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ORIGINAL ARTICLE

Adverse events and mortality: comparative analysis between diagnostic and interventional endoscopic ultrasound

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ABSTRACT

Background and aims: Escalating an indication of EUS for diagnosis and treatment justifies the evaluation of the conditions associated with the adverse events (AE) and related deaths. The aim is to evaluate and compare the incidence of AE and deaths after diagnostic-EUS (D-EUS) and interventional-EUS (I-EUS).

Methods: This retrospective study included patients undergoing D-EUS and I-EUS, in two centers for 28 years (03/1992 to 12/2019). Were noted parameters such as: age, gender, indication of EUS, modality, time of occurrence and severity of AE, type of treatment imposed and whether there was death. Descriptive analysis was performed using means, standard deviation and frequencies of the variables of interest.

Results: 13,196 procedures performed, 9843 D-EUS and 3353 I-EUS. Thirty-seven (0.3%) had AE with six deaths (0.04%). The overall rate of AE for D-EUS and I-EUS was 0.08% and 0.86%, respectively ($p > .05$). Three deaths (0.03%) occurred after D-EUS and three (0.09%) after I-EUS. AE were immediate and early in 70% and 30%, respectively, with no late complications. Perforation was detected immediately in 80% and early in 20%, being more frequent after D-EUS than I-EUS. Acute pancreatitis occurred immediately in 70% and early in 30%. The AE were mild, moderate, and severe in 35.1%, 27%, and 37.8%, respectively. Overall, D-EUS presented the majority of AE as severe (87.5%), while I-EUS presented mild AE in most cases (41.4%), followed by severe complications (24.1%).

Conclusions: Despite the low incidence of AE and mortality after EUS, the occurrence of severe complications, especially perforation in D-EUS, may support the review of therapeutic protocols, aiming to ensure that a quality and safety process is implemented in the practice of EUS.

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Endoscopic ultrasound; adverse events; mortality; diagnostic; intervention

Introduction

Endoscopic ultrasound (EUS) stands out as a resource for the diagnosis, staging and treatment of digestive diseases [1] and is considered safe, effective, and minimally invasive compared with operative procedures with the same purpose [2]. Moreover, EUS is a complex endoscopic procedure used for at least three decades which presents rare adverse events (AE) when performed by experienced specialists [2]. Most AE are described as sporadic observations in individual centers [3–11]. Their modality, severity and period of occurrence are specific to each EUS [12], and the major ones are perforation, bleeding, infection, acute pancreatitis (AP), subepithelial hematomas and neoplastic cell seeding [13]. Few studies are evaluating the immediate, early, and late AE of EUS. There is a lack of data on possible measures that could improve the safety of EUS before, during, and after the procedure. No studies are evaluating the occurrence of AE comparing diagnostic-EUS (D-EUS) and interventional-EUS (I-EUS).

This study aimed to consecutively evaluate the occurrence and severity of AE, determining the mortality rate in D-EUS and I-EUS in two endoscopy referral centers and therefore subsidize and ameliorate the quality and safety protocols that regulate the EUS practice.

Subjects and methods

This is an observational cohort study of patients consecutively treated at the Endoscopy Department of Hospital 9 de Julho and the Digestive Endoscopy Section of the Department of Surgery and Anatomy of the Clinical Hospital of Ribeirão Preto Medical School – University of São Paulo (HCFMRP-USP), private and public institutions, respectively, both tertiary health services and teaching hospitals, from March 1992 to December 2019. Approval for the study was offered by the Research Ethics Committee of the 9 de Julho Hospital (number 3.845.367) and the HCFMRP-USP (number 3.892.649). The evaluation includes the registry of age, sex,

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indication, procedure performed, modality and severity of AE, and the occurrence of deaths in patients who underwent D-EUS and I-EUS.

Diagnostic–endoscopic ultrasonography

Combination of endoscopy with high-resolution ultrasound through a thin and flexible endoscope specially equipped with a miniature ultrasound probe (transducer) coupled to the end of the device, which allows ultrasound scanning inside the digestive system [13]. Conventional EUS is limited to the insertion of a sectorial or radial echoendoscope and obtaining ultrasound images that allow the diagnosis of certain diseases of the digestive system.

Interventional–endoscopic ultrasonography

It encompasses a wide range of procedures evolved from the insertion of a fine needle (EUS-FNA) to obtain tissue samples, drain abdominal collections, and create fistulas. EUS-INJ can be used for alcohol injection in the treatment of pancreatic cysts and absolute alcohol for celiac plexus neurolysis (EUS-CPN) [5]. EUS-NEC and EUS-DRA (pancreatic pseudocyst and/or abdominal collection) are techniques for approaching abdominal collections with the aid of sectorial EUS by creating a fistula between the collection and the wall of the digestive system [14]. EUS-BPD also consists of the use of FNA to drain the biliary and pancreatic contents by creating a fistula between the bile duct, the main pancreatic duct, and the intrahepatic biliary tree with the digestive wall [15].

Adverse events

AE were considered immediate if they occurred during the procedure or within 24 h, early if they occurred between 1 and 7 days and late if they occurred after 7 days of the procedure. Immediate, early, and late AE were documented at the time of the procedure and at the time of hospitalization or were noted through telephone follow-up from the first 24 h through the following 30 days. The severity classification was based on the length of hospitalization: mild if the patient remained less than 3 days, moderate if the patient remained between 4 and 10 days and severe if more than 10 days; surgery or intensive care units were required [16].

The expected and studied AE were bleeding, AP, infection, perforation, choleperitoneum and bruising of the digestive system wall. The presence or hypothesis of AE was evaluated considering the clinical, laboratory, and imaging criteria and may in some cases have indicated hospitalization or even surgical treatment according to the evaluation of the teams involved in the treatment.

Among the AE found, AP was considered in the presence of two of the following criteria: upper abdominal pain, alteration in imaging and amylase or lipase at threefold of the reference value [17]. Bleeding was considered such as the presence of blood in the intestinal lumen during or after the procedure (recognized in stool or vomiting). Perforation, such as severe abdominal pain, altered imaging exam, and positive 'Joubert' sign on clinical examination, as well as the observation of discontinuity tissue lesion of the digestive wall during EUS. Infection, such as fever, tachycardia, dyspnea, or leukocyte abnormality associated with isolation of the infectious agent or positive culture. Choleperitoneum was defined as any abdominal pain, fever, and signs of peritoneal irritation, which was confirmed by paracentesis. Finally, the hematoma was detected on the intraluminal wall during the procedure.

Follow-up

A strict interview protocol was applied after conducting the EUS. Patients submitted to D-EUS and I-EUS in the outpatient care regimen received a return guide with the registry of the procedure, AE information and a phone for contact. They were asked to contact the hospital immediately in case of abdominal discomfort, pain, or fever. In addition, they were seen at the outpatient clinic between 1 and 2 weeks after the procedure for discussion of results, survey of AE, and additional management decisions with their respective attending physicians.

Occurrence of AE by periods

The occurrence of AE was analyzed in three different periods. The first period is from March 1992 to December 2001 (10 years), the time when the EUS method was incorporated in the daily clinical practice of specialized centers of endoscopy and gastroenterology. At this time, the procedures were made with radial mechanical devices with oblique vision. From 1997 on, there is the introduction of the EUS-FNA, as well as the implementation of therapeutic procedures such as EUS-DRA, EUS-FNI, and EUS-CPN, simultaneously to the technique consolidation. The second period comprises January 2002 to December 2011 (10 years), marked by the evolution of EUS and the beginning of our postgraduate training of D-EUS and I-EUS. By last, from January 2012 to December 2019 (8 years), the third period encompasses the period of amplification of I-EUS indications.

Statistical analysis

Descriptive analysis was performed using means, standard deviation, and frequencies of the variables of interest. Mortality calculation for each endoscopic procedure was performed with the proportions of occurrence of each event in relation to the total procedures performed. In the detailed statistical analysis of the AE, we used a subsample containing only the cases that presented some AE ($n = 37$). Fischer's exact test was used to assess the association between the studied variables. The value of statistical significance adopted was 95%. The analyses were conducted using STATA 14 software.

Results

Patients

During the study period, 13,196 patients underwent EUS. D-EUS account for 9843 patients (74.6%), where radial and sectorial endoscopic scanning were used in 5,493 (41.6%) and 4,350 (33%), respectively. In 3353 patients (25.4%), there was some type of intervention during EUS. EUS-FNA was performed in 3,082 (23.3%), EUS-CPN in 88 (0.66%), EUS-DRA in 66 (0.5%), EUS-NEC in 52 (0.4%), EUS-BPD in 38 (0.3%), and EUS-INJ in 27 (0.2%).

Adverse events

Among the 13,196 patients who underwent D-EUS and I-EUS, 37 (0.28%) patients had AE (Table 1). The overall rate of AE for D-EUS and I-EUS was 0.08% ($n = 8$) and 0.86% ($n = 29$), respectively. The mean age was 65.3 (27–89 years) with 19 men and 18 women. EUS indication for classificatory diagnosis of pancreatic cyst occurred in 18 patients (48.6%), for pseudocyst drainage in six (16.2%) patients, due to endoscopic retrograde cholangiopancreatography (ERCP) failure in three (8.1%) requiring EUS-BPD, EUS-NEC in three (8.1%), to determine the type of subepithelial tumor in three (8.1%), staging of gastric neoplasia in one (2.7%), diagnosis of biliary cancer in one (2.7%), follow-up of operated GIST in one (2.7%), and suspected choledocholithiasis in a patient undergoing Billroth II gastrectomy in one (2.7%).

Most AE had as main EUS indication the classification of a pancreatic cyst, corresponding to 37.5% ($n = 3$) of D-EUS and 51.7% ($n = 15$) of I-EUS ($p = .021$). The most common AE occurring during D-EUS and I-EUS was perforation 87.5% ($n = 7$) and bleeding 44.8% ($n = 13$), respectively ($p < .001$).

During D-EUS, the sectorial technique presented the highest number of AE 87.5% ($n = 7$), and for I-EUS, EUS-FNA presented 55.2% ($n = 16$) of all AE, determining an association between the modality of EUS and the type of AE ($p < .001$).

Severity of adverse events

D-EUS presented the majority of AE as severe 87.5% ($n = 7$), whereas I-EUS presented mild AE in most cases in 41.4% ($n = 12$) with $p = 0.001$ (Table 1). The AE were mild, moderate, and severe in 35.1% ($n = 13$), 27% ($n = 10$), and 37.8% ($n = 14$), respectively (Table 2). We considered all perforation cases ($n = 10$) as severe. AP was considered moderate, mild, and severe in five (50%), four (40%), and one (10%) patient, respectively. Bleeding was mild, moderate, and severe in seven (53.8%), four (30.8%) and two (15.4%), respectively. Choleperitoneum ($n = 3$) was mild in one, moderate in one, and severe in another, and esophageal intraparietal hematoma was mild in one (Table 3).

Adverse events moment of occurrence

There were no late complications. AE were immediate and early in 70.3% ($n = 26$) and 29.7% ($n = 11$), respectively. Bleeding occurred immediately and early in 76.9% ($n = 10$) and 23.1% ($n = 3$), respectively. Perforation was identified immediately in 80% ($n = 8$) and early in 20% ($n = 2$). AP occurred up to 24 h in 70% ($n = 7$) and early in 30% (3). Choleperitoneum (2) and esophageal parietal hematoma (1) were identified early after abdominal pain and fever in the first case and dysphagia in the second (Table 4).

Adverse events time period of occurrence

The occurrence of AE and lethality in D-EUS and I-EUS were analyzed in three different time periods over 28 years. In the first decade, D-EUS comprised 85% of procedures performed, with a rise of I-EUS in the subsequent periods. By the time of the last 8 years, 40% of procedures were I-EUS (Table 5).

Discussion

D-EUS and I-EUS have become an integral part of daily medical practice in numerous centers of excellence in digestive endoscopy and the disclosure of their therapeutic potential has increased significantly. However, data regarding patient safety in these procedures are still scarce [12]. The evolution of D-EUS and I-EUS morbidity and mortality along 30 years in the studied centers, one public and other private hospital, are representative of the population and care profile of the Brazilian Unified Health system and therefore provide relevant information about the usefulness and performance of these procedures to managers, auditors and specialists.

The study design and the distinct operational model of the centers evaluated may limit the generalization of its results. However, the fact that one of the study's author (JCA) coordinates both centers endoscopy departments in similar ways can mitigate these biases. The general occurrence of AE was 0.28% (37/13196) and the mortality rate 0.04% (6/13196). From the first to last decade, it was seen an increase from 15% to 40% on the proportion of I-EUS, with a decrease in the AE and mortality rates for both EUS modalities during the intervening decade. Comparatively, a 10 years prospective study showed similar rates of global occurrence of AE 0.3% (10/3324) and mortality 0.06% (2/3324) [12]. These results are comparable to those from other EUS series [3–11] and are lower than the observed in the ERCP [18] and colonoscopy [19] series.

An association between the type of EUS performed and the occurrence of some type of AE must be highlighted, since the occurrence of AE was significantly lower in D-EUS compared with I-EUS. Only 0.08% of the patients who underwent D-EUS had some type of AE, whereas in I-EUS the rate rose to 0.86% ($p < .001$). This reveals that the development of new therapeutic methods determined more invasion and hence a higher probability of occurrence of AE.

Although there are variations in patient selection, target organ of the exam and modality of I-EUS, the general morbidity and mortality estimates range from 0% to 5% and 0% to 1%, respectively, but with a clear tendency to zero mortality and a morbidity below 1% [3–11]. In the data obtained through the present study, six deaths were recorded as a final consequence of the occurred AE, representing 0.04% of

Table 1. Gender, age, year, indication, type, severity of adverse events, modality of endosonography and treatment performed in the 37 patients who presented adverse events.

Patient	G	Age	Year	Indication	AE	Severity	D-EUS	I-EUS	Outcome
1	M	65	1998	Junctional gastric cancer	Gastric perforation	Severe	Radial scanning	No	Full recovery
2	F	87	2000	Gallbladder carcinoma	Choleperitoneum	Severe	No	EUS-FNA	Death after surgical treatment—acute myocardial infarction
3	M	58	2000	Pancreatic cystic lesion (IPMN)	Acute pancreatitis	Moderate	No	EUS-FNA	Full recovery after conventional treatment
4	F	57	2001	Pancreatic cystic lesion (SCA)	Intracystic bleeding with abdominal pain	Mild	No	EUS -FNA	Full recovery after conventional treatment
5	M	87	2002	Pancreatic cystic lesion (malignant IPMN)	Perforation (Esophagus)	Severe	Sectorial scanning	No	Death after surgical treatment—infectious complication
6	M	68	2002	Pancreatic cystic lesion (MCA)	Acute pancreatitis	Mild	No	EUS -FNA	Full recovery after conventional treatment
7	M	59	2003	Pancreatic pseudocyst	Perforation (gastric)	Severe	No	EUS -DRA	Death from infection after surgical treatment—infectious complication
8	F	64	2004	Follow up of operated duodenal GIST	Perforation (duodenum)	Severe	Sectorial scanning	No	Death 90 days after surgery—infection, diabetes and hypothyroidism
9	M	47	2004	GIST	Perforation (duodenum)	Severe	Sectorial scanning	No	Full recovery after surgery
10	M	67	2004	Pancreatic Pseudocyst	Bleeding of the cyst wall	Moderate	No	EUS -DRA	Full recovery after endoscopic treatment
11	M	62	2004	Pancreatic cystic lesion (SCA)	Intracystic bleeding with abdominal pain	Mild	No	EUS-FNA	Full recovery after conventional treatment
12	F	89	2005	Pancreatic cystic lesion (SCA)	Perforation (Esophagus)	Severe	Sectorial scanning	No	Full recovery after surgery
13	F	63	2006	Pancreatic pseudocyst	Bleeding of the cystic wall	Mild	No	EUS-DRA	Full recovery after conventional treatment
14	M	76	2006	Pancreatic carcinoma (ERCP failure)	Bleeding (intracavitary)	Moderate	No	EUS-BPD	Full recovery after conventional treatment
15	M	65	2009	GIST	Intraparietal giant Esophagus hematoma)	Mild	Sectorial scanning	No	Full recovery after conventional treatment
16	F	56	2009	Pancreatic cystic lesion (IPMN)	Acute pancreatitis	Moderate	No	EUS-FNA	Full recovery after conventional treatment
17	M	65	2010	Pancreatic pseudocyst	Bleeding of the cyst wall	Moderate	No	EUS-DRA	Full recovery after endoscopic treatment
18	F	47	2010	Pancreatic cystic lesions (IPMN)	Acute pancreatitis	Moderate	No	EUS -FNA	Full recovery after conventional treatment
19	M	67	2010	Pancreatic cystic lesion (IPMN)	Acute pancreatitis	Mild	No	EUS -FNA	Full recovery after conventional treatment
20	F	87	2011	Pancreatic cystic lesion (IPMN)	Acute pancreatitis	Mild	No	EUS -FNA	Full recovery after conventional treatment
21	M	65	2012	GIST	Bleeding	Mild	No	EUS -FNA	Full recovery after endoscopic treatment
22	M	64	2013	Walled off necrosis	Bleeding (intracavitary)	Moderate	No	EUS -NEC	Full recovery after endoscopic treatment
23	M	54	2013	Walled off necrosis	Bleeding (intracavitary)	Mild	No	EUS -NEC	Full recovery after endoscopic treatment
24	F	87	2013	Pancreatic cystic lesion (IPMN)	Acute pancreatitis	Moderate	No	EUS-FNA	Full recovery after conventional treatment
25	M	73	2014	Choledocholithiasis in patients with Billroth II (dubious MRCP)	Perforation (Jejunum)	Severe	Sectorial scanning	No	Death after surgical treatment—acute myocardial infarction
26	F	27	2014	Pancreatic cystic lesion (MCA)	Perforation (Gastric)	Severe	No	EUS -DRA	Fully recovery after surgery
27	M	74	2014	Pancreatic carcinoma (ERCP failure)	Perforation (choledochal wall)	Mild	No	EUS-BPD	Fully recovery after percutaneous Intrahepatic drainage
28	F	73	2014	Pancreatic cystic lesions (IPMN)	Acute pancreatitis	Moderate	No	EUS-FNA	Full recovery after conventional treatment
29	F	78	2014	Pancreatic cystic lesions (IPMN)	Acute pancreatitis	Severe	No	EUS-FNA	Full recovery after conventional treatment
30	F	72	2015	Pancreatic cystic lesions (IPMN)	Acute pancreatitis	Mild	No	EUS-FNA	Full recovery after conventional treatment
31	F	54	2016	Pancreatic cystic lesions (SCA)	Intracystic bleeding with abdominal pain	Mild	No	EUS-FNA	Full recovery after conventional treatment
32	F	69	2016	Pancreatic carcinoma (ERCP failure)	Choleperitoneum	Mild	No	EUS-BPD	Full recovery after conventional treatment
33	F	79	2017	Pancreatic pseudocyst	Bleeding of the cyst wall	Severe	No	EUS-DRA	Fully recovery after surgery
34	M	57	2017	Walled off necrosis	Bleeding of the mesentery axis after LAMS insertion	Severe	No	EUS-NEC	Death after surgery
35	M	48	2017	Pancreatic cystic lesions (SCA)	Abdominal pain from interstitial bleeding	Mild	No	EUS-FNA	Full recovery after conventional treatment
36	F	65	2017	Pancreatic pseudocysts	LAMS disinsertion of from the pseudocyst wall	Severe	No	EUS-DRA	Full recovery after surgery
37	F	67	2019	Pancreatic cystic lesions (SCA)	Perforation (duodenum)	Severe	Sectorial scanning	No	Full recovery after endoscopic treatment

EUS-FNA: Endosonography-guided fine needle aspiration; IPMN: intraductal papillary mucinous neoplasia; SCA: serous cystadenoma; MCA: mucinous cystadenoma; GIST: gastrointestinal stromal tumor; ERCP: endoscopic retrograde cholangiopancreatography; EUS-DRA: endosonography-guided pancreatic fluid drainage; EUS-NEC: endosonography-guided necrosectomy; EUS-BPD: endosonography-guided biliopancreatic drainage.

Table 2. Patient characteristics, indications, modality of endosonography, modality and severity of adverse events, treatment imposed, and deaths occurred in the 37 patients who presented adverse events divided in EUS-D and EUS-I.

Characteristics	Total	D-EUS (9.843)	I-EUS (3.353)	*p value
Patients (N)	37	8	29	
Median age (years)	65.3 (27–89)	69.6 (47–89)	65 (27–87)	
Gender (male/female)	19/18	05/3	14/15	
Indication		*N* (%)	*N* (%)	.021
Pancreatic cyst	18	3 (37.5)	15 (51.7)	
Pseudocyst drainage	6	0	6 (20.7)	
ERCP failure	3	0	3 (10.3)	
EUS – necrosectomy	3	0	3 (10.3)	
Subepithelial tumor	3	2 (25)	1 (3.5)	
Gastric cancer staging	1	1 (12.5)	0	
Cholangiocarcinoma	1	0	1 (3.5)	
Follow up of operated GIST	1	1 (12.5)	0	
Choledocholitiasis suspicion	1	1 (12.5)	0	
Modality of Adverse event		*N* (%)	*N* (%)	<.001
Perforation	10	7 (87.5)	3 (10.3)	
Acute pancreatitis	10	0	10 (34.5)	
Bleeding	13	0	13 (44.8)	
Choleperitoneum	3	0	3 (10.3)	
Esophageal Intraparietal hematoma	1	1 (12.5)	0	
Adverse event Severity		*N* (%)	*N* (%)	.001
Severe	14	7 (87.5)	7 (24.1)	
Mild	13	1 (12.5)	12 (41.4)	
Moderate	10	0	10 (34.4)	
Modality of endosonography		*N* (%)	*N* (%)	<.001
EUS-FNA	16	0	16 (55.2)	
Radial scanning	1	1 (12.5)	0	
Setorial scanning	7	7 (87.5)	0	
EUS-BPD	3	0	3 (10.3)	
EUS-DRE	7	0	7 (24.1)	
USE-NEC	3	0	3 (10.3)	
Management of Adverse event		*N* (%)	*N* (%)	.028
Conventional treatment	18	1 (12.5)	17 (58.6)	
Endoscopic treatment	6	1 (12.5)	5 (17.2)	
Percutaneous transhepatic treatment	1	0	1 (3.5)	
Surgery	12	6 (75)	6 (20.7)	
Death after complications		N (%)	N (%)	.101
Yes	6	3 (37.5)	3 (10.3)	
No	31	5 (62.5)	26 (89.7)	

EUS-FNA: Endosonography-guided fine needle aspiration; EUS-DRA: endosonography-guided pancreatic fluid drainage; EUS-NEC: endosonography-guided necrosectomy; EUS-BPD: endosonography-guided biliopancreatic drainage.
*p-value according to Fisher's exact test.

Table 3. Severity of AE.

Adverse Events	*N*	Mild (%)	Moderate (%)	Severe (%)
Perforation	10	0	0	10 (100)
Acute pancreatitis	10	4 (40)	5 (50)	1 (10)
Bleeding	13	7 (53.8)	4 (30.8)	2 (15.4)
Choleperitoneum	3	1 (33.3)	1(33.3)	1 (33,3)
Intraparietal hematoma (esophagus)	1	1 (100)	0	0
Total	37	13 (35.1%)	10 (27%)	14 (37.8%)

Severity was based on days of hospital stay mild, <3 days; moderate, 4–10 days; severe, >10 days or need of ICU or surgery [16].

Table 4. Adverse events moment of occurrence.

Adverse Events	*N*	Immediate	Early	Late
Perforation	10	8 (80)	2 (20)	0
Acute pancreatitis	10	7 (70)	3 (30)	0
Bleeding	13	10 (76.9)	3 (23.1)	0
Choleperitoneum	3	1 (33.3)	2 (66.6)	0
Intraparietal hematoma (esophagus)	1	0	1 (100)	0
Total	37	26 (70.3%)	11 (29.7%)	0

Immediate: occurring during or up to 24 h after the procedure; Early: occurring from 1 to 30 days after procedure; Late: occurring after 30 days from the procedure.

the total. Of these cases, three occurred after D- EUS, representing 0.03% and three after I-EUS, representing 0.09% of the total ($p = .101$).

The three cases of deaths resulting from D-EUS occurred during sectoral EUS. One had an indication to evaluate supposedly malignant intraductal papillary mucinous neoplasia,

Table 5. Adverse events by time of occurrence.

Period (years)	1992–2001 (10)		2002–2011 (10)		2012–2019 (8)		Total (28)	
Number of procedures	5835		2946		4415		13,296	
Modality of procedure	D-EUS	I-EUS	D-EUS	I-EUS	D-EUS	I-EUS	D-EUS	I-EUS
Number	4981	854	2209	737	2653	1762	9843	3353
Adverse events *N* (%)	1 (0.02)	2 (0.24)	3 (0.13)	11 (1.49)	1 (0.03)	13 (0.74)	5 (0.05)	26 (0.77)
Death *N* (%)	0 (0)	1 (0.11)	2 (0.09)	1 (0.13)	1 (0.03)	1 (0.05)	3 (0.03)	3 (0.08)

and the passage of the apparatus caused perforation of the proximal esophagus due to an osteophyte of the cervical spine in an elderly patient. This patient underwent surgery and presented infectious complications. Another had EUS indication for follow-up of an operated GIST of the second duodenal portion and presented lacerations of the region, which evolved with perforation and infection, being then submitted to surgery. The latter died from heart complications on the post-operative follow up of surgical correction of a jejunal perforation consequent to a sectoral EUS-D for the research of choledocholithiasis in a Billroth II gastrectomy.

I-EUS, the first occurred after inadvertent puncture of the gallbladder in a patient with gallbladder cancer, evolving to choleperitoneum. The patient presented an acute myocardial infarction during surgical treatment. The second occurred after gastric perforation during drainage of a pancreatic pseudocyst, evolving to death after postoperative infectious complications. The third presented laceration of the upper mesenteric artery after insertion of a metallic stent in a patient undergoing EUS-NEC, who had necrotizing pancreatitis consecutive to a bariatric surgery [20]. These findings corroborate those already seen in other studies with smaller populations [12,13], in which regardless of the exam modality (D-EUS or I-EUS), perforation followed by conventional surgical treatment is associated with lethality, ($p = .101$). Therefore, safety-based techniques to avoid perforation or minimally invasive treatment, through endoscopy, can mitigate lethality (21).

Regarding the severity of the AE, D-EUS presented the majority of severe AE 87.5% ($n = 7$) and mild AE 12.5% ($n = 1$). Perforation occurred in seven cases: duodenum (three), esophagus (two), stomach (one) and jejunal (one), and all cases were considered severe, as they required surgery for correction (six) or remained more than 10 days hospitalized after endoscopic treatment of duodenal perforation (one) [21]. Of the seven cases of perforation that occurred during D-EUS, only one of them occurred with the radial scanning with oblique vision (mechanical radial scanning), during the staging of an esophagogastric junction cancer. All others were consequent to the introduction of sectoral scanning EUS.

The other cases of perforation occurred after I-EUS in three cases (10.3%). There were two gastric perforations: one recovered after surgical treatment, and the other died because of severe infectious complications. Most of the AE that occurred after I-EUS were mild in 41.4% ($n = 12$), evidencing that, although less frequent, AE in diagnostic procedures may be more severe, once they are mostly perforation cases.

There were no late complications reported in the analysis of the moment of occurrence. The AE were immediate and early in 70.3% ($n = 26$) and 29.7% ($n = 11$), respectively. These data show the importance of immediate and early follow-up after each procedure is performed, which is efficient in detecting and approaching the AE.

This data corroborates our adoption of a regulatory protocol that has been in practice for many years, which involves a good medical history, judicious analysis of procedure indication and detailed understanding of the imaging exams performed (CT, MRI or abdominal US). During the exam, the precepts of a good endoscopic technique must be followed, respecting all steps of the procedure and thus perform it with excellence. In the recovery room, physical examination must be performed to identify signs and symptoms such as abdominal distension, abdominal pain, nausea, and vomiting, up to 2 h after the procedure. After this, patients must be oriented to return to the hospital in case of the presence of any of those symptoms. It is extremely important to search actively for AE through telephone contact, up to 48 h, by the attending physician or nurse staff. Unquestionably, the adoption of these measures is crucial in diminishing the occurrence of AE and improving the recovery after they do occur.

Another fundamental point in the analysis was the decrease in the occurrence of AE as time went by, resultant from the gain of experience and the evolution of the apparels used for therapeutic interventions in EUS. The initial insertion of these new techniques determined, at least in the first time, the increment in the occurrence of AE, with a later decline explained by a learning curve that culminated in greater expertise. D-EUS and I-EUS are safe procedures capable of providing low morbidity rates and a mortality rate close to zero, with a rate of occurrence of AE comparable with those of upper digestive endoscopy [22–27]. In this present study, the incidence of AE and mortality after EUS were low. The occurrence of severe AE in D-EUS decurrent from perforation of the GI tract may justify the similar rates of mortality between this modality and EUS-I.

Thus, as the majority of D-EUS and I-EUS are performed on an outpatient basis, the adoption of protocols to identify AE in the immediate and early stages are essential to increase their safety and effectiveness. Additionally, the adoption of minimally invasive treatments, especially for perforations, can reduce lethality.

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