


## ORIGINAL ARTICLE

## Gastroenterology

# Pediatric retrograde cricopharyngeal dysfunction diagnosed by high-resolution impedance manometry

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**Abstract**

**Objectives:** The inability to burp, known as retrograde cricopharyngeal dysfunction (R-CPD), was initially described in adults. The proposed clinical diagnostic criteria for R-CPD include belching inability, abdominal bloating and discomfort/nausea, postprandial chest pain, and involuntary noises. Botulinum toxin injection to the cricopharyngeal muscle has been reported to be beneficial. High-resolution esophageal impedance-manometry (HRIM) features in adolescent patients with R-CPD have not been described yet. The aim of our study was to describe the clinical and HRIM findings of pediatric patients with R-CPD.

**Methods:** Clinical and manometric features of five pediatric patients diagnosed with R-CPD were reviewed. HRIM study protocol was modified to include the consumption of carbonated drink to provoke symptoms and distinctive manometric features.

**Results:** We report five female patients aged 15–20 years who presented with an inability to burp and involuntary throat sounds. HRIM revealed normal upper esophageal sphincter (UES) relaxation during swallowing, but abnormal UES relaxation with concurrent high esophageal impedance reflecting air entrapment and secondary peristalsis following the carbonated drink challenge. Four patients exhibited esophageal motility disorder. All patients reported improvement or resolution of symptoms after botulinum toxin injection to the cricopharyngeus muscle.

**Conclusions:** Adolescents with an inability to burp, reflux-like symptoms, bloating, and involuntary throat noises should be assessed for R-CPD by pediatric gastroenterologists with HRIM. The relatively recent recognition of this novel condition is the likely reason for its under- and misdiagnosis in children.

## Diagnosing Pediatric Retrograde Cricopharyngeal Dysfunction (R-CPD)

- Diagnosis of R-CPD in adults is based mainly on clinical criteria
- Esophageal High-Resolution Impedance Manometry (HRIM) with carbonation protocol was proposed for diagnosis
- Manometric and impedance features of pediatric patients with R-CPD were not described



- Distinct features on HRIM were noted with carbonation protocol
- Adolescent patients with inability to burp - should be assessed by HRIM
- Botulinum toxin injection of the cricopharyngeus muscle was beneficial



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### KEYWORDS

belch, burp, dysphagia, esophageal motility disorders, upper esophageal sphincter

## 1 | INTRODUCTION

Inability to belch was first described by Kahrilas et al. in 1987.<sup>1</sup> While several case reports and series have been published since then, it was over 30 years later that a cohort of 51 adult patients with the inability to belch was reported and the authors proposed clinical diagnostic criteria for retrograde cricopharyngeal dysfunction (R-CPD).<sup>2-4</sup> The clinical diagnosis is based on typical symptoms including the inability to belch, abdominal bloating and discomfort/nausea, postprandial chest pain, socially awkward gurgling noises from the chest and lower neck, excessive flatulence, or difficulty vomiting in some.<sup>5</sup> While some adult studies report female predominance, others describe similar prevalence among the sexes.<sup>6,7</sup>

Improvement after botulinum toxin injection into the cricopharyngeus muscle was suggested as confirmation of diagnosis and as a treatment,<sup>2</sup> with reported relief of symptoms after injection in 95% and retaining ability to burp after 6 months in 80% after a single injection.<sup>6</sup> Adverse events reported after Botox injection included: transient dysphagia which resolved within days to weeks, reflux symptoms, and regurgitation with no association between Botox dose and side effects.<sup>7</sup> Characteristic findings on high-resolution impedance manometry (HRIM) and on 24 h pH impedance studies have been recently published.<sup>5</sup> However, there is no consensus regarding the need for manometric evaluation of patients with typical symptoms of R-CPD.

A single pediatric case series of patients with R-CPD has been published based on clinical diagnosis

### What is Known

- Retrograde cricopharyngeal dysfunction (R-CPD) has been described in adults.
- Diagnosis is based mainly on clinical criteria.
- Esophageal high-resolution impedance manometry (HRIM) with modified carbonation protocol was proposed to support the diagnosis of R-CPD in adults.

### What is New

- Adolescent patients and youth with R-CPD present distinct features on HRIM.
- HRIM with a modified carbonation protocol is helpful in the diagnosis of R-CPD in adolescent patients, concomitant with the reproduction of their symptoms.
- Adolescent patients with an inability to burp and involuntary throat noises should be assessed for R-CPD by HRIM.
- Botulinum toxin injection of the cricopharyngeus muscle is a potential treatment that should be considered after confirmation of the diagnosis on HRIM or impedance.

alone.<sup>8</sup> Manometric features of pediatric patients with R-CPD have not been previously described. The aim of our study is to describe the clinical and esophageal manometry findings of pediatric patients with R-CPD.

## 2 | METHODS

We describe pediatric patients presenting with the inability to burp and socially embarrassing throat noises who were diagnosed with R-CPD based on clinical symptoms and demonstrated characteristic findings on HRIM.

Data were retrospectively collected from electronic medical records, including basic clinical characteristics, past medical history, clinical and laboratory findings, comorbidities, treatment regimens in the past and present, 24-h pH impedance and HRIM tracings, treatment, outcomes, and adverse effects.

For all patients, HRIM studies were performed according to published consensus guidelines using Laborie (Medical Measurement System) systems.<sup>9,10</sup> Solid state 36 channel, 1 cm spaced catheters were used for all patients. For the interpretation of the metrics, Chicago Classification 4.0 normative values were used.<sup>10</sup> No sedation or anesthetic agent was administered before performing the manometry studies. Metrics calculated included: Pharyngeal contractile integral, upper esophageal sphincter (UES) relaxation time and integrated relaxation pressures (IRPs), proximal contractile integral, distal contractile integral, lower esophageal sphincter (LES) IRPs, and LES baseline pressure. Modified carbonated protocol: at the end of the standard HRIM protocol, consumption of 500 mL of carbonated drink was performed, to provoke symptoms.<sup>5</sup> Patients' symptoms were monitored and documented throughout the provocation study.

Twenty-four-hour pH impedance was performed utilizing Laborie (Medical Measurement System) systems with eight sensors catheter.

The study was reviewed and approved by the Cincinnati Children's Hospital Institutional Review Board.

## 3 | RESULTS

Five patients met the inclusion criteria. All five were females, aged 15–21 years, and all reported inability to burp and daily involuntary sounds from the throat causing social embarrassment. Symptoms duration before diagnosis was more than 1 year in all patients with one patient with mental health comorbidities describing symptoms for her “whole life”. None of the other four patients had other medical or mental health issues. Four patients were treated with proton pump inhibitors (PPI) for suspected GERD with no improvement in their symptoms.

Endoscopic evaluation was performed in three patients and was normal in all three. Additional testing included esophagram in one patient with minimally delayed clearance of esophageal contrast and normal video fluoroscopy swallow study in another patient. Patients' characteristics are present in Table 1.

Three patients had 24-h pH impedance study, showing air entrapment in all with evidence for aerophagia in two. None of the patients reported nocturnal symptoms and this was reflected in normal impedance parameters during sleep (Table 2).

### 3.1 | Manometric characteristics

All five patients underwent HRIM. Abnormal findings were noted in four patients: ineffective esophageal motility (IEM) was noted in two and incomplete bolus clearance was noted in three patients. Resting UES pressure and UES relaxation with swallowing was normal in all patients. UES relaxation is expected during normal burping, but an absence of UES relaxation with paradoxical increase in UES pressure and concurrent high impedance after carbonation challenge representing air entrapment in the esophagus was noted in all five patients. Symptoms were provoked in four patients during the carbonation protocol and characteristic manometric features were noted in two even before carbonation protocol. Secondary peristalsis provoked by air entrapment was noted among all patients. Baseline resting LES pressures, before carbonation protocol, were within normal range in all subjects. Following carbonation drink ingestion, LES pressures were low.

All except one patient had typical symptoms including involuntary sounds during provocation protocol, concomitant with an increase in esophageal impedance (representing air). Symptoms reported during the study were similar to the symptoms that patients were being evaluated for. Manometric findings of patients are presented in Table 1 and Figure 1. For comparison, esophageal manometry findings following carbonated HRIM protocol, of an 18-year-old female, with dysphagia and normal burping is presented in Figure 2. Manometry tracings for all five patients are provided as Figure S1 to this manuscript.

### 3.2 | Outcome

All five patients had botulinum toxin injection into the cricopharyngeus under anesthesia by an otolaryngologist in our center. The median follow-up period for four patients was 6.25 months (range 2–9 months) with one patient having reported improvement of symptoms 2 days after injection before being lost to follow-up. All reported symptom improvement within days after the injection. Short-term adverse event of dysphagia was reported by one patient which resolved after a short course of oral steroids. One patient (20%) had a second botulinum toxin injection due to recurrent symptoms 8 months after the first injection. Summary of outcomes is presented in Table 3. One patient had

**TABLE 1** Clinical, manometric, and impedance features of pediatric patients with retrograde cricopharyngeal dysfunction (R-CPD).

Patient	1	2	3	4	5
Age	15	16	15	16	20
Sex	F	F	F	F	F
Inability to burp	Yes	Yes	Yes	Yes	Yes
Vocal symptoms	Gurgling noises coming from her throat that are "embarrassing" and uncomfortable	"Frog-like" noises	gurgling sensation	"Throat popping," "frog-like" noises, sporadic and embarrassing	Audible throat sounds
Additional symptoms	None	None	Epigastric discomfort, chest pain, heartburn, and reflux	GERD, chest pain	Abdominal distention
Symptoms duration	Several years	2 years	3 years	1 year	All her life
Comorbidities	None	None	None	None	Juvenile idiopathic arthritis, bi-polar disorder, joint hypermobility
Previous treatment	PPI	Simeticone, PPI	PPI, calcium carbonate	Famotidine, PPI	None
Previous diagnosis	GERD	GERD	GERD	GERD	None
Bowel movements	Alternating—diarrhea/constipation	Normal	Normal	Normal	Normal
EGD/colonoscopy	Normal	Not performed	Normal (EGD only)	Normal	Not performed
Additional test	Dissaccharidases:Lactase—13.7 (norm = 15)—mild lactase deficiency	Gastric emptying study: delayed gastric emptying of the liquid phase VFSS—normal dual phase liquid/solid meal	Esophagram—minimally delayed clearance of esophageal contrast toward the end of the exam	None	None
Manometric and impedance features	UES resting pressure, 94 mmHg	89	34	72	34
Normal deglutition	Yes	Yes	Yes	Yes	Yes
UES relaxation	1	7	-1	-3	-1
UES IRP 0.2 mean (mmHg)	9	14	2	-1	2
UES IRP 0.4, mean (mmHg)					

TABLE 1 (Continued)

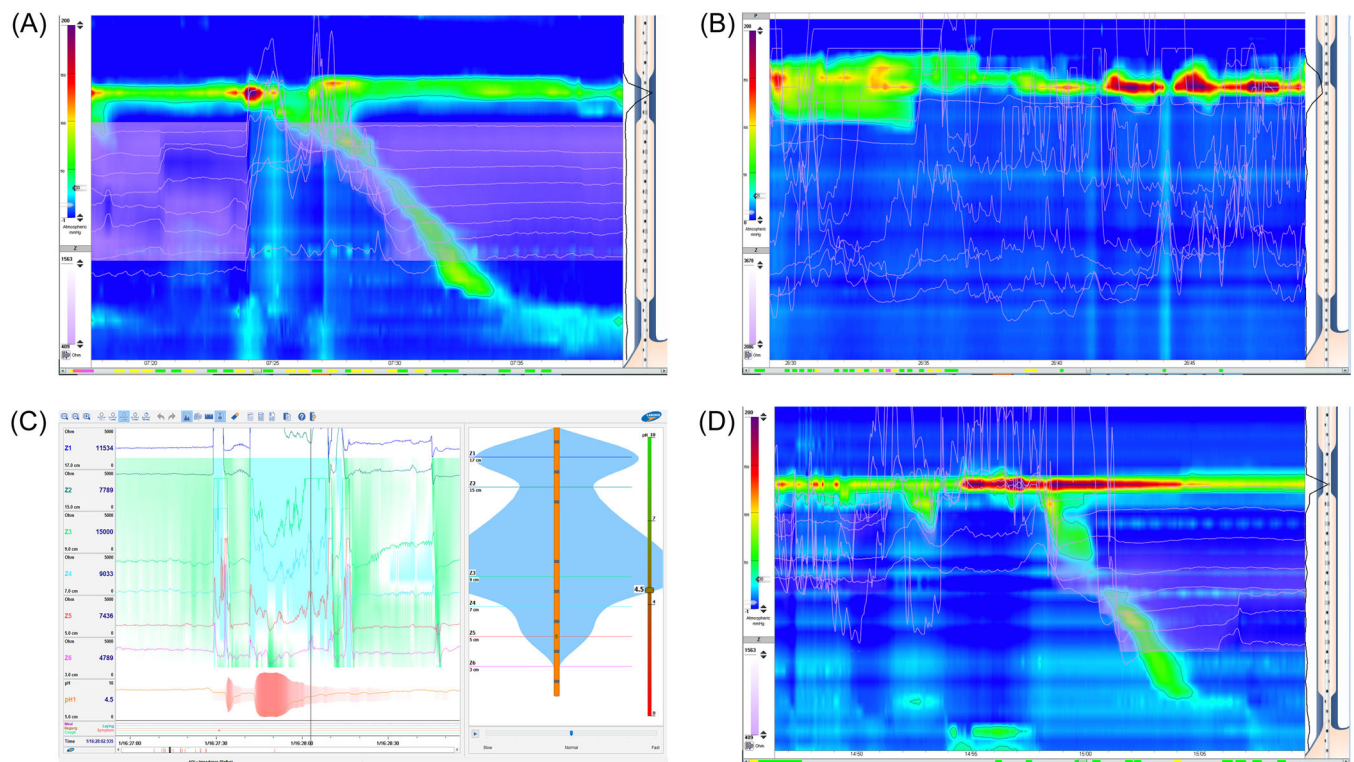
Patient	1	2	3	4	5
UES relaxation time, mean (s)	0.4	0.4	0.4d	0.5	0.5
Absence of UES relaxation after carbonation challenge	Yes	Yes	Yes	Yes	Yes
Normal spontaneous UES relaxation before challenge	Occasional	No	Occasional	Occasional	Occasional
Symptoms during challenge	None	Yes—frog noise	Yes—noises	Yes—noises, pressure in throat, loud croaking	Yes—nausea, gurgling in throat, feels air in throat, discomfort, bloating
Secondary peristalsis with air entrapment	Yes	Yes	Yes	Yes	Yes
LES resting pressures before carbonated protocol, mean (mmHg)	14	11	10	12	26
Diagnosis without carbonation protocol	Yes	Yes	No	No	No
Manometric diagnosis based on CC 4.0 v	Normal	IEM	Normal	IEM	Normal
Bolus clearance	Incomplete	Incomplete	Incomplete	Normal	Normal
24-h pH impedance	Not performed	Prolonged air entrapment. None during sleep	Frequent prolonged air entrapment, no symptom correlation with reflux. None during sleep	Prolonged air entrapment in the esophagus, rarely during sleep. No correlation between symptoms and reflux events	Not performed

Abbreviations: CC, Chicago classification; EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease; IEM, ineffective esophageal motility; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; PPI, proton pump inhibitor; UES, upper esophageal sphincter.

**TABLE 2** 24-h pH impedance results in pediatric patients with retrograde cricopharyngeal dysfunction (R-CPD).

Patient	2	3	4
Acid suppression during study	Yes	No	No
Study length, h:min	23:22	22:11	25:11
Total episodes of reflux ( <i>n</i> )	38	12	69
Acidic reflux events ( <i>n</i> )	8	4	15
Weakly acid ( <i>n</i> )	22	8	50
Proximal reflux episodes, <i>n</i> (%)	10 (26%)	4 (33%)	24 (35%)
RI (%)	0.40%	0.60%	1.20%
Prolonged reflux events (>5 min) ( <i>n</i> )	0	0	0
SAP (%)	99%	66%	86.30%
Air entrapment events	Present	Present	Present

Abbreviations: RI, reflux index; SAP, symptom association probability.

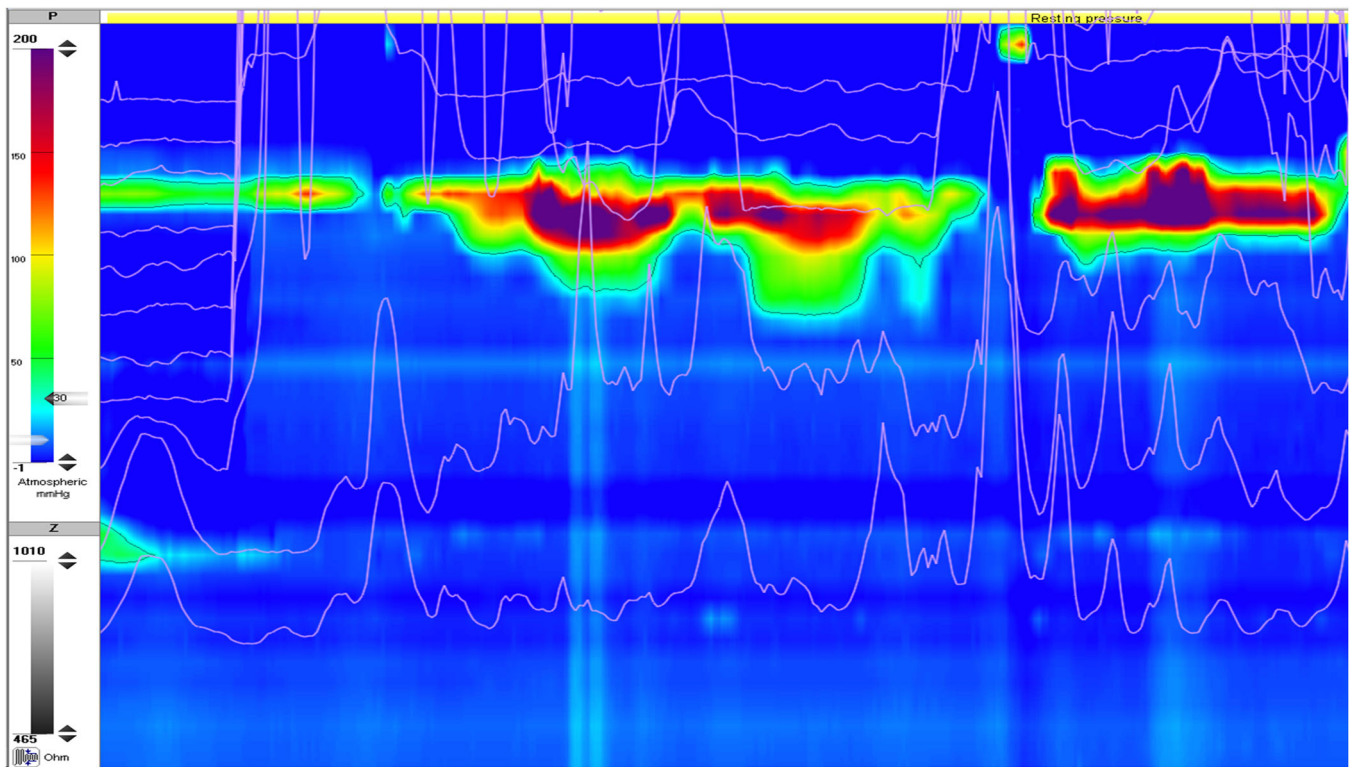


**FIGURE 1** (A) Secondary esophageal peristalsis provoked by air entrapment and low lower esophageal sphincter (LES) pressures in patient 1 with normal esophageal manometry per Chicago classification 4. (B) Air entrapment represented by high esophageal impedance without relaxation of the upper esophageal sphincter (UES) and low LES pressure in patient 4 with ineffective esophageal motility per Chicago classification 4. (C) Air entrapment in 24-h pH impedance study in patient 3 with normal esophageal manometry per Chicago classification 4. (D) Increase in UES pressure during esophageal air entrapment with low LES pressures and secondary peristalsis in patient 2 with ineffective esophageal motility per Chicago classification 4.

repeated esophageal manometry due to residual symptoms 2 months after botulinum toxin injection, which demonstrated normal burping and low upper pressures in the upper third of the esophagus (Figure 3).

## 4 | DISCUSSION

It had been previously suggested that R-CPD may be diagnosed based on characteristic clinical criteria alone.<sup>2,8</sup> This is the first study describing esophageal



**FIGURE 2** Normal upper esophageal sphincter relaxation during burping with low lower esophageal sphincter pressures as noted in an 18-year-old female with dysphagia, during provocation protocol.

manometric and impedance features in pediatric patients with R-CPD.

There is exclusive adolescent female prevalence of R-CPD in our series. Some previous adult studies have reported female predominance, while another reported similar distribution.<sup>5,7</sup> The lack of male patients in our cohort may be incidental due to the small number of patients but it may also represent a true higher prevalence among females, as seen in other disorders of gut-brain interaction such as irritable bowel syndrome.<sup>11</sup>

On HRIM with provocation test in our series, manometric features included lack of UES relaxation with concordant high impedance on esophageal impedance channels, secondary peristalsis provoked by air entrapment and reduction in LES resting pressure during air entrapment episodes. Normal UES resting pressures and relaxation with swallowing were noted. In four patients we did observe occasional normal UES relaxation, but this occurred before carbonation challenge. We observed a decrease in LES pressures during provocation test, which is an appropriate response when attempting to burp, as it permits the entry of air into the esophagus. The persistent decrease in LES pressure during failed attempts to burp is probably caused by air entrapment and may represent a protective phenomenon to prevent excessive pressure build up in the esophagus

or the stomach from the carbonation. Abnormal UES relaxation, on the other hand, kept the air trapped in the esophagus and the LES open in an effort to dissipate the pressure build up. These findings provide compelling supportive objective criteria for a definitive diagnosis of R-CPD in children.

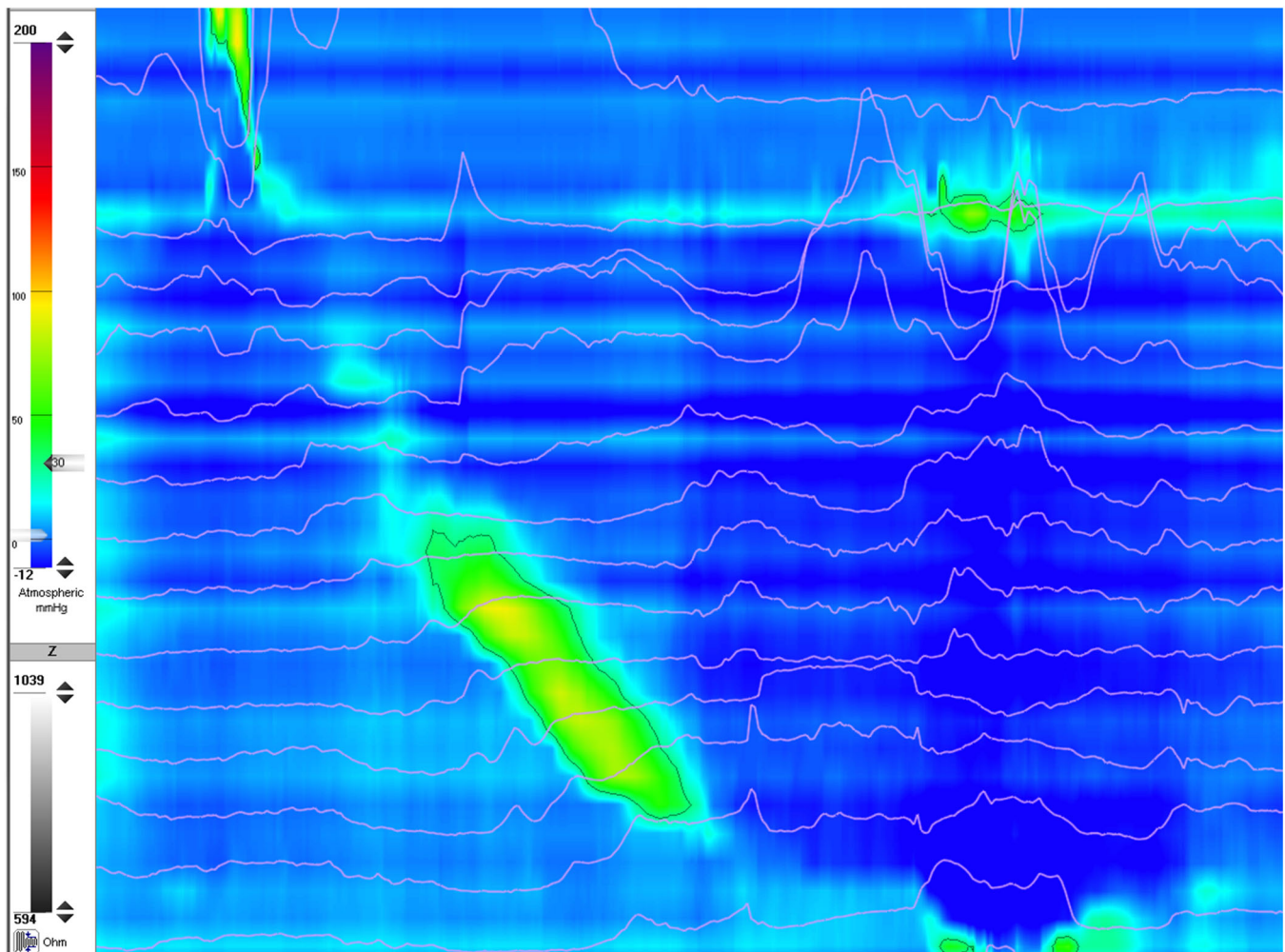
Modified, carbonated protocol which was previously proposed by Oude Nijhuis et al.<sup>5</sup> was well tolerated in our adolescent patients and provoked characteristic findings in all of them, confirming diagnosis in three patients who did not demonstrate characteristic findings on HRIM before carbonation challenge. The significance of conducting a carbonated provocation test is underscored by these findings, as it enables the identification of unique manometric characteristics and the induction of symptoms that would have otherwise gone undiagnosed. Further validation of the protocol with possible volume adjustment is needed in younger patients.

Ineffective esophageal motility was diagnosed in two of our patients, and abnormal bolus clearance was noted in three, with only one of them having normal esophageal peristalsis. It should be mentioned that Chicago classification 4.0, which is used for diagnosis of esophageal dysmotility, was not validated in pediatric patients, and extrapolating adult metrics to children may not be accurate.<sup>10</sup> Abnormal esophageal motility was previously reported in seven out of eight adult

**TABLE 3** Patient outcomes after botulinum toxin injection.

Patient	1	2	3	4	5
Botox injection	Yes	Yes	Yes	Yes	Yes
Botox units	65	70	60	75	70
Ability to burp	Yes (within 2 days)	Yes (within a week)	Yes (within days)	Yes	Yes (within a week)
Outcome	Improved	Resolved	Resolved	Improved	Improved
Remaining symptoms	Yes (gurgling)	None	No	Involuntary sounds—daily (more moderate)	Occasional gurgling (1/week)
Worsening over time	N/a	No	yes	No	No
Adverse events	None	None	None	None	Dysphagia for 3 days, resolved after steroid treatment
Repeated esophageal manometry	No	No	No	Yes (2 months post procedure)	No
Repeated botox injection	No	No	Yes (after 8 months, 80 units of botox)	No	No
Repeated botox outcome	Not performed	Not performed	Significant improvement, occasional gurgling (1/week)	Not performed	Not performed
Follow-up length (months)	0.1	6.5	9	6	2





**FIGURE 3** Esophageal manometry of patient number 4, 2 months after botox injection, showing low upper esophageal sphincter pressures, low proximal esophageal pressures, and burping.

patients with R-CPD with IEM being the most common finding.<sup>5</sup> Abnormality in primary esophageal peristalsis seems to be commonly associated with the R-CPD but it is unclear if it is primary or secondary to continuous air entrapment in these patients. It is of interest that secondary peristalsis was intact in all our patients on HRIM. Thus far there has been no data on long-term follow-up of this condition or its response to botulinum toxin injection or behavioral therapy in children.

While inability to burp and involuntary noise production was reported by all our patients, two patients also reported chest pain, heartburn, and reflux and one patient reported abdominal bloating. Four patients were initially clinically diagnosed with gastroesophageal reflux disease but had no response to proton pump inhibitors for at least a 6-week trial. While chest pain is an uncommon symptom in pediatrics, R-CPD should be considered in the differential diagnosis of this presentation in patients who also complain of inability to burp. The prevalence of chest pain in the adult population with R-CPD has not been described

and no reports of chest pain were published in the pediatric series either.<sup>8</sup> This may reflect co-existent sensory hypersensitivity induced by the trapped air.

Response to Botulinum toxin injection to the UES has been reported in cases of cricopharyngeal achalasia.<sup>12</sup> A large series of 200 patients reporting long-term efficacy of botox injection in patients with R-CPD included six pediatric patients.<sup>6</sup> In an additional report of five pediatric patients with clinical R-CPD, all patients responded to botox injection.<sup>8</sup> No data is available on the role or success of behavioral therapy in this condition. Our cohort exhibited comparable outcomes, with complete symptom resolution observed in two patients (40%) and symptom improvement in the remaining three patients. The need for repeated botulinum toxin injection which was noted in one patient (20%) is similar to the rate of 20.1%, reported by Hoesli et al. who did not maintain satisfactory ability to burp after 6 months follow-up.<sup>6</sup>

The introduction of HRIM has allowed better understanding and diagnosis of R-CPD. The increasing

availability of HRIM worldwide and the growing evidence of successful treatment of R-CPD after Botox injections into the UES, warrants the use of HRIM to confirm the diagnosis of R-CPD before proceeding to invasive treatment options and monitoring long-term outcomes.

The ability to burp should be enquired by pediatric gastroenterologists in patients presenting with other upper esophageal symptoms, especially with GERD-like symptoms, bloating, and reporting involuntary noises from the throat or chest. Due to lack of awareness and objective criteria, R-CPD is probably under- and misdiagnosed in the pediatric population, and providers should be aware of this condition.

Our case series is constrained by its limited number of patients and the absence of male patients, despite previous case series documenting the presence of male pediatric patients with R-CPD. Nevertheless, our findings might represent a true female preponderance in pediatric patients with R-CPD, as reported in adult literature.

While optimal treatment is not currently fully understood, the ability to ease symptoms with Botox injection and the reported safety is reassuring. We believe that a combined treatment with behavioral therapy and Botox injection may provide optimal results, but further research is needed to confirm this proposition.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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## REFERENCES

1. Kahrilas PJ, Dodds WJ, Hogan WJ. Dysfunction of the belch reflex. *Gastroenterology*. 1987;93(4):818-822.
2. Bastian RW, Smithson ML. Inability to belch and associated symptoms due to retrograde cricopharyngeus dysfunction: diagnosis and treatment. *OTO Open*. 2019;3(1):2473974X19834553. doi:10.1177/2473974X19834553

3. Tomizawa M, Kusano M, Aoki T, et al. A case of inability to belch. *J Gastroenterol Hepatol*. 2001;16(3):349-351.
4. Waterman DC, Castell DO. Chest pain and inability to belch. *Gastroenterology*. 1989;96(1):274-275.
5. Oude Nijhuis RAB, Snelleman JA, Oors JM, et al. The inability to belch syndrome: a study using concurrent high-resolution manometry and impedance monitoring. *Neurogastroenterol Motil*. 2022;34(5):e14250. doi:10.1111/nmo.14250
6. Hoesli RC, Wingo ML, Bastian RW. The long-term efficacy of botulinum toxin injection to treat retrograde cricopharyngeus dysfunction. *OTO Open*. 2020;4(2):2473974X20938342. doi:10.1177/2473974X20938342
7. Siddiqui SH, Sagalow ES, Fiorella MA, Jain N, Spiegel JR. Retrograde cricopharyngeus dysfunction: the Jefferson experience. *Laryngoscope*. 2023;133(5):1081-1085.
8. Hoffman MR, Schiffer B, Patel RA, Smith ME. "I've never been able to burp": preliminary description of retrograde cricopharyngeal dysfunction in children. *Int J Pediatr Otorhinolaryngol*. 2022;161:111261.
9. Rosen R, Garza JM, Tipnis N, Nurko S. An ANMS-NASPGHAN consensus document on esophageal and antroduodenal manometry in children. *Neurogastroenterol Motil*. 2018;30(3):13239. doi:10.1111/nmo.13239
10. Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago classification version 4.0©. *Neurogastroenterol Motil*. 2021;33(1):e14058.
11. Sperber A. Epidemiology and burden of irritable bowel syndrome: an international perspective. *Gastroenterol Clin North Am*. 2021;50(3):489-503. doi:10.1016/j.gtc.2021.04.001
12. Messner A, Ho AS, Malhotra PS, Koltai PJ, Barnes MA. The use of botulinum toxin for pediatric cricopharyngeal achalasia. *Int J Pediatr Otorhinolaryngol*. 2011;75(6):830-834.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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