Annals of Case Reports
Seraphim AM, et al. Ann Case Rep: 9: 102046
www.doi.org/10.29011/2574-7754.102046
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Research Article

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Performance of Endoscopic Dilation in Patients with Esophageal Stenosis due to Radiotherapy for Aerodigestive Tract Malignancy: Retrospective Cohort

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Citation: Seraphim AM, Andrade JDO, De Castro JSM, De Andrade ERA, Cabral JGGAL, et al (2024) Performance of Endoscopic Dilation in Patients with Esophageal Stenosis due to Radiotherapy for Aerodigestive Tract Malignancy: Retrospective Cohort. Ann Case Report. 9: 2046. DOI:10.29011/2574-7754.102046

Received: 28 October 2024, **Accepted:** 01 November 2024, **Published:** 04 November 2024

Abstract

This retrospective study aimed to evaluate the outcome of dysphagia after endoscopic dilation (ED) in patients with esophageal stricture (ES) after radiotherapy (RDT) for malignancies of the aerodigestive tract (MAT) and the secondary objectives: rates of adverse events and risk factors. We included patients aged > 18 years who underwent ED in ES after RDT for MAT within a one-year period. A total of 191 endoscopic esophageal dilations (EED) were performed in 63 patients. Twenty individuals were included in the study, 14 (70%) men, with a mean age of 67.2 years. All underwent treatment with RDT 16 (80%) underwent surgery and 14 (70%) chemotherapy. They complained of dysphagia and before starting treatment, 7 (35%) were able to swallow some solid foods, 6 (30%) swallowed semi-solids and 7 (35%) reported complete dysphagia for liquids. In the endoscopic aspect prior to the first dilation, 6 (30%) had simple stenosis and 14 (70%) complex, the latter being significantly related to the factors of refractoriness (p 0.05) and recurrence (p 0.04). The instrument used in the first session of 12 (60%) patients was a Savary-Gilliard dilators, 5 (25%) started with a hydrostatic balloon and 3 (15%) with the passage of the endoscope. After the procedure, only 1 (5%) patient had suspected perforation, which was ruled out after computed tomography. During the study period, 4 (20%) participants were lost to follow-up, 3 (15%) died, 6 (30%) had resolution of dysphagia complaints and 7 (35%) continued to perform ED. We conclude that EED in patients with MAT after RDT treatment is common and multifactorial. EED remains the treatment of choice in these cases; however, it is observed that this is a distinct group of patients, in which there is a higher rate of refractoriness and recurrence when compared with EED for other benign causes of stenosis. However, there are few case series describing the effect of dilation procedures in this group of patients.

Keywords: Endoscopic Dilation; Esophageal Dilation; Radiotherapy; Aerodigestive Tract Neoplasms; Cohort.

Introduction

Neoplasms of the upper aerodigestive tract (lip, oral cavity, pharynx, salivary glands and larynx), esophagus and stomach had a worldwide incidence in 2018 of 4.9, 3.2 and 5.7% respectively [1]. These generally originate from the epithelial layer of the mucosa and traditionally receive multimodal treatment, with surgical resections, radiotherapy and/or chemotherapy [2,3].

As a consequence of the aforementioned therapies, a frequently reported sequela is dysphagia, which may be due to neuromuscular damage, impairing the propulsion of the hypopharyngeal region, formation of pseudodiverticula; reduction in the quality and/or quantity of saliva; and obstruction by stenosis [3,4].

EE is characterized by a reduction in the lumen of the organ and can be estimated by endoscopy and measured through contrast radiological examinations [5,6]. Risk factors that can predict the development of dysphagia include: age, laryngeal or hypopharyngeal tumors, tumor size, and amount of radiation administered. Dysphagia management includes techniques such as swallowing readaptation, neuromuscular electrostimulation, dietary modification, and endoscopic and surgical procedures.

Upper gastrointestinal endoscopy (EGD) dilation is frequently used to treat dysphagia due to stenosis. This therapeutic option, although routine, presents a risk of complications, considerably increasing the morbidity and mortality of patients undergoing the procedure [3].

This study addressed the clinical evolution of patients after endoscopic treatment of dysphagia associated with EE after radiotherapy.

Materials and Methods

This is a retrospective study conducted at a single Center specializing in cancer treatment with data collected in a database. All individuals who underwent ED were initially selected.

The study was approved by the Research Ethics Committee of the same hospital (no. 009813/2021).

Individuals aged > 18 years who underwent the first ED in EE after radiotherapy for malignancies in the AT between April 10, 2019 and April 10, 2020 at the Endoscopy Service of the AC Camargo Cancer Center - São Paulo (SP) - Brazil were included in this study. Patients with ED due to causes other than radiotherapy and strictures due to neoplasms not located in the AT were excluded.

Variables analysed

Dysphagia will be assessed according to the Ogilvie et al [7] scale (grade 0, able to eat a normal diet; grade 1, able to eat some solid foods; grade 2, able to eat semi-solids only; grade 3, able to eat only liquids; grade 4, complete dysphagia for liquids).

The refractoriness and recurrence rates will also be analysed. Patients who reached a diameter of 11 mm in up to 5 ED sessions and did not achieve resolution of the dysphagia were considered refractory, and patients who dilated at least 11 mm but were unable to remain without new dilations for more than 4 weeks were considered recurrent.

The adverse events considered were bleeding, infection and perforation. The presence of adverse events was evaluated considering clinical, laboratory and imaging criteria, indicating hospitalization or even surgical treatment according to the assessment of the teams involved in the treatment.

Statistical analysis

Initially, a descriptive analysis of the variables was performed, presenting the absolute (n) and relative (%) frequency distributions for the qualitative variables, and the main summary measures, such as mean, standard deviation, median, minimum and maximum values, for the quantitative variables.

To assess the association between qualitative variables, the chi-square test or Fisher's exact test was used, when appropriate.

To compare the distribution of qualitative variables in relation to qualitative variables, the non-parametric Mann-Whitney test was used.

The significance level adopted was 5% and the statistical analyses were performed using SPSS software version 25.

Results

In the period of one year, 191 EEDs were performed in the Digestive Endoscopy sector of the AC Camargo Cancer Center, in 63 patients. Among these, 23 patients who started esophageal dilation therapy before the date determined for the study were excluded, 9 individuals for not having undergone radiotherapy in their oncological treatment, 10 for having other oncological diagnoses other than MAT and 1 for inability to access the information in their medical records, leaving 20 people of interest for this research. Of the 20 patients studied, 6 (30%) were women and 14 (70%) were men, with a mean age of 67.2 years (minimum of 42 and maximum of 87 years). Among them, 3 (15%) had a diagnosis of oral cavity tumors, 8 (40%) laryngeal squamous cell carcinoma (SCC), 6 (30%) esophageal SCC, 2 (10%) gastric adenocarcinoma and 1 (5%) sarcomatoid carcinoma of the glottic larynx.

All patients underwent RDT treatment, with an average of 31.5 sessions (minimum 5 and maximum 61 sessions). In addition to this

therapy, 16 (80%) underwent surgery and 14 (70%) chemotherapy. The surgeries performed were: 1 (5%) hemilaryngectomy, 11 (55%) total laryngectomy, 1 (5%) subtotal esophagectomy with gastric tube reconstruction, 2 (10%) total gastrectomies with Roux-en-Y reconstruction and 1 (5%) right partial pelvisglossectomy. Seven (35%) individuals had second primary neoplasia, namely early gastric adenocarcinoma, breast carcinoma, papillary thyroid carcinoma, laryngeal SCC, tongue SCC, hypopharyngeal SCC and Hodgkin lymphoma.

At EDA, the stenoses were located in: hypopharyngeal anastomosis in 8 (40%) patients, esophagogastric anastomosis in 1 (5%), esophagojejunal anastomosis in 2 (10%) and upper third of the esophagus in 9 (45%) cases. These stenoses were 6 (30%) simple and 14 (70%) complex.

The instrument used in the first ED session of 12 (60%) patients was a Savary-Gilliard dilators, 5 (25%) began treatment with a hydrostatic balloon and 3 (15%) with the passage of the endoscope. The average diameter with which the first dilation session was initiated was 10.6 mm (minimum 5 and maximum 16 mm). And the average number of diameters progressed in the first session was 1.7 (minimum 1 and maximum 3).

After the first dilation session, the following change in the dysphagia pattern was observed: 5 (25%) patients had no dysphagia (OS: grade O), 4 (20%) were able to swallow some solid foods (OS: grade 1), 6 (30%) were able to swallow semi-solid foods (OS: 2) and 3 (15%) had complete dysphagia for liquids (OS: 4), 2 (10%) individuals were lost to follow-up.

The mean number of sessions performed was 4.2 (minimum 1 and maximum 14 sessions) over one year. The maximum dilated diameter in all sessions was on average 13.8 mm (minimum 9 and maximum 18 mm). The average time intervals between sessions were also evaluated, and it was found that 20.5 days passed between the first and second dilation, 48.4 days passed between the second and third, and 74.9 days passed between the third and fourth.

After the dilation procedure, all patients presented lacerations and self-limited bleeding, and only 1 (5%) had a deep laceration with suspected perforation, which was ruled out after a computed tomography scan. Three (15%) patients who presented recurrent stenosis underwent applications of Triamcinolone (100mg/5ml) associated with dilation in 3 sessions. In 4 (20%) patients, self-expanding metal prostheses were used to treat the stenosis and 8 (40%) used gastrostomy as an alternative feeding route.

Dysphagia symptoms were evaluated before and after the esophageal dilation session in 18 patients. It was observed that among the 6 patients who presented dysphagia for solid foods (EO: grade 1) before the EED session, 3 (50%) denied dysphagia after the procedure (EO: grade 0), 1 (16.6%) was able to swallow some solid foods (EO: grade 1), 1 (16.6%) was able to swallow semi-solids (EO: 2) and 1 (16.6%) had dysphagia for liquids (EO: grade 4). Among the 5 individuals who were able to ingest semi-solid foods (OS: grade 2), 2 (40%) developed no dysphagia (OS: 0), 1 (20%) swallowed some solid foods (OS: grade 1) and 2 (40%) semi-solids (OS: grade 2). Among the 7 patients who complained of difficulty swallowing liquid foods (OS: grade 4), after endoscopic therapy, 2 (28.5%) were able to ingest some solid foods (OS: grade 1), 3 (42.8%) semi-solids (OS: grade 2) and 2 (28.5%) maintained complete dysphagia for liquids (OS: grade 4).

Of the participating patients, 7 (38.9%) were refractory to treatment. They had a mean age of 55.8 years, p: 0.69, with 1 (14.3%) woman and 6 (85.7%) men, p: 0.35. Of these, 1 (14.3%) had an oncological diagnosis of oral cavity tumor, 2 (28.6%) laryngeal SCC, 3 (42.9%) esophageal SCC and 1 (14.3%) sarcomatoid carcinoma of the glottic larynx, p: 0.53. As for the location of the luminal narrowing, 3 (42.9%) had stenosis of the hypopharyngeal anastomosis, 1 (14.3%) stenosis of the esophagogastric anastomosis and 3 (42.9%) stenosis in the proximal third of the esophagus, p: 0.61. Five (71.5%) patients underwent surgical treatment (p: 0.58): 4 (80%) total laryngectomy and 1 (20%) subtotal esophagectomy with gastric tube reconstruction. Regarding complaints of dysphagia prior to the start of dilation, 2 (28.6%) reported being able to swallow some solid foods (EO: grade 1), 1 (14.3%) semi-solid foods (EO: grade 2) and 4 (57.1%) complete dysphagia for liquids (EO: grade 4), p: 0.38. Afterwards, 2 (28.6%) swallowed some solid foods (EO: grade 1), 4 (57.1%) semi-solid foods (EO: grade 2) and 1 (14.3%) had difficulty swallowing liquids (EO: grade 4), p: 0.14. Regarding the endoscopic aspect of esophageal stricture before the first dilation session, all refractory patients had complex strictures, p: 0.05. In the first ED, 5 (71.4%) patients started the procedure with Savary-Gilliard dilators and 2 (28.6%) with a hydrostatic balloon, p: 0.65. Two (28.6%) patients used intralesional corticosteroid, p: 0.27.

Eight (44.4%) patients were recurrent, with a mean age of 68.5 years, p: 0.79, of which 1 (12.5%) was a woman and 7 (87.5%) were men, p: 0.32. These patients had as their underlying disease 1 (12.5%) oral cavity tumor, 3 (37.5%) laryngeal SCC, 3 (37.5%) esophageal SCC and 1 (12.5%) sarcomatoid carcinoma of the glottic larynx, p: 0.78, and as the cause of esophageal lumen narrowing, 4 (50%) hypopharyngeal anastomotic strictures, 1 (12.5%) esophagogastric anastomotic strictures and 3 (37.5%) strictures of the upper third of the esophagus, p: 0.50. Six (75%) patients underwent surgery, p: 1, namely: 5 (83.3%) total laryngectomy and 1 (16.7%) subtotal esophagectomy with gastric tube reconstruction. Regarding complaints of dysphagia prior to the start of therapy, 2 (25%) reported ingesting some solid foods (EO: grade 1), 1 (12.5%) semi-solid foods (EO: grade 2) and 5 (62.5%)

were unable to ingest liquids (EO: grade 4), p: 0.14. Regarding dysphagia after the first dilation, 3 (37.5%) were able to ingest some solid foods (EO: grade 1), 4 (50%) semi-solid foods (EO: grade 2) and 1 (12.5%) was completely unable to ingest liquids (EO: grade 4), p: 0.07. At the initial endoscopic appearance, all presented complex stenoses, p: 0.04. In 5 (62.50%) patients the first dilation was performed with Savary-Gilliard dilators, 2 (25%) with a hydrostatic balloon and 1 (12.5%) with the adult endoscope, p: 1.

The patients were followed up for up to one year, 4 (20%) were lost to follow-up and 3 (15%) died.

Six (46.2%) patients had resolution of dysphagia complaints, with a mean age of 64.7 years, p: 0.53, 4 (66.7%) women and 2 (33.3%) men, p: 0.10. Among these, 1 (16.7%) had oral cavity tumor, 2 (33.3%) laryngeal SCC, 2 (33.3%) esophageal SCC and 1 (16.7%) gastric adenocarcinoma, p: 1. Two (33.3%) had stenosis of the hypopharyngeal anastomosis, 1 (16.7%) of the esophageal-jejunal anastomosis and 3 (50%) stenosis of the proximal third of the esophagus, p: 0.42. Five (83.3%) underwent surgery, p: 1, of which 1 (20%) was a hemilaryngectomy, 3 (60%) was a total laryngectomy and 1 (20%) was a total gastrectomy with Roux-en-Y reconstruction. Before the first dilation, 1 (16.7%) swallowed some solid foods (EO: grade 1), 4 (66.7%) had some semi-solids (EO: grade 2) and 1 (16.7%) had complete dysphagia for liquids (EO: grade 4), p: 0.11. Regarding the appearance of the stenosis before the first dilation, 3 (50%) had simple stenosis and 3 (50%) had complex stenosis, p: 0.07. Regarding the instruments used in the first dilation session, 5 (83.3%) started with Savary-Gilliard dilators and 1 (16.7%) with a hydrostatic balloon, p: 1. It was noted that all patients who had their complaints resolved underwent up to five dilation sessions, p: 0.02.

Discussion

Radiotherapy treatment, with or without surgery and/or chemotherapy, is part of the treatment of several neoplasms of the neck and thorax [8]. It is expected that, after therapy, patients will have a normal diet, however some have difficulty swallowing, so that dysphagia is the most serious functional consequence associated with this therapy [9,10]. It may be due to anatomical changes such as strictures, formation of pseudo-diverticula, changes in the quality or quantity of saliva, reduced pressure at the base of the tongue or loss of muscle contraction of the neopharynx [9]. This disorder appears to be associated with chronic inflammation and formation of local fibrosis, generally occurring between 3 and 8 months after the end of radiotherapy [8]. More than 50% of patients treated with radiotherapy for head and neck neoplasms presented strictures, since local radiation induces dysmotility and esophageal stenosis [9,11].

Radiation-induced esophageal stenosis has a significant impact on the patient's life and can be managed with dilations guided by silicone tubes, hydrostatic balloons and even surgical resection [8]. Dilation, however, is the modality associated with the lowest morbidity and mortality rate, the fastest improvement of symptoms and the shortest hospital stay [8].

We can see here the description of the epidemiological profile of patients who underwent esophageal dilations in the period of one year. As seen in the literature, the majority of patients are male; Martins et al show in their work that 86.2% of the patients studied were men [12]. Regarding age range, the present study had a mean age of 67.2 years of participants, compared to 66 years presented by Kim et al in their work on predictors of stenosis in patients with cervical esophageal neoplasia after high doses of radiotherapy [11].

The data presented by Martins et al. in 2017 regarding the oncological diagnosis of patients with EE after RDT are in line with the findings of this study, with 75% of individuals having laryngeal and pharyngeal tumors in the former and 55% in the latter, and 20% having esophageal neoplasms in the latter and 30% in the former [12].

As identified in the study, Martins et al. show silicone dilators (e.g. Savary-Gilliard) as the preferred dilation instrument, being 96% of their sample and 60% in the latter, hydrostatic balloons (through-the-scope) represent 4% for them and 25% for us [12].

Martins et al. present similar results regarding the minimum mean diameter of the first dilation, 10 mm, and an average number of dilation sessions of 4, ranging from 2 to 9 sessions with patient follow-up for at least 12 months [12]. While Petersen et al have an average number of dilations performed of 3 sessions, varying between 1 and 113 with follow-up for an average period of 81 months [9].

The literature shows that the main complications associated with ED are aspiration, bleeding and perforation, the latter being the most serious [13]. It is reported that the perforation rate after EED varies between 0.1 and 0.4% and its risk is associated with the characteristics of the stenosis, being higher when complex [14]. Complex stenoses are more difficult to treat and tend to be refractory, as observed in the study, in which all refractory patients presented endoscopic appearance of complex stenoses before starting therapy. ED is the first choice in a less invasive approach, but in cases of refractoriness, therapies such as the use of steroids, incisional therapy, placement of esophageal prostheses and even self-dilation may be necessary. It is noted that the treatment of refractory benign EE remains a challenge [15].

A study published in 2003 demonstrated that non-peptic strictures were more likely to recur in the first year after ED, being related to lower transmural compliance due to local fibrosis, as occurs

in radiation-related strictures. It was observed that the average number of ED sessions required achieving adequate esophageal patency and improvement in dysphagia was higher in non-peptic strictures when compared with peptic strictures [16].

A meta-analysis published in 2017 shows that some studies considered that EED were successful when the patient reported any improvement in the dysphagia pattern [17]. Thus, it can be considered that the ED results presented here were positive, since most patients showed improvement in their swallowing pattern after the procedures, some even evolving with resolution of the dysphagia complaint.

Conclusions

EE in patients with MAT after RDT treatment is common and multifactorial [18]. EED remains the treatment of choice in these cases; however, it is observed that this is a distinct group of patients, in which there is a higher rate of refractoriness and recurrence when compared with EED for other benign causes of stenosis. However, there are few case series describing the effect of dilation procedures in this group of patients [17,18].

In view of the above, it was considered that the dilations performed during the study period obtained good results, since most of the patients had an improvement in their swallowing pattern according to the Olgivie scale, and some had resolution of dysphagia complaints.

Disclosure

Author Contributions: Conceptualization: A.M.S., J.O.A. and J.S.L.C.; methodology: E.R.A.A. and L.S.B.; software: L.K.L and A.G.P.; validation: C.Z.; formal analysis and resouces: A.M.S., J.O.A.., J.S.L.C, J.G.G.A.L.C, C.Z; writing-original draft preparation: A.M.S. and J.O.A.; writing-review and editing: A.M.S., J.S.L.C; supervision: A.G.P and C.Z.

Funding: This research received no external funding.

Institutional Review Board Statement: All experimental procedures were approved by the Human Research Ethics Committee of the ACCamargo Cancer Center and conformed to the principles outlined in the Declaration of Helsinki (approval number approval number 4.354.386). This study was guided by ethical standards and national and international laws. All athletes signed the consent form after receiving instructions regarding the possible risks and benefits and were granted privacy, confidentiality, and anonymity rights. The participants were free to stop participating any stage of the experiment without giving reasons for their decision.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data supporting the study results can be provided followed by request sent to the corresponding author's e-mail.

Acknowledgments: None.

Conflicts of Interest: None.

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