atrial appendage, bicaval cannulation, main pulmonary artery, or femoral vein.

5) *Venting*. Venting of the heart was performed either through the right superior pulmonary vein, main pulmonary artery, or left ventricle (LV) apex via a mini left thoracotomy.

6) *Conduct of cardiopulmonary bypass*. Cardiopulmonary bypass was initiated following full heparinization (300 U/kg) to an activated clotting time > 450, and during active cooling, alpha stat was maintained. Warming was commenced ensuring no excessive differential between peripheral and core temperatures.

7) *Cardioplegia*. Intermittent cold blood cardioplegia was administered anterogradely at induction and retrogradely during maintenance. Anterograde cardioplegia was supplemented into the right coronary system throughout cases where possible. A “hot shot” of warm blood cardioplegia was administered prior to reflow.

8) *Monitoring*. It is our practice to monitor a radial and femoral arterial trace as well as central venous cannulation and central venous pressure. A nasopharyngeal and bladder/rectal catheter are used to monitor temperature. Near infrared spectroscopy (NIRS) was employed beginning in

2008. Transeosophageal echocardiography is routinely utilized unless contraindicated.

9) *Brain protection*. Our approach to neuroprotection is centered around deep hypothermic circulatory arrest; however, adjuncts include CO_2 flooding of operative field, packing of head in ice, phenobarbitone prior to circulatory arrest, and supplementary cerebral perfusion as indicated below:

- *Anterograde cerebral perfusion*. This is administered in total arch surgery. Cold blood is administered via the head and neck vessels directly or via clamping of the brachiocephalic artery and perfusing the axillary artery. The left subclavian artery is temporarily occluded or may be perfused if NIRS is suboptimal. Target flows of 10 mL/kg/min are used; however, this is modified according to perfusion pressure (target mean, 50-60 mm Hg) and NIRS response.

- *Retrograde cerebral perfusion*. This technique is used for simple hemiarch surgery or acute pathologies where tissue quality of arch vessels may be poor. The superior vena cava (SVC) is cannulated with a 15 French cannula and a small clamp placed between SVC and right atrial appendage. Flow is commenced at 10 mL/kg/min aiming for a central venous pressure (CVP) between 25 and 50 mm Hg and an acceptable NIRS reading.

10) *Temperature*: Our core (urinary or rectal) target temperatures for hemiarch and total arch surgery have evolved over the time of the study. During early periods, target temperature for all procedures was less than 18°C (deep hypothermia). Currently, our typical target for an elective hemiarch is 25°C (moderate hypothermia), elective total arch is 20°C (moderate hypothermia), and for emergency cases, 20°C. Rewarming was aided with external warmers.

11.7 Costing Definitions

1. **Cost driver:** Cost drivers are the structural determinants of the cost of an activity, reflecting any linkages or interrelationships that affect it; therefore, we could assume that the cost drivers determine the cost behaviour within the activities, reflecting the links that these have with other activities and relationships that affect them.

2. **Cost pool:** A cost pool is a group of individual costs that is allocated to cost objectives (like patient episode) using a single cost driver. For example, building rent, utilities cost, and janitorial services may be in the same cost pool because all are allocated on the basis of square meters of space occupied.

3. **Tracing:** Direct tracing requires that, by physical observations, a cost can easily and accurately be related to a cost object.

11.8 Costing Methodology

11.8.1 Estimation of Costs for Pre-SLR Period Patients

Although data on clinical outcomes were available for all cases between 1999 and the present day, only on the more recent cases could resource use be identified through PLICS, because SLR data was available for only from 2009. Costs for the cases prior to 2009 were estimated.

The method of cost estimation was as follows. Firstly, some preliminary analyses were undertaken to determine the most significant drivers of cost. This required the collaboration of both clinicians and members of the finance department to determine which aspects of the treatment and perioperative care drive cost. Factors like Cutting time (the length of time in surgery), intensive care unit (ICU) length of stay, and ward length of stay were found to be the major drivers of cost. Cost lines which are impacted by these factors are considered as relevant costs for this study. Cost lines like cost of valves and high cost antibiotic drugs will remain the same on either side of sub specialisation (when inflation adjusted) and hence are considered irrelevant costs for this study. All cost analysis in this study is based only on the relevant costs. Although the cardiac database at LHCH is invaluable for analysis of clinical outcomes, this prospectively collected data was not designed to support economic analysis. Hence we added costs to the available time values found in the cardiac database for each episode based on the current rates derived from PLICS from 2009 when the PLICS data is readily available. This process ensured all rates in this study are inflation adjusted.

Costs of primary and secondary measures as defined above will be sought and compared for the two groups. Using PLICS cost data from Liverpool Heart and Chest Hospital's service line reporting (SLR) system, enabling detailed micro-costing that is far superior to the use of NHS reference costs. SLR allows the trust to analyze cost and profitability at patient level of each service it provides rather than just overall profitability. Costs of resources that can be directly attributed to particular patient episode are 'traced', that is, they are allocated to the episode without any treatment or manipulation. Such costs include the likes of prostheses and consumables.

The use of consumables dispensing and supply tracking technologies assigns costs on the fly and allows precise tracing of resource use to the patient and episode on which they were used.

This applies to drugs, and in surgery, where surgical consumables, valves, prostheses, anaesthetic drugs etc. are all automatically attributed to the patient and procedure as they are used. Staff time is allocated with reference to employment contracts and the proportion of the time that is to be dedicated to each duty. That is, the cost of a particular surgeon for a given procedure is a function of his salary, the proportion of his contract he is to operate, and the time the procedure takes. Similarly, the ward costs of clinician can be allocated in the same way. These costs are then allocated based on the observed values of time for each patient episode. Indirect costs such as utilities and trust overheads are allocated/absorbed – although some of them are not directly attributable to any particular episode /service lines, they are divided up and shared amongst all episodes.

11.8.2 Estimation of Costs for Aortic Arch Aneurysm and Acute Type A Dissection Patients

The method of cost estimation is as follows. Firstly, some preliminary analyses will be undertaken to determine the most significant drivers of cost. Factors like cutting time (the length of time in surgery), intensive care unit (ICU) length of stay, and ward length of stay were previously found from parallel and confounding research to be the major drivers of cost. Cost lines which are impacted by these factors are considered as relevant costs for this study. Relevant cost is the cost which is impacted by the quality of service provided per unit of time spent in the theatre, critical care and ward. Actual data of times spent in these three areas recorded and the current rates per unit of time is applied on all cases to arrive at the comparable cost adjusted for inflation.

All cost analysis in this study is based only on the relevant costs. Although the cardiac database at LHCH is invaluable for analysis of clinical outcomes, this prospectively collected data was not designed to support economic analysis.

Hence we added costs to the available time values found in the cardiac database for each episode based on the current rates derived from PLICS from 2009 when the PLICS data is readily available.

CHAPTER TWELVE

12. RESULTS

12.1 Development and Validation of Elective and non-Elective Risk Prediction Models for in-Hospital Mortality in Proximal Aortic Surgery Using the National Institute for Cardiovascular Outcomes Research (NICOR) Database

The number of patients undergoing aortic surgery has increased greatly since the 1990's[192]. As the discipline has developed from a subsection of cardiovascular surgery to an established speciality with many individualised techniques and treatment models [193,194,195], there has naturally been a corresponding focus on clinical outcomes in both the overall patient group and within the individualised

192 Czerny M, Bachet J, Bavaria J, Bonser RS, Borger MA, De Paulis R et al. The future of aortic surgery in Europe European Journal of Cardio-Thoracic Surgery. 2013; 43; 226–230
193 Borst HG, Heinemann MK, Stone CD. Surgical Treatment of Aortic Dissection, 1st edn. Churchill Livingstone, 1995
194 Bachet J, Guilmet D, Goudot B, Termignon JL, Teodori G, Dreyfus G et al. Cold cerebroplegia. A new technique of cerebral protection during operations on the transverse aortic arch. *J Thorac Cardiovasc Surg* 1991; 102 : 85–93
195 Dubost C. The first successful resection of an aneurysm of the abdominal aorta followed by re-establishment of continuity using a preserved human arterial graft. *Ann Vasc Surg* 1986; 1 : 147–49.

pathologies and treatments that are available. Several recent publications continue to demonstrate this important approach to surgical quality[196,197,198,199].

Meanwhile, the application of statistical models to produce risk adjusted outcomes has become an established practice in many healthcare disciplines[200201202203], especially cardiac surgery. These models are typically used to inform patients, to give clinical assurance and to allow benchmark comparisons between institutions. Several risk adjustment models have been published which would allow risk prediction in certain types of aortic patient, or in patients undergoing vascular surgery[204,205,206,207,208,209,210].

196 Hughes GC, Zhao Y, Rankin JS, Scarborough JE, O'Brien S, Bavaria JE, *et al*. Effects of institutional volumes on operative outcomes for aortic root replacement in North America. *J Thorac Cardiovasc Surg*. 2013 Jan;145(1):166-70

197 Chikwe J, Cavallaro P, Itagaki S, Seigerman M, Diluozzo G, Adams DH. National outcomes in acute aortic dissection: influence of surgeon and institutional volume on operative mortality.
Ann Thorac Surg. 2013 May;95(5):1563-9

198 Kilic A, Tang R, Whitson BA, Sirak JH, Sai-Sudhakar CB, Crestanello J, Higgins RS. Outcomes in the current surgical era following operative repair of acute Type A aortic dissection in the elderly: a single-institutional experience. *Interact Cardiovasc Thorac Surg*. 2013 Jul;17(1):104-9

199 Canaud L, Karthikesalingam A, Jackson D, Cresswell L, Cliff M, Markar SS, *et al* Clinical outcomes of single versus staged hybrid repair for thoracoabdominal aortic aneurysm. *J Vasc Surg*. 2013 Nov;58(5):1192-200

200 Tian WJ, Chi DS, Sehouli J, Tropé CG, Jiang R, Ayhan A, *et al* A risk model for secondary cytoreductive surgery in recurrent ovarian cancer: an evidence-based proposal for patient selection. *Ann Surg Oncol*. 2012 Feb;19(2):597-604

201 Teguh DN, Levendag PC, Ghidey W, van Montfort K, Kwa SL. Risk model and nomogram for dysphagia and xerostomia prediction in head and neck cancer patients treated by radiotherapy and/or chemotherapy. *Dysphagia*. 2013 Sep;28(3):388-94

202 Shahian DM, Edwards FH The Society of Thoracic Surgeons 2008 Cardiac Surgery Risk Models: Introduction. *Ann Thorac Surg* 2009;88:1

203 Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg*. 1999 Jul;16(1):9-13

204 Mehta RH, Suzuki T, Hagan PG, Bossone E, Gilon D, Llovet A, *et al*. Predicting death in Patients with Acute Type A Aortic Dissection. *Circulation*. 2002 Jan 15;105(2):200-6

205 Giles KA, Schermerhorn ML, O'Malley AJ, Cotterill P, Jhaveri A, Pomposelli FB, *et al* Risk prediction for perioperative mortality of endovascular vs open repair of abdominal aortic aneurysms using the Medicare population. *J Vasc Surg*. 2009 Aug;50(2):256-62.

206 Choke E, Lee K, McCarthy M, Nasim A, Naylor AR, Bown M, *et al*. Risk models for mortality following elective open and endovascular abdominal aortic aneurysm repair: a single institution experience. *Eur J Vasc Endovasc Surg*. 2012 Dec;44(6):549-54

207 Grant SW, Hickey GL, Grayson AD, Mitchell DC, McCollum CN. National risk prediction model for elective abdominal aortic aneurysm repair. *Br J Surg*. 2013 Apr;100(5):645-53

208 Bala Ramanan B, Gupta PK, Sundaram A, Gupta H, Johanning JM, Lynch TG, *et al* Development of a risk index for prediction of mortality after open aortic aneurysm repair *Journal of Vascular Surgery*; 2013; 58(4); 871–878

209 Williams JB, Peterson ED, Zhao Y, O'Brien SM, Andersen ND, Miller DC, Chen EP, Hughes GC Contemporary results for proximal aortic replacement in North America. J Am Coll Cardiol. (2012) 60:1156–1162

210 Kunihara T, Aicher D, Asano M, Takahashi H, Heimann D, Sata F & Schäfers HJ Risk factors for prophylactic proximal aortic replacement in the current era. Clinical Research in Cardiology (2014), 103(6), 431-440

We conducted a retrospective analysis of aortic surgery data submitted to the National Institute for Cardiovascular Outcomes Research (NICOR) National Adult Cardiac Surgery Audit (NACSA) database by all cardiac centres in the UK. The primary aim of the study was to develop and validate a risk prediction model for post-operative mortality following open surgery on the proximal aorta (i.e. root, ascending or arch aortic segments).

12.1.1 NICOR Database.

For this study, records were included that met the following criteria: operation on one or more of the root, ascending or arch aortic segments that were performed in England and Wales between 1 April 2007 and 31 March 2013. As only non-identifiable patient data were used for this research, formal ethical approval was not required. This project was approved by the NICOR research board.

12.1.2 Study and Outcome Variables

For each operation, data are recorded on patient characteristics, comorbidities, surgical team, intraoperative factors and postoperative outcomes. For this study, we extracted data on patient age at the time of operation (years), gender, body mass index [BMI, defined as weight (kg) / height2 (m2)], Canadian Cardiovascular Society (CCS) angina class, dyspnoea (New York Heart Association grade), recent myocardial infarction (defined as within 90 days of surgery), history of cardiac procedures, diabetes (diet- or insulin controlled), smoking status, history of hypertension, serum creatinine >200 μmol/l, history of renal dysfunction, history of pulmonary disease, history of neurological dysfunction, extracardiac arteriopathy, preoperative heart rhythm (classified for the purposes of this study as sinus rhythm or non-sinus rhythm. Non-sinus rhythm includes: atrial fibrillation, atrial flutter, complete heart

block, presence of a pacing device, ventricular fibrillation, ventricular tachycardia or any other abnormal rhythm), left ventricular ejection fraction (classified as <30, 30–50 and >50%), use of preoperative IV nitrates, IV inotropes prior to anaesthesia, preoperative ventilation, pre-operative cardiogenic shock, operative urgency, concomitant CABG and valve procedures. Further details of variable definitions are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets.

Missing data were assumed to be absent for categorical variables or replaced with the mean value for continuous variables. Ejection fraction was the categorical variable with the highest incidence of missing data (3.5%). The proportions of missing data for continuous variables were: age, 0%; BMI, 3.6%; cardiopulmonary bypass time, 2.3%; and aortic cross clamp time = 2.9%. The outcome for this study was in-hospital mortality, defined as death due to any cause during admission to the operating hospital for cardiac surgery.

Records were excluded from the analysis if in-hospital mortality status was missing. Data on cause of death were unavailable.

12.1.3 Developing the Model

Continuous variables were dichotomised where appropriate; a left ventricular ejection fraction of >50% was categorised as good, 30-50% was categorised as moderate and <30% was categorised as poor. Age at operation, body mass index (BMI) and operative times were retained as continuous variables. Pre-operative heart rhythm was dichotomised into sinus rhythm (normal) and non-sinus rhythm as detailed above. Similarly, the pathology of the aortic segments was dichotomised into aneurysmal or normal pathologies and other pathologies which included: chronic dissection, acute dissection, trauma, coarctation, penetrating atheromatous ulcer, pseudoaneurysm, intramural haematoma and “other” pathology. Ordinal variables were dichotomised as follows: NYHA category, which classifies heart

failure, was grouped into no or mild symptoms (Class I and II) and moderate or severe symptoms (Class III and IV) and the CCS angina grade into stable (Class I to III) and unstable (Class IV). The data were split into an elective group and a non-elective group. The non-elective group included urgent, emergency and salvage surgery. Separate multiple logistic regression models were fitted for elective and non-elective surgery using the backwards elimination procedure for variable selection; all preoperative patient variables listed above were offered to the analysis.

12.1.4 Assessing Model Performance

Model performance was assessed using bootstrap methodology, the complete datasets were sampled from repeatedly and the final multivariate logistic regression model was refit 100 times. Model performance summary statistics were calculated for each iteration with the average across all the bootstrapped samples then calculated. Model calibration was assessed in three ways. Firstly, a Hosmer-Lemeshow goodness-of-fit test where the overall differences between the observed mortality rate and the mortality rate predicted by the risk model are evaluated using a $\chi 2$ test[211].

The second method involved visual inspection of a calibration plot. The calibration plot shows the mean predicted probability of outcome against the observed proportion of outcomes for ten equally sized groups based on the ranked predicted risks calculated by the models. Thirdly, the datasets were divided into three groups based on their predicted risk of in-hospital death (low, medium and high risk). For each group the observed mortality rate was compared with the mortality rate predicted by the risk model and goodness-of-fit was evaluated using a $\chi 2$ test. Model discrimination was evaluated by calculating the ROC curve, which is summarised by

211 Hosmer D, Lemeshow S. Applied Logistic Regression. John Wiley: New York, 1989

the area under the curve (AUC)[212]. In all cases, $P < 0.05$ was considered significant. All statistical analyses were carried out using SAS software for Windows, version 9.3 (SAS Institute Inc., Cary, NC, USA).

12.1.5 Patient Characteristics

In total 8641 records were identified as meeting the study criteria. Two records were missing in-hospital mortality status and were excluded, leaving 8639 records for analysis. Over the six year study period 44 hospitals contributed data. The largest contribution from a single centre was 638 cases and the smallest contribution from a single centre was two. A summary of patient characteristics is shown in Table 12.1.5. There were 775 in-hospital deaths giving an in-hospital mortality rate of 8.97% (95% CI = 8.35% to 9.63%). There were 5463 elective patients identified with 250 deaths (4.6% (95% CI = 4.0% to 5.2%)) and 3176 non-elective patients with 525 deaths (16.5% (95% CI = 15.3% to 17.9%)).

12.1.6 Univariable and Multivariable Analyses

Risk factors for in-hospital mortality based on univariate analysis are shown in Tables 12.1.5 and 12.1.6a. The final risk prediction models with estimated model coefficients, odds ratios, approximate 95% CI, corresponding P values, and the model equation itself are shown in Tables 12.1.6b and 12.1.6c.

212 Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982; 143: 29–36

12.1.7 Overall Performance of the Risk Models

Both models demonstrated good calibration according to the Hosmer–Lemeshow $\chi 2$ (elective model P = 0.427 and non-elective model P = 0.616. The calibration plots for both models are shown in Figure 12.1.7. and demonstrated good calibration for both models. The low, medium and high risk group assessments also supported the assumption of satisfactory calibration for both models as shown in Table 12.1.7. The AUC for the elective model was 0.805 (95% CI: 0.802 to 0.807), for the non-elective model the AUC was 0.761 (95% CI: 0.761 to 0.765) with bias-corrected values calculated using the bootstrap method of 0.795 and 0.756, respectively, indicating good discrimination

The risk models share five common risk factors: age, additional CABG surgery, poor ejection fraction, preoperative arrhythmia and previous cardiac surgery. These factors will be familiar to healthcare professionals involved in the care of patients with cardiac disease and are well represented in previously developed risk models [213,214,215,216]24, 26, 27, 28. It is no surprise that older, sicker patients with more complicated presentation are at an increased risk of in-hospital mortality. Among the elective cohort, the remaining factors of lung disease, female gender, NYHA class, current smoker, neurological disease, triple vessel disease, surgery on the aortic arch and more complicated pathologies are similarly understandable contributors to increased patient risk. Within the non-elective model: renal disease, peripheral vascular disease, cardiogenic shock and increasingly critical presenting priority are all intuitively reasonable inclusions.

213 Huijskes RV, Wesselink RM, Noyez L, Rosseel PM, Klok T, van Straten BH, Nesselaarg A and Tijssen JG. Predictive models for thoracic aorta surgery. Is the Euroscore the optimal risk model in the Netherlands? Interactive cardiovascular and thoracic surgery 4(6) (2005): 538-542.
214 Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR and Lockowandt U. Euroscore II. European Journal of Cardio-Thoracic Surgery 41 (2012) 1–12
215 Roques F, Nashef SA, Michel P, Gauducheau E, de Vincentiis C, Baudet E et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15:816–22; discussion 22–3
216 Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999;16:9–13.

12.2 National Outcomes in Acute Type A Dissection

This section aims to report the national UK outcomes in the operated ATAD patients' population and explore the relationship between adjusted in-hospital mortality for ATAD repair and case volume at both a hospital and surgeon level.

12.2.1 NICOR Database

For this section, records were included that corresponded to the following criteria: operation on one or more of the root, ascending or arch aortic segments with a recorded pathology of Acute Dissection that were performed in England and Wales between 1st April 2007 and 31st March 2013. Records missing responsible consultant cardiac surgeon data (recorded in the form of General Medical Council registration number) or vital status at discharge were excluded.

12.2.2 Study and Outcome Variables

For each operation, data are recorded on patient characteristics, comorbidities, surgical team, intraoperative factors and postoperative outcomes. For this study, we extracted data on patient age at the time of operation (years), gender, body mass index [BMI, defined as weight (kg) / height2 (m2)], Canadian Cardiovascular Society (CCS) angina class, dyspnoea (dichotomised as New York Heart Association (NYHA) grade < III and NYHA grade ≥ III), recent myocardial infarction (defined as within 90 days of surgery), history of major cardiac surgery, diabetes (diet- or insulin controlled), smoking status, history of hypertension, serum creatinine >200 μmol/l, history of renal dysfunction, history of pulmonary disease, history of neurological dysfunction, extracardiac arteriopathy, preoperative heart rhythm,

left ventricular ejection fraction (classified as <30, 30–50 and >50%), use of preoperative IV nitrates, IV inotropes prior to anaesthesia, preoperative ventilation, pre-operative cardiogenic shock, operative urgency, concomitant CABG and valve procedures, cardiopulmonary bypass time, aortic cross-clamp time and circulatory arrest time. Operative times were dichotomised using the third quartile as an upper boundary, rounded to the nearest five minutes. Administrative data were also extracted including: patient admission, procedure and discharge dates, responsible consultant cardiac surgeon and anonymised hospital identifier.

The outcome for this study was in-hospital mortality, defined as death due to any cause during admission to the base hospital for cardiac surgery. Follow-up data up until the point of discharge was collected by the NACSA clinical registry system. Data on cause of death were unavailable.

12.2.3 Statistical Analysis

Categorical and dichotomous variables are summarized as absolute number and percentage. Non-normally distributed continuous data are summarized as median and inter-quartile range (IQR). The univariate associations of each variable to in-hospital mortality are reported as odds ratios with 95% confidence intervals (CIs) along with their respective p-values. Due to the relatively low number of missing data items for the majority of the variables, missing data was assumed not to be present for binary variables and imputed with the mean value for continuous variables before calculations were performed. Where categorical comparisons are made, the chi-squared test was used to obtain p-values. Scatterplots were generated to assess the relationship between observed in-hospital mortality and volume, and locally weighted scatterplot smoothing (LOWESS) curves for visual inspection were included.

12.2.4 Characteristics of the Study Population

1632 patients were identified from the NACSA database as having an aortic dissection during the time period. After excluding patients who had surgery on the descending and thoracoabdominal segments of the aorta, and records that lacked discharge or responsible clinician data, a total of 1386 patients were included in the study. These patients were admitted to 33 different hospitals throughout England and Wales and were under the care of by 218 different consultant cardiac surgeons. During this time period, the mean number of acute dissection operations performed by a hospital was 42, with 21 out of 33 (63.6%) performing fewer than 40 operations. The minimum hospital activity was 8 and the maximum activity was 103. The average number of operations performed by a surgeon was 6.4, with 171 of 218 surgeons (78.4%) performing fewer than 10 operations. The minimum surgeon activity was 1 (34 (15.6%) of surgeons performed a single acute dissection operation) and the maximum activity was 32.

The median age of the patient cohort was 63 (Q1 = 52, Q3 = 72), 446 (32.2%) were female, 1362 (98.3%) of patients were recorded as being non-elective priority, with 97 (7.0%) being salvage operations. 463 (33.4%) underwent a procedure that involved the aortic root segment, 1202 (86.7%) the ascending aorta segment and 176 (12.7%) the aortic arch segment. 569 (41.1%) had a concomitant cardiac valve operation and 181 (13.1%) a concomitant CABG. The median cardiopulmonary bypass time was 197 (Q1 = 152, Q3 = 257) minutes. Patient pre-operative and operative characteristics are shown in Tables 12.2.4a and 12.2.4b.

12.2.5 Univariate Predictors of in-Hospital Mortality by Patient-Level Factors and Clinical Factors

Unadjusted associations between patient-level characteristics and in-hospital mortality from univariate logistic regression analyses are shown in Tables 12.2.4a and 12.2.4b. The following pre-operative characteristics were found to be associated with in-hospital mortality: age, NYHA class ≥ III, previous MI, recent MI, previous cardiac surgery, preoperative creatinine > 200 μmol/L, history of renal dysfunction, peripheral vascular disease, pre-operative non-sinus heart rhythm, impaired left ventricular ejection fraction, pre-operative IV inotropes, pre-operative ventilation and pre-operative cardiogenic shock. The following operative characteristics were found to be similarly associated with in-hospital mortality: salvage operation, concomitant CABG operation, cardiopulmonary bypass time, circulatory arrest time and operating consultant having fewer than 10 acute dissections in the dataset.

12.2.6 Patient Outcomes

In-hospital mortality occurred in 246 (17.7%) patients and 165 (11.9%) suffered a post-operative stroke. 7 (0.5%) patients suffered paraparesis and 3 (0.2%) paraplegia. 198 (14.3%) patients required post-operative dialysis. 236 (17.0%) required a return to theatre during their hospital stay with the majority of these being for bleeding (n=198; 14.3%). Outcome data is presented in Table 12.2.6. Figure 12.2.6a. and 12.2.6b show the relationship between acute dissection volume and in-hospital mortality for hospitals and consultant cardiac surgeons, respectively.

12.2.7 Medium Term Survival

Along with in-hospital mortality, survival rates at 90 days, 1 year and 3 years are shown in Table 12.2.7. Responsible consultant activity is categorised into 3 groups: 1 to 9 operations, 10 to 19 operations and >20 operations over the study period. In-hospital mortality rates in the lower activity group are 20.2% vs. 13.2% in the higher activity group and similarly at 3 years the mortality rate is 29.2% vs. 21.2%. Associated p-values suggest that this difference has some statistical significance at 0.049 and 0.047, respectively.

Table 12.2.7. Survival rates by consultant activity

	Overall (n=1386)	**1 - 9 procedures (n=699)**	**10 - 19 procedures (n=536)**	**20 or more procedures (n=151)**
In-hospital mortality	246 (17.8)	141 (20.2)	85 (15.9)	20 (13.2)
90 day mortality	286 (20.6)	160 (22.9)	102 (19.0)	24 (15.9)
1 year mortality	332 (24.0)	182 (26.0)	121 (22.6)	29 (19.2)
3 year mortality	368 (26.6)	204 (29.2)	132 (24.6)	32 (21.2)

12.3 Is the Volume-Outcome Relationship Cost-Effective and Can It be a Template of Quality Improvement in Acute Type A Aortic Dissection and Aortic Arch Surgery.

In 2007, a specialised aortic service line was established at our institution in response to perceived poor outcomes from acute Type A aortic dissection repair. Prior to the change all elective and emergency aortic surgery were performed by 13 general cardiac surgeons. Following the specialised team formation the majority of elective aortic surgery and all emergency aortic surgery were performed by 4 aortic surgeons. The primary aim was to reduce operative mortality and associated morbidity and consequently to improve long term survival. In addition to improving quality of outcomes, our aim was to assess whether such primary goals were mirrored with cost-effectiveness arm.

12.3.1 Study Population

We identified 135 patients who underwent emergency surgery for acute Type A aortic dissection and 232 patients who underwent aortic arch surgery at our institution between October 1998 and August 2012. Patients were divided into two groups based on the time period in which they were operated. Prior to August 31st 2007 Acute Type A aortic dissection repair (ATADR) and aortic arch surgery was performed by 13 surgeons on a general cardiac on call rota. Subsequent to this date, a specialist aortic on call rota was established with 4 aortic consultants. These surgeons performed the majority of the elective and all non-elective thoracic aortic surgery.

12.3.2 Data Collection

All study data were prospectively entered into an electronic database by the operating surgeon during the study period. The database was validated retrospectively by case notes review. Outcomes evaluated for the purposes of this study included key quality markers as defined by STS (www.sts.org) for coronary surgery: in-hospital mortality, stroke, re-exploration for bleeding, sternal wound infections, renal failure and prolonged ventilation times.

12.3.3 Survival Data

Follow up survival was derived by linking patient records to a national spine via the Demographics Batch Service (DBS). Records were linked using National Health Service number, name, and date of birth, gender and postcode. The DBS returns a variety of patient demographics, including date of death.

12.3.4 Costing Methodology

12.3.4.1 Service Level Reporting & Patient Level Costing Information System

We utilize and employs Patient Level Costing Information System (PLICS) and Service Level Reporting (SLR) systems, enabling detailed micro-costing. SLR allows the hospital to analyze cost and profitability at a patient level of each service it provides rather than just overall profitability. Costs of resources can be directly attributed to particular patient episodes. The use of sophisticated consumables dispensing and supply tracking technologies assigns costs and allows precise tracing of resource use to the patient and episode on which they were used.

Staff time is allocated with reference to employment contracts and the proportion of the time that is to be dedicated to each duty. That is, the cost of a particular surgeon for a given procedure is a function of his salary, the proportion of his contract he is to operate, and the time the procedure takes. Similarly, the ward costs of clinician can be allocated in a similar way. These costs are then allocated based on the observed values of time for each patient episode. Indirect costs such as utilities and hospital overheads are allocated/absorbed – although some of them are not directly attributable to any particular episode /service lines, they are divided up and shared amongst all episodes.

12.3.4.2 Estimation of Costs for pre-SLR Period Patients

Data on clinical outcomes was available for all cases between 1999 and the present day. Resource use identified through PLICS was only obtainable from 2009 due to availability of SLR data from 2009. Costs for the cases prior to 2009 were estimated. The method of cost estimation was as follows. Firstly, preliminary analyses were undertaken to determine the most significant drivers of cost. This required the collaborative involvement of clinicians and members of the finance department to agree which treatment and perioperative processes drive cost. Factors included, "cutting time" (the length of time in surgery), intensive care unit (ICU) length of stay, and ward length of stay were found to be the major drivers of cost. These variables were considered the "cost drivers" accounting for approximately 80% of the true cost. Cost lines such as involving consumables will remain the same on either side of sub specialisation time line, adjusted for inflation and hence are considered irrelevant costs for this study.

12.3.5 Statistical Analysis

Due to non-normal distributions (tested using the Shapiro-Wilk test), continuous variables are shown as median with 25th and 75th percentiles and comparisons were made with Wilcoxon rank-sum tests. Categorical variables are shown as a percentage and comparisons were made with chi-squared tests or Fisher's exact tests as appropriate. Patients from the pre-specialisation era were propensity-matched with unique post-specialisation patients. To do this, logistic regression was used to develop a propensity score.

The propensity score was constructed using all the pre-operative variables listed in Table 12.3.5. In all cases a p-value less than 0.05 was considered significant. All statistical analyses were performed with SAS for Windows Version 9.2 (SAS, Cary, NC).

12.3.6 Patient Characteristics

Patient preoperative and operative characteristics for ATAD and aortic arch surgery are shown in Table 12.3.5 and table 12.3.6 respectively. In the unmatched groups of ATAD, there was a higher incidence of hypertension and cerebrovascular disease in the pre-subspecialisation era (both p=0.01). For the aortic arch group NYHA class III and above and respiratory disease was significantly higher but was not evident post match. For both aortic arch surgery and ATAD the operative variables, cardiopulmonary bypass and aortic cross clamp time were all significantly increased in the post- subspecialisation era (p=0.002, p<0.001 and p=0.001, respectively). The propensity-matched analysis provided 51 patients from the post-subspecialisation era successfully matched to 51 who were operated on pre-subspecialisation.

The patient characteristics of the propensity matched groups are also in Table 12.3.5 and table 12.3.6, showing both groups were well matched with respect to major preoperative characteristics such as age, gender, left ventricular function and comorbidities such as: diabetes, peripheral vascular disease, respiratory and renal dysfunction. Previous cardiac surgery and BMI were also well matched.

12.3.7 Patient Outcomes

There was no difference in the extent of procedures performed pre and post-subspecialisation after matching. However, operative times, cardiopulmonary bypass times and aortic cross clamp times were significantly longer in the post–subspecialisation cohort after matching in ATAD patients however this was only true of aortic cross clamp time in the Arch Surgery group.

Patient outcomes are shown in Table 12.3.7a. and 12.3.7b. for ATAD and aortic arch respectively. Patients who underwent repair of acute Type A aortic dissection in the post-subspecialisation era were less likely to suffer in-hospital mortality in both the matched and unmatched groups (p=0.001 and p=0.007, respectively). Fourteen (17.5%) patients suffered a post-operative permanent stroke in the pre-subspecialisation cohort, compared to only five (9.6%) patient's post-subspecialisation (p=0.21). In the aortic arch surgery group, the significant outcomes from the post-match were; renal failure, prolonged ventilation and composite outcome (mortality, stroke, prolonged ventilation or renal failure) (Table 12.3.7b.).

Re-operation for bleeding was performed in 10 (13%) patients in pre-subspecialisation compared to 5(9.6) patients in post-subspecialisation (p=0.58) for ATAD. Intensive care unit and hospital length of stay were different between the 2 groups in ATAD however, when aligned using propensity matching there was no statistical significance.

Table 12.3.7a. Patient Outcomes in Acute Aortic Dissection

	Before Match			After Match		
	Pre-Subspecialisation (n=80)	**Post-Subspecialisation (n=55)**	**P value**	**Pre-Subspecialisation (n=51)**	**Post-Subspecialisation (n=51)**	**P value**
ITU stay (days)	4 (2, 7)	5 (2, 15)	0.06	5 (2, 8)	5 (2, 15)	0.07
Post-operative stay (days)	12 (7, 19)	13 (10, 28)	0.26	12.5 (7, 23)	13 (10, 27)	0.27
Re-exploration for bleeding	10 (12.5)	5 (9.1)	0.54	6 (11.8)	5 (9.8)	0.75
Prolonged ventilation (> 48 hours)	26 (32.5)	5 (9.1)	0.002	17 (33.3)	5 (9.8)	0.004
Renal failure	21 (26.3)	6 (10.9)	0.03	16 (31.4)	6 (11.8)	0.02
Stroke	14 (17.5)	5 (9.1)	0.17	7 (13.7)	5 (9.8)	0.54
In-hospital mortality	27 (33.8)	5 (9.1)	0.001	16 (31.4)	5 (9.8)	0.007

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;

Categorical data shown as percentage (number), comparisons made with Chi-square tests and Fishers exact tests as appropriate

Table 12.3.7b. Patient Outcomes in Aortic Arch Repair

	Before Match			After Match		
	Pre-Subspecialisation (n=73)	Post-Subspecialisation (n=159)	P value	Pre-Subspecialisation (n=71)	Post-Subspecialisation (n=71)	P value
ITU stay (days)	3 (2, 5)	3 (1, 6)	0.29	3 (2, 5)	3 (1, 5)	0.28
Post-operative stay (days)	11 (9, 16)	10 (7, 16.5)	0.04	11 (9, 18)	10 (7, 15)	0.14
Re-exploration for bleeding	7 (9.6)	7 (4.4)	0.14	7 (9.9)	5 (7.0)	0.55
Prolonged ventilation (> 48 hours)	14 (19.2)	9 (5.7)	0.001	13 (18.3)	3 (4.2)	0.008
Renal failure	11 (15.1)	3 (1.9)	<0.001	11 (15.5)	2 (2.8)	0.009
Stroke	6 (8.2)	5 (3.1)	0.10	6 (8.5)	1 (1.4)	0.12
In-hospital mortality	6 (8.2)	8 (5.0)	0.38	6 (8.5)	1 (1.4)	0.12
Composite outcome (Mortality, Stroke, Prolonged ventilation or Renal failure)	18 (24.7)	22 (13.8)	0.043	17 (23.9)	6 (8.5)	0.01

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;
Categorical data shown as percentage (number), comparisons made with Chi-square tests and Fishers exact tests as appropriate

12.3.8 Survival

Mid-term survival is shown in Figure 12.3.8a. and Figure12.3.8b. We found a significant improvement in 5-year survival for the pre and post-subspecialisation in both matched and unmatched patients (p=0.002 and p=0.01, Log-Rank test).

12.3.9 Cost Drivers

Table 12.3.9a. displays the median (IQR) comparisons of relevant costs were £28,784 (£21,431, £44,381) pre-subspecialisation compared to £31,648 (£20,184, £47,882) in a matched group of patient's post-subspecialisation, p=0.70 for ATAD. In addition, Table 12.3.9b. displays the median (IQR) comparisons of relevant costs for aortic arch surgery cost. This reveals that cost comparison between the two groups was non-significant and cost neutral. The improvement in the outcomes and survival between the two groups was cost effective.

The average cost per patient in the post–subspecialisation era has not varied significantly. With no notable change in resource cost resulting from the change in the clinical re-organization, it is perhaps reasonable to deduce that the introduction of subspecialisation was cost neutral to the hospital.

The improvement in clinical outcomes would seem to have two separate effects on costs. The effect of reduced mortality is, "ceteris paribus", an increase in length of stay and therefore an increase in costs. However, also present is the effect of a reduction in adverse events and other complications, which works to reduce length of stay by improving recovery time. Another consequence is that where mortality is not avoided, it may be postponed, thereby increasing the average length of stay.

Table 12.3.9a. Patient Cost in Acute Aortic Dissection (currency shown as £ sterling)

	Before Match			After Match		
	Pre-Subspecialisation (n=80)	**Post-Subspecialisation (n=55)**	**p value**	**Pre-Subspecialisation (n=51)**	**Post-Subspecialisation (n=51)**	**P value**
Cost Drivers						
Critical Care	8185 (3727, 13863)	9235 (4180, 24475.5)	0.19	8185 (3274, 14630)	8020 (4180, 25236)	0.25
Theatre costs	6762 (4713, 9207)	6932.5 (5705, 9234)	0.27	7450 (5272, 9241)	7037 (5751, 9234)	0.75
Ward costs	2103 (1176, 3490.5)	2101.5 (1611, 4323.5)	0.34	1911 (1176, 3675)	2058 (1584, 3829)	0.42
Other Costs						
Pathology	785 (366, 1334.5)	809.5 (418, 1881)	0.29	785 (314, 1463)	748 (418, 1881)	0.22
Medical Staffing	2332.5 (1474.5, 3289)	2660 (1850, 3369)	0.62	2689 (1625, 3372)	2710 (1927, 3369)	0.71
Other Clinical Supplies & service	4460 (2295.5, 10949)	4043 (2579.5, 10767)	0.48	8404 (2409, 11642)	4109 (2561, 11642)	0.10
Other Diagnostics	149 (86, 224)	168 (109, 227.5)	0.57	144 (88, 243)	163 (108, 224)	0.56
Pharmacy services	198 (104, 305.5)	234 (151.5, 413.5)	0.21	195 (104, 324)	216 (142, 387)	0.38
Therapies	390 (224.5, 584.5)	426.5 (261, 870)	0.46	377 (232, 667)	404 (239, 841)	0.45
Total relevant costs	26428 (19152.5, 40873.5)	31131 (20273, 47882)	0.22	28784 (21431, 44381)	31648 (20184, 47882)	0.70

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;

Table 12.3.9b. Patient Cost in Aortic Arch Repair (currency shown as £ sterling)

	Before Match			After Match		
	Pre-Subspecialisation (n=73)	**Post-Subspecialisation (n=159)**	**p value**	**Pre-Subspecialisation (n=71)**	**Post-Subspecialisation (n=71)**	**p value**
Cost Drivers						
Critical Care	3531 (2354, 5885)	3531 (1839, 7520)	0.99	3531 (2354, 5885)	3531 (1968, 8239)	0.85
Theatre costs	5996 (5358, 7120)	6556 (5034, 8226)	0.17	5996 (5358, 7120)	6554 (4855, 7691)	0.49
Ward costs	2769 (2130, 3834)	2343 (1704, 3834)	0.04	2769 (2130, 3834)	2537 (1917, 4473)	0.38
Other Costs						
Pathology	416 (338, 624)	391 (260, 641)	0.17	416 (338, 624)	380 (260, 588)	0.09
Medical Staffing	1948 (1740, 2313)	2129 (1661, 2534)	0.27	1948 (1740, 2313)	2146 (1749, 2513)	0.25
Other Clinical Supplies & service	2841 (2539, 3374)	3106 (2394, 3622)	0.42	2841 (2539, 3374)	3110 (2471, 3671)	0.41
Pharmacy services	208 (169, 312)	192 (130, 324)	0.15	208 (169, 312)	196 (130, 351)	0.55
Therapies	240 (195, 360)	207 (135, 409)	0.08	240 (195, 360)	248 (150, 482)	0.99
Total relevant costs	18812 (15896, 22666)	19579 (15495, 26017)	0.46	18812 (15804, 23422)	19579 (15504, 26640)	0.49

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;

12.4 Contemporary Hospital Outcomes and Survival Following Open Aortic Arch Surgery in a Specialized UK Thoracic Aortic Centre

As a marker for comparison between open arch surgery and the endovascular approach the aim of this section is not to draw bench-marking among LHCH and those around the country, however, it's to illustrate our experience and practice in addition to documenting our outcomes in terms of mortality, postoperative morbidity and survival. It's also our aim to demonstrate that provided the expertise and the available resources open repair aortic arch surgery outcomes in the UK could be of international standards.

12.4.1 Study Population

This study looked at all patients who had undergone aortic arch surgery under deep hypothermic circulatory arrest with the aid of cardiopulmonary bypass.
All study data were entered into an electronic database by the operating surgeon, prospectively during the period of the study (June 1999 - November 2012). The database was validated retrospectively by a case notes review.

12.4.2 Data Collections and Outcomes

Methods of data collection and definitions have been published previously. In brief, each operation had a dataset collected that included relevant demographics, indicators of heart disease severity, acuity, comorbidities and procedural details along with all relevant in-hospital outcomes. Outcomes evaluated for the purposes

of this study included in-hospital reoperations, sternal wound infections, neurological and renal complications, post-operative ventilation times and in-hospital mortality. In-hospital outcomes and survival were stratified by elective and non-elective total arch replacement (TAAR) and elective and non-elective hemiarch replacement (HAAR), (Figure 11.5). Receiver operating characteristic (ROC) analysis was also performed to establish a suitable age cut-off for elective follow up survival, which is also presented. Follow up survival was derived by linking patient records to a national spine via the Demographics Batch Service (DBS). Records were linked using National Health Service number, name, and date of birth, gender and postcode. The DBS returns a variety of patient demographics, including date of death.

12.4.3 Statistical Analysis

Continuous data are shown as median (inter-quartile range), comparisons are made using Wilcoxon's Signed Rank tests and students t-tests as appropriate. Categorical variables are shown as frequency and percentage, comparisons are made with chi-squared tests and Fisher's exact tests as appropriate. Follow-up mortality rates are presented using the Kaplan-Meier method. In all cases a p-value less than 0.05 was considered significant. All statistical analyses were performed with SAS for Windows Version 9.2 (SAS, Cary, NC).

12.4.4 Patient Characteristics

Of the 276 patients analysed (Figure 12.4.4.), 110 (39.9%) underwent TAAR and 166 (60.1%) underwent HAAR. 35 (31.8%) of the TAAR and 26 (15.7%) of the HAAR operations were performed non-electively. Patients were mostly male (60.1%) and had a median age of 61.2 (range, 16.7 to 87.3) years. Patient characteristics, co-morbidities and aortic aetiologies are collected in Table 12.4.4. Notable differences between the elective and non-elective TAAR groups include; a higher proportion of

current smokers and patients with a left ventricular ejection fraction between 30% and 50% in the non-elective group (9.3% vs. 28.6%; p=0.009 and 8.0% vs. 22.9%; p=0.06, respectively), together with a higher proportion of patients with respiratory disease in the elective group (40.0% vs. 14.3%; p=0.007) and a higher proportion of patients having undergone previous cardiac surgery (32.0% vs. 14.3%; p=0.0495). In the HAAR procedures, non-elective patients were more likely to suffer from renal dysfunction and peripheral vascular disease (2.1% vs. 19.2%; p=0.003 and 4.3% vs. 15.4%; p=0.052, respectively), while elective patients were more likely to suffer from hypercholesterolaemia (55.0% vs. 19.2%; p=0.001).

12.4.5 Operative Procedures

Repair of the ascending aorta was the most common concomitant procedure (Table 12.4.5a), it was performed respectively in 97.3% and 94.3% of elective and non-elective TAAR, and in 99.3% and 100% of elective and non-elective HAAR. Operative times were typically observed to be shorter in the elective groups (also Table 12.4.5b), time on cardiopulmonary bypass for non-elective patients saw a significant increase in both the TAAR and HAAR cohorts (358 minutes (IQR, 272 to 435) vs. 398 minutes (IQR, 338 to 479); p=0.006 and 299 minutes (IQR, 256 to 341) vs. 340 minutes (IQR, 283 to 440); p=0.004, respectively). In the HAAR cohort, median circulatory arrest times were significantly lower in elective patients compared to non-elective (29 minutes (IQR, 23 to 36) vs. 46 minutes (IQR, 26 to 66); p<0.001).

Table 12.4.5a Operative Variables and Times

Variable	Total Arch Replacement			Hemi-Arch Replacement		
	Elective (n=75)	Non-elective (n=35)	p-value	Elective (n=140)	Non-elective (n=26)	p-value
Concurrent procedures						
Aortic valve replacement	49 (65.3)	21 (60.0)	0.59	112 (87.1)	21 (80.8)	0.37
Aortic root	43 (57.3)	20 (57.1)	0.99	104 (74.3)	18 (69.2)	0.59
Ascending	73 (97.3)	33 (94.3)	0.59	139 (99.3)	26 (100)	>0.99
Other concomitant procedure	10 (13.3)	5 (14.3)	>0.99	29 (20.7)	5 (19.2)	0.86
Operative times						
Circulatory arrest	71 (56, 99)	88 (62, 120)	0.11	29 (23, 36)	46 (26, 66)	<0.001
Cardiopulmonary bypass	358 (272, 435)	398 (338, 479)	0.006	299 (256, 341)	340 (283, 440)	0.004
Aortic crossclamp	205.5 (135, 267)	219 (157, 305)	0.35	174 (138, 207)	190.5 (149, 209)	0.25

Categorical variables shown as n (%), comparisons made with chi-squared and Fisher's exact tests as appropriate;

Continuous variables shown as median (25th percentile, 75th percentile), comparisons made with Wilcoxon's Signed Rank test and t-tests as appropriate

A conventional elephant trunk (ET) procedure was performed in 49.3% and 37.1% of elective and non-elective TAAR procedures respectively. ET activity and outcomes, including frozen and reverse procedures, are shown in Table 12.4.5b.

Table 12.4.5b Elephant Trunk (ET) Post-Operative Complications

Variable	Total Arch Replacement		
	Elective (n=75)	Non-elective (n=35)	p-value
Conventional ET	**37 (49.3)**	**13 (37.1)**	**0.23**
Stroke	2/37 (5.4)	1/13 (7.7)	>0.99
In-hospital mortality	4/37 (10.8)	1/13 (7.7)	>0.99
30 day mortality	3/37 (8.1)	1/13 (7.7)	>0.99
Frozen ET	**7 (9.3)**	**5 (14.3)**	**0.52**
Stroke	0/7 (0)	0/5 (0)	-
In-hospital mortality	0/7 (0)	1/5 (20.0)	0.42
30 day mortality	0/7 (0)	1/5 (20.0)	0.42
Reverse ET (2nd stage)	**2 (2.7)**	**0 (0)**	**>0.99**
Stroke	0/2 (0)	0 (0)	-
In-hospital mortality	0/2 (0)	0 (0)	-
30 day mortality	0/2 (0)	0 (0)	-

Categorical variables shown as n (%), comparisons made with chi-squared and Fisher's exact tests as appropriate

12.4.6 Outcomes

In the TAAR group, in-hospital mortality occurred in 6.7% of elective patients and 25.7% of non-elective patients (p=0.01). In the HAAR group, in-hospital mortality occurred in 2.1% of elective patients and 19.2% of non-elective patients (p=0.003). Post-operative stroke occurred in 4.0% of elective TAAR's and 14.3% of non-elective (p=0.11), 2.9% of elective HAAR's suffered a stroke compared with 11.5% non-elective (p=0.08), as shown in Table 12.4.6.

Median intubation times were significantly shorter in elective TAAR patients when compared to non-electives (16 hours (IQR, 12 to 38) vs. 27.5 hours (IQR, 16 to 99.5); p=0.045). Median ITU stay was significantly longer in non-elective HAAR patients when compared to electives (4 days (IQR, 3 to 13.5) vs. 2 days (IQR, 1 to 4); p=0.001). Significantly higher rates of postoperative bleeding requiring reoperation were seen in non-elective HAAR patients when compared to electives (19.2% vs. 4.3%; p=0.015). Similar postoperative rates of acute renal failure were seen when comparing priority in the TAAR group (6.7% vs. 22.9%; p=0.02). Figure 12.4.6a. and Figure 12.4.6b. respectively show the 5-year survival for TAAR stratified by priority and, in the elective group only, age <65 or >=65. After an early divergence, the survival curves based on priority reintersect and ultimately result in no significant difference (p=0.69).

Elective survival based on age, however, does result in significantly poorer outcomes in the older group (p=0.006). Figure 12.4.6c and Figure 12.4.6d. similarly show the 5-year survival for HAAR stratified by priority and, in the elective group only, age <65 or >=65.

In this cohort, the non-elective group have consistently poorer survival over 5 years than the elective group (p=0.03). But in contrast to the TAAR cohort, elective survival based on age does not result in any significant difference (p=0.16). In our conventional ET subcategory, 5 patients died in-hospital; 4 (10.8%) were elective and 1 (7.7%) was non-elective (p>0.99).

12.4.7 Paraplegia Rate

No patients sustained paraplegia or paraparesis.

12.4.8 Our Hospital Outcome

This is the first UK publication of detailed outcomes and survival from a series of contemporary patients undergoing aortic arch surgery in a specialized thoracic aortic centre. Acute aortic dissection patients have been excluded from this series unless documentation of a formal hemiarch or total arch surgery took place. Typically, these patients have a simple open distal anastomosis under circulatory arrest.

12.4.9 Hemiarch versus total Arch

Median age of elective patients was not significantly different at 64.3 (53.7, 71.9) versus 64.5 (46.4, 71.0) respectively. Elective hospital mortality is very acceptable at 1.5% and 7.5% respectively for hemiarch and total arch surgery. Similarly stroke rate was 3% versus 4.5% in elective patients. A high proportion of both groups underwent concomitant procedures on the aortic valve, root and ascending aorta. Not unsurprisingly, the need for arch vessel reimplantation results in longer periods on cardiopulmonary bypass and deep hypothermic circulatory arrest with consequent higher morbidity and mortality.

12.4.10 Elective versus Non-Elective

Non-elective surgery was associated with much high mortality and morbidity. Mortality and stroke rate for total arch as an urgent/emergency were 31% and 17.2 % respectively. For hemiarch these were 20% and 12% respectively. This reflects the nature of emergency work with acute Type A dissection, leaking aneurysms, pseudoaneurysms and endocarditis.

12.4.11 Elephant Trunk Procedures

More than 50% of our elective and non-elective patients undergoing total arch replacement underwent some form of elephant trunk procedure. A proportion (43.1%) of these were "prophylactic" and simply placed to aid possible further surgery on the thoracoabdominal aorta. Others (31.4%) were placed with the intention of a planned second stage intervention on the descending thoracic aorta allowing guaranteed placement of a proximal clamp and left heart bypass rather than cardiopulmonary bypass. Mean delay between first and second stages was 12.4 months.

12.5 Influences on Early and Medium-Term Survival Following Surgical Repair of the Aortic Arch

Surgery to replace the proximal or total aortic arch has become relatively commonplace, with many examples of international centers publishing excellent morbidity and mortality outcomes in large series**254256**[217,,218] compared with the very early series[96]. Underpinning these patient outcomes are a host of improvements in surgery, anaesthesia, nursing, perfusion, and intensive care, all well described by Coselli and LeMaire [219]in *Aortic Arch Surgery: Principles, Strategies and Outcomes*. This success with clinical morbidity and mortality outcomes has allowed the development of more sophisticated quality measures of the "process" and "structure" of care delivered by institutions published in the form of guidelines on performing and reporting of thoracic aortic surgery [220].

217 Estrera AL, Miller CC 3rd, Lee TY, Shah P, Safi HJ. Ascending and transverse aortic arch repair. *Circulation*. 2008; 118:S160–S166

218 Ma WG, Zhu JM, Zheng J, Liu YM, Ziganshin BA, Elefteriades JA, et al.. Sun's procedure for complex aortic arch repair: total arch replacement using a tetrafurcate graft and stented elephant trunk implantation. *Ann Cardiothorac Surg* 2013; 2:642–648.

219 Coselli JS, LeMaire SA. Aortic arch surgery: principles, strategies and outcomes, Ed 1. London: Blackwell Publishing Ltd, 2008.

220 Svensson LG, Adams DH, Bonow RO, Kouchoukos NT, Craig Miller D, O'Gara PT, et al.. Aortic valve and ascending aorta guidelines for management and quality measures. *Ann Thorac Surg*. 2013; 95:1–66.

However, reporting of contemporary survival following aortic arch surgery, and the factors which influence it, remains limited [165,221].

This work has three aims: 1) report, compare and analyse our morbidity and mortality outcomes for hemiarch and total aortic arch surgery; 2) examine the survival benefit of hemiarch and total aortic arch surgery compared to age- and sex-matched controls; and 3) define factors which influence survival in these two groups and, in particular, identify those that are modifiable and potentially actionable.

12.5.1 Patient Population and Data

We performed a retrospective study on 287 consecutive patients who underwent aortic arch surgery at Liverpool Heart and Chest Hospital between June 15, 1999 and December 31, 2012. All relevant clinical data were collected prospectively and entered into a local hospital database from which, periodically, core datasets were validated and submitted to The Society for Cardiothoracic Surgery (UK). In brief, for each operation, a dataset was collected that included relevant demographics, indicators of disease severity, acuity, comorbidities, and procedural details, along with all relevant in-hospital outcomes. Outcomes evaluated for the purposes of this study include in-hospital reoperations for bleeding, sternal wound infections, neurological and renal complications, postoperative ventilation times, and both in-hospital and follow-up mortality.

221 Patel HJ, Deeb GM. Open aortic arch reconstruction. Ann Cardiothorac Surg. 2013; 2:181–183. doi:

12.5.2 Preoperative and Postoperative Criteria

Indications for surgery. Indications for isolated elective aortic aneurysm surgery were: aneurysmal size greater than 5.5 cm in nonconnective tissue disorders, size greater than 4.5 cm with connective tissue disorders. Attributable symptoms were an indication for surgery. Other indications were acute aortic syndromes, infection, fistula, and pseudoaneurysms. In patients in whom the principal indication for surgery was severe disease in the aortic valve, mitral valve, or tricuspid valve and/or coronaries, the threshold for intervention on the aorta was lowered to 4.0-4.5 cm. Similarly, when the primary indication for surgery was the aorta, the threshold for cardiac intervention was lowered; i.e., moderate aortic valve disease, one and two vessel or proximal left anterior descending coronary artery disease. Nonelective surgery was performed based on the presence of acute aortic syndrome or decompensation of nonaortic cardiac-related factors such as aortic valve disease and pulmonary oedema or coronary disease with recent non-ST elevation myocardial infarction. We currently adhere to the American Heart Association Guidelines[11] on indications for aortic surgery which, although presented in 2009, broadly reflected our practice prior to publication.

Patient follow-Up. To establish follow-up vital status, patient records were linked to the national Personal Demographic Service (PDS). Patients were matched to the PDS (http://systems.hscic.gov.uk/demographics/pds) based on National Health Service number, patient name and date of birth, gender, and postcode.

12.5.3 Indications for Surgery

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12.5.5 Statistical Methods

Continuous data that are not normally distributed are reported as median (25^{th} percentile, 75^{th} percentile) with Wilcoxon's signed rank test used for comparisons. Categorical variables are shown as frequency and percentage, while comparisons are made with chi-square (χ^2) tests and Fisher‘s exact tests as appropriate.

Follow-up mortality rates are presented using the Kaplan-Meier method[222] and comparisons are made using the log-rank test. Cox proportional hazards analysis with forward stepwise selection of covariates was used to calculate adjusted hazard ratios (HRs). Limits for entry to and removal from the model were set at $P < 0.10$ and $P > 0.05$, respectively. In all cases a p-value less than 0.05 was considered significant. All statistical analyses were performed with SAS for Windows Version 9.2 (SAS Institute, Cary, NC, USA).

12.5.6 Demographic Data

Within the study period we performed a total of 1240 operations on thoracic aortic aneurysms, of which 287 involved the aortic arch and circulatory arrest and were included in this study. Preoperative patient characteristics, including comorbidities and disease etiology, are presented in Table 12.5.6a, along with operative data. "All AAR" (all aortic arch Aneurysms, $n = 287$) is presented in column 1, followed by a spilt of "Elective HAAR" (elective hemi-aortic arch resection) and "Elective TAAR" (elective total aortic arch resection). Nonelective patients undergoing HAAR ($n = 30$) and TAAR ($n = 36$) are described in Table 12.5.6b.

12.5.7 Comorbidities

Of 287 patients included in the present study, 115 (40.1%) of patients were female. Median age was 63.7 years. A total of 76 (26.5%) patients had a New York Heart Association (NYHA) class ≥ III, 100 (34.8%) suffered from respiratory disease, and 48 (16.7%) had undergone a surgical cardiac procedure in the past. There were no major differences in comorbidity as defined between elective hemiarch and total

222 Kaplan E, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958; 53:547–581.

aortic arch patients apart from a slightly higher incidence of peripheral vascular disease in the elective total arch group ($P < 0.03$). Also, previous cardiac surgery was more common in the elective TAAR group (30.9%) versus the elective HAAR group (10%, $P < 0.001$). In the non-elective cohort, all variables were similar apart from a significantly higher incidence of current smoking in the TAAR group (33.3%) versus the HAAR group (6.7%, $P < 0.008$).

12.5.8 Aetiology

A total of 147 (51.2%) patients had simple age-related degenerative disease in which we also included atherosclerotic aneurysms and bicuspid valve syndrome-related aneurysms. Of these, 138 (48.1%) were non-degenerative disease including such diagnoses as Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome, infection, inflammation, and pseudoaneurysms. Two patients had iatrogenic disease. Aetiology was poorly specified in our database, principally because it is often uncertain, and in 13.6%, aetiology was not recorded. There was no significant difference between the TAAR and HAAR elective groups.

12.5.9 Concomitant Procedures

A high proportion of patients required intervention on the aortic valve (76.7%), and this was significantly different between the two elective groups (HAAR, 87.1%; TAAR, 64.2%, $P < 0.001$). This was typically associated with aortic root replacement in the two groups together (76.7%), although this was not statistically different between the two elective groups (Table 12.5.6a). A similar trend was observed in the non-elective cohort (Table 12.5.6b). Coronary artery bypass graft (CABG) was required in 16% of the entire group, and this was not significantly different between elective HAAR and TAAR.

12.5.10 Preoperative Outcomes

Non-normally distributed variables are shown as median (interquartile range); thus, time on cardiopulmonary bypass was 330 (272, 394) min (for completeness, the mean ± standard deviation (SD) was 337.5 ± 98.9 min). Similarly, time for circulatory arrest was 38 (24, 68; 50 ± 38.5) min. Cardiopulmonary bypass time and circulatory arrest time were significantly longer in the TAAR group than in the HAAR group for both elective and non-elective cohorts.

12.5.11 In-Hospital and Survival Outcomes

Median (interquartile range; mean ± SD) stay in intensive care was 3 (2, 6; 6.4 ± 10.7) days, while overall postoperative length of stay in hospital was 11 (8, 17; 15.2 ± 15.4) days. A total of 35 (12.2%) patients remained on mechanically assisted ventilation for more than 48 hours, 21 (7.3%) suffered acute renal failure, 18 (6.3%) patients required a re-exploration for bleeding, 16 (5.6%) patients suffered a stroke [CVA = 13 (4.5%), TIA = 3 (1.1%)], 19 (6.6%) patients experienced postoperative confusion, and there was 1 (0.7%) deep sternal wound infection. A total of 23 (8.0%) patients died in-hospital, and survival at 1, 3 and 5 years was 87.5%, 80.8%, and 79.1%, respectively. The mean (+/- standard error) survival period was 3.9 (0.12) years.

When looking at elective HAAR versus TAAR, the ITU length of stay was significantly longer in the latter group; however, key outcomes such as mortality, stroke, acute renal failure, prolonged ventilation, re-intubation, and re-exploration for bleeding did not reach statistical significance. In-hospital mortality in HAAR and TAAR was significantly and dramatically higher in non-elective groups versus elective groups (Tables 12.5.11a and 12.5.11b)

In-hospital mortality, 30-day mortality, and 1 year and 5-year survival were not different between elective HAAR and TAAR groups.

We matched the 287 patients by age and gender to the UK population life tables available from the United Kingdom Office of National Statistics (http://www.ons.gov.uk/). The resulting Kaplan-Meier chart comparing survival is shown in Figure 12.5.11. The median follow-up period for aortic arch patients was 2.8 years. 11.9a and 11.9b how sex- and age- matched survival broken down into elective HAAR and TAAR.

12.5.12 Univariate and Multivariate Analysis

Table 12.5.12a shows the univariate analysis of risk factors for overall survival. Nine perioperative factors were identified to be statistically significant: age at operation ≥ 65 years (P = 0.007), angina class IV (P = 0.005), NYHA class ≥ III (P = 0.002), diabetes (P = 0.038), respiratory disease (P = 0.02), peripheral vascular disease (P < 0.001), preoperative renal dysfunction (defined as patients with a functioning renal transplant and patients with acute or chronic renal failure or insufficiency; P < 0.001), concurrent CABG operation (P = 0.029), circulatory arrest time > 100 min (P = 0.001), and cardiopulmonary bypass time > 450 minutes (P < 0.001).

Multivariate analysis of patient risk factors revealed 5 variables independently associated with overall follow-up survival (Table 12.5.12b): renal dysfunction [HR = 3.11; 95% confidence interval (CI) = 1.44 to 6.73; P < 0.001], NYHA class ≥ III (HR = 2.25; 95% CI = 1.38 to 3.67; P = 0.002), circulatory arrest time > 100 min (HR = 2.92; 95% CI = 1.57 to 5.43; P = 0.001), peripheral vascular disease (HR = 2.44; 95% CI = 1.25 to 4.74; P = 0.004), and concomitant CABG operation (HR = 2.14; 95% CI = 1.20 to 3.80; P = 0.008) (Table 12.5.12b). The c-statistic for the Cox model was 0.72, indicating an acceptable level of discrimination.

12.5.13 Elephant Trunk Procedures

A total of 117 patients of the entire cohort (81 electives and 36 non-elective) included either a conventional or frozen elephant trunk. Table 12.5.13 shows selected and important clinical outcomes from these procedures. No patients suffered paraplegia following these procedures.

12.5.14 Characteristics of the Cohort

The median age of our patients was 63.7 years with 40.1% being female. Apart from previous cardiac surgery, there were no significant differences in comorbidities between those patients undergoing elective hemiarch and total aortic arch surgery (Table 12.5.6a). In the non-elective patients, current smoking was significantly more common in the total aortic arch group (6.7% versus 33.3%, $P < 0.008$; Table 12.5.6b). Of significant interest in our cohort was the presence of symptoms in the form of breathlessness (NYHA class ≥ III). Typically, thoracic aortic aneurysms have been thought of as largely asymptomatic. This feature of our cohort is multifactorial.

The most likely cause is the high incidence of aortic valve disease with 76.7% of our entire cohort undergoing aortic valve surgery. In addition to that, 16% underwent concomitant coronary artery bypass grafting, thus ischemic heart disease had been a likely additional cause of symptoms. Two other characteristics important in conferring symptoms are the left ventricular dysfunction (ejection fraction < 50% in 20.2%) and the incidence of respiratory disease (34.8%). Current smoking was documented in 13.6% of the entire group. These data confirm that a good proportion of our patients underwent surgery on both symptomatic and prognostic grounds.

This feature is contrary to common dogma that thoracic aortic aneurysm patients are largely asymptomatic, although this is likely true absent the additional factors enumerated above.

The entire cohort of patients (287) undergoing some form of aortic arch surgery under deep hypothermic circulatory arrest had an in-hospital mortality of 8% and stroke rate of 5.6%. Other key outcome measures were prolonged ventilation (12.2%), acute renal failure (7.3%), re-exploration for bleeding (6.3%), and deep sternal wound infection (0.4%). Stroke rate in the entire group was 5.6% with an additional 1.1% suffering TIA and 6.6% confusion.

Our institution has developed a "Quality Outcomes Framework" (QOF), broadly based on Society of Thoracic Surgeons (STS) Quality Performance Measures in cardiac surgery (www.sts.org/quality), for internal reporting of annualized data from aortic arch surgery. Unlike the STS measures, which include indicators of process, structure, and outcome, our QOF concentrates on outcomes, annualized, and is presented as a "Statistical Process Control Chart" (Appendices). These include in-hospital mortality, 30-day mortality and 1-year mortality, stroke, re-exploration, postoperative renal failure, and prolonged ventilation. This mechanism allows us to monitor the stability of our outcomes annually and investigate and modify processes when deviation is observed. These data are presented in Appendices and not only demonstrate our increasing annual activity over time but also the relative stability of outcomes with little influence of the change in service provision from 2007 (see Methods). Stability of outcomes, particularly major morbidity and mortality, is an important platform for interpreting our survival data and the influences on it.

An interesting aspect of our outcomes is seen when the elective hemiarch and total arch cohorts are examined separately. There were no significant differences in our QOF measures of in-hospital mortality, 30-day mortality, 1-year mortality, prolonged ventilation, acute renal failure, re-exploration bleeding, or stroke (Table 12.5.15). Even more surprising, although the absolute differences in these two groups within the nonelective cohort were significantly different (Table 12.5.11b),

the relative difference between hemiarch and total arch were nonsignificant. This has informed our consent process and operative strategies. It gives assurance that organ protection strategies are sufficiently robust to allow resection of the total arch where indicated, at the price of a small but nonsignificantly higher morbidity and mortality.

12.5.15 Survival Outcomes

12.5.15.1 Age- and Sex-Matched Survival

Our data as an entirety show that survival following some form of aortic arch surgery, under hypothermic circulatory arrest, matched to age and sex of the UK population (Fig. 19), is parallel beyond 2 years with a disparity of approximately 20%. The reasons underlying this effect at 2 years are seen in Figure 12.5.15a and Figure 12.5.15b. These figures demonstrate survival in hemiarch and total aortic arch groups matched by age and sex. While the hemiarch group survival is fairly flat and parallel with controls, separated by 10%, the survival in total aortic arch patients is somewhat different, albeit on an expanded Y-axis.

Survival in the total aortic arch group drops off quickly over the first 24 months to approximately 70% and then remains fairly flat out to 5 years. In absolute terms, the 5-year survival of 70% is comparable with other published series[,221,238]; however, the shape of the survival curve for this subset of patients of ours is unusual. The Safi group[165,217] reported a 72% and 71% survival at 5 and 10 years, respectively, from 1991 to 2001. A separate report from the Mount Sinai group described long-term survival in 206 aortic arch patients, reporting a 6-year survival rate of 75%. In a large study of 721 patients followed over 17 years, Patel et al.[221] reported survival at 5 years to be 80%, with 10 and 12-year survival of 65% and 51%, respectively.

Our captured follow-up data systems do not allow us to easily determine the cause of this early attrition in our total arch cohort. Future enquiry will focus on causes of early death in this group and act as a focus of effort to identify modifiable risk factors. For the present, these data allow us to better inform the consent process.

12.5.15.2 Univariate and Multivariate Analysis of Survival

Univariate analysis of the entire cohort found significant relationships between survival and age (65 years), NYHA class ≥ III, diabetes, respiratory disease, peripheral vascular disease, renal dysfunction, concomitant CABG, circulatory arrest time (> 100 min) and cardiopulmonary bypass (> 450 min). Multivariate analysis demonstrated that independent factors associated with survival were renal dysfunction (HR 3.11), NYHA class ≥ III (HR 2.25), circulatory arrest time (> 100 min; HR 2.92), peripheral vascular disease (HR 2.44), and concomitant CABG (HR 2.14).

Safi's group[165],[217] identified increasing age, chronic obstructive pulmonary disease, concurrent unoperated aneurysm, arch involvement, pump time, concurrent aortic valve replacement, and postoperative renal failure to negatively affect survival following aortic arch repair. Interestingly, Crawford's group, of which Safi was a part, published a similar paper on influences on survival in 1989 [223], showing independent predictors of follow-up survival were: aneurysm symptoms, preoperative angina, extent of proximal replacement, associated residual distal aneurysm, balloon pump, renal dysfunction, cardiac dysfunction, and stroke. Several predictors of late mortality identified by Patel et al. [221] included increasing age, preoperative renal function, history of CABG or descending aortic replacement, prolonged circulatory arrest time, and postoperative tracheostomy.

223Crawford ES, Svensson LG, Coselli JS, Safi HJ, Hess KR. Surgical treatment of aneurysm and/or dissection of the ascending aorta, transverse aortic arch and ascending aorta and transverse arch. Factors influencing survival in 717 patients. J Thorac Cardiovasc Surg. 1989; 98:659–673.

12.5.15.3 Independent Influences on Survival

- **NYHA class ≥ III.**

The finding of NYHA class ≥ III+ as an independent risk factor for survival (HR 2.25, P < 0.002) is most likely a surrogate marker for a multitude of pathologies underlying this symptom—a composite variable—which independently are not significant. These include aortic valve disease, ischemic heart disease, impaired left ventricular function, and respiratory disease. By far, the largest proportion of patients, however, required aortic valve replacement, but this did not come out as an independently significant variable with respect to survival. A recent study examining NYHA class at the time of aortic valve repair (AVR) for severe aortic stenosis[224] demonstrated that patients with NYHA III–IV had significantly impaired short- and long-term survival compared to those with NYHA I–II, even with preserved left ventricular function. Ischemic heart disease, ventricular dysfunction, and respiratory compromise might all be expected to negatively impact prognosis independent of aortic disease. A study by Leavitt et al. 2006[225] has shown that in patients who have undergone CABG, survival over 10 years is significantly impaired in those patients with a diagnosis of COPD. Similarly, survival has been shown to be impacted by ischemic heart disease and ventricular dysfunction[226].

Unlike most series, a good proportion of our patients were symptomatic from concomitant disease rather than aneurysm per se, and these data suggest that earlier intervention before development of symptoms is appropriate. Interestingly,

224 Piérard S, de Meester C, Seldrum S, Pasquet A, Gerber B, Vancraeynest D, et al.. Impact of preoperative symptoms on postoperative survival in severe aortic stenosis: implications for the timing of surgery. *Ann Thorac Surg*. 2014; 97:803–809

225 Leavitt BJ, Ross CS, Spence B, Surgenor SD, Olmstead EM, Clough RA, et al.. Long term survival of patients with chronic obstructive pulmonary disease undergoing coronary artery bypass surgery. *Circulation*. 2006; 114:1430–1434

226 Emond M, Mock MB, Davis KB, Fisher LD, Holmes DR Jr, Chaitman BR, et al.. Long-term survival of medically treated patients in the Coronary Artery Surgery Study (CASS) Registry. Circulation. 1994; 90:2645–2657.

Crawford's original series[223] did demonstrated the presence of symptoms in the form of angina as an independent variable in long-term survival following aortic arch surgery.

Preoperative investigation and aggressive optimization of causes of breathlessness may represent an opportunity to improve not only perioperative morbidity and mortality, but also longer-term survival in these patients.

- **Postoperative renal dysfunction.**

Preoperative renal impairment has the highest hazard ratio in our multivariate model (3.11, P < 0.0001) of risk factors for follow-up survival. A recent study [227] in which a large cohort of patients undergoing cardiac surgery, including aortic surgery, were examined for a relationship between renal impairment and survival showed that, preoperative renal dysfunction is a predictor of long-term mortality in cardiac surgery patients. Indeed, in a large series of aortic patients presented by Patel et al.[221], preoperative renal impairment was an independent predictor of survival. In the original Crawford series[223], renal dysfunction was a significant variable. Interestingly, Estrera et al[217], in 2002, found postoperative renal failure but not preoperative renal impairment as a risk factor for follow-up survival. Certainly, Loef et al [228], in 2005, drew a similar conclusion in a large series of patients undergoing cardiac surgery: immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and long-term survival (HR 1.83). While postoperative renal failure and its relationship to survival are, of course, interesting, this points us to providing excellent preoperative and postoperative care. Preoperative renal impairment and its relationship to survival offer us an opportunity to modify and improve the health status of the patient with a view to improving long-term survival.

227 Dhanani J, Mullany DV, Fraser JF. Effect of preoperative renal function on long-term survival after cardiac surgery. *J Thorac Cardiovasc Surg*. 2013; 146:90–95.
228 Loef BG, Epema AH, Smilde TD, Henning RH, Ebels T, Navis G, et al.. Immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and long-term survival. *J Am Soc Nephrol*. 2005; 16:195–200

Taken together, evidence suggests that meticulous attention to modifying or maintaining renal function in the perioperative period is crucial to long-term survival.

- **Circulatory arrest time > 100 min.**

Intuitively, prolonged periods of circulatory arrest will cause significant physiological distress. Indeed, numerous studies have discussed durations of circulatory arrest as significant predictors of death and morbidity such as stroke, many of these summarized in systematic reviews[229][230]. Such morbidity will of course have consequences for survival. While prolonged circulatory arrest times may simply reflect complex anatomy and pathologies such as acute Type A dissection, chronic Type A dissection or infective processes, these times are also determined by the orchestration of the operation in terms of early distal body perfusion, use of various branched configurations for arch vessels, or the Carrel patch technique. The definition of the circulatory arrest time is also important in understanding and interpreting studies. In this study, we have taken circulatory arrest time as the time taken to re-establish distal body perfusion. In the case of hemiarch, this definition is easily understood as completion of the anastomosis is the point of return of distal body perfusion and cerebral perfusion. When total arch with Carrel patch is employed, again, the definition is easily understood as completion of the distal anastomosis and patch is the point at which distal and cerebral perfusion is established. However, in total arch replacement, when separate branches were employed, distal perfusion was re-established on completion of the distal anastomosis. Each head vessel was then anastomosed sequentially with ongoing anterograde cerebral perfusion, and in these cases, the circulatory arrest time was less than the "assisted cerebral perfusion time" by the duration of time it took to re-anastomose 1-3 cerebral vessels. In terms of modifiable risk factors, the more

229 Ziganshin BA, Elefteriades JA. Deep hypothermic circulatory arrest. *Ann Cardiothorac Surg*. 2013; 2:303–315.
230 Tian DH, Wan B, Bannon PG, Misfield M, Lemaire SA, Kazui T, et al.. A meta-analysis of deep hypothermic circulatory arrest alone versus with adjunctive selective anterograde cerebral perfusion. Ann Cardiothorac Surg. 2013; 2:261–270

frequent use of individual branches as opposed to a Carrel patch has allowed us to reduce our circulatory arrest times, although we have yet to see this translate into survival benefit. We have not yet acquired an easy, safe, and reproducible mechanism to establish distal perfusion during construction of the distal anastomosis, but this would effectively reduce circulatory arrest time further, as defined in our series.

- **Peripheral vascular disease.**

With the exception of one small study of 62 patients, which revealed that peripheral vascular disease was significantly associated with transient neurological dysfunction following arch surgery[231], little has been published. This may be because of the small number of patients with peripheral vascular disease in other studies, and even with our patient cohort, only 7.3% were found to have peripheral vascular disease. Clearly, atherosclerotic burden might be expected to influence follow-up survival. A study by Kurra et al [232] studied computed tomography imaging data on 862 patients undergoing cardiac surgeries and quantified a "plaque burden score." They concluded that the extent of thoracic atheroma burden is independently associated with increased long-term mortality in patients following cardiothoracic surgery. This again provides opportunity to modify survival by careful investigation and treatment of peripheral vascular disease both preoperatively and postoperatively.

- **Concomitant CABG operation.**

In our study, 16% of patients underwent concomitant CABG. A number of previous studies have described outcomes from concomitant CABG and aortic surgery. As far

231 Matalanis G, Hata M, Buxton BF. A retrospective comparative study of deep hypothermic circulatory arrest, retrograde and anterograde cerebral perfusion in aortic arch surgery. Ann Thorac Cardiovasc Surg. 2003; 9:174–179.
232 Kurra V, Lieber ML, Sola S, Kalahasti V, Hammer D, Gimple S, et al.. Extent of thoracic aortic atheroma burden and long-term mortality after cardiothoracic surgery: a computed tomography study. JACC Cardiovasc Imaging. 2010; 3:1020–1029

back as 2002, Hitoshi Yokoyama[233] summarized the outcomes of 6 studies between 1989 and 2001 demonstrating higher operative mortality and morbidity from concomitant CABG. Our study demonstrates that concomitant CABG is not associated with higher operative mortality but is associated with worse postoperative follow-up survival, with a hazard ratio of 2.14 ($P < 0.008$). There is a wealth of data from numerous studies demonstrating that concomitant CABG at the time of AVR is negatively associated with survival [233,234], and data from the Bristol group[235] have reported reduced 3-year survival in patients undergoing concomitant CABG at the time of ascending/arch surgery. Coronary grafting at the time of aortic arch surgery is required for symptomatic reasons and to aid myocardial protection at the time of surgery; it does not, however, appear to be associated with prognostic benefit. On the face of it, this does not appear to be a modifiable risk factor coming into surgery.

Managing Perioperative Risk Factors for Long-term Survival— "Primary and Secondary Prophylaxis"

Good long-term survival does not just happen. Careful attention is required to modifiable risk factors preoperatively, and the best possible pre- and postoperative care is crucial. Care for these patients should not end on discharge from hospital. Lifelong follow-up and attention to ongoing secondary prophylaxis is important.

233 De Waard GA, Jansen EK, de Mulder M, Vonk AB, Umans VA. Long term outcomes of isolated aortic valve replacement and concomitant AVR and coronary artery bypass grafting. *Neth Heart J*. 2012; 20:110–117.
234 Jones JM, Lovell D, Cran GW, Macgowan SW. Impact of coronary artery bypass grafting on survival after aortic valve replacement. *Interact Cardiovasc Thorac Surg*. 2006; 5:327–330.
235 Narayan P, Rogers CA, Caputo M, Angelini GD, Bryan AJ. Influence of concomitant coronary bypass graft on outcome of surgery of the ascending aorta/arch. *Heart*. 2007; 93:232–237

CHAPTER THIRTEEN

13. DISCUSSION

13.1 The LHCH Experience of Sub-Specialisation

Liverpool Heart and Chest Hospital (LHCH) is the only cardiothoracic stand-alone centre in the UK with independent trust status. The hospital covers a population of 2.8 million, performing approximately 1800 cardiac and thoracic surgical procedure a year of which 180 cases are elective and non-elective thoracic and thoracoabdominal aortic aneurysm repairs. Despite the high volume of general and conventional cardiac surgery that is being performed by 10 surgeons on general cardiac rota, it was felt that the hospital mortality for acute Type A aortic dissection was excessive at around 30%. Hence, in 2007, LHCH became the first in the UK to implement a subspecialised twenty-four hour on-call rota for acute Type A aortic dissection. The primary objective was to reduce morbidity and mortality of this dire operation to an acceptable national and international level. Hence, the trust underwent and approved a radical rearrangement to try and achieve the aforementioned. The aortic team was formed and which more or less were performing the highest volume of procedures relating to elective and non-elective aortic aneurysm surgery. The team which currently comprises of four aortic surgeons performs solely all non-elective and elective procedures. In addition, the surgical team is supported by dedicated anaesthetists and nursing staff. Subsequent to this re-organisation within the service delivered by LHCH, the mortality and morbidity for both elective and non-elective complex aortic surgery has dramatically improved. Pertaining to the scope of this study, we have clearly presented in our

results the significant reduction in mortality after acute Type A aortic dissection falling from 33.8% to 9.6% after implementation of the specialised rota. We also demonstrated the same effect to aortic arch aneurysm surgery cohort and as such we demonstrated that the mortality and morbidity following aortic arch aneurysm repair is equivalent to international level and is below the national average. The subspecialisation model improved the 5 years' actuarial survival of effected patients and that truly relates to the effectiveness arm of this subspecialised and high volume service and centre.

Subsequently, this improvement I results and outcomes observed in our elective and non-elective surgery paved the way for the aortic aneurysm service and team to accept higher volume of referral from the region and from the country at large. Putting this concept into perspective, one would deduce that concentration of expertise and volume to the appropriate surgeons who provide a well-rounded service perform increasing more work and complex aortic cases than the rest of cardiac surgeons within the same centre have the tendency to support the linearity seen with volume versus outcomes. The volume trends increased with time as one would expect with increasingly better outcomes.

No wonder the expertise of the team and the establishment of better outcome emerged from not only volume, referral and skills but also due to a very subtle fact that the three surgeons were all trained by one senior surgeon. Aortic arch operations were preformed among three aortic surgeons who were all trained by a principle surgeon who had transferred his skills to the subspecialised team as of 2005. Interestingly, while the extent of surgical intervention did not change between the two eras (before and after subspecialisation), the time spent in surgery noted as cutting time was prolonged. Certainly, the cardiopulmonary bypass times and cross clamp times were significantly prolonged in equally acute type A dissection repair and elective aortic arch surgery. The reason behind this paradoxical observation is suspected due to the adoption and evolution of skills to initiate a robust and reliable prophylactic techniques, such as routine buttressing of suture lines, developed

during elective aortic cases and also applied to the emergency situation. This operative techniques development aims to minimise bleeding and malperfusion. Bleeding being the commonest reason why patients are returned to theatre for re-exploration and for targeting the actual cause. This take back approach although it's aimed at saving the patient's lives, it comes at a monetary cost. Which is why the aortic team at Liverpool Heart and Chest Hospital adopted a very rigid protocol for haemostasis by adding two double layers to avert bleeding and hence the increment in cost as seen in the pre and post subspecialised era. While this added cost as reflected by increased theatre time, clearly it is a very reliable approach and is cost-effective in the sense that such approach led to improvement in surgical outcomes and overall survival as elaborated in the sections above.

The only published paper on standardization of care for aortic dissection comes from Minneapolis (11), where a regional protocol was instituted in August 2005. This began with the suspicion of the diagnosis in community hospitals where a single telephone call activated the protocol, leading to operation by one of 4 specialist cardiovascular surgeons. The group demonstrated significantly reduced times from diagnosis to surgery but no significant reduction in mortality rates so far. A clear issue in comparing studies is the different patient groups. Typically, young, low risk patients are thought to be referred for surgery, with older higher risk patients undergoing endovascular treatment. We would suggest all patients undergoing total arch/proximal descending aortic intervention to be discussed at a truly multi-disciplinary meeting with cardiac surgeons, vascular surgeons, interventional radiologists and intensivists. Ideally, patients should be assessed and treated on the basis of their pathology and fitness for intervention at a national level rather than availability and success of local services.

Arguably, prospective randomised trials have never been performed in acute aortic dissection, and realistically are not likely due to their ethical controversies. As such reporting of aneurysm surgery experience from each and every centre worldwide is a form of accepted evidence based medicine.

We acknowledge the fact that current reported results in the literature might be due to better developments in anaesthetic agents and drugs employed, the understanding of brain protection and perfusion techniques over the last few years. However, all of the aforementioned could be grouped as adjuncts to the fact the practice does make perfect and more volume reflects better outcomes. This will be discussed in details in the section below.

13.2 Factors Underlying Improved Clinical Outcomes

There are multiple factors that ought to be highlighted in this context that collectively attributed to the overall success of the working model of subspecialisation. Of these aspects are the following:

1. **Volume:** The major contributing factor amongst other is the large number of volume of case load that was initiated following the concept of subspecialisation at Liverpool Heart & Chest Hospital. The analysis has identified a significant improvement in clinical outcomes resulting from the introduction of a sub-specialised aortic surgical team. As we demonstrated, the increase in volumes, with published evidence on relationship between the hospital volume of procedures and outcomes for elective and non-elective surgeries is the most forward concept to explain the rearrangement in service and reduction in mortality and morbidity. It relevant to mention that the team non-aortic elective and non-elective work remained within national standards for mortality and morbidity. This is clearly reflected in the CUSSUM curves that the team of non-aortic conventional work is regularly audited and the quality of the service provision is not compromised. This rearrangement of service that complies with standard of care and better service provision didn't come at the stake of more concentrated and conventional work is being directed to other consultants hence creating a pseudo-subspecialisation to the rest of the cardiac surgeons on the

rota. This was a divisional and strategic operational move that ultimately concentrated the expertise from one end to aortic aneurysm service provision without alteration of normal conventional cardiac work load.

2. **Multidisciplinary Team Process:** Other related factor is the strong multidisciplinary team (MDT) processes in cardiothoracic surgery practice in the UK that has a strong tradition with involvement in MDTs particularly in lung cancer surgery and oesophageal cancer surgery. In addition, new European Guidelines on the management of ischaemic heart disease place the MDT at the heart of decision-making[236]. Liverpool has a strong MDT process ensuring intervention is personalized to patients depending on pathology and co-morbidities. Key to this is preoperative assessment by anaesthetics/intensivists and their inclusion in the whole perioperative process. On the opposite end, the only international guidelines on thoracic and thoracoabdominal aortic aneurysm intervention published by the American Heart Association make no mention of involvement of an MDT in managing cases.
3. **Quality Outcomes Framework:** Our institution has developed a "Quality Outcomes Framework" (QOF), broadly based on Society of Thoracic Surgeons (STS) Quality Performance Measures in cardiac surgery (www.sts.org/quality), for internal reporting of annualized data from aortic arch surgery. Unlike the STS measures, which include indicators of process, structure, and outcome, our QOF concentrates on outcomes, annualized, and is presented as a "Statistical Process Control Chart" (Appendices). These include in-hospital mortality, 30-day mortality and 1-year mortality, stroke, re-exploration, postoperative renal failure, and prolonged ventilation. This mechanism allows us to monitor the stability of our outcomes annually and investigate and modify processes when deviation is observed. These data are presented in Appendices and not only demonstrate our increasing annual activity over time but also the relative stability of outcomes with little influence of the change in service provision from

236 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013 Oct;34(38):2949-3003

2007. Stability of outcomes, particularly major morbidity and mortality, is an important platform for interpreting our survival data and the influences on it.

4. **Subspecialised Clinical Disciplines and other Allied Teams:** The advent of the subspecialised aortic team that jointly perform aortic work-loads on complex thoracic and thoracoabdominal aortic aneurysm cases, advertently had to be met with the surge of anaesthetic expertise, clinical radiology, perfusion innovation and implementation and most importantly the efforts made from allied health professionals to implement protocols and intensive surgical care structure. Although this thesis can't support the aforementioned in terms of robust data and analysis seen from different disciplines, it's the overall presupposition of all these services that worked together in a coherent and homogenous team effort that inadvertently supported the subspecialised team and concept.
5. **Innovation in Thoracic Aortic Aneurysm Surgery:** Its inconceivable that the model of subspecialisation revealed out to be an impact model which allowed for the morbidity and mortality figures to be restored to and beyond national and international levels. Yet, this not only was accomplished through rearrangement in the service and the development of specialised area and clinical settings that supported this rearrangement but also due the fundamental fact that innovation and evolution of device technology, anaesthetic agents, perfusion techniques, brain protection methods, neuromonitoring advancement and post-operative monitoring techniques all contributed to this impact model. Hence, all the aforementioned co-existed to supplement the advancement of the aortic surgery team and impact the model of subspecialisation. Also, this moves in conjunction with the uniformity on the surgical and technical skills. The intricacy of this uniform surgical practices and skills see applied amongst different surgeon who perform aortic complex procedures using same skills and abilities explains why such impact model is attained. The primary senior surgeon who aided in the development of this team passed on his skills that were transferred amongst the team. Hence, its inarguably correct that the uniformity of the skills executed in between the surgeons and that was transcribed from their predecessor would undoubtedly correlate to the improvement in quality outcomes as conveyed

thought in this thesis.

13.3 Subspecialisation Enhances Cost-Effectiveness

The increase of referral of elective and non-elective workload to the specialised aortic team contributed to enhancing the improvement seen on outcomes level and influenced the survival of our patient cohort. One could argue that the operative characteristic has been prolonged in a sense due to extra haemostatic control intra-operatively that impacted the reoperation and re-exploration rate for bleeding in a positive sense.

Yet, if more time is being spent in theatre while surgeons take extra care in making sure that re-exploration is minimised to subliminal levels that afford the patient better outcomes and the surgeons' better results. The cost of theatre time increased as it's a mere reflection of the length of operation and due to the fact that more of the subspecialised team patients surviving longer, one would expect that the post-operative lengths of stay, both on the ward and on the ICU to increase significantly as a consequence. However, the analysis revealed that the cost between the two group before and after the subspecialisation remained to be neutral and no meaningful cost incurrence occurred. This leads us to say that the subspecialisation certainly led to improvement in outcomes and survival benefits were enhanced. This was accomplished at cost neutral effect between the two groups. This will lead us to conclude that subspecialisation has certainly been demonstrated to be an important factor in enhancement of cost-effectiveness.

There have been significant clinical and economic benefits as a resultant to a dedicated sub-specialised surgical service and team in aortic surgery at Liverpool Heart & Chest Hospital. It would be superb if such cost-effective model could be transferred to other organisations with the National Health Service. It's demonstrated across the country that other specialities such as the hepatobialiary and pancreatic surgery benefited profoundly from developing a subspecialised and

concentrated services. This is also true for vascular service throughout the UK and their establishment of new era of vascular breed through their instrumental training system that was initiated in 2011. Hence, reaping the benefits from similar centralization and reorganisation of their service and expertise in cardiothoracic and in particular aortic surgery will certainly follow pursuit.

However, the overall centralisation that was viewed at LHCH affected positively other service delivery by attaining improvements in parallel reorganization of associated services, such as interventional radiology and specialist critical care. Radiology at LHCH offer and due to wide range of expertise and experience the ability to aid in diagnostic measures and resources. This surely would require some degree of scale measurement in terms of costing and manpower. Yet, it's my insight that such reorganisation in manpower and parallel and allied speciality will all fall under one umbrella of being cos-effective and overall will provide patient with better quality of care provision.

13.4 Standardization and Centralization of Thoracic Aortic Aneurysm

The aim and strong rationale of subspecialisation and centralization is to provide centres with a large and reaching catchment areas that has a reciprocal effect on the subspecialised unit. It allows more robust referral to influx and hence will maintain an adequate voluminous exposure. Essentially, thoracic aortic aneurysm service is in much need of such approach and a national policy and mandate that would support such programs across the UK. Hence, this will provide a sustained and increasing in volume to concentrated expertise that will allow the possibility to address dire surgical diseases and avert associated complications.

It will then reciprocate this arrangement that will ultimately reduce mortality and improve long term survival following aortic surgery.

The advent of technological superiority in aiding the diagnosis and surgical planning of aortic surgery and the understanding of the natural history resulted in personalised and targeted therapies and surgical procedures to be done on wider range of the affected population. This allowed for such cost-effective diagnostic tests to be distributed to a smaller number of regional centres to attempt on operating on such patients' cohort. Hence this has titrated the inexistence of specialist centres and diverted a large number of patients to be operated at local low- volume institutions.

The development of standardization subspecialisation requires a comprehensive assessment of the current status in aortic surgery in the UK.

This thesis illustrated this from the wider literature review. The aforementioned, should it be a mandate and a national policy would irrevocably prevent unnecessary death related event due to lack of available resources, expertise at the centre or hospital that provide[237]. This initiative has ultimately to be mandated as a governance policy in the NHS and to be commissioned to supra-regional centres or hospitals with intent to treat the wide array of aortic pathologies and established framework of referral and robust mechanism to refer patients.

The quality and measured outcomes from such national reorganisation that was demonstrated at a smaller scale in this thesis i.e. at LHCH provides a platform for such transfer of quality and expert skills to other much need population across the region and the country. This will impact the utilisation of resources and direct it to the much needed and debilitated patients. It will allow an analysis to be made on large scale nationally to attain a better understanding albeit on cost and outcome measures.

237 CIS Meadows, W Rattenberry, C Waldmann. Centralisation of specialist critical care services, JICS 2011;12:2,

However, centralisation and subspecialised service has its own at a drawback; this includes displacement of families and relatives, together with increased travel times and costs to meet with a specialist. This is not easy to quantify and is beyond the scope of this thesis but surely will need to be considered. The emphasis of importance of concentration of experts in a suitably subspecialised and central service might be met in the public eye and media perception as negative. This could be attributed to loss of local services. However, the 'hub and spoke' model of specialist service delivery is characterised by close links between regional referring hospitals and specialist centres and is exemplified by percutaneous coronary intervention networks[238,239].

The introduction of such a network for cardiac surgery in Italy had a positive effect on patients' outcomes, with a 22% reduction in hospital mortality rates[240].

13.5 Is the LHCH Subspecialized Model Generalizable throughout the NHS?

A key to answering this question is in deciding whether we believe there is evidence that intervention can alter the natural history of this disease process to provide either symptomatic or prognostic benefit. As suggested earlier, the international literature does document particularly poor survival for patients managed medically and improved significantly following intervention. There are no data published on survival with and without intervention in the UK; however, published survival in our own group of postoperative aortic patients in Liverpool compares favourably

238 De Maria E, Ricci S, Capelli S et al. Feasibility of transradial approach in a hub and spoke cath lab network. Minerva Cardioangiol 2010;58:11-15
239 Morgan KP, Leahy MG, Butts JN, Beatt KJ. The cost-effectiveness of primary angioplasty compared to thrombolysis in the real world: one year results from West London. Eurointervention 2010;6:596-603
240 Nobilio L, Fortuna D, Vizioli M et al. Impact of regionalisation of cardiac surgery in Emilia-Romagna, Italy. J Epidemiol Community Health 2004; 58:97-102

with published survival for medically treated patients. At present, it is necessary to accept that international data on clinical effectiveness of intervention on thoracic and thoracoabdominal aneurysms may be extrapolated to the English NHS; however, this is the subject of a recent call by the UK National Institute for Health Research. Having drawn the tentative conclusion that survival following intervention in the UK is improved is there sufficient volume to underpin acceptable outcomes. This is uncertain, however, the Liverpool model, which predominantly accepts patients from The North West (population 7 million), has an annual activity of between 150 and 180 shared between four surgeons.

Providing this model can be duplicated it would suggest that in a population of over 50 million in England there is roughly sufficient volume for 4 – 5 centres. Interestingly, NHS Scotland, with a population of around five million, commissioned the Vascular Surgery Unit at the Royal Infirmary of Edinburgh to perform 25 interventions per year on the thoracoabdominal aorta from April 2001 (www.nsd.scot.nhs.uk). In their government review in 2007 their service was deemed clinically robust and offered value for money. These figures are comparable with the population in the North West and the activity through Liverpool.

Based on this, we believe there is sufficient international evidence for intervention, sufficient UK volume and proof that acceptable outcomes can be achieved in the UK NHS framework.

Generalizability of this subspecialised model could potentially be achievable. Accepting the change and limitations of surgical ability are amongst the factors that might tip sub-speciality in thoracic aortic aneurysm as a favourable and sensible trend. This was the bottom element that rerouted surgical expertise in aneurysm repair at LHCH. This initiative further led to a local generalizability of a consensus that was made in harmony between a group of skilful individuals, the managers and local commissioners. Yet, such change was met by another challenge that is the opportunity cost if surgeons are moved away from other therapeutic areas.

To divert this, surgeons were being as effective as needed in other conventional surgeries. Their results were also audited and quality monitored.

Hence, opportunity cost and service provision was balanced and overall welfare gain and quality outcomes were set and met. We feel however, that the development of standard surgical techniques and the regular performance of these on a weekly basis as well as the increased number of cases per surgeon are the major contributing factors to the improvement in results. This might stand out as a challenge to other centres.

We acknowledge that this model of care might not be appropriate to every trust and that ours is one of the largest cardiothoracic units in the country. It may however, be regionally applied in order to provide consistent subspecialist out of hours, year round cover. If such model could be disseminated to other service providers across generality across the wide service in the NHS might be achieved with limited modification.

Overall, the patients' needs and expectation are constantly changing and the need for specialised and cost effective model with new treatment and technological advancement is the future of the NHS. This would be viable in a financial constraint environment that aimed at delivering safe options and world class service.

This thesis has demonstrated that given the significant clinical and economic benefits of a subspecialised team can result in quality service and outcomes. The fact that such improved surgical outcomes can be achieved with little or no change in resource use suggests that sub-specialisation holds the potential to be a highly cost-effective structure of surgical care.

CHAPTER FOURTEEN

14. CONCLUSION

Subspecialisation in aortic aneurysm surgery has been demonstrated as an impact model that certainly seems to function within the framework of NHS. Crucial to this service provision is the team approach and the volume of cases referred. Yet, a very important contributing factor manifesting is the inclusive and comprehensive multidisciplinary team (MDT) discussion on every patient.

We demonstrated that simple changes in service provision has led to a significant improvement in outcome and survival amongst our elective and non-elective case mix. The contemporary aortic outcomes accomplished are directly related to the increasing volume of cases being operated on at LHCH. This volume outcome relationship has been well established in literature and has been at the centre of attention in many speciality including vascular speciality that underwent rigorous steps to re-align the provision of services in the UK. This has provided ample of lessons to be learned from and how a speciality has moved to effectively be centralised and subspecialized at national scale.

The development of a robust referral system and the increasing of volume of aortic cases has allowed us to produce an initiative to hospital managers and commissioners. The initiative that rearrangement in the way we offer aortic service is crucial to attempt to reduce morbidity and mortality from dissection and non-dissection work load. This has led to the establishment of a UK first specialised service with a dedicated 24 hours' acute aortic service. The subspecialisation initiative stood ground not only due to our commitment to offer better service but due to factors that the team has standardized in between them. Such factors are

attributable to the fact that the aortic surgeons were all trained by one principle surgeon whose skills has been passed on. Other factors include the uniformity in the surgical techniques and additional higher number of cases per surgeon per year were amongst the major contributing factors to the improvement in results.

The outlined results that were demonstrated between the before and after subspecialisation rota are sufficient evidence that indicate quality improvement that impacted patient outcomes, survival benefit at cost neutral implications.

The introduction of subspecialisation was expected to have direct impact on cost distribution in our division. Although the introduction of a separate aortic on call rota resulted in some change in how surgeons were remunerated, this was merely to reflect the change in their on call case load. Surgeons on the aortic team would see their on call case load go up as a result of all aortic cases being directed their way. To reflect this, the on call premium they are paid above their basic salary was increased. However, this increase in on call caseload for the newly created aortic team naturally coincided with an equal and opposite reduction for the non-aortic surgeons. Hence, the change was once again achieved at cost neutral level. The average cost per patient in the post subspecialisation has not varied significantly as seen in our analysis and with no notable change in resource cost resulting from the change in the clinical re-organization, it is perhaps reasonable to deduce that the introduction of subspecialisation was cost neutral to the hospital as well. The improvement of our patients' cohort outcomes had two separate effects on cost implication. The effect of reduced mortality is, "ceteris paribus", an increase in length of stay and therefore an increase in costs. However, also present is the effect of a reduction in adverse events and other complications, which works to reduce length of stay by improving recovery time.

The idea of producing aortic supercentre that follows pursuit the model seen in the United States could not be achievable at the NHS service level due to multitude of factors at the centre of which is cost and the fact that aortic subspecialisation model has been floated in the United Kingdom so that the highest quality of preoperative

evaluation, operative management, and follow-up can be provided patients. Yet we look at our experience and results in the elective and non-elective open thoracic aortic surgery and can deduce that at our regional unit including patient demographics, in- hospital results such as mortality and postoperative outcomes, as well as survival are equivalent to worldwide published results.

It's undeniable that a surplus of other relevant changes had to be implemented to support our concept of subspecialisation and to help in the consistency of the volume of our cases and such changes occurred at other similar speciality including anaesthesia and operative perfusion scientist. We have specialised aortic anaesthetist and perfusionist that assist in every case albeit on thoracic and thoracoabdominal cases. This increased in volume has mirrored our results and their expertise has also been well concentrated. This is in addition to our well-resourced critical care area whose staff are well trained to delineate critical phases in the post-operative management of our aortic patient that certainly influenced our patient outcome and longevity of their survival. Another major contributing factor that supported the subspecialisation of our aortic service is the multidisciplinary team meeting that allowed cases to be openly discussed and for the best intervention and case management to be achieved. The eventuality of the improvement of our results culminated in our dedicated aortic clinics and we at LHCH are amongst the top hospitals in the world to follow-up our patients and screen for their aneurysm changes and intercept any change that require immediate attention and surgical intervention that potentially avert the patient futile outcomes. In a nutshell, all the aforementioned factors contributed significantly to subspecialised initiative that evolved rapidly and allowed for our results to be superior to national published aortic outcomes and survival.

We believe there is sufficient volume and evidence of adequate outcomes for the UK to offer a comprehensive service for intervention on thoracic aortic aneurysms. Indeed, the UK has several facets of service provision that would allow for development of an internationally unique and effective system.

However, we suggest there is a need for a review of service provision by all stakeholders and a rationalization of services. A comprehensive and inclusive MDT must be central to the process.

AREAS FOR FUTURE RESEARCH

This thesis opens a significant number of areas for future research. Such areas can be categorized in broad terms as “clinical research”, and 'economic/health policy research'. Throughout this study we demonstrated the current evidence that thoracic aortic aneurysm service at LHCH became an evolving subspecialty. A case for a national strategy with a few designated regional centres in a system analogous to provide aortic specialism has to be mandated. The cluster of specialism should be related to the expertise offered, hence, each patient should be matched to appropriate treatment regimens and adequately consented. Each centre should be subject to regular audit to ensure adequate activity monitoring and outcomes. All national centres should commit to regular bench-marking exercises, exchange of processes, audit and provide training.

In the UK, thoracic aortic surgery remains a part of cardiothoracic surgery in general, rather than an independent sub-specialty. Proposals for the centralization or subspecialisation of aortic aneurysm surgery as a subspecialty is underway. We acknowledge that our model of care may not be appropriate to every trust and that ours is one of the largest cardiothoracic units in the country. It may however, be regionally applied in order to provide consistent subspecialist out of hours, year round cover. We have demonstrated that simple changes in service provision can lead to significant improvement in outcome for this lethal condition.

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APPENDICES

TABLES

Table 7.1. The Yearly Risk of Aortic Rupture, Dissection and Death Correlated to Aortic Aneurysm Size

	Aortic size			
Yearly Risk	> 3.5cm	>4.0cm	>5.0 cm	> 6.0cm
Rupture	0.0%	0.3%	1.7%	3.6%
Dissection	2.2%	1.5%	2.5%	3.7%
Death	5.9%	4.6%	4.8%	10.8%
Any of the above	7.2%	5.3%	6.5%	14.1%

(Taken from Division of Cardiothoracic surgery at St. Roosevelt Aneurysm Centre. USA)

Table 9.1. Table Displaying the Common Economic Methods Utilised Particular in Health Ecomonics

Method	Outcome measure	Application/interpretation
Cost-minimisation analysis	Evidence is available that outcomes for competing therapies are equivalent	Given the evidence of output equivalence (and only when such evidence is available), the cheapest therapy is preferred
Cost-effectiveness analysis	Health benefits are measured in natural units, reflecting a dominant common therapeutic goal for competing therapies	How much more does it cost (incremental cost) to achieve an additional unit (incremental effectiveness) of the common therapeutic good (incremental cost-effectiveness ratio)?
Cost–utility analysis	In the absence of a common therapeutic goal, outcome is measured through the effect of any intervention on mortality (quantity of life) and morbidity (quality of life)	The quality-adjusted life-year measures the number of additional life years weighted by the quality of life (value) of the health state experienced in each year
Cost–benefit analysis	Both costs and benefits are measured in the same unit – money – with the financial value of the costs being compared with the financial value of the benefits	An intervention should be undertaken if the (financial) value of the benefits exceeds the (financial) value of the costs. If only one intervention can be funded, choose the activity with the highest excess financial benefit over costs

Table 9.3. Thoracic and thoraco-abdominal aortic surgery OPCS 4 Procedures and HRGs analysis *(1 of 4)*

Operations	Relative Clinical complexity	Emergency Coding- Liverpool	Emergency Coding - Royal Brompton	Elective Codes- Liverpool	Elective Codes- Royal Brompton	Proposed HRG groupings
AAo	Simple	L181 EA20Z/EA22Z	L181 EA20Z/EA22Z	L191 EA20Z/EA22Z	L191 EA20Z/EA22Z	Group A1, modify if complications
AAo+AVR	Simple	L181 + K263 EA20Z/EA22Z	L181 + K263 EA20Z/EA22Z	L191 + K263 EA20Z/EA22Z	L191 + K263 EA20Z/EA22Z	
AAo+hemiarch	Complex	L181+L188 +Z34.2 EA20Z/EA22Z	L181+L188 +Z34.2 EA20Z/EA22Z	L191+L198 +Z34.2 EA20Z/EA22Z	L191+L198 +Z34.2 EA20Z/EA22Z	Group A2, higher risk of significant complications, so need to modify HRG is complications
AAo+AVR+hemiarch	Complex	L181 +L188 +Z34.2+ K263 EA20Z/EA22Z	L181 +L188 +Z34.2+ K263 EA20Z/EA22Z	L191+L198 +Z34.2 + K263 EA20Z/EA22Z	L191+L198 +Z34.2 + K263 EA20Z/EA22Z	
AAo+total arch	Complex	L181 + L188 + Z342 EA20Z/EA22Z	L181 + L188 + Z342 EA20Z/EA22Z	L191 + L198 + Z342 EA20Z/EA22Z	L191 + L198 + Z342 EA20Z/EA22Z	
AAo+total arch +AVR	Complex	L181 + L188 + Z342 + K263 EA20Z/EA22Z	L181 + L188 + Z342 + K263 EA20Z/EA22Z	L191 + L198 + Z342 + K263 EA20Z/EA22Z	L191 + L198 + Z342 + K263 EA20Z/EA22Z	
AAo+total arch +ET	Complex	L181 + L188 + L761+ Z342- EA20Z/EA22Z	L181 + L188 + L761+ Z342- EA20Z/EA22Z	L191 + L198 + L761+Z342- EA20Z/EA22Z	L191 + L198 + L761+Z342- EA20Z/EA22Z	
AAo+total arch+ET+AVR	Complex	L181 + L188 + L761+Z342 + K263 EA20Z/EA22Z	L181 + L188 + L761+Z342 + K263 EA20Z/EA22Z	L191 + L198 + L761+.K263+Z342 EA20Z/EA22Z	L191 + L198 + L761+.K263+Z342 EA20Z/EA22Z	
Root	Simple/ Complex	K334 Mechanical / K335 Tissue / K33.3 homograft, EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft, EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft EA20Z/EA22Z	Group B1, modify if complications
Root+AVR	Simple/ Complex	K334 Mechanical / K335 Tissue / K33.3 homograft + K263 EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft + K263 EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft + K263 EA20Z/EA22Z	K334 Mechanical / K335 Tissue / K33.3 homograft + K263 EA20Z/EA22Z	
Root+ AAo	Simple/ Complex	L181+ K334 Mechanical / K335 Tissue, EA20Z/EA22Z	L181+ K334 Mechanical / K335 Tissue, EA20Z/EA22Z	L191+ K334 Mechanical / K335 Tissue EA20Z/EA22Z	L191+ K334 Mechanical / K335 Tissue EA20Z/EA22Z	

Table 9.3. Thoracic and thoraco-abdominal aortic surgery OPCS 4 Procedures and HRGs analysis *(2 of 4)*

Operations	Relative Clinical complexity	Emergency Coding- Liverpool	Emergency Coding - Royal Brompton	Elective Codes- Liverpool	Elective Codes- Royal Brompton	Proposed HRG groupings
Root +AAo+AVR	Major complex	L181 + K334 Mechanical / K335 Tissue + K263, EA20Z/EA22Z	L181 + K334 Mechanical / K335 Tissue + K263, EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	Group B2, modify if complications
Root +AAo+hemiarch	Major complex	L181 + K334 Mechanical / K335 Tissue+L188 +Z34.2, EA20Z/EA22Z	L181 + K334 Mechanical / K335 Tissue+L188 +Z34.2, EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue + L198 + Z34.2 EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue + L198 + Z34.2 EA20Z/EA22Z	
Root +AVR+AAo+ hemiarch	Major complex	L181 + K334 Mechanical / K335 Tissue +L188 +Z34.2+ K263 , EA20Z/EA22Z	L181 + K334 Mechanical / K335 Tissue +L188 +Z34.2+ K263 , EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue +L198 +Z34.2+ K263 EA20Z/EA22Z	L191 + K334 Mechanical / K335 Tissue +L198 +Z34.2+ K263 EA20Z/EA22Z	
Root+AAo+total arch	Major complex	L181 + L188 +Z342 + K334 Mechanical / K335 Tissue, EA20Z/EA22Z	L181 + L188 +Z342 + K334 Mechanical / K335 Tissue, EA20Z/EA22Z	L191 + L198 + Z342 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	L191 + L198 + Z342 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	
Root+AVR+ AAo+total arch	Major complex	L181 + L188+Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L181 + L188+Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L191 + L198 + Z342 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L191 + L198 + Z342 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	
Root+AAo + total arch + ET	Major complex	L181 + L188+ L761+Z34.2 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	L181 + L188+ L761+Z34.2 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	L191 + L198 + L761 + Z34.2 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	L191 + L198 + L761 + Z34.2 + K334 Mechanical / K335 Tissue EA20Z/EA22Z	Group B2, modify if complications
Root+AVR+AAo + total arch + ET	Major complex	L181 + L188 + L761+Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L181 + L188 + L761+Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L191 + L198 + L761 + Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	L191 + L198 + L761 + Z34.2 + K334 Mechanical / K335 Tissue + K263 EA20Z/EA22Z	
Isolated arch	Complex	L188 QZ01A/QZ01B	L188 + Z342QZ01A/QZ01B	L198 + Z342QZ01A/QZ01B	L198 QZ01A/QZ01B	Group C 1, Modify if complications
Frozen elephant trunk	Complex	L188 + L27/L28		L198 + L27/L28		

Table 9.3. Thoracic and thoraco-abdominal aortic surgery OPCS 4 Procedures and HRGs analysis *(3 of 4)*

Operations	Relative Clinical complexity	Emergency Coding- Liverpool	Emergency Coding - Royal Brompton	Elective Codes- Liverpool	Elective Codes- Royal Brompton	Proposed HRG groupings
Aortic surgery as above+ other (CABG, MVR, TVR)	Complex	K401 - K469 (CABG) EA14Z/EA16Z	K401 - K469 (CABG) EA14Z/EA16Z	K401 - K469 (CABG) EA14Z/EA16Z	K401 - K469 (CABG) EA14Z/EA16Z	Group D1, modify if complications
	Complex	K251 - K259 (Mitral Valve) EA17Z/EA19Z	K251 - K259 (Mitral Valve) EA17Z/EA19Z	K251 - K259 (Mitral Valve) EA17Z/EA19Z	K251 - K259 (Mitral Valve) EA17Z/EA19Z	
	Complex	K271 - K279 (Tricuspid Valve) EA17Z/EA19Z	K271 - K279 (Tricuspid Valve) EA17Z/EA19Z	K271 - K279 (Tricuspid Valve) EA17Z/EA19Z	K271 - K279 (Tricuspid Valve) EA17Z/EA19Z	
	Complex	K281 - K289 (Pulmonary Valve) EA17Z/EA19Z	K281 - K289 (Pulmonary Valve) EA17Z/EA19Z	K281 - K289 (Pulmonary Valve) EA17Z/EA19Z	K281 - K289 (Pulmonary Valve) EA17Z/EA19Z	
	Complex	K301 - K309 Revision of Repair of Valve EA20Z/EA22Z	K301 - K309 Revision of Repair of Valve EA20Z/EA22Z	K301 - K309 Revision of Repair of Valve EA20Z/EA22Z	K301 - K309 Revision of Repair of Valve EA20Z/EA22Z	Group D2, modify if complex
	Complex	K341 - K343 Annuloplasty EA17Z/EA19Z	K341 - K343 Annuloplasty EA17Z/EA19Z	K341 - K343 Annuloplasty EA17Z/EA19Z	K341 - K343 Annuloplasty EA17Z/EA19Z	
Redo		Depends on the previous procedure	Depends on the previous procedure	Depends on the previous procedure	Depends on the previous procedure	Modify due to increased complexity and higher risk of complications
Other Aortic Aneurysm Procedures	Complex	L183, L184, L185, L186 QZ01A/QZ01B	L183, L184, L185, L186 QZ01A/QZ01B	L193, L194, L195, L196 QZ01A/QZ01B	L193, L194, L195, L196 QZ01A/QZ01B	Group C, modify if complications

Table 9.3. Thoracic and thoraco-abdominal aortic surgery OPCS 4 Procedures and HRGs analysis *(4 of 4)*

Operations	Relative Clinical complexity	Emergency Coding- Liverpool	Emergency Coding - Royal Brompton	Elective Codes- Liverpool	Elective Codes- Royal Brompton	Proposed HRG groupings
Other Aortic Bypass Procedures	Complex	L201 - L209 EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L201 - L209 (L20.1&L20.2 = EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (L21.1= EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	Group D, modify if complications
Isolated DTA(Thoracic aortic dissection) Medical management	Simple	L201 - L209 EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L201 - L209 (L20.1&L20.2 = EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (L21.1= EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	Group E 1, modify if complications
Isolated DTA(Thoracic aortic dissection) Surgical management	Complex	L201 - L209 EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L201 - L209 (L20.1&L20.2 = EA20Z/EA22Z, L20.3 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	L21.1 - L219 (L21.1= EA20Z/EA22Z, L20.2 to L20.9 = QZ01A/QZ01B)	Group E2, modify if complications
TAAA (thoraco abdominal aortic aneurysm)	Major complex	L181 / L182 + L185 EA20Z/EA22Z or QZ01A/QZ01B	L181 / L182 + L185 EA20Z/EA22Z or QZ01A/QZ01B	L191 / L192 + L195 EA20Z/EA22Z or QZ01A/QZ01B	L191 / L192 + L195 EA20Z/EA22Z or QZ01A/QZ01B	Group F, modify if complications

Table 10.5. Outcomes following aortic arch surgery and cerebral protection method used since 1997 to current date in the published literature *(1 of 2)*

Author	Year	Site	Method	Mortality	References
Hayashi	1997	Arch	SCP	24% (137)	([241])
Sadahiro	1997	Ascending/ arch	SCP	10% (91)	([242])
Ohkita	1998	Arch	HCA+RCP	9% (129)	
Crawford	1998	Ascending/ arch	HCA	7% (596)	
Ehrlich	2000	Ascending/ arch	HCA	9% (311)	([243])
Yamashiro	2001	Arch	SCP	20% (25)	
Czerny	2003	Ascending/ arch	HCA	11.6% (369)	([244])
Ueda	2003	Arch	SCP	12% (103)	([245])
Griepp	2004	Arch	HCA/SCP/T	14% (150)	([246])
Elefteriades	2007	Ascending/ arch	HCA/SCP	3% (360)	([247])
Minatoya	2006	Arch	SACP	2.3% (271)	([248])

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Table 10.5. Outcomes and cerebral protection method used since 1997 to current date in the literature *(2 of 2)*

Author	Year	Site	Method	Mortality	References
Sundt	2008	Arch	SCP	2.9% (347)	([249])
Minatoya	2010	Arch	HCA	7.9% (114)	([250])
Bischoff	2010	Arch		7% (50)	([251])
Kulik	2011	Arch		6% (67)	([252])
Zierer	2011	Arch	UACP/HCA	4% (44)	([253])
LeMaire	2011	Arch		2% (200)	([254])
Misfeld	2012	Arch	UACP/BACP/HCA	11% (636)	([255])
Thomas	2012	Arch/DTA	UACP/BACP/HCA	8% (20)	([256])
Iba	2013	Arch		6% (67)	([257])
Urbanski	2013	Arch	HCA/SCP	7% (50)	([258])

HCA: hypothermic circulatory arrest, tRCP: retrograde cerebral perfusion, T: Trifurcated Graft

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Table 12.1.5. Patient characteristics and univariable analysis of risk factors for in-hospital mortality after proximal aortic surgery in the UK

		No. of patients*	Odds ratio (95% CI) for in-hospital mortality	P value
Age (years)	< 70	5723 (66.3)	Reference	
	≥ 70	2916 (33.8)	1.98 (1.70, 2.29)	<0.001
	Continuous	64 (51, 73)	1.03 (1.02, 1.03)	<0.001
Gender	Male	5784 (67.0)	Reference	
	Female	2855 (33.0)	1.06 (0.91, 1.24)	0.48
Admission type	NHS patient	8269 (95.7)	Reference	
	Private patient	370 (4.3)	0.39 (0.23, 0.67)	<0.001
BMI	<30	6460 (74.8)	Reference	
	≥ 30	2179 (25.2)	0.90 (0.76, 1.07)	0.24
	Continuous	26.9 (24.1, 30.1)	1.00 (0.98, 1.01)	0.57
Angina CCS class	I to III	8232 (95.3)	Reference	
	IV	407 (4.7)	2.56 (1.98, 3.32)	<0.001
New York Heart Association (NYHA) class	< III	6014 (69.6)	Reference	
	≥ III	2625 (30.4)	1.80 (1.55, 2.09)	<0.001
Previous myocardial infarction	No	7978 (92.3)	Reference	
	Yes	661 (7.7)	2.36 (1.91, 2.93)	<0.001
Myocardial infarction within last 90 days	No	8344 (96.6)	Reference	
	Yes	295 (3.4)	2.97 (2.23, 3.96)	<0.001
Previous angioplasty	No	8363 (96.8)	Reference	
	Yes	276 (3.2)	1.65 (1.16, 2.35)	0.005
Previous cardiac surgery	No	7419 (85.9)	Reference	
	Yes	1220 (14.1)	2.80 (2.37, 3.32)	<0.001
Diabetes	No	8042 (93.1)	Reference	
	Yes	597 (6.9)	1.46 (1.13, 1.88)	0.004
Current smoker	No	7671 (88.8)	Reference	
	Yes	968 (11.2)	1.10 (0.88, 1.39)	0.39
Hypertension	No	3335 (38.6)	Reference	
	Yes	5304 (61.4)	1.50 (1.27, 1.75)	<0.001
Creatinine > 200 µmol / L	No	8386 (97.1)	Reference	
	Yes	253 (2.9)	3.82 (2.86, 5.11)	<0.001
History of renal impairment	No	8471 (98.1)	Reference	
	Yes	168 (1.9)	2.96 (2.04, 4.30)	<0.001
Pulmonary disease	No	7624 (88.3)	Reference	
	Yes	1015 (11.8)	1.35 (1.09, 1.66)	0.005
History of neurological disease	No	7913 (91.6)	Reference	
	Yes	726 (8.4)	2.04 (1.65, 2.53)	<0.001
Neurological dysfunction	No	8297 (96.0)	Reference	
	Yes	342 (4.0)	2.36 (1.77, 3.13)	<0.001
Peripheral vascular disease	No	7268 (84.1)	Reference	
	Yes	1371 (15.9)	1.79 (1.51, 2.14)	<0.001
Preoperative non-sinus rhythm	No	7604 (88.0)	Reference	
	Yes	1035 (12.0)	2.14 (1.77, 2.57)	<0.001
Triple vessel disease	No	8244 (95.4)	Reference	
	Yes	395 (4.6)	2.62 (2.02, 3.40)	<0.001
Left main stem disease	No	8472 (98.1)	Reference	
	Yes	167 (1.9)	1.99 (1.31, 3.03)	0.001
Left ventricular ejection fraction 30%-50%	No	6933 (80.3)	Reference	
	Yes	1706 (19.7)	1.78 (1.49, 2.12)	<0.001
Left ventricular ejection fraction <30%	No	8251 (95.5)	Reference	
	Yes	388 (4.5)	3.50 (2.69, 4.55)	<0.001
Presence of IV nitrates	No	8171 (94.6)	Reference	
	Yes	468 (5.4)	2.60 (2.04, 3.32)	<0.001
Presence of IV inotropes	No	8404 (97.3)	Reference	
	Yes	235 (2.7)	6.09 (4.61, 8.04)	<0.001
Cardiogenic shock	No	8253 (95.5)	Reference	
	Yes	386 (4.5)	6.32 (5.05, 7.90)	<0.001
Preoperative ventilation	No	8472 (98.1)	Reference	
	Yes	167 (1.9)	6.08 (4.39, 8.42)	<0.001

*With percentages in parentheses; non-normallly distributed continuous data are presented as median (IQR)

Table 12.1.6a. Operative factors and univariable analysis of risk factors for in-hospital mortality after proximal aortic surgery from the NICOR database in the UK

		No. of patients*	Odds ratio (95% CI) for in-hospital mortality	P value
Operative details				
Priority	Elective	5461 (63.2)	Reference	
	Urgent	1412 (16.3)	2.52 (2.04, 3.11)	<0.001
	Emergency	1615 (18.7)	4.76 (3.98, 5.69)	<0.001
	Salvage	149 (1.7)	20.03 (14.18, 28.29)	<0.001
	MISSING	2 (0.02)		
Concomitant procedures	No CABG operation	7000 (81.0)	Reference	
	CABG operation	1639 (19.0)	2.10 (1.79, 2.47)	<0.001
	No Valve operation	2642 (30.6)	Reference	
	Valve operation	5997 (69.4)	0.59 (0.50, 0.68)	<0.001
	No Other operation	5841 (67.6)	Reference	
	Other operation	2798 (32.4)	1.02 (0.87, 1.19)	0.47
Aortic pathology				
Aneurysm	No	3604 (41.7)	Reference	
	Yes	5035 (58.3)	0.27 (0.23, 0.32)	<0.001
Chronic dissection	No	8299 (96.1)	Reference	
	Yes	340 (3.9)	1.37 (0.98, 1.93)	0.07
Acute dissection	No	7071 (81.9)	Reference	
	Yes	1568 (18.2)	3.02 (2.58, 3.54)	<0.001
Trauma	No	8603 (99.6)	Reference	
	Yes	36 (0.4)	3.94 (1.9, 8.21)	<0.001
Coarctation	No	8636 (99.97)	Reference	
	Yes	3 (0.03)	5.09 (0.46, 56.14)	0.18
Penetrating Atheromatous Ulcer	No	8599 (99.5)	Reference	
	Yes	40 (0.5)	2.97 (1.41, 6.26)	0.004
Pseudoaneurysm	No	8592 (99.5)	Reference	
	Yes	47 (0.5)	2.77 (1.37, 5.59)	0.005
Intramural haematoma	No	8611 (99.7)	Reference	
	Yes	28 (0.3)	1.70 (0.59, 4.90)	0.33
Other	No	7161 (82.9)	Reference	
	Yes	1478 (17.1)	1.51 (1.26, 1.80)	<0.001
Aortic segment				
Root	No	4354 (50.4)	Reference	
	Yes	4285 (49.6)	0.89 (0.76, 1.03)	0.11
Ascending	No	2214 (25.7)	Reference	
	Yes	6425 (74.4)	0.90 (0.76, 1.06)	0.22
Arch	No	7801 (90.3)	Reference	
	Yes	838 (9.7)	1.72 (1.39, 2.13)	0.004

*With percentages in parentheses; non-normally distributed continuous data are presented as median (IQR)

Table 12.1.6b. Final multivariable logistic regression model for risk prediction in elective patients. Data taken from the NICOR database.

Parameter	Odds Ratio	95% CI	Co-efficient	P
Intercept	-	-	-6.6707	<0.001
Age at operation (years)	1.04	1.02, 1.05	0.0345	<0.001
Female gender	1.49	1.13, 1.98	0.4002	0.005
NYHA class > 2	1.45	1.10, 1.92	0.3721	0.009
Previous cardiac surgery	4.10	2.97, 5.67	1.4118	<0.001
Current smoker	1.61	1.04, 2.48	0.475	0.032
Pulmonary disease	1.50	1.07, 2.12	0.4081	0.02
History of neurological disease	2.12	1.46, 3.08	0.7518	<0.001
Preoperative non-sinus rhythm	1.61	1.15, 2.26	0.4765	0.006
Triple vessel disease	2.29	1.49, 3.52	0.8296	<0.001
Left ventricular ejection fraction < 30%	2.46	1.43, 4.25	0.9011	0.001
Concomitant CABG operation	2.29	1.68, 3.13	0.8275	<0.001
Surgery on the arch segment of the aorta	2.39	1.68, 3.41	0.8719	<0.001
Aortic pathology other than 'Aneurysm'	1.86	1.28, 2.70	0.619	0.001

Calculation of predicted risk using patient data and logistic regression coefficients: odds of in-hospital death = exp(-6.6707+[0.0345*age (continuous in years)]+[0.4002*Female gender]+ [0.3721*NYHA Class > 2]+[1.4118*Previous cardiac surgery]+[0.475*Current smoker]+[0.4081*History of pulmonary disease]+[0.7518*History of neurological disease]+[0.4765*Non sinus rhythm]+[0.8296*Triple vessel disease]+[0.9011*Left ventricular ejection fraction < 30%]+[0.8275*Concomitant CABG operation]+[0.8719*Surgery on the arch segment of the aorta]+[0.619*Aortic pathology other than 'Aneurysm'])

Table 12.1.6c. Final multivariable logistic regression model for risk prediction in non-elective patients

Parameter	Odds Ratio	95% CI	Co-efficient	P
Intercept	-	-	-4.666	<0.001
Age at operation (years)	1.03	1.02, 1.03	0.0251	<0.001
Previous cardiac surgery	3.86	2.99, 4.98	1.3506	<0.001
Creatinine > 200 µmol / L	1.73	1.21, 2.48	0.5483	0.003
Peripheral vascular disease	1.43	1.11, 1.83	0.3548	0.005
Preoperative non-sinus rhythm	1.74	1.32, 2.31	0.5563	<0.001
Left ventricular ejection fraction < 30%	1.52	1.06, 2.19	0.4187	0.024
Cardiogenic shock	1.87	1.42, 2.48	0.6265	<0.001
Emergency priority	2.77	2.17, 3.53	1.0186	<0.001
Salvage priority	9.90	6.46, 15.18	2.2928	<0.001
Concomitant CABG operation	2.17	1.69, 2.79	0.7739	<0.001

Calculation of predicted risk using patient data and logistic regression coefficients: odds of in-hospital death = exp(-4.666+[0.0251*age (continuous in years)]+[1.3506*Previous cardiac surgery]+[0.5483*Creatinine > 200 µmol / L]+[0.3548*Peripheral vascular disease]+[0.5563*Non sinus rhythm]+[0.4187*Left ventricular ejection fraction < 30%]+[0.6265*Cardiogenic shock]+[1.0186*Emergency priority]+[2.2928*Salvage priority]+[0.7739*Concomitant CABG operation])

Table 12.1.7. Risk group assessment demonstrating good calibration of the risk prediction model ultising NICOR data

Risk Group	n	Score Range	Observed mortality	Predicted mortality	P
Elective cohort					
Low	4047	0%-5%	1.75	2.01	0.398
Medium	624	5%-8%	7.69	6.29	0.331
High	792	>8%	16.54	16.36	0.923
Non-elective cohort					
Low	1547	0%-12%	6.33	7.09	0.401
Medium	823	12%-20%	15.8	15.14	0.713
High	806	>20%	36.85	36.13	0.764

Table 12.2.4a. Patient characteristics showing univariate odds ratios for in-hospital mortality

	All Type A Acute Dissections (n=1386)	Missing Data	Odds ratio (95% CI)	p-value
Age at operation (years)	63 (52, 72)	0 (0)	1.02 (1.01, 1.03)	<0.001
Female gender	446 (32.2)	0 (0)	0.91 (0.68, 1.23)	0.53
Body mass index (kg/m2)	26.3 (23.8, 29.4)	48 (3.5)	1.01 (0.98, 1.04)	0.55
Angina class IV	215 (15.5)	17 (1.2)	1.37 (0.96, 1.96)	0.09
NYHA class ≥ III	360 (26.0)	23 (1.7)	1.45 (1.07, 1.95)	0.02
Previous Q-wave MI	140 (10.1)	13 (0.9)	2.37 (1.61, 3.49)	<0.001
Recent MI (within 90 days)	71 (5.1)	10 (0.7)	3.28 (1.99, 5.39)	<0.001
Previous PCI	45 (3.3)	39 (2.8)	1.17 (0.55, 2.45)	0.69
Previous cardiac surgery	85 (6.1)	97 (7.0)	1.68 (1.01, 2.79)	0.04
Diabetes (diet or insulin controlled)	63 (4.6)	11 (0.8)	1.48 (0.81, 2.69)	0.20
Current smoker	246 (17.8)	53 (3.8)	0.88 (0.61, 1.28)	0.50
History of hypertension	964 (69.6)	8 (0.6)	1.15 (0.85, 1.56)	0.37
Creatinine > 200 µmol/L	72 (5.2)	111 (8.0)	1.99 (1.18, 3.38)	0.01
History of renal dysfunction	33 (2.4)	60 (4.3)	2.73 (1.33, 5.63)	0.006
History of pulmonary disease	152 (11.0)	9 (0.7)	1.00 (0.64, 1.56)	>0.99
History of neurological disease	145 (10.5)	19 (1.4)	1.01 (0.65, 1.59)	0.95
History of neurological dysfunction	103 (7.4)	15 (1.1)	1.28 (0.79, 2.10)	0.32
Peripheral vascular disease	283 (20.4)	16 (1.2)	1.48 (1.07, 2.04)	0.02
Non-sinus heart rhythm	126 (9.1)	92 (6.6)	2.00 (1.32, 3.03)	0.001
Triple vessel disease	30 (2.2)	324 (23.4)	1.16 (0.47, 2.88)	0.74
Left ventricular ejection fraction 30% - 50%	267 (19.3)	23 (1.7)	1.45 (1.04, 2.03)	0.03
Left ventricular ejection fraction <30%	47 (3.4)	23 (1.7)	3.96 (2.17, 7.22)	<0.001
Intravenous nitrates or any heparin	190 (13.7)	6 (0.4)	1.01 (0.68, 1.51)	0.95
Intravenous inotropes prior to anaesthesia	100 (7.2)	8 (0.6)	3.33 (2.17, 5.12)	<0.001
Pre-operative ventilation	81 (5.8)	6 (0.4)	2.97 (1.85, 4.76)	<0.001
Pre-operative cardiogenic shock	235 (17.0)	13 (0.9)	2.76 (2.00, 3.79)	<0.001

Table 12.2.4b. Operative characteristics showing univariate odds ratios for in-hospital mortality

	All Type A Acute Dissections (n=1386)	Missing Data	OR (95% CI)	p-value
Elective operation	24 (1.7)	0 (0)	2.21 (0.90, 5.41)	0.08
Urgent operation	189 (13.6)	0 (0)	0.74 (0.47, 1.19)	0.21
Emergency operation	1076 (77.6)	0 (0)	1 (referent category)	-
Salvage operation	97 (7.0)	0 (0)	5.05 (3.28, 7.76)	<0.001
Root segment	463 (33.4)	0 (0)	1.13 (0.84, 1.51)	0.38
Ascending segment	1202 (86.7)	0 (0)	1 (referent category)	-
Arch segment	176 (12.7)	0 (0)	1.20 (0.80, 1.78)	0.38
Concomitant CABG	181 (13.1)	27 (2.0)	2.72 (1.92, 3.84)	<0.001
Concomitant Valve	569 (41.1)	26 (1.9)	0.96 (0.73, 1.27)	0.78
Concomitant Other cardiac procedure	428 (30.9)	31 (2.2)	1.08 (0.99, 1.18)	0.08
Cardiopulmonary bypass time > 260 mins	324 (24.1)	39 (2.8)	2.04 (1.51, 2.75)	<0.001
Aortic cross clamp time > 145 mins	329 (24.5)	45 (3.2)	1.10 (0.80, 1.52)	0.55
Circulatory arrest time > 35 mins	252 (24.0)	335 (24.2)	1.55 (1.11, 2.16)	0.01

Table 12.2.6. Post-operative outcomes from NICOR in all patients under going Type A Acute Dissection Surgery in the UK. A separate column for missing data is provided

	All Type A Acute Dissections (n=1386)	Missing Data
In-hospital mortality	246 (17.8)	0 (0)
All stroke	165 (11.9)	169 (12.2)
TIA	57 (4.1)	169 (12.2)
CVA	108 (7.8)	169 (12.2)
Paraparesis	7 (0.5)	169 (12.2)
Paraplegia	3 (0.2)	169 (12.2)
Post-operative dialysis	198 (14.3)	156 (11.3)
Return to theatre (RTT)	236 (17.0)	74 (5.3)
RTT for bleeding	198 (14.3)	74 (5.3)
RTT for valvular problems	4 (0.3)	74 (5.3)
RTT for graft problems	3 (0.2)	74 (5.3)
RTT for other cardiac problems	33 (2.4)	74 (5.3)
RTT for other sternal resuturing	11 (0.8)	74 (5.3)
RTT for deep sternal wound infection	3 (0.2)	74 (5.3)

Table 12.3.5. Patients Demographics of LHCH patients pre and post match *(1of 2)*

	Before Match			After Match		
	Pre-Subspecialisation (n=80)	Post-Subspecialisation (n=55)	P value	Pre-Subspecialisation (n=51)	Post-Subspecialisation (n=51)	P value
Pre-operative						
Age at operation (years)	62.8 (53.3, 67.9)	58.4 (52.5, 72.5)	0.69	62.1 (53.3, 68.7)	58.5 (52.5, 72.6)	0.72
Body mass index (kg/m2)	27.0 (24.3, 29.3)	26.7 (23.6, 31.6)	0.66	27.5 (24.6, 29.4)	26.6 (23.6, 31.2)	0.76
Female gender	24 (30.0)	23 (41.8)	0.16	15 (28.9)	21 (40.4)	0.22
Angina class IV	8 (10.0)	6 (10.9)	0.86	7 (13.5)	6 (11.5)	0.77
Previous myocardial infarction	4 (5.0)	1 (1.8)	0.65	1 (1.9)	1 (1.9)	>0.99
Myocardial infarction within the last 30 days	2 (2.5)	1 (1.8)	>0.99	0 (0)	1 (1.9)	>0.99
NYHA class ≥ III	12 (15.0)	6 (10.9)	0.49	6 (11.5)	6 (11.5)	>0.99
Current smoker	23 (28.8)	11 (20.0)	0.25	14 (26.9)	10 (19.2)	0.35
Diabetes	1 (1.3)	3 (5.5)	0.30	1 (1.9)	3 (5.8)	0.62
Hypercholesterolaemia	16 (20.0)	14 (25.5)	0.45	11 (21.2)	13 (25.0)	0.64
Hypertension	56 (70.0)	27 (49.1)	0.01	34 (65.4)	27 (51.9)	0.16
Respiratory disease *	16 (20.0)	9 (16.4)	0.59	10 (19.2)	9 (17.3)	0.80
Cerebrovascular disease	9 (11.3)	0 (0)	0.01	0 (0)	0 (0)	-
Peripheral vascular disease	7 (8.8)	2 (3.6)	0.31	6 (11.5)	2 (3.9)	0.27
Renal dysfunction †	9 (11.3)	12 (21.8)	0.10	7 (13.5)	12 (23.1)	0.20
Left ventricular ejection fraction <30%	3 (3.8)	1 (1.8)	0.65	1 (1.9)	1 (1.9)	>0.99
Logistic EuroSCORE	19.1 (12.2, 31.0)	22.5 (9.2, 32.1)	0.90	18.4 (12.2, 29.2)	22.8 (11.7, 32.8)	0.46

(Continued…)

Table 12.3.5. Patients Demographics *(2 o 2)*

	Before Match			*After Match*		
	Pre-Subspecialisation (n=80)	***Post-Subspecialisation (n=55)***	***P value***	***Pre-Subspecialisation (n=51)***	***Post-Subspecialisation (n=51)***	***P value***
Operative						
Prior surgery	*3 (3.8)*	*1 (1.8)*	*0.65*	*2 (3.9)*	*1 (1.9)*	*>0.99*
Cutting time	*480 (420, 610)*	*583 (520, 675)*	*0.002*	*510 (421, 617)*	*598.5 (502.5, 682.5)*	*0.038*
Cardiopulmonary bypass time	*291 (240.5, 353)*	*345 (305, 425)*	*<0.001*	*303.5 (261, 353)*	*342.5 (305, 425)*	*0.01*
Aortic crossclamp time	*145 (119, 194)*	*204 (147, 258)*	*0.001*	*151.5 (112.5, 201)*	*203 (142, 258)*	*0.004*

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;

Categorical data shown as percentage (number), comparisons made with Chi-square tests and Fishers exact tests as appropriate

*** Respiratory disease defined as patient having FEV1<75, asthma, emphysema, chronic obstructive airway disease or being on respiratory medications**

† Renal dysfunction includes patients with a functioning renal transplant and patients with acute or chronic renal failure or insufficiency

Table 12.3.6. Patients Demographics Aortic Arch before and after matching for both pre and post subspecialisation*(1 of 2)*

	Before Match			After Match		
	Pre-Subspecialisation (n=73)	Post-Subspecialisation (n=159)	P value	Pre-Subspecialisation (n=71)	Post-Subspecialisation (n=71)	P value
Pre-operative						
Age at operation (years)	62.2 (52.4, 69.8)	63.1 (48.9, 71.5)	0.95	62.1 (52.1, 69.7)	64.9 (54.9, 74.5)	0.07
Body mass index (kg/m2)	26.2 (23.7, 29.7)	26.9 (23.9, 30.0)	0.57	26.2 (23.5, 29.7)	27.1 (23.8, 29.4)	0.57
Female gender	34 (46.6)	61 (38.4)	0.24	32 (45.1)	33 (46.5)	0.87
Angina class IV	1 (1.4)	1 (0.6)	0.53	1 (1.4)	1 (1.4)	>0.99
Previous myocardial infarction	0 (0)	4 (2.5)	0.31	0 (0)	2 (2.8)	0.50
Myocardial infarction within the last 30 days	0 (0)	0 (0)	-	0 (0)	0 (0)	-
NYHA class ≥ III	28 (38.4)	33 (20.8)	0.005	26 (36.6)	26 (36.6)	>0.99
Current smoker	8 (11.0)	24 (15.1)	0.40	8 (11.3)	11 (15.5)	0.46
Diabetes	2 (2.7)	8 (5.0)	0.73	2 (2.8)	3 (4.2)	>0.99
Hypercholesterolaemia	29 (39.7)	70 (44.0)	0.54	29 (40.9)	35 (49.3)	0.31
Hypertension	41 (56.2)	77 (48.4)	0.27	40 (56.3)	36 (50.7)	0.50
Respiratory disease *	34 (46.6)	43 (27.0)	0.003	32 (45.1)	31 (43.7)	0.87
Cerebrovascular disease	9 (12.3)	9 (5.7)	0.08	9 (12.7)	6 (8.5)	0.41
Peripheral vascular disease	3 (4.1)	11 (6.9)	0.56	3 (4.2)	2 (2.8)	>0.99
Renal dysfunction †	3 (4.1)	10 (6.3)	0.76	3 (4.2)	3 (4.2)	>0.99
Left ventricular ejection fraction <30%	1 (1.4)	3 (1.9)	>0.99	1 (1.4)	2 (2.8)	>0.99
Logistic EuroSCORE	17.4 (10.0, 24.8)	11.7 (6.2, 23.6)	0.009	16.8 (9.6, 24.8)	13.8 (7.2, 24.9)	0.30

Table 12.3.6. Patients Demographics Aortic Arch before and after matching for both pre and post subspecialisation (2 of 2)

	Before Match			After Match		
	Pre-Subspecialisation (n=73)	Post-Subspecialisation (n=159)	P value	Pre-Subspecialisation (n=71)	Post-Subspecialisation (n=71)	P value
Operative						
Non-elective	11 (15.1)	43 (27.0)	0.045	11 (15.5)	12 (16.9)	0.820
Prior surgery	10 (13.7)	32 (20.1)	0.24	10 (14.1)	10 (14.1)	>0.99
Cutting time	400 (358, 475)	437 (371, 491)	0.24	400 (358, 475)	416 (359, 467)	0.99
Cardiopulmonary bypass time	289 (230, 341)	335 (275, 409)	0.001	289 (230, 341)	308 (269, 369)	0.06
Aortic crossclamp time	157 (119, 205)	185 (145, 239)	0.004	157 (119, 199)	183 (138, 239)	0.045

Continuous data shown as median (25th to 75th percentile), comparisons made with Wilcoxon rank sum tests;

Categorical data shown as percentage (number), comparisons made with Chi-square tests and Fishers exact tests as appropriate

*** Respiratory disease defined as patient having FEV1<75, asthma, emphysema, chronic obstructive airway disease or being on respiratory medications**

† Renal dysfunction includes patients with a functioning renal transplant and patients with acute or chronic renal failure or insufficiency

Table 12.4.4. Patient Demographics for total and hemi arch replacement at LHCH in both elective and non elective surgeries

Variable	Total Arch Replacement			Hemi-Arch Replacement		
	Elective (n=75)	Non-elective (n=35)	p-value	Elective (n=140)	Non-elective (n=26)	p-value
Age at operation (years)	64.5 (46.4, 71.0)	60.0 (52.1, 69.0)	0.59	64.3 (53.7, 71.9)	60.6 (52.7, 74.3)	0.54
Female gender	37 (49.3)	16 (45.7)	0.72	48 (34.3)	9 (34.6)	0.95
Comorbidities						
Body mass index (kg/m2)	26.0 (23.1, 30.0)	26.6 (23.8, 29.1)	0.96	27.5 (24.9, 30.4)	27.8 (24.7, 31.7)	0.57
Angina class IV	2 (2.7)	1 (2.9)	>0.99	3 (2.1)	2 (7.7)	0.17
Previous Q-wave MI	4 (5.3)	0 (0)	0.30	5 (3.6)	2 (7.7)	0.30
Left ventricular ejection fraction 30% - 50%	6 (8.0)	8 (22.9)	0.06	27 (20.0)	9 (34.6)	0.10
Left ventricular ejection fraction <30%	2 (2.7)	0 (0)	>0.99	3 (2.1)	1 (3.9)	0.50
NYHA class ≥ III	20 (26.7)	7 (20.0)	0.45	41 (29.3)	8 (30.8)	0.88
Current smoker	7 (9.3)	10 (28.6)	0.009	19 (13.6)	2 (7.7)	0.53
Diabetes	4 (5.3)	2 (5.7)	>0.99	8 (5.7)	2 (7.7)	0.66
Hypercholesterolaemia	32 (42.7)	13 (37.1)	0.58	77 (55.0)	5 (19.2)	<0.001
Hypertension	43 (57.3)	20 (57.1)	0.99	76 (54.3)	14 (53.9)	0.97
Cerebrovascular disease	5 (6.7)	2 (5.7)	>0.99	12 (8.6)	2 (7.7)	>0.99
Respiratory disease	30 (40.0)	5 (14.3)	0.007	50 (35.7)	9 (34.6)	0.91
Peripheral vascular disease	10 (13.3)	1 (2.9)	0.17	6 (4.3)	4 (15.4)	0.052
Renal dysfunction	3 (4.0)	5 (14.3)	0.11	3 (2.1)	5 (19.2)	0.003
Previous cardiac surgery	24 (32.0)	5 (14.3)	0.0495	14 (10.0)	3 (11.5)	0.73
Aetiology						
Degenerative	42 (56.0)	18 (51.4)	0.65	74 (52.9)	13 (50.0)	0.79
Non-Degenerative	33 (44.0)	16 (45.7)	0.87	65 (46.4)	13 (50.0)	0.74
Other	0 (0)	1 (2.9)	0.32	1 (0.7)	0 (0)	>0.99

Categorical variables shown as n (%), comparisons made with chi-squared and Fisher's exact tests as appropriate;

Continuous variables shown as median (25th percentile, 75th percentile), comparisons made with Wilcoxon's Signed Rank test and t-tests as appropriate

Table 12.4.6. Post-Operative Complications And Length Of Stay

Complication	Total Arch Replacement			Hemi-Arch Replacement		
	Elective (n=67)	Non-elective (n=29)	p-value	Elective (n=133)	Non-elective (n=25)	p-value
Intubation time (hours)	16 (11, 38)	44 (18, 120)	0.03	16 (11, 23)	10 (9, 20)	0.33
ITU stay (days)	3 (2, 7)	5 (2, 10)	0.17	2 (1, 4)	4 (3, 15)	0.002
Post-operative stay (days)	11 (9, 20)	12 (9, 20)	0.77	10 (7, 14)	11.5 (7.5, 19.5)	0.25
Re-intubation	7 (10.5)	2 (6.9)	0.72	6 (4.5)	4 (16.0)	0.053
Prolonged ventilation (> 48h)	11 (16.4)	7 (24.1)	0.37	12 (9.0)	3 (12.0)	0.71
Acute renal failure	5 (7.5)	7 (24.1)	0.04	6 (4.5)	2 (8.0)	0.61
Deep sternal wound infection	3 (4.5)	0 (0)	0.55	2 (1.5)	0 (0)	>0.99
Re-exploration for bleeding	4 (6.0)	3 (10.3)	0.43	6 (4.5)	5 (20.0)	0.02
Stroke	3 (4.5)	5 (17.2)	0.052	4 (3.0)	3 (12.0)	0.08
Local readmission within 30 days	3 (4.5)	3 (10.3)	0.36	9 (6.8)	1 (4.0)	>0.99
In-hospital mortality	5 (7.5)	9 (31.0)	0.005	2 (1.5)	5 (20.0)	0.001

Categorical variables shown as n (%), comparisons made with chi-squared and Fisher's exact tests as appropriate;

Continuous variables shown as median (25^{th} percentile, 75^{th} percentile), comparisons made with Wilcoxon's Signed Rank test and t-tests as appropriate

Table 12.5.6a. Aortic Arch Characteristics and Activity

Variables	All AAR (n=287)	Elective HAAR (n=140)	Elective TAAR (n=81)	p-value
Age at operation (years)	63.7 (52.4, 71.5)	64.3 (53.7, 71.9)	65.3 (46.6, 72.1)	0.25
Female gender	115 (40.1)	48 (34.3)	40 (49.4)	0.03
Comorbidities				
Body mass index (kg/m2)	26.9 (24.3, 30.1)	27.5 (24.9, 30.4)	26.0 (23.2, 29.3)	0.03
Left ventricular ejection fraction < 50%	58 (20.2)	31 (22.1)	9 (11.1)	0.04
NYHA class ≥ III	76 (26.5)	41 (29.3)	20 (24.7)	0.46
Current smoker	39 (13.6)	16 (11.4)	9 (11.1)	0.94
Diabetes	16 (5.6)	8 (5.7)	4 (4.9)	>0.99
Hypercholesterolemia	133 (46.3)	77 (55.0)	36 (44.4)	0.13
Hypertension	159 (55.4)	76 (54.3)	47 (58.0)	0.59
Cerebrovascular disease	23 (8.0)	12 (8.6)	6 (7.4)	0.76
Respiratory disease	100 (34.8)	52 (37.1)	34 (42.0)	0.48
Peripheral vascular disease	21 (7.3)	6 (4.3)	10 (12.4)	0.03
Renal dysfunction†	17 (5.9)	3 (2.1)	3 (3.7)	0.67
Previous cardiac surgery	48 (16.7)	14 (10.0)	25 (30.9)	<0.001
Aetiology				
Degenerative	147 (51.2)	72 (51.4)	44 (54.3)	0.68
Non-degenerative	138 (48.1)	67 (47.9)	37 (45.7)	0.75
Iatrogenic	2 (0.7)	1 (0.7)	0 (0)	>0.99
Priority				
Non-elective procedure	66 (23.0%)	-	-	-
Extent of arch				
Total arch	117 (40.8)	-	81 (100)	-
Hemi-arch	170 (59.2)	140 (100)	-	-
Concomitant procedures				
Aortic valve replacement	220 (76.7)	122 (87.1)	52 (64.2)	<0.001
Mitral valve replacement/ repair	4 (1.4)	2 (1.4)	1 (1.2)	>0.99
Tricuspid valve	2 (0.7)	1 (0.7)	1 (1.2)	>0.99
Pulmonary valve	1 (0.4)	0 (0)	1 (1.2)	>0.99
CABG	46 (16.0)	26 (18.6)	10 (12.4)	0.23
Aortic root	220 (76.7)	114 (81.4)	58 (71.6)	0.09
Thoracic aorta	18 (6.3)	1 (0.7)	2 (2.5)	0.56
Operative times				
Circulatory arrest	38 (24, 68)	28 (20, 34.5)	68 (45, 99)	<0.001
Cardiopulmonary bypass	330 (272, 394)	299 (256, 341)	358 (280, 434)	<0.001
Aortic cross clamp	185 (140, 238)	174 (138, 207)	201 (135.5, 267.5)	0.02

Categorical variables shown as n (%)

Continuous variables shown as median (25th percentile, 75th percentile)

Table 12.5.6b. Pre- And Peri-Operative Patient Data In Non-Elective Hemi-Arch (HAAR) And Total Arch (TAAR) Repair

Variables	Non-elective HAAR (n=30)	Non-elective TAAR (n=36)	p-value
Age at operation (years)	60.6 (52.1, 74.3)	59.3 (53.1, 67.2)	0.58
Female gender	10 (33.3)	17 (47.2)	0.25
Comorbidities			
Body mass index (kg/m2)	27.8 (24.2, 31.6)	26.7 (24.1, 29.0)	0.28
Left ventricular ejection fraction <50%	10 (33.3)	8 (22.2)	0.31
NYHA class ≥ III	8 (26.7)	7 (19.4)	0.49
Current smoker	2 (6.7)	12 (33.3)	0.008
Diabetes	2 (6.7)	2 (5.6)	>0.99
Hypercholesterolaemia	7 (23.3)	13 (36.1)	0.26
Hypertension	16 (53.3)	20 (55.6)	0.86
Cerebrovascular disease	3 (10.0)	2 (5.6)	0.65
Respiratory disease	9 (30.0)	5 (13.9)	0.11
Peripheral vascular disease	4 (13.3)	1 (2.8)	0.17
Renal dysfunction	6 (20.0)	5 (13.9)	0.51
Previous cardiac surgery	4 (13.3)	5 (13.9)	>0.99
Etiology			
Degenerative	13 (43.3)	18 (50.0)	0.59
Non-degenerative	17 (56.7)	17 (47.2)	0.44
Iatrogenic	0 (0)	1 (2.8)	>0.99
Concomitant procedures			
Aortic valve replacement	24 (80.0)	22 (61.1)	0.10
Mitral valve replacement / repair	0 (0)	1 (2.8)	>0.99
Tricuspid valve	0 (0)	0 (0)	-
Pulmonary valve	0 (0)	0 (0)	-
CABG	5 (16.7)	5 (13.9)	>0.99
Aortic root	22 (73.3)	26 (72.2)	0.92
Thoracic aorta	0 (0)	1 (2.8)	>0.99
Operative times			
Circulatory arrest	44 (25, 56)	79.5 (52, 114)	<0.001
Cardiopulmonary bypass	340 (283, 440)	399 (348.5, 473)	0.01
Aortic crossclamp	184 (147, 207)	223 (157, 309)	0.04

Table 12.5.11a. In-Hospital And Follow-Up Outcomes In All Patients And Elective Hemi-Arch (HAAR) And Total Arch (TAAR) Repair

Variables	All AAR (n=287)	Elective HAAR (n=140)	Elective TAAR (n=81)	p-value
Intubation time (hours)	16 (11, 28)	16 (10.5, 23)	16 (12, 38)	0.17
ITU stay (days)	3 (2, 6)	2 (1, 4)	4 (2, 7)	<0.001
Post-operative stay (days)	11 (8, 17)	10 (7, 14)	12 (9, 21)	<0.001
Re-intubation	22 (7.7)	6 (4.3)	9 (11.1)	0.052
Prolonged ventilation (> 48h)	35 (12.2)	12 (8.6)	13 (16.1)	0.09
Acute renal failure	21 (7.3)	6 (4.3)	5 (6.2)	0.54
Deep sternal wound infection	1 (0.4)	0 (0)	1 (1.2)	0.37
Re-exploration for bleeding	18 (6.3)	6 (4.3)	4 (4.9)	>0.99
All stroke	16 (5.6)	4 (2.9)	4 (4.9)	0.47
CVA	13 (4.5)	3 (2.1)	4 (4.9)	0.26
TIA / RIND	3 (1.1)	1 (0.7)	0 (0)	>0.99
Confusion	19 (6.6)	5 (3.6)	10 (12.4)	0.01
In-hospital mortality	23 (8.0)	3 (2.1)	5 (6.2)	0.15
30 day mortality	19 (6.6)	3 (2.1)	3 (3.7)	0.67
1 year mortality	36 (12.5)	11 (7.9)	9 (11.1)	0.42
5 year mortality	60 (20.9)	22 (15.7)	21 (25.9)	0.065

Categorical variables shown as n (%)

Continuous variables shown as median (25th percentile, 75th percentile)

Table 12.5.11b. In-Hospital And Follow-Up Outcomes In Non-Elective Hemi-Arch (HAAR) And Total Arch (TAAR) Repair

Variables	Non-elective HAAR (n=30)	Non-elective TAAR (n=36)	p-value
Intubation time (hours)	10 (8, 24)	27 (14, 79)	0.03
ITU stay (days)	4 (3, 11.5)	5 (2, 8.5)	0.81
Post-operative stay (days)	11 (8, 19)	11 (9, 19.5)	0.62
Re-intubation	4 (13.3)	3 (8.3)	0.69
Prolonged ventilation (> 48h)	3 (10.0)	7 (19.4)	0.33
Acute renal failure	2 (6.7)	8 (22.2)	0.10
Deep sternal wound infection	0 (0)	0 (0)	-
Re-exploration for bleeding	5 (16.7)	3 (8.3)	0.45
All stroke	3 (10.0)	5 (13.9)	0.72
CVA	2 (6.7)	4 (11.1)	0.68
TIA / RIND	1 (3.3)	1 (2.8)	>0.99
Confusion	1 (3.3)	3 (8.3)	0.62
In-hospital mortality	6 (20.0)	9 (25.0)	0.63
30 day mortality	5 (16.7)	8 (22.2)	0.57
1 year mortality	7 (23.3)	9 (25.0)	0.88
5 year mortality	8 (26.7)	9 (25.0)	0.88

Table 12.5.12a. Univariate Analysis Showing Significant Risk Factors For Follow Up Survival In All AAR Patients

Variables	Patients	Median Follow up	Survival Rate %			p-value
	n	(Months)	1 Year	3 Years	5 Years	
Total	**287**	**33.4**	**87.5**	**80.8**	**79.1**	
Age at operation (years)						
≤65	155	35.3	90.3	85.2	84.5	0.007
>65	132	27.2	84.1	75.8	72.7	
NYHA class ≥ III						
No	211	33.8	89.1	84.4	83.4	0.002
Yes	76	29.7	82.9	71.1	67.1	
Diabetes						
No	271	34.8	88.2	81.9	80.1	0.038
Yes	16	14.8	75	62.5	62.5	
Respiratory disease						
No	187	31.6	89.3	84.5	84	0.02
Yes	100	35.3	84	74	70	
Peripheral vascular disease						
No	266	34.5	88.4	82.3	81.2	<0.001
Yes	21	25.6	76.2	61.9	52.4	
Preoperative renal dysfunction						
No	270	35.4	89.6	82.6	80.7	<0.001
Yes	17	6	52.9	52.9	52.9	
Concomitant CABG procedure						
No	241	33.8	89.6	83.4	81.7	0.029
Yes	46	28.4	76.1	67.4	65.2	
Circulatory arrest (minutes)						
≤100	251	37.5	88.8	83.3	81.3	0.001
>100	36	18.8	77.8	63.9	63.9	
Cardiopulmonary bypass (minutes)						
≤450	251	35.1	90.4	84.5	82.5	<0.001
>450	36	19.3	66.7	55.6	55.6	

Table 12.5.12b. Multivariable Analysis Showing Risk Factors For Follow Up Survival In All AAR Patients

Risk Factors	Hazard Ratio	95% CI	p-value
Pre operative renal dysfunction	3.11	1.44, 6.73	<0.001
NYHA class ≥ III	2.25	1.38, 3.67	0.002
Circulatory arrest time > 100 minutes	2.92	1.57, 5.43	0.001
Peripheral vascular disease	2.44	1.25, 4.74	0.004
Concomitant CABG operation	2.14	1.20, 3.80	0.008

C-index = 0.72

Table 12.5.13. Elephant trunk (ET) post-operative complications

Variable	Total Arch Replacement		
	Elective (n=81)	Non-elective (n=36)	p-value
Conventional ET	**37 (49.3)**	**13 (37.1)**	**0.23**
Stroke	2/37 (5.4)	1/13 (7.7)	>0.99
In-hospital mortality	4/37 (10.8)	1/13 (7.7)	>0.99
30 day mortality	3/37 (8.1)	1/13 (7.7)	>0.99
Frozen ET	**7 (9.3)**	**5 (14.3)**	**0.52**
Stroke	0/7 (0)	0/5 (0)	-
In-hospital mortality	0/7 (0)	1/5 (20.0)	0.42
30 day mortality	0/7 (0)	1/5 (20.0)	0.42
Reverse ET (2nd stage)	**2 (2.7)**	**0 (0)**	**>0.99**
Stroke	0/2 (0)	0 (0)	-
In-hospital mortality	0/2 (0)	0 (0)	-
30 day mortality	0/2 (0)	0 (0)	-

Categorical variables shown as n (%)

Comparisons made with chi-squared and Fisher's exact tests as appropriate

FIGURES

Figure 2.3.1. Annual % Expenditure

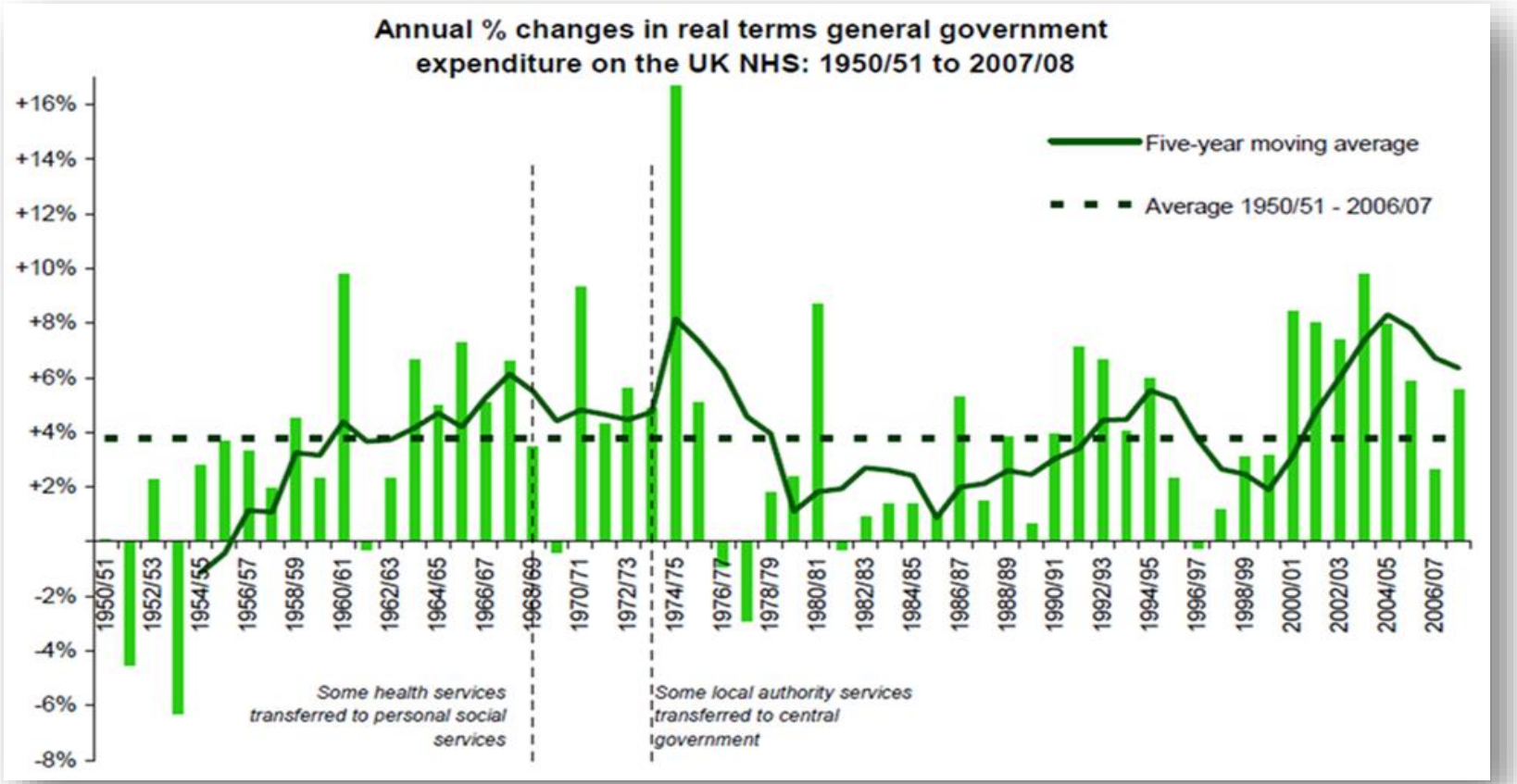


Figure 3.2. Type of Thoracic Aortic Aneurysms

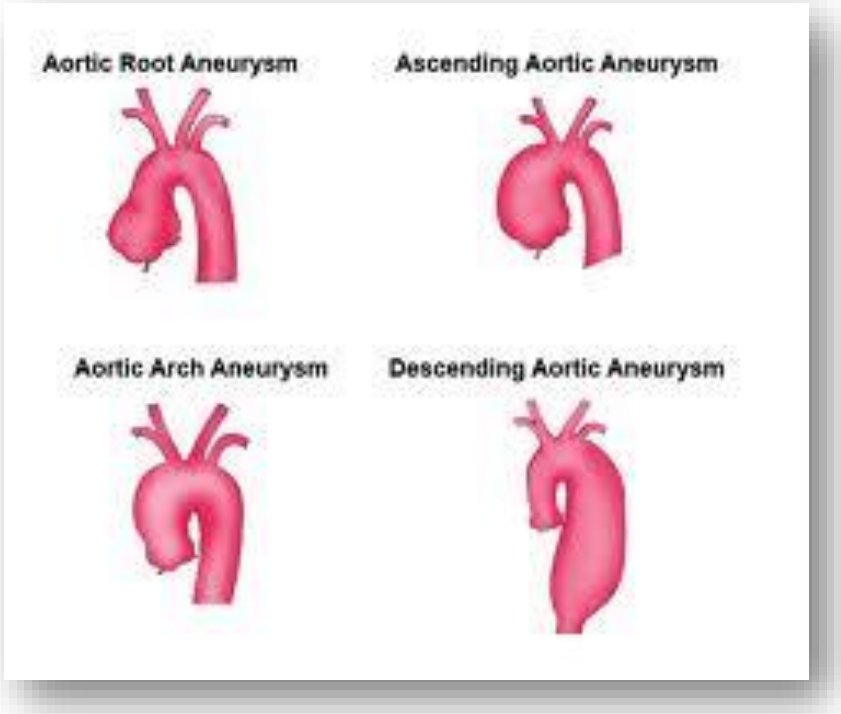


Figure 3.8. Aneurysmal Disease (indicated by the red arrows)

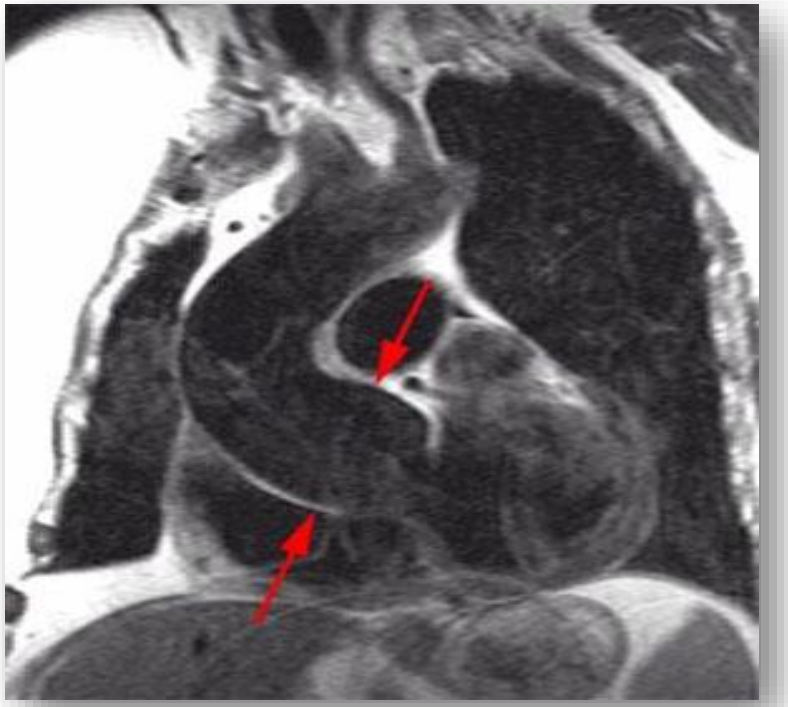


Image taken from St. Roosevelt Aneurysm Centre. USA

Figure 7.3a. Postoperative mortality in Marfan patients as high as 6.8% in those undergoing composite valve grafts in a retrospective group of 119 patients (114)

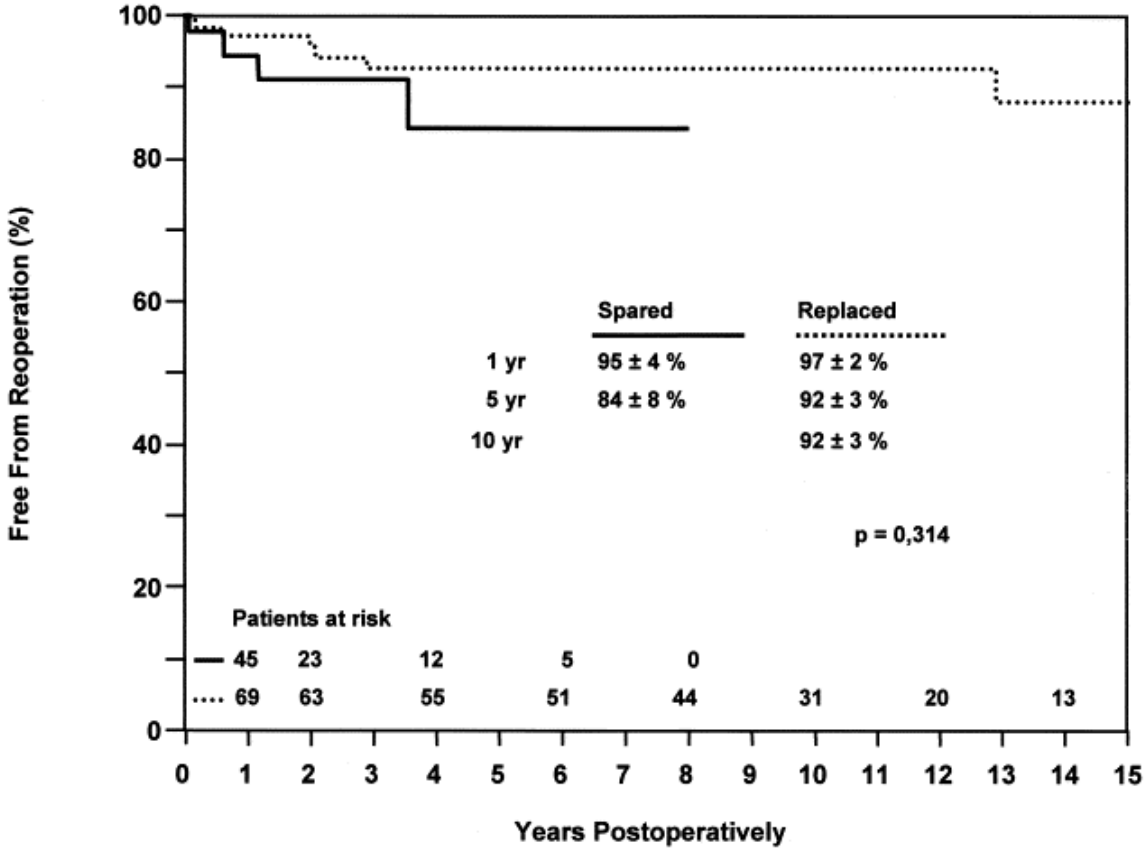
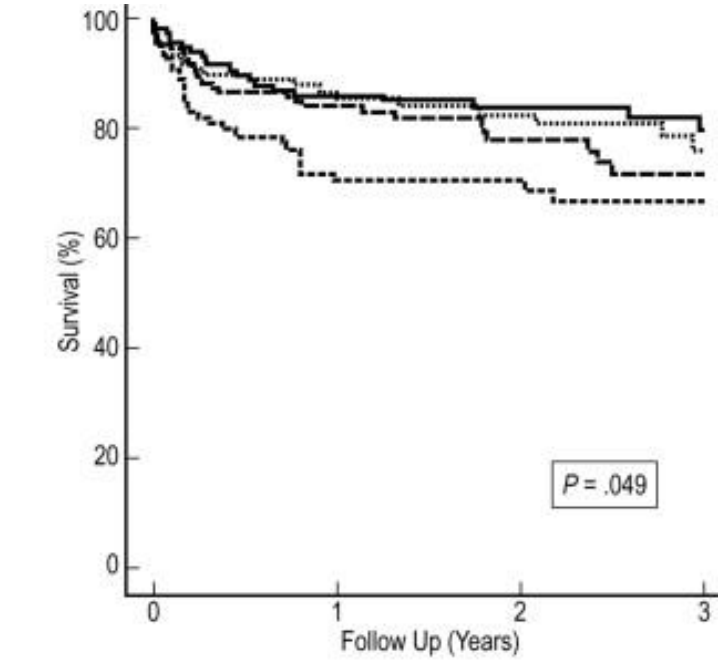


Figure 7.3b. Survival after repair of thoracoabdominal aortic aneurysm among 509 patients, stratified by extent of repair. (122)



Extent I	129	85	58	35
Extent II	161	87	53	21
Extent III	94	53	38	13
Extent IV	125	73	49	26

Figure 7.4. Distribution of interventional activity on all thoracic aortic aneurysms by centre within England

Figure 7.4

Distribution of interventional activity on all thoracic aortic aneurysms by centre within England (Dr Foster)

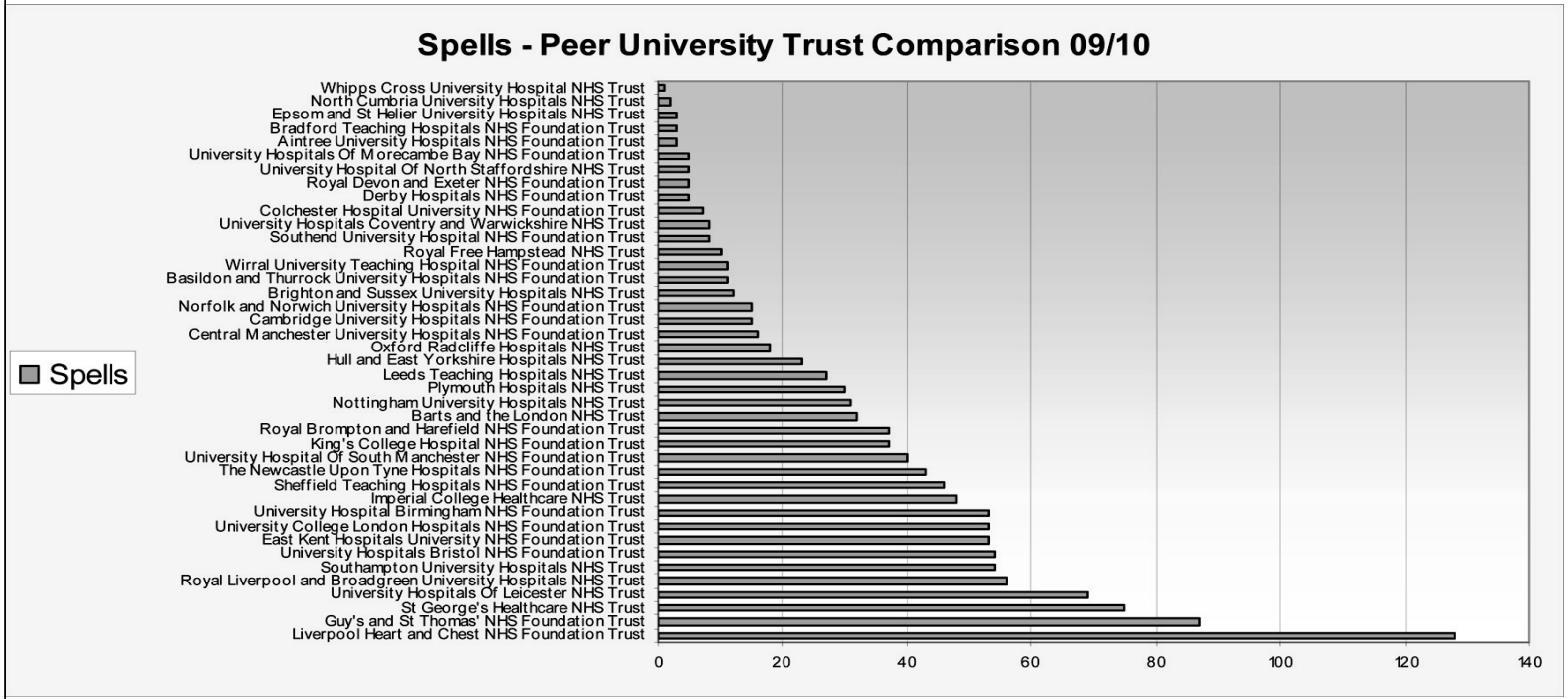
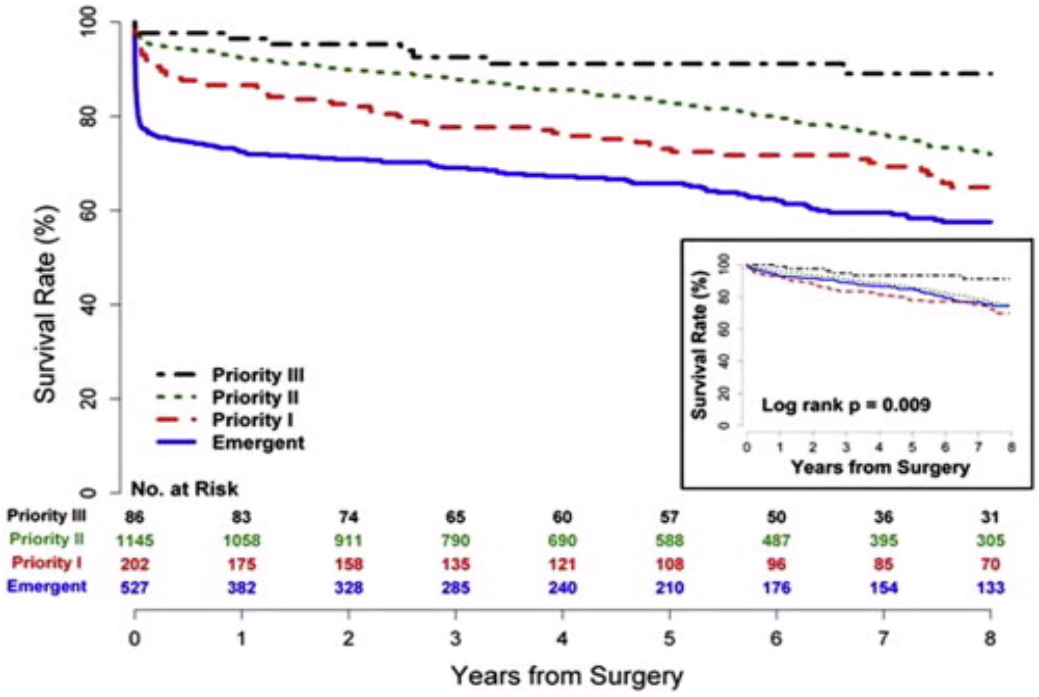


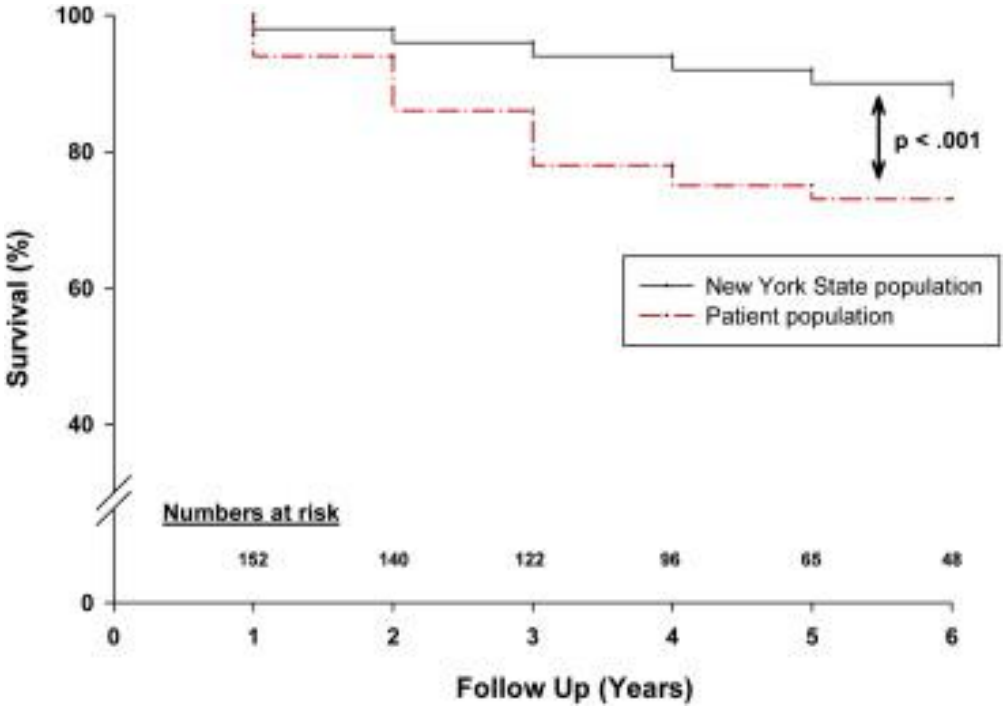
Figure 7.8a. Kaplan-Meier Survival Curve Stratified By Urgency Of Surgery.

Insert, Kaplan-Meier survival curve stratified by urgency for those surviving beyond the first 30 postoperative days.



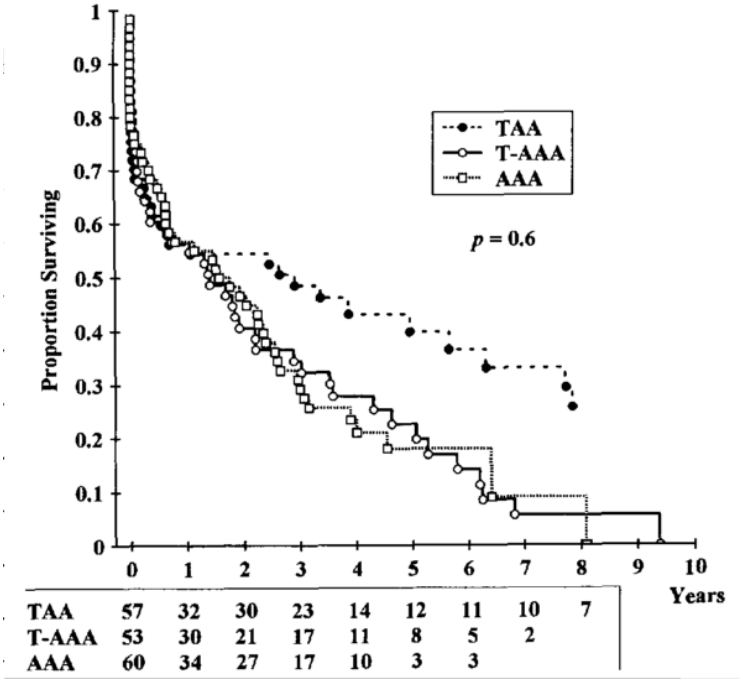
From Higgins et al with permission.

Figure 7.8b. Aortic Arch Replacement with a TG: Kaplan–Meier curve of 152 1-year survivors versus New York State population.



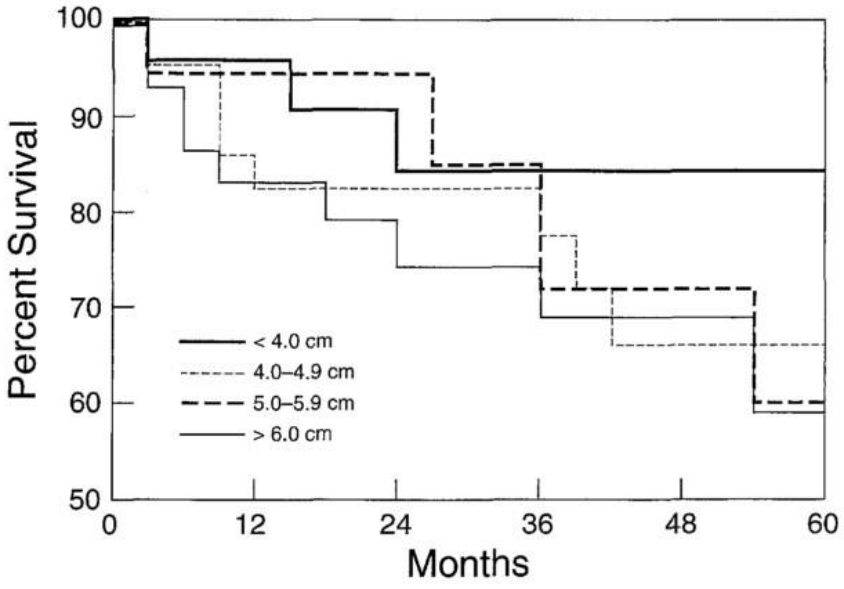
From Bischoff et al with permissions.

Figure 8.1.3. Kaplan-Meier Cumulative Survival displaying the dismal prognosis of unoperated patients with Thoracic Aortic Aneurysms (TAA), Thoraco-Abdominal Aneurysms (T-AAA), and Abdominal Aortic Aneurysms (AAA).



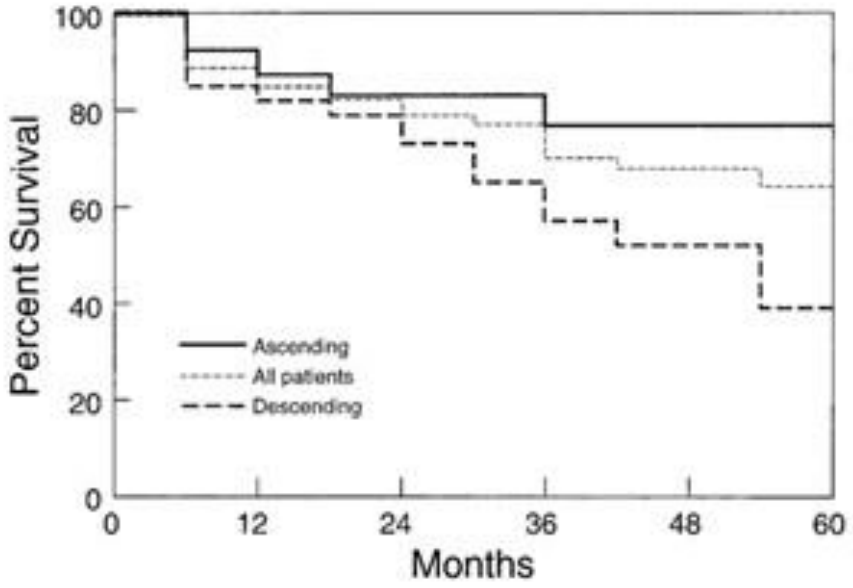
From Perko et al[173].

Figure 8.1.4a. Kaplan-Meier cumulative survival for 5 year survival in TAAs of varying size between 4 to 6cms.



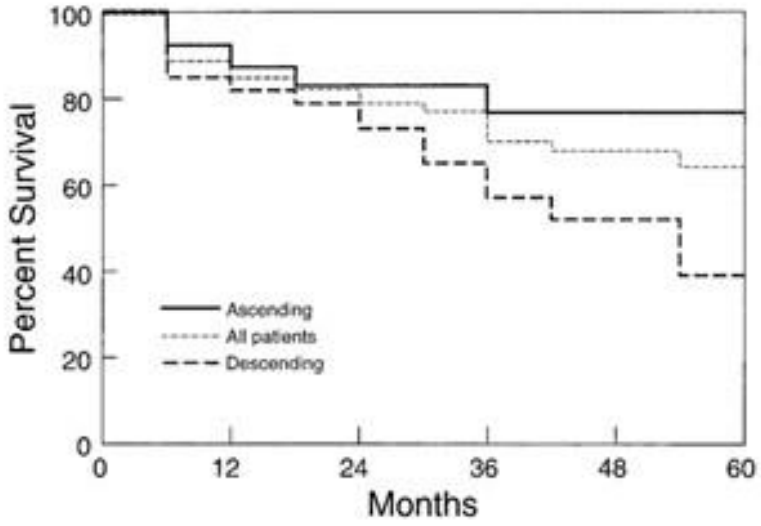
From Coady et al[171]

Figure 8.1.4c. Kaplan-Meier Cumulative Survival displaying 5 year survival for patient suffering from ascending and descending thoracic aortic aneurysms.



From Coady et al[171].

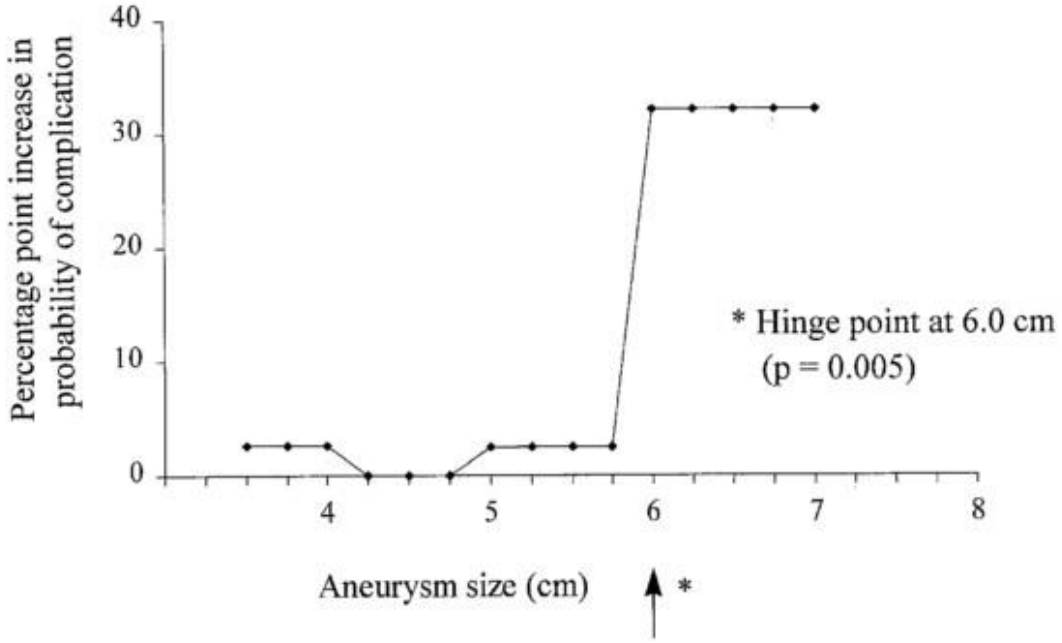
Figure 8.1.5a. Kaplan-Meier Cumulative Survival displaying 5 year survival for patient suffering from ascending and descending thoracic aortic aneurysms.



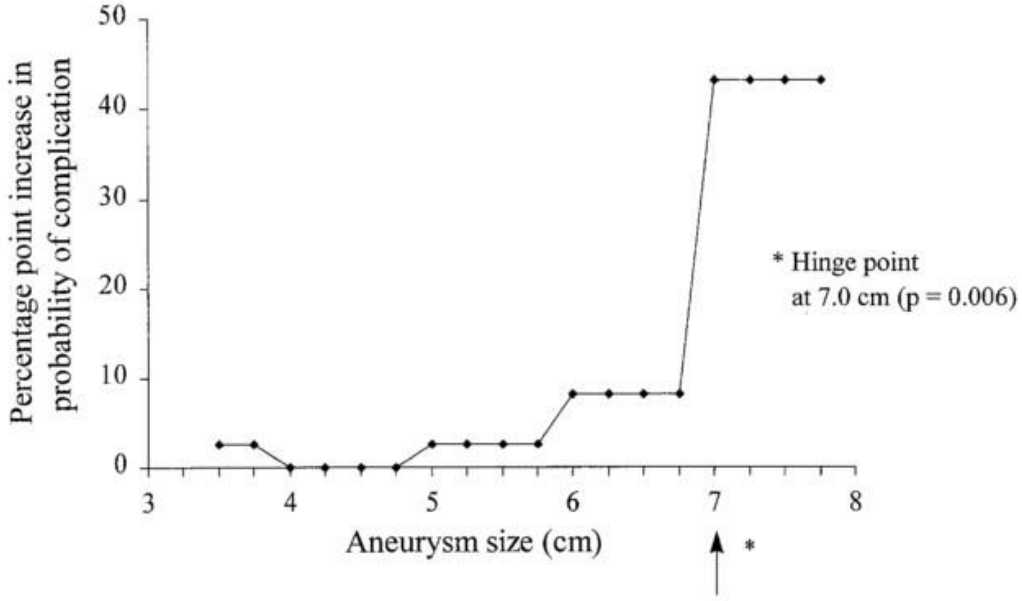
From Coady et al171.

Figures 8.1.5b. & 8.1.5c. The Percentage Risk Of Complications for Ascending (b) and Descending (c) Aortic Aneurysms according to aneurysm size.

b) Ascending Aortic Aneurysm



c) Descending Aortic Aneurysm



From Coady et al.

Figure 12.1.7. Calibration plot comparing observed and predicted in-hospital deaths, the bold black line represents perfect calibration

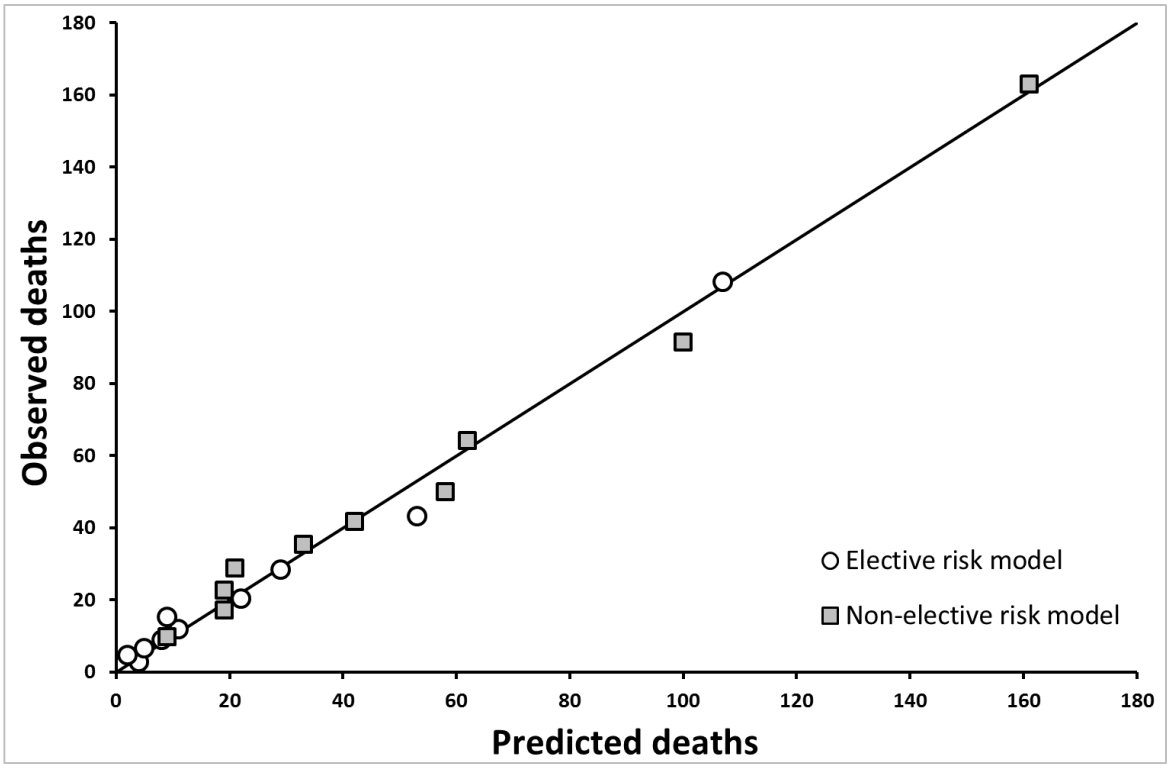


Figure 12.2.6a. Bar chart showing acute dissection volume categories and in-hospital mortality rates for UK hospitals, dashed line indicates overall mortality rate (17.8%)

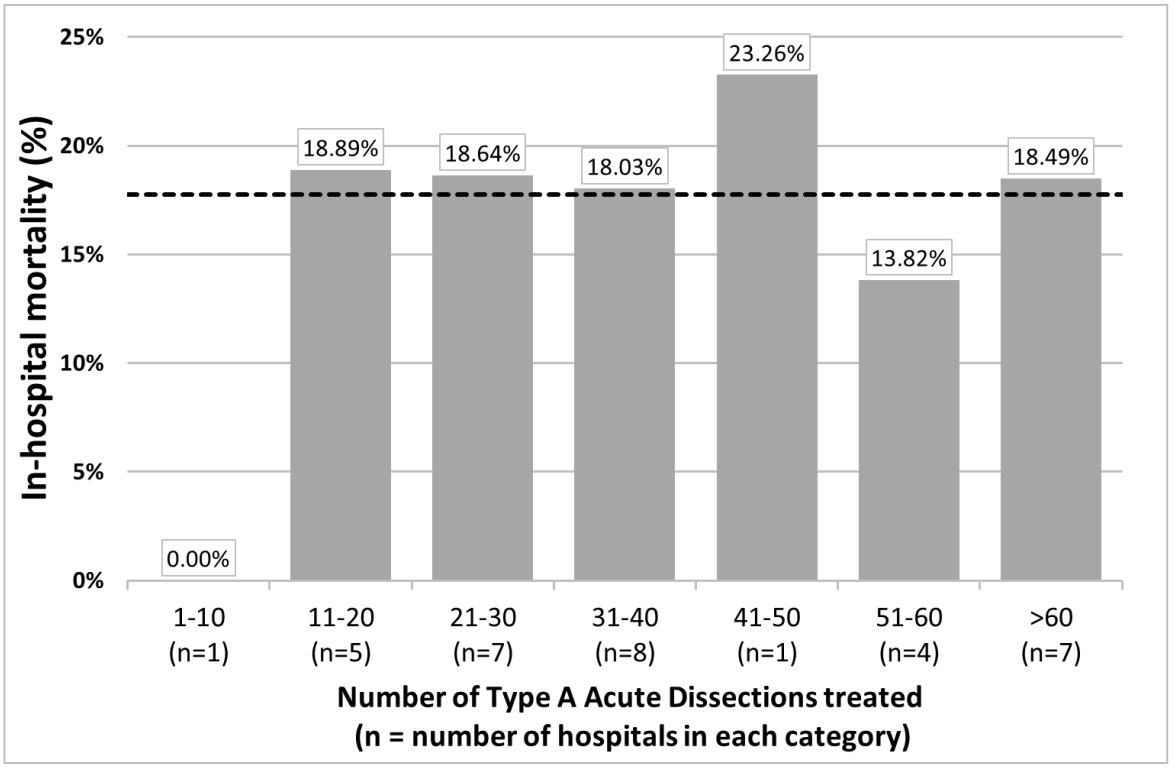
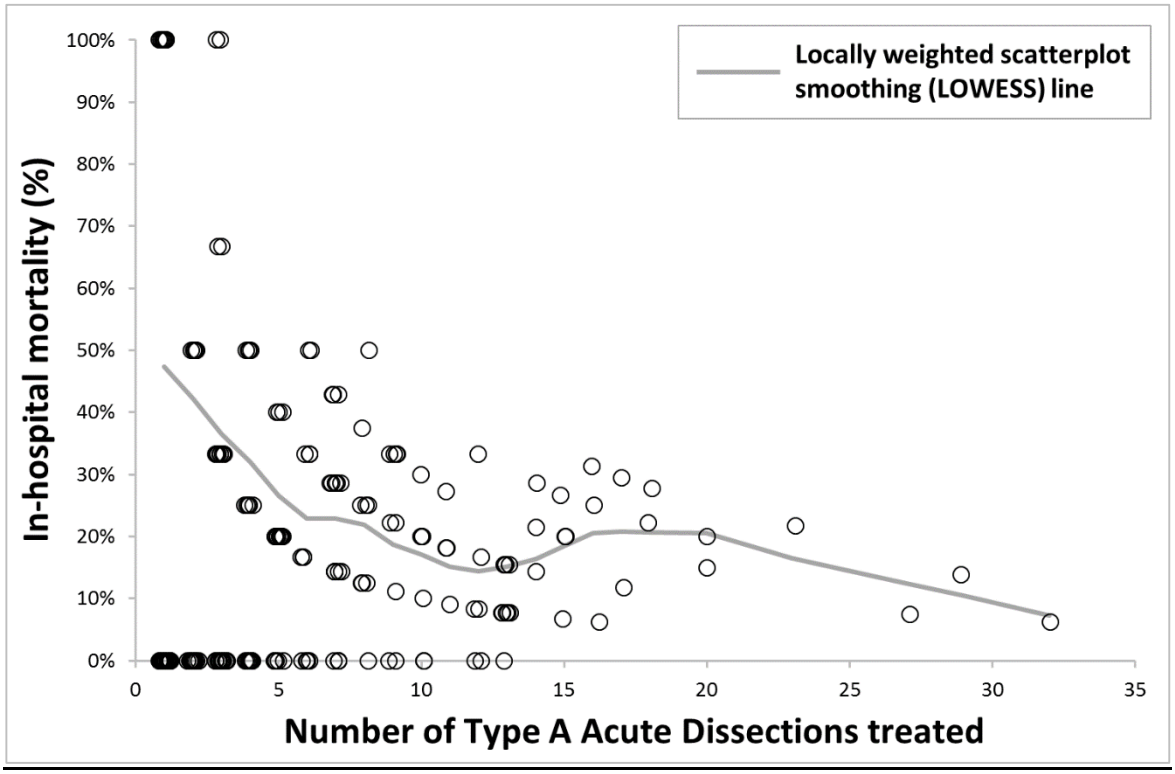
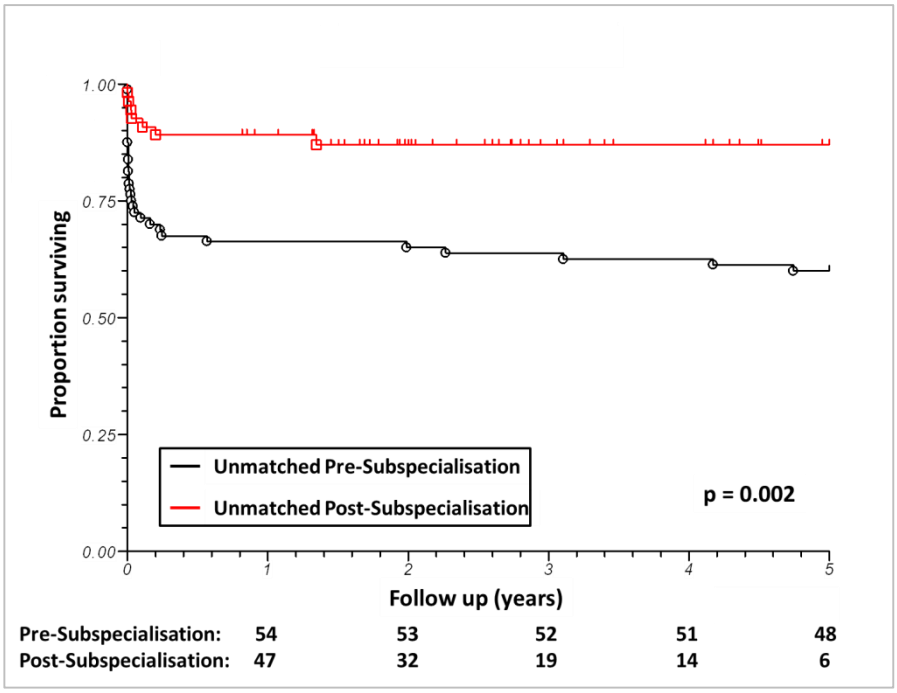


Figure 12.2.6b. Scatterplot showing the relationship between acute dissection volume and in-hospital mortality for consultant cardiac surgeons, each point represents an individual surgeon. (NB: points are jittered to highlight overlapping data)



Figures 12.3.8a & 12.3.8b. Unmatched (a) and Matched (b) 5 Year Survival

a) Unmatched 5 year survival



b) Matched 5 year survival

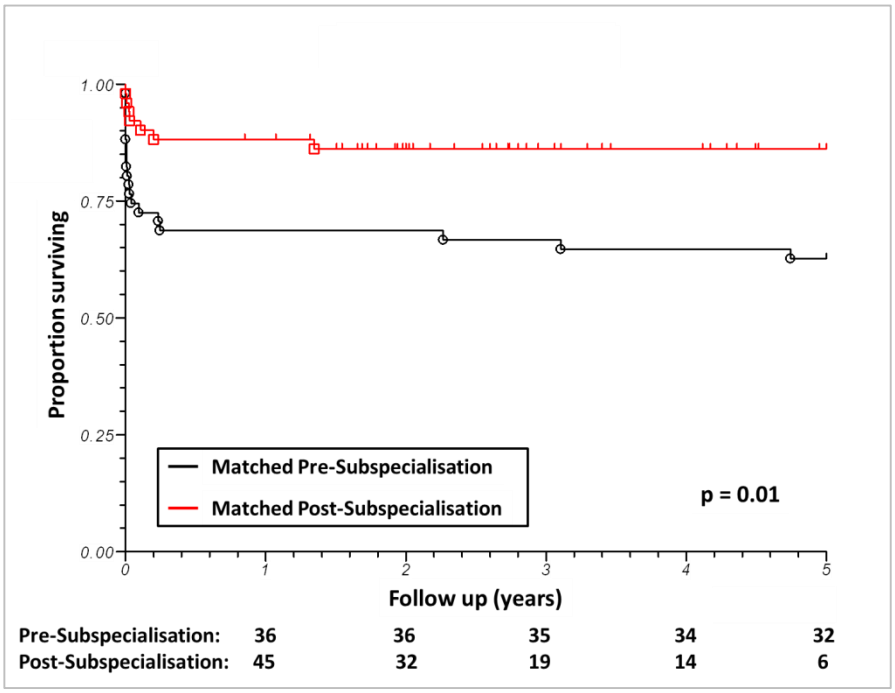


Figure 12.4.4. Study Flow Chart

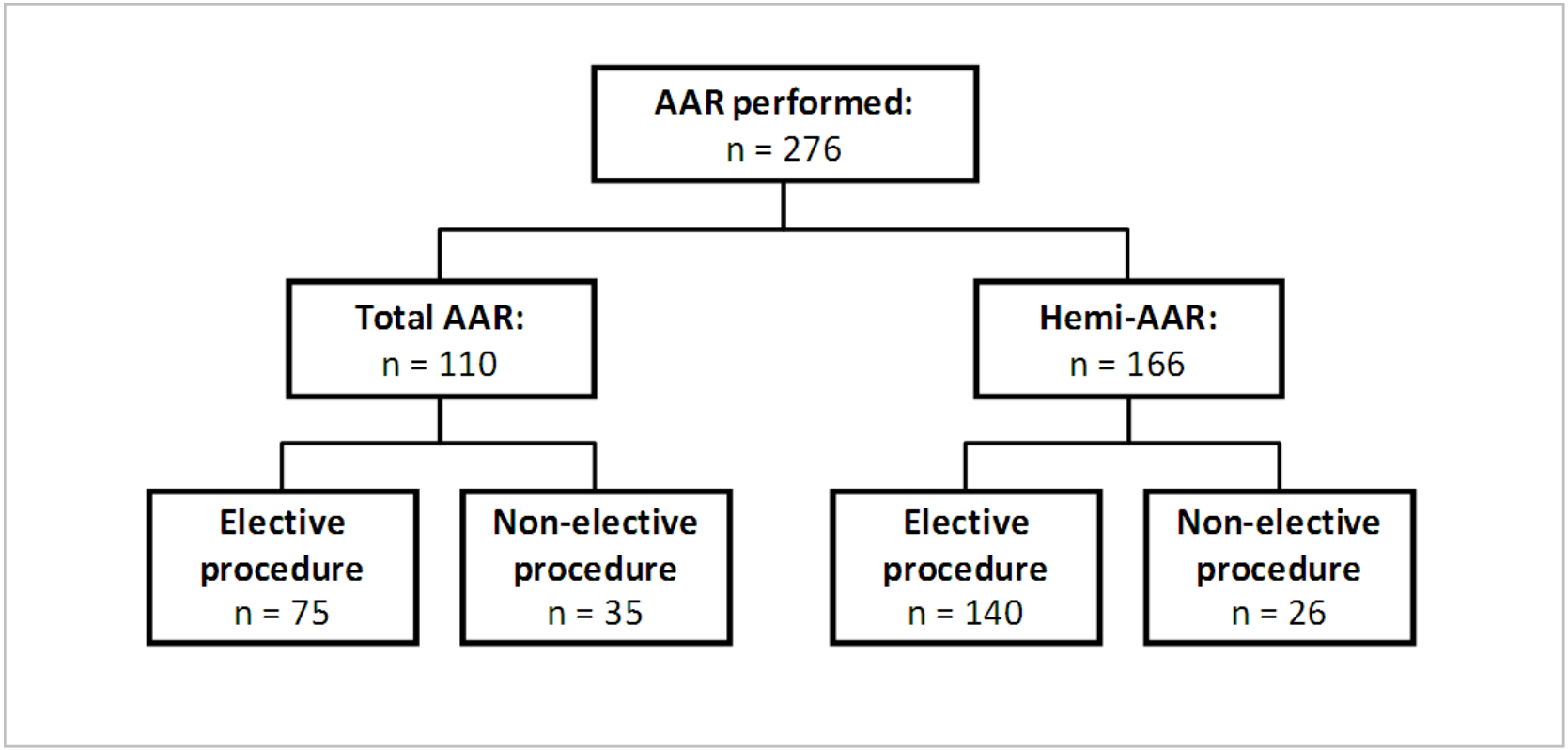


Figure 12.4.6a. Kaplan-Meier survival chart – TAAR's stratified by priority

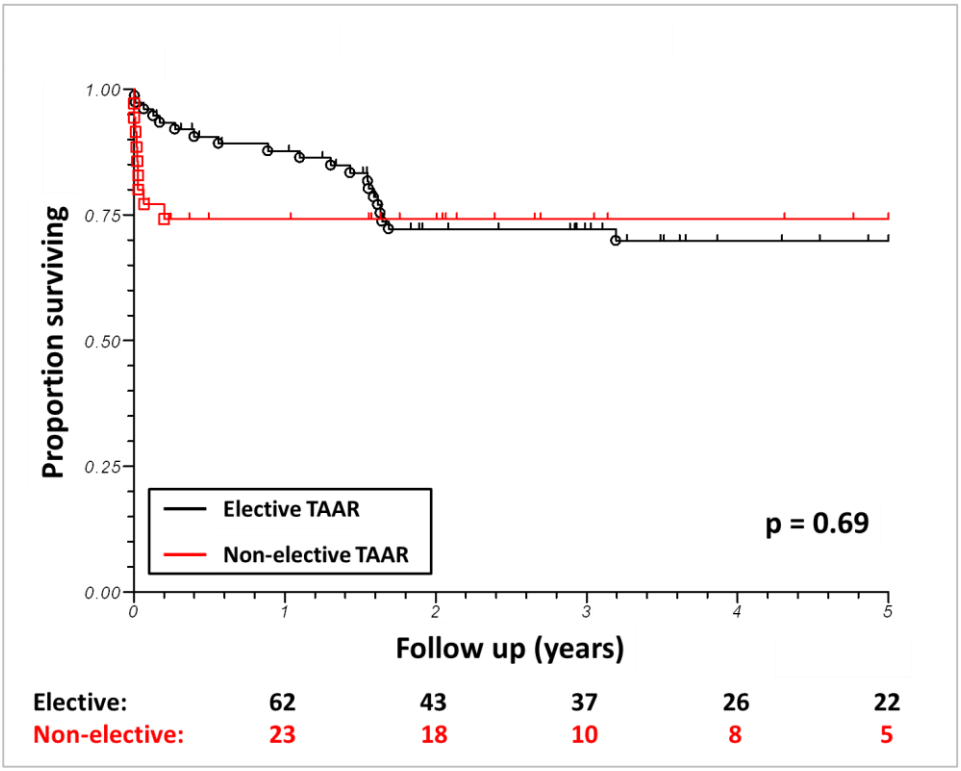


Figure 12.4.6b. Kaplan-Meier survival chart –Elective TAAR's stratified by age

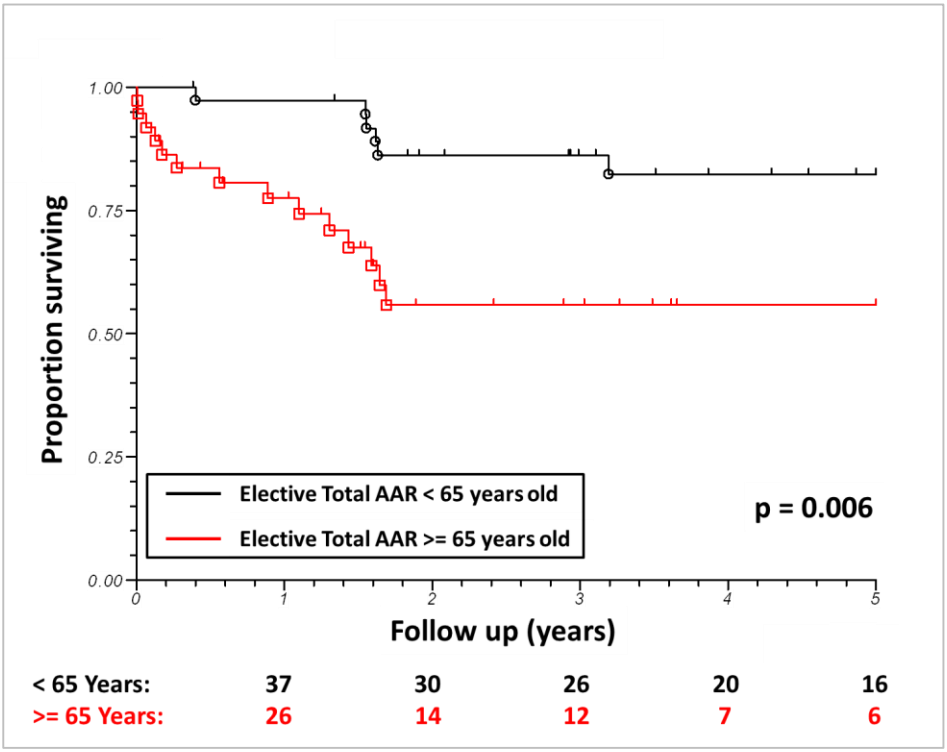


Figure 12.4.6c. Kaplan-Meier survival chart – HAAR's stratified by priority

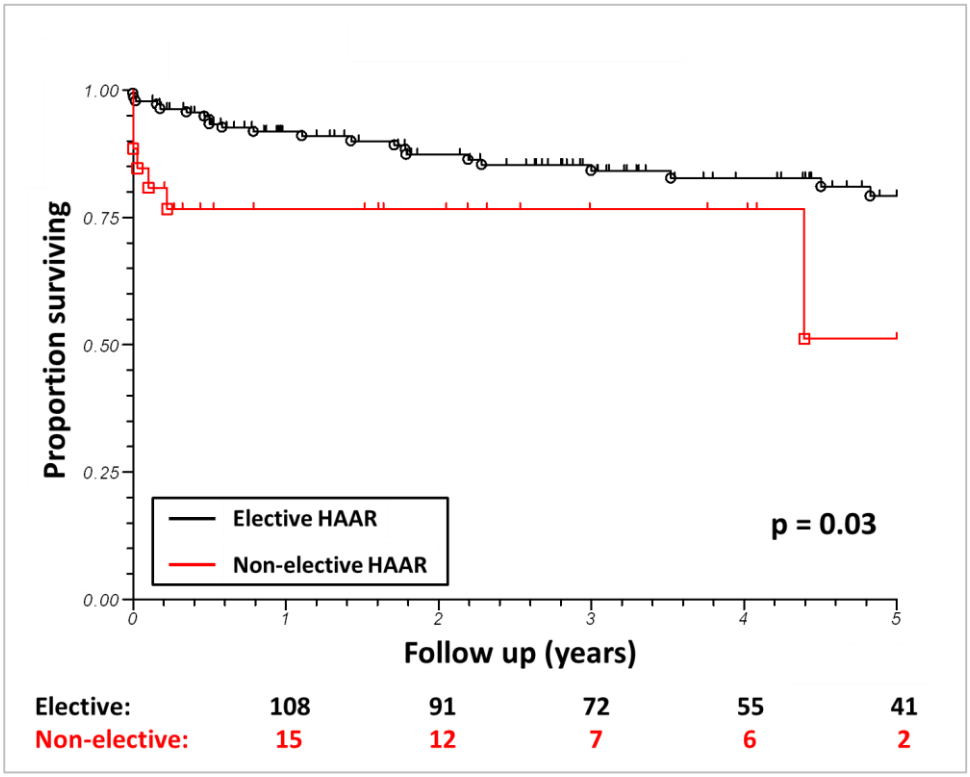


Figure 12.4.6d. Kaplan-Meier survival chart –Elective HAAR's stratified by age

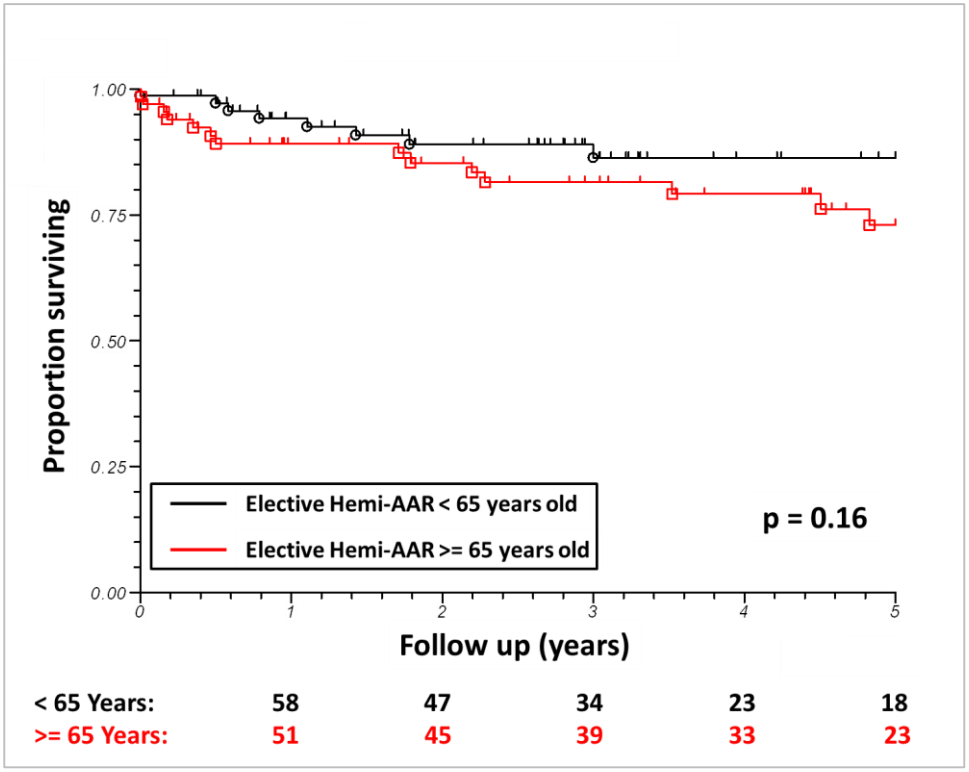


Figure 12.5.11. Aortic Arch Replacement Kaplan Meier chart with age and sex matched general population comparator (note truncated axis)

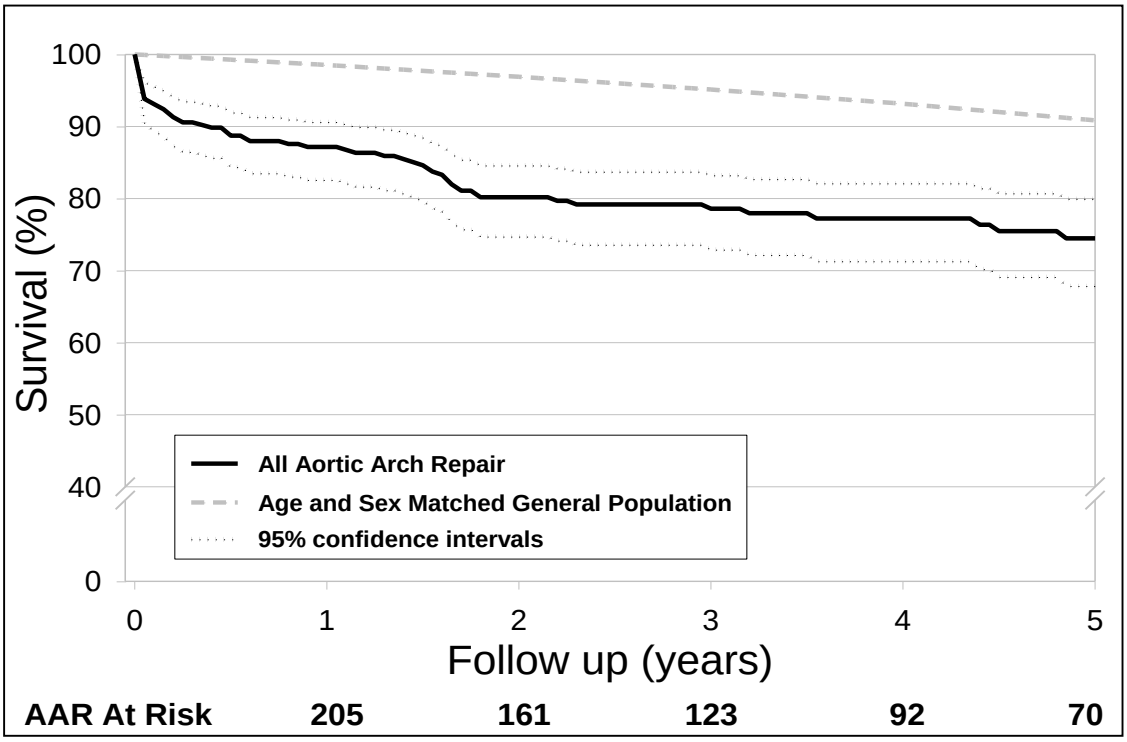


Figure 12.5.15a. Elective Hemi-AAR chart with age and sex matched general population comparator (note truncated axis)

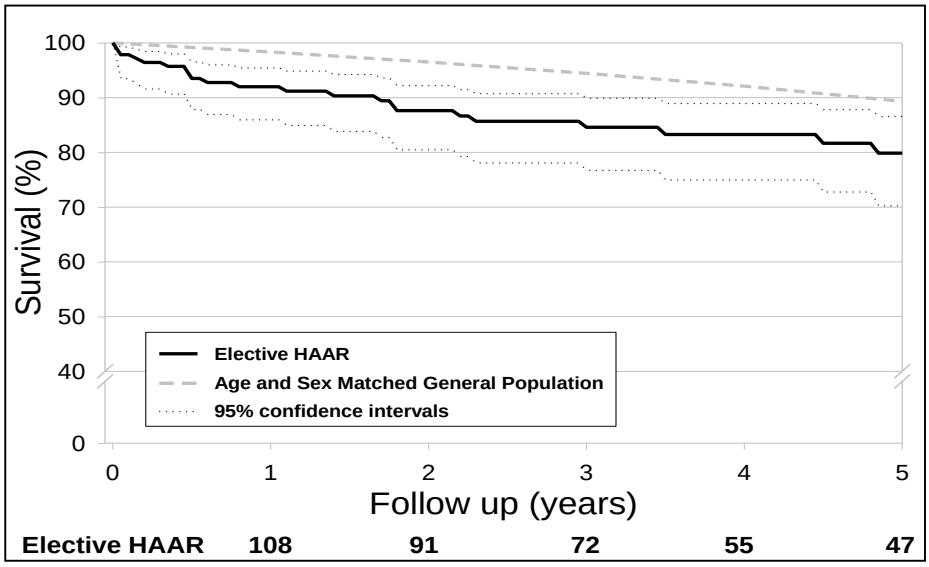


Figure 12.5.15b. Elective Total-AAR chart with age and sex matched general population comparator (note truncated axis)