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Upper Esophageal Sphincter and Esophageal Motility Pathology on Manometry in Retrograde Cricopharyngeal Dysfunction

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Abstract

Objective.—There exists a paucity of data regarding the mechanism and manometric findings in retrograde cricopharyngeal dysfunction (RCPD). In this study, we aimed to compare esophageal physiologic findings between patients with RCPD compared to an asymptomatic cohort.

Study Design.—Case-control study.

Setting.—Tertiary Care Center.

Methods.—Esophageal high-resolution impedance manometry was completed preoperatively in patients diagnosed with RCPD. Manometric data were compared between the RCPD and asymptomatic cohorts. A 2:1 age-sex-matched asymptomatic cohort was used as the control group. Treatment response was assessed among the RCPD cohort.

Results.—Thirty-nine patients are included: 13 RCPD [mean age: 31.1 (SD: 12.6) years, female sex: 11 (85%)] and 26 asymptomatic [mean age: 32.1 (SD: 1.5) years, female sex: 22 (85%)]. The RCPD cohort, compared to the asymptomatic cohort, exhibited significantly greater upper esophageal sphincter (UES) length [4.5 (SD: 0.7) vs 3.7 (0.9) cm, $P = .01$] and higher UES basal pressures [91.9 (35.0) vs 49.7 (25.5) mm Hg, $P = .002$]. Patients with RCPD demonstrated higher rates of ineffective swallows [70.0% (31.6%) vs 15.4% (21.6%), $P < .001$] and incomplete bolus clearance [81% (22.0%) vs 21.8% (30.0%), $P < .001$]. All patients who underwent cricopharyngeal botulinum injections experienced initial improvement of symptoms with 3 patients requiring repeat intervention.

Conclusion.—RCPD is associated with a longer UES, elevated UES basal pressures, and an increased incidence of ineffective esophageal motility. This study is the first to compare

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Author Contributions

Andrew Yousef, contributed to study design, analysis, and interpretation of data, and writing of the manuscript; **Amanda Krause**, contributed to study design, interpretation of data, statistical analysis, and writing of the manuscript; **Rena Yadlapati**, contributed to the study design, study recruitment, critical revisions of the manuscript, and study supervision; **Priya Sharma**, contributed to statistical analysis and review of the manuscript; **Philip A. Weissbrod**, contributed to the study design, study recruitment, critical revisions of the manuscript, and study supervision.

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preoperative manometry results among patients with RCPD to those of an asymptomatic cohort, providing insights into the mechanism of RCPD.

Keywords

belching disorders; diagnostic tools; high-resolution manometry; upper esophageal sphincter

Retrograde cricopharyngeal dysfunction (RCPD) is a relatively novel clinical entity that has garnered increasing attention in recent years. Characterized by the inability to belch, often accompanied by abdominal discomfort, this condition has presented unique diagnostic and therapeutic challenges for health care providers.[1,2] Despite its clinical significance, RCPD remains an understudied disorder within the realm of gastroesophageal and upper esophageal sphincter (UES) dysmotility.

Patients afflicted by RCPD often experience a range of distressing symptoms, including chronic bloating, abdominal discomfort, and excessive flatulence.[1] These symptoms not only affect patients' physical well-being but also have substantial psychosocial implications, as they may lead to social embarrassment and decreased overall quality of life.[3]

Despite the clinical significance of RCPD, the pathophysiology and underlying mechanisms of this condition remain poorly understood. Prior to 2019, there were only 3 isolated case reports describing patients with symptoms now recognized as consistent with RCPD.[4–6] In 2019, Bastian et al published a series of patients with a constellation of symptoms (inability to belch, bloating, gurgling, flatulence) that improved with cricopharyngeal botulinum injections, subsequently coining the diagnosis "retrograde cricopharyngeal dysfunction." This diagnosis was made on symptoms alone, lacking confirmatory physiological testing.[1] Subsequently, several studies have reported similar findings with symptom presentation and improvement postbotulinum injections serving as the primary diagnostic criteria.[2,3,7–10] However, the precise etiology of RCPD, its clinical presentation, diagnostic abnormalities, and the optimal management strategies remain subjects of ongoing investigation. There also remains a significant need for an objective diagnostic modality for RCPD and a means to monitor treatment response.

Considering these challenges and the limited research available on RCPD, the present study aims to use esophageal high-resolution manometry (HRM) to expand our understanding of this condition. Through a comprehensive examination of patient characteristics, clinical presentation, diagnostic approaches, and therapeutic interventions, we compare HRM findings in patients with RCPD to age and sex-matched asymptomatic controls.

Methods

Study Design and Setting

This single-center retrospective case-control study included adult case and control patients that underwent HRM. The case group included patients with history of RCPD that were treated at UCSD over 1 year (August 2022 to August 2023). The control group included patients without esophageal symptoms that had undergone HRM at UCSD between December 2015 and June 2020. The a priori design was to include 2 controls for every

1 case with an age and sex match. Approval for this study was obtained from the UCSD Institutional Review Board.

Case Cohort: RCPD

The case cohort included adult patients with a clinical diagnosis of RCPD as previously defined by Bastian et al.[1] All patients were evaluated by a laryngologist and esophagolologist. Assessments included a preoperative appointment where a history, physical exam, and flexible laryngoscopy were completed, as well as an HRM study. Additionally, patients completed the Eating Assessment Tool (EAT-10) at their intake visit.[11] Exclusion criteria included patients with any pertinent esophageal or hypopharyngeal treatment history in the past year, evidence of oropharyngeal dysphagia, diagnosis of any neurologic conditions, history of head and neck cancer treatment, or history concerning for iatrogenic esophageal injury.

Patients with symptomatology consistent with RCPD, regardless of HRM findings, were offered cricopharyngeal botulinum toxin injections. Cricopharyngeal botulinum toxin injections were completed in the operating room. Briefly, after induction of general anesthesia, a laryngoscope was used to view the cricopharyngeus. Once the cricopharyngeal prominence was clearly visualized and palpated, injections were performed with a 26 G Xomed Injection Needle (Medtronic). Injections were placed at 5 and 7 O'clock within the operative field directly into the cricopharyngeal muscle under direct visualization. Botulinum toxin (Allergan Inc., Botox, onabotulinumtoxinA, 2009) was typically diluted to 100 U/1 mL of preservative free saline. On initial operative intervention, patients were injected between 50 and 100 U of botulinum depending on surgeon preference. This was based on prior studies given that there is no current consensus on the optimal dosing of botulinum for RCPD.[1–3] Patients were discharged on the same day of surgery. Postoperatively, they were clinically evaluated in the UCSD Voice and Swallow Center. Treatment response was assessed by subjective improvement of symptoms based on patient interviews. All patients were seen for at least 1 postoperative visit.

Control Cohort: Asymptomatic

Data on an asymptomatic cohort of obese patients who were undergoing HRM for bariatric surgery evaluation were also collected at UCSD between December 2015 and June 2020. Patients were excluded if they had any symptoms including dysphagia, heartburn, regurgitation, atypical chest pain, cough, voice changes, globus sensation, throat clearing, odynophagia, or belching. In addition, patients were excluded if they were unable to undergo HRM, had a prior foregut surgery, or were <18 years of age. Asymptomatic controls were first matched via sex, followed by age, with 2 asymptomatic controls for every 1 RCPD patient. If there was more than 1 patient that fit these criteria, the patient with the lowest body mass index (BMI) was chosen.

HRM

HRM was completed using the Medtronic system. A solid-state assembly with 36 circumferential pressure sensors at 1-cm intervals, 18 impedance sensors at 2-cm intervals, and 3 intragastric pressure sensors, according to the Chicago Classification version 4.0

(CCv4.0), was utilized.[12] The procedure was performed after a minimum of a 6-hour fast. The HRM catheter was placed transnasally and positioned so that data could be recorded from the hypopharynx to the stomach. After 2 minutes of baseline records, the HRM protocol was performed with ten 5-mL liquid swallows in the supine position and five 5-mL liquid swallows in the upright position. HRM studies were analyzed using ManoView analysis software (Medtronic). Diagnoses were based on CCv4.0.[12] HRM variables assessed included hiatal hernia size, LES integrated relaxation pressure (IRP), UES length, UES basal pressure, UES IRP, distal contractile integral (DCI), distal latency (DL), percentage of ineffective, failed, weak, fragmented, intact, and hypercontractile swallows, as well as percent of incomplete bolus clearance. Briefly, DCI is a measure of esophageal peristalsis evaluating the contractile vigor of the esophagus, IRP assesses the relaxation pressure across the esophagogastric junction in response to deglutition, and DL assesses the latency of deglutitive inhibition.[12] Ineffective swallows were defined as a weak, failed, or fragmented swallow based on DCI as previously described.[12]

Data Collection

Demographic data collected included age, sex, race, BMI, smoking history, use of acid-suppressive medications, and anxiety or depression. HRM variables were collected as shown above. Barium swallow and computed tomography of the chest and abdomen were also included if completed. If patients opted for operative intervention, operative data including date of surgery, units of botulinum toxin injected, postoperative improvement of symptoms, temporary side effects of surgery, postoperative complications, and need for repeat intervention were collected.

Statistical Analysis

Primary analyses aimed to compare manometric findings between the RCPD cohort and the asymptomatic control cohort. Secondary analyses included assessing treatment outcomes in the RCPD group and assessing factors associated with treatment response. Missing data were not imputed. Descriptive statistics including means, medians, and frequencies were calculated as appropriate. Mann-Whitney U tests were used to compare means of groups for continuous variables and Fisher Exact Tests were used for categorical variables. Not all exact P values could be computed for the Mann-Whitney U test due to ties and a small sample size. Odds ratios were calculated to determine the odds of ineffective esophageal motility (IEM) or absent contractility on HRM. Statistical analyses were performed using R v4.2.0.

Results

Baseline Demographics RCPD

A total of 13 patients were included in the RCPD cohort; the mean age was 31.1 (SD: 12.6) years, the mean BMI was 24.6 (2.8) kg/m^2, and there were 11 (85%) females (Table 1). Five patients (5/13, 38%) were either on a proton pump inhibitor (PPI) or histamine H2 receptor blocker at time of evaluation. The most common symptoms at time of initial presentation were inability to belch (100%), bloating (92%), flatulence (62%), and gurgling (46%). Flexible laryngoscopy was completed in all patients with 12 patients having normal exams

with no nasopharyngeal, supraglottic, hypopharyngeal, or glottic anatomic abnormalities. There was 1 patient with an abnormal finding of a small aryepiglottic fold cyst. Three patients had a modified barium swallow and 2 patients had imaging of the chest and abdomen completed by the time they were referred to our institution with no abnormalities identified on any of these studies. Patients had EAT-10 scores completed at their intake visit with a minimally elevated mean of 1.6.

Baseline Demographics Asymptomatic Cohort

A total of 26 asymptomatic patients, sex and age-matched to the RCPD cohort, were included; the mean age was 32.1 (SD: 11.5) years, the mean BMI was 45.1 (5.5) kg/m^2, and there were 22 (85%) females (Table 1). Five patients (19%) were either on a PPI or H2 blocker at time of evaluation.

Primary Analysis: Manometric Data between RCPD and Asymptomatic Cohorts

In terms of UES findings on HRM, the RCPD cohort compared to the asymptomatic cohort had significantly greater UES length [4.5 cm (0.7) vs 3.7 (0.9), $P = .01$] and significantly higher UES basal pressures [91.9 mm Hg (35.0) vs 49.7 (25.5), $P = .002$] (Table 2). In terms of esophageal peristalsis, the RCPD cohort compared to the asymptomatic cohort had significantly lower mean DCI [747.4 mm Hg cm s (717.3) vs 2264.9 (1758.5), $P = .003$] and a significantly greater proportion of ineffective swallows [70.0% (31.6%) vs 15.4% (21.6%), $P = .002$] and incomplete bolus clearance [81.1% (22.0%) vs 21.8% (30.0%), $P = .001$; Figure 1]. Patients in the RCPD cohort had an increased odds of IEM or abstract contractility when compared to the asymptomatic cohort (odds ratio: 37.5, 95% confidence interval: 3.5, 399.4, $P < .001$). No significant difference was found in hiatal hernia size between the RCPD and asymptomatic cohort [1.1 cm (1.2) vs 0.8 (1.9), $P = .18$]. In the RCPD cohort, there was no evidence of spasticity (0% hypercontractile or premature peristalsis) in the esophageal body.

Operative and Postoperative Results

Eight RCPD patients (62%) elected to proceed forward with surgery. The mean botulinum toxin injected was 75.6 (SD: 10.5) units. Of this group, 100% reported complete resolution or partial improvement of their symptoms as assessed at their initial postoperative appointment. Seven patients (88%) had temporary side effects after botulinum injection: 6 patients (75%) experienced short-lived dysphagia and 4 patients (50%) endorsed temporary regurgitation. All side effects were temporary and self-resolved without intervention. Three patients (37.5%) had return of symptoms between 3 and 20 weeks postoperatively (Table 3). Patients with symptom recurrence had higher rates of ineffective swallows [90.0% (14.1) vs 50.0 (26.5), $P = .20$) when compared to patients with sustained symptom resolution. A diagnosis of IEM or absent contractility was more commonly found in patients with symptom recurrence than those with sustained symptom resolution [2 (67%) vs 1 (20%), $P = .46$].

All 3 patients that had repeat operative intervention received 80 U of botulinum at an average of 11.7 months (SD: 9.4 months) following initial surgery. After repeat intervention, all patients had improvement in their symptoms. Two patients had improvement, but not

resolution with repeat injections. Patients were followed for an average of 222 (272) days postoperatively.

Discussion

RCPD is a relatively recent entity that is currently diagnosed clinically based on symptom presentation.[3,7–9,13] However, the mechanistic underpinnings of RCPD remain poorly understood, emphasizing the necessity for additional research to elucidate the pathophysiology of this disorder. This is the first study to compare preoperative manometry results with those of a normal cohort, providing additional insights into the underlying pathophysiology of RCPD.

In this case-control study of 39 patients, the key findings are that patients with RCPD exhibit greater UES length and basal pressure as well as higher rates of IEM. We also find that patients with symptom recurrence had a trend to have higher rates of ineffective swallows. The impact of the present study is 2-fold: (1) this study highlights the potential importance of HRM prior to cricopharyngeal botulinum injections to identify pathology; (2) this study contributes to our understanding of the underlying mechanism of RCPD generating the hypothesis that poor EM and obstructive UES physiology could lead to air trapping and the inability to belch.

Our findings of greater UES length, higher UES basal pressures, and higher rates of ineffective swallow and incomplete bolus clearance in patients with RCPD is a novel finding not previously well described in the literature. A solitary prior study by Oude Nijhuis et al examined HRM results in patients with RCPD, albeit without a control group for comparison.[14] Despite no formal analysis comparing their results to a normal cohort, their findings of preoperative UES basal pressures of 95.7 mm Hg is similar to our findings in our cohort with preoperative UES basal pressures of 91.9. Their study also shows a decrease in UES basal pressures following treatment with cricopharyngeal botulinum injections indicating the potential importance of the UES in the pathophysiology of this disease. Furthermore, these findings corroborate with earlier physiological studies investigating manometric patterns during belching. These previous studies demonstrate that retrograde gaseous distension of the esophagus and UES relaxation are fundamental aspects of normal belching physiology.[10,15] Given the need for UES relaxation to allow for belching and our findings of higher UES basal pressures and UES length in RCPD patients, we hypothesize that the mechanism of RCPD may be related to an inability to release built-up pressure in the esophagus leading to air trapping and associated discomfort. This air trapping then can lead to more downstream gastrointestinal discomfort causing the bloating and flatulence symptoms that we see in RCPD patients (Figure 2).

Similarly, we see high rates of dysfunctional swallows in our patients with RCPD. This finding was similarly seen in Oude Nijhuis et al with high rates of IEM and absent contractility, though again further analysis is limited due to a lack of a comparison group in their study.[14] During normal swallowing, the cricopharyngeus relaxes and the UES opens from the forces of the bolus as it enters the esophagus.[14,16,17] With higher UES basal pressures and length in RCPD, higher pressures from deglutition may be needed to

overcome the UES basal pressures and thereby there may be a mechanistic relationship with hypomotile primary peristalsis. Similarly, in these patients, the feedback mechanism of air in the esophagus that leads to UES relaxation may also be impaired. This again lends further credence to our theory for RCPD that higher UES pressures lead to the inability of the upper esophagus to open and can cause air trapping in the esophagus.

HRM plays a crucial role in distinguishing swallowing disorders, such as achalasia or EM disorders. Understanding the manometric findings in RCPD is of clinical relevance for several reasons. First, HRM can aid in the identification of suitable candidates for RCPD treatment, as distinguishing RCPD from other disorders can sometimes prove to be clinically challenging. Ensuring patients with an unclear diagnosis have manometric findings consistent with RCPD can ensure patients are receiving appropriate treatment. For example, it can be difficult to confirm an RCPD diagnosis in a patient with some, but not all of the classical symptoms.[1] HRM can be used as an adjunct tool that can guide the clinician if they see similarly elevated UES basal pressures, UES length, and a dysfunctional swallow. Second, HRM may be able to aid with providing the prognostic value of botulinum injections for RCPD. Potentially, patients with more pronounced abnormalities on HRM, such as extremely elevated UES basal pressures or a higher frequency of ineffective swallows, may have more substantial benefits from treatment. Conversely, patients without abnormal manometric findings may be less likely to have symptomatic improvement based on our limited observations. However, additional studies are needed to further assess the role of HRM in the diagnosis and treatment of RCPD.

As a secondary aim, we sought to provide additional information on patient presentation, clinical course, and postoperative improvement in patients with RCPD. At this point, there are few studies that look at long-term outcomes in patients with RCPD[1–3,7] and our long follow-up time for our patients provides additional support for the use of botulinum injections for symptom improvement in RCPD. Among our RCPD cohort, the most common symptoms were inability to belch (100%) and bloating (92%), aligning with prior research that assessed preoperative symptoms and reported similar rates of inability to belch and bloating.[1,3] Patients who underwent operative intervention received an average of 76 U of botulinum injection. This is again similar to prior studies with mean units injected between 50 and 100 U depending on the study.[1–3] While there is a single case report describing the use of only 10 U of botulinum toxin to treat RCPD, this low dose remains an outlier in the existing literature.[13] Among patients that underwent operative management in our study, 75% endorsed temporary dysphagia and 50% experienced temporary regurgitation. Temporary dysphagia and regurgitation after cricopharyngeal botulinum injections have been documented in prior studies as well, though rates vary between studies.[1,3] Anecdotally, dysphagia symptoms are well tolerated, in particular, in this young patient population. Finally, all of our patients had initial complete or partial resolution of their symptoms after initial operative intervention, though 3 required repeat injection for return of symptoms. After repeat injection, all patients had improvement of their symptoms. This is again consistent with prior studies reporting symptom resolution rates ranging from 88% to 96%.[1–3,7] We did have patients that had improvement but did not have complete resolution of their symptoms with repeat intervention. Of note, one of these patients had evidence of dysmotility on manometry. Due to few patients needing repeat surgical intervention,

we are limited in our ability to determine factors associated with the need for repeat surgical intervention. However, we did see higher rates of ineffective and failed swallow in patients requiring repeat intervention. Additional areas of future research would be to determine if patients with dysmotility and higher UES pressures have differences in results with botulinum injections compared to patients without dysmotility and only elevated UES pressures.

Strengths of this study include the age and sex-matched case-control study design which enables meaningful comparisons as well as the well-characterized study population and HRM data. Limitations of this study include those inherent to a retrospective study including the potential for selection bias, as well as the small sample size. However, we present a relatively robust sample size of RCPD in light of disease prevalence. In addition, the asymptomatic cohort was a population with obesity undergoing evaluation for bariatric surgery and thus we were unable to match for BMI. Future prospective studies with larger cohorts that are matched for BMI are warranted to validate our findings, explore potential subtypes within RCPD, and identify factors and manometry findings associated with treatment response.

Conclusion

Objective data in the setting of RCPD is an under described etiology. This study provides significant evidence of abnormal manometric findings in patients with RCPD, emphasizing the potential clinical utility of manometry in the diagnosis and confirmation of RCPD. These findings contribute to the ongoing efforts to improve the management and outcomes of patients with RCPD. Further research in this field is essential to refine our understanding of this condition and to develop additional diagnostic and therapeutic strategies.

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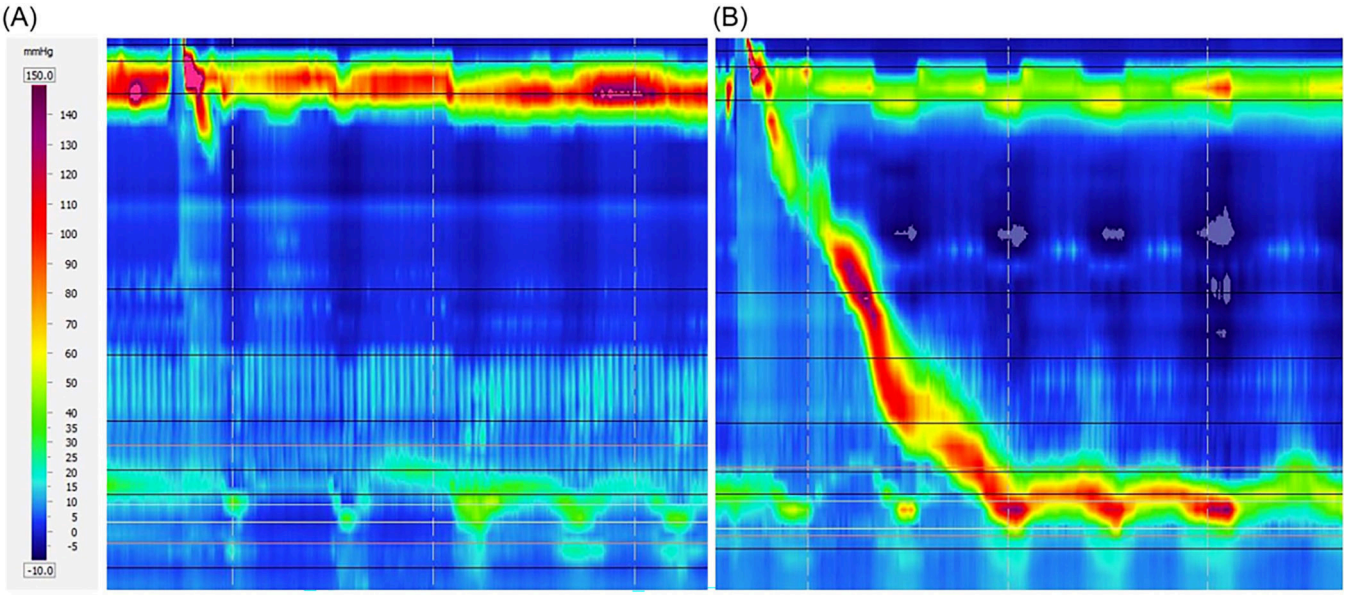

Figure 1.

High-resolution manometry. (A) Retrograde cricopharyngeal dysfunction patient with ineffective esophageal motility. Upper esophageal sphincter (UES) basal pressure 92.7 mm Hg; UES length 4.2 cm. (B) Age-matched control patient with normal esophageal motility. UES basal pressure 59.7 mm Hg; UES length 3.1 cm.

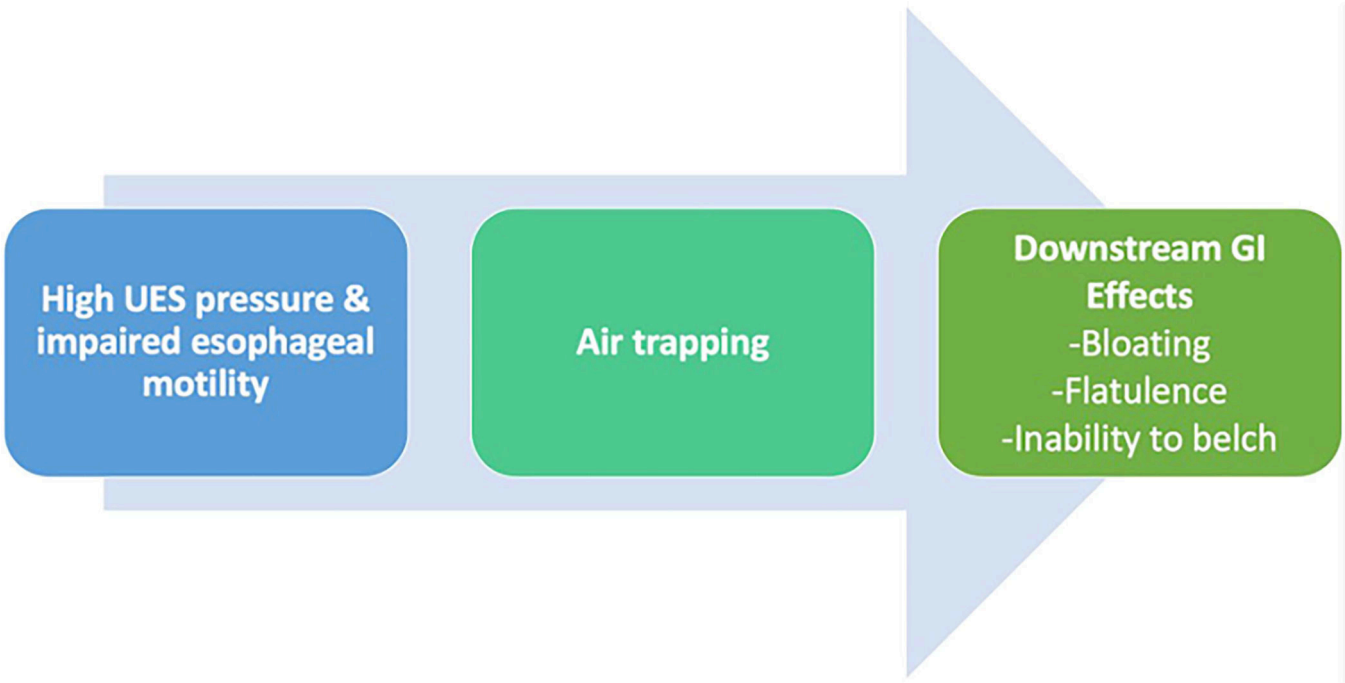

Figure 2.
Theoretical pathophysiology of retrograde cricopharyngeal dysfunction. Higher upper esophageal sphincter (UES) pressures and impaired motility lead to air trapping in the esophagus. This air trapping then leads to downstream effects of an inability to belch, bloating, and flatulence.

Table 1.

Patient Demographics and Preoperative Evaluation

	RCPD cohort (n = 13)	Asymptomatic cohort (n = 26)	*P* value
Demographics			
Age, y	31.1 (12.6)	32.1 (11.5)	.60
Sex, female	11 (85%)	22 (85%)	1.00
Ethnicity			
Hispanic	0 (0%)	12 (46%)	<.001
Asian	0 (0%)	5 (19%)	
Native Hawaiian/Pacific Islander	1 (8%)	0 (0%)	
Black	0 (0%)	2 (8%)	
White	11 (85%)	5 (19%)	
Other/unknown	1 (8%)	2 (8%)	
BMI, kg/m^2	24.6 (2.8)	45.1 (5.5)	<.001
Medications			
Proton pump inhibitor	4 (31%)	5 (19%)	-
H2 blocker	1 (8%)	0 (0%)	
Anxiety/depression	4 (31%)	8 (31%)	1.0
Smoking			
Never	12 (92%)	16 (61%)	.02
Former	1 (8%)	9 (35%)	
Current	0 (0%)	1 (4%)	
Symptoms			
Inability to belch	13 (100%)		-
Bloating	12 (92%)		-
Flatulence	8 (62%)		-
Gurgling	6 (46%)		-
Nausea	5 (38%)		-
Dysphagia	3 (23%)		-
Globus	3 (23%)		-
Difficulty vomiting	2 (15%)		-

	RCPD cohort (n = 13)	Asymptomatic cohort (n = 26)	*P* value
RSI	9.8 (7.3)		-
EAT-10 score	1.6 (2.8)		-

Abbreviations: BMI, body mass index; EAT-10, Eating Assessment Tool; RSI, reflux symptom index.

Table 2.

HRM Results

	RCPD cohort (n = 13)	Asymptomatic cohort (n = 26)	*P* value
HRM			
UES length, cm	4.5 (0.7)	3.7 (0.9)	.01
UES basal pressure, mm Hg	91.9 (35.0)	49.7 (25.5)	.0016
UES IRP, mm Hg	−2.4 (6.2)	0.4 (5.3)	.22
Hiatal hernia size, cm	1.1 (1.2)	0.8 (1.9)	.18
LES IRP, mm Hg	9.6 (3.8)	8.6 (5.4)	.67
DCI, mm Hg cm s	747.4 (717.3)	2264.9 (1758.5)	.0027
Distal latency, s	6.4 (0.4)	6.9 (1.4)	.80
% Ineffective swallows (failed, weak, fragmented)	70.0 (31.6)	15.4 (21.6)	.0002
% Failed swallows	48.9 (37.2)	3.8 (9.0)	.0003
% Weak swallows	18.9 (15.4)	9.2 (13.5)	.049
% Fragmented swallows	2.2 (4.4)	2.3 (6.5)	.58
% Intact swallows	30.0 (31.6)	84.6 (21.6)	.0002
% Premature swallows	0.0 (0.0)	0.0 (0.0)	-
% Hypercontractile swallows	0 (0)	1.9 (9.8)	.60
% Incomplete bolus clearance	81.1 (22.0)	21.8 (30.0)	.00017
Diagnosis			
Achalasia (Types I-III)	0 (0%)	0 (0%)	
Esophagogastric junction outflow obstruction	0 (0%)	0 (0%)	.00067
Diffuse esophageal spasm	0(0%)	0 (0%)	
Hypercontractile esophagus	0 (0%)	1 (4%)	
IEM or absent contractility	6 (50%)	1 (4%)	
Normal	4 (50%)	24 (92%)	

HRM data available for each metric varied.

Abbreviations: DCI, distal contractile integral; HRM, high-resolution manometry; IEM, ineffective esophageal motility; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; RCPD, retrograde cricopharyngeal dysfunction; UES, upper esophageal sphincter.

Table 3.

Factors Associated With Repeat Intervention in RCPD Patients

	RCPD patients with improvement after 1 intervention (n = 5)	RCPD patients requiring repeat intervention (n = 3)
Demographics		
Age, y	21.2 (2.3)	39.3 (20.3)
Sex, female	5 (100%)	3 (100%)
BMI, kg/m^2	23.6 (1.7)	25.7 (4.0)
Medications		
Proton pump inhibitor	2 (40%)	0 (0%)
H2 blocker	1 (20%)	0 (0%)
Anxiety/depression	1 (20%)	2 (67%)
Smoking		
Never	5 (100%)	3 (100%)
Symptoms		
Inability to belch	5 (100%)	3 (100%)
Bloating	4 (80%)	3 (100%)
Flatulence	3 (60%)	3 (100%)
Gurgling	3 (60%)	1 (33%)
Nausea	3 (60%)	2 (67%)
Dysphagia	1 (20%)	1 (33%)
Globus	1 (20%)	1 (33%)
Difficulty vomiting	0 (0%)	2 (67%)
RSI	11.3 (10.3)	4.5 (3.5)
High-resolution manometry		
UES length, cm	4.8 (1.1)	4.6 (0.6)
UES basal pressure, mm Hg	122.1 (20.0)	98.4 (49.6)
% Ineffective swallows (failed, weak, fragmented)	50.0 (26.5)	90.0 (14.1)
% Failed swallows	23.3 (25.2)	80.0 (28.3)
% Weak swallows	26.7 (20.8)	10.0 (14.1)
% Intact swallows	50.0 (26.5)	10.0 (14.1)
% Incomplete bolus clearance	63.3 (25.2)	80 (28.3)

	RCPD patients with improvement after 1 intervention (n = 5)	RCPD patients requiring repeat intervention (n = 3)
Operative findings		
Units of botulinum injected at first operative intervention	80 (0.0)	68.3 (16.1)
Postoperative temporary complications		
Dysphagia	5 (100%)	1 (33%)
Regurgitation	2 (40%)	2 (67%)
Days between operative intervention	-	350.0 (283.1)
Units of botulinum injected at second operative intervention	-	80.0 (0.0)

Abbreviations: BMI, body mass index; RSI, reflux symptom index; UES, upper esophageal sphincter.