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Randomised clinical trial: comparison of acceptability, patient tolerance, cardiac stress and endoscopic views in transnasal and transoral endoscopy under local anaesthetic

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SUMMARY

Background
Transnasal endoscopy (TNE) with ultrathin endoscopes has been advocated as an attractive alternative, for diagnostic upper endoscopy.

Aim
To assess tolerability, acceptability and quality of TNE, in comparison with standard upper endoscopy (SOGD, standard oesophago-gastro-duodenoscopy) under local anaesthetic.

Methods
We prospectively recruited 157 patients (83 females/74 males) mean age 57 years. The Fujinon EG530N (5.9 mm) and EG530WR (9.4 mm) endoscopes were used. The endoscopist and all patients completed detailed questionnaires regarding tolerability, acceptance and quality of endoscopy using standard visual analogue scales (VAS). Oxygen saturation (SaO_2), heart rate (HR) and systolic blood pressure (SBP) were recorded. Quality of biopsies was evaluated.

Results
Analysis included 161 procedures (TNE:79, SOGD:82) with duodenal intubation achieved in all patients. VAS scores for patient comfort were significantly better in the TNE group (7.3 vs. 5.3 respectively, $P < 0.001$). Twenty patients with previous experience of standard endoscopy were randomised to TNE and 19 of them (95.5%) preferred the TNE. Gagging was significantly less in the TNE group (0.12 vs. 3.41 respectively, $P < 0.001$). Cardiovascular stress was significantly less in the TNE group irrespective of the degree of gagging or comfort. TNE biopsies were smaller, but adequate for definitive diagnosis, similarly to standard endoscopy.

Conclusions
Transnasal endoscopy is superior to SOGD in terms of comfort and patient acceptance with significantly less cardiovascular stress. TNE can routinely be used as alternative to SOGD under local anaesthetic, for diagnosis and should be preferentially offered in cardiorespiratory compromised patients.

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INTRODUCTION

Oesophago-gastro-duodenoscopy (OGD) is the routine method for investigating the upper digestive system either under local anaesthetic or conscious sedation. Local anaesthetic is favoured by some patients to shorten recovery times and in those with cardiorespiratory comorbidity likely to be adversely affected by sedation.[1] However, it can be poorly tolerated due to gag reflex being triggered with contact to the soft palate and the back of the tongue.

Recent improvements in camera technology, have led to the development of 4-way angulation ultrathin endoscopes (<6 mm at the distal tip) while maintaining high resolution, thus making the transnasal route for OGD (TNE, transnasal endoscopy) a viable alternative. This technique is especially compelling[2] as it combines avoidance of sedation and is more patient friendly.[3]

Transnasal endoscopy has mostly been validated in Japan,[4] where it is used to screen for early gastric cancer. However, in Europe (including UK), TNE is not fully established. This is due to limited data from prospective randomised control studies assessing standard oesophago-gastro-duodenoscopy (SOGD) with TNE.

In this trial, we compared TNE with SOGD under local anaesthetic in a prospective randomised controlled single centre study. Our primary outcome was to assess patient's acceptability and procedure comfort. Secondary outcomes included cardiovascular stress, the endoscopist assessment of technical difficulty, image quality and biopsy adequacy.

METHODS

This study is a prospective randomised controlled trial of out-patients undergoing unsedated diagnostic upper gastrointestinal endoscopy. The study protocol was approved by the Lothian Research Ethics Committee, and has also been registered in ISRCTN (Reference number 08227262).

To avoid any bias, all patients were enrolled and all standard and transnasal endoscopic procedures were carried out by a single, experienced endoscopist (EA), within a dedicated endoscopy research area, in the Royal Infirmary of Edinburgh, Wellcome Trust Clinical Research Facility (RIECRF). All questionnaires before and after the procedure were collated by the research nursing staff of the RIECRF.

Study population

Invitations were sent to 700 random patients referred from the out-patient clinic for an SOGD as per routine indications between 1 February 2011 and 31 January 2012 (end of recruitment date). All out-patients over the age of 18 years who required an elective diagnostic upper endoscopy and were agreeable to unsedated endoscopy were eligible. Exclusion criteria included pregnancy, patients deemed high risk for vCJD, patients with psychiatric disorders, unable to give informed consent or a documented allergy to local anaesthetic. Patients with previous nasal surgery/fractures or nose malformations, a history of previous epistaxis, bleeding disorders, currently prescribed warfarin or low molecular weight heparin were also excluded.

Although the recruitment target was a maximum of 250 patients, 157 enrolled in the study by the recruitment closing date.

Randomisation and statistical analysis

All patients were randomised by the principal investigator, using the 'Random Allocation Software',[5] into two groups, one group undergoing SOGD under local (pharyngeal) anaesthesia and a second group having a TNE. Following recruitment and randomisation, three to five patients were booked onto each endoscopy list. The endoscopist was only informed of procedure allocation on the day and each list contained a mix of procedure types as assigned by randomisation. If a follow-up endoscopy was clinically necessary, patients had the follow-up procedure performed by the alternative endoscopic method in a cross-over fashion.

The study was powered to pick up a 10% difference in the primary outcomes between TNE and SOGD. Allowing for a 5% type I error with 90% statistical power required a minimum of 75 patients in each group as calculated by the study statistician. This number was exceeded in both groups by the end of the recruitment period.

Comparisons between groups were done using two-sample *t*-test where data are continuous; where data are categorical either χ^2 tests (more than two categories) or test for comparison of proportion (two categories) were used. Fisher's exact test was used to calculate the *P*-values if *n* were less than 10 in subgroup analyses. Results were displayed as a mean ± standard deviation (s.d.), unless stated otherwise and $P < 0.05$ was taken as significant (two-tail test of significance).

Endoscopic procedure

The EG-530WR endoscopes (Fujifilm, Japan) were used for the SOGD. The EG-530N ultrathin endoscopes (Fujifilm, Japan) were used for TNE. Both scopes were connected to an EPX-4400HD endoscopic processor and

light source stacking system (Fujifilm, Japan). Images were captured from each anatomical area (as per Figure 1) and stored in a digital image archiving system (ADAM, Fujifilm, Japan). Endoscopic reports were generated using Unisoft (Middlesex, UK) and included representative images of clinical relevance.

A Welch Allyn Propaq-CS was used to monitor blood pressure, heart rate (HR) and oxygen saturation by pulse oximetry. The blood pressure was recorded preceding intubation, when the endoscope reached the second part of the duodenum (D2) and immediately post-endoscope withdrawal.

For standard endoscopy, 50–100 μg of Xylocaine spray (2%) was used as local anaesthetic. A mouthguard was used in all transoral procedures and oxygen was administered at 2 L/min via a nasal cannula. External suction of saliva was applied as required.

For TNE, four to six puffs of Lidocaine hydrochloride/phenylephrine hydrochloride (5%/0.5%) spray was applied to both nostrils. Nostril patency was tested using a pre-treatment transnasal catheter of comparable scope diameter (N18F-SS 6.0 mm-18F; TOP Corporation, Tokyo, Japan) lubricated with 2% lidocaine gel. External suction was used, if required.

Patients in both arms were discharged an hour after the endoscopy. This included a 30-min observation period, a satisfactory swallow assessment and completion of research questionnaires.

Patient questionnaire

All patients completed a questionnaire at 30 min and 7 days post-procedure. A visual analogue scale (VAS) was used to rate aspects of the procedure from 0 to 10, with 0 denoting poor and 10 high comfort and tolerability. Patients rated their procedural experiences including comfort levels, anxiety pre- and post-procedure, procedure tolerance and preference in a future endoscopy. Patients with previous history of SOGD who were randomised to the TNE arm were asked to compare their TNE experience with that of the previous endoscopy.

Endoscopist/nurse questionnaire

A questionnaire was completed by the endoscopist to rate and comment on procedural aspects including: ease of pyloric intubation, overall scope handling, effectiveness of suction and air insufflation and adequacy and ease of biopsy sampling. In addition, the endoscopist assessed live endoscopic image quality, in terms of light, contrast, resolution and the adequacy of visualising each anatomical region, i.e. hypopharynx and epiglottis, oesophagus, gastric fundus, gastric body, antrum, pylorus, duodenal bulb and second part of duodenum.

The attending nurses performed an independent assessment of the patient's comfort and gagging using VAS scales. Comfort was rated by VAS; gagging was rated as 0 for no gagging and 10 for severe gagging.

Biopsy assessment

Tissue samples were obtained using either standard biopsy forceps (2.4 mm jaw diameter) for SOGD or paediatric forceps (1.8 mm jaw diameter) for TNE. The pathologist blindly reported on all received biopsy specimens. A repeat endoscopy for further biopsies was considered a biopsy failure. The number of biopsies taken was at the endoscopist's discretion.

Cardiac-respiratory assessment

The HR, arterial blood pressure and oxygen saturation were assessed, pre-, during and post-procedure, in all patients. For each patient, the 'double product' (DP) was calculated at each point of the procedure, from the systolic blood pressure and heart rate (SBP × HR).

Standard endoscopy	Transnasal endoscopy
0*	10*
4.68 ± 3.82	10*
4.71 ± 3.82	10*
9.72 ± 1.26	9.95 ± 0.32
9.85 ± 0.75	9.97 ± 0.27
9.96 ± 0.33	10*
10*	9.97 ± 0.23
9.98 ± 0.17	10*
9.89 ± 0.53	10*
9.91 ± 0.48	10*

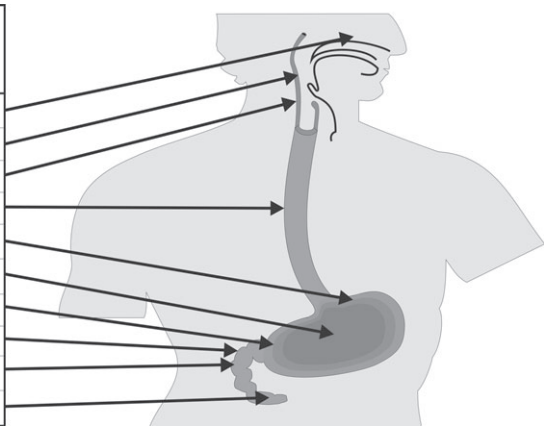

Figure 1 | Endoscopist VAS scoring for visualisation of the upper digestive system. Hypopharynx, epiglottis, vocal cords and cricopharyngeal views were superior by TNE. VAS, visual analogue scale; TNE, transnasal endoscopy.

The DP reflects myocardial oxygen consumption and cardiac output in treadmill test,[6] and is a useful prognostic mortality tool in cardio-compromised patients both during exercise and rest.[7] A value greater than 15 000 was taken as indicative of cardiovascular stress.

It was hypothesised that changes in cardiac output from baseline (pre-procedure) would reflect the level of stress incurred by the patient undergoing the procedure.[8] The study also looked at the association of the DP with the gagging and comfort scores recorded by the endoscopy nurse.

RESULTS

Demographics

One hundred and fifty-seven patients were recruited into the study and underwent a total of 161 endoscopies (82 standard and 79 transnasal). Of the four patients requiring follow-up, only three proceeded to have the cross-over procedure. The fourth patient opted to have a repeat SOGD out with the trial.

The demographics are detailed in Table 1. Both groups were similar in terms of age, gender and past medical history, with 27% of patients having a diagnosis of ischaemic heart disease. The indications for referral are displayed in Table 2. Endoscopic diagnoses are displayed in Table 3. There were no differences in the indications, history of ischaemic heart disease of endoscopic findings between the two groups.

Procedure characteristics

In both study arms, success rate was 100% in an intention-to-treat basis with no complications. In the TNE arm, two procedures failed transnasally due to resistance in the insertion of the nasal dilator. In both cases, a transoral endoscopy was performed successfully using the TNE scope. Standard OGD arm had 100% success rate.

Time from insertion to withdrawal of scope was longer in the transnasal group (mean time: 8.8 ± 3.2 min) in comparison with the standard endoscopy group (mean time: 7.7 ± 3.4 min, $P = 0.02$). The mean distance to the gastro-oesophageal junction was 39 ± 2.7 cm from the incisors for the SOGD and 42 ± 3.4 cm from the nostrils for the TNE, which is in concurrence with previous studies.[9] Although all patients remained for 1 h post-procedure, 80% of both groups were happy to be discharged less than 20 min post-procedure.

Patient comfort

Patients in the TNE group reported a higher mean comfort score compared with SOGD (7 ± 2.3 vs. 5.4 ± 2.7, $P < 0.001$). Seven days post-procedure, the mean VAS score remained largely unchanged (7.3 ± 2.1 vs. 5.3 ± 2.7, $P < 0.001$).

Data were analysed further, by grouping the comfort score into three tolerance bands; low (0–3), mid (>3 to 7) and high (>7 to 10). There were significantly more

Table 1 | Study demographics

	Standard	TNE
Total patients	80	77
Total procedures	82	79
Mean age (years)	57 ± 13.8	56 ± 15.8
Males (%)	43	52
Females (%)	57	48
Past medical history		
Lung disease	5	7
Cardiovascular disease	12	8
Current drug therapy		
Beta blocker	10	7
Calcium antagonist	11	7

TNE, transnasal endoscopy.

Table 2 | Referral indications for endoscopy

Indications	Standard ($n = 82$)	TNE ($n = 79$)
Symptoms of acid reflux	29	20
Epigastric pain	11	11
Anaemia	8	7
Dysphagia	14	18
Dyspepsia	11	13
Coeliac	3	4
Other	6	6

TNE, transnasal endoscopy.

Table 3 | Endoscopic diagnoses in each arm of the study

Diagnosis	Standard	TNE
Normal	27	41
Oesophagitis	20	20
Barrett's	8	4
Gastritis	9	3
Benign stricture	6	2
Oesophageal carcinoma	1	4
Other	6	2

TNE, transnasal endoscopy.

patients reporting a low comfort score in the SOGD group compared with the TNE group (23% vs. 9%, $P < 0.02$). Similarly there was a statistically significant difference between SOGD and TNE groups in the number of patients reported high comfort scores in favour of TNE (33% vs. 57%, $P < 0.0025$).

Patients in the TNE study arm had minimal gagging (0.12 ± 0.7) compared with the SOGD group (3.41 ± 3.34) ($P < 0.001$, χ^2 test). More specifically, 59 TNE patients (77%) vs. 21 SOGD patients (26%) experienced no gagging ($P < 0.001$, χ^2 test).

Procedure preference

When patients were asked regarding future endoscopic examinations (if clinically indicated) at day 7 post-procedure, 74% of the standard endoscopy group were prepared to have the test again and 26% stated only if absolutely necessary. In the TNE group, the corresponding numbers were 87% and 9% respectively ($P = 0.009$). Three patients in the TNE study arm did not complete the 7 day questionnaire.

Forty-six participants had a standard endoscopy in the past 5 years. Twenty were randomised into the TNE arm, and 95% (19/20) of these patients stated they clearly preferred the transnasal approach.

Endoscopist assessment

Image quality. The picture quality was comparable in both techniques in terms of light contrast and resolution (VAS scores for TNE light 9.94, contrast 9.93, resolution 9.90 vs. SOGD light 9.76, contrast 9.82 and resolution 9.82, NS).

Visualisation. Figure 1 details the VAS score for the visualisation and image quality of the examined anatomical regions. A significant difference was obtained at the hypopharynx, epiglottis, vocal cords and cricopharyngeal area ($P < 0.001$). There was no difference in the visualisation and image quality obtained with both techniques regarding oesophagus, stomach and duodenum.

The mean VAS score for the ability to complete the examination was 10 in both techniques. No difficulty was encountered with pyloric intubation with either technique and both techniques equally satisfied the endoscopist that the upper gastrointestinal tract was adequately examined.

Biopsy quality. Biopsy samples were taken as per standard protocols for disease diagnosis (e.g. four biopsies from D2 for diagnosis of coeliac disease). Biopsy samples were visually assessed for size adequacy by the endoscopist. The pathologist reported on all samples submitted unaware of the procedure type.

In the SOGD group, all biopsies were adequate for diagnosis, while in the TNE group, two cases were deemed inadequate. In the first case, four duodenal biopsies were considered inadequate for a definitive diagnosis of coeliac disease. However, repeat biopsies in a subsequent SOGD also failed to confirm diagnosis. In the second case, biopsies of a probable high oesophageal carcinoma were inconclusive. A repeat SOGD was performed out with the trial for additional biopsies, but histology was again inconclusive. It is therefore probable that it was the nature of the underlying disease rather than the biopsy size that lead to diagnostic uncertainty.

Cardiac-respiratory tolerance

No differences were found in the oxygen saturation levels (SaO_2) between the TNE procedure (average of 98% without supplementary oxygen) and SOGD (average of 99% with supplementary oxygen flow at 2 L/min). Both peak HR and peak SBP were statistically significantly higher in the SOGD group at the mid of procedure ($P < 0.0001$ for HR and $P < 0.0048$ for SBP) (Table 4).

Table 4 | Changes in heart rate and systolic BP during endoscopy. Mid-procedure heart rate and systolic BP were significantly higher in standard ($n = 80$) vs. TNE ($n = 77$) endoscopy

Patient stats (pre-, during and post-procedure)	Standard		Transnasal		
	Average (mean ± s.d.)	Range (min/max)	Average (mean ± s.d.)	Range (min/max)	*P*-value
Heart rate					
Pre	73.1 ± 13.2	40/110	72.6 ± 11.9	49/108	NS
Mid	89.9 ± 18.1	51/140	77.6 ± 13.5	56/118	<0.0001
Post	75.2 ± 13.6	54/122	72.8 ± 12.7	48/139	NS
Systolic BP					
Pre	139.2 ± 22.1	98/201	138.5 ± 20.9	98/198	NS
Mid	155.9 ± 25	103/225	144.3 ± 26.1	95/211	0.0048
Post	144.3 ± 22.8	105/200	145.1 ± 23	104/228	NS

The mean SOGD DP baseline was 10 190 ± 2540, this rose by an average of 3566 at mid-procedure. In comparison, the mean TNE DP baseline was 10 040 ± 2206, but only rose by an average of 801 at mid-procedure ($P < 0.0001$). DP was significantly lower over the entire range of comfort scores for TNE ($P < 0.001$) (Figure 2). Only six (8%) TNE patients exceeded the DP threshold of 15 000, whereas 32 (41%) SOGD patients had a DP score above that threshold ($P < 0.0001$).

Double product was significantly lower over the entire range of nurse assessed gagging scores for TNE ($P < 0.001$) (Figure 3). There was no correlation between the degree of gagging and DP value. Over 75% of TNE patients did not experience any gagging at all (VAS score = 0), compared with only 22% of standard endoscopy patients ($P < 0.0001$).

In the three cases that had both endoscopies in a cross-over fashion smaller incremental changes in DP were recorded mid-procedure with TNE, indicating less cardiovascular stress for the same patient (Figure 4).

DISCUSSION

This is the first prospective, randomised, control study comparing TNE with standard upper endoscopy (SOGD) under local anaesthetic carried out in a UK population who had been referred for elective diagnostic endoscopy. We have demonstrated that TNE is better tolerated, with high levels of patient comfort and acceptability and can be safely performed. It has a comparable success rate to SOGD, provides better visualisation of the hypopharynx and is associated with less cardiac stress. This study provides evidence to support TNE as a first line alternative to SOGD for

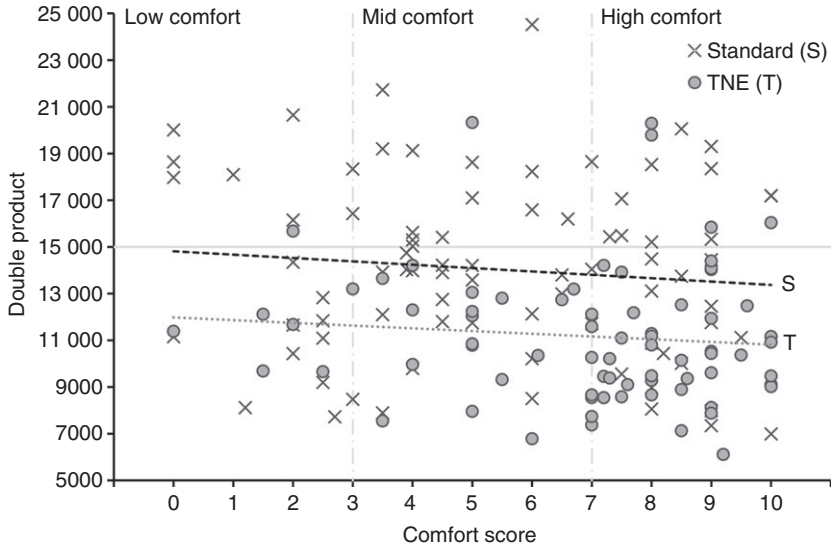

Figure 2 | Patient assessed comfort score plotted against double product for standard and transnasal endoscopies. Double product was significantly lower over the entire range of comfort scores for TNE ($P < 0.001$). TNE, transnasal endoscopy.

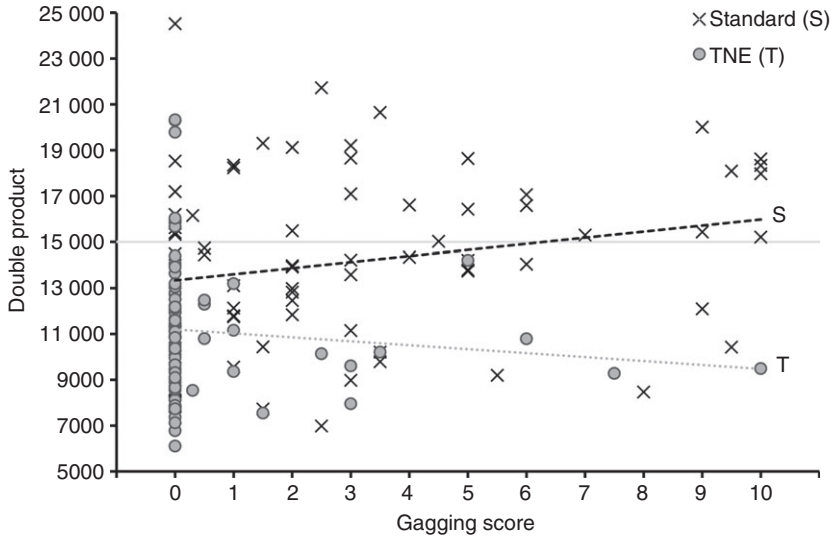

Figure 3 | Nurse assessed gagging score plotted against double product for standard and transnasal endoscopies. Double product was significantly lower over the entire range of gagging scores for TNE ($P < 0.001$). TNE, transnasal endoscopy.

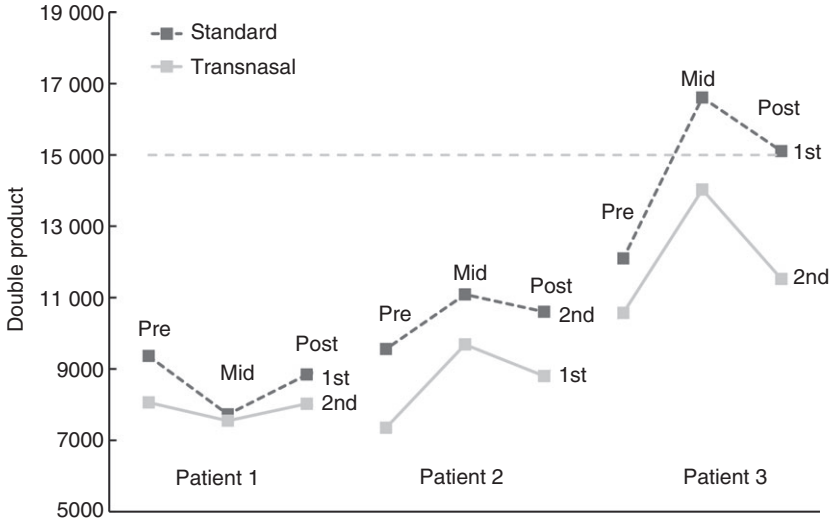

Figure 4 | The double product values pre-, during and post-procedure for three patients who had both endoscopies in a cross-over fashion.

diagnostic endoscopy particularly in cardiorespiratory compromised patients.

Since the first report of TNE in 1994 by Shaker,[2] few studies evaluated and compared this technique with standard transoral endoscopy particularly in the West. Although prospective, many studies included relatively small numbers of patients often in a nonrandomised manner with inconsistent comparisons such as different calibre endoscopes and a variety of sedation protocols. Furthermore, it is difficult to interpret results from studies using previous generation endoscopic technology and compare with studies using modern ultrathin endoscopes.[3, 4] In those early studies, transnasal intubation rate was variable (78–94%) and epistaxis was commonly reported. The most recent large prospective randomised study comes from China[10] and confirmed that TNE has comparable diagnostic effectiveness to standard endoscopy, and was associated with less cardiopulmonary stress and was more comfortable and cost-effective.

Although all TNE trials have showed promise, the technique has only gained wider acceptance in certain geographical areas (South East Asia and mainly Japan, and only parts of France and the US) so far.

In our study, the transnasal endoscope was found of comparable quality in terms of contrast, light and resolution to the standard endoscope including the application of image enhancement techniques (Fuji Intelligent Colour Enhancement). TNE performed significantly better when examining the hypopharynx, epiglottis and vocal cords, because of minimal gagging. Although this is an advantage of the technique, it emphasises the importance for the gastroenterologist practising TNE should be able to recognise pathology within the nasal cavity and hypopharynx. The recent introduction of the EG-530NW has seen further improvements to field of view (from 120 to 140°) identical to standard endoscopy.

In our study, TNE was successful via the nasal route in 97% of cases and 100% on 'the intention to treat' basis, this is at the high end of previously reported studies (82–100%).[11, 12] The duration of TNE procedure was 1 min longer which is in contrast to other studies.[13, 14] This could partly be attributed to the endoscopist performing a more detailed examination, including the hypopharynx, with less pressure from a less distressed patient.

Patients in the TNE group reported higher overall comfort and significantly lower levels of gagging. Of this group, 87% (compared to 74% in SOGD group) also indicated preference to a subsequent endoscopy via the nasal route. Furthermore, those patients in the TNE group who had previously experienced a standard endoscopy, reported that TNE was definitely more comfortable. This result was mirrored in the 7 days post-endoscopy questionnaire.

Previous studies[15–17] reported some pain during insertion of the endoscope to the nasal cavity, although this did not alter the higher satisfaction with TNE. In our study, nasal discomfort during scope insertion was low (<20%). However, this was identified as the most unpleasant part of the procedure. As such, we recommend the application of adequate local anaesthesia, using additional lignocaine spray into the nostril along with avoidance of touching the nasal septum with the endoscope, as key factors to improve TNE tolerance. While testing nostril patency was performed in our study, it is debatable and not used routinely elsewhere. It does have a role in preventing discomfort from endoscope insertion in anatomically narrow or distorted nasal cavities,

although failure to insert the flexible plastic catheter does not preclude a successful TNE examination.

The overall better tolerance seen in the TNE group, is in agreement with other studies in diverse patient groups.[3, 15, 18–20] The main positive points in favour of the TNE procedure included minimal gagging, lack of choking feeling, and the opportunity to communicate with the endoscopy staff during the procedure; all of which contributed to a less stressful procedure, and less apprehension regarding future endoscopies. These advantages imply that TNE is ideal for screening and surveillance programmes (varices or Barrett's) as it is not uncommon for such patients to become increasingly anxious after multiple repeat endoscopies. A recent small randomised trial from Turkey with similar design to our study which included endoscopy-experienced patients also confirmed that TNE was better tolerated when compared with unsedated standard endoscopy.[21]

Failure to intubate the nose is limiting factor and has been reported in 3–8% of patients.[15, 21–23] In our study, two TNE procedures failed, but were successful transorally using the ultrathin endoscope.

Complications reported in other studies included self-limited epistaxis (0.85–2%), vasovagal events (0.3%), and a single oesophageal perforation.[11, 21–23] No complications were reported in this study.

Diagnostic yield was similar in both groups (Table 3). This is in agreement with current literature for the detection of Barrett's oesophagus (BO), gastric cancer,[24, 25] and gastro-oesophageal reflux associated diseases.[26] Other studies, although consisting of small numbers, found that ultrathin endoscopes had similar diagnostic abilities.[27–30] Two of these studies applied a randomised design,[24, 31] found moderate or excellent agreement in diagnostic accuracy between TNE and SOGD (kappa score 0.94; 95% CI: 0.85–1.00).

Transnasal endoscopy has been shown to be feasible and safe[32] in primary care. Due to increasing incidence of oesophageal adenocarcinoma (sevenfold over the last 35 years) with poor survival rates[33], screening for BO has long been considered, but at present, screening of the general population in the UK for BO is not recommended. This may change in the future as wider use of endoscopic treatments such as Radio-frequency ablation for low grade dysplasia, or even for nondysplastic BO, may warrant the implementation of screening programmes for which TNE can prove an ideal option.

Use of TNE for Barrett's surveillance is based on the assumption that less gagging reduces oesophageal movement permitting more accurate assessment of BO. The British Society of Gastroenterology guidelines currently do not recommend TNE as a replacement for transoral endoscopy due to lack of supporting evidence.[34] A later UK study however looked at the rates of dysphasia between TNE and standard endoscopy in Barrett's surveillance and found to be similar despite smaller size biopsies obtained by TNE.[35]

In agreement with the previously mentioned study,[35] our study showed that the diagnostic accuracy biopsy material was similar in both groups, although the biopsies obtained by TNE were smaller. With technological advances, it is expected that next generations of ultrathin endoscopes will have wider biopsy channels allowing for use of standard biopsy forceps. Our study adds further weight to the evidence that TNE should be considered as an equal alternative to transoral endoscopy for diagnostic purposes including BO.

An important study aim was to assess cardiovascular stress during TNE and standard endoscopy. We opted for a simple measurement (DP) derived from routinely recorded cardiovascular parameters (HR and SBP pre-, mid and post-endoscopy). This has been previously used to assess myocardial functional reserve during exercise.

Although the pre-procedure resting HR and SBP were comparable in both groups, the mid-procedure peak HR and SBP were significantly higher in the SOGD group. Only 8% of TNE patients exceeded the DP threshold (15 000), whereas it was exceeded by 41% of SOGD patients. When DP was plotted against patient reported comfort (Figure 2) or nurse assessed gagging (Figure 3), no correlation was found suggestive that the lower DP value observed in TNE is related to the type of procedure rather than the degree of patient comfort or gagging. Furthermore, the three patients with cross-over endoscopies had lower DP values recorded mid-procedure during TNE.

No study patient had a hospital admission attributed to cardiac causes within 80 days of the index endoscopy. However, standard endoscopy could cause cardiovascular stress equivalent to a treadmill test for some of our patients. Previous studies confirmed that TNE causes fewer cardiovascular adverse effects than SOGD.[36, 37] TNE has also been shown to cause minimal increases in SBP and less sympathetic stimulation than SOGD,[38] possibly associating with fewer cardiovascular adverse events.

Given the increasing prevalence of ischaemic heart disease in an ageing western population, the impact of cardiac stress during endoscopy cannot be ignored. A recent study evaluating TNE in the elderly, reported it to be safe and well accepted in this population[39], but lacked objective cardiovascular data. Coupled with our observa-

tions, we recommend that TNE should be the preferred endoscopic method in patients with established cardiovascular disease or significant cardiorespiratory compromise.

As TNE is more widely adopted, it is important to consider the financial implications of implementation. Presently, no data exist regarding the cost benefits of TNE, and has not been addressed in this study. However, we found that most TNE patients can be immediately discharged without risk. This translates to a reduced requirement for recovery space, healthcare personnel. Although we conducted the trial with two attending nurses as per national guidelines, it is feasible to run a diagnostic TNE list with one nurse assisting, as we have found that this is a well-tolerated procedure requiring minimal or no oral suction or oxygen administration. This represents potential cost savings and increased operational effectiveness which translates to increased capacity.

Other studies support the notion that TNE is associated with shorter overall procedure times and lower procedure costs due to avoiding sedation and minimising post-procedure observation.[13, 14]

A limitation of our study was the modest sample size although the study numbers gave adequate statistical power to avoid type I or II errors. In addition only a small number of patients crossed-over within the trial. A factor not investigated in this study was the contribution of endoscope insertion tube diameter to the procedure tolerability. A recent study[40] from Taiwan implied that per os intubation using a 5-mm ultrathin endoscopy achieves comparable patient tolerance, acceptance and satisfaction as with TNE intubation, in addition to lower intubation failure and epistaxis. However, in that study no assessment of cardiovascular stress was made which from our data is associated to the insertion route rather than the degree of comfort or gagging.

In conclusion, TNE is a safe and potentially cost-effective alternative to SOGD, with excellent patient tolerability in a UK population. We have demonstrated that TNE is associated with lower cardiac stress and therefore recommend that TNE should be considered first line investigation in cardiopulmonary compromised patients.

AUTHORSHIP

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Author contributions: Dr Alexandridis was the trial endoscopist and contributed to ethics submission and writing of the manuscript. Dr Inglis contributed to the study design, analysis of data and the writing of the manuscript. Dr McAvoy conducted a literature review and contributed to the writing of the manuscript. Dr Falconer conducted a review of the cardiac history, medication and post-endoscopy follow-up of complications. Miss Graham contributed to the statistical design and analysis. Prof. Hayes contributed to the study design and critical evaluation of the manuscript. Prof. Plevris was the principal investigator and contributed to the study design, ethics application, analysis of data and writing of the manuscript. All authors have reviewed and approved the final version of the article.

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