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SCIENTIFIC REVIEW

Esophageal Duplication Cysts in 97 Adult Patients: A Systematic Review

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Abstract

Background Esophageal duplication cysts are a rare congenital cystic malformation from faulty intrauterine recanalization of the esophagus during the 4-8th weeks of development. They account for 20% of all gastrointestinal duplication cysts and commonly involve the distal esophagus. Presenting symptoms may be related to size and location.

Materials and Methods Following the PRISMA guidelines, a systematic review was performed by searching published literature in various databases. Data from 97 reported case reports were pooled to present a descriptive and statistical analysis.

Results Patient population was composed of 51(52.5%) males and 46 (47.5%) females, and mean ages was 42.3 years (18–77). Distal cysts were the most prevalent. Seventy-nine (81.4%) patients were symptomatic; common symptoms included dysphagia, chest pain, cough and weight loss. Fifteen (15.5%) patients were treated conservatively and 75 (84.5%) by surgical treatment, among them thoracotomy in 30 (30.9%) patients and VATS in 17 (17.5%) patients. Mean length of hospital stay was 8.6 days (range: 1–26 days). One fatality was registered. Location, unlike size, was not found to influence presenting symptoms or treatment employed. Frequency of conservative treatment was not significantly different between symptomatic and asymptomatic patients. Open approaches were associated with longer stays than their minimally invasive counterparts.

Conclusion Esophageal duplication cysts remain rare in adults and are frequently located in the distal esophagus. Larger cysts are more likely to cause symptoms. Various surgical techniques may successfully be employed in the treatment of this pathology. Minimally invasive procedures have a shorter hospital stay.

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Introduction

Esophageal duplication cysts (EDCs) are congenital malformations of the posterior primitive foregut and often within the thoracic esophagus. EDC is a congenital cystic malformation of the alimentary tract consisting of a duplication of the segment to which it is adjacent, being the result of faulty intrauterine recanalization of the esophagus, during the fourth to eighth week of embryonic development [1]. EDC are the third most common esophageal mass after leiomyoma and benign polyps, accounting for 0.5% to 2.5% of all esophageal tumors. They have a male-to-female ratio of 2:1, and they are more commonly found in the distal esophagus [2]. Autopsy studies have shown a prevalence of approximately 1:4500 and esophageal duplications occur even less frequently, 1:8200. They account for 20% of all the gastrointestinal duplication cysts. Less than 7% of EDCs remain asymptomatic until adolescences. EDCs most frequently involve the distal esophagus and may generate a wide group of symptoms depending on their size and location [3]. These symptoms may include dysphagia, respiratory distress, failure to thrive and retrosternal pain [4]. Cysts may cause various complications such as esophageal stenosis, respiratory system compression, rupture, infarction or malignancy [5]. Diagnosis is usually made by an imaging study: furthermore, total surgical or endoscopic excision represents the treatment of choice for these cysts [4, 6].

A few case reports have been reported in the literature, with only one series consisting of 4 asymptomatic patients, which were no treated [4]. Herein, we present a systematic review of all adult patients that have been reported in the literature, to our knowledge, with EDC, describing demographics, form of presentation, treatment and perioperative outcomes. Furthermore, this review aims to summarize and analyze published data to determine possible relations in location with presentation, diagnosis, treatment and outcomes.

Materials and methods

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we searched for published manuscripts using the Mesh terms "esophageal duplication cyst," "enteric cyst" "esophageal cyst" in PubMed, Google Scholar, Scopus, NCBI databases, using snowballing method as well as a manual search to avoid losing reports, with no language restrictions. Investigators were not blinded to the journal, author or institutions. We identified potentially eligible studies by examining titles and abstracts. Full articles were obtained to assess eligibility criteria before the critical appraisal. Data extraction of every case report or case series was performed and analyzed by all investigators to ensure quality data extraction. The primary analysis of adult patients with EDC included variables such as gender, age, comorbidities, main symptom, time of symptoms to diagnosis, image study, size, location, treatment, complications, length of hospital stayed and mortality. For those cases with a noticed successful treatment without complications, we assumed a favorable outcome.

We limited inclusion to published material of adult patients and of real EDC diagnosed by histopathologic examination. Studies whose histopathologic analysis was anything other than EDC were discarded. Studies not providing histopathologic analysis, but corresponding image diagnoses were included. We excluded any cyst or tumor mimicking EDC, patients who did not meet the established criteria for diagnosing an EDC, patients < 18 years old.

Palmer's pathologic criteria are useful for diagnosing this type of cyst; these criteria include (1) attachment to the esophageal wall; (2) presence of gastrointestinal tract epithelium; non-keratinizing squamous or ciliated columnar epithelium; and (3) existence of two layers of smooth muscle. [7] We excluded case reports that initially had a diagnosis of EDC, but final pathology did not meet Palmer's criteria, thus classifying them as bronchogenic cysts or other types of cysts.

A narrative description of findings was performed, and statistical analysis was carried out using the SPSS Statistics version 25 (IBM Corp., Armonk, USA) software. No assessment for risk of bias was performed. Kolmogorov–Smirnov test of normality was performed before data analysis to assess for normality of distribution. Testing of parametric variables was performed using Student T and ANOVA with Tukey's post hoc tests when applicable. Nonparametric testing was performed through Mann–Whitney U and Kruskall–Wallis. Nominal and ordinal variables were tested using Chi-square or Fisher's exact where applicable. Continuous variables were expressed as means or medians when appropriate. Ordinal and nominal variables were expressed as frequencies and percentages. A P value< 0.05 was considered statistically significant.

All procedures performed in studies involving human participants were in accordance with the ethical standards of Tecnologico de Monterrey ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Results

We carried out the systematic review until May 10, 2020. Shown in Fig. 1 is the flowchart, including the four phases of PRISMA, and obtained, eliminated and excluded duplicated records. In the identification phase, we collected 182 records from PubMed, Google Scholar and Scopus. We excluded a total of 104 of this first query. Due to incomplete information, no access to full text and pediatric patients, the pathology report came out inconclusive or did not include such information.

Remaining were 78 full-text articles that were assessed entirely for eligibility, which had basic and extended terms. We included another 14 articles from the NCBI database. We extracted evidence for this review, a total of 92 case reports and two case series, with the first case report published in 1973.

Patients characteristics, demographics, image studies and treatment

A total of 97 cases from 92 publications were included. The population was composed of 51 (52.5%) males and 46 (47.5%) females. Mean age was 42.3 years (range: 18 to 77 years). Cysts were located at various levels of the esophagus, being most frequently encountered in the distal third, middle third and proximal third of the esophagus, in 82 (84.5%), 10 (10.3%) and 5 (5.2%) of the cases, respectively (Fig. 2). Seventy-nine (81.4%) patients were symptomatic and 18 (18.5%) asymptomatic. Common symptoms included dysphagia, chest pain, cough and weight loss, which were presented in 50 (51.5%), 29 (29.8%), 5 (5.1%) and 15 (15.4%) of the cases, respectively. Six (6.1%) patients presented fever. Mean time from initial symptoms until diagnosis was 17.3 months (range 1 to 243.3 months). Several diagnostic studies were used, such as esophagogram in 72 (74.2%) patients, endoscopy in 49 (50.5%) patients, endoscopic ultrasound (EUS) in 54 (55.6%) patients, magnetic resonance imaging (MRI) in 16 (16.4%) patients, computed tomography in 77 (79.3%) patients and chest X-ray in 26 (26.8%) patients. Fine needle aspiration biopsy was performed in 17 (17.5%) patients.

In regard to the treatment employed, 15 (15.5%) patients were managed conservatively (antibiotics, percutaneous drainage or expectant) and 75 (84.5%) by surgical treatment. The most common therapeutic choice was thoracotomy in 30 (30.9%) patients, followed by video-assisted thoracoscopic surgery (VATS) in 17 (17.5%) patients. Endoscopic primary excision or aspiration of the cyst was performed in 12 (12.4%) cases, and a laparoscopic approach was employed in 11 (11.3%) of the cases. Laparotomy was done in five (5.2%) cases. In seven (7.2%) patients, the surgical method was not specified. Figure 3 displays trends in the treatment during the years.

Mean length of hospital stayed (LOS) was 8.6 days (range: 1 to 26 days). There were seven spontaneous cyst complications, including two cyst infections, one rupture of the cyst, one hemorrhage from the cyst, one ischemic perforation of the cyst, one hematoma, one rupture of esophageal muscle, one postoperative esophagus leakage and one fatality.

Analysis by symptomatology and cyst location

Grouping patient data in symptomatic and asymptomatic and subsequent analysis revealed no significant differences in symptoms in gender, age or location. However symptomatic patients had larger cystic dimensions 3.70 ± 1.58 vs 5.81 ± 3.03 ($P = 0.009$). Group analysis by location revealed no differences in demographic data such as gender or age, nor morphological characteristics or symptoms (Table 1). Symptomatic cysts more frequently underwent surgical management (Table 2).

Analysis by Treatment Employed

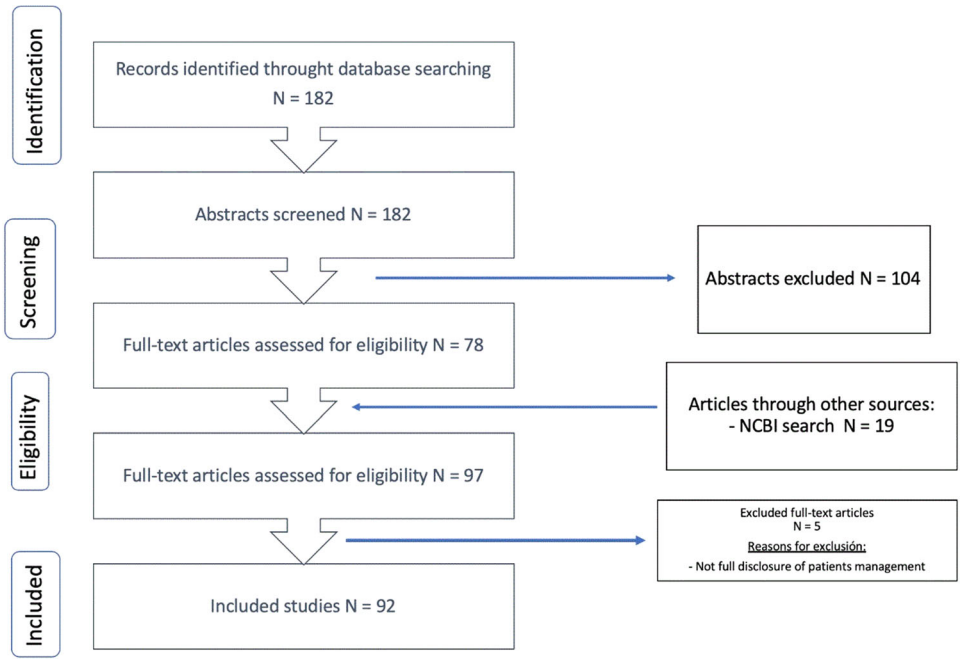
Analyzing patient characteristics and outcomes of patients grouped into treatment type revealed no differences of statistical significance in age and location or certain cystic dimensions. Furthermore, when analyzing separately length of hospital stay between conventional method or minimally invasive surgery, differences were nonsignificant. There was only one postoperative complication and one mortality. These findings are summarized in Table 3.

Discussion

EDC are the second most common duplication cysts of the digestive tract after their ileal equivalents, and these types of cysts are rarely seen in adults [2, 7, 8]. In this systematic review, almost all of the patients had EDC in the distal part of the esophagus; nevertheless, the male-to-female ratio was nearly 1:1.

While the current literature suggests most cysts are asymptomatic, our review found the opposite, with 81% symptomatic cases, probably from reporting bias in that symptomatic cases are more likely to be diagnosed and treated, and thus most likely to be reported. In this review, 18% of patients were asymptomatic upon diagnosis, and most of these diagnoses were incidentally made when performing an imaging study. Some patients who underwent routine checkup with endoscopy [4, 9, 10] or chest X-ray [11] were diagnosed with an incidental mass. For

Fig. 1 PRISMA flowchart



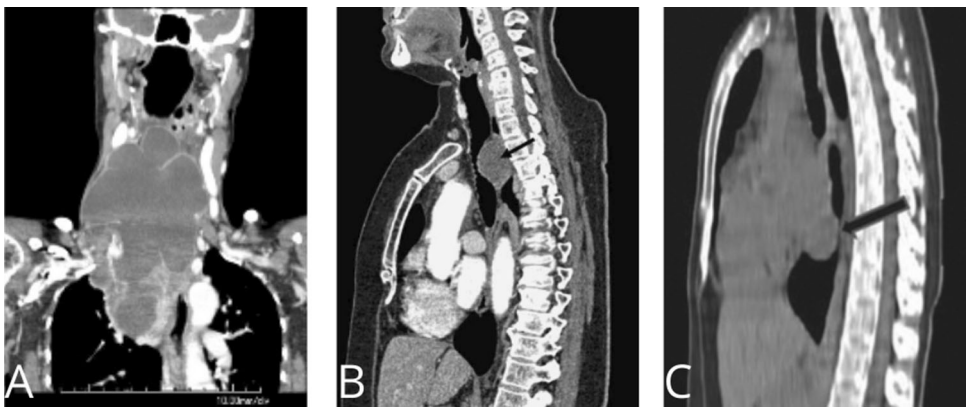


Fig. 2 **a** Coronal CT section illustrating complex loculated proximal oesophageal duplication cyst. Reprinted with permission. Prasai et al. Eur Arch Otorhinolaryngol. 2014;2. **b** Sagittal CT scan showing a cyst in the middle esophagus. Reprinted with permission. Espeso et al. Eur Arch Otorhinolaryngol. 2007; 264: 1357–60. **c** Sagittal CT scan showing a cyst in the distal esophagus. Reprinted with permission. Markinez-Gordobil et al. Cir Esp. 2011;89: 408–410

other patients in whom a CT scan was performed for various reasons such as renal transplant protocol [6], urolithiasis [12], lumbar back pain [13], staging breast cancer [14] and pneumonia [15], incidental masses were also detected. For some other patients who underwent cardiac imaging studies such as cardiac MRI [16], echocardiography [17] or carotid ultrasound [18], masses in their esophagus were incidentally encountered.

EDC may cause symptoms like chest pain and dysphagia, because of direct compression of the esophagus. Moreover, patients may experience weight loss because of a lack of food intake due to fear of experiencing dysphagia [19–26]. If the cyst is not promptly diagnosed, it might cause severe complications such as perforation [20, 27–30], mild bleeding [31, 32] intramural hematoma [33] and massive hemorrhage into the pleura space [34]. Infection is another known complication of EDC [35–38]. Agarwal et al. [39] and Tomar et al. [40] reported two young adults who presented with an EDC masquerading pericarditis and post-infective bronchiectasis, respectively. Nasr et al. [27] reported a 30-year-old man with an EDC penetrating the thorax causing a pyothorax, and the final specimen revealed an EDC along with a squamous cell carcinoma. Malignant transformation within these cysts is extremely rare and has been rarely reported before. Two 61-year-old patients presented with dysphagia and significant weight

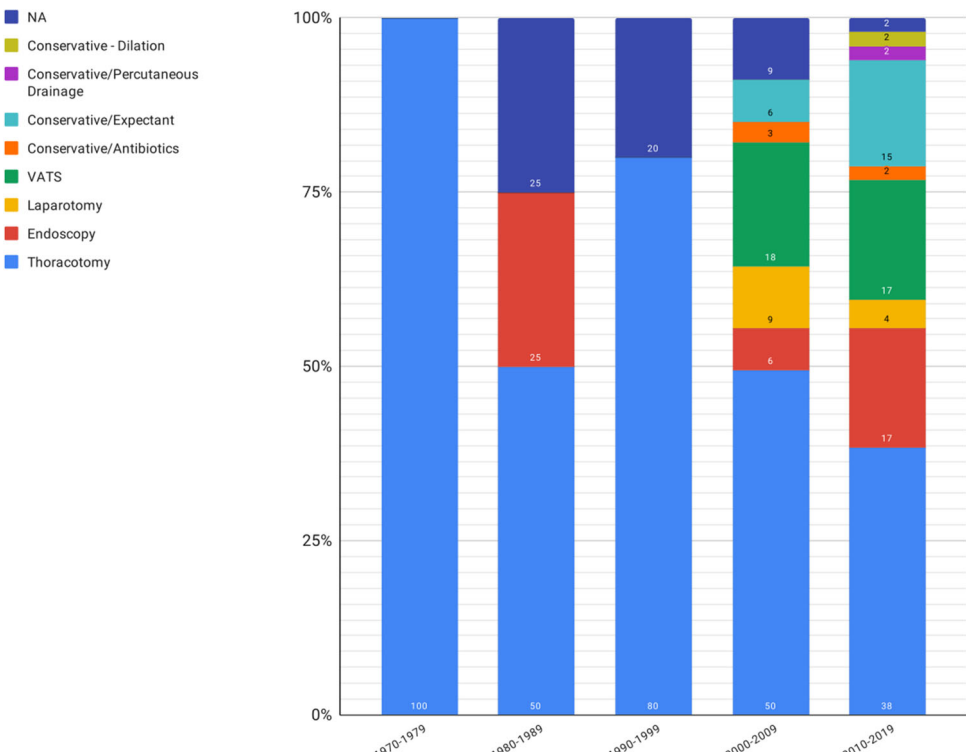


Fig. 3 Trends in treatment of esophageal duplication cyst during the years

Table 1 Patients' characteristics by symptoms and location regarding gender, symptoms, location and size

	Asymptomatic N (%) mean (SD)	Symptomatic N (%) mean (SD)	P	Proximal N (%) mean (SD)	Medial N (%) mean (SD)	Distal N (%) mean (SD)	P
Gender			.800				.914
Males	10 (55.6%)	41 (51.9%)		3 (60.0%)	6 (60%)	42 (51.2%)	
Females	8 (44.4%)	38 (48.1%)		2 (40.0%)	4 (40%)	40 (48.8%)	
Age(years)	47.9 (15.8)	41.1 (14.8)	.085	46.6 (12.4)	43.2 (18.2)	42.0 (15.1)	.226
Location			.866				
Proximal	1 (5.6%)	4 (5.1%)		–	–	–	
Medial	1 (5.6%)	9 (11.4%)		–	–	–	
Distal	16 (88.9%)	66 (83.5%)		–	–	–	
Size							
Width (cm)	3.7 (1.5)	5.8 (3.0)	.009	3.8 (2.1)	6.5 (2.9)	5.3 (2.9)	.355
Length cm)	3.0 (1.4)	5.4 (2.8)	.004	6.3 (2.9)	6.9 (2.9)	4.7 (2.5)	.297
Height (cm)	3.4 (1.5)	6.7 (4.0)	.095	4.7 (2.5)	4.7 (2.5)	4.7 (2.5)	.840

loss, with a proximal and distal mass in the esophagus; on the former, biopsies were taken revealing a duplication cyst with squamous cell carcinoma, so chemo-radiation was given with complete response [41], and on the latter, a complete surgical resection by thoracotomy was achieved, with the same histopathologic diagnosis [8].

Several ways of resecting the cyst have been reported, including thoracotomy, VATS, abdominal approach or more recently endoscopic resection. In this systematic review, we observed patients with cysts in the distal [22, 42–45] and middle esophagus [21] who underwent endoscopic resections. In one patient, a VATS with an endoscopic approach was made for treating a bleeding

Table 2 Patients' characteristics by symptoms and location regarding diagnosis and treatment

	Asymptomatic N (%) mean (SD)	Symptomatic N (%) mean (SD)	P	Proximal N (%) mean (SD)	Medial N (%) mean (SD)	Distal N (%) mean (SD)	P
Imaging							
Esophagogram	12 (16.7%)	60 (83.3%)	.758	4 (80.0%)	10 (100%)	58 (71.6%)	.133
Endoscopy	6 (33.3%)	43 (54.4%)	.124	2 (40%)	6 (60%)	41 (50%)	.834
Endoscopic ultrasound	11 (61.1%)	43 (54.4%)	.793	2 (40%)	3 (30%)	49 (59.8%)	.173
Magnetic resonance imaging	5 (27.8%)	11 (13.9%)	.291	0	1 (10%)	15 (18.3%)	.735
Computed tomography	10 (55.6%)	67 (84.8%)	.010	5 (100%)	8 (80%)	64 (78%)	.759
Chest X-ray	1 (5.6%)	25 (31.6%)	.036	1 (20%)	3 (30%)	22 (26.8%)	.916
Treatment							
Conservative	5 (31.3%)	10 (13.5%)	.001	3 (75%)	2 (20%)	10 (13.2%)	.007
Thoracotomy	0	30(40.5%)		1 (25%)	4 (40%)	25 (32.9%)	
VATS	5 (31.3%)	12 (16.2%)		0	1 (10%)	16 (21.1%)	
Laparotomy	0	5 (6.8%)		0	1 (10%)	4 (5.3%)	
Laparoscopy	5 (31.3%)	6 (8.1%)		0	0	11 (14.5%)	
Endoscopy	1 (6.3%)	11 (14.9%)		0	2 (20%)	10 (13.2%)	

VATS: video-assisted thoracoscopic surgery

Table 3 Patients' characteristics by treatment employed

	Conservative	Thoracotomy	VATS	Laparotomy	Laparoscopy	Endoscopy	P
Length of hospital stay (days)	5.5 ± 2.1	12.7 ± 7.6	6.7 ± 5.0	13.0 ± 4.0	6.1 ± 3.3	2	.055
Postoperative complications	0	0	0	1 (16.7%)	0	0	.077
Mortality	0	1 (16.7%)	0	0	0	0	.056

VATS: video-assisted thoracoscopic surgery

caused during the surgical excision [46]. Laparotomy was performed in six patients with distal cysts [10, 26, 47, 48].

A laparoscopic approach was performed in 11 patients; most of them used intraoperative endoscopies to monitor the integrity of the esophageal walls [7, 13, 14, 24, 49–52]. One patient with an EDC at the lower left cervical region underwent surgical excision of the mass, through a "Y" cervical incision, completely enucleating the tumor, with a favorable postoperative evolution, without any complication [23].

A thoracic approach was chosen in half of the patients, being more frequently employed a conventional method [19, 30, 33, 34, 53–57]. There are known advantages associated with the minimally invasive approach, such as a short hospital stay, minimal postoperative discomfort, fast recovery and return to regular activities [11, 15, 17, 58–62].

Endoscopic therapeutic approaches were employed in 12 patients, of which 4 underwent endoscopic drainage [63–65]. Eight patients underwent endoscopic resection, in one of them a fully covered, lumen-apposing, metal stent was inserted transluminally into the lesion, creating an endoscopic cystogastrostomy to facilitate drainage [66]. In one patient, a cervical EDC drainage was made by a percutaneous ultrasound-guided method. [67]. On two patients, antibiotics were only given, and ten patients were expectantly managed [40, 68]. While we cannot draw strong recommendations when using an endoscopic approach for treating this disease, we can demonstrate that most patients who underwent endoscopic treatment had EDC in the distal third of the esophagus, with a mean size of 5.3 cm × 4.7 cm × 4.7 cm; however, we hope that this review allows for future higher-quality studies by pointing out new questions in treatment.

One postoperative complication was reported in a 35-year-old woman, who developed chest pain and fever on her POD 10. A swallow study revealed a leakage into the posterior mediastinum, which was successfully resolved by endoscopy applying metallic clips [35]. One 30-year-old male patient died in whom a thoracotomy was performed for resecting an EDC. On POD 5, the patient developed respiratory distress, and a chest CT scan showed large pleural effusion. The patient was reoperated, draining a pyothorax. The patient developed a septic shock and died on POD 10 [27].

Limitations of our study include the short number of patients, the long study period, which entails different imaging and treatment modalities. Another limitation is the nature of the case reports, and even though we advocate for the use of CARE guidelines to improve the quality of them, a potential loss of reports from search engines is possible. Another important limitation in our study is that our database was built using published cases; thus, publication bias may be present in cases with suboptimal outcomes or managed conservatively that were not reported/published. Furthermore, symptomatic patients are most likely to be worked up and treated, while asymptomatic patients may rely on an incidental diagnosis. Efforts must be made to estimate the prevalence and presenting symptoms of this disease.

In conclusion, this is the only review to date of EDC in adult patients, describing, to our knowledge, all published cases in the medical literature. EDC is more frequently found in the distal third of the esophagus. In this systematic review, most of the patient presented symptoms, being chest pain and dysphagia the most common of them. CT scan was the image modality more frequently employed in all the cases; nevertheless, some other image studies may be done to achieve the diagnosis, such as endoscopy or MRI. There are several ways to treat EDCs, and treatment should be individualized to each patient.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00268-021-06325-8.

Author contribution MGU and DEHG performed research database and wrote the first draft. DPPA collected and analyzed the data on the methods and result section. ALA wrote discussion section and edited the final version of the manuscript. MRS designed the manuscript and performed research database. JRM helped with the design of the figures and tables, as well as edited the final version of the manuscript. All authors contributed to the design and interpretation of the study and to further drafts. MGU is the guarantor.

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Declarations

Conflict of interest The author(s) declare(s) that there is no conflict of interest.

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