



Cricopharyngeal myotomy and toxin botulinum injection for the treatment of upper esophageal sphincter disorders: a narrative review

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Abstract: To assess the indications, safety, and results of cricopharyngeal myotomy (CPM) and toxin botulinum injection (TBI) for the treatment of upper esophageal sphincter (UES) abnormalities. The UES disorders can provoke overwhelming consequences such as bronchopulmonary aspiration, malnutrition, impaired quality of life or even death. The best treatment modality for UES disorders remains unclear. The purpose of this review was to assess indications and outcomes of CPM and TBI for the treatment of UES abnormalities. We performed a review of the literature regarding the outcomes of CPM and TBI for UES disorders. All articles between 1990 and 2020 describing CPM, TBI, or those comparing both techniques were analyzed. Treatment indications, safety, and outcomes of both procedures were evaluated as primary endpoints. Quality of life improvement was evaluated as a secondary endpoint. Outcomes after CPM and TBI for UES disorders are heterogeneously reported. Data suggest that both surgical and endoscopic CPM are safe and have encouraging long-lasting results in terms of symptoms relief and quality of life improvement. TBI is also a safe procedure, with good but temporary postoperative results. Current data are heterogeneous and show that both CPM and TBI are safe and effective treatment modalities for UES disorders. Better long-lasting effects, however, seem to be achieved with CPM.

Keywords: Upper esophageal sphincter (UES); cricopharyngeal myotomy (CPM); toxin botulinum injection (TBI)

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Introduction

The upper esophageal sphincter (UES) is mostly formed by the cricopharyngeal muscle (CM) which at rest, keeps a continuous tone with the underneath esophageal lumen closed, allowing automatic relaxations when swallowing (1).

Normal swallowing involves the relaxation of the CM, thereby sphincter relaxation failure or cricopharyngeal

dysfunction leads to dysphagia and obstruction of food passage. The UES disorders can provoke overwhelming consequences such as bronchopulmonary aspiration, malnutrition, impaired quality of life or even death. Patients with cricopharyngeal dysfunction may refer upper esophageal reflux, coughing, halitosis (especially if associated with a Zenker's diverticulum) or progressive swallowing

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weakness in neurological disorders. Several studies can be used to reach the diagnosis, such as flexible endoscopy, manometry, videofluoroscopy, and manofluorography. In patients with UES abnormalities, several treatments have been described being the surgical myotomy and the toxin botulinum injection (TBI) the most widely accepted (2).

Since its introduction in 1951 for the treatment of post-poliomyelitis dysphagia, surgical cricopharyngeal myotomy (CPM) has been considered the treatment of choice for patients with deficient CM relaxation (3). Since 1994, endoscopic laser-assisted transmucosal myotomy has been increasingly replacing the open approach (4). On the other hand, TBI into the CM has also been described with promising results (5). However, indications techniques and outcomes have varied among different studies (6-8).

We performed a review of the literature to assess the indications, safety and outcomes of CPM and TBI for the treatment of UES disorders. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://aoe.amegroups.com/article/view/10.21037/aoe-21-8/rc>).

Methods

A literature search using the Medline database was performed to identify articles evaluating surgical myotomy and TBI for the treatment of UES disorders. Electronic searches in PubMed and Cochrane Central Register of Controlled Trials were performed using the following Medical Subject Headings (MeSH): “Upper esophageal sphincter disorders”, “Cricopharyngeal myotomy”, “Surgical myotomy”, “Toxin botulinum injection”, “Surgical myotomy vs. Toxin botulinum injection”. Each set of keywords was used to obtain the maximal number of articles. The search was limited to the adult population and to the English language.

All articles between 1990 and 2020 describing CPM, TBI, or those comparing both techniques were analyzed. A total of 237 articles were initially screened; after removing duplicates and excluding titles and abstracts that did not meet the inclusion criteria, 66 articles were revised based on the methodological quality of the publications. Finally, 42 articles were included in the review. The inclusion flowchart is displayed in *Figure 1*.

Treatment indications, safety and outcomes of surgical myotomy and TBI were evaluated as primary endpoints. Quality of life improvement was evaluated as a secondary endpoint.

Surgical CPM

Several treatment modalities for UES disorders have been described, being the CPM the most frequently used (9). Historically, CPM has been performed by an open approach through a left-sided cervical incision and has been recognized as a definitive treatment option for UES swallowing disorders. It was first described in 1951 by Kaplan *et al.* for the treatment of a patient with post-poliomyelitis deglutition paralysis with substantial symptoms improvement (10).

CPM has also been used to treat oropharyngeal dysphagia in neurogenic, idiopathic, structural, and/or myogenic disorders. It is also indicated in patients with moderate or severe pharyngeal dysphagia associated with a defective UES opening with a normal swallowing, in patients with manometric, electromyographic, and/or radiological abnormalities, in those with severe complications due to progressive dysphagia (pneumonia, weight loss, significant impairment of quality of life), or in patients with associated comorbidities (3,10,11).

Surgical technique

The open technique for the CPM is usually performed through a left cervical incision as the preferred approach. After separating the sternocleidomastoid muscle and dividing the omohyoid muscle, the posterior portion of the pharyngo-esophagus is exposed by rotating and retracting the carotid sheath posteriorly and the larynx anteriorly. The extramucosal myotomy of the CM is performed extending the incision 3–4 cm above the esophagus. A proper division of the muscle fibers is crucial for success (11,12).

Outcomes

Since Kaplan *et al.* described the surgical technique in 1951 (10), several studies have been published analyzing CPM results. In 1988, Duranceau and colleagues reported a total of 188 patients undergoing CPM for UES disorders of different etiologies, with a success rate of 73% (13). Similarly, Buchholz reported 79% of success in 244 patients undergoing CPM for neurological UES disorders (14).

A previous study analyzed 28 patients who underwent CPM for dysphagia or aspiration secondary to UES abnormalities. Every patient had a pre- and postoperative video-fluoroscopy and manometry to evaluate postoperative results. Treatment success was defined as complete

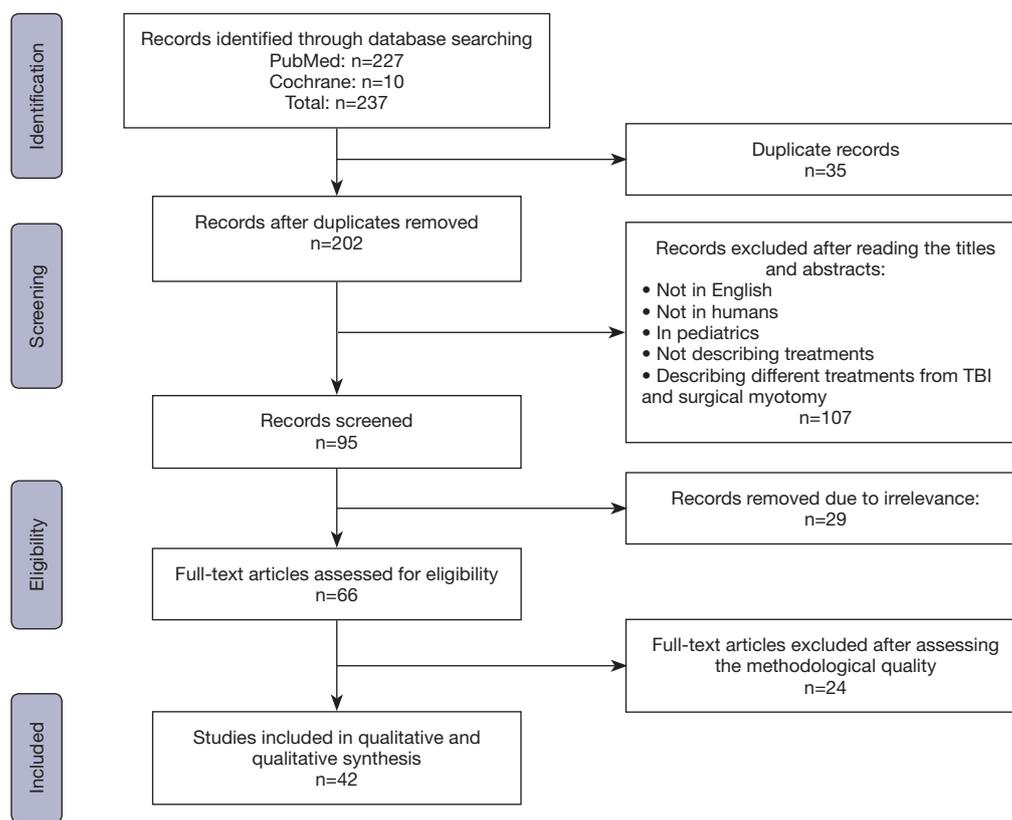


Figure 1 PRISMA flowchart. TBI, toxin botulinum injection.

symptoms resolution (dysphagia and/or aspiration), and results showed a success rate of 75% (21/28) (4).

Even when cricopharyngeal disorders are associated with a Zenker's diverticulum, surgical myotomy results are encouraging. A prospective study was conducted comparing the results between the surgical myotomy in patients with and without Zenker's diverticulectomy and a normal control group, evaluating the impact of the myotomy in the UES opening. Twenty patients were included (12/20 had a Zenker's diverticulum), and after the myotomy, UES opening was comparable with control healthy patients (15).

Although most studies analyzed post-myotomy outcomes, only a few included objective measurement instruments. Interestingly, Jiang *et al.* conducted a retrospective study measuring reflux symptoms and dysphagia with the Reflux Symptom Index and the Eating Assessment Tool 10, respectively, after an open CPM. Twenty patients underwent transcervical CPM, with or without Zenker's diverticulectomy, with statistically significant improvement of reflux and dysphagia symptoms [21.8 to 8.9 and 19.1 to 5 pre- and post-operatively, respectively ($P < 0.001$)] (16).

Overall, data suggest that surgical CPM is safe, with encouraging postoperative results in terms of symptoms relief and quality of life improvement. Studies describing surgical CPM are summarized in *Table 1*.

Endoscopic CPM

Based on the promising results published by Dohlman treating Zenker's diverticulum endoscopically, Halvorson in 1994 using the KTP laser, and Herberhold in 1995 using the CO₂ laser, described the endoscopic laser-assisted myotomy (18,31). However, controversy arises regarding safety and efficacy of this highly demanding technique (24,25).

Technique

A laryngoscope is positioned at the post-cricoid place. A vertical midline incision over the mucosa covering the CM is then performed with the laser, exposing the muscle. After that, a submucosal resection of the CM is performed with

Table 1 Evidence regarding cricopharyngeal surgical and endoscopic myotomy

Author	Year	Number of patients	Surgical or endoscopic myotomy	Complications	Success rate (%)	Follow-up (months)
St Guily <i>et al.</i> (17)	1994	11	Surgical	None	72	5–53
Herberhold <i>et al.</i> (18)	1995	32	Endoscopic	Mediastinitis, supraglottic edema	97	>84
Lim <i>et al.</i> (19)	1995	40	Endoscopic	Esophageal perforation	90	2–22
Poirier <i>et al.</i> (20)	1997	40	Surgical	Retropharyngeal hematoma	72.5	1–255
Ali <i>et al.</i> (21)	1997	8	Surgical	Not available	75	1.5
Halvorson <i>et al.</i> (22)	1998	18	Endoscopic	Not available	78	NA
Mason <i>et al.</i> (23)	1998	31	Surgical	Pneumonia, neck hematoma, pulmonary edema	77	2–48
Lawson <i>et al.</i> (24)	2003	29	Endoscopic	None	88	1–36
Zaninotto <i>et al.</i> (1)	2004	11	Surgical	None	73	6–31
Takes <i>et al.</i> (25)	2005	10	Endoscopic	None	60	2–24
Dauer <i>et al.</i> (26)	2006	22	Surgical and endoscopic	Chest pain, fever, pharyngocutaneous fistula, tracheotomy	58	NA
Munoz <i>et al.</i> (27)	2007	14	Surgical	Not available	25	6–10
Lawson <i>et al.</i> (28)	2008	31	Endoscopic	None	64.5	12–23
Kos <i>et al.</i> (4)	2010	28	Surgical	Aspirative pneumonia, mucosal fistula, fever	79	2.5–203
Ozgursoy <i>et al.</i> (29)	2010	14	Endoscopic	None	100	6
Bachy <i>et al.</i> (30)	2013	32	Endoscopic	Bleeding	84	6–99
Jiang <i>et al.</i> (16)	2017	41	Surgical and endoscopic	Not available	97.5	5.4
Shibata <i>et al.</i> (9)	2020	14	Surgical	Pneumonia, fever, nerve paralysis	100	66

the laser as extensively as possible. Finally, the incised area is covered with the incised mucosa (32).

Outcomes

Originally, CPM has been performed using potassium-titanyl-phosphate lasers. Over the years, CO₂ lasers have gained popularity due to their reduced postoperative morbidity (33).

Gilheaney *et al.* conducted a systematic review analyzing effectiveness of endoscopic CPM in patients with neurological disorders. Two studies were included, both of them using CO₂ laser for CPM. Reduction of food aspiration and laryngeal penetration with no adverse events were reported. However, evidence is still scarce to strongly recommend the endoscopic approach for CPM in patients with neurological UES disorders (33).

A retrospective study was published in 2000, including 17 patients with UES disorders related to different etiologies. All the patients but one, improved swallowing characteristics and quality of life after the procedure, and no complications were reported, suggesting that the endoscopic CPM was a safe approach (34). Another retrospective review of patients undergoing CPM was conducted in the Mayo Clinic of Jacksonville in 2006, comparing the open myotomy versus the endoscopic approach. Eight patients underwent an open surgical myotomy, whereas 14 underwent an endoscopic approach. Improvements in swallowing function were similar between groups (objectively evaluated by the Functional Outcome Swallowing Scale), and there were 3 minor complications in the endoscopic group and 3 complications (1 minor and 2 major) in the open group (26). According to the published data, the endoscopic approach seems to be safe

and effective. Studies describing endoscopic CPM are summarized in *Table 1*.

TBI

TBI has emerged as a less invasive treatment modality for patients with UES disorders (35). Toxin botulinum inhibits the release of acetylcholine, blocking the neuromuscular transmission and inhibiting the active contraction of the muscles and their tonicity; helping patients with hypertonicity of the UES (35).

TBI is often used for patients with transitory CM dysfunction and/or for those who are not candidates for a procedure under general anesthesia. TBI might also be helpful to select patients who could benefit from a definitive surgical myotomy (1,2).

TBI technique

Administered doses of toxin botulinum vary among authors, from 2.5 to 100 Botox units, and the injection technique is also diverse. Some authors prefer injecting botulinum neurotoxin under direct vision with an endoscopic approach, and others perform a percutaneous technique. TBI can be performed under electromyographic, fluoroscopic, and/or imaging guidance (36).

Outcomes

Zaninotto and colleagues, conducted one the largest series of patients with oropharyngeal dysphagia undergoing TBI. Twenty-one patients were included in the analysis, and 43% showed an improvement of the dysphagia. One patient died due to bronchopulmonary aspiration, and 12 failed to improve dysphagia symptoms [11 of these patients underwent a surgical myotomy of the CM, with a swallowing improvement of 72.7% (8/11)] (1).

Another study included 34 patients with symptomatic dysphagia, and analyzed cricopharyngeal electrophysiological characteristics to predict the efficacy of the cricopharyngeal TBI. Improvement of dysphagia two months after TBI was observed in 50% of the patients, with no complications reported in this series (37).

Restivo *et al.* published the results of 14 patients with UES disorders associated with multiple sclerosis, who underwent percutaneous TBI guided by electromyographic control. After two years follow-up, all patients (100%) showed

significant improvement of the swallowing mechanism with no complications related to the procedure (38).

Finally, Kelly and colleagues published the outcomes of the largest series of patients undergoing TBI for UES disorders: 65% of patients showed symptom's improvement after the treatment (32/49 patients) (3). Studies describing TBI are summarized in *Table 2*.

TBI for the treatment of CM dysfunction seems to be safe and effective, with success rates comparable to surgical myotomy. Although one of the most important disadvantages is its temporary effect, it is a valid and less invasive alternative to surgical myotomy. In addition, in case of failure, a surgical myotomy can always be attempted.

Expert commentary

We intended to analyze all the available literature regarding CPM and TBI for the treatment of UES disorders. With all the existing data, it is hard to give an evidence-based recommendation for this complex and poorly understood entity. However, we were able to draw some conclusions.

The TBI for the treatment of CM dysfunction is safe and effective. However, it offers only a temporary resolution of the symptoms. On the other hand, the CPM offers more durable results of the cricopharyngeal dysfunction. We often use the TBI as well as the cricopharyngeal dilation to select which patients might be benefited from surgical treatment. Overall, we prefer a myotomy as definitive treatment.

Promising results are reported regarding novel techniques such as the Z-POEM, which consists of an endoscopic myotomy through a submucosal tunnel for the treatment of Zenker's diverticulum. Although we do not have experience with this treatment modality, we strongly believe that this kind of novel procedures should be explored in the future.

Overall, further studies analyzing diverse treatment modalities for UES disorders with objective assessments of their outcomes are still needed.

Conclusions

Current data are heterogeneous and show that both CPM and TBI are safe and effective treatment modalities for UES disorders. Better long-lasting effects, however, seem to be achieved after surgical or endoscopic myotomy, as compared to TBI.

Table 2 Evidence regarding UES toxin botulinum injection

Author	Year	Number of patients	Cause of UES dysfunction	Complications	Symptom's improvement (%)	Follow-up (months)
Schneider <i>et al.</i> (5)	1994	7	Heterogeneous	None	71	2.5
Atkinson and Rees (39)	1997	5	Heterogeneous	Left vocal paralysis and pneumonia secondary to aspiration when injection effect ended	80	N/A
Brant <i>et al.</i> (40)	1999	1	Stroke	None	100	12
Alberty <i>et al.</i> (7)	2000	10	Heterogeneous	None	100	N/A
Shaw and Searl (41)	2001	12	Heterogeneous	Worsening dysphagia and pharyngeal laceration	83	N/A
Haapaniemi <i>et al.</i> (42)	2001	4	Heterogeneous	None	75	N/A
Moerman <i>et al.</i> (43)	2002	4	Heterogeneous	None	100	N/A
Parameswaran and Soliman (8)	2002	12	Heterogeneous	Neck cellulitis	92	N/A
Zaninotto <i>et al.</i> (1)	2004	21	Heterogeneous	Death secondary to a bronchopulmonary aspiration	43	17
Liu <i>et al.</i> (44)	2004	2	Inclusion body myositis	None	100	23
Chiu <i>et al.</i> (45)	2004	1	Stroke	None	100	12
Murry <i>et al.</i> (35)	2005	13	Heterogeneous	None	85	5–9
Kim <i>et al.</i> (46)	2006	8	Stroke	None	62.5	1–3
Masiero <i>et al.</i> (12)	2006	2	Stroke	None	100	24
Restivo <i>et al.</i> (47)	2006	12	Diabetic neuropathy	None	100	6
Suzukia <i>et al.</i> (48)	2007	1	Type 2 spinal muscular atrophy	Temporary worsening of dysphagia	100	1
Krause <i>et al.</i> (49)	2008	1	Subarachnoid hemorrhage spasticity	None	100	N/A
Alfonsi <i>et al.</i> (37)	2010	34	Heterogeneous	None	50	2
Restivo <i>et al.</i> (38)	2011	14	Multiple sclerosis	None	100	6
Woisard-Bassols <i>et al.</i> (50)	2013	11	Heterogeneous	Worsening dysphagia and GERD	45	12
Kelly <i>et al.</i> (3)	2000	49	Heterogeneous	Worsening dysphagia	65	N/A
Terré <i>et al.</i> (51)	2013	23	Stroke	None	82	12
Kim <i>et al.</i> (52)	2017	10	Heterogeneous	Unilateral vocal fold paralysis	63.9	6
Wei <i>et al.</i> (53)	2019	1	Stroke	None	100	6

UES, upper esophageal sphincter; GERD, gastroesophageal reflux disease.

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