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REVIEW ARTICLE

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Retrograde cricopharyngeal dysfunction (R-CPD): What do we know so far?

Fahad Z. Alotaibi

Department of Otolaryngology–Head and Neck Surgery, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia

Correspondence
Fahad Z. Alotaibi, Department of Otorhinolaryngology–Head and Neck Surgery, Imam Mohammad Ibn Saud Islamic University, Othman Bin Affan Rd, Alnada-7544, Riyadh 13317-4233, Saudi Arabia.
Email: fzalotaibi@imamu.edu.sa

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Abstract

Objective: This comprehensive review aims to explain the disease pathophysiology, clinical presentation, and management options.

Methods: A review was carried out in the following databases: Medline, Scopus, Web of Science, and Cochrane. The following terms were used alone and combined: Retrograde, Cricopharyngeus muscle, Dysfunction, Abelchia, and inability to burp.

Results: A total of 68 articles were identified, and only 11 were found to be relevant and included in writing this review. Retrograde cricopharyngeal dysfunction (R-CPD) is a relatively new disease entity that has recently been described in clinical literature. It is caused by the inability of the cricopharyngeus muscle to relax. Unlike cricopharyngeal dysfunction (CPD), which is well-known and characterized by dysphagia, R-CPD is characterized by the inability to belch in almost all patients, which is considered diagnostic for the condition.

Conclusions: High-resolution manometry (HRM) is the definitive diagnostic modality. Most patients reported in the literature responded well to treatment with botulinum toxin injection.

KEYWORDS

botulinum toxin, cricopharyngeal dysfunction, pharyngoesophageal segment, R-CPD, retrograde

Key Points

- Retrograde cricopharyngeal (R-CPD) dysfunction is a newly described condition.
- The inability to belch is the most common symptom.
- High-resolution manometry (HRM) provides the most accurate diagnostic information.
- Botulinum toxin injection is an effective treatment.

INTRODUCTION

Retrograde cricopharyngeal dysfunction (R-CPD) also can be more accurately described as retrograde upper esophageal sphincter dysfunction (R-UESD) is a disorder that Bastian recently described in 2019. It results from the abnormal retrograde function of the upper esophageal sphincter, which does not relax to permit eructation. This results in a significant impact on the patient's quality of life, as demonstrated by the ratings of severity and motivation of patients to solve this issue.[1] Unfortunately, there is little knowledge of this disorder in the medical community, and very few publications have addressed this issue. The first mention of the symptoms of what can now be recognized as R-CPD was in a case report by Kahrilas, who described a patient with an inability to burp, chest pain, and gurgling noises.[2] That study was followed by three other gastroenterological case reports, each describing an individual patient with the inability to belch, abdominal pain/bloating, and gurgling noises.[3–5] In these studies, manometry revealed an absence of relaxation of the upper esophageal sphincter (UES), but again, no treatments were attempted.

Bastian and Smithson were the first to describe clinical diagnostic criteria and introduce botulinum toxin (BT) injection into the cricopharyngeal muscle as a potent confirmatory diagnostic test and effective treatment.[1] A larger case series came out last year with more than 270 patients from the United States and the United Kingdom.[6–8] These large series relied mainly on the diagnostic criteria proposed by Bastian in his initial work.[1] This paper provides a comprehensive review of this condition's pathophysiology, clinical presentation, and management options based on a thorough search of all literature on this condition.

METHODS

Search strategy

A literature review was carried out in September 2022 in the following databases: Medline, Scopus, and Web of Science using the following terms: Retrograde AND cricopharyngeal dysfunction, Abelchia, and Inability to Burp. All reviewed articles and cross-referenced studies were screened for relevant data.

Inclusion criteria

We included studies that described Children and Adults diagnosed with R-CPD. Case reports, pilot studies, randomized and nonrandomized controlled trials were included. We excluded review articles. Studies considered for inclusion were published in any language.

Data and items collection

The following data items were extracted from each study: study author, year of publication, study design, subjects, mean age, presenting symptoms, diagnostic workup, treatment provided, and follow-up period.

RESULTS

A study identification, screening, eligibility, and inclusion flow diagram is shown in Figure 1. A total of 68 studies were identified and assessed for inclusion. After the exclusion on the title and abstract stages, 14 articles were retrieved for the full review. Three were later excluded after a full-text review because they mainly discussed classical cricopharyngeal dysfunction. Therefore, only 11 articles met the inclusion criteria set for this study. The included articles' key methodological and descriptive characteristics are presented in Tables 1–3.

All included articles were published between 1987 and 2022, with most of the articles being published after 2017. All studies were in the English language. Four articles were case reports, and four were case series. In these studies, 382 patients were investigated and diagnosed with R-CPD. The mean age of the patients was 26 years (range 7–68), with a slightly male predominance of 52%. A summary of patient demographics is provided in Table 1.

DISCUSSION

The pharyngoesophageal segment (PES) is a high-pressure area measuring 2.5–4.5 cm in diameter that connects the proximal esophagus to the distal pharynx. Another name for this anatomical area is the upper esophageal sphincter (UES). The cricopharyngeus muscle (CPM) is positioned in the transition zone between the inferior pharyngeal constrictor and cervical esophageal musculature, and these three muscles compose the PES. The CPM is 1–2 cm wide and C shaped, attaching to the lateral portions of the cricoid cartilage without a median raphe.[13] It comprises a horizontal portion and an oblique portion. CPM receives dual innervation from the ipsilateral pharyngeal plexus and the recurrent laryngeal nerve (RLN). Sensory information is carried along the glossopharyngeal nerve and cervical sympathetic.

UES relaxation during swallowing is the result of a cessation in neural input along with the activation of the strap muscles which will cause hyolaryngeal elevation that will actively pull the sphincter apart. During belching, proximal gastric air distension induces lower esophageal sphincter relaxation which causes a retrograde air movement through the esophagus to the pharynx. R-CPD is a dysfunction of the UES and involves failure to recognize and release the trapped gas below the UES, leading to retrograde dysfunction of the UES. In his initial work, Kahrilas suggested that the absent belch reflex is secondary to a defect in the sensory afferent neurons in the esophageal wall or the long vagal reflex arc.[11,14]

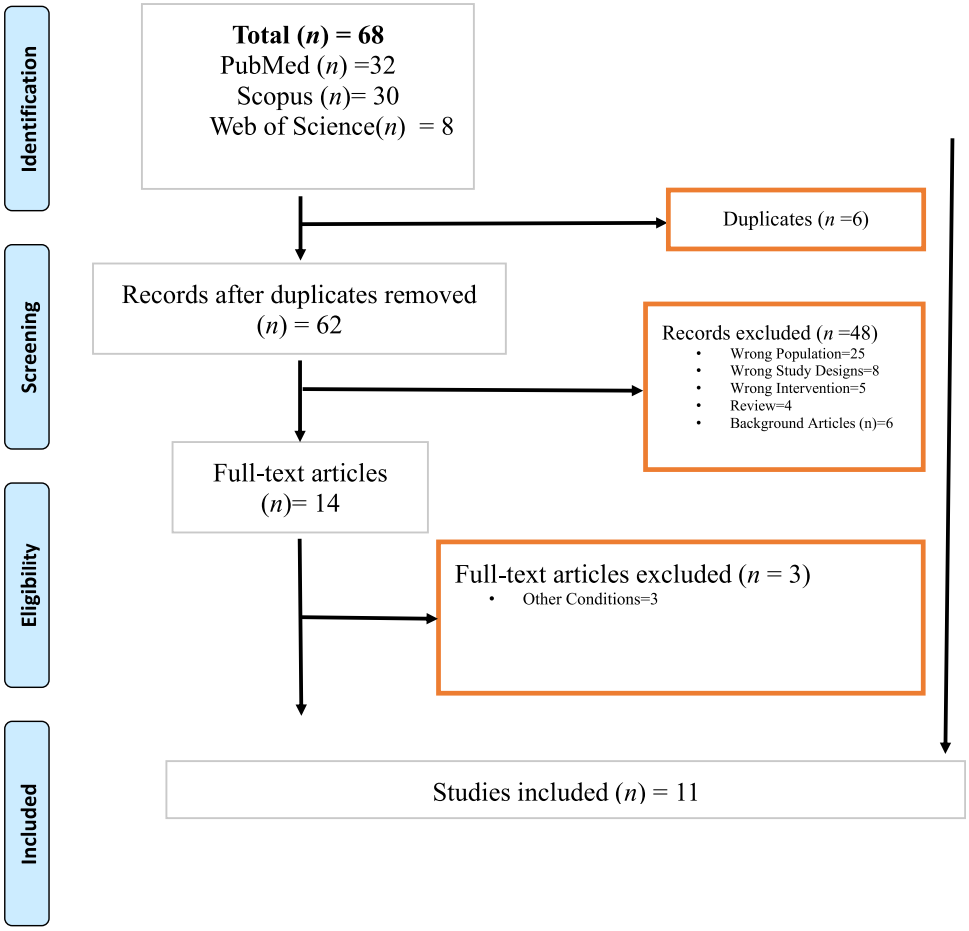

FIGURE 1 Flow diagram derived from PRISMA. This diagram reports the results of a search for published adaptive design clinical trials in PubMed, CENTRAL (Cochrane), Scopus, and Web of Science on September 2022.

The disease tends to affect young individuals (mean age 26 years), with a slightly higher rate of 52% in males compared to 48% in females. The inability to burp is a presenting feature in almost all patients in the literature (99%). Other symptoms include bloating, abdominal and retrosternal or chest pain/discomfort, gurgling noise in the throat, and excessive flatulence. Bastian suggested a clinical diagnostic criterion for R-UES. Most patients described an onset of symptoms in early childhood.[7] The disease was also described to affect the pediatric age group, and it could be a possible cause for parents' inability to burp their infants.

Diagnostic test battery for patients with esophageal and pharyngeal disorders involves high-resolution manometry (HRM) which is the most accurate method for assessing R-CPD. HRM assesses pharyngeal and esophageal motor functions, including UES relaxation and UES coordination. In R-CPD, elevated basal UES pressure and failure of relaxation were established in earlier reports. Recently, Oudi Nijhius et al. also provided a detailed description of the HRM findings in R-CPD dysfunction both at rest and in a carbonated-drink provocation test. They noted an increase in UES pressure instead of the expected UES relaxation.[11] These changes were resolved completely after BT injection.

Esophagoscopy is another investigation that can be performed as an in-office procedure using or under sedation. Esophageal lumen dilation below the UES was noted by Karagama et al. in all of his R-CPD patients.[6] The same finding was reported by Bastian et al., who noticed dilation below the CPM during injection under general anesthesia.[1]

Other diagnostic modalities such as functional endoscopic evaluation of swallowing and videofluoroscopic swallowing study, had been used in previous studies to help in ruling out other pharyngeal and esophageal pathologies.

Management of R-CPD is directed towards decreasing CPM activity by either using medication such as BT or through surgical division of the muscle. Avoidance of carbonated drinks and position change was suggested as an effective therapy for this condition when it was first described as lying down in a supine position directing the air down to the small intestine and relieving patient symptoms.

BT injection into the CPM has both confirmatory (diagnostic) and therapeutic advantages and represents the most effective treatment modality for this condition so far. It can be performed as an in-office procedure with EMG guidance or, most commonly, under general anesthesia. Most patients may require a single treatment of BT

TABLE 1 Clinical presentation of patients diagnosed with R-CPD in the literature.

No.	Author	Year	Study type	Number/ sex	Age (mean)	Clinical presentation
1	Kahril et al.[2]	1987	Case report	1F	25	Episodic chest pain while eating inability to belch gurgling noises in the chest. Shortness of breath
2	Tomizawa et al.[3]	1989	Case report	1M	21	Chest pain inability to belch
3	Waterman and Castell[4]	2001	Case report	1M	22	Abdominal bloating Inability to belch
4	Sato et al.[5]	2018	Case report	1F	17	Abdominal bloating gurgling noises in the chest
5	Bastian and Smithson[1]	2019	Case series	51 30 (M) 21 (F)	30	Inability to belch neck pain excessive flatulence gurgling noise
6	Wajsberg et al.[9]	2020	Case report	1M	32	Inability to belch abdominal and chest pressure gurgling noise Abdominal bloating
7	Karagama[6]	2021	Cases series	72 50 (M) 22 (F)	30	Retrosternal pain after eating Abdominal bloating inability to belch
8	Hoesli et al.[7]	2021	Case series	200 105 (M) 95 (F)	31	Inability to belch, abdominal and chest pressure, gurgling noise, and bloating
9	Wajsberg et al.[9]	2021	Case series 6 patients reported in 8	18 11 (M) 7 (F)	32.5	All symptoms mentioned in Table 1
10	Hoffman et al.[10]	2022	Case series	5 3F 2M	14	Inability to belch, bloating Gurgling noises Symptoms aggravated by carbonated drinks
11	Siddiqui et al.[8]	2022	Retrospective cohort	85 54F 31M	26.7	Inability to belch Chest pain Abdominal bloating Gurgling noises in the abdomen Excessive flatulence Dysphagia Globus sensation
12	Oudi Nijhius et al.[11]	2022	Case series	8 4M 4F	27	Inability to belch

Abbreviations: F, female; M, male; R-CPD, retrograde cricopharyngeal dysfunction.

injection. High doses (50–100 units) injected in the posterior and lateral parts of the CPM provided patients with complete symptom resolution within the first 48 h postinjection.[1] Most BT injection-related complications are well known in otolaryngology literature from experience with classic CPD management. The most frequent complication is mild, temporary, mostly solid food dysphagia in one-third of patients. Most of the side effects resolve within the first few weeks after injection. The probability of effectiveness of injection is excellent, ranging from 88.2% to 100% at the initial postoperative appointment in previous reports (Table 3).

CPM myotomy is a substantially effective treatment for refractory R-CPD that does not respond to BT injection. The surgery is performed under general anesthesia with either transoral approach after adequate exposure of CPM, the muscle divided using a cold technique or a CO_2 laser. Another approach is the transcervical approach. Only one patient received CO_2 laser-assisted endoscopic partial cricopharyngeal myotomy, and there was a complete resolution of symptoms after the surgery.[12] However, this option should be reserved for patients who fail to respond to repeated BT injections.

Study limitations

There are a few drawbacks to this research. the majority are case reports and case series. Second, there has been limited follow-up of the patients in the mentioned studies.

TABLE 2 Diagnostic modalities and terminology used to describe the condition.

No.	Author	Field	Workup	Diagnosis terminology
1	Kahrilas et al.[2]	Gastroenterology	Manometry, esophagrogram	Inability to belch
2	Tomizawa et al.[3]	Gastroenterology	Manometry, esophagoscopy	Inability to belch
3	Waterman and Castell[4]	Gastroenterology	Manometry, UGI series	Inability to belch
4	Sato et al.[5]	Gastroenterology	HRM, esophageogram	Inability to belch
5	Bastian and Smithson[1]	Otolaryngology	VFSS, TNFL	R-CPD
6	Bastian and Hoesli[12]	Otolaryngology	Clinical/botox inj	R-CPD
7	Karagama[6]	Otolaryngology	TNFL, TNO	Abelchia
8	Hoesli et al.[7]	Otolaryngology	VFSS, clinical	R-CPD
9	Wajsberg et al.[9]	Otolaryngology	VFSS, clinical	R-CPD
9	Hoffman et al.[10]	Otolaryngology	Clinical	R-CPD
10	Siddiqui et al.[8]	Otolaryngology	Clinical	R-CPD
11	Oudi Nijhius et al.[11]	Gastroenterology	HRM Ambulatory 24-h pH-impedance monitoring	Inability to belch syndrome

Abbreviations: HRM, high-resolution manometry; R-CPD, retrograde cricopharyngeal dysfunction; UGI, upper gastrointestinal; VFSS, videofluoroscopic swallowing study.

TABLE 3 Method and response to botulinum toxin injection.

Study	Number of patients	Injection technique	BT dose	Response to treatment
Hoesli et al.[7]	800	GA	50 IU	99% one w, 80% 6 m
Karagama[6]	72	GA	50–100 IU	100%, 96% at 3 m
Wajsberg et al.[9]	18	In office - EMG guided	50–75 IU	80% at 6 m
Siddiqui[8]	85	GA	25–100 IU	88.2%
Hoffman et al.[10]	5	GA	25–50 IU	100%
Oude Nijhuis et al.[11]	8	GA	50 IU	100%

Abbreviations: BT dosing and response to treatment. Botox (Allergan).

CONCLUSIONS

The diagnosis of R-CPD is mainly dependent on the assessment of the patient's symptoms and confirmed by HRM. Initiating the treatment using BT injection can confirm the diagnosis in addition to its therapeutic effect, resulting in almost complete resolution of the symptoms. Unifying the disease terminology will also help improve communication and collaboration between otolaryngologists and gastroenterologists. Further large-sample studies will provide a better understanding of the pathogenesis, diagnosis, and treatment approach.

AUTHOR CONTRIBUTIONS

Fahad Z. Alotaibi conceived and designed the study idea and wrote and edited the manuscript.

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The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

The author declares no conflict of interest.

DATA AVAILABILITY STATEMENT

All data are available upon request.

ETHICS STATEMENT

Given the deidentified and publicly available nature of this database, this study was exempted from Institutional Review Board approval.

ORCID

Fahad Z. Alotaibi http://orcid.org/0000-0001-6310-8252

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