

## ORIGINAL ARTICLE

## Gastroenterology

# Persistent and newly developed gastrointestinal symptoms after surgery for intestinal malrotation in children: Dysmotility or disorders of gut and brain interaction?

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## Abstract

**Objectives:** Surgery for intestinal malrotation (IM) aims to correct the defect and improve symptoms; however, many have persistent gastrointestinal (GI) symptoms postoperatively. We evaluated the incidence, clinical presentation, and long-term outcomes of children with surgically repaired IM and its possible association with disorders of gut and brain interaction (DGBI).

**Methods:** Multicenter retrospective study was conducted in patients from 0 to 21 years old, who had surgery for IM from 2000 to 2021 across three pediatric tertiary care centers. Data analyzed included demographics, time to diagnosis, idiopathic diagnosis, incidental diagnosis, postoperative follow-up, surgical time, and the need for surgery including bowel detorsion. Outcome variables were the presence of postoperative GI symptoms and DGBIs, and overall resolution of symptoms. We also evaluated the potential association of demographics and other included variables with our outcome variables.

**Results:** Ninety-two patients with surgically corrected IM were included, 54% were male, and median age of diagnosis and surgical correction was 4.9 and 7.8 months, respectively. Median follow-up after surgery was 64 months. A total of 77% had postoperative GI symptoms, and notably, 78% of patients without symptoms before surgery (incidental diagnosis) developed GI symptoms postoperatively and 27% of patients met Rome IV criteria for a one or more DGBI. No factors were associated to the presence of postoperative symptoms or DGBIs in multivariate analysis. Female gender was the only factor associated with lack of resolution of symptoms at follow-up.

**Conclusion:** Pediatric IM is commonly associated with postoperative GI symptoms and DGBI well beyond surgery. An increased awareness about the prevalence of DGBI in these patients may help reach a prompt and accurate diagnosis, and improve their quality of life.

## KEYWORDS

disorders of the gut and brain interaction (DGBI), functional gastrointestinal disorders, GI motility, neurogastroenterology and motility, pediatrics

Dhiren Patel and Darnna Banks shared first authorship.

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## 1 | INTRODUCTION

Intestinal malrotation (IM) is a spectrum of congenital abnormalities of intestinal rotation and/or fixation classified by the embryonic stage of developmental arrest. Malrotation may lead to the formation of Ladd's bands and increased risk of midgut volvulus.<sup>1</sup> Symptoms at the time of diagnosis may include abdominal pain, distention, vomiting, and feeding intolerance. Seventy-five percent to 90% of patients are diagnosed within the first year of life.<sup>2,3</sup> The true incidence of malrotation outside of this age is unknown, as some of these patients are asymptomatic or present with atypical symptoms, and some are diagnosed incidentally.<sup>2,3</sup> Malrotation is managed surgically with the Ladd's procedure and, although surgery improves symptoms in more than 50% of patients, many have persistent gastrointestinal (GI) symptoms.<sup>2</sup> Little is known about the prevalence and etiology of persistent GI symptoms after surgery for IM in children. Although the prevalence of disorders of gut–brain interaction (DGBI, formerly known as functional GI disorder) in children range from 9.9% to as high as 87%, to the best of our knowledge, there are no pediatric studies that have explored the prevalence of DGBIs after surgery for IM and the potential factors associated to those disorders.<sup>4</sup> Few studies have reported dysmotility as a possible etiology for the persistence of symptoms after surgical correction of malrotation.<sup>5,6</sup> We conducted a multicenter study describing the long-term outcomes of children after surgery for IM and its possible association with DGBIs.

## 2 | METHODS

This was a multicenter retrospective study. Each center (Saint Louis University, Yale University, and University of Washington, Seattle) obtained Institutional Review Board approval for the study and appropriate inter-institutional data use agreements. The data analysis of patients with IM was conducted across these three pediatric motility and tertiary care centers.

### 2.1 | Patient population

Patients up to 21 years of age, who were diagnosed and had surgery for malrotation, were included over a 21-year period, from 2000 to 2021 across three tertiary care centers. Operative reports of those patients who underwent surgical intervention were reviewed. Surgical finding of malrotation included the presence of Ladd bands, narrow mesenteric root, presence of midgut volvulus, and abnormal position of duodenojejunal junction. We evaluated specific intestinal orientation and included patients that met criteria for abnormalities of the second stage of intestinal rotation. Patients with abdominal wall defects such as omphalocele and

### What is Known

- Intestinal malrotation (IM) in children remains a relatively common diagnosis, although the exact incidence is unknown.
- Patients with IM continue to experience persistence gastrointestinal symptoms well beyond initial surgical interventions.

### What is New

- We evaluated the incidence, clinical presentation, and long-term outcomes of children with surgically repaired IM.
- We found greater than a quarter of patients in this cohort from three tertiary pediatric GI centers met the criteria for disorders of gut and brain interaction (DGBI).
- An increased awareness about the prevalence of DGBI in these patients may help reach an accurate diagnosis and improve the quality of life of patients with IM.

gastroschisis, congenital diaphragmatic hernia, situs inversus, cecal and sigmoid volvulus, prune belly syndrome, extensive intestinal resection (deemed as having short bowel syndrome), patients with history of intestinal atresia or stenosis (with or without short bowel syndrome), hiatal hernia, imperforate anus, and those with <6 months of follow-up after surgery were excluded from the analysis.

### 2.2 | Record review

An electronic medical record search was performed using the International Classification of Disease Tenth Revision (ICD-10) using the following diagnosis codes for malrotation: K56.2 (volvulus), Q43.3 (congenital malformations of intestinal fixation), and K31.5 (volvulus of duodenum). A records search was also performed using Current Procedural Terminology code: 44055 (Ladd procedure) to be able to capture all patients undergoing surgery for malrotation. We used combination of both, ICD-9 codes (for data before 2015) and ICD-10 codes (after 2015), considering the major change in ICD codes in 2015. Three reviewers independently performed eligibility assessment and data extraction.

### 2.3 | Variables

Data analyzed included demographics (age, gender), time to IM diagnosis, idiopathic diagnosis or not

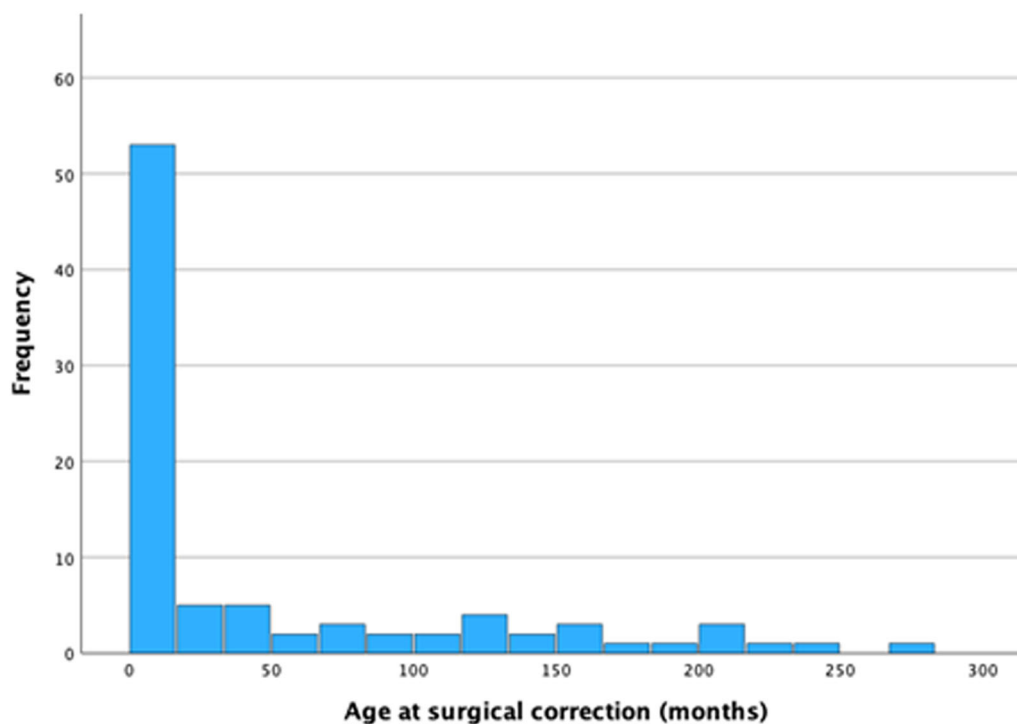
(including associated syndromes), presenting symptoms, diagnosis as incidental (no GI symptoms and found during imaging studies obtained for another indication) or found during imaging triggered by GI symptoms, type of surgical correction (including detorsion or not), surgical time, complications, and surgical outcomes. Postoperative data included length of postoperative follow-up, presence of GI symptoms, therapeutic interventions, and the response to those as well as any further surgical intervention. Postoperative GI symptoms were defined as persistent when present for more than 4 weeks after surgery. We evaluated three outcome variables in our cohort: the presence of postoperative GI symptoms, presence of DGBIs, and therapeutic outcomes (overall resolution of symptoms at last follow-up). Presence and quality of postoperative GI symptoms were analyzed by investigators to assess eligibility of patients to meet diagnostic criteria for DGBIs according to the Rome IV criteria at the clinical evaluations after surgery. We then evaluated the potential association of demographics and other included variables with our outcome variables.

### 3 | RESULTS

A total of 92 patients were included, median age at diagnosis was 4.9 months, and for surgical correction was 7.8 months (please refer to Figure 1), and 54%

were male. See Table 1. A total of 28 (30%) of patients had malrotation associated to another condition. The diagnosis was considered incidental (asymptomatic at diagnosis) in 23 (25%) patients and the remainder 69 (75%) had GI symptoms prompting further investigations, leading to the diagnosis of malrotation. The median time for surgical repair was 100 min. All patients underwent surgery for malrotation and 16 (17%) of those included detorsion of midgut volvulus with 2 of those also undergoing minor intestinal resection. Median follow-up after surgery was 64 months, 88 of the 92 (96%) had follow-up > 12 months. A total of 71 (77%) had GI symptoms after surgery and 21 (23%) had no GI symptoms after surgery.

A total of 34 patients underwent a second surgery after initial correction of malrotation—16 for GI symptoms or related to previous surgery for malrotation (exploratory laparoscopy to evaluate and/or treat for bowel obstruction in 12, redo Ladds procedure in two, and diverting ileostomy in two, with later ostomy closure in one, and wound and abdominal abscess drainage in one) and 18 for reasons unrelated to malrotation surgery (gastrostomy tube placement in 10, gastrojejunostomy tube placement in two and jejunostomy in one, umbilical hernia repair in two, laparoscopic cholecystectomy in one, intussusception reduction in one, and para-duodenal hernia repair in one). From the asymptomatic group, five had surgery for reasons unrelated to previous surgery for malrotation or GI



**FIGURE 1** Age in months at surgical correction. Note that the majority underwent surgery in the first few months of life.

**TABLE 1** Demographic data for patients with IM.

	Median	IQR
Age at diagnosis	4.9 months	76.51 months
Age at surgical correction	7.8 months	76.74 months
Surgical repair time	100 min	67 min
Follow-up after surgery	64 months	60.76 months
	Number	Percentage
Gender		
• Male	55/92	54%
• Female	37/92	46%
Race		
• Caucasian	65/92	71%
• African American	20/92	22%
• Asian	7/92	7%
Malrotation diagnosis		
• Symptoms present at the time of diagnosis	69/92	75%
• Absent GI symptoms (incidental diagnosis)	23/92	25%
Isolated vs. associated to congenital anomalies		
• Isolated malrotation	64/92	70%
• Malrotation associated with other conditions: Trisomy 21 and 18, genetic syndromes (Barth, Coffin-Siris and Cornelia de Lange), and multiple gene deletions, mutations and chromosomal anomalies	28/92	30%

Abbreviation: IQR, interquartile range.

symptoms and two for malrotation or GI symptoms, and from the symptomatic group 14 had surgery related to malrotation or GI symptoms and 13 for unrelated reasons.

### 3.1 | Postoperative GI symptoms

After surgery, most patients (77%) had GI symptoms. The predominant symptom was vomiting in 20, followed by constipation in 18, abdominal pain in 17, feeding problems in 10, nausea in four, and gastroesophageal reflux disease (GERD) in two patients. Despite the presence of GI symptoms, only two patients underwent advanced motility studies (one had a normal colon manometry and another had normal colon manometry and antroduodenal manometry that showed normal presence of the migrating motor

complex, and only some decrease in antral postprandial response) and only two underwent a colon transit study with radiopaque markers (normal in both). We found no association between presence of postoperative GI symptoms and age at diagnosis, age at surgery, race, time from diagnosis to surgery, duration of surgical procedure and need for second surgical procedure, surgery with detorsion of volvulus, follow-up duration, and idiopathic malrotation in univariate analysis. See Table 2. We also found no association between postoperative GI symptoms and incidental diagnosis (78% had persistent GI symptoms after surgery in the incidental diagnosis group and 77% in the symptomatic group,  $p=0.86$ ). It is important to highlight that 78% of patients without GI symptoms before surgery developed GI symptoms after surgery. We only found an association between presence of postoperative GI symptoms and female gender ( $p=0.034$ ) in univariate analysis (see Table 2), but logistic regression demonstrated no factors were associated with presence of postoperative GI symptoms (Table 3).

### 3.2 | Rome IV DGBIs

A total of 27 (29%) patients met Rome IV criteria for DGBI of which 16 (59%) were female ( $p=0.109$ ). Twenty-three patients met criteria for one DGBI and four met criteria for more than one DGBI. Of the 23 meeting criteria for one DGBI, nine met criteria for functional constipation, eight for functional abdominal pain not otherwise specified, three for functional dyspepsia, two for irritable bowel syndrome, and one for abdominal migraine. The four patients who met criteria for more than one DGBI had both functional dyspepsia and functional constipation. Please refer to Figure 2. There was no association between meeting Rome IV criteria for DGBI's and gender, age at surgery, idiopathic presentation, incidental diagnosis, follow-up duration, time from diagnosis to surgery, surgical repair time, and subsequent surgical procedures in univariate analysis (see Table 2). There was an association between DGBI's and older age (age at DGBI meeting criteria) and race in univariate analysis, ( $p=0.012$  and  $p=0.024$ , respectively) but logistic regression demonstrated no factors were associated with meeting Rome IV criteria for any DGBI, although we observed a tendency towards an association for race ( $p=0.055$ ) (see Table 3).

### 3.3 | Response to therapy

Medications were used (alone or in combination) at different times in 65 patients in our cohort, including a proton pump inhibitor (PPI), cyproheptadine, gastric

**TABLE 2** Univariate analysis evaluating the association between demographics and other factors and postoperative GI symptoms, meeting Rome IV criteria for DGBIs and symptom resolution.

	Postoperative GI symptoms			Meet Rome IV criteria for DGBIs			Symptom resolution		
	Yes	No	<i>p</i>	Yes	No	<i>p</i>	Yes	No	<i>p</i>
Median age at diagnosis (months)	7.00	1.23	0.111	125.62	86.62	0.012	115.16	97.73	0.208
Gender			0.034			0.201			0.012
	<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)	
Male	32/47 (68)	15/47 (32)		11/47 (23)	36/47 (77)		7/47 (15)	40/47 (85)	
Female	39/45 (87)	6/45 (13)		16/45 (36)	29/45 (64)		17/47 (36)	28/47 (64)	
Race			0.326			0.024			0.083
African American	15/20 (75)	5/20 (25)		1/20 (5)	19/20 (95)		9/20 (45)	11/20 (55)	
Caucasian	49/65 (75)	16/65 (25)		23/65 (35)	42/65 (65)		13/65 (20)	52/65 (80)	
Asian	7/7 (100)	0 (0)		3/7 (43)	4/7 (57)		2/7 (29)	5/7 (71)	
Idiopathic			0.453			0.545			0.501
	<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)	
Yes	48/64 (75)	16/64 (25)		20/64 (31)	44/64 (69)		18/64 (28)	46/64 (72)	
No	23/28 (82)	5/28 (18)		7/28(25)	21/28 (75)		6/28 (21)	22/28 (79)	
Incidental diagnosis			0.886			0.895			1.000
	<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)	
Yes	18/23 (78)	5/23 (22)		7/23 (30)	16/23 (70)		6/23 (26)	17/23 (73)	
No	53/69 (77)	16/69 (23)		20/69 (29)	49/69 (71)		18/69 (26)	51/69 (74)	
Median follow-up (months)	63.64	64.70	0.759	75.80	60.88	0.158	72.94	54.06	0.088
Median surgical time (minutes)	100.50	95.00	0.986	101.00	94.00	0.585	84.00	101.00	0.353
Median time from diagnosis to surgery (months)	0.07	0.00	0.118	0.33	0.00	0.263	0.23	0.00	0.010
Volvulus detorsion			0.460			0.103			0.504
	<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)	
Yes	63/80 (79)	17/80 (21)		26/80 (33)	54/80 (67)		20/80 (25)	60/80 (75)	
No	8/12 (67)	4/12 (33)		1/12 (8)	11/12 (92)		4/12 (33)	8/12 (67)	
Required more surgery			0.695			0.348			0.358
	<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)		<i>N</i> (%)	<i>N</i> (%)	
Yes	44/58 (76)	14/58 (24)		19/58 (33)	39/58 (67)		17/58 (29)	41/58 (71)	
No	27/34 (79)	7/34 (21)		8/34 (24)	26/34 (76)		7/34 (21)	27/34 (71)	

Abbreviations: DGBI, disorders of gut and brain interaction; GI, gastrointestinal.

prokinetic (erythromycin, azithromycin, metoclopramide), polyethylene glycol (PEG), and stimulant laxatives (sennosides or bisacodyl). A PPI was used alone in 19 patients, eight of those responded. Cyproheptadine was used alone in 11 patients and five of those had a positive response. A gastric prokinetic was used alone in 12 patients and only four had a positive response. PEG was used alone in 20 patients and 13 responded to it. A stimulant laxative was used alone in

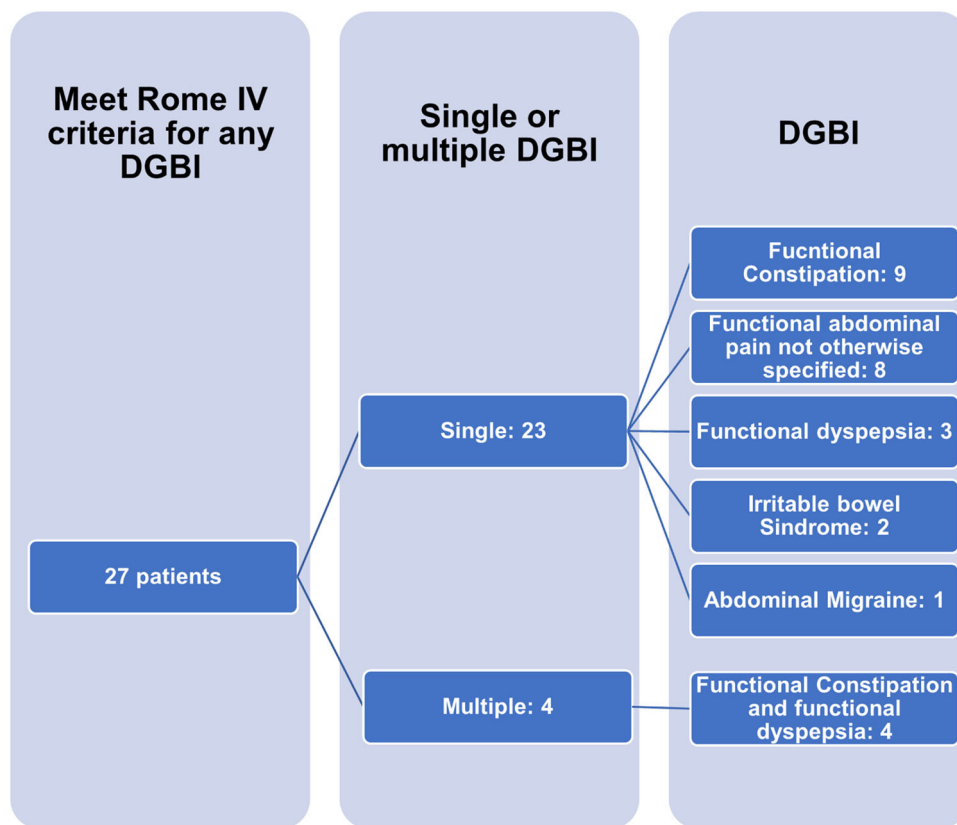
11 patients and only four had a positive response. Overall, a total of 33 patients were treated with a promotility agent. Of 71 patients with persistent GI symptoms, 24 (34%) had complete symptom resolution while on therapy at last follow-up. We found no association between symptom resolution and age at diagnosis, age at surgical correction, race, follow-up duration, idiopathic malrotation, surgery requiring volvulus detorsion, surgical time, and requirement of

**TABLE 3** Joint effect of factors associated to postoperative GI symptoms, Rome IV criteria for DGBIs, and symptoms resolution in children after surgery for IM.

	Postoperative GI symptoms				Meet Rome IV criteria (DGBIs)				Symptom resolution			
	<i>p</i>	OR	95% CI		<i>p</i>	OR	95% CI		<i>p</i>	OR	95% CI	
			Upper	Lower			Upper	Lower			Upper	Lower
Age at diagnosis	0.25	1.01	0.996	1.015	0.38	1.00	0.995	1.013	0.11	1.01	0.998	1.017
Male gender	0.35	0.57	0.174	1.862	0.94	0.96	0.306	2.995	0.04	0.26	0.070	0.945
Caucasian	0.95	1.04	0.251	4.350	0.05	0.12	0.014	1.054	0.02	0.15	0.040	0.590
Idiopathic	0.17	0.36	0.083	1.555	0.42	1.74	0.447	6.799	0.18	0.19	0.017	2.111
Incidental diagnosis	0.94	0.94	0.222	3.995	0.22	0.41	0.098	1.719	0.83	1.31	0.104	16.56
Follow-up (months)	0.71	1.00	0.982	1.012	0.17	1.01	0.996	1.025	0.44	1.83	0.402	8.316
Surgical time (minutes)	0.46	1.00	0.988	1.005	0.49	1.00	0.995	1.011	0.29	2.26	0.497	10.29
Volvulus detorsion	0.14	3.50	0.661	18.49	0.99	3.76	0.264	6.356	0.18	1.01	0.995	1.028

Note: Male gender and Caucasians are associated with lack of symptom resolution.

Abbreviations: CI, confidence interval; DGBI, disorders of gut and brain interaction; GI, gastrointestinal; IM, intestinal malrotation; OR, odds ratio.

**FIGURE 2** Description of disorders of gut–brain interactions (DGBIs) in our cohort of patients with postoperative symptoms after surgery for intestinal malrotation.

second surgery. We did find an association between male gender and longer time from diagnosis to surgery and lack of resolution of symptoms ( $p=0.012$  and  $p=0.010$ , respectively) in univariate analysis but in multivariate analysis only male gender and race (Caucasian) were associated to lack of resolution of symptoms (see Table 3).

## 4 | DISCUSSION

IM is a spectrum of congenital abnormalities of intestinal rotation and/or fixation that is often diagnosed and repaired during infancy. Some IM patients have reported persistent GI symptoms after surgery.<sup>1–3</sup> In our multicenter retrospective study, we describe the

long-term outcomes of children who have undergone surgery for IM and the association with DGBI. The present study shows that after surgery for IM a very high proportion (77%) of patients have postoperative GI symptoms and many of them (29%) meet ROME IV criteria for a DGBI. We found no association between all variables evaluated and the presence of persistent GI symptoms after surgery for IM and DGBIs.

Symptomatic IM in neonates occurs with a frequency of about one in 6000 live births.<sup>7</sup> Beyond the neonatal age, malrotation may present as an incidental finding in an asymptomatic patient or with chronic or intermittent GI symptoms, which can result in delayed diagnosis and surgical repair.<sup>8–12</sup> In our study, 25% of patients were asymptomatic at diagnosis (incidental diagnosis) and 75% had GI symptoms that ultimately led to the diagnosis of malrotation. These chronic or intermittent symptoms in undiagnosed or unrepaired patients with IM are thought to be due to repeated twisting/untwisting sequences resulting in intermittent volvulus. Since its first description in the 1930s, operative management with the Ladd's procedure has been standard therapy for IM and consists of volvulus detorsion (if present), Ladd's bands division, straightening of the duodenum, widening of mesentery root, positioning of the bowel in a systematic position within the abdominal cavity, and possible prophylactic appendectomy.<sup>1</sup> Nagdeve et al.<sup>3</sup> reported that as many as 30% of patients older than 2 years of age had midgut volvulus found during the surgical correction of malrotation. We also report that 17% of patients in our cohort had an operative finding of midgut volvulus at the time of malrotation repair, but such finding did not seem to have relevant clinical significance in our cohort.

Following surgery, patients may have persistence of GI symptoms that could be challenging to differentiate from a structural or anatomic abnormality. Dekonenko et al.<sup>2</sup> and Nagdeve et al.<sup>3</sup> reported that 25% and 40% of their patient cohorts respectively had persistence of GI symptoms following surgery for IM. In our cohort, 77% had postoperative GI symptoms, a strength of our study is the long term follow-up with the majority of patients (96%) followed for longer than 12 months. The predominant symptoms were vomiting, constipation, abdominal pain, feeding problems, nausea, and GERD. To our knowledge, the prevalence of DGBIs in patients after surgery for IM is unknown. In our study, 29% of patients with postoperative GI symptoms met Rome IV criteria for one or more DGBIs, specifically functional constipation, functional abdominal pain not otherwise specified, functional dyspepsia, irritable bowel syndrome, and abdominal migraine. Moreover, only 34% of patients with postoperative GI symptoms had resolution of symptoms at last follow-up, and other than gender and race no other factors were associated to symptom resolution. Based on the results of this

study, identifying, and treating DGBIs in these patients might be warranted after reasonable investigations to rule out mechanical and anatomical etiologies.

We found an equivalent proportion of patients with postoperative GI symptoms after surgery for malrotation between those with an incidental diagnosis (asymptomatic before surgery) and those symptomatic before surgery. Notably, 78% of patients without GI symptoms before surgery (incidental diagnosis) developed symptoms postoperatively. This suggests that factors other than malrotation may be linked to development of GI symptoms. We found that longer time from diagnosis to surgery (delay in surgery) was associated to lack of resolution of symptoms with univariate but not with multivariate analysis, suggesting that delaying surgery may be a factor associated to treatment and overall outcomes. There is some evidence of chronic GI dysfunction particularly chronic nausea, vomiting, or diarrhea after major abdominal surgeries including pancreatic resection, cardiac surgery, and lung transplant.<sup>13–16</sup> Most of these studies did not identify the clear etiology of chronic and debilitating GI symptoms in their patient cohorts. We postulate that the stress related to surgery (abnormal neuroinflammatory response in the setting of significant intestinal manipulation) could result in altered sensory response/visceral hyperalgesia predisposing these patients to develop DGBIs. We did observe those with symptom resolution had a longer median follow-up compared to those that did not resolve but did not reach significance ( $p=0.088$ , Table 2), suggesting symptoms may resolve over time but perhaps our study did not have a large enough sample size to detect that association.

There is very limited evidence that persistence or development of GI symptoms after surgical repair may be secondary to dysmotility or aberrant early development of the enteric nervous system (ENS).<sup>5</sup> Devane et al.<sup>5</sup> conducted antroduodenal manometry in eight patients who had persistent GI symptoms following surgical repair of malrotation. Authors reported results ranging from normal motility to no detectable activity to slow and disorganized propagation and low amplitude of MMC phase 3. Seven out of eight patients demonstrated findings on antroduodenal manometry consistent with neuropathic changes of intestinal pseudo-obstruction. Even though the number of patients in the study is very small, one can consider GI dysmotility as one of the potential mechanisms leading to symptoms in these groups of patients. Altered ENS development may account for abnormal motility since the embryological maturation timing for enteric neuronal innervation and the rotation of midgut and return to abdominal cavity are similar around 10th–12th weeks of gestation.<sup>17,18</sup> In another study, Coombs et al.<sup>6</sup> conducted four antroduodenal manometry studies in patients with persistent GI symptoms including vomiting,

failure to thrive, diarrhea and possible pseudo-obstruction. They concluded that all four patients had abnormal motility ranging from nonpropagation to random neuropathic abnormal cluster activity. They concluded that this group of patients did not benefit from the operation of malrotation and in fact it could be an incidental finding although it prevents complications such as volvulus.<sup>6</sup> In a national series of children with pediatric intestinal pseudo-obstruction, 15% of children were found to have malrotation.<sup>19</sup> However, in our cohort, only two patients underwent advanced motility studies, most with transit studies had normal results and a third required promotility agents with only few responding satisfactorily to those, suggesting dysmotility may not play an important role and other etiologies must be considered.

Notably, there is a high rate of associated anomalies reported in infants with malrotation.<sup>20</sup> In our cohort, 30% of patients had malrotation associated with another condition, including chromosomal anomalies. Having genetic abnormalities concurrently with IM may increase the risk of upper GI dysmotility.<sup>21</sup> In addition, other motility disorders such as Megacystis Microcolon Hypoperistalsis Syndrome are commonly associated with IM.<sup>22,23</sup> Further studies are needed to substantiate the claims of increased foregut dysmotility in these patients.

## 5 | LIMITATIONS

This study is limited primarily by its retrospective nature, also by the lack of motility studies to identify and typify any possible bowel dysmotility as a potential mechanism for dysfunction and symptom development. The study also lacks detailed information on the timing of symptom onset relative to surgery, as well as change in symptoms over time. Nevertheless, the strengths of this study are the long follow-up time, multicenter collaboration yielding a large population of patients with malrotation from birth to 21 years of age, and the much-needed information on the long-term outcomes and prevalence of DGBIs. Multicenter longitudinal studies are needed to further delineate the natural course and possible etiologies of persistent and de novo GI symptoms in children following surgery for IM.

## 6 | CONCLUSIONS

Pediatric IM is a relatively common diagnosis in children. These patients continue to have persistent GI symptoms and some develop new symptoms after surgery. Due to the lack of studies evaluating this condition and its natural course, etiologies remain unclear. Intestinal dysmotility and abnormal sensory responses secondary to ENS insult (in utero due to the disruption of the normal developmental intestinal

rotation and intermittent volvulus and from surgical stress) are possible theories to explain such symptoms. In our study, including long follow-up, a large proportion of patients had persistent or developed new GI symptoms and many met Rome IV criteria for DGBI. After a reasonable evaluation for mechanical and anatomical causes, it is important to screen and treat patients with DGBI to improve their symptoms and quality of life. Future research exploring GI motility in these patients is warranted.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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