

Title Page

Pilot Randomized Cross-over study comparing the efficacy of transnasal disposable endosheath to standard endoscopy to detect Barrett's oesophagus

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Abstract:

Background and study aims: The transnasal endoSheath endoscope (TEE) is a new disposable technology with potential applicability to primary care setting. To evaluate the efficacy of this new technology for detection of Barrett's Oesophagus (BO), this study compared the diagnostic accuracy of TEE with standard endoscopy (SE).

Patients and methods: This was a prospective, randomized, cross-over study performed in a single, tertiary referral center. Consecutive patients undergoing surveillance for BO or referred for diagnostic assessments were recruited. All patients were randomized to have TEE followed by SE or the reverse. Endoscopic experiences and patient preferences were evaluated using a single questionnaire. Endoscopic and histologic diagnosis of BO, including optical image quality of both endoscopic procedures were compared.

Results: 21 of 25 patients completed the study. TEE had sensitivity and specificity of 100% for an endoscopic diagnosis of BO and of 66.7% and 100%, respectively, for histologic diagnosis of BO. Mean optical quality of SE was significantly better than TEE (7.11 ± 0.42 vs. 4.06 ± 0.27), ($p < 0.0001$). However, following endoscopy patients reported a significantly better experience with TEE compared to SE (7.05 ± 0.49 vs. 4.35 ± 0.53), ($p = 0.0006$) with 60% preferring TEE and 25% sedated SE.

Conclusions: In this study TEE had equal accuracy for an endoscopic diagnosis of BO compared to SE, at the expense of reduced image quality and a lower yield of intestinal metaplasia (IM) on biopsy. TEE was better tolerated and preferred by patients. Hence, TEE needs further evaluation in primary care as an initial diagnostic tool.

Introduction

The incidence of oesophageal adenocarcinoma (OAC) has increased dramatically in Western Countries over the last 30 years. However, despite advances in staging and treatment strategies, the 5-year survival of patients with this diagnosis remains poor, indicating the need to detect this cancer early to improve outcomes [1, 2]. Barrett's oesophagus (BO) is the only recognized precursor to this cancer and can be monitored over time endoscopically with the aim to detect neoplastic changes at an early curable stage. Retrospective series have showed that endoscopic surveillance of BO leads to early detection of EAC at an earlier clinical stage [3, 4], however the data on survival benefit remains controversial [5, 6]. The discrepancy among studies can be explained by the evidence that surveillance only improves survival from OAC if it is conducted with strict adherence to the recommended protocol [7]. Within this context, screening programs for BO have the potential to reduce mortality from OAC.

A valid screening test needs to be cheap, accurate, well tolerated and applicable to primary care [8]. Currently, the only validated screening test for BO is standard endoscopy (SE), which has major limitations. It requires sedation that increases the risk of adverse events, prolongs the length of the procedure and adds direct and indirect costs [9-11]. In addition, the standard endoscopic equipment requires decontamination, which is labour intensive, time consuming, with additional costs related to reprocessing machines. Hence, population screening by SE remains controversial, and specialist societies recommend it only in high risk individuals [12, 13].

Unsedated ultrathin transnasal endoscopy has been shown to be feasible, well tolerated, safe and accurate in evaluating BO [14-16]. In addition, TNE is estimated to be cost-effective compared with SE [17]. However, these endoscopes require the same decontamination process as standard endoscopes. A novel transnasal endoSheath® endoscope (TEE) has been developed to circumvent the need for reprocessing and allow use in a portable office-based setting. It has a reusable ultrathin endoscope with an outer disposable sterile sheath. The processor, light source and screen are integrated in a portable digital processing unit with the size of a briefcase. The TEE system has not yet been evaluated in a randomized cross-over design for the diagnosis of BO.

The primary aim of the study was to evaluate the sensitivity and specificity of TEE in diagnosing BO with reference to the endoscopic diagnosis made by SE;

The secondary aims of the study were:

1. To evaluate the sensitivity and specificity of TEE for a histologic diagnosis of BO with intestinal metaplasia with reference to the histopathology assessed on two random biopsies taken during SE
2. To compare the optical quality of TEE with SE;
3. To compare the patient tolerability and preference for the two procedures.

Patients and Methods

Design and Participants

This was a prospective randomized cross-over study performed in a tertiary referral centre. The study was approved by the Cambridgeshire 2 research ethics committee, Cambridge, U.K. All patients were over the age of 18 years and provided individual, informed consent for the study.

Two groups of patients were eligible for this study: a) Patients who were scheduled to have a diagnostic endoscopy for indications including dyspepsia, anaemia, suspected coeliac disease and abdominal pain, who were not known to have BO and b) Patients with a previous diagnosis of BO with a minimum length of at least 2 cm. This length cut-off was chosen to limit the impact of very short segments or an irregular Z-line which are known to lead to poor diagnostic agreement [18, 19]. However, if at the time of the research endoscopy their BO was found to be shorter than 2cm, they would still be included in the study.

Exclusion criteria were:

Known upper GI tract abnormality (e.g. pharyngeal pouch or previous esophagectomy);

Coagulopathy or anticoagulant treatment;

Active or severe cardiopulmonary or liver disease;

Active GI bleeding;

Referral to fast track service with alarm symptoms or dysphagia;

High grade dysplasia or intramucosal carcinoma in BO requiring extensive evaluation and biopsy.

After written informed consent was obtained, randomization was performed using a computer-generated randomization (www.randomization.com web-site), which allocated patients on a 1 to 1 basis to TEE followed by SE ("TEE first" group) or the reverse order of investigations ("SE first" group). The two procedures were performed by different endoscopists. The second procedure was undertaken at least 2 weeks later to allow for

mucosal healing if biopsies had been taken, thus ensuring that the endoscopists were blind to the indication. For practical reasons, the endoscopists were assigned to the first or second procedure based on their availability and not by a second independent randomization; however endoscopists were blind to the order of the procedures and were provided with the same clinical information. In addition the endoscopists were blinded to the indication to the procedure and the outcome of the other endoscopy test. A dedicated research nurse was present at all procedures to maintain the blinding of both the order and indication of procedure.

Endoscopy procedures

All SE procedures were performed by three experienced endoscopists (MKS, SV and MDP). The TEE procedures were performed by two endoscopists (MKS or SV), who had performed at least 50 procedures prior to the study.

Ultrathin unsedated Transnasal EndoSheath® Endoscopy (TEE): the EndoSheath® technology (TNE – 5000) consists of a 'D' shaped ultrathin scope (outer diameter of 4.7mm x 5.8mm) with a working length of 650mm, a two way distal angulation (140° up and 215° down) and a disposable sheath with two channels for insufflation, suction and biopsy forceps (Vision® Sciences, Inc, New York, USA). The endoscope handle has two push buttons to control insufflation and suction. Prior to each procedure the endoscope was placed in the sterile disposable sheath The patient's nasal cavity was sprayed with a combination of a local anaesthetic and decongestant and the procedure was performed in the sitting or left lateral position. The examination was limited to the oesophagus and the proximal stomach.

Endoscopists located the following landmarks and made a note of their distance from the nares: (a) the diaphragmatic pinch; (b) the gastro-esophageal junction (GEJ), corresponding to the top of the proximal gastric folds on minimal distension[19] , and (c) the squamo-columnar junction or 'Z' line[20]. A still image of the 'Z' line or the BO segment was taken to evaluate the optical quality. On endoscopic evidence of columnar-lined oesophagus 2 targeted biopsies were taken with a paediatric biopsy forceps within the BO segment to look for intestinal metaplasia (IM).

Standard endoscopy (SE): was performed using a 9.8 mm diameter endoscope (GIF-Q240Z, Olympus Inc.) with complete intubation of the second part of the duodenum according to standard practice. The procedure was performed under local anaestheticLidocaine spray

(Xylocaine®, Astrazeneca, U.K.) or conscious sedation using midazolam according to patient preference as per standard practice. If BO was detected 2 biopsies were taken within the segment of columnar-lined oesophagus to compare with TEE for presence of IM. This was followed by surveillance biopsies taken according to the Seattle protocol[21]. This allowed for direct comparison between TEE and SE without subjecting BO patients to two sets of surveillance biopsies. Still images of the 'Z' line and BO were captured as mentioned above. Any serious adverse events related to both procedures were recorded. Any failure to complete the procedure, including the reason for the failure, was recorded by the endoscopist.

Diagnostic criteria: a hiatal hernia was documented as viewed on the instructional video available on the international working group website for the classification of oesophagitis (www.iwgco.org) and the length was recorded according to the Prague C&M classification[19]. For the analysis the maximal length was used. The presence of oesophagitis was documented using the LA Classification [11]. Biopsies were evaluated by a single expert GI pathologist (MO'D) who was blinded to the endoscopic findings and endoscopy type, according to 2005 British Society of Gastroenterology guidelines [22], since this study was completed prior to the publication of the most recent 2014 guidelines [12].

Optical quality: The still images taken at both procedures were transferred onto Microsoft power point maintaining the same quality. The images were placed in a random order and evaluated by MDP and SV. The quality of the image was scored on a 10-cm visual analogue scale with 10 being excellent and 0 poor (VAS)[16]. The evaluators were asked to comment on the presence or absence of BO on TEE to estimate the interobserver agreement.

Patient acceptability: Following both of the procedures the participants completed a 10-point visual analogue scale (VAS), where 0 represented the worst experience and 10 the best experience ever. One week (+/- 2 days) after the completion of both the procedures patients were asked a single question addressing preferences for endoscopy.

Statistics: Continuous data were reported as mean with standard error of mean (SEM) or as median with range according to the type of distribution of variables. To compare groups Student's t test and Chi-square was used depending on the variables. All P-values were 2-sided and assumed to be significant if $p \leq 0.05$. Statistical analyses were performed using

GraphPad Prism 6 (La Jolla, CA, USA). Bland and Altman's limits_of agreement method was used to assess agreement of the two procedures in assessing the length of BO. For the endoscopic findings, the diagnosis made by SE was regarded as the reference. For the pathological findings, the histology based on the 2 research biopsies taken at SE was regarded as the reference. The sensitivity, specificity and diagnostic accuracy for detecting BO using TEE when compared to the reference SE was calculated along with 95% Clopper-Pearson confidence intervals. Interobserver agreement was estimated using k values with 95% confidence intervals.

The study was powered to address the primary aim of the study (endoscopic diagnosis of BO). Previous studies have showed that TNE has a sensitivity and a specificity for Barrett's of 90% and 95% [23-26]. Even though this may not be directly applicable to the TEE technology, we used this information to calculate the sample size. With this level of diagnostic accuracy we expected to recruit at least 12 patients with BO and 7 patients without BO to show a sensitivity and a specificity of at least 0.65 or better at a significance level of 0.05.

Briefly, if we assume that the true sensitivity is 90%, then testing 12 BO patients will result in at least 11 positive test results with a probability of 69.8%. In this case, the one-sided upper tail of a binomial distribution, under the null hypothesis of a sensitivity of 65% or less, results in a p-value of 0.042 or less. Under these circumstances, we will be able to demonstrate a sensitivity of at least 0.65 at a significance level of 0.05. Similarly, when recruiting 7 patients without BO and assuming a true specificity of 0.95, we anticipate 7 negative test results with a probability of 65.9%. Under these circumstances we will be able to demonstrate a specificity of at least 65% with a p-value of 0.049, obtained from the upper tail of the binomial distribution.

Results

Recruitment and participants

98 patients who fulfilled the criteria for inclusion were approached and 25 consented to participate in the study. Among those who declined participation, 20 patients were specifically asked to disclose the reason and the two main motivations were time constraints to commit for a second visit and the reluctance to have a second procedure. Four withdrew from the study, 3 after SE and 1 after TEE, none of whom had BO. 21 patients completed both the procedures. Patient demographics are shown in Table 1.

Diagnostic accuracy and optical quality of TEE

13 participants had endoscopic evidence of BO on SE and all these cases were correctly detected by TEE, which yielded a sensitivity and specificity of 100% for an endoscopic diagnosis of BO by TEE (95% CI, 75.3 – 100%) (Table 2). Biopsies taken at SE found histological evidence of IM in 9 cases [69.2% (9/13)] of which 6 were also confirmed by biopsies taken at TEE. This translated into a sensitivity and specificity of 66.7% (95% CI, 29.9 – 92.5%) and 100% (95% CI, 79.4 – 100%), respectively (Table 2). Of the three cases in which IM was not detected on TEE-directed biopsies, two had short tongues of columnar-lined oesophagus (COM1), of which in one case no biopsies were taken due to the difficulty in targeting the sampling, and the other was a C1M2 segment.

The median length of BO was 3cm (interquartile range [IQR] 1.5-4 cm) on SE and 2 cm on TEE (IQR 1-3 cm) The agreement between TEE and the reference standard SE is shown in figure 1. Overall we found a good level of agreement, with a discrepancy between the two technologies which is not dissimilar from the reported inter- and intra-observer variability for BO length estimation on SE [18]. In addition there was no trend in the difference of length between the procedures excluding systematic error

16 images were available for evaluation of optical quality. The mean optical quality score as measured by VAS for SE was 7.11 (SEM \pm 0.42). This was significantly better than the mean optical quality of TEE, which was 4.06 (SEM \pm 0.27) ($p = <0.0001$) (Fig 2 and 3). The interobserver agreement for diagnosis of BO on TEE endoscopic images between the two endoscopists was good with a κ of 0.738 (95% CI, 0.41 to 1.00).

Patient endoscopic experience and preference

Of the 21 patients that completed the study, 20 completed the post endoscopy visual analogue experience scale. The patient reported endoscopy experience following TEE was 7.05 (SEM \pm 0.49). This was significantly better than the level of experience following SE of 4.35 (SEM \pm 0.53), ($p = 0.0006$) (Fig 4A). Following the second endoscopy 20 patients returned their endoscopy preference questionnaire. 12 participants (60%) reported a preference for TEE with local anaesthesia, 5 (25%) preferred SE with sedation and 3 (15%) had no preference (Fig 4B). Among the patients who preferred TTE, one third ($n=4$) had SE under sedation, whereas all patients who preferred SE over TTE had their clinically indicated diagnostic procedure under sedation. None preferred SE without sedation. Common comments recorded by those who preferred TEE were “nasal felt less intrusive”, “easier to tolerate” and “I was able to talk”.

Discussion

This is the first study to look at the accuracy of TEE to diagnose BO in a randomized design. Our study demonstrates that TEE is as good as SE for an endoscopic diagnosis of BO with a sensitivity and specificity of 100%, even with a lower optical quality. The instrument allows for the use of paediatric sized biopsy forceps and can detect IM with a sensitivity and specificity of 0.67 and 1.00, respectively. Patients tolerated TEE significantly better than SE and most preferred TEE.

There are only two other studies which investigated the same technology used in this trial. One of these evaluated the feasibility of the endoscopic system, the time taken for processing and carrying out the procedures and the safety of TEE compared to SE. This study found that TEE significantly reduced the total time (time to set up, perform procedure and reprocess the endoscope) needed to perform upper GI endoscopy when compared to SE (18.8 vs 56.4 minutes, $p < 0.05$), without compromising safety [27]. A more recent cross-sectional study on a cohort of 426 patients evaluated TEE feasibility, safety and tolerability within a screening setting in tertiary care. TEE was able to diagnose BO in 4% of the participants and was tolerated well with only 0.7% reporting minor epistaxis and 0.2% reporting nasal irritation [28]. However, this study aimed to screen for esophageal pathologies in general and did not specifically look at detection of BO. Of the 426 participants included in this study, only 18 cases of BO were detected by TEE. Also, patients did not receive a standard endoscopy, therefore the study did not investigate the diagnostic accuracy of TEE as compared with the current gold standard. The results of our study are similar to those of previous trials using different types of ultrathin transnasal endoscopy. Four non-randomized studies reported a sensitivity and specificity for histologic or endoscopic diagnosis of BO of >89% and >95%, respectively [23-26]. However, one study which used an ultrathin calibre size of 3.1mm reported a sensitivity of 55% [29]. Two additional studies evaluated transnasal endoscopy using a similar design to the present study and demonstrated a sensitivity of 83.3% to 91% for detection of BO [15, 16]. In these studies patient tolerability of transnasal endoscopy was similar to SE and preference for transnasal endoscopy varied between 59% to 71%. There are some differences between this study and the two randomized studies previously published. First, we used a disposable system, totally applicable to primary care, as opposed to a TNE that needs reprocessing. Secondly, the scope diameter of the present study was 4.7mm x 5.8mm, compared to a 5.1mm used in the above studies.

The findings related to the quality of the image point to the fact that TEE is significantly inferior to the SE. While this is expected due to the obvious technological differences and

perhaps within an acceptable limit for a screening test, it is possible that this study has underestimated the image quality as its assessment was done on still images rather than videos. Future studies on this technology should assess optical quality based on video sequences.

This study has some limitations. First, we had a small number of participants, which may bias the results in favour of TEE. It is important to test new technologies in pilot randomized studies before proceeding to larger multicenter trials. We had difficulty in recruiting patients to the study and from our analysis of questionnaires; we found that the main barrier to recruitment was the reluctance by patients to undergo two procedures, rather than the reluctance to have TEE. Second, the endoscopists were not randomized to the type of procedure due to practical reasons, however the two endoscopists performing TEE did an equal number of cases (n=11). In addition, a dedicated research nurse was present throughout the procedures and ensured that the endoscopists were blinded to the indication and the order of endoscopy. Third, all endoscopists worked in tertiary care with a special interest in BO and the cases of BO included were artificially high due to enrichment, hence the results of this study cannot be generalized to a primary care setting for which this technology is intended. Fourth, three participants who had SE first withdrew from the study; if all of them had preferred SE this would drop the percentage of preference for TEE from 60% to 45%. Finally, the comparison between SE and TEE for the histologic diagnosis relied only on two random biopsies each rather than on the full biopsy protocol. This was decided a priori to avoid submitting patients to two consecutive endoscopies with multiple biopsies. The limited number of samples may in part explain the lower sensitivity of TEE compared to SE for a histologic diagnosis of BO [and the wide 95% CI](#), considering that the distribution of IM in BO is patchy and subject to sampling error. However, it should be noted that the lower yield of IM by TEE would preclude its use as surveillance tool. [It is reasonable to hypothesize that with a sufficient number of biopsies the sensitivity and the 95% CI of TEE for a histologic diagnosis of BE might improve.](#)

This study did not aim to assess diagnostic accuracy for other oesophageal diseases, which is relevant when the technology is intended as screening modality in primary care. We have looked at other oesophageal findings in our small patient cohort and the only other diagnoses made by SE were one case of grade A oesophagitis, which was correctly identified and graded by the TEE, and one proximal oesophageal web which was missed by the TEE. Future studies will need to address this important issue.

Other non-endoscopic imaging technologies that have been tested for BO screening in comparative clinical studies include the esophageal video capsule, and tethered capsule endomicroscopy. The esophageal capsule suffers from low sensitivity and specificity for diagnosing BO (78% and 73% respectively), requires further endoscopy with biopsy, is expensive and applicable mainly to secondary care [30]. The tethered capsule endomicroscopy has recently been proposed as a screening device for BO, but the interpretation of the imaging output is not straightforward and formal studies are yet to be conducted to prove its feasibility [10].

In conclusion, our pilot study has shown that TEE allows accurate diagnosis of BO. TEE can be safely performed without sedation and, given its portability, it is potentially feasible as screening tool in primary care and may be used in office-based setting. It will be interesting in the future to compare accuracy, acceptability and costs of TEE with other screening tests.

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Competing interests:

There are no conflicts of interest for any author relevant to this study. RCF is named on patents relating to the Cytosponge technology. Vision Sciences had no involvement in the conduct of the study or in the interpretation of the data.

References

1. Pohl H, Sirovich B, Welch HG. Esophageal adenocarcinoma incidence: are we reaching the peak? *Cancer Epidemiol Biomarkers Prev* 2010; **19**: 1468-70.
2. Eloubeidi MA, Mason AC, Desmond RA, El-Serag HB. Temporal trends (1973-1997) in survival of patients with esophageal adenocarcinoma in the United States: a glimmer of hope? *Am J Gastroenterol* 2003; **98**: 1627-33.

3. Cooper GS, Kou TD, Chak A. Receipt of previous diagnoses and endoscopy and outcome from esophageal adenocarcinoma: a population-based study with temporal trends. *Am J Gastroenterol* 2009; **104**: 1356-62.
4. Fountoulakis A, Zafirellis KD, Dolan K et al. Effect of surveillance of Barrett's oesophagus on the clinical outcome of oesophageal cancer. *The British journal of surgery* 2004; **91**: 997-1003.
5. Corley DA, Mehtani K, Quesenberry C et al. Impact of endoscopic surveillance on mortality from Barrett's esophagus-associated esophageal adenocarcinomas. *Gastroenterology* 2013; **145**: 312-9 e1.
6. Bhat SK, McManus DT, Coleman HG et al. Oesophageal adenocarcinoma and prior diagnosis of Barrett's oesophagus: a population-based study. *Gut* 2015; **64**: 20-5.
7. Verbeek RE, Leenders M, Ten Kate FJ et al. Surveillance of Barrett's esophagus and mortality from esophageal adenocarcinoma: a population-based cohort study. *Am J Gastroenterol* 2014; **109**: 1215-22.
8. Dellon ES, Shaheen NJ. Does screening for Barrett's esophagus and adenocarcinoma of the esophagus prolong survival? *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2005; **23**: 4478-82.
9. Eisen GM, Baron TH, Dominitz JA et al. Complications of upper GI endoscopy. *Gastrointest Endosc* 2002; **55**: 784-93.
10. Gora MJ, Sauk JS, Carruth RW et al. Imaging the upper gastrointestinal tract in unsedated patients using tethered capsule endomicroscopy. *Gastroenterology* 2013; **145**: 723-5.
11. Rubenstein JH, Inadomi JM, Brill JV, Eisen GM. Cost utility of screening for Barrett's esophagus with esophageal capsule endoscopy versus conventional upper endoscopy. *Clin Gastroenterol Hepatol* 2007; **5**: 312-8.
12. Fitzgerald RC, di Pietro M, Ragnunath K et al. British Society of Gastroenterology guidelines on the diagnosis and management of Barrett's oesophagus. *Gut* 2014; **63**: 7-42.
13. Spechler SJ, Sharma P, Souza RF et al. American Gastroenterological Association technical review on the management of Barrett's esophagus. *Gastroenterology* 2011; **140**: e18-52.
14. Saeian K, Staff DM, Vasilopoulos S et al. Unsedated transnasal endoscopy accurately detects Barrett's metaplasia and dysplasia. *Gastrointest Endosc* 2002; **56**: 472-8.
15. Jobe BA, Hunter JG, Chang EY et al. Office-based unsedated small-caliber endoscopy is equivalent to conventional sedated endoscopy in screening and surveillance for Barrett's esophagus: a randomized and blinded comparison. *Am J Gastroenterol* 2006; **101**: 2693-703.
16. Shariff MK, Bird-Lieberman EL, O'Donovan M et al. Randomized crossover study comparing efficacy of transnasal endoscopy with that of standard endoscopy to detect Barrett's esophagus. *Gastrointest Endosc* 2012; **75**: 954-61.
17. Nietert PJ, Silverstein MD, Mokhashi MS et al. Cost-effectiveness of screening a population with chronic gastroesophageal reflux. *Gastrointest Endosc* 2003; **57**: 311-8.
18. Dekel R, Wakelin DE, Wendel C et al. Progression or regression of Barrett's esophagus--is it all in the eye of the beholder? *Am J Gastroenterol* 2003; **98**: 2612-5.
19. Sharma P, Dent J, Armstrong D et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. *Gastroenterology* 2006; **131**: 1392-9.
20. Meining A, Ott R, Becker I et al. The Munich Barrett follow up study: suspicion of Barrett's oesophagus based on either endoscopy or histology only--what is the clinical significance? *Gut* 2004; **53**: 1402-7.

21. Levine DS, Haggitt RC, Blount PL et al. An endoscopic biopsy protocol can differentiate high-grade dysplasia from early adenocarcinoma in Barrett's esophagus. *Gastroenterology* 1993; **105**: 40-50.
22. Watson A HR, Shepherd NA. Guidelines for diagnosis and management of Barrett's columnar-lined oesophagus. 2005 [cited; Available from: <http://www.bsg.org.uk>
23. Wildi SM, Wallace MB, Glenn TF et al. Accuracy of esophagoscopy performed by a non-physician endoscopist with a 4-mm diameter battery-powered endoscope. *Gastrointest Endosc* 2003; **57**: 305-10.
24. Catanzaro A, Faulx A, Isenberg GA et al. Prospective evaluation of 4-mm diameter endoscopes for esophagoscopy in sedated and unsedated patients. *Gastrointest Endosc* 2003; **57**: 300-4.
25. Sorbi D, Gostout CJ, Henry J, Lindor KD. Unsedated small-caliber esophagogastroduodenoscopy (EGD) versus conventional EGD: a comparative study. *Gastroenterology* 1999; **117**: 1301-7.
26. Mokhashi MS, Wildi SM, Glenn TF et al. A prospective, blinded study of diagnostic esophagoscopy with a superthin, stand-alone, battery-powered esophagoscope. *Am J Gastroenterol* 2003; **98**: 2383-9.
27. Mayinger B, Strenkert M, Hochberger J et al. Disposable-sheath, flexible gastroscope system versus standard gastroscopes: a prospective, randomized trial. *Gastrointest Endosc* 1999; **50**: 461-7.
28. Peery AF, Hoppo T, Garman KS et al. Feasibility, safety, acceptability, and yield of office-based, screening transnasal esophagoscopy (with video). *Gastrointest Endosc* 2012; **75**: 945-53 e2.
29. Catanzaro A, Faulx A, Pfau PR et al. Accuracy of a narrow-diameter battery-powered endoscope in sedated and unsedated patients. *Gastrointest Endosc* 2002; **55**: 484-7.
30. Bhardwaj A, Hollenbeak CS, Pooran N, Mathew A. A meta-analysis of the diagnostic accuracy of esophageal capsule endoscopy for Barrett's esophagus in patients with gastroesophageal reflux disease. *Am J Gastroenterol* 2009; **104**: 1533-9.

Table 1 – Participant demographics

Table 2 – The efficacy of TTE for detecting endoscopic BO and IM, compared to SE

Figure 1 – The agreement between TEE and SE for estimation of BO length was analysed with a Bland-Altman plot. The dotted lines represent the 95% CI of limits of agreement.

Figure 2 – Comparison of the mean optical quality scores (on visual analogue scale) of TEE and SE

Figure 3 – Representative endoscopic images of normal GEJ and BO as seen on TEE and SE

Figure 4 – Endoscopy experience and preference. A) The mean post endoscopy experience scores following TEE and SE, B) Preference of type of endoscopy as recorded by participants following the last endoscopy

Table 1

	SE first	TEE first	Total	P Value
Number of patients	12	13	25	
Median age (range)	58.5 (24-76)	58.5 (33-74)	58.5 (24-76)	p=0.90
Male: Female (ratio)	5:7 (0.56)	10:3 (3.9)	15:10 (2.6)	p=0.11

Table 2

	Sensitivity % (95 % CI)	Specificity % (95 % CI)	Diagnostic accuracy % (95 % CI)

Endoscopic BO	100.0 (75.3 – 100.0)	100.0 (73.5 – 100.0)	100.0 (86.3 – 100.0)
Histologically confirmed BO	66.7 (29.9 – 92.5)	100.0 (79.4 – 100.0)	88.0 (68.8 – 97.5)

Figure 1

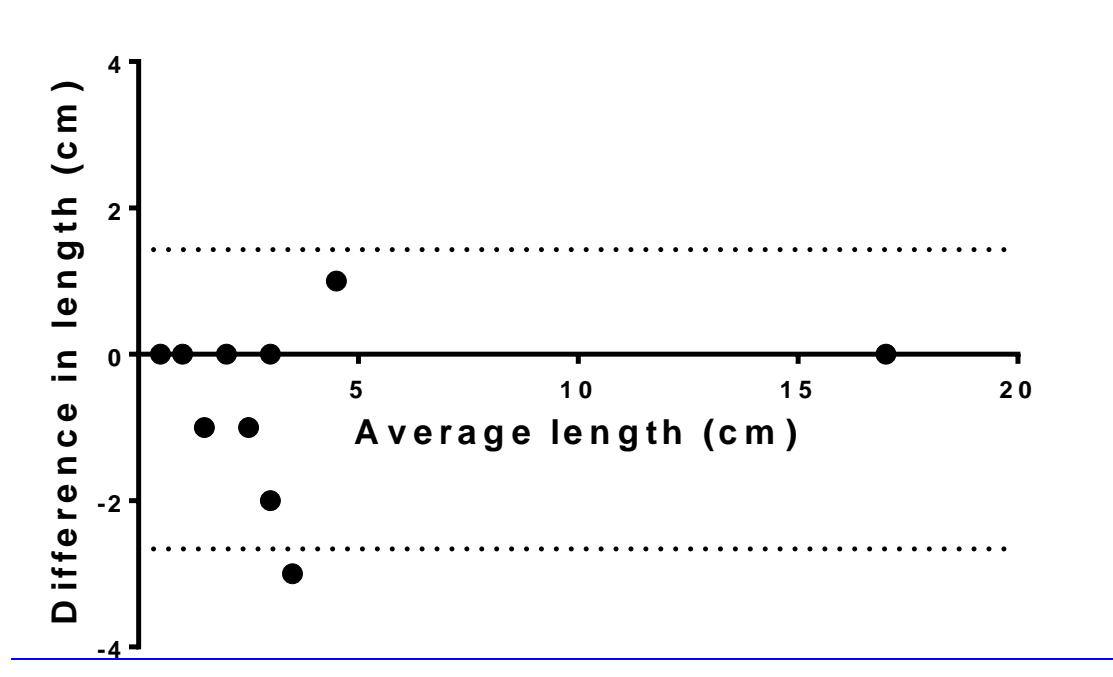
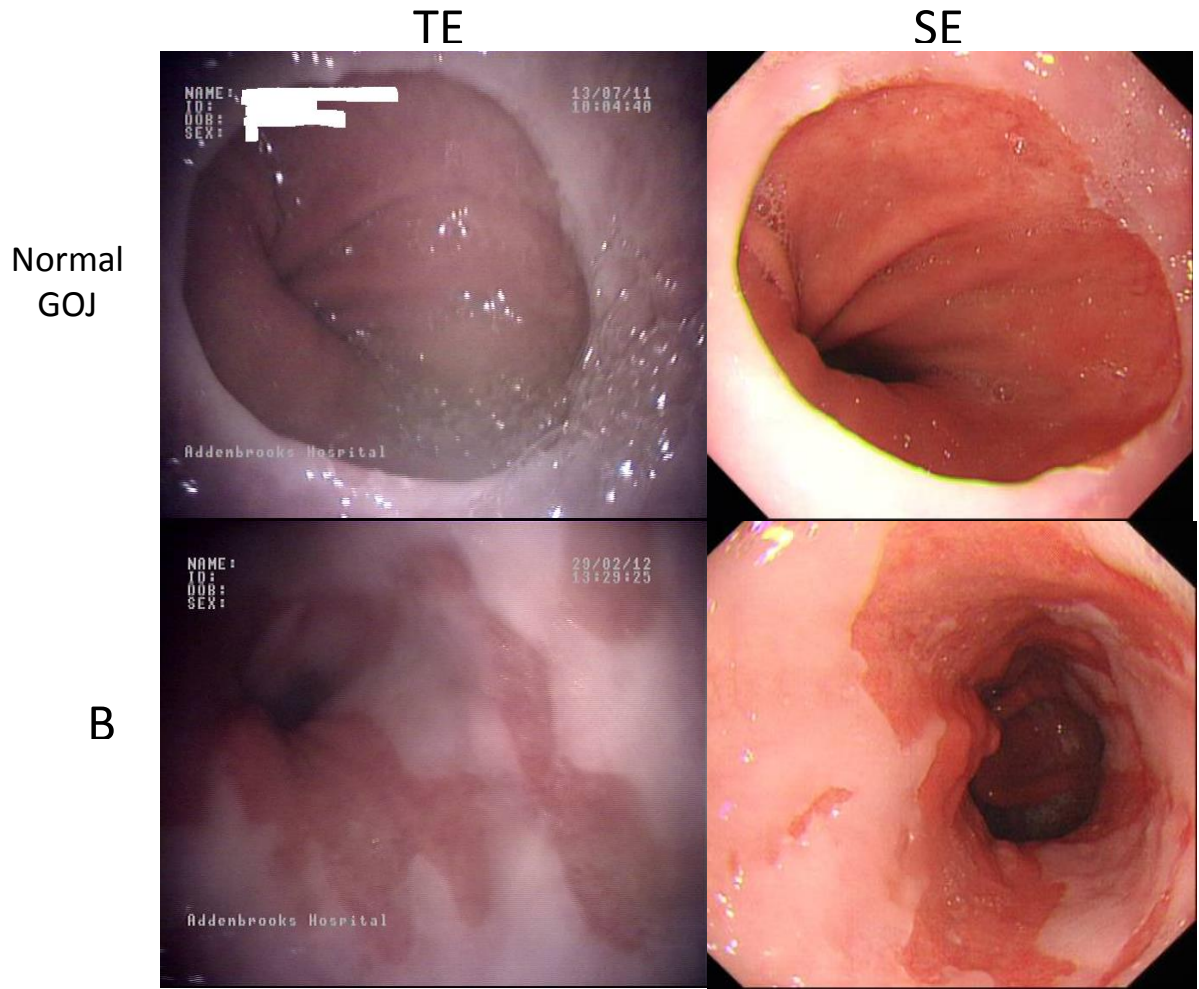


Figure 2



TEE – transnasal endoscopy; SE – standard endoscopy;
BO – Barrett’s oesophagus; GEJ – gastroesophageal junction

Figure 4

