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ORIGINAL ARTICLE

Gastroenterology



Esophago-gastric junction findings on high resolution impedance manometry in children with esophageal atresia

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Abstract

Objectives: Using high resolution impedance manometry (HRIM), this study characterized the esophago-gastric junction (EGJ) dynamics in children with esophageal atresia (EA).

Method: Esophageal HRIM was performed in patients with EA aged less than 18 years. Objective motility patterns were analyzed, and EGJ data reported. Controls were pediatric patients without EA undergoing investigations for consideration of fundoplication surgery.

Results: Seventy-five patients (M:F = 43:32, median age 1 year 3 months [3 months–17 years 4 months]) completed 133 HRIM studies. The majority (64/75, 85.3%) had EA with distal tracheo-esophageal fistula. Compared with controls, liquid swallows were poorer in patients with EA, as evident by significant differences in distension pressure emptying and bolus flow time (BFT). The integrated relaxation pressure for thin liquid swallows was significantly different between EA types, as well as when comparing patients with EA with and without previous esophageal dilatations. The BFT for solid swallows was significantly different when compared with EA types.

Conclusions: We have utilized HRIM in patients with EA to demonstrate abnormalities in their long-term EGJ function. These abnormalities correlate with poorer esophageal compliance and reduced esophageal peristalsis across the EGJ. Understanding the EGJ function in patients with EA will allow us to tailor long-term management to specific patients.

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JPGN



KEYWORDS esophagus, motility, pediatric

1 | INTRODUCTION

Esophageal atresia (EA) is the most significant congenital anomaly of the esophagus, and affects up to 1 in 2600 Australian newborns.¹ Congenital impairment of neural innervation, as well as narrowing and reduced compliance at the surgical anastomosis, may impact upon the mechanism of the esophago-gastric sphincter, particularly in patients with long-gap EA. Such changes, including changes in tension in the esophagus, may also lead to increased susceptibility to gastro-esophageal reflux (GER). It is not uncommon for patients with EA to have severe enough GER to warrant fundoplication, which may occur in 10%–45% of patients with EA.^{2,3}

Currently, there are no published objective motility data that have assessed the esophago-gastric junction (EGJ) in patients with EA. The development of high resolution impedance manometry (HRIM) have facilitated accurate and reliable measurement of the EGJ mechanics.⁴ These include contractility and relaxation, as well as esophageal bolus transport and emptying. HRIM has been utilized in children to assess for dysphagia in other conditions, such as achalasia and diffuse esophageal spasm, and in pre- and postfundoplication settings.⁵⁻⁷ The HRIM technique has yet to be systematically applied in patients with EA.

The aim of our study, as part of a larger HRIM study investigating patients with EA, was to understand the motility mechanics in EA, with a particular focus on the EGJ.

2 | METHODS

Eligible patients with EA were identified from the Nate Myers Oesophageal Atresia Database, at The Royal Children's Hospital, Melbourne (RCH). This is the

What is Known

- Swallowing difficulties in children with repaired esophageal atresia suggest the mechanism of the sphincter at esophago-gastric junction may be disrupted in these patients.
- Objective data that characterize the esophagogastric junction in children with esophageal atresia are lacking from the literature.

What is New

- Poorer liquid swallow function in the esophageal atresia group compared with the control group was detected for distension pressure emptying (mean difference 6.65 mmHg) and bolus flow time (mean difference –0.86 min).
- Integrated relaxation pressure for thin liquid swallows was significantly different when compared with esophageal atresia types.

world's largest single-center prospective database of patients with EA, with data collected from 1948 onwards. Carers of eligible patients were contacted for recruitment, via letters and phone calls, or face-toface discussions if they were present in the hospital for clinical indications (outpatient visits, inpatient admissions). Data for both asymptomatic and symptomatic patients were collected.

Patients up to 18 years old were eligible to participate. The study employed a prospective longitudinal cohort study design. This study was approved by the RCH Human Research Ethics Committee (HREC 35089A and HREC 35089B).

HRIM was performed with a pediatric solid-state catheter (8 Fr, 2.7 mm diameter; with 32×1 cm spaced

pressure sensors; 16×2 cm impedance electrode segments; UniSensor) linked to a Medical Measurement Systems (MMS) program (Laborie). Catheter placement was performed by an experienced manometry nurse, and correct placement determined by the pressures recorded on the MMS program. Esophageal body motor activity and bolus transport patterns were collected.

Participants sat upright during the study and followed the following protocol for swallows: 10 swallows of thin standardized bolus medium (SBM) or equivalent [IDDSI (International Dysphagia Diet Standardization Initiative)] 0; 10 swallows of thick SBM or equivalent (IDDSI 4); and 5 swallows of solids (bread) or equivalent (IDDSI 7). Liquid volumes were standardized at 5 mL when the child was able to swallow this volume. This was delivered either via a syringe or spoon, at one go, depending on child cooperation. Solid swallows (bread) were given to the child to take a bite from, and swallows recorded after a period of mastication.

Limitations in the pediatric setting were also accounted for, and the protocol adjusted according to the individual child's ability to swallow and/or cooperate. The catheter was removed before the conclusion of the study recording. At the time of the study, parents (or patients who were old enough) also completed a validated dysphagia questionnaire modeled on the composite dysphagia score of Dakkak and Bennett (Supporting Information: Content 1).⁸ The questionnaire assessed dysphagia for nine different food types with increasing viscosity (water to meat; scale 0–45; no dysphagia = 0). This questionnaire was utilized as it provides a quick and convenient assessment with accuracy and clinical utility.⁸

Each deidentified study was uploaded to Swallow Gateway[™] (swallowgateway.com; version© 2020), a web-based application for HRIM analysis and multidisciplinary communication.⁹ Analysis was undertaken in collaboration by three to five clinicians (STT, NS, AC, TO, and/or SK). All clinical data were obtained from the RCH electronic medical record (Epic). Data points included gestational age, birth weight, VACTERL association (vertebral anomalies, anorectal malformation, cardiac anomalies, tracheo-esophageal fistula, renal anomalies, limb anomalies), chromosomal abnormalities, intraoperative findings, postoperative complications, need for esophageal dilatations, swallowing difficulties, and choking episodes. Types of EA were classified according to the Gross classification: Type A—pure EA, Type B—EA with proximal tracheoesophageal fistula (TEF), Type C-EA with distal TEF, Type D—EA with double TEF, Type E—isolated TEF.¹⁰ Patients with EA and VACTERL association were identified in accordance with current clinical definitions for VACTERL association, that is, three or more of the aforementioned VACTERL anomalies.¹¹ Esophageal dilatations typically focused on addressing the area of previous surgical anastomosis, given its propensity for 3

narrowing and reduced compliance. Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools, hosted at the Murdoch Children's Research Institute (MCRI).¹²

For the analysis of HRIM metrics, patients with good quality studies were assessed. This was defined by having undertaken at least three analyzable bolus swallows of thin SBM, thick SBM, or solids.^{9,13} Due to the invasive nature of HRIM, generating normative data in healthy children is not ethical. Therefore, as controls, data were utilized from a previous cohort of children without EA. These children had undergone HRIM for GER symptoms as part of a series of investigations for consideration of a fundoplication surgery. Metrics pertaining to EGJ function analyzed have been previously described and included the EGJ resting pressure, EGJ contractile integral (CI), integrated relaxation pressure over 4 s (IRP4s), intrabolus distension pressure during esophageal emptying (DPE), and bolus flow time (BFT).9,14-22

Statistical analysis was conducted utilizing Minitab Statistical Software for Mac© (2020). Descriptive statistics are median and ranges for patient demographics and mean and standard error for HRIM metrics. Analysis was undertaken with a general linear model. Esophageal length was included as a co-variate in the analysis, as it is known to affect biomechanical findings on HRIM.⁹ Esophageal length is thought to influence metrics such as EGJ resting pressure, IRP4s, and distension pressures. Since esophageal length will be expectedly variable across children of different ages, we controlled for length to allow the detection of differences in metrics independent of this factor.

3 | RESULTS

A total of 75 patients underwent 133 HRIM studies over the period of November 2015 to April 2021-35 patients underwent one study, 24 patients underwent two studies, 14 patients underwent three studies, and 2 patients underwent four studies. There were 80 control patients [M:F 38:42, median age 13 years (range 1-18 years, IQR 9 years 6 months-15 years 8 months)] that each underwent one study. Patient demographics are described in Table 1. There were 33 patients with documented endoscopic findings, of which 7 (21.2%) showed evidence of esophagitis. Of the 75 initial studies, 64 (85.3%) were considered "good guality" for inclusion in the analysis. Of the 80 control studies. 76 (96.0%) were considered "good quality." Analysis of the EGJ metrics, and comparison between EA and control groups, are presented in Table 2 and Figure 1.

We demonstrated that the distension pressure emptying (DPE) for thin (IDDSI 0) and thick (IDDSI 4) liquid swallows were significantly different, with patients



TABLE 1 Demographics for the EA group (N = 75).

	Number	Percentage
Male	43	57
EA type		
Туре А	5	7
Туре В	2	3
Туре С	64	85
Type D	0	0
Туре Е	4	5
VACTERL	23	31
Requirement for ≥1 esophageal dilatation	9	12
Requirement for fundoplication surg	ery 45	60
	Median	Range
Gestational age (weeks)	38	31–41 ⁺⁵
Birth weight (kg)	2.9	1.2–4.5
Age at time of study (years)	1.25	0.25–17.33
		IQR 1-7

Abbreviation: EA, esophageal atresia.

TABLES	EG I motrice All	\mathbf{P}	compared with controls
IADLEZ	EGJ metrics—All	patients with EA	compared with controls.

with EA having a higher DPE compared with controls [mean difference: 6.65 mmHg, 95% CI: (4.02, 9.27) mmHg, p < .01 (IDDSI 0); mean difference 4.41 mmHg (IDDSI 4); 95% CI: (1.22, 7.59) mmHg, p = .01 (IDDSI 4)]. Additionally, the BFT for thin (IDDSI 0) and thick (IDDSI 4) liquid swallows were also significantly different, with patients with EA having a lower BFT compared with controls [mean difference: -0.86 s, 95% CI (-1.43, -0.30) s, p < .01 (IDDSI 0); mean difference: -0.66 s, 95% CI (-1.22, -0.09) s, p = .02 (IDDSI 4)]. Only 27/64 (42.2%) patients with EA were able to complete the solid swallow protocols.

A subgroup analysis of only patients with Type C EA was also undertaken and compared with the control group; Type C EA is the most common EA variant, in which the EA is associated with a distal TEF. Among the 64 initial studies that were deemed "good quality," 53 (82.8%) were patients with Type C EA (Supporting Information: Content 2). In this subgroup analysis, the DPE for thin (IDDSI 0) and thick (IDDSI 4) swallows were significantly different, with patients with Type C EA having a higher DPE compared with controls [mean difference: 6.28 mmHg, 95% CI: (3.38, 9.18) mmHg, p < .01 (IDDSI 0); mean difference 3.77 mmHg (IDDSI 4); 95% CI: (0.31, 7.23) mmHg, p = .03 (IDDSI 4)]. Additionally, the BFT for

	EA		Control		EA minus control		
	Mean	SE	Mean	SE	Mean difference	95% CI	p Value
EGJ, n	64		76				
Resting pressure (mmHg)	38.99	3.86	47.08	3.44	-8.09	-19.86, 3.69	0.18
CI (mmHg.cm)	51.65	5.17	54.83	4.61	-3.18	-18.96, 12.60	0.69
IDDSI 0, n	60		75				
IRP4s (mmHg)	9.23	1.10	9.87	0.95	-0.64	-3.92, 2.65	0.70
DPE (mmHg)	11.26	0.87	4.61	0.75	6.65	4.02, 9.27	<0.01
BFT (s)	1.52	0.19	2.38	0.16	-0.86	-1.43, -0.30	<0.01
IDDSI 4, n	61		75				
IRP4s (mmHg)	9.06	0.97	10.08	0.84	-1.02	-3.94, 1.90	0.49
DPE (mmHg)	12.07	1.06	7.66	0.92	4.41	1.22, 7.59	0.01
BFT (s)	1.77	0.19	2.43	0.17	-0.66	-1.22, -0.09	0.02
IDDSI 7, n	27		73				
IRP4s (mmHg)	9.76	2.03	13.04	1.15	-3.28	-8.17, 1.61	0.19
DPE (mmHg)	12.22	1.96	9.90	1.11	2.32	-2.40, 7.04	0.33
BFT (s)	1.96	0.24	1.83	0.14	0.13	-0.45, 0.71	0.66

Abbreviations: BFT, bolus flow time; CI, contractile integral; EA, esophageal atresia; EGJ, esophago-gastric junction; IDDSI, International Dysphagia Diet Standardization Initiative; IRP4s, integrated relaxation pressure.



FIGURE 1 EGJ metrics—Mean differences of all patients with EA compared with controls. EA, esophageal atresia; EGJ, esophago-gastric junction.

IDDSI 0 swallows were significantly different, with patients with Type C EA having a lower BFT compared with controls (mean difference: -0.69 s, 95% CI (-1.43, -0.04) s, p = .04). When BFT was compared with Dakkak dysphagia scores, no significant differences were found (IDDSI 0: p = .21, IDDSI 4: p = .13, IDDSI 7: p = .07).

Within the EA group, we also investigated the association between the EGJ parameters with EA type, and any previous esophageal dilatations (Table 3 and Supporting Information: Content 3). We demonstrated that the IRP4s for thin (IDDSI 0) swallows was significantly different among the EA types: Type E had the highest IRP4s (22.88 ± 3.77 mmHg) when compared with the other EA types (Type A or B $13.03 \pm 3.02 \text{ mmHg}$, Type C $9.56 \pm 1.04 \text{ mmHg}$, p = .01).

In addition, the BFT for IDDSI 7 swallows was significantly different among the EA types. Type C EA had the highest BFT (2.03 ± 0.33 s) when compared with the other types (Type A or B 0.07 ± 0.65 s, Type E 1.92 ± 1.15 s, p = .04). The IRP4s for thin (IDDSI 0) swallows was lower in the group with prior esophageal dilatations when compared with the group without previous dilatations [mean difference -4.29 mmHg, 95% CI (-8.40, -0.19) mmHg, p = .04].

4 | DISCUSSION

In our study, we aimed to characterize EGJ function in patients with EA and compare these findings with controls. The few published studies that have utilized HRIM in children with EA have suggested abnormalities in gastro-esophageal function within this patient cohort.²³⁻²⁷ In our study, the DPE and the BFT for liquid swallows differed significantly between the EA and control groups. When Type C EA was specifically compared with control groups, DPE for liquid swallows differed, and BFT differed for only the thin liquid swallows. Distension pressure during esophageal emptying was higher in the EA group, suggesting a poorer compliance in this group of patients, when the food bolus empties from the esophagus into the stomach. This finding was only limited to liquid swallows, as there insufficient patients able to complete solid swallows to accurately perform a comparison. The higher DPE in liquid swallows in the EA group was not unexpected, due to the predictable impairment of bolus clearance.

BFT predicts the period of esophageal bolus emptying across the EGJ and may also be related to

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	Type #	V or B	Type C		Type E		Type C minu	s Type A or B		Type E minu	s Type A or B		Type E minu	us Type C	
	Mean	SE	Mean	L S	Mean Sl	, <u> </u>	dean lifference	95% CI	p Value	Mean difference	95% CI	p Value	Mean difference	95% CI	p Value
EGJ, <i>n</i>	7		53		4										
Resting pressure (mmHg)	42.60	11.10	46.85	4.00	63.40 14	4.90 ∠	1.30	-24.30, 32.80	0.93	20.80	-22.80, 64.50	0.49	16.60	-20.90, 54.10	0.54
CI (mmHg.cm)	53.60	13.40	54.72	4.84	87.60 15	3.10 1	.10	-33.50, 35.80	1.00	34.00	-18.90, 86.90	0.28	32.80	-12.60, 78.30	0.20
IDDSI 0, <i>n</i>	9		50		4										
IRP4s (mmHg)	13.03	3.02	9.56	1.04	22.88 3.	- 22	-3.47	-11.22, 4.27	0.53	9.85	-1.49, 21.19	0.10	13.33	3.84, 22.81	0.00
DPE (mmHg)	14.12	2.77	13.74	0.95	15.92 3.	45 -	-0.38	-7.48, 6.71	0.99	1.80	-8.60, 12.19	0.91	2.18	-6.51, 10.87	0.82
BFT (s)	0.83	0.49	1.40	0.17	1.13 0.	.62 C	.57	-0.70, 1.83	0.53	0.29	-1.56, 2.15	0.92	-0.28	-1.83, 1.27	06.0
IDDSI 4, <i>n</i>	9		51		4										
IRP4s (mmHg)	11.21	2.70	10.24	0.92	15.62 3.	37 -	-0.97	-7.89, 5.94	0.94	4.40	-5.73, 14.53	0.55	5.38	-3.10, 13.85	0.29
DPE (mmHg)	15.80	3.04	14.34	1.04	16.48 3.	- 62	-1.47	-9.25, 6.32	0.89	0.68	-10.71, 12.07	0.99	2.15	-7.38, 11.68	0.85
BFT (s)	0.58	0.22	1.51	0.80	1.60 0.	72 1	.49	-0.24, 3.04	0.11	0.93	-1.47, 3.33	0.62	-0.47	-2.48, 1.54	0.84
IDDSI 7, <i>n</i>	S		20		2										
IRP4s (mmHg)	12.72	3.67	11.56	1.87	13.03 6.	52 -	-1.16	-11.51, 9.19	0.96	0.31	-18.25, 18.88	1.00	1.47	-15.87, 18.82	0.98
DPE (mmHg)	16.44	4.05	13.34	2.06	11.37 7.	20	-3.10	-14.52, 8.32	0.78	-5.07	-25.55, 15.42	0.81	-1.97	-21.11, 17.17	0.96
BFT (s)	0.07	0.65	2.03	0.33	1.92 1.	15 1	.97	0.13, 3.80	0.03	1.85	-1.44, 5.14	0.36	-0.12	-3.19, 2.95	1.00
Abbreviations: BFT, bc	olus flow tir	ne; Cl, cor	tractile int	egral; E	EA, esopha	igeal atr	esia; EGJ, eso	phago-gastric junc	tion; IDDSI,	International Dy	/sphagia Diet Stand	ardization I	nitiative; IRP4s,	, integrated relaxatic	n pressure.

Effect of EA type within EA cohort.

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increased resistance at the EGJ.^{28,29} This suggests a possibility that the EGJ may be a potential therapeutic target for managing dysphagia in patients with EA; however, lowering the EGJ pressure may increase the likelihood of GER in a patient group already prone to GER and its associated short- and long-term morbidities.³⁰ One study in an adult population by Cock et al. (in asymptomatic healthy volunteers over 80 years of age) found that BFT and bolus presence time (BPT) may be utilized to differentiate individuals with failed bolus clearance.¹⁵ However, this has yet to be found as predictive in the pediatric population.²⁹ In patients with ineffective peristalsis and/or incomplete EGJ relaxation, a short BFT may indicate impairment of flow across the EGJ, with some residual bolus left within the body of the esophagus.

There was no significant difference found in the BFT in the solid swallows when patients with EA were compared with controls, though differences were demonstrated between EA types. This may relate to the fact that only 42% of our patients were able to complete solid swallows, due to their stage of development and/or limitations with patient cooperation. It should also be noted that BFT has not been validated for accuracy of solid bolus emptying. A study by Lin et al. suggested that the BFT is correlated with dysphagia severity, as a marker of EGJ function.³¹ However, we found no correlation between BFT and Dakkak dysphagia scores in our cohort. We propose several key methodological distinctions which may reconcile the apparent differences between the findings of the current study and those reported by Lin et al. The study by Lin et al., which did correlate BFT with nonobstructive dysphagia, was conducted in a distinctly different patient population, namely adults with a diagnosis of achalasia. In our study, dysphagia was assessed with a different questionnaire (Dakkak dysphagia questionnaire). Our Dakkak dysphagia questionnaires were completed by caregivers, which may reflect an inability or refusal to swallow rather than a true perception of bolus hold-up, which may occur even when the food bolus transits. However, with dysphagia symptoms being multi-factorial, there may also be a contribution from EGJ resistance and/or resistance at the esophageal anastomosis.

We have found that the IRP4s for thin swallows was significantly different within the EA cohort, both when comparison was made between the types of EA, and when there was a history of previous esophageal dilatations. The IRP4s describes relaxation of the EGJ during swallowing and may be used to identify issues with the structural function of the esophagus, such as esophageal outflow obstruction. The difference that was found with Type E EA, when compared with other EA types, is likely due to these patients having an isolated tracheoesophageal fistula (without EA). Surgical correction of Type E EA is typically via a cervical incision rather than thoracotomy and does not involve either traction on the EGJ or esophageal anastomosis to restore esophageal continuity. As such the distinctly different surgery for Type E EA would not be expected to impact the anatomy or function of the EGJ, in the same fashion as surgery for other types of EA.

The difference in IRP4s found among EA types needs to be interpreted with care, as we had a small sample size for subgroup analysis here, and there were only four patients with Type E EA. Further, the IRP4s for thick and solid swallows were not different across the EA types. This may have implications for parental counseling during the period of introduction of solids, especially with parents who are hesitant to introduce more solid foods, but are feeding their child thick pureed food. This information may reframe the thinking on the well-understood and documented challenges faced by children with repaired EA in transitioning from swallowing thick pureed food to swallowing more solid foods. This may focus the attribution of these challenges to other areas, such as the anastomosis rather than the EGJ. If trials of solid foods do indeed manifest with difficulties with swallowing, we would focus our therapeutic attention on the anastomosis as a more likely root cause of the difficulties.

Further, when comparing for previous esophageal dilatations, the group with previous esophageal dilatations had a lower IRP4s. As IRP4s is influenced by contact and intrabolus pressures, this lower value may reflect ineffective peristalsis which leads to lower intrabolus pressures and lower IRP4s. This may be an indication of dysmotility in patients with EA, affecting symptomatology. Dysmotility, which manifests as dysphagia and/or food bolus obstruction, then in turn affected dilatation requirement, as dilatations did not typically directly impact the EGJ. We acknowledge that these findings are limited by the small sample size of patients with EA who had undergone dilatation (nine patients).

In our study, we factored esophageal length into the analysis. While adult studies may have little need to compare esophageal length and its impact on metrics, this is important in the pediatric population, as it has been shown to affect HRIM metrics.^{9,24} In our analysis, using the general linear model, we adjusted for esophageal length as a potential confounder. Therefore, we are confident that our findings are independent of the influence of esophageal length, which is highly variable in a cohort of children from 0 to 18 years of age, and is highly likely to differ between children with repaired EA and their age matched peers without EA. We do, however, acknowledge that the median age at the time of study was 1.25 years in the EA group and 13 years in the control group.

Our study is limited by challenges faced within the pediatric population. The standardization of HRIM in children is affected by child cooperation, taking into



account age and developmental stage, which may be exacerbated by parental anxiety and/or previous traumatic experiences with healthcare. As such, obtaining many data points can be a challenge. We do appreciate that the more data points, the better for internal consistency of measurements. However, due to this challenge, we have included patients with at least three analyzable bolus swallows - in our experience, this is sufficient for meaningful analysis. Additionally, SBM was not used for all studies, either because those studies predated the development and utilization of SBM or because a child's distaste for SBM resulted in pragmatic exchange of SBM for the patient's own food to ensure meaningful, good swallow analysis. Nonetheless, we hypothesize that the impact on our findings does not negate the clinical implications of our results.

Controls in our study were children who had undergone HRIM for reflux symptoms as part of a work-up for possible fundoplication. In this case, the EGJ is not expected to be fully representative of the healthy (i.e., "normal") population. However, given that this group of patients are presurgery, the EGJ would not have been impacted by those anatomical and physiological changes resulting from surgical dissection, traction, and esophageal anastomosis, unlike the EA group. Therefore, the control group was deemed representative of the non-EA population, bearing this limitation in mind.

Further, we acknowledge that a large proportion of patients with EA have undergone a Nissen fundoplication (60%), which changes the anatomy of the EGJ. This can affect the HRIM results and may make it difficult to determine if the HRIM findings reflecting EGJ dysfunction is attributable to EA alone of fundoplication changes. Acknowledging this limitation, we also note that patients within the EA cohort undergo different surgical changes depending on gap length and need for repeat surgeries, and that fundoplication adds to this already varied factor. We also acknowledge that a limited number of our patients had documented endoscopic findings. Therefore, it was not possible to undertake meaningful analysis to compare the presence of mucosal abnormalities with EGJ morphology.

The application of HRIM to patients with EA has several important benefits, and we have now demonstrated its specific utility in understanding EGJ function. This may help target the management of EA patients, if HRIM identifies EGJ dysfunction as contributing to patient symptoms. It may aid in the decision to perform fundoplication, assess postfundoplication changes, or even need for revision surgery subsequently. With the increasing availability of HRIM, its application offers an improved understanding of the swallowing in these patients, and the potential to direct and improve patient care.³²

5 | CONCLUSION

This is the largest study of its kind, understanding the metrics of esophageal contraction in patients with EA. Utilizing HRIM, we have objectively characterized the EGJ. Distension pressure emptying and BFT for liquid swallows were significantly different between the EA and control groups. Integrated relaxation pressure for thin liquid swallows was significantly different when compared for EA types, as well as a previous history of esophageal dilatations. Understanding the EGJ function in patients with EA will facilitate individualized long-term management.

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CONFLICT OF INTEREST STATEMENT

Professor Omari holds inventorship of the international patent family that covers the analytical methods described. The Swallow GatewayTM software service is owned and provided by Flinders University. The remaining authors declare no conflict of interest.

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REFERENCES

- 1. Riley M, Halliday J. Birth defects in Victoria 2005-2006. *Victorian Perinatal Data Collection Unit*. Victoria Government Department of Human Services; 2008.
- 2. Rintala RJ. Fundoplication in patients with esophageal atresia: patient selection, indications, and outcomes. *Front Pediatr.* 2017;5:109.
- 3. Pellegrino SA, King SK, McLeod E, et al. Impact of esophageal atresia on the success of fundoplication for gastroesophageal reflux. *J Pediatr.* 2018;198:60-66.

- Rogers BD, Gyawali CP. Evaluation of the esophagogastric junction on high resolution manometry. *J Clin Gastroenterol*. 2021;55(2):e8-e18.
- Bagucka B, Badriul H, Vandemaele K, et al. Normal ranges of continuous pH monitoring in the proximal esophagus. J Pediatr Gastroenterol Nutr. 2000;31(3):244-247.
- Goldani HAS, Staiano A, Borrelli O, Thapar N, Lindley KJ. Pediatric esophageal high-resolution manometry: utility of a standardized protocol and size-adjusted pressure topography parameters. *Am J Gastroenterol.* 2010;105(2):460-467.
- Staiano A, Boccia G, Miele E, Clouse RE. Segmental characteristics of oesophageal peristalsis in paediatric patients. *Neurogastroenterol Motil.* 2008;20(1):19-26.
- 8. Dakkak M, Bennett JR. A new dysphagia score with objective validation. *J Clin Gastroenterol*. 1992;14(2):99-100.
- Singendonk MMJ, Ferris LF, McCall L, et al. High-resolution esophageal manometry in pediatrics: effect of esophageal length on diagnostic measures. *Neurogastroenterol Motil*. 2020; 32(1):e13721.
- 10. Gross ER. The Surgery of Infancy and Chilhood. Saunders; 1962.
- 11. Solomon BD. VACTERL/VATER association. Orphanet J Rare Dis. 2011;6(1):56.
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inf. 2009;42(2):377-381.
- Ferris L, King S, McCall L, et al. Piecemeal deglutition and the implications for pressure impedance dysphagia assessment in pediatrics. J Pediatr Gastroenterol Nutr. 2018;67(6):713-719.
- Wang D, Xu H, Tang T, Wang J, Yu Y, Gyawali CP. Assessment of the esophagogastric junction (EGJ) using the EGJ contractile integral (EGJ-CI) following per-oral endoscopic myotomy (POEM) in achalasia. *Rev Esp Enferm Dig.* 2018; 110(11):706-711.
- Cock C, Besanko LK, Burgstad CM, et al. Age-related impairment of esophagogastric junction relaxation and bolus flow time. World J Gastroenterol. 2017;23(15):2785-2794.
- Singendonk MMJ, Omari TI, Rommel N, et al. Novel pressureimpedance parameters for evaluating esophageal function in pediatric achalasia. *J Pediatr Gastroenterol Nutr.* 2018;66(1): 37-42.
- Rayyan M, Omari T, Debeer A, et al. Characterization of esophageal motility in infants with congenital diaphragmatic hernia using high-resolution manometry. *J Pediatr Gastroenterol Nutr.* 2019;69(1):32-38.
- 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.
- Lin Z, Imam H, Nicodème F, et al. Flow time through esophagogastric junction derived during high-resolution impedancemanometry studies: a novel parameter for assessing esophageal bolus transit. *Am J Physiol Gastrointest Liver Physiol*. 2014;307(2): G158-G163.
- Nicodème F, Pipa-Muniz M, Khanna K, Kahrilas PJ, Pandolfino JE. Quantifying esophagogastric junction contractility with a novel HRM topographic metric, the EGJ-Contractile Integral: normative values and preliminary evaluation in PPI non-responders. *Neurogastroenterol Motil.* 2014;26(3):353-360.
- Rogers BD, Rengarajan A, Abrahao L, et al. Esophagogastric junction morphology and contractile integral on high-resolution manometry in asymptomatic healthy volunteers: an international multicenter study. *Neurogastroenterol Motil.* 2021;33(6):e14009.

- 22. Kou W, Carlson DA, Kahrilas PJ, Patankar NA, Pandolfino JE. Normative values of intra-bolus pressure and esophageal compliance based on 4D high-resolution impedance manometry. *Neurogastroenterol Motil*. 2022;34(10):e14423.
- Kawahara H, Kubota A, Hasegawa T, et al. Lack of distal esophageal contractions is a key determinant of gastroesophageal reflux disease after repair of esophageal atresia. *J Pediatr Surg*. 2007;42(12):2017-2021.
- 24. Pedersen RN, Markøw S, Kruse-Andersen S, et al. Esophageal atresia: gastroesophageal functional follow-up in 5-15 year old children. *J Pediatr Surg*. 2013;48(12):2487-2495.
- 25. Tambucci R, Thapar N, Saliakellis E, et al. Clinical relevance of esophageal baseline impedance measurement: just an innocent bystander. *J Pediatr Gastroenterol Nutr.* 2015;60(6): 776-782.
- 26. Tovar JA, Diez Pardo JA, Murcia J, Prieto G, Molina M, Polanco I. Ambulatory 24-hour manometric and pH metric evidence of permanent impairment of clearance capacity in patients with esophageal atresia. *J Pediatr Surg.* 1995;30(8): 1224-1231.
- Lemoine C, Aspirot A, Le Henaff G, Piloquet H, Lévesque D, Faure C. Characterization of esophageal motility following esophageal atresia repair using high-resolution esophageal manometry. J Pediatr Gastroenterol Nutr. 2013;56(6):609-614.
- Rommel N, Omari TI, Selleslagh M, et al. High-resolution manometry combined with impedance measurements discriminates the cause of dysphagia in children. *Eur J Pediatr.* 2015;174(12):1629-1637.
- 29. Courbette O, Omari T, Aspirot A, Faure C. Characterization of esophageal motility in children with operated esophageal atresia using high-resolution impedance manometry and pressure flow analysis. *J Pediatr Gastroenterol Nutr.* 2020;71(3): 304-309.
- Tovar J, Fragoso A. Gastroesophageal reflux after repair of esophageal atresia. *Eur J Pediatr Surg.* 2013;23(3):175-181.
- Lin Z, Carlson DA, Dykstra K, et al. High-resolution impedance manometry measurement of bolus flow time in achalasia and its correlation with dysphagia. *Neurogastroenterol Motil.* 2015; 27(9):1232-1238.
- Rommel N, Rayyan M, Scheerens C, Omari T. The potential benefits of applying recent advances in esophageal motility testing in patients with esophageal atresia. *Front Pediatr.* 2017;5:137.

SUPPORTING INFORMATION

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

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