

Cervical Esophageal Perforations at the Time of Endoscopic Ultrasound: A Prospective Evaluation of Frequency, Outcomes, and Patient Management

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- OBJECTIVES:** With the exception of one retrospective survey, there are currently no prospectively published data about the frequency of cervical esophageal perforation at the time of endoscopic ultrasound (CEP-EUS). We prospectively investigated the frequency of CEP-EUS and the outcomes and management of patients sustaining CEP-EUS.
- METHODS:** All patients that underwent upper EUS by a single experienced endosonographer over a 7-year period were enrolled. All indications and immediate complications encountered, the baseline demographics, indication of the procedures, surgical interventions, length of hospital stay, and the final outcomes of the patients were prospectively recorded.
- RESULTS:** A total of 5,225 EUS procedures were performed. Lower gastrointestinal tract EUS procedures ($n=331$) were excluded from the analysis, and thus 4,894 upper EUSs constitute this study. The mean age of the patients was 59.7 years (s.d. 14.3 years); 54% patients were men and 79% were white. Indications for EUS included pancreaticobiliary (58%), esophageal (14%), mediastinal (14%), gastric (9%), celiac blocks (1%), and other (4%). Of 4,894 patients, 3 (0.06%, exact 95% confidence interval: 0.01–0.18) suffered CEP-EUS. The curvilinear echoendoscope was used in all three patients. All patients were octogenarians and women. All perforations were suspected at the time of intubation. Esophagogram confirmed contained perforation in all patients. All patients were immediately admitted and underwent surgical repair with a neck incision and recovered completely. The length of hospital stay was 6, 11, and 23 days, respectively. All patients resumed swallowing without complications. One patient died from progressive pancreatic cancer 6 months after Whipple's procedure. The two other patients remained alive and well 12 and 22 months after the procedure.
- CONCLUSIONS:** CEP-EUS is rare but a potentially devastating event for the patient and the treating physician. Although rare, the incidence is 2- to 3-fold higher than what has been reported in the survey literature. Early recognition and treatment is crucial for prompt intervention and complete recovery from CEP-EUS. These data can be used by endosonographers to counsel their patients about frequency, management, and outcomes of CEP-EUS.

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INTRODUCTION

Endoscopic ultrasound (EUS) has been used as a diagnostic tool since the early 1980s for the evaluation and staging of

GI malignancies, benign disorders of the pancreaticobiliary system, and the evaluation of subepithelial lesions of the GI tract. With the introduction of the curvilinear echoendoscope, the

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interest in EUS has increased and the applications and indications of diagnostic EUS-fine needle aspiration (FNA), EUS-guided fine needle injection, and interventional endosonography are rapidly increasing. We and others have shown that EUS and EUS-guided FNA exams provide a cost-effective and safe approach, minimize more invasive procedures, and impact patient management in various GI and lung malignancies (1–3).

Fortunately, EUS-related complications are uncommon, particularly in the case of diagnostic EUS procedures, which are associated with a similar risk to EGD (4). Despite recent advances in the echoendoscope technology, and due to their oblique viewing nature, intubation of the esophagus with the echoendoscope remains a partially blind maneuver, and hence the risk of inadvertent cervical esophageal perforation. With the exception of a retrospective survey performed in 1999 (5), there are currently no prospectively published data about the risk of cervical esophageal perforation at the time of endoscopic ultrasound (CEP-EUS). Therefore, our aims were to study the frequency of CEP-EUS and to report on the outcomes and management of patients sustaining CEP-EUS.

METHODS

This is an institutional review board-approved prospective study (protocol X010924009) of the frequency and management of CEP-EUS by a single experienced endosonographer (M.A.E.). All patients consented to undergo EUS. All indications and immediate complications encountered at the time of EUS were prospectively recorded over a 7-year period (from July 2000 to July 2007). The majority of the procedures were performed on an outpatient basis and under conscious sedation. Meperidine and midazolam were routinely used for sedation. Droperidol or ketamine were used as adjuncts in difficult to sedate cases according to the judgment of the endoscopist. General anesthesia was rarely used <1% of the cases. Physicians or nurse-administered propofol were not utilized. For the first 3 years of the study, and when indicated for staging, the radial echoendoscope was first used. However, after July 2003, in cases where there was a clear indication for possible FNA, the curvilinear echoendoscope was used as the sole echoendoscope to enhance the efficiency of the EUS operation. Regardless of whether the EUS examination was performed with either the curvilinear or the radial echoendoscopes or both, each patient was counted as one entry for the sake of the analysis. Thus, the patient is the unit of analysis and not the procedure. Intravenous antibiotics were administered when pancreatic or other cystic lesions were aspirated during the procedure these patients also received an oral course of the same antibiotic for 5 additional days (usually ciprofloxacin). The baseline demographics, indication for the procedures, and surgical interventions were recorded. In patients where we suspect a possible perforation, our protocol is to obtain an esophagogram to rule out perforation before discharge. When the esophagogram shows a perforation, then a CT scan

of the neck and chest was performed to determine the extent of fluid collection and perforation. In the event of a perforation, all operations were performed by a single thoracic surgeon (R.J.C.). The length of hospital stay as well as the final outcomes of the patient was documented.

Statistical analysis

In addition to determining the perforation incidence in our population, we divided our cases into two groups: the first 2,500, and the remaining 2,394 to examine the potential role of a learning curve with EUS. Fisher's exact test for proportions was used to determine whether more perforations occurred in the second group. We calculated exact 95% confidence interval for proportions. Statistical significance was set at 0.05. The analysis was conducted with SAS statistical software (version 9.13; Cary, NC).

RESULTS

A total of 5,225 patients underwent EUS procedures by a single experienced endosonographer over the study period. Lower GI tract EUS procedures ($n = 331$) were excluded from the analysis, and thus 4,894 patients that underwent upper EUS procedures constituted this study. The mean age of the patients was 59.7 years (s.d. 14.3 years); 54% patients were men and 79% were white. Indications for EUS included pancreaticobiliary (58%), esophageal (14%), mediastinal (14%), gastric (9%), celiac blocks (1%), and other (4%). Of 4,894 patients, 3 (0.06%, exact 95% confidence interval: 0.01–0.18) suffered cervical esophageal perforation at the time of intubation with EUS. All perforations occurred after the first 2,500 procedures were performed (0/2,500 vs. 3/2,394, $P = 0.12$), suggesting that the perforations were not learning curve related. Two patients were suspected to have pancreatic cancer; the third patient had a history of cervical cancer and recurrence of her disease was suspected in an enlarged celiac lymph node. The curvilinear echoendoscope was used in all three patients (Olympus UC-140T, or Olympus, UC-30 P echoendoscopes). All perforations were suspected at the time of intubation. Typically, a yellowish area is noted in the posterior hypopharynx suggesting that the endoscope had penetrated into the mediastinum.

All patients were octogenarians and women. Of the patients that suffered a perforation, they were neither known to have cervical osteophytes nor known to suffer from kyphosis of the spine. The procedure was completed in only one patient. One of three patients reported chest pain. The two other patients had excessive salivation and sore throat. Physical examination at the bedside showed crepitus in only one patient. Water-soluble esophagograms confirmed a contained perforation in each patient. It showed a fluid collection in the superior mediastinum consistent with an upper esophageal perforation (**Figure 1a**). CT scan of the chest was urgently obtained in all patients (**Figures 1b** and **c**). All patients were immediately admitted, underwent surgical repair with a neck incision, and recovered completely. The length of hospital stay was 6, 11, and 23 days

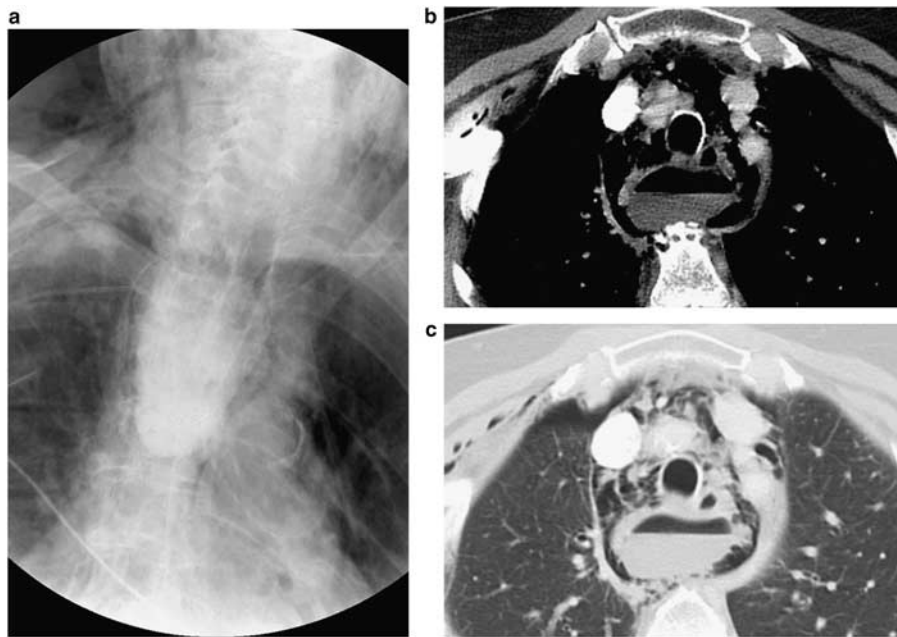


Figure 1. An 80 year-old woman with proximal esophageal perforation during attempted intubation during endoscopic ultrasound (EUS). **(a)** Post-endoscopy water-soluble contrast swallow demonstrates gas within the lower cervical soft tissues and mediastinum. Contrast is seen within a collection in the upper mediastinum, located posterior to the esophageal lumen. **(b)** Axial CT image through the upper mediastinum demonstrates the focal fluid collection located immediately anterior to the thoracic vertebral column and posterior to the trachea. Note proximal thoracic esophageal lumen located to the left of the trachea. **(c)** Axial CT image of same level filmed at lung windows reveals pneumomediastinum and small right pneumothorax. An air-fluid level is noted in the mediastinal collection that promptly required surgical evacuation.

respectively. All patients resumed swallowing without complications. One patient died from progressive pancreatic cancer 6 months after Whipple's procedure. The two other patients remained alive and well 12 and 22 months after the procedure.

DISCUSSION

EUS has become a mainstream procedure used in the management of complex GI disorders as well as staging and work up of GI and lung malignancies. In addition, many applications such as EUS-guided FNA therapy and interventional endosonography are emerging rapidly.

Fortunately, even with utilization of EUS-guided FNA, EUS carries a reasonable risk profile in experienced hands (6,7). Survey data tend to underestimate the risk of complications; this is well documented in survey literature regarding development of acute pancreatitis after EUS-guided FNA of solid pancreatic masses (8,9). Although the risk of esophageal perforation related to staging of esophageal cancer has been well evaluated, few studies, restricted to survey data, have evaluated the risk of cervical esophageal perforation at the time of EUS (2,5).

Several studies have reported perforation rate during EUS (2,5). In their prospective study of more than 428 patients, the American Endosonography Club found a perforation rate of 0.03% (2). The case of perforation in that study was a perforation due to esophageal cancer staging. Das *et al* (5) performed

a national survey of The American Endosonography Club in 1999 and found a cervical perforation rate of 0.03% as well. All perforations in that study were in patients older than 65 years of age (5). Our results are similar in that regard; all of our patients suffering from a CEP-EUS were octogenarians. In addition, and in retrospect, the three patients in our cohort had a short and webbed-appearing neck, which from our observations supports the anatomical limitation in intubating the esophagus with a long a semirigid tipped echoendoscope. That these perforations occurred in elderly patients can be supported by the fact that these patients had hyperextension of the cervical spine, which increases the risk of crushing trauma caused by the rigid tip of the echoendoscope on the posterior hypopharynx against the hyperextended cervical spine (5). In a normal esophagus, the location at greatest risk of instrumental injury is Killian's triangle, which is formed by the inferior constrictor pharyngeus and the cricopharyngeus muscles. In this region, the posterior esophageal mucosa is unprotected by muscularis, and is separated from the retroesophageal space by buccopharyngeal fascia only. Cervical osteophytic spurs, kyphosis of the spine, or hyperextension of the neck can further increase the risk of perforation in this area (10).

It is important to note that the excellent outcomes of our patients are consistent with observations and findings from the literature describing esophageal perforations during endoscopy (10). Cervical perforations tend to have a better prognosis compared to intrathoracic or intraabdominal perforations. The

anatomic location affects the mortality associated with esophageal perforation. In 397 patients, cervical esophageal perforations were associated with a mortality of 6% whereas thoracic and abdominal perforations were associated with mortality of 27% and 21%, respectively (10). This difference in mortality results from containment of contamination by the fascial planes of the neck following cervical perforation. By contrast, contamination secondary to intrathoracic or intraabdominal esophageal perforation is poorly contained and rapidly results in systemic complications of sepsis if treatment is delayed (10).

We suggest below a few remedies that we currently and routinely utilize to minimize the risk of perforation during intubation at the time of EUS. First, a careful history of swallowing difficulties, prior esophageal stricture, esophageal surgery, or radiation to the neck and mediastinum must be obtained at the time of consent. In the case of reported dysphagia, upper endoscopy is initially performed before EUS. We also perform EGD routinely in any EUS esophageal indication, particularly when staging esophageal cancer. Second, the endoscopist must insure adequate position of the patient before attempting intubation. The patient is positioned on the endoscopy table so that his or her body is straight and perpendicular to the table and the chin needs to be flexed 45° in the plane of scope advancement. Gentle adjustment of patient neck position might be needed during intubation. Too much flexion or extension of the neck might prohibit successful intubation. Third, adequate sedation of the patient must be achieved, so that the patient is optimally relaxed at the time of intubation. If intubation is not accomplished with two attempts, inflating the balloon slightly may induce a swallowing reflex as suggested by Sahai (11). Otherwise, a wire-guided approach can be used to help stabilize the echoendoscope and allow it to go more easily in the direction of the esophagus. A Savary wire is preloaded and passed under direct vision in the esophagus whereas the echoendoscope is in the hypopharynx. The echoendoscope is then advanced over the wire smoothly. We found this method to be extremely useful for the successful intubation when the echoendoscope would not pass spontaneously. Finally, when difficulty is further encountered, consider aborting the procedure and obtaining a contrast swallow evaluation. We have encountered a few patients who had cricopharyngeal achalasia that precluded successful intubation of the esophagus with the echoendoscope or even a regular endoscope.

In summary, this study suggests that cervical esophageal perforations during EUS are rare, but a potentially devastating event for the patient and the treating physician. Although uncommon, these proximal perforations occur at a rate 2- to 3-fold higher than that reported in the survey literature. Early recognition and treatment is crucial for early intervention and complete recovery. These data can be used by endosonographers to counsel their patients about frequency, management, and outcomes of cervical esophageal perforation at the time of EUS.

CONFLICT OF INTEREST

Guarantor of the article: Mohamad Eloubeidi, MD, MHS.

Specific author contributions: Mohamad Eloubeidi:

designed and initiated the study, enrolled patients, analyzed the results of the statistical analysis, wrote and edited the paper, and approved the final version; Ashutosh Tamhane: performed the statistical analysis, revised, edited, and approved the paper; Tercio Lopes: helped with data collection, revised, edited, and approved the paper; Desiree Morgan: provided professional images and their legends, revised, edited, and approved the paper; Robert Cerfolio: revised, edited, and approved the paper.

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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

✓ Based on a survey published in 2000, the risk of cervical esophageal perforation by endoscopic ultrasound (EUS) is 0.03%.

WHAT IS NEW HERE

✓ This paper provides evidence that the rate of cervical esophageal perforation by EUS is 2–3 times higher than what is suggested in the survey literature.

✓ This paper also reviews the pathophysiology of cervical esophageal perforations and suggests ways to avoid them at the time of intubation with EUS instruments.

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