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A Randomized Comparative Effectiveness Trial of Novel Endoscopic Techniques and Approaches for Barrett's Esophagus Screening in the Community

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Abstract

Objectives—To compare participation rates and clinical effectiveness of sedated endoscopy (sEGD) versus unsedated transnasal endoscopy (uTNE) for esophageal assessment and Barrett's esophagus (BE) screening in a population-based cohort.

Methods—Prospective, randomized, controlled trial in a community population. Subjects, ≥ 50 years of age who previously completed validated gastrointestinal symptom questionnaires were randomized (stratified by age, sex and reflux symptoms) to one of three screening techniques (either sEGD, or uTNE in a mobile research van (muTNE), or uTNE in a hospital outpatient endoscopy suite (huTNE)) and invited to participate.

Results—209 of 459 (46%) subjects agreed to participate (muTNE n=76, huTNE n=72, sEGD n=61). Participation rates were numerically higher in the unsedated arms of muTNE (47.5%) and huTNE (45.7%) compared to the sEGD arm (40.7%), but were not statistically different (p=0.27).

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Prasad G. Iyer contributed to study concept and design; acquisition of data; analysis and interpretation of data; critical revision of the manuscript for important intellectual content; obtained funding; study supervision.

Complete evaluation of the esophagus was similar using muTNE (99%), huTNE (96%) and sEGD (100%) techniques (p=0.08). Mean recovery times (minutes) were longer for sEGD (67.3) compared to muTNE (15.5) and huTNE (18.5) (p<0.001). Approximately, 80% of uTNE subjects were willing to undergo the procedure again in future. 29% and 7.8% of participating subjects had esophagitis and BE respectively.

Conclusions—Mobile van and clinic uTNE screening had comparable clinical effectiveness with similar participation rates and safety profile to sEGD. Evaluation time with uTNE was significantly shorter. Prevalence of BE and esophagitis in community subjects ≥ 50 years of age was substantial. Mobile and outpatient unsedated techniques may provide an effective alternative strategy to sEGD for esophageal assessment and BE screening.

Keywords

Esophageal adenocarcinoma; Barrett's esophagus; transnasal endoscopy; screening; mobile van screening

Introduction

The incidence rate of esophageal adenocarcinoma (EAC) has rapidly risen over the past 3 decades, exceeding that of melanoma, lung, colon and breast cancers(1). Five year survival remains below 20% for EAC cases diagnosed after the onset of symptoms, while early stage EAC has a 5-year survival exceeding 80%(2). Barrett's esophagus (BE) is the strongest and only known precursor of EAC. However, cancer progression rates in clinically diagnosed BE are as low as 0.33% per year(3), hence endoscopic surveillance alone may not have an impact on survival rates from EAC(4). Moreover, it is estimated that only a third of patients with BE in the population are detected clinically, with the rest remaining undiagnosed, despite the substantial increase in the use of endoscopy (5). Indeed, up to 90% of patients who present with EAC do not have a previous diagnosis of BE(6), despite its presence on histology, an indication of the underlying challenge for early detection.

Screening for BE in high-risk individuals coupled with curable endotherapy of early neoplasia may represent an alternative strategy to reduce mortality from this lethal cancer. This was endorsed by recent guidelines from gastroenterology societies (7, 8). However, several questions remain to be addressed before such an approach can be considered or implemented. To this date, the true population prevalence of BE in the United States remains unknown partly due to the lack of suitable screening tests to replace sedated endoscopy (sEGD) for use in the community. Current BE risk prediction models are derived from patients seen at referral centers undergoing endoscopy for clinical indications and may not be representative for use at a population level (9, 10). Finally, The lack of real data on participation rates and yield of different screening modalities for assessment in the community limits the validity of assumptions utilized in modeling studies which have found screening to be cost effective(11).

Unsedated transnasal endoscopy (uTNE) has been proposed as an acceptable and accurate alternative to sEGD for detection of BE(12, 13). The feasibility and acceptability of this technique was demonstrated in a pilot randomized trial in Olmsted County(14). A survey

study in this population showed the potential for increased participation if screening was provided closer to home(15). The EndoSheath® transnasal esophagoscope (Vision-Sciences Inc., Orangeburg, New York) has recently become available. It utilizes a novel disposable sheath that encases the endoscope and completely isolates it from patient contact, obviating the need for decontamination and reprocessing facilities. It utilizes a more compact processing system allowing for easy portability, rendering it suitable for widespread use. Initial reports on the clinical utility of this device in an office-based setting have been encouraging(16).

The comparative clinical effectiveness of uTNE compared to sEGD in community screening for BE specifically participation rates, diagnostic yield, tolerability, and safety has not been studied before. While prior studies have used either uTNE alone or in tandem with sEGD (12, 16); this does not allow a simultaneous and systematic comparison of both approaches separately. Furthermore, the clinical utility and effectiveness of using a mobile van unit for screening with uTNE closer to the patient's home also remains unknown.

The aims of our study were: 1. To assess participation rates in BE screening using uTNE in a mobile van unit (muTNE), uTNE in a hospital endoscopy unit (huTNE) and conventional sEGD; and 2. To compare the clinical effectiveness of these techniques in a population based randomized trial.

Methods

Trial Design and Settings

This was a prospective, randomized, controlled trial conducted in Olmsted County, MN. The study took place between April 1st 2011 and October 30th 2013. The Olmsted County population comprises approximately 144,000 persons of whom 86% are white (2010 US Census data). County residents receive their medical care almost exclusively from two group practices: the Mayo Medical Centre and Olmsted Medical Center. The Mayo Clinic has maintained a common medical record system with its two affiliated hospitals. The system was further developed by the Rochester Epidemiology Project (REP), which created indices for the records of other providers of medical care to local residents. Annually, over 80% of the entire population is attended by one or both of these two practices, and nearly everyone is seen at least once during any given 4-year period(17). Therefore, the REP medical records linkage system provides an enumeration of the population from which samples can be drawn. All participants gave informed consent and the study received approval from the Mayo Clinic and Olmsted Medical Center Institutional Review Boards. The trial was registered on clinicaltrials.gov (identifier: NCT01288612).

Participants

Using the REP resources, age- and gender-stratified random samples of Olmsted County residents were previously drawn, and those subjects were mailed validated gastrointestinal symptom questionnaires from 1988 to 2009 (5, 18, 19). Those population-based surveys have allowed identification of a cohort of community subjects, well characterized by the

frequency of reflux symptoms, without history of endoscopic evaluation and not known to have BE.

Subjects 50 years or older in this cohort (n= 1157) were randomized - stratified by age, sex, and reflux symptoms- and assigned to muTNE, huTNE, or sEGD groups. Within each group, patients were sorted in a random order, and an initial sample of 450 potential participants was obtained (150 per group) to contact for recruitment to the study. Medical chart review was performed to check for exclusion criteria, namely: history of progressive dysphagia; known Zenker's or epiphrenic diverticulum; history of recurrent epistaxis; moved out of Olmsted County or deceased; significant illness that may impair ability to complete questionnaires (e.g. metastatic cancer, major stroke, and dementia); and coagulopathy.

Successive patients who met the inclusion and exclusion criteria in each of the 3 groups were initially sent generic invitation letters asking if “they agree to be contacted by phone in two weeks' time to inform them about a research study run by Mayo Clinic”. Subjects who explicitly declined to be contacted regarding research were excluded from the study, while others who agreed or did not respond after 2 weeks were considered eligible to be contacted. Details of patient flow are shown in figure 2.

Eligible patients received a telephone call from a research coordinator who was blinded to the primary hypothesis of the study. One of 3 standardized telephone scripts were used depending on the group assignment. Subjects were only offered the technique that they had been randomized to. These scripts included information on the rationale of the study and details on the procedure and its potential adverse effects. In each group, the order for contacting patients was randomized. Patients who declined participation or could not be reached by telephone after 3 attempts were not further contacted. Patients in all 3 groups were treated and followed up in the same manner.

Interventions

Prior to endoscopic procedures, participants filled out the GERQ questionnaire(18), a validated measure of reflux and somatic symptoms. Reflux symptoms were classified into: frequent (≥ one episode/week of heartburn or acid regurgitation); infrequent (< one episode/ week of heartburn or acid regurgitation); or absent (No Heartburn or acid regurgitation).

The sEGD procedures were performed using a conventional high definition endoscope (GIF-180, Olympus America, Center Valley, PA) under conscious sedation with intravenous midazolam and fentanyl. uTNE was performed using the EndoSheath® transnasal esophagoscope (TNE-5000, Vision Sciences, Orangeburg, NY). The working length is 650 mm with 140° up & 215° down tip deflection and 120° field of view. The insertion diameter is 4.7 mm when using a sheath with no working channel, and this increases to 5.4 mm or 5.8 mm when using a sheath containing 1.5 mm or 2.1 mm working channel, respectively. All procedures were performed by expert gastroenterologists, who had performed over 1000 upper gastrointestinal endoscopic examinations. Topical anesthetic aerosol spray (Benzocaine 20%; Topex®, Sultan Healthcare Inc., Hackensack, NJ, USA) was applied to the posterior pharynx and nasal spray mixture (Phenylephrine 1.0%, Leader®, Cardinal

Health, Dublin, Ohio, USA; and Lidocaine 4%, Hospira Inc., Lake Forest, IL, USA) was applied to the patient's nares (6–8 sprays) 10–15 minutes prior to uTNE.

The uTNE procedure was performed with the patient lying in the left lateral position. The endoscope was introduced into the right or left nares and advanced into the proximal esophagus under direct vision. Prior to every procedure, the esophagoscope was placed inside a new, sterile sheath. Following the procedure, the esophagoscope was removed from the sheath, which is then discarded, and the endoscope was cleaned with a 70% ethyl alcohol wipe after every use.

The muTNE group underwent the research procedures in a mobile research vehicle (MRV) that is staffed by a registered nurse. The MRV contains two exam rooms with cardio respiratory monitoring equipment, a private area for patient interviews and audiovisual technology for patient education (figure 1). Eligible subjects were divided into 4 groups geographically in Olmsted County (on the basis of residential address: northwest, northeast, southwest and southeast quadrants,) and were approached consecutively by group. Screening exams in this group were conducted in the exam room space, in sets of 5–6 subjects to maximize efficiency. Once 5 subjects consented to participate in this arm of the study, the MRV was driven to a geographical location in close proximity to the subjects' residence and stationed in a suitable area with convenient parking. A maximum of 6 screening procedures were conducted in one muTNE session over a 4–5 hour period. Fifteen sessions were conducted to screen 76 subjects.

Biopsies were taken from any endoscopically suspected BE and from the GE junction and squamous mucosa in all subjects. The length of BE segment was defined using the Prague criteria(20). All participants received a telephone call from the research coordinator 1 and 30 days after the procedure, to complete validated tolerability scales(21) and adverse events questionnaires.

Outcome Measures

The primary outcome measure was participation rate. This was estimated as the proportion of subjects who agreed to undergo esophageal assessment in the three groups (muTNE, huTNE, sEGD) out of those who were eligible to be contacted for participation in screening. Additional analysis was performed to identify clinical and demographic factors associated with higher participation rates in screening.

The secondary outcome measure was clinical effectiveness. This was evaluated by assessing both the quality and yield of esophageal assessment with muTNE, huTNE and sEGD. All parameters were recorded by the trial coordinator for all procedures.

Endpoints for procedure quality were: rate of successful intubation (the ability to traverse the upper esophageal sphincter and visualize the esophageal mucosa) classified as successful or unsuccessful; rate of complete evaluation (visualization of the whole esophagus and identification of landmarks: squamocolumnar junction, gastroesophageal junction [upper margin of gastric folds with stomach deflated] and the diaphragmatic hiatus) classified as complete = all three landmarks identified, incomplete = some landmarks identified, or

unsuccessful; rate of successful acquisition of biopsies scored as successful = all biopsies obtained, incomplete = some biopsies are obtained, or unsuccessful = no biopsies can be obtained; duration of procedure in minutes (time from the beginning of procedure [initiation of sedation or local anesthesia] to extubation, and time from extubation to discharge [recovery time]); tolerability (validated pain scales(21) - where “0” is none and “10” is severe - were used to assess the degree of pain, choking, gagging, and anxiety experienced during the procedure, overall tolerance was rated on a scale from 0–10, where “0” is good and “10” is poor tolerance); acceptability (proportion of patients willing to undergo the procedure again in the future); safety (adverse events including pain, abdominal discomfort, bleeding, perforation, or need for hospitalization) was assessed 1 and 30 days after the procedures in all subjects.

Endpoints for procedure yield included: reflux esophagitis (graded using the Los Angeles classification(22)); suspected BE (presence of columnar mucosa at least 1 cm length in the tubular esophagus); and confirmed BE (presence of intestinal metaplasia with goblet cells in biopsies on Hematoxylin and Eosin stains). All patients with suspected BE in the muTNE and huTNE groups were offered a “confirmatory” clinical sEGD with histology in 2 weeks' time. Histology was interpreted by a gastrointestinal pathologist blinded to the cohort assignment.

Randomization and Sample Size Estimation

Subjects eligible to be contacted were randomly assigned to one of three procedures (muTNE, huTNE and sEGD) stratified by sex, presence of GERD, and age group (≥65 vs. <65). The assignments were generated via a computer algorithm (SAS®) by the study statistician and sent to the study coordinator via an EXCEL spreadsheet (Excel 2010, Microsoft, Redmond, WA).

In a prior pilot study done by us (14), the participation rate for using sEGD was 37% compared with 47% for uTNE. A sample size of 150 subjects (eligible to be invited for participation) in each group provided 80% power to detect a 20% increase in screening participation using uTNE (thought to be clinically significant) over sEGD, using a two sample test of proportions at an alpha level of 0.0125, accounting for four comparisons (1. sEGD versus huTNE, 2. sEGD versus muTNE, 3. sEGD versus huTNE and muTNE combined, and 4. huTNE versus muTNE).

Statistical Analysis

Pair wise comparisons of participation proportions in the three study arms were assessed. These proportions were compared using a chi square test (or a Fisher's exact test as appropriate). Logistic regression analysis was utilized to identify factors predicting participation. Several logistic regression models were examined, each one including the procedure group and one of a fixed (a-priori selected) set of predictor variables to identify factors associated with participation in screening. We assessed the following a-priori selected variables: age, gender, education level, employment, marital status, reflux symptoms, use of PPI drugs, randomization group, SSC score, and Charlson comorbidity index.

The performance characteristics and yield of muTNE, huTNE, and sEGD were summarized either as proportions (95% confidence intervals) for categorical characteristics, or as mean (standard deviation), or median (interquartile range) depending on their distribution, for continuous characteristics. These characteristics were compared across the three groups using a Kruskal-Wallis test for the continuous characteristics and a chi-square test for categorical characteristics. Given the need for multiple comparisons to assess this hypothesis, statistical significance was defined using an alpha level of 0.01 (adjusting for testing multiple measures of performance). The statistical software (SAS® version 9.3, SAS Institute, Cary NC) was used for analysis.

Results

Participation Rates and Predictors

459 subjects were eligible to be contacted and invited for screening in their allocated study arm (muTNE n=158, huTNE n=151, sEGD n=150). 43 (9.4%) had frequent reflux symptoms (≥1/week), while 197 (42.9%) had infrequent (<1/week) and 219 (47.7%) had no reflux symptoms in this cohort. Baseline characteristics were comparable among the three groups (table 1).

Of the 459 subjects contacted, 209 (46%) agreed to undergo study procedures (muTNE n=76, huTNE n=72, sEGD n=61). The mean (+/− SD) age of this cohort of “participants” was 65 years (+/− 9) and 45.9% were males. 29 (13.9%) had frequent reflux symptoms, 86 (41.1%) had infrequent and 90 (43%) had no reflux symptoms in this cohort Baseline characteristics were also comparable among the three groups of participants (table 2).

Though participation rates were numerically higher in the unsedated arms of muTNE (48.1%) and huTNE (47.7%) compared to the sEGD arm (40.7%), these differences were not statistically significant on pair wise comparisons (sEGD vs. muTNE, p=0.25; sEGD vs. huTNE, p=0.42; sEGD vs. muTNE or huTNE, p=0.27; muTNE vs. huTNE, p=0.82). Factors which independently predicted higher participation rates included presence of frequent reflux symptoms (OR 2.94, 95%CI 1.47–5.88,) and being either unemployed or a homemaker (OR 2.48, 95%CI 1.07–5.77). Age, gender, education level, marital status, current PPI use, SSC score and Charlson co morbidity index were not associated with significant differences in participation rates (table 3).

Quality and Yield of Endoscopic Assessment

Complete evaluation of the esophagus (intubation, visualization of the mucosa and landmark identification) was comparable using muTNE (n=75, 98.7%), huTNE (n=69, 95.8%) and sEGD (n=61, 100%) techniques (p=0.08). However, successful biopsy acquisition was lower in the muTNE (n=60, 79%) and huTNE (n=60, 83.3%) groups compared to sEGD (n=61, 100%) (p=0.001), due to inability to advance the TNE scope with the biopsy sheath through narrow nasal passages and patient intolerance. Recovery times (from extubation to discharge) were significantly longer following sEGD (67.3 +/−5.9) compared to muTNE (15.5 +/−2.8) and huTNE (18.5 +/− 4.2) techniques (p<0.001).

Though the overall tolerability scores (mean +/−SD) for sEGD was better than muTNE and huTNE (0.4 +/−0.6 vs. 1.9 +/−2.2 and 2.2 +/−2.2 respectively, p<0.001), uTNE was well tolerated. Moreover, a substantial majority of patients undergoing muTNE and huTNE were willing to undergo TNE again (78.9% and 83.3%, respectively, compared to 93% with sEGD). No serious adverse events were reported in any of the three arms (table 4).

There was no difference in procedure yield between the three study arms with regards to suspected (p=0.37) and confirmed (p=0.44) BE. However, the yield for erosive esophagitis was higher in the huTNE and sEGD arms compared to muTNE (p=0.003). Overall, 16 subjects (5 females and 11 males) were diagnosed with BE (7.8%). Median segment length (using Prague classification) was C0 (range 0–8) M2 (range 1–10). One patient was found to have low grade dysplasia and one patient was diagnosed with high grade dysplasia. The rates of detection of manifestations of GERD-induced esophageal injury in subjects with and without reflux symptoms are shown in table 5. Erosive esophagitis was seen in several subjects with (35%, 17% LA Grade B, C) and without reflux symptoms (23%, 10% LA grade B, C).

Discussion

We report results from the first large prospective randomized trial evaluating novel approaches to assess GERD complications (including BE) in a population cohort in the United States. In this study we have demonstrated comparable participation rates, clinical effectiveness and safety of unsedated TNE (performed in both the hospital and in a mobile setting) to sedated EGD for the assessment of GERD complications. Though the participation rates were numerically higher in the unsedated techniques (muTNE and huTNE) compared to sEGD, the difference was not statistically significant. The patient's visit was significantly shorter using uTNE techniques with adequate tolerability and acceptability. Patients with frequent heartburn or acid regurgitation were significantly more likely to participate in screening compared to those with infrequent or no reflux symptoms. The overall proportion of subjects in the study population who had BE was 7.8%, with 4.4% of subjects without reflux symptoms being diagnosed with BE.

In this study, subjects were randomized and offered their allocated screening test only, as opposed to offering all three to every patient (with the patient choosing the technique). This design was chosen in order to obtain comparative and valid estimates of participation rates for each one of the three techniques separately. Results from this study are concordant with the previous pilot trial comparing uTNE, video capsule endoscopy (VCE) and sEGD screening (14). Though VCE was the most acceptable in this study, given its suboptimal accuracy for the detection of BE (23), this technique was not assessed in the current study.

Development of non-invasive screening tests over the past few years have led to renewed interest in screening for BE and EAC. The Cytosponge™ is a capsule cell-sampling device, coupled with a biomarker(24). In a primary care study involving 12 UK general practices, 18% of invited subjects agreed to take part. The sensitivity and specificity of the test for the detection of Barrett's epithelium was 73.3% and 93.8% (24). 3.0% of participants (15/501) had a confirmed diagnosis of BE. Cytosponge™ screening was also found to be cost-

effective in a recent economic modeling study (25). This device is promising given its low cost and potential widespread applicability. Nonetheless, it is a non-endoscopic technique and hence will still need a confirmatory endoscopy.

BE prevalence rates between 6–25% have been reported from U.S. referral center cohorts (26, 27). Population studies from Europe have reported lower prevalence (1.3%–1.6%) for BE (28, 29). This may reflect differences in risk factors such as obesity, Helicobacter pylori and differences in endoscopic and histological assessment(30). The reasons for higher BE prevalence in our study (7.6%) compared to the Cytosponge™ study are not fully clear. Participants in both studies had comparable sociodemographic characteristics but all patients in the Cytosponge™ study had history of reflux symptoms or receiving acid suppressive medication prescriptions. Participation rates in the current study were substantially higher than in the Cytosponge™ study. Prevalence of BE while higher in those with frequent and infrequent reflux symptoms (10%), was also substantial on those without reflux symptoms (4.4%).

Unsedated TNE has been shown to be an accurate alternative to sEGD for the diagnosis of BE (12, 13). However, comparative data on technical success rate, tolerability and acceptability of uTNE with respect to sEGD in the population are lacking. While uTNE screening was found to be more cost effective than screening using sEGD(11), assumptions such as a 95% participation rate in screening were used. Our study provides the first real data on participation and completion rates of uTNE in the community, in addition to demonstrating the comparable clinical effectiveness of uTNE to sEGD. Although a substantial majority of patients who underwent muTNE and huTNE were willing to undergo the test again in future if necessary (78.9% and 83.3%, respectively), acceptability of sEGD was significantly higher (93.4%, p=0.001). It is likely that the use of sedation for sEGD may explain this as it makes the procedure more comfortable to patients, and likely impairs memory and re-collection of the event.

Mobile screening vans have been found to be effective instruments in increasing population participation in screening (in and outside the U.S.) for cervical(31), colon(32), breast(33) and lung(34) cancer with no decrement in accuracy, in a cost-effective manner(35). A survey study conducted by us previously suggested that participation in BE screening may increase by the use of mobile screening(15). Therefore we elected to evaluate this technique by incorporating the portable and disposable EndoSheath system in a mobile research van,. We did not find a statistically significant increase in uptake rates between the hospital and mobile TNE arms. This may be a result of the excellent access to medical care and endoscopy in Olmsted County and should be tested in more medically underserved populations with limited access to screening tests. Despite this, an important finding of our study was the reduction in recovery and overall patient visit duration achieved by using the muTNE and huTNE techniques compared to sEGD, without any substantial decrement in yield, tolerability and safety. Furthermore, uTNE can be performed by non-gastroenterology physicians as well as by physician extenders raising the possibility of this being a truly community based screening tool (36).

Successful biopsy acquisition remains a limitation of the current uTNE device. This was lower in the muTNE (79%) and huTNE (83.3%) groups compared to sEGD (100%) (p=0.001), primarily due to inability to intubate the esophagus with the larger biopsy sheath. In those cases, the endoscopist switched to the thinner channel-free sheath to enable successful intubation and visualization of the esophagus, without biopsies being taken. If screening is to be implemented in practice, then the issue of biopsy acquisition using uTNE becomes less important because all subjects with endoscopically suspected BE on uTNE screening will likely require a clinical sEGD for surveillance biopsies(7).

There was a higher yield of erosive esophagitis with the hospital based techniques compared to the mobile technique. The reasons for this remain unclear, in particular, as the proportion of subjects with reflux symptoms and other baseline characteristics were comparable across the three study arms. Better visualization of the esophagus in studies conducted in the hospital may be a potential explanation.

This study provides an insight into the potential subset of undetected BO in the community(37) and helped us to determine the acceptability of screening in a previously untested segment of the population. Given the demographic make- up of Olmsted County, our study sample is representative of the US white population, which is the likely target population for future screening efforts for BO and OAC. Although response bias is a possibility because the cohort consisted of responders to previous health questionnaires, this is unlikely because of the lack of difference between responders and non-responders that has been demonstrated in this population(38).

In conclusion, in this prospective randomized population based study utilizing state-of-the-art novel minimally invasive endoscopic techniques in a hospital and mobile setting, we demonstrate comparable clinical effectiveness, safety and participation rates with uTNE. Data from this study may help inform future economic and risk stratification modeling studies. BE and esophagitis prevalence in the community is substantial, in both those with and without reflux symptoms.

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Abbreviations

BE	Barrett's Esophagus
EAC	esophageal adenocarcinoma
GERD	gastroesophageal reflux disease
GERQ	gastroesophageal reflux questionnaire
huTNE	unsedated transnasal endoscopy in hospital outpatient endoscopy suite
MRV	mobile research vehicle
muTNE	unsedated transnasal endoscopy in mobile research van
REP	Rochester Epidemiology Project
sEGD	sedated endoscopy
uTNE	unsedated transnasal endoscopy

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Study Highlights

What is current knowledge?

- Screening for BE with unsedated transnasal endoscopy (uTNE) has been found to be cost effective, but assumptions such as a 95% participation rate and up to 15% prevalence rates were used.
- The comparative effectiveness of esophageal assessment by uTNE compared to sedated endoscopy is not known.
- Existing uTNE devices are not suitable for widespread use in the community setting due to limited portability and need for decontamination equipment.
- Mobile screening vans have increased participation in screening for cervical, colon, breast, and lung cancers with no decrement in accuracy.

What is new here?

- The clinical effectiveness of uTNE is comparable to that of sedated endoscopy, enabling the use of uTNE in BE screening of high risk individuals.
- uTNE screening using the novel EndoSheath® (portable and disposable) esophagoscope is effective and acceptable both in the hospital and community settings
- Overall participation in uTNE screening was substantial (but lower than previously assumed), and prevalence of BE in our population-based study sample was 7.8%.
- Mobile van screening for BE and esophageal adenocarcinoma (EAC) may be an effective alternative to hospital or clinic-based techniques.

Figure 1.
Mobile research vehicle: A) outside view, B) view of exam room inside

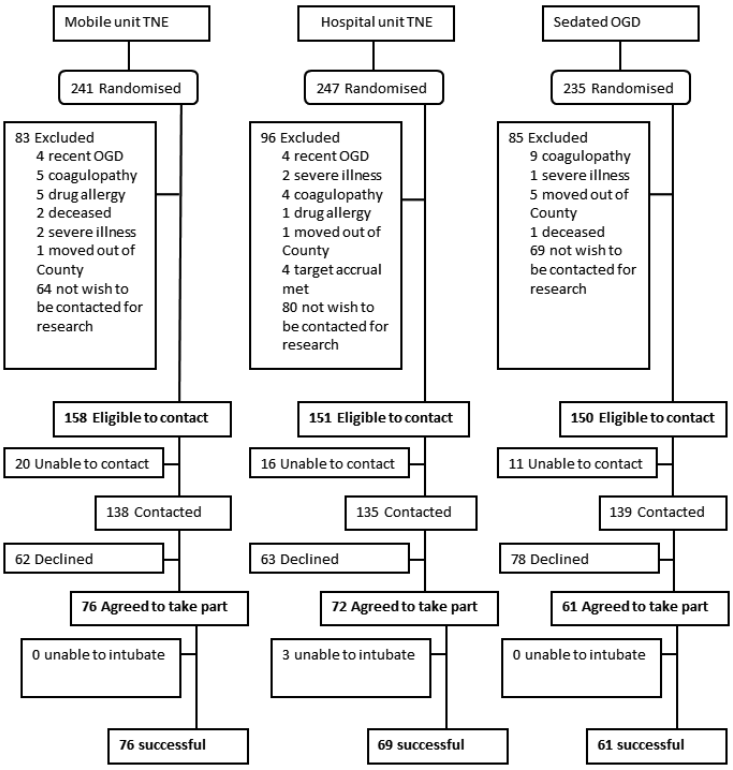

Figure 2.
Study flowchart describing patient identification and recruitment.

Table 1

Baseline characteristics of subjects who were invited for screening in their allocated study arm

Variable	muTNE (N=158)	huTNE (N=151)	sEGD (N=150)
Mean age, years (SD)	64 (10)	64 (10)	65 (9)
Male Sex, N (%)	71 (44.9%)	69 (45.7%)	69 (46.0%)
Education N (%)			
Less than high school	7 (4.6%)	3 (2.0%)	2 (1.4%)
High school or some college	72 (47.1%)	76 (52.0%)	77 (53.8%)
College/professional training	74 (48.4%)	67 (45.9%)	64 (44.8%)
Employment N (%)			
Employed	56 (36.6%)	63 (43.2%)	48 (33.6%)
Unemployed/homemaker	11 (7.2%)	8 (5.5%)	8 (5.6%)
Retired	86 (56.2%)	75 (51.4%)	87 (60.8%)
Marital status N (%)			
Married	116 (73.9%)	118 (78.2%)	115 (77.2%)
Not married (single, widowed, divorced, separated)	41 (26.1%)	33 (21.8%)	34 (22.8%)
Reflux symptoms N (%)			
Heartburn or acid regurgitation >= 1/week	15 (9.5%)	16 (10.6%)	12 (8.0%)
Heartburn or acid regurgitation < 1 / week	68 (43.0%)	67 (44.4%)	62 (41.3%)
No Heartburn or acid regurgitation	75 (47.5%)	68 (45.0%)	76 (50.7%)
Current use PPI drugs N (%)	28 (18.2%)	23 (15.5%)	25 (16.9%)
SSC score, mean (SD)	0.8 (0.6)	0.7 (0.5)	0.8 (0.6)
Charlson comorbidity index, mean (SD)	0.9 (1.5)	1.0 (1.5)	1.2 (1.9)

(n=459), PPI, proton pump inhibitors; SSC, somatic symptom checklist; sEGD, sedated endoscopy; muTNE, mobile unitTNE; huTNE, hospital unitTNE; SD, standard deviation; N, number.

Table 2

Baseline characteristics of subjects participating in the three arms of the randomized trial

Variable	muTNE (N=76)	huTNE (N=72)	sEGD (N=61)
Mean age (years), mean (SD)	65 (9)	64 (9)	66 (9)
Male Sex N (%)	32 (42.1%)	35 (48.6%)	29 (47.5%)
White ethnicity N (%)	73 (96.0%)	72 (100%)	61 (100%)
BMI mean (SD)	29.0 (5.6)	30.5 (13.9)	28.8 (5.8)
Waist to hip ratio, mean (SD)	0.91 (0.09)	0.92 (0.11)	0.91 (0.09)
Education N (%)			
Less than high school	2 (2.7%)	1 (1.4%)	1 (1.7%)
High school or some college	37 (49.3%)	40 (55.6%)	33 (55.0%)
College/professional training	36 (48.0%)	31 (43.1%)	26 (43.3%)
Employment N (%)			
Employed	23 (30.7%)	29 (40.3%)	17 (28.3%)
Unemployed/homemaker	6 (8.0%)	6 (8.3%)	5 (8.3%)
Retired	46 (61.3%)	37 (51.4%)	38 (63.3%)
Marital status N (%)			
Married	57 (76.0%)	62 (86.1%)	42 (70.0%)
Not married (single, widowed, divorced, separated)	18 (24.0%)	10 (13.9%)	18 (30.0%)
Frequency of reflux symptoms N (%)			
≥1/week	11 (14.5%)	10 (13.8%)	8 (13.1%)
<1/week	26 (34.2%)	32 (44.4%)	28 (45.9%)
None	38 (50%)	27 (37.5%)	25 (41.0%)
Current use PPI drugs N (%)	15 (19.7%)	9 (12.5%)	11 (18.0%)
Current aspirin use N (%)	38 (50.0%)	37 (51.4%)	36 (59.0%)
SSC score, mean (SD)	0.8 (0.6)	0.8 (0.6)	0.8 (0.5)
Charlson comorbidity index, mean (SD)	0.9 (1.3)	0.9 (1.4)	1.3 (2.0)

(n=209). PPI, proton pump inhibitors; SSC, somatic symptom checklist; sEGD, sedated endoscopy; muTNE, mobile unitTNE; huTNE, hospital unitTNE; SD, standard deviation; N, number.

Table 3

Proportions and predictors of participation in screening.

Variable	Proportion of participants	OR for participation (95%CI)[a]	P value[a]
Age [b]		1.09 (0.90,1.31)	0.39
Sex			
Male	45.4%	1.0 (ref)	
Female	44.0%	0.94 (0.65,1.36)	0.75
Education			
Less than high school	33.3%	0.60 (0.17,2.06)	0.41
High school or some college	48.0%	1.17 (0.80,1.71)	0.42
College/professional training	44.0%	1.0 (ref)	
Employment			
Employed	40.7%	1.0 (ref)	
Unemployed/homemaker	63.0%	2.48 (1.07,5.77)	0.03
Retired	47.6%	1.34 (0.90,2.00)	0.15
Marital status			
Married	45.6%	1.23 (0.79,1.90)	0.36
Not married (single, widowed, divorced, separated)	40.7%	1.0 (ref)	
Reflux symptoms			
Heartburn or acid regurgitation >= 1 / week	67.4%	2.94 (1.47,5.88)	0.002
Heartburn or acid regurgitation < 1 / week	43.6%	1.10 (0.75,1.63)	0.62
None	41.1%	1.0 (ref)	
Current use PPI drugs			
PPI user	46.0%	1.02 (0.62,1.68)	0.93
PPI non-user	45.4%	1.0 (ref)	
Randomization group			
muTNE	48.1%	1.32 (0.84,2.07)	0.23
huTNE	47.7%	1.23 (0.78,1.94)	0.38
sEGD	40.7%	1.0 (ref)	
SSC score [c]		1.01 (0.73,1.41)	0.93
Charlson comorbidity index [d]		0.99 (0.89,1.12)	0.94

OR, odds ratio; CI, confidence interval; PPI, proton pump inhibitors; SSC, somatic symptom checklist; sEGD, sedated endoscopy; muTNE, mobile unitTNE; huTNE, hospital unitTNE

[a] multiple variable model.

[b] per 10 years of age.

[c] per unit score.

[d] per unit of the index.

Table 4

Quality and safety parameters in the three study arms.

Variable	muTNE (n=76)	huTNE (n=72)	sEGD (n=61)	P value[§]
Rate of successful intubation	76 (100%)	69 (95.8%)	61 (100%)	0.06
Rate of complete evaluation				
Complete	75 (98.7%)	69 (95.8%)	61 (100%)	0.08
Incomplete[*]	1 (1.3%)	0 (0%)	0 (0%)	
Unsuccessful[**]	0 (0%)	3 (4.2%)	0 (0%)	
Rate of successful acquisition of biopsies from the oesophagus	60 (79.0%)	60 (83.3%)	61 (100%)	0.001
Duration of procedure				
Mean duration of procedure (SD).	8.5 (2.5)	8.0 (2.7)	9.3 (1.6)	<0.001
Mean duration from extubation to discharge (SD)	15.5 (2.8)	18.5 (4.2)	67.3 (5.9)	<0.001
Tolerability scores				
Pain	3.2 (8.8)	2.7 (2.3)	0.1 (0.5)	<0.001
Choking	0.6 (1.9)	0.8 (1.8)	0 (0)	<0.001
Gagging	1.3 (2.3)	1.2 (2.4)	0.1 (0.6)	<0.001
Anxiety	2.8 (2.8)	2.3 (2.2)	0.8 (1.5)	<0.001
Overall tolerance	1.9 (2.2)	2.2 (2.2)	0.4 (0.6)	<0.001
N (%) willing to have procedure again in future	60 (78.9%)	60 (83.3%)	57 (93.4%)	0.001
Patient reported procedure related adverse events				
Sore throat	12 (15.8%)	10 (13.8%)	8 (13.1%)	0.97
Bloating	3 (4.0%)	4 (5.6%)	2 (3.3%)	0.83
Epistaxis (self-limiting nose bleed)	1 (1.3%)	1 (1.4%)	0 (0%)	1.00
Nasal pain	1 (1.3%)	0 (0%)	0 (0%)	1.00
Abdominal/chest discomfort	2 (2.7%)	4 (5.6%)	4 (6.6%)	0.51
Headache	4 (5.3%)	1 (1.4%)	0 (0%)	0.16
Serious adverse events (bleeding, perforation, hospitalization)	0 (0%)	0 (0%)	0 (0%)	

Data presented as number (percentage) or mean (+/− standard deviation). sEGD, sedated endoscopy; muTNE, mobile unit TNE; huTNE, hospital unit TNE; SD, standard deviation; N, number..

[§] Fisher's Exact test (discrete variables) or Kruskal-Wallis test (quantitative variables)

[*] unable to intubate with biopsy sheath, but able to intubate with non-biopsy sheath.

[**] unable to intubate with either biopsy or non-biopsy sheath.

Table 5

The rates of detection of manifestations of GERD-induced esophageal injury in subjects with and without reflux symptoms.

Findings	Frequent reflux ≥1/week (n=29)	Infrequent reflux <1/week (n=86)	No reflux (n=90)	P value§
Normal GE junction	13 (44.8%)	44 (51.2%)	59 (65.6%)	0.06
Hiatus hernia present	22 (75.9%)	43 (50.0%)	58 (64.4%)	0.03
Mean (SD) Hiatus hernia length (cm)	2.4 (1.7)	1.4 (1.6)	1.9 (2.1)	0.03
Suspected BE on endoscopy	7 (24.1%)	17 (19.8%)	14 (15.6%)	0.53
Confirmed BE on histology	6 (20.7%)	6 (7.0%)	4 (4.4%)	0.03
Erosive Esophagitis	11 (37.9%)*	29 (33.7%) **	21 (23.3%) ***	0.18

Data presented as number of patients (percentage) or mean (+/−SD, standard deviation).

§Fisher's Exact test (discrete variables) or Kruskal-Wallis test (quantitative variables).

*11 patients [Grade A= 5, Grade B= 4, Grade C=2].

**29 patients [Grade A=15, Grade B=13, Grade C=1].

***21 patients [Grade A=12, Grade B=8, Grade C=1].