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Endoscopic spray cryotherapy for dysphagia palliation in esophageal cancer: Systematic review and meta-analysis

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ABSTRACT

Background and study aims Endoscopically delivered liquid nitrogen spray cryotherapy is reported to be a safe and possibly more effective strategy for dysphagia palliation in patients with advanced esophageal cancer. This systematic review and meta-analysis aimed to pool all available data to evaluate the impact of this treatment modality.

Methods Electronic databases (PubMed, Embase, and Cochrane Library) from January 2005 through June 2023 were searched for studies evaluating endoscopically delivered liquid nitrogen spray cryotherapy for dysphagia palliation in patients with advanced esophageal cancer. Pooled proportions were calculated using random-effects (DerSimonian-Laird) model.

Results From an initial 895 studies, data were extracted and analyzed from five studies comprising a total of 230 patients that met inclusion criteria. In this pooled analysis, dysphagia improved or did not deteriorate in 81.40% of patients (95% confidence interval [CI] 73.75–87.99). Significant improvement in dysphagia was reported by 55.19% of patients (95% CI 29.62–79.37). An alternate method of dysphagia palliation despite spray cryotherapy was required in 18.78% of patients (95% CI 8.09–32.63) with 10.56% (95% CI 2.53–23.18) requiring esophageal stents. The weighted mean number of spray cryotherapy sessions per patient was 3.37 (95% CI 2.55–4.18). The pooled major adverse event rate was 3.26% (95% CI 0.15–10.14).

Conclusions Endoscopic liquid nitrogen spray cryotherapy can effectively and safely treat dysphagia in esophageal cancer. It can be considered an option for dysphagia palliation in centers with expertise and equipment.

Introduction

Esophageal cancer is the eighth most common cancer worldwide and the sixth leading cause of cancer-related deaths [1]. It makes up about 1% of all cancers diagnosed in the United States, with an incidence of about 4.2 per 100,000 men and women per year [2]. With a 5-year survival rate of only about 21%, it is one of the most lethal forms of cancer [2]. More than 50% of patients with esophageal cancer are diagnosed at an advanced stage, and the primary debilitating symptom at the

time of diagnosis is dysphagia, which predominantly results from local tumor burden and extension [3,4]. As cancer progresses, dysphagia worsens and is a crucial component leading to malnutrition and a diminished quality of life (QoL). Patients often have unresectable locally advanced or metastatic disease. They are usually not candidates for esophagectomy or do not eventually undergo esophagectomy due to disease progression, malnutrition, or poor functional status [5].

Current preferred treatments for dysphagia palliation in advanced esophageal cancer include systemic chemotherapy with or without external beam radiation therapy, expandable esophageal stents, dilation, and brachytherapy [6,7]. Among these, esophageal stenting is the most widely used and provides instant relief of dysphagia. However, adverse events (AEs) such as chest pain, reflux, aspiration pneumonia, bleeding, perforation, fistula formation, stent obstruction from tissue ingrowth, and stent migration can happen infrequently [8,9]. Some studies have reported that self-expanding metal stents (SEMS), when used as a bridge to surgery, may result in higher postoperative mortality, morbidity, lower R0 resection rates, and reduced overall survival [10]. Radiation and chemotherapy can have a substantial delay before noticeable symptom improvement. Furthermore, poor nutritional or functional status, a common situation in this population, can also preclude patients from receiving chemoradiation therapy. Brachytherapy has been reported to be an effective and relatively safe treatment option, but it is underutilized for managing malignant dysphagia, possibly because of the unawareness of its usefulness and lack of expertise [3]. Other options include argon plasma coagulation, laser treatment, radioactive esophageal stents, and photodynamic therapy, but they have fallen out of favor due to limited efficacy, prohibitive cost, or high AE rates [11,12]. None of the currently preferred treatment options have demonstrated clear superiority over the others, and the treatment decision depends on multidisciplinary input depending on local expertise and availability.

Endoscopic spray cryotherapy is a relatively new modality that has been used for palliating dysphagia in patients with advanced esophageal cancer [6]. Cash et al. first described endoscopic spray cryotherapy as a palliative option for recurrent unresectable esophageal cancer in 2007 [13]. Endoscopic spray cryotherapy involves using an endoscopically delivered low-pressure 7F catheter that sprays liquid nitrogen at –196°C in a non-contact fashion directed to the area of interest by the endoscopist [14]. This process also requires placing a decompression tube into the stomach to evacuate nitrogen gas during the procedure. The area of interest is typically treated with 2 to 5 cycles of 20 to 30 seconds of cooling followed by 60 seconds of thawing [14,15]. The duration of cryotherapy application and the number of cycles has not been standardized and they are decided by the performing endoscopist [16,17,18]. Studies have demonstrated the safety and efficacy of liquid nitrogen spray cryotherapy to induce tumor necrosis and have been used to treat Barrett's esophagus and superficial esophageal cancer [19,20,21]. In addition, studies have also suggested that cryotherapy, when combined with chemoradiation, can result in a complete response even in locally advanced disease [15]. By preserving the tissue architecture of the surrounding squamous layers, this targeted approach reduces tissue damage, potentially contributing to a lower rate of stricture formation associated with this modality. Cryoablation has also been postulated to stimulate an antitumor immune response based on clinical observations that distant diseases often regress after cryoablation of a primary tumor [22]. In 2018, Kachaamy et al. reported the safety and efficacy of liquid nitrogen spray cryotherapy as a primary modality for dysphagia palliation in inoperable esophageal cancer [14]. Other studies have subsequently shown that spray cryotherapy can be an effective strategy for managing dysphagia in esophageal cancer [15,16,17,18]. This meta-analysis aimed to synthesize and highlight the current data on spray cryotherapy in managing dysphagia due to advanced esophageal cancer.

Materials and methods

Search methodology

A literature search was conducted using the electronic database engines MEDLINE through PubMed, Ovid, Cochrane Library (Cochrane Central Register of Controlled Trials and Cochrane Database of Meta-Analysis), EMBASE, ACP journal club, Database of Abstracts of Reviews of Effects (DARE) according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines from January 2005 through June 2023 to identify studies evaluating the use of endoscopically delivered liquid nitrogen spray cryotherapy for the palliation of dysphagia due to inoperable esophageal cancer [23]. The keywords used were "Cryoablation," "endoscopic spray cryotherapy," "dysphagia," "esophageal adenocarcinoma," "esophageal squamous cell carcinoma" and "esophageal stent." References of reviewed articles were further scanned for additional studies. The retrieved studies were carefully examined to exclude potential duplicates or overlapping data.

Study eligibility

Published studies were eligible if they reported the use of endoscopically delivered liquid nitrogen spray cryotherapy for the palliation of dysphagia due to esophageal cancer. Articles were excluded if they were not in the English language. Studies in animal models, editorials, abstracts with incomplete data, and comments were excluded. Two authors reviewed full-text articles independently (HG, HK). Differences were resolved by mutual agreement or review by a third author (SP).

Data extraction and quality assessment

The following data were independently abstracted by two authors (HG, HK) into a standardized form: Study characteristics (primary author, period of study, year of publication, and country of the population studied), study design, baseline characteristics of the study population (number of patients enrolled, participant demographics), intervention details (number of cryotherapy sessions, indications, experience of the operator), outcomes (improvement in dysphagia or prevention of further deterioration in dysphagia, significant improvement in dyspha-

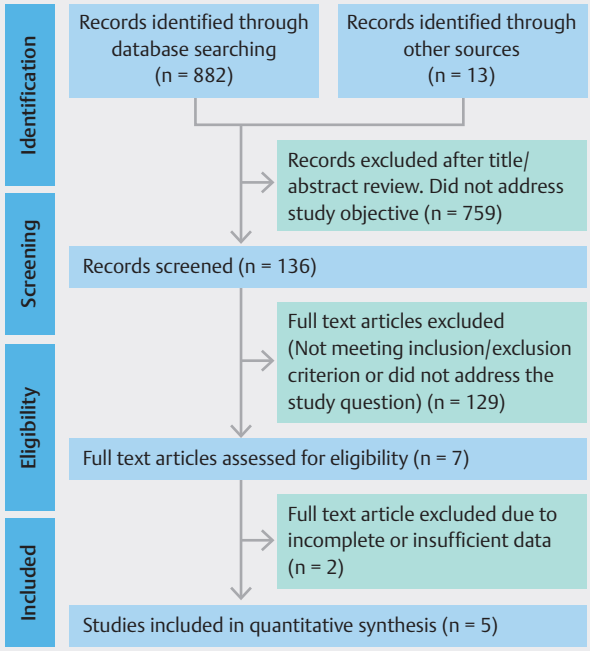
gia, need for alternate method of dysphagia palliation), and AEs.

Outcomes evaluated

The primary outcomes evaluated were the pooled proportion of patients reporting an overall improvement or prevention of further deterioration in dysphagia and the proportion of patients reporting significant improvement in dysphagia. The degree of dysphagia was defined by the included studies using dysphagia scores on a 4-point Likert scale: 0, no dysphagia; 1, dysphagia to solids; 2, dysphagia to semi-solids; dysphagia to liquids; 4, dysphagia to own saliva. Significant improvement in dysphagia was arbitrarily defined by a reduction in the dysphagia score by at least one point on the Likert scale in keeping with the standard definition used in the included studies or as defined by the authors. Secondary outcomes evaluated were the pooled proportion of patients who required an alternative method of dysphagia palliation (e.g., dilation, esophageal stent) despite initial treatment with liquid nitrogen stray cryotherapy and the AEs attributed to the use of spray cryotherapy. AEs were rated as mild or severe, and the severe AEs were further characterized and individually analyzed.

Statistical analysis

This pooled analysis of single-arm studies was performed by calculating weighted pooled effects. Individual study proportions were transformed into a quantity using the Freeman-Turkey variant of the arcsine square-root transformed proportion. The pooled proportion is calculated as the back-transform of the weighted mean of the transformed proportions, using the DerSimonian-Laird method for the random-effects model. As all available studies were single-arm non-comparative observational studies with the inherent risk of heterogeneity, we performed this meta-analysis using the random-effects model. The heterogeneity of the studies was evaluated by Cochran's Q test based on inverse variance weights and by calculating the I^2-statistic. I^2 values of 0% to 39% were considered non-significant heterogeneity, 40% to 75% moderate heterogeneity, and 76% to 100% considerable heterogeneity. The null hypothesis on which the I2 statistics is performed assumes that there is heterogeneity in the included studies. $P>0.10$ rejects this null hypothesis and shows that there is no evidence of heterogeneity. Furthermore, given the presence of considerable heterogeneity, we also calculated the prediction interval for each of the effect sizes calculated. Forest plots were drawn to show the point estimates in each study in relation to the summary of pooled estimate. The width of point estimates in the forest plots indicates the assigned weight to that study. The Egger bias indicator and Begg-Mazumdar bias indicator tested the effects of publication and selection bias on the summary estimates. Funnel plots were constructed to assess potential publication bias. The quality of included studies was evaluated using the Newcastle-Ottawa scale for non-randomized studies. The interobserver variability was assessed using Cohen's κ. Microsoft Excel 2019 was used to perform the statistical analysis for this study.



▶ **Fig. 1** Study flow diagram according to the PRISMA guidelines [23].

Results

The initial search identified 895 studies, of which 136 relevant articles were reviewed. Data were extracted from five studies comprising patients meeting inclusion criteria and included in the final analysis. PRISMA describing the details of the review process are shown in ▶ **Fig. 1**. Four of the five included studies are available in full-text articles [14, 15, 17, 18], while the one by Eluri et al. is available as published abstract [16]. The characteristics of the included studies are given in ▶ **Table 1**. The quality of studies was good as evaluated using the Newcastle-Ottawa scale shown in ▶ **Table 2**. All the pooled estimates given are estimates calculated by the random-effects model. The estimates calculated using fixed and random-effects models were similar. The agreement between reviewers was 1.0, as measured by Cohen's κ.

The total sample size was 773 endoscopic liquid nitrogen spray cryotherapy sessions performed on 230 patients. The mean patient age was 68.57±8.51 years with males constituting 82% of the study population. These data included spray cryotherapy performed in the esophagus for palliation of significant symptoms of dysphagia in patients with adenocarcinoma (86.52%), squamous cell carcinoma (13.47%), and two patients with neuroendocrine carcinoma. The weighted mean number of cryotherapy sessions per patient was 3.37 (95% confidence interval [CI] 2.55–4.18). The mean follow-up duration was 351 ±286 days. The operators in all the included studies were experts from centers with extensive experience in the endoscopic management of esophageal cancers.

▶ **Table 1** Basic characteristics of studies included in this meta-analysis.

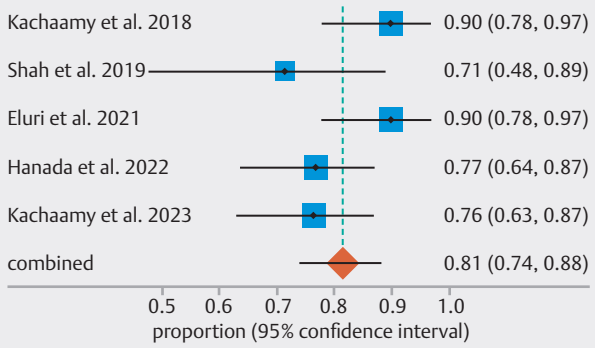
Author, year	Study design, location	Patients (n)	Males (n)	Adenocarcinoma (n)	Squamous cell carcinoma (n)	Concurrent chemotherapy (n)	Dysphagia improved or maintained (n)	Overall adverse events (n)	Patients requiring alternate method of dysphagia palliation (n)
Kachaamy et al. 2018 [14]	Multicenter retrospective USA	49	39	47	2	33	44	8	5
Shah et al. 2019 [15]	Multicenter prospective USA	21	20	15	6	0	15	2	0
Eluri et al. 2021 [16]	Multicenter prospective USA	49	43	45	4	0	44	19	18
Hanada et al. 2022 [17]	Single-center retrospective USA	56	40	41	15	0	43	9	16
Kachaamy et al. 2023 [18]	Multicenter prospective USA	55	47	51	3	44	42	2	13

▶ **Table 2** Modified Newcastle-Ottawa scale assessing the quality of included studies.

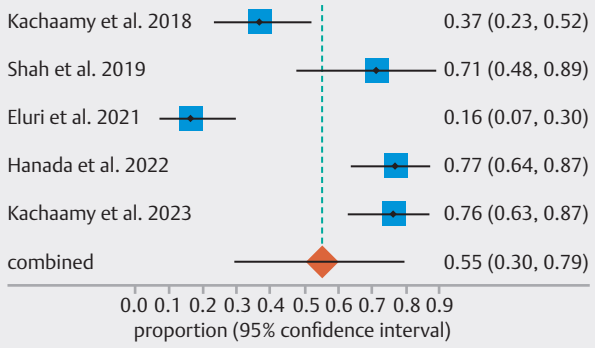
	Representativeness of the exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Assessment of outcome	Was follow-up long enough for outcome to occur	Adequacy of follow-up	Quality score	Quality
Kachaamy et al. [14]	*	*	*	*	*	*	*	7	High
Shah et al. [15]	*	*	*	*	*	*		6	High
Eluri et al. [16]	*	*	*	*	*	*	*	7	High
Hanada et al. [17]	*	*	*	*	*	*	*	7	High
Kachaamy et al. [18]	*	*	*	*	*	*	*	7	High

*Indicates that the criterion in the corresponding column was satisfied by the study.

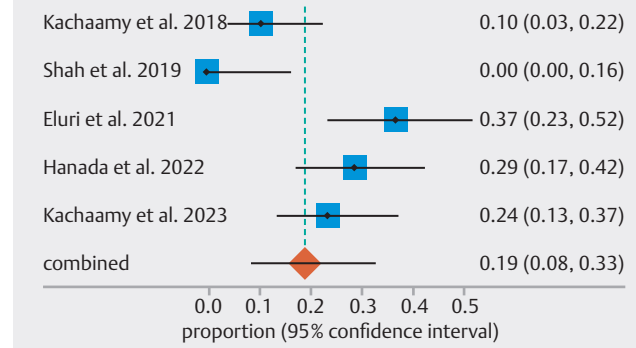
The pooled rate of overall dysphagia improvement or prevention of deterioration was 81.40% (95% CI 73.75–87.99). The forest plot showing individual study estimates and the pooled estimate for overall dysphagia improvement or prevention of worsening is shown in ▶ **Fig. 2**. There was no publication bias when calculated using the Egger bias indicator; –4.05 (95% CI -9.87–1.77, $P = 0.11$) or Harbord bias indicator; -2.33 (95% CI –13.89–9.22, $P = 0.62$). There was moderate heterogeneity with an I^2 score of 49.5% (95% CI 0–79.70). A significant improvement in dysphagia was noted in 55.19% (95% CI 29.62–79.37) patients. The forest plot for significant improvement in dysphagia is shown in ▶ **Fig. 3**. Despite spray cryotherapy, the pooled rate of need for an alternate method of dysphagia palliation was 18.78% (95% CI 8.09–32.63). The individual and pooled estimate of the rate of need for an alternate method of dysphagia palliation despite spray cryotherapy is represented on the forest plot shown in ▶ **Fig. 4**. Esophageal stents were eventually required for the management of dysphagia in 10.56% of patients (95% CI 2.53–23.18) who were initially treated with spray cryotherapy. Pooled minor AE rate was 10.60% (95% CI 1.41–26.80) and the pooled major AE rate was 3.26% (95% CI 0.15–10.14). The forest plot showing the individual



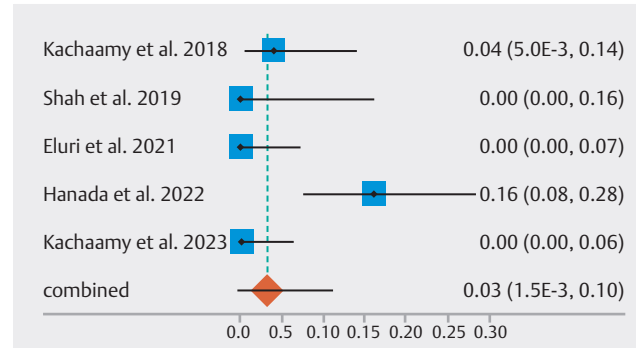
▶ **Fig. 2** Forest plot showing the individual and pooled rate of overall dysphagia improvement or prevention of worsening.



▶ **Fig. 3** Forest plot showing the individual and pooled rate of significant improvement in dysphagia.



▶ **Fig. 4** Forest plot showing the individual and pooled rate of need for an alternate method of dysphagia palliation despite spray cryotherapy.



▶ **Fig. 5** Forest plot showing the individual and pooled rate of major complications.

and pooled rate of major complications are shown in ▶ **Fig. 5**. The major AEs were bleeding, perforation, and delayed post-procedure stricture formation, with pooled rates of 1.14% (95% CI 0.18–2.91), 1.35% (95% CI 0.27–3.23), and 2.41% (95% CI 0.20–6.94), respectively. Overall, there was evidence of considerable heterogeneity in the outcomes evaluated. ▶ **Table 3** summarizes the estimates of heterogeneity and prediction intervals of all reported outcomes.

Discussion

Dysphagia is one of the most debilitating symptoms of advanced esophageal cancer and can often be challenging to manage [7]. Partially covered and fully covered SEMS are the most preferred modality for palliating symptomatic dysphagia in inoperable esophageal cancer [8]. It can provide prompt symptom relief in most cases but can also be associated with AEs such as pain, bleeding, unacceptable gastroesophageal reflux symptoms, recurrent dysphagia due to tissue ingrowth/overgrowth and stent migration [8, 9]. SEMS-related AEs can be seen in up to 40% to 50% of the patients with severe AE rates reported to be up to 20% [24]. In a recent network meta-analysis of randomized control trials evaluating the various types of esophageal stents used in the treatment of malignant dysphagia, ultraflex stent + radiotherapy and irradiation stent were reported to be the better treatment options in terms of survival [25]. However, the choice is often based on availability or endoscopist's preference and experience. Systemic chemotherapy can improve dysphagia, but this typically happens at a slow pace and can often be incomplete, resulting in the need for alternate intervention [7]. A Cochrane systematic review concluded that systemic therapy improves dysphagia but recommended against using chemotherapy alone in dysphagia palliation for esophageal cancer due to high incidence of recurrence and unclear impact on QoL [26].

Although guidelines from the National Comprehensive Cancer Network have described cryoablation as an option for dysphagia palliation in esophageal cancer since 2015, data regarding its efficacy remain scarce [27]. Our analysis shows that about 82% of patients treated with endoscopic spray cryotherapy showed improvement in their dysphagia score or maintained the level of dysphagia without further deterioration. Furthermore, 55% of patients reported significant improvement in dysphagia. A 1-point improvement in dysphagia score defined significant improvement. This would mean that a patient who

▶ **Table 3** Values estimating the heterogeneity and prediction intervals of reported outcomes.

Sl. no	Outcome analyzed	Pooled rate (%)	95% confidence interval	95% prediction interval	I2 (%)	95% confidence interval
1	Improvement in dysphagia or prevention of deterioration	81.40	73.75–87.99	52.20–94.50	49.50	0–79.70
2	Significant improvement in dysphagia	55.19	29.62–79.37	1.90–98.80	93.80	89.10–95.90
3	Need for an alternate method of dysphagia palliation	18.78	8.09–32.63	3.60–68.80	83.30	53.20–91.10
4	Requiring esophageal stents	10.56	2.53–23.18	0.40–78.80	85.50	62.60–92.00
5	Minor adverse event	10.60	1.41–26.80	0.10–91.40	90.60	80.50–94.30
6	Major adverse event	3.26	0.15 – 10.14	0.10–74.90	78.90	31.00–89.40
7	Bleeding	1.14	0.18–2.91	Not applicable	0	0–64.1
8	Perforation	1.35	2.73–3.23	Not applicable	0	0–64.1
9	Delayed post-procedure stricture formation	2.41	0.20 – 6.94	0.10 – 54.50	65	0 – 84.5

could tolerate only semisolid food was now eating solid food or that a patient who would tolerate only liquid food could now eat semisolid food. Only about 19% of patients required additional methods of dysphagia palliation in the form of stents (12%) or endoscopic dilation. These findings are comparable or better than that reported from other modalities currently used for dysphagia palliation.

The results of this pooled analysis also included a combination of patients who received endoscopic spray cryotherapy in a neoadjuvant setting (9.1%) or as concurrent therapy while they underwent systemic chemotherapy (33%). Kachaamy et al. reported that there were no specific AEs related to the use of SC in the adjuvant setting [14, 18]. These findings can be particularly relevant given that stent migration during chemoradiation is one of the main drawbacks of SEMS with rates up to 30% to 50% [28]. Although not immediate as seen with SEMS, the onset of improvement in dysphagia is also relatively rapid with Shah et al. reporting that 50% of patients had a 1-point improvement in dysphagia by 2 weeks post cryotherapy [15]. The persistent improvement or maintenance in the ability to swallow at a mean follow-up duration of about 1 year without the need for additional interventions also support that the effects of spray cryotherapy in dysphagia palliation are sustainable.

The findings from this study also show that spray cryotherapy delivered endoscopically is safe with a reported major AE (perforation, bleeding, and delayed post-procedural stricture formation) rate of about 2.5%. This is substantially lower that current standard of care with SEMS which has a reported severe AE rate up to 20% [24]. The etiology of esophageal stricture after spray cryotherapy can be challenging to discern in esophageal cancer, as the progression of primary malignancy alone could also result in malignant stricture formation. There was a higher proportion of stricture formation on long-term follow-up in the study by Hanada et al., with six cases of esophageal strictures at the site of spray cryotherapy. In contrast, only one case of esophageal stricture was reported in all the other studies combined.

There are a few limitations to this study. The data from two of the studies are limited by their retrospective nature. Furthermore, the available studies included in this pooled analysis were all single-arm and non-comparative, which limits our ability to directly compare these results with more common methods such as esophageal stents. A major limitation to this study is the presence of considerable heterogeneity which can limit the generalizability of findings from this meta-analysis. QoL assessment is as important a measure of a palliative strategy in esophageal cancer as dysphagia. This is especially relevant as esophageal stenting and radiation, which is currently the preferred method for dysphagia palliation and has been associated with poor QoL. Although QoL was evaluated by Kachaamy et al [18], there was paucity of uniform data across the studies for us to formally analyze this in the current study. As endoscopic spray cryotherapy is a relatively new method for dysphagia palliation in esophageal cancer, the number of patients enrolled in the included studies and the total number of available studies are low which could also limit the generalizability of our findings. Another limitation was that the data for this study come from experts in high-volume centers with experience in endoscopic management of esophageal cancer. This introduces the risk of selection bias. Whether the technical success and low AE rates demonstrated by them can be replicated in the community is a question that needs further research. Although a promising alternative with potential benefit over standard of care, more data are required from well-designed studies before wider adoption of this technique can be considered.

To our knowledge, this is the first meta-analysis of all available data on endoscopic spray cryotherapy using liquid nitrogen to palliate dysphagia due to inoperable esophageal cancer. This study shows that cryotherapy can be a safe and effective option for relieving dysphagia in patients with inoperable esophageal cancer, including those receiving systemic therapy. Further research is needed to standardize the dosimetry and define the appropriate indications so that this effective strategy

with minimal AE can be incorporated earlier in the course of this debilitating disease.

Conclusions

Endoscopic liquid nitrogen spray cryotherapy can effectively and safely treat dysphagia in esophageal cancer. It could be considered as an option for dysphagia palliation in centers with expertise and equipment.

Conflict of Interest

Dr. Neil R Sharma is a consultant for Boston Scientific, Medtronic, Steris, and Olympus. All other authors of this article do not have any conflict of interest with the publication of this manuscript or any institution or product that is mentioned in this manuscript and/or is important to the outcome of the study presented.

References

[1] Uhlenhopp DJ, Then EO, Sunkara T et al. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. Clin J Gastroenterol 2020; 13: 1010–1021 doi:10.1007/s12328-020-01237-x

[2] Siegel RL, Miller KD, Wagle NS et al. Cancer statistics, 2023. CA Cancer J Clin 2023; 73: 17–48 doi:10.3322/caac.21763

[3] Fuccio L, Mandolesi D, Farioli A et al. Brachytherapy for the palliation of dysphagia owing to esophageal cancer: A systematic review and meta-analysis of prospective studies. Radiother Oncol 2017; 122: 332–339 doi:10.1016/j.radonc.2016.12.034

[4] Ahmed O, Lee JH, Thompson CC et al. AGA Clinical Practice Update on the Optimal Management of the Malignant Alimentary Tract Obstruction: Expert Review. Clin Gastroenterol Hepatol 2021; 19: 1780–1788 doi:10.1016/j.cgh.2021.03.046

[5] Depypere L, Thomas M, Moons J et al. Analysis of patients scheduled for neoadjuvant therapy followed by surgery for esophageal cancer, who never made it to esophagectomy. World J Surg Oncol 2019; 17: 89

[6] Greenwald BD. Spray cryotherapy for dysphagia palliation in esophageal cancer prior to systemic therapy: is it ready for prime time? Endosc Int Open 2020; 8: E122–E123 doi:10.1055/a-0966-8457

[7] Mohapatra S, Santharaman A, Gomez K et al. Optimal management of dysphagia in patients with inoperable esophageal cancer: current perspectives. Cancer Manag Res 2022; 14: 3281–3291

[8] Kumar S, Bahdi F, Emelogu IK et al. How much progress have we made?: a 20-year experience regarding esophageal stents for the palliation of malignant dysphagia Dis Esophagus 2022; 35

[9] Mwachiro M. Through-the-scope esophageal stents for malignant dysphagia: A double-edged sword? Gastrointest Endosc 2019; 90: 980–982 doi:10.1016/j.gie.2019.08.022

[10] Mariette C, Gronnier C, Duhamel A et al. Self-expanding covered metallic stent as a bridge to surgery in esophageal cancer: impact on oncologic outcomes. J Am Coll Surg 2015; 220: 287–296 doi:10.1016/j.jamcollsurg.2014.11.028

[11] Rupinski M, Zagorowicz E, Regula J et al. Randomized comparison of three palliative regimens including brachytherapy, photodynamic therapy, and apc in patients with malignant dysphagia (CONSORT 1a) (Revised II). Am J Gastroenterol 2011; 106: 1612–1620

[12] Yang ZM, Geng HT, Wu H. Radioactive stent for malignant esophageal obstruction: a meta-analysis of randomized controlled trials. J Laparoendosc Adv Surg Tech A 2021; 31: 783–789 doi:10.1089/lap.2020.0666

[13] Cash BD, Johnston LR, Johnston MH. Cryospray ablation (CSA) in the palliative treatment of squamous cell carcinoma of the esophagus. World J Surg Oncol 2007; 5: 34 doi:10.1186/1477-7819-5-34

[14] Kachaamy T, Prakash R, Kundranda M et al. Liquid nitrogen spray cryotherapy for dysphagia palliation in patients with inoperable esophageal cancer. Gastrointest Endosc 2018; 88: 447–455

[15] Shah T, Kushnir V, Mutha P et al. Neoadjuvant cryotherapy improves dysphagia and may impact remission rates in advanced esophageal cancer. Endosc Int Open 2019; 7: E1522–E1527 doi:10.1055/a-0957-2798

[16] Eluri S, Kaul V, Sharma N et al. Palliative endoscopic spray cryotherapy to prevent worsening of dysphagia and improve quality of life in esophageal cancer. J Clin Oncol 2021; 39: 219–219

[17] Hanada Y, Leggett CL, Iyer PG et al. Spray cryotherapy prevents need for palliative stenting in patients with esophageal cancer-associated dysphagia. Dis Esophagus 2022; 35

[18] Kachaamy T, Sharma NR, Shah T et al. A prospective multicenter study to evaluate the impact of cryotherapy on dysphagia and quality of life in patients with inoperable esophageal cancer. Endoscopy 2023: doi:10.1055/a-2105-2177

[19] Shaheen NJ, Greenwald BD, Peery AF et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. Gastrointest Endosc 2010; 71: 680–685

[20] Tsai FC, Ghorbani S, Greenwald BD et al. Safety and efficacy of endoscopic spray cryotherapy for esophageal cancer. Dis Esophagus 2017; 30: 1–7 doi:10.1093/dote/dox087

[21] Greenwald BD, Dumot JA, Abrams JA et al. Endoscopic spray cryotherapy for esophageal cancer: safety and efficacy. Gastrointest Endosc 2010; 71: 686–693 doi:10.1093/dote/dox087

[22] Sabel MS. Cryo-immunology: a review of the literature and proposed mechanisms for stimulatory versus suppressive immune responses. Cryobiology 2009; 58: 1–11 doi:10.1016/j.cryobiol.2008.10.126

[23] Page MJ, McKenzie JE, Bossuyt PM et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71 doi:10.1136/bmj.n71

[24] Reijm AN, Didden P, Schelling SJC et al. Self-expandable metal stent placement for malignant esophageal strictures - changes in clinical outcomes over time. Endoscopy 2019; 51: 18–29 doi:10.1055/a-0644-2495

[25] Doosti-Irani A, Mansournia MA, Cheraghi Z et al. Network meta-analysis of palliative treatments in patients with esophageal cancer. Crit Rev Oncol Hematol 2021; 168: 103506

[26] Dai Y, Li C, Xie Y et al. Interventions for dysphagia in oesophageal cancer. Cochrane Database Syst Rev 2014; 2014: Cd005048 doi:10.1002/14651858.CD005048.pub4

[27] Ajani JA, D'Amico TA, Almhanna K et al. Esophageal and esophagogastric junction cancers, version 1.2015. J Natl Compr Canc Netw 2015; 13: 194–227 doi:10.6004/jnccn.2015.0028

[28] Huddy JR, Huddy F, Markar SR et al. Nutritional optimization during neoadjuvant therapy prior to surgical resection of esophageal cancer – a narrative review. Dis Esoph 2018; 31: dox110