**Outcomes and Adverse Factors for Endoscopic Mucosal Resection (EMR) of Colorectal Polyps in Elderly Patients**

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**Running title:** Endoscopic mucosal resection in the Elderly

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**ABSTRACT**

**Introduction**

Endoscopic Mucosal Resection (EMR) is an invaluable technique. However, it is associated with significant risks. In the Elderly in particular, the long-term survival benefits of polyp resection with EMR is unknown. The aim of this study was to determine the long-term outcomes in elderly patients that had undergone EMR and to identify any adverse factors.

**Method**

A retrospective observational study on patients of 75 years of age or greater, who underwent EMR of colorectal polyps, in a single tertiary centre, from 2005 to 2014. Demographics of the patients, including Charlson Comorbidity Index (CCI), endoscopic, and histological data were reviewed to identify potential factors predicting outcomes.

**Results**

The patients’ median age was 80 years. In total 239 procedures were performed in 206 unique patients. The complication rate was 1.6%. Mean overall survival was 6.7 years with only 1 patient dying from metastatic colorectal cancer (0.5%) and 49 dying from non-colorectal cancer conditions (24%). Age more than 79 years and CCI more than 2 were independent predictors of significantly shorter survival (p= <0.01). Gender, size of the removed polyps and total number of polyps were not statistically significantly affecting survival. Patients who had more than 2 colonoscopies were found to have a survival benefit (p=0.02).

**Conclusion**

EMR of colonic polyps is safe even for elderly patients. However, the decision to proceed to complex endoscopic therapy should be individualised considering the patients’ age and comorbidities. CCI can help to objectively assess the comorbid state of a patient prior to such decisions.

**Introduction**

Removal of adenomatous polyps can prevent advancement to malignancy [1] and thus reduce morbidity and mortality from CRC [2-6] as demonstrated by the bowel cancer screening. Endoscopic mucosal resection (EMR) is an invaluable technique in removing large or complex polyps, however, it is not without risks. A recent systematic review of 50 studies outlined significant risks associated with the procedure such as perforation (1.5%), bleeding (6.5%) and even mortality (0.08%) [7]. In view of these risks, each case needs to be selected individually with a risk to benefit basis.

Age is an important in the pathophysiology of colorectal cancers (CRC). It has been shown that there is an increased incidence of CRC arising from sporadic adenomatous polyps with age [8,9]. With an aging population in the UK, the occurrence of adenomatous polyps and consequently, the need for intervention with polypectomy and advanced techniques such as EMR is increasing. Studies have underlined the importance and benefits of screening for colorectal cancer, however, identifying an age of cessation of screening, when the benefits no longer justify its continuation remain controversial. Age alone cannot be the only factor when considering the eligibility of screening, as pre-existing comorbidities are an important cofounder in predicted survival. Consequently, a number of scoring systems have been developed to standardise the assessment of co-morbidities, for example, the Charlson Comorbidity Index (CCI) [10] in order to take this into account within studies.

In the elderly, the long-term survival benefits of polyp resection with EMR are unknown given their potential life expectancy. The aim of this study was to determine the long-term outcomes in elderly patients that undergone EMR and to identify any adverse factors.

**Methods**

**Setting & Patient Selection:** This was a single centre study performed at the Royal Liverpool University Hospital as part of a registered service evaluation audit with a study period between July 2005 and November 2014.

Patients selected were all patients aged 75 years and above, undergoing EMR of colonic polyps. The patients were identified through the audit tools of the endoscopy reporting software (GI Reporting Tool - UNISOFT Medical Systems)

**Study design:** A retrospective observational approach was adopted to complete this study. Data was collected from patients’ notes and their electronic patient record, including clinic letters, trust results system, discharge summaries and the GI Reporting tool report of their procedure. The data collected included: patients age at the procedure, gender, co-morbidities, performing endoscopist, bowel preparation used, reported ASA score, polyp size and polyp characteristics, reported immediate complications, number of subsequent endoscopies, histology, readmission within 7 days, 30 day mortality, last follow up date, date of death and cause of death.

The CCI [11] for each patient was retrospectively calculated according to relevant clinical information from the time period at which the EMR was performed. All subjects were followed until death or study censure date. Survival time was calculated as the interval from the index colonoscopy to death or study censure date; subjects with incomplete follow-up were censored at the time of their last documented follow-up. The underlying distribution of each continuous variable was assessed. These variables were modelled as continuous, but results are presented as post-hoc categorised data. Size of polyps was handled as a categorical variable due to reasons of clinical interpretability.

**Definition of terms**

Elderly - Defined as any patient equal or above 75 years of age

Endoscopic Mucosal Resection (EMR) – Any colonic polypectomy coded by the endoscopist, on the UNISOFT report, as an EMR during a flexible sigmoidoscopy or a colonoscopy

Charlson Comorbidity Index (CCI) – Calculated based on the original Charlson Comorbidity Index (CCI) [11] with information extracted from the endoscopy report, the clinic letters and the previous investigations.

Complication - Immediate complication reported on the endoscopy report by the operating endoscopist. Later complications were recorded as a result of post procedural hospitalisation.

7-day readmission – Re-attendance in the institution and admission, directly associated with the procedure.

30-Day Mortality – Date of death documented and reported within 30 days from the procedure.

Survival - The interval from the index colonoscopy to death or study censure date.

Histology – The histological report of the resected lesion. In cases were more than one lesions were resected the worst prognostic histology was recorded i.e. cancer > high grade dysplasia > low grade dysplasia

Cause of death: As recorded on the death certificate.

**Inclusion & Exclusion Criteria**

Inclusion Criteria:

All patients of at least 75 years of age, who underwent an EMR colonic polypectomy as defined above from July 2005 to November 2014.

Exclusion Criteria:

Patients younger than 75 years old were excluded from the study.

Polypectomies, which were not classified as EMR by the performing endoscopist on the endoscopy report.

**Statistical Analysis**

Descriptive statistics were used to characterise the demographic and clinical features of the cohort. The mean survival time and associated standard deviation were calculated using a restricted approach with upper limit of the maximum observed time.

Cox regression was used to analyse the predictors of mortality after the index colonoscopy. Backwards selection via Akaike’s Information Criterion was used to select each variable in the multivariable model. The Kaplan-Meier method was used to estimate overall survival. All statistical analyses were performed with R version 3.2.3 software. Patients with missing values for any of the covariates were removed from the analysis. A p value of <0.05 was considered to be significant.

**Results**

**Patient & Polyp Demographics**

Two hundred and thirty-nine (239) procedures were included; these were performed in 206 unique patients. Patient characteristics can be seen in table 1. The median age of the patients was 80 (range 78-83) and there was a slight male preponderance (55%).

The median follow up was 30 months (IQR 15, 51). The median size of the polyp resected was 20mm (IQR 12, 30). Eighteen percent (18%) were found to have high-grade dysplasia with seven percent (7%) having a malignant component. The vast majority was low-grade dysplasia (71%)

**Procedural Outcomes, Complications & Mortality**

Total Number of Procedures:

Sixty-five (65) patients (31.6%) had a single EMR procedure and had no further endoscopies. Fifty-eight patients (28.2%) had one more endoscopy after the EMR and the remaining 83 patients (40.2%) had 2 or more endoscopies after the EMR.

Complications:

Four of the cases had reported complications (1.6%). In 2 cases (0.8%), bleeding was reported as an immediate complication but was managed conservatively. Another 2 cases (0.8%) had cardiopulmonary complications, one of which was respiratory depression related to the sedation and the other a cardiovascular compromise related to a hyoscine butylbromide induced arrhythmia. Ten patients (4.2%) were readmitted within 7 days. None of the patients required surgery due to a complication.

Histological Outcomes:

The majority of the resected lesions were low-grade dysplasia (LGD), but 37 patients had lesions with high-grade dysplasia (HGD) and 14 with confirmed malignancy.

Patients with malignancy:

Of the 14 patients with malignancy, 4 had a surgical resection and at the study censure date were all still alive. The remaining ten patients were not operated on and 4 of them died during the study period. Two of the deaths were unrelated to colorectal cancer (Post renal transplant lymphoproliferative disease, cardiac disease) and 2 died due to unknown causes (one 2 years and one 9 years after the original procedure).

Patients with HGD:

Of the 37 patients with high-grade dysplasia, 3 underwent a surgical resection. One of them died, 42 months later, due to sepsis. The remaining 34 patients did not undergo surgery and 8 of them died. Six of the deaths were unrelated to colorectal cancer, 1 was due to unknown causes and 1 was due to metastatic colorectal cancer.

Mortality:

Two patients died in a relatively short period post the procedures. An 82 year old and a 78 year old who both died from cardiac causes within 1 and 2 months respectively.

The 10 year mortality in our cohort was 26.4% and the 5 years mortality was 21.6%. One patient died as a result of colorectal cancer. 53 patients died during the follow up period of the study. The main causes of death of all patients are described in table 2. The cause of death could not be identified in 8 cases, who moved out of area of our institution, and the death certificate was could not be retrieved.

**Predictive Factors for Outcomes**

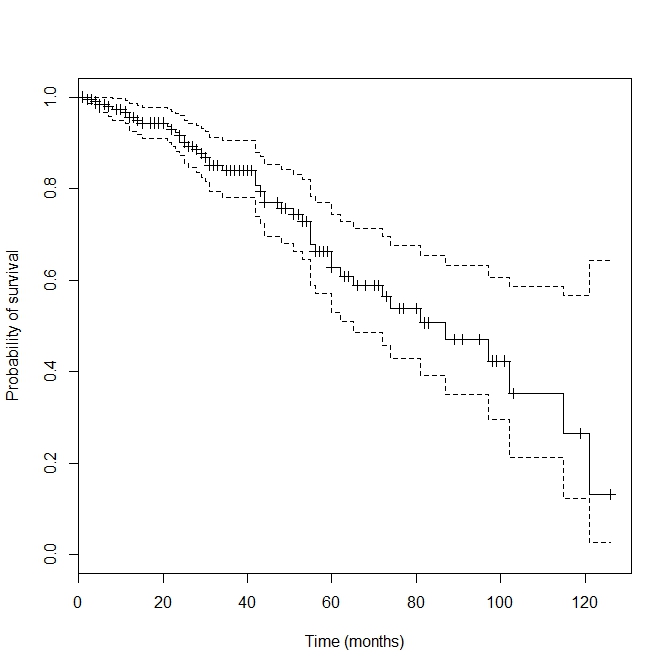


Figure 1: Probability of survival curve for all patients following EMR for colonic polyp.

*The solid line is the mean survival, with the dotted lines illustrating 95% confidence intervals*

The results of the univariable and multivariable analysis can be seen in table 3.Univariable analysis demonstrated age, CCI, repeat colonoscopies and the presence of high-grade dysplasia were risk factors for mortality following polypectomy. Specifically patients aged 80 and above were more likely to die than those age <80 (p<0.01) (HR 1.39 - 95%CI - 1.09, 1.77). A CCI of three or four was associated with death following polypectomy (p<0.01) (HR 1.14 95%CI 1.04, 1.25) as was a CCI of more than four (HR1.29 95%CI 1.09, 1.53). Patients with at least one repeat colonoscopy were less likely to die than those with none (p<0.02 HR 0.84 95%CI 0.73, 0.98)

Multivariable analysis demonstrated age, CCI and repeat colonoscopies to be significant with a Hazard risk of 1.28 1.14 and 0.85 respectively. The directions of effect were as per the univariable results. The occurrence of a complication did not predict mortality and only one of the 4 reported complications died up to the censure date of this study, 1 year later from respiratory sepsis.

Interaction between age and Charlson index, and their impact upon survival post EMR, was assessed by creating patient subgroups as seen in table 4. Those patients with a score of <3, irrespective of age had the longest survival post EMR. CCI did not predict risk of complication (p=0.5), readmission (p=0.3) or the presence of carcinoma and HGD (p=0.5). When considering those with an individual polyp greater than 20mm, application of the CCI is a strong predictor of mortality. This can be seen in figure 2 with immediate separation in the Kaplan Meier curve. This begins to maximise by 5 years and is greater still by 10 years (p=0.0126).



Figure 2: Kaplan Meier curve based upon those with an individual polyp ≥20mm.

**Discussion**

Considering outcomes of EMR for colorectal polyps in elderly patients is important due to their potential longevity, the high preponderance of polyps in this age group and the risks of the procedure. We have presented the largest dedicated cohort of elderly patients undergoing colonic polyp EMR. Our study has demonstrated that elderly patients, as defined by patient of 75 years of age or greater, that underwent EMR for colonic polyps, had low complication rates and post procedural survival exceeding 5 years in the vast majority (78.6%). It has also highlighted the importance of CCI and advancing age as independent risk factors for predicting survival post procedure.

The definition of age and ageing often categorise ‘older or elderly people’ as being above a certain age. The Office for National Statistics (ONS) commonly quote data on individuals aged over 65, whilst World Health Organization (WHO) have defined an ‘older person’ as someone ‘whose age has passed the median life expectancy at birth’, which in the UK is currently 81.2 for men and women combined [12]. Defining elderly at 75 years therefore falls between these two definitions. Other studies that have examined outcomes in an “elderly” cohort have defined elderly as > 75 years [13]. Moreover, British Society of Gastroenterology (BSG) guidelines recommend that patients should be offered surveillance until age 75 years and beyond if they are well enough and have a reasonable life expectancy [14]. Some have suggested that there is little benefit from polypectomy in patients over the age of 85 years because of the very low likelihood of progression to cancer during their remaining life.

As with many countries around the world, female life expectancy in the UK is greater than males. Despite this we report a male predominance in an elderly cohort undergoing EMR. This male predominance is explained by the increase in colorectal cancer in males, compared to females [9] the majority of which arise, as a result of sporadic adenomas and the adenoma-carcinoma pathway [15]. Such male predominance has been reported in similar studies examining outcomes of EMR in elderly patients [13].

Inclusion in this study was not based upon polyp size, but instead upon the recording of EMR as the mode of polyp removal. As a result, 14% of polyps were <10mm, however, 55% were >20mm. The potential for a patient to have a CRC associated death from a polyp <10mm is low in a cohort >75 years old and more so in those >80 years of age. Risk of advanced dysplasia and colorectal cancer increases with an increase in polyp size, particularly those >20mm [16]. Polyp size at EMR did not influence mortality in our study. Other studies examining outcomes following EMR have also included polyps <20mm [17] like in our study. These studies reported the outcomes whereby the majority of lesions resected were >20mm. Other such studies only included polyps identified to be >20mm [18,19]. None of these studies were specifically examining outcomes in the elderly or subsequent mortality. All of these studies reported post procedural outcomes, namely procedural complications and local adenoma recurrence. Finding increased polyp size, specifically those >40mm were associated with increased complications and polypectomy site recurrence [18-20].

Co-morbidity is an important factor that determines the survival of patients and a number of scoring systems have been developed to standardise the assessment of co-morbidities [11]. In this study we used the Charlson Comorbidity Index (CCI), which is a weighted index that takes into account the number and the severity of comorbid diseases. It predicts the cumulative mortality attributable to comorbid disease. The estimated increment in the relative risk of death, from an increase of one in CCI proved approximately equal to that from an additional decade of age [10,11]. The score has been validated and shown to independently predict adverse outcomes across a broad spectrum of conditions [21-25], including colorectal cancer [26,27]

Histology identified 18% of resected polyps to contain high-grade dysplasia (HGD). This was identified to be associated with increased risk of post procedural death (p=0.03). The same was not identified for lesion found to contain established cancer. A study in 2014 reported mortality following polypectomy. The adenoma cohort consisted of 40,826 patients with a total follow-up time of 334,154 person-years. HGD in the resected polyp was identified as a predictor of death in both univariate and multivariate analysis [28]. A small number of our cohort had a malignant component in the resected specimen, this did infer future risk of death but did not achieve statistical significance. HGD as a predictor of future mortality may be related to the inferred risk of future neoplasia and in particular CRC [29]. The greater risk inferred by HGD may be as a consequence of those with cancer undergoing surgical resection, by merit of being less co-morbid and suitable for surgical resection. Thus, a lower CCI, which in turn is an independent predictor of survival.

Colonoscopy is considered to a be a relatively safe procedure, however EMR of larger polyps has been reported to have an overall risk of bleeding of up to 7% [30] but has also been reported to be as low as 0.44% [31]; an overall risk of perforation of up to 1.5% and a risk of post-polypectomy coagulation syndrome of up to 3.7% [30-32]*.* Studies examining the outcomes of EMR in elderly patients are retrospective and sparse within the literature. They have differing complication rates in this cohort of patients. One study of 412 adenoma resections in 343 patients, included a sub-cohort of elderly patients as defined as 74 years of age or greater (n=80) [13]. They demonstrated a perforation rate of 1.2% (5/412) and bleeding rates of 8%(28/412) (4.6% early bleeding and 2.2% delayed bleeding) [13]. Another study examined 50 patients of which 32 patients were 65 years or greater. They reported no perforations and a bleeding rate was 4% [33]. By comparison our study was favourable with an overall complication rate of just 1.6%, with no reported perforations and a bleeding rate of 0.8%. Our other main complication was cardiopulmonary compromise, which is unsurprising in this cohort at a rate 0.8%. Our study also included additional performance indicators including a 7-day re-admission rate of 4.2% and 30-day mortality of 0.4%.

Considering that patients with multiple comorbidities are less likely to be suitable candidates for surgery or prolonged chemo-radiotherapy, therefore endoscopic treatment is an appealing approach. In our cohort, patients with a higher CCI had significantly worse 5-year survival rates compared to healthier patients. The 5-year survival rate of patients with a high CCI (>3) who underwent an EMR polypectomy of a larger polyp (>20cm) was 62%. For patients with a low CCI the 5-year survival was significantly better at 83.5%. A Danish population study revealed that after diagnosis of colorectal cancer in patients with a CCI ≥3, the 5-year survival rate was up to 28% [34]. In our study, patients aged 75-79 with a high CCI, had a comparable 5-year survival compared to patients aged 80+ with a small CCI. Therefore, the decision on the appropriate management of a large colonic polyp should take under careful consideration the co-existent comorbidities as they play a crucial role in the outcome. This underlines the importance of careful assessment and reporting of all known comorbidities before undertaking endoscopy in patients of these characteristics. This further emphasises that age alone should not be used as the sole determining factor for suitability for colonic polyp EMR.

Patients who had >1 colonoscopy had increased survival following their EMR. This likely represents less co-morbidities and thus more suitability for the index and any subsequent colonoscopies. Moreover, repeated colonoscopies would ensure complete excision by removal residual disease at the site, detect local recurrence and reduce the risk of missed adenomatous or even malignant lesions. In our study, 44.6% of patients who underwent EMR for a larger polyp (>2cm) underwent at least 2 more subsequent endoscopies for surveillance or treatment of recurrence while 22.3% underwent at least 3 more procedures. Only one patient subsequently died of colorectal cancer. A lower CCI is likely to mean the patient would be more eligible for repeated procedures and we have demonstrated that a CCI of <3 is associated with prolonged survival.

The retrospective nature of our study infers some limitations. Due to the nature of our service and the wide geographic catchment of the referral area cause of death could not be recorded in all cases. Follow up time after EMR was also truncated in some cases as some of the procedures occurring within 1 year of the closure of the study.

In conclusion, Endoscopic Mucosal Resection of colonic polyps can be safely performed in an elderly population, without excessive complication or readmission rates. When considering a patient’s suitability for the procedure their age and CCI can be independently considered as risk factors for reduced survival following the procedure. This study therefore suggests that both age and CCl are important factors for decision making in the elderly when considering EMR in this population.

Table 1: Patient demographics, colonic polyp details and survival outcomes.

|  |  |
| --- | --- |
|  | Number |
| Age (years) – median (IQR) | 80 (78 – 83) |
| Charlson Index – median (IQR) | 1 (0 – 2) |
| Repeat Colonoscopies – median (IQR) | 1 (0 – 2) |
| Gender:  Male  Female | 114 (55%)  92 (45%) |
| Size of polyps 1 (categorical):  1-9mm  10-19mm  ≥ 20mm  Missing | 28 (14%)  61 (30%)  114 (55%)  3 (1%) |
| Number of polyps:  1  ≥ 2 | 121 (59%)  85 (41%) |
| Histology:  Low grade dysplasia  High grade dysplasia  Malignancy  Hyperplastic | 146 (71%)  38 (18%)  14 (7%)  8 (4%) |
| Mean survival, months (standard error) | 80.63 (4.49) |

Table 2: Causes of death

|  |  |
| --- | --- |
| Cause of Death | Number |
| Sepsis | 19 |
| Cardiac Causes | 9 |
| Cancer:  Lung  Prostate  Cholangiocarcinoma  Pancreas  Colorectal | 3  2  1  1  1 |
| Other Causes:  Advanced dementia  Pancreatitis  PTLD  Renal failure  Duodenal bleed  Respiratory Failure  Suicide | 2  1  1  1  2  1  1 |
| Unknown | 8 |

Table 3: Univariable and multivariable analysis of risk factors of death following EMR of colonic polyp in patients >75 years of age.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variable | | p-value | Univariable  HR (95% CI) | Multivariable  HR (95% CI) |
| Age | 76-79  ≥80 | <0.01 | 1.00  1.39 (1.09, 1.77) | 1.00  1.28 (1.00, 1.64) |
| Charlson Index | <3  3-4  >4 | <0.01 | 1.00  1.14 (1.04 1.25)  1.29 (1.09, 1.53) | 1.00  1.14 (1.04 1.25)  1.28 (1.07, 1.54) |
| Repeat Colonoscopies | 0  1  ≥2 | 0.02 | 1.00  0.84 (0.73, 0.98)  0.70 (0.52, 0.95) | 1.00  0.85 (0.74, 0.99)  0.72 (0.53, 0.97) |
| Gender | Male  Female | 0.28 | 1.00  0.72 (0.39, 1.31) | N/A |
| Size of Polyps | 1-9mm  10-19mm  ≥ 20mm | 0.59  0.67 | 1.00  1.36 (0.45, 4.17)  1.26 (0.44, 3.61) | N/A |
| Number of Polyps | 1  ≥ 2 | 0.84 | 1.00  0.94 (0.53, 1.68) | N/A |
| Histology | Low grade dysplasia  High grade dysplasia  Malignancy  Other | 0.03  0.51  0.66 | 1.00  2.16 (1.07, 4.36)  1.33 (0.57, 3.08)  1.57 (0.21, 11.71) | N/A |

Table 4: Patient subgrouping according to age and Charlson Index. Includes mean survival (months) for each patient subgroup.

|  |  |  |  |
| --- | --- | --- | --- |
| Age | Charlson Index | Patients | Mean survival, months  (standard error) |
| 75-79 | <3 | 67 | 87.7 (5.1) |
| 75-79 | 3-4 | 11 | 61.6 (6.2) |
| 75-79 | >4 | 10 | 63.9 (12.1) |
| ≥80 | <3 | 87\* | 84.3 (8.1) |
| ≥80 | 3-4 | 18 | 47.5 (5.3) |
| ≥80 | >4 | 12 | 68.5 (14.2) |

**References:**

1. Alonso-Abreu I, Alarcon-Fernandez O, Gimeno-Garcia AZ et al. Early Colonoscopy Improves the Outcome of Patients With Symptomatic Colorectal Cancer. Dis Colon Rectum 2017; 60: 837-844

2. Logan RF, Patnick J, Nickerson C et al. Outcomes of the Bowel Cancer Screening Programme (BCSP) in England after the first 1 million tests. Gut 2012; 61: 1439-1446

3. Rees CJ, Bevan R. The National Health Service Bowel Cancer Screening Program: the early years. Expert Rev Gastroenterol Hepatol 2013; 7: 421-437

4. Lee TJ, Rutter MD, Blanks RG et al. Colonoscopy quality measures: experience from the NHS Bowel Cancer Screening Programme. Gut 2012; 61: 1050-1057

5. Bond A, Sarkar S. New technologies and techniques to improve adenoma detection in colonoscopy. World journal of gastrointestinal endoscopy 2015; 7: 969-980

6. Bond A, Sarkar S. How Can We Improve Adenoma Detection Rate? Curr Colorectal Cancer Rep 2016, DOI: 42-50

7. De Ceglie A, Hassan C, Mangiavillano B et al. Endoscopic mucosal resection and endoscopic submucosal dissection for colorectal lesions: A systematic review. Critical reviews in oncology/hematology 2016; 104: 138-155

8. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013; 49: 1374-1403

9. Parkin DM, Bray F, Ferlay J et al. Global cancer statistics, 2002. CA: a cancer journal for clinicians 2005; 55: 74-108

10. Charlson M, Szatrowski TP, Peterson J et al. Validation of a combined comorbidity index. Journal of clinical epidemiology 1994; 47: 1245-1251

11. Charlson ME, Pompei P, Ales KL et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40: 373-383

12. Association BM. Growing older in the UK: A series of expert-authored briefing papers on ageing and health In. London; 2016

13. Bronsgeest K, Huisman JF, Langers A et al. Safety of endoscopic mucosal resection (EMR) of large non-pedunculated colorectal adenomas in the elderly. Int J Colorectal Dis 2017; 32: 1711-1717

14. Baker G, Valori R, Brooklyn T. Learning from adverse outcomes: guidelines on colonoscopic polypectomy in patients aged 85 years and older. Frontline Gastroenterol 2016; 7: 199-201

15. Fearon ER. Molecular genetics of colorectal cancer. Annu Rev Pathol 2011; 6: 479-507

16. Bretagne JF, Manfredi S, Piette C et al. Yield of high-grade dysplasia based on polyp size detected at colonoscopy: a series of 2295 examinations following a positive fecal occult blood test in a population-based study. Dis Colon Rectum 2010; 53: 339-345

17. Nesargikar P, Amadio L, Noble C et al. PTH-003 Outcomes following endoscopic mucosal resection (emr) of colonic polyps in a tertiary centre: a three year experience. In: BMJ Publishing Group; 2015

18. Kim B, Choi AR, Park SJ et al. Long-Term Outcome and Surveillance Colonoscopy after Successful Endoscopic Treatment of Large Sessile Colorectal Polyps. Yonsei Med J 2016; 57: 1106-1114

19. Longcroft-Wheaton G, Mead R, Duku M et al. Endoscopic mucosal resection of colonic polyps: a large prospective single centre series. Gut 2011; 60: A14-A15

20. Zhan T, Hielscher T, Hahn F et al. Risk Factors for Local Recurrence of Large, Flat Colorectal Polyps after Endoscopic Mucosal Resection. Digestion 2016; 93: 311-317

21. Ng AC, Chow V, Yong AS et al. Prognostic impact of the Charlson comorbidity index on mortality following acute pulmonary embolism. Respiration; international review of thoracic diseases 2013; 85: 408-416

22. Vaquero-Herrero MP, Ragozzino S, Castano-Romero F et al. The Pitt Bacteremia Score, Charlson Comorbidity Index and Chronic Disease Score are useful tools for the prediction of mortality in patients with Candida bloodstream infection. Mycoses 2017; 60: 676-685

23. Kahl A, du Bois A, Harter P et al. Prognostic Value of the Age-Adjusted Charlson Comorbidity Index (ACCI) on Short- and Long-Term Outcome in Patients with Advanced Primary Epithelial Ovarian Cancer. Ann Surg Oncol 2017; 24: 3692-3699

24. Chuang M-H, Chuang T-L, Huang K-Y et al. Age-adjusted Charlson Comorbidity Index scores predict major adverse cardiovascular events and all-cause mortality among systemic lupus erythematosus patients. Tzu-Chi Medical Journal 2017; 29: 154

25. Takemura K, Takenaka Y, Ashida N et al. Age-adjusted Charlson Comorbidity Index predicts prognosis of laryngopharyngeal cancer treated with radiation therapy. Acta oto-laryngologica 2017; 137: 1307-1312

26. Huang Y, Zhang Y, Li J et al. Charlson comorbidity index for evaluatiomicronn omicronf the outcomes of elderly patients undergoing laparoscopic surgery for colon cancer. J BUON 2017; 22: 686-691

27. Tian Y, Xu B, Yu G et al. Age-adjusted charlson comorbidity index score as predictor of prolonged postoperative ileus in patients with colorectal cancer who underwent surgical resection. Oncotarget 2017; 8: 20794

28. Loberg M, Kalager M, Holme O et al. Long-term colorectal-cancer mortality after adenoma removal. N Engl J Med 2014; 371: 799-807

29. Fairley KJ, Li J, Komar M et al. Predicting the risk of recurrent adenoma and incident colorectal cancer based on findings of the baseline colonoscopy. Clin Transl Gastroenterol 2014; 5: e64

30. Metz A, Bourke M, Moss A et al. Factors that predict bleeding following endoscopic mucosal resection of large colonic lesions. Endoscopy 2011; 43: 506-511

31. Derbyshire E, Hungin P, Nickerson C et al. Post-polypectomy bleeding in the English National Health Service Bowel Cancer Screening Programme. Endoscopy 2017; 49: 899-908

32. Xie HQ, Zhong WZ. Outcomes of Colonic Endoscopic Mucosal Resection for Large Polyps in Elderly Patients. J Laparoendosc Adv Surg Tech A 2016; 26: 707-709

33. Pontone S, Palma R, Panetta C et al. Endoscopic mucosal resection in elderly patients. Aging clinical and experimental research 2017; 29: 109-113

34. Ostenfeld EB, Norgaard M, Thomsen RW et al. Comorbidity and survival of Danish patients with colon and rectal cancer from 2000-2011: a population-based cohort study. Clin Epidemiol 2013; 5: 65-74