

Dual-focus magnification, high-definition endoscopy improves pathology detection in direct-to-test diagnostic upper gastrointestinal endoscopy.

A. Bond,^{1,2,}, M. D. Burkitt^{1,2,*}, T.Cox³, H.L. Smart¹, C. Probert^{1,2}, N. Haslam¹ and S. Sarkar¹*

1) Department of Gastroenterology , Royal Liverpool and Broadgreen University Hospital Trust

2) Clinical Cancer Trials Unit, University of Liverpool, Liverpool

3) Unit of Gastroenterology Research, Department of Cellular and Molecular Physiology, Institute of Translational Medicine, University of Liverpool

* these authors contributed equally to this manuscript

Contributions

AB was responsible for data collection, data analysis, writing and editing the manuscript. MDB performed data analysis, wrote and edited the manuscript. TC provided statistical support and analysis. HLS, NH and SS devised the study and were responsible for editing the manuscript. CP assisted with editing manuscript prior to submission.

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Corresponding author

Dr Sanchoy Sarkar

Dept of Gastroenterology

Royal Liverpool and Broadgreen University Hospital Trust

Prescot Street

Liverpool

UK

sanchoy@aol.com

Abstract

Introduction. In the UK, the majority of diagnostic upper gastrointestinal (UGI) endoscopy is a result of direct-to-test referral from the primary care physician. The diagnostic yield from these tests is relatively low, and the burden high on endoscopy services. Dual-focus magnification, high-definition endoscopy is expected to improve detection and classification of UGI mucosal lesions and also help minimize biopsies by allowing better targeting.

Methods. A retrospective study of patients attending for direct-to-test UGI endoscopy from January 2015 to June 2015. The primary outcome of interest was the identification of significant pathology. Detection of significant pathology was modelled using logistic regression.

Results. 500 procedures were included. The mean age of patients was 61.5 (+/-15.6) years, 60.8 % of patients were female. Ninety four gastroscopies were performed using dual-focus magnification high-definition endoscopy. Increasing age, male gender, type of endoscope, and type of operator were all identified as significant factors influencing the odds of detecting significant mucosal pathology. Use of dual-focus magnification, high-definition endoscopy was associated with an odds ratio of 1.87 (95% CI 1.11-3.12) favouring the detection of significant pathology. Subsequent analysis suggested that the increased detection of pathology during dual-focus magnification, high-definition endoscopy also influenced patient follow-up and led to a 3.0 fold ($p=0.04$) increase in proportion of patients entered into an UGI endoscopic surveillance program.

Conclusion. Dual-focus magnification, high-definition endoscopy improved the diagnostic yield for significant mucosal pathology in patients referred for direct-to-test endoscopy. If this finding is recapitulated elsewhere it will have substantial impact on the provision of UGI endoscopic services.

Introduction

There is increasing demand upon gastrointestinal diagnostic services, including diagnostic UGI endoscopy. The majority of new referrals for UGI endoscopy originate from primary care physicians' who refer via a direct-to-test pathway. In the UK direct-to-test UGI endoscopy can be accessed through two distinct pathways: referrals are made either through a routine "open access" (OA) referral system, or through a fast tracked, cancer exclusion service in which patients receive their gastroscopy within 2 weeks of referral (2WR)[1]. As a result the majority of studies assessing dual focus endoscopy are conducted using such a referral population.

These referral pathways aim to reduce unnecessary outpatient consultations and streamline the diagnostic algorithm for patients[2], and have been adopted globally[3,4]. However the effectiveness of direct-to-test referral has been refuted by some authors because of a perceived increase in inappropriate referrals when comparing direct-to-test endoscopy to endoscopy with a prior GI consultation[5].

Both the American Society for Gastrointestinal Endoscopy (ASGE) and National Institute for Health and Care Excellence (NICE) have produced guidance documents which support the use of direct-to-test referral routes for diagnostic UGI endoscopy[6], and adherence to these guidelines has been shown to improve the yield of clinically relevant findings at UGI endoscopy[6-8].

These guidelines focus on appropriateness of referral, patient acceptance and preparedness for endoscopy, informed consent, and assurance of appropriate follow-up, however in addition to these service level factors recent technical advances in endoscope design may also influence the diagnostic yield of UGI endoscopy. High-definition, high-magnification endoscopy, with or without mucosal enhancement techniques by indigo carmine

chromoendoscopy or blue light endoscopy, enable more detailed visualization of GI mucosa than was achievable using earlier generation endoscopic equipment, and may allow improved detection and classification of GI mucosal lesions leading to better biopsy targeting[9].

Since January 2015, patients attending our teaching hospital for direct-to-test UGI endoscopy have been allocated either an Olympus GIF-HQ290 dual-focus magnification, high-definition gastroscope or an older generation video gastroscope (Olympus GIF-H260 or GIF-Q240). We aimed to establish whether the use of dual-focus magnification, high-definition endoscopy influenced the diagnostic yield in patients attending our service for open access diagnostic UGI endoscopy.

Method

A retrospective observational study of factors that influence identification of significant pathology during direct-to-test UGI endoscopy was performed in a university teaching hospital. Endoscopists consisted of nurses, specialist gastroenterology trainees and consultants. All of which were Joint Advisory Group (JAG) accredited endoscopists. All patients referred, between January 2015 and June 2015, through a direct-to-test pathway and who underwent a completed UGI endoscopy were included. Data were collected using the Unisoft endoscopy reporting software and hospital pathology database. The primary outcome of interest was the identification of significant pathology, defined as mucosal ulceration, stricture formation, biopsy proven cancer, biopsy proven Barrett's oesophagus or *Helicobacter pylori* positive gastritis, The latter two diagnoses were included due to their pre-malignant potential.

Any other findings were defined as non-significant and are summarised in supplementary table 1.

During this period an updated video-endoscopy system (EVIS LUCERA ELITE, CV-290, Olympus) was incorporated into our endoscopy department. A newly released dual-focus magnification, high-definition gastroscope (GIF-HQ290, Olympus) was used alongside existing models of video endoscopes (GIF-H260, GIF-Q260 & GIF-Q240, Olympus). Their usage was allocated based on availability post decontamination and the requirements of the lists being conducted. There was no blinded randomisation of the scope systems. The GIF-HQ290 endoscope allows for x45-fold magnification at the touch of a button on the endoscope. For the purposes of this study this endoscope was compared to all other endoscope technologies in use within the department. Recorded variables included endoscope type, age, gender, endoscopist, mode of referral (OA or 2WR) and primary symptoms prompting referral. Along with the finding of significant pathology, secondary measures were site of pathology and outcome after endoscopy.

Statistical analysis

Numerical summaries of the data were made. Categorical variables have been summarised as frequency (%) and continuous variables as mean (+/- SD). Univariate analysis was performed by Student's *t*-test, Fisher's exact test and χ^2 test as described in the text. Multivariate analysis was performed by modelling significant pathology (yes/no) using nominal logistic regression and contingency table analysis incorporating the factors age, gender, endoscope model, mode of referral and type of operator. Odds ratios were estimated from the fitted model. JMP (SAS Inc.) v11.0.0 and Prism (Graphpad Software Inc) v.6.0f were used for statistical analyses. A *p* value of <0.05 was considered as statistically significant.

Results

Patient demographics

500 endoscopies were included in the study. In keeping with our known departmental practice 77% of procedures were performed by nurse endoscopists, the remainder being performed by a mixture of training grade (16%) and non-training grade (7%) doctors.

Ninety four gastroscopies were carried out using the dual-focus magnification, high-definition gastroscope, the remaining 406 were conducted with, for the purposes of this study, standard Olympus gastroscopes (260 series, n=343 and 240 series, n=63). Significant pathology was identified in 122 (24.4%) patients. Seventy three percent of these significant pathologies were identified by nurse endoscopists, whilst training grade and non-training grade doctors identified 23 and 4% respectively. No other mucosal enhancement techniques were recorded as being used during any of the recorded procedures.

The mean age of patients was 61.5 (SD 15.6) years, with 304 (60.8 %) female patients. There was no significant difference in age between male and females ($p=0.97$ by Student's t -test, Figure 1A). The majority of patients (69.8%) were referred via open access, rather than the 2 week rule pathway. Mode of referral was similar for male and female patients ($p=0.2$ by Fisher's exact test, Figure 1B).

The two commonest indications for endoscopy were dyspepsia and dysphagia, accounting for 48% and 27% of referrals respectively. Men and women were equally likely to be referred for each of these indications (figure 2A, $p=.49$ by χ^2 test), and, in our dataset, individuals were at similar risk of being diagnosed with significant pathology irrespective of the indication for which the procedure was performed (figure 2B, $p=.29$ by χ^2 test). Of the 8 patients found to have an UGI cancer, 5 were referred with dysphagia, 2 with weight loss and anaemia and 1 with dyspepsia.

Univariate analysis of impact on diagnostic yield.

To characterise which factors influenced the diagnostic yield of direct-to-test UGI endoscopy we performed contingency table analyses or student *t*-tests to determine whether there were correlations between age, gender, mode of referral, operator and type of endoscope used and the identification of significant pathology (table 1). Whilst the group with significant pathology were marginally older than those without significant pathology (mean age 63.6 vs 61.0 years, $p=0.12$ by Student's *t*-test) there was no significant difference in ages. Male patients were more likely to have significant pathology than female patient ($p=0.02$ by Fisher's exact test). Mode of referral was not associated with a difference in diagnostic yield ($p=0.50$ by Fisher's exact test), whilst the type of operator was significantly associated with differences in diagnostic yield with nurse endoscopists identifying significant pathology in 23% of procedures, training grade doctors identifying pathology in 35% of procedures and consultants (who performed the fewest procedures in this cohort) identifying significant pathology at 14% of procedures ($p=0.04$ by χ^2 test). The use of dual-focus magnification, high-definition endoscopes was also associated with increased identification of significant pathology compared to other endoscope series ($p=0.02$ by Fisher's exact test).

Multivariate analysis

As univariate analysis identified a number of potentially confounding factors that influenced the frequency of identifying significant pathology in direct-to-test UGI endoscopy we built a logistic regression model to determine what impact specific variables had on diagnostic yield (Table 2).

In this model advancing age was identified as a statistically significant risk factor for the identification of pathology, though the effect size was extremely small (OR 1.01 (95% CI 1.00-1.02)). In keeping with previous literature, male gender was also identified as a risk

factor for the identification of significant pathology and conferred an odds ratio of 1.59 (95% CI 1.04-2.43). As in the univariate analysis, mode of referral did not influence the risk of identifying significant pathology. The type of operator did contribute to diagnostic yield in the multivariate analysis, with training grade doctors 3.7 (1.34-12.05) times more likely to identify pathology than their non-training grade colleagues. The use of dual-focus magnification, high-definition endoscopes was also identified as an independent factor in the identification of significant UGI pathology and conferred an odds ratio of 1.87 (95% CI 1.11-3.12) for identifying significant pathology over the use of other endoscope series.

Dual-focus magnification, high-definition endoscopy influences outcome following endoscopy

Having identified that the identification of significant pathology is influenced by the use of dual-focus magnification, high-definition endoscopy we wanted to characterise whether this endoscopy system also influenced the ongoing care provided to patients. We therefore categorised patient outcomes following endoscopy into hospital outpatient or MDT follow-up, an acute repeat UGI endoscopy, repeat endoscopy for surveillance, or discharge to the primary care physician. Acute repeat gastroscopies were defined as a further procedure within three months, and were requested either for interventional therapies including oesophageal dilatation, or to assess healing of mucosal lesions identified in the initial endoscopy.

There was a significant ($p=0.04$, χ^2 test) difference in the outcome of endoscopies following dual-focus magnification, high-definition endoscopy with a 3.0-fold increase in the proportion of patients entering an endoscopic surveillance program than in the group who were examined with conventional endoscopes (figure 3).

Non-trainee doctors discharged a higher percentage of patients, followed by nurse and trainee doctors (91.42, 83.72 and 78.2% respectively). Nurses and non-trainee doctors enrolled

patients into surveillance at a very similar rate, 2.84 and 2.85% respectively. With trainee doctors having the greatest rate of surveillance enrolment at 5.12%.

Dual-focus magnification, high-definition endoscopy aids diagnosis of significant oesophageal and gastric pathology

To determine whether dual-focus magnification, high-definition endoscopy might have an impact on the identification of lesions in a specific part of the UGI tract we categorised pathology by location and performed contingency table analyses. This demonstrated significant differences in distribution ($p=0.01$ by χ^2 test) with a 1.3 fold higher proportion of procedures identifying significant oesophageal pathology when procedures were performed with endoscopy compared to other endoscope series and a 2.7 fold increase in identification of gastric pathology (Table 3 and Figure 4). Significant duodenal pathology was identified in less than 1% of procedures and was not identified during any of the 94 endoscopies performed using a high-definition, high-magnification endoscope, hence this site was excluded from this analysis.

Comparing the standard and high definition scopes, all endoscopic findings were also subjected to univariate analysis (Table 4). This demonstrated a superior ability for the high definition scope to identify Barrett's oesophagus, gastric ulcers and gastritis. There was no difference in the identification of established oesophageal cancer. Insufficient duodenal pathology was identified to characterise statistically significant differences.

Discussion

This study demonstrates dual-focus magnification, high-definition endoscopy as an independent factor in the identification of significant mucosal pathology in patients attending for direct-to-test UGI endoscopy. In a multivariate analysis these endoscopes conferred a 1.87

fold increased odds of identifying pathology over the previously adopted standard endoscopes in our department. This increased ability to detect pathology also appears to have influenced the outcomes for patients included in the study. People who were examined with a dual-focus magnification, high-definition endoscope were approximately 3 times as likely to be entered into a Barrett's oesophagus surveillance programme as those in whom their endoscopy was performed with a standard endoscope. This is in keeping with previous data which have demonstrated utility for this type of endoscope in surveillance of Barrett's oesophagus [10].

In addition, an increased rate of mucosal pathology was identified in patient's stomachs when dual-focus magnification, high-definition endoscopes were used. The gastric mucosa is recognised to be a particularly challenging area to examine well, with reports of up to 7% of gastric cancers being missed when endoscopy was performed within a year of diagnosis[11]. Because of this, there has been a drive amongst policy makers to try to improve UGI endoscopy service provision[12], the data presented here suggest that there may be a role for dual-focus magnification, high-definition endoscopes in this. In our study advanced imaging techniques, such as NBI or AFI, were not utilised. Therefore we are unable to comment on the utility of this system to endoscopically determine malignant potential of neoplastic lesions or significant pathology.

The retrospective design of this study accurately reflects practice in our unit, but does introduce limitations to the study. Of particular note, the distribution of dual-focus magnification, high-definition endoscopes between different users was not random, and we identified a preponderance for their use by non-training grade doctors.

This observation may reflect the fact that more experienced endoscopists are more comfortable with using new equipment, but we cannot exclude that dual-focus magnification,

high-definition endoscopes were used for patients thought to have a higher pre-procedure index of suspicion for pathology.

In this study the majority of procedures were performed by nurse endoscopists, with non-training grade doctors conducting the smallest number of procedures. This is representative of the workload in the Royal Liverpool and Broadgreen University Hospitals Trust, and may well be representative across UK university hospital departments where non-training grade doctors conduct more complex therapeutic endoscopies, whilst other endoscopists perform the bulk of open-access endoscopy. The logistic regression analysis, which corrected for type of endoscope used, demonstrated that training grade doctors identified more epithelial pathology than non-training grade doctors, but no differences were identified between the diagnostic abilities of nurse endoscopists and non-training grade doctors. This supports the logistic regression's assertion that the type of endoscope used is an independent factor for the likelihood of making a diagnosis.

One of the benefits of dual-focus magnification, high definition endoscopy over other types of image enhancement, particularly chromoendoscopy, is the limited additional training and procedural time required. This means that adoption of this technology may have relatively little impact on direct provision of procedures, and that endoscopists of all levels of experience are likely to derive benefit from this technology. However the observation that more patients entered a Barrett's oesophagus surveillance programme could, if replicated, have a profound impact on the provision of UGI endoscopic services in the future.

Further research is therefore indicated to understand what the impact of introducing dual-focus magnification, high-definition endoscopy will be on service provision in the future. In the first instance similar studies need to be replicated in other settings, preferably adopting a prospective study design and a multicentre approach.

Conclusion

Dual-focus magnification, high-definition endoscopy increased the yield of significant pathology in patients referred by their primary care physician for direct-to-test UGI endoscopy. This altered clinical outcomes, and if recapitulated across services would have an impact on the provision of UGI endoscopy services in general, and the provision of Barrett's oesophagus surveillance in particular.

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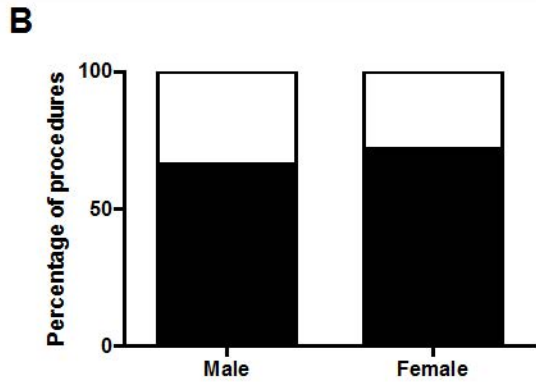
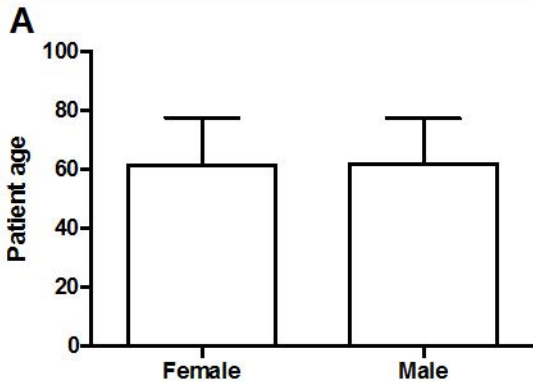
Figure Legends

Figure 1 A: Bar chart representing the age of patients at endoscopy according to gender (mean +/- standard deviation). No significant differences were identified between groups by Student's *t*-test $p=.77$. B: Bar chart showing the proportion of patients referred by gender and referral pathway. No significant differences identified between groups, $p=.19$ by Fisher's exact test.

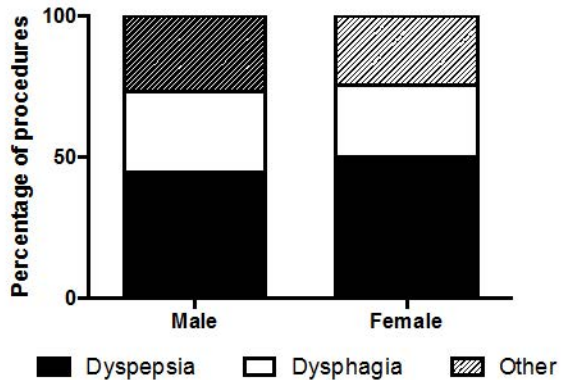
Figure 2A: Bar chart showing the proportion of male and female patients referred with dyspepsia, dysphagia or other indications. No significant differences identified between proportions of men and women referred with each indication, $p=.49$ by χ^2 test B: Bar chart showing the proportion of patients referred with dyspepsia, dysphagia or another indication who were found to have significant pathology following endoscopy. No significant differences identified between groups, $p=.29$ by χ^2 test.

Figure 3: Outcome of UGI endoscopies segregated by endoscope type. * denotes $p<0.05$ by χ^2 test.

Figure 4: Bar chart showing distribution of pathology in the UGI tract segregated by anatomical site. ** denotes $p<0.01$ by χ^2 test.



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