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Methods in pediatric surgery 2022

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Azygos vein preservation is feasible and beneficial in esophageal atresia with tracheoesophageal fistula: A meta-analysis of randomized controlled trials

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Background: Esophageal atresia (EA) with tracheoesophageal fistula (TEF) is a common congenital anomaly. It is still unknown whether azygos vein preservation will increase the difficulty or time of operation and reduce the quality of anastomosis. Thus, we conducted this meta-analysis to explore the puzzle.

Methods: Two researchers independently searched the databases. Randomized controlled trials were included if these studies applied thoracotomy to perform operations and compared the outcomes in patients with EA/TEF between azygos vein preservation groups and azygos vein ligation groups. The Jadad score was used to assess the quality of the included studies. Statistical heterogeneity was evaluated using the I^2 value. A fixed or random-effect model was applied regarding the I^2 value.

Results: Four studies involving 286 patients were included. The pooled estimates indicated that preservation of the azygos vein decreased the incidence of anatomic leakage with a pooled risk ratio (RR) of 0.54 (95% CI 0.29–0.99, $P = 0.05$) and mortality with an RR of 0.51 (95% CI 0.29–0.90; $P = 0.02$). Preservation of the azygos vein might not require a longer operative time than ligation of the azygos vein.

Conclusions: This research certifies that preservation of the azygos vein is able to reduce the prevalence of anastomotic leakage and mortality.

KEYWORDS

esophageal atresia, azygos vein, complication, anatomic leak, mortality

Introduction

Esophageal atresia (EA) is a common congenital anomaly of the digestive tract, with a prevalence of 1 in 3,500 births (1). EA with tracheoesophageal fistula (EA/TEF) accounts for ~70–90% of cases of EA (2, 3). Operation is indispensable to save the patient's life. The azygos vein is usually ligated and divided to facilitate operation during the repair procedure of EA/TEF (4).

The azygos vein is an important vein that ascends in the posterior region of the right thorax and next to the vertebral column. It drains blood from all of the posterior intercostal veins but the first intercostal vein in the right thorax into the superior vena cava. Some investigators maintain that the azygos vein is a major vessel and should be preserved if preservation does not augment the incidence of postoperative complications (5). Anastomotic leakage is one of the most frequent postoperative complications and significantly increases postoperative hospitalization time and cost (6, 7). Some researchers believe that ligation of the azygos vein will aggravate postoperative edema at the anastomosis and chest congestion and consequently lead to higher incidences of complications, including anastomotic leakage and pneumonitis (5, 8). Although a series of studies have been performed to verify this assumption, those studies have failed to achieve consistent conclusions (5, 8–11). Concerns are raised regarding whether azygos vein preservation will increase the difficulty or time of operation and reduce the quality of anastomosis. A longer operative time results in longer anesthetic exposure. Longer anesthetic exposure may augment the risk of impairment in neural development (12). With the view that more than 90% of pediatric surgeons preferring thoracotomy to thoracoscopy to deal with EA, (13) in the present study, we conducted this meta-analysis to investigate whether azygos vein preservation would be feasible with no increased risks or even reduced risks of postoperative complications in patients undergoing thoracotomy.

Methods

Study selection

This review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (14). Randomized controlled trials (RCTs) were included if these studies applied thoracotomy to perform operations and compared the outcomes in patients with EA/TEF between azygos vein preservation groups and azygos vein ligation groups. Patients in the included studies should receive primary repair procedures rather than staged procedures. Meanwhile, eligible studies were mandatory to report at least one of the predetermined outcomes, including operative time, anastomotic leak and mortality. The included studies were restricted to studies published in English.

Abbreviations: CI, Confidence interval; EA, Esophageal atresia; TEF, Tracheoesophageal fistula; RCT, Randomized controlled trial; RR, Risk ratio.

Search strategy

The search strategy was designed and conducted by two researchers (C.W. and J.W.). We independently searched databases including PubMed, EMBASE and the Cochrane Library. The keywords containing "azygos vein" and "esophageal atresia" were combined with the Boolean operator AND to identify published potential studies. Each of the two researchers independently reviewed the titles and abstracts to refine the results. Full-text manuscripts of the relevant studies were scrutinized to identify potential studies that met the inclusion criteria. Reference lists of included studies were inspected to screen additional studies.

Data extraction and quality assessment

Anastomotic leakage was defined as the primary outcome. Operative time and mortality were defined as the secondary outcomes. Two authors (C.W. and J.W.) independently abstracted and documented the following information from eligible studies: lead author, publication year, sample size, study design and outcomes. The Jadad score was adopted to assess the quality of the included studies. The Jadad score, ranging from 0 to 5, was applied to evaluate the quality of RCTs, and a study with a score >2 was regarded as a "high quality" study (15).

Statistical analysis and exploration of heterogeneity

Reviewer Manager 5.3 from the Cochrane Collaboration was applied to perform the meta-analysis. We adopted the Mantel–Haenszel statistical method to calculate risk ratios (RRs) and 95% confidence intervals (CIs) for the pooled results of all outcomes in the meta-analysis. The potential bias for publication was evaluated by employing funnel-plot symmetry. Statistical heterogeneity among summary data was assessed by the I^2 method, with an I^2 value higher than 50%, suggesting substantial heterogeneity. If the I^2 value was higher than 50%, a random-effects model of analysis was applied; if not, a fixed-effects model was applied.

Results

Study selection and the results of selection are shown in Figure 1. Forty-eight potentially eligible records were identified by using the search strategy. After carefully reviewing the titles and abstracts of these publications, the full texts and reference lists of 7 records were scrutinized, and 4 articles

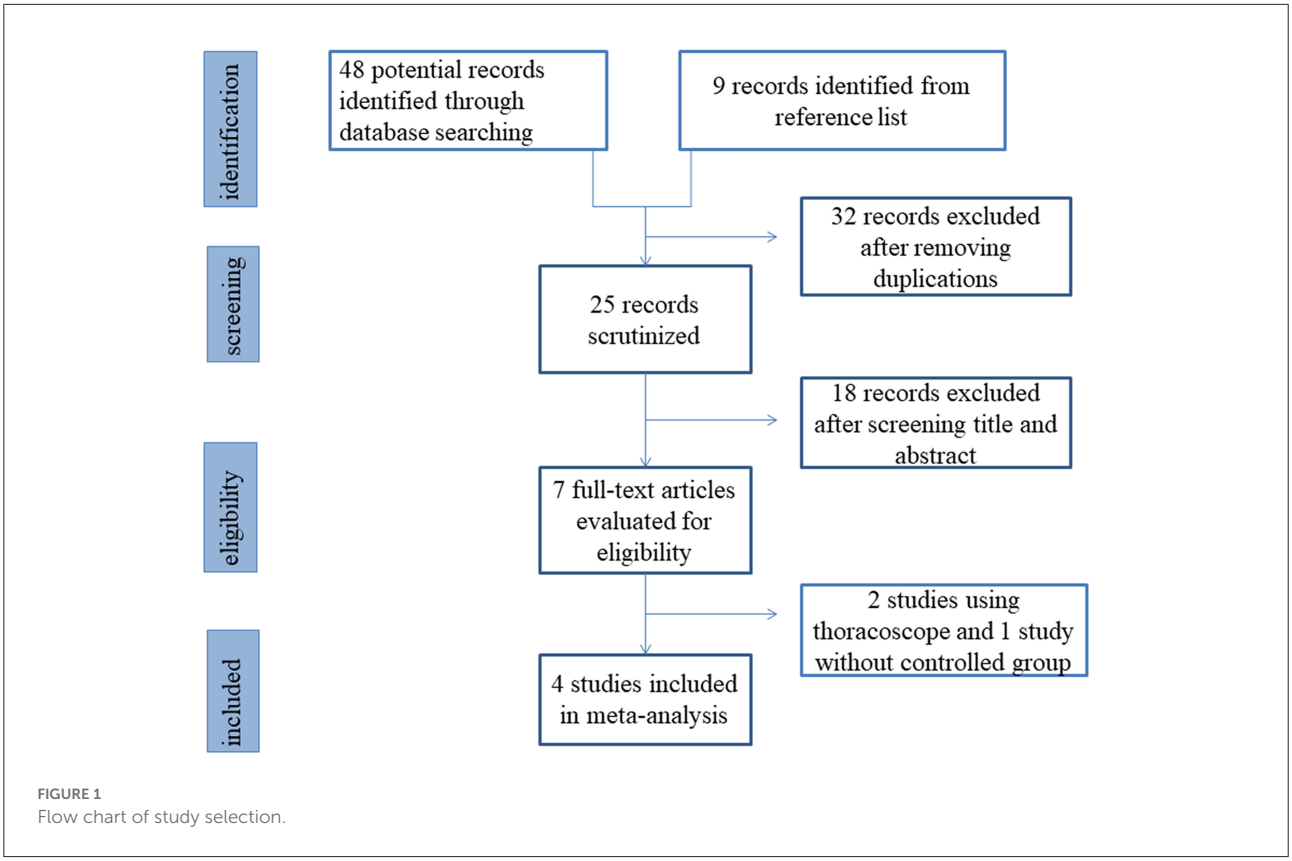

FIGURE 1
Flow chart of study selection.

TABLE 1 Characteristics of included studies.

Study	Study type	Surgery approach	Sample size	Mean age (h)	Sex	Weight (kg)	Associated anomalies	Gap length (cm)	JS
Upadhyaya et al. (8)	RCT	Thoracotomy	Preservation: 25	NA	Male/Female:NA	NA	8	NA	3
			Ligation: 25	NA	Male/Female:NA	NA	9	NA	
Sharma et al. (5)	RCT	Thoracotomy	Preservation: 46	NA	Male/Female:33/13	2.32	12	NA	8
			Ligation: 50	NA	Male/Female:27/23	2.52	14	NA	
Rashid et al. (11)	RCT	Thoracotomy	Preservation: 81	41.07	Male/Female:49/32	2.66	24	1.33	2
			Ligation: 35	37.93	Male/Female:22/13	2.48	13	1.43	
Fathi et al. (10)	RCT	Thoracotomy	Preservation: 12	36.25	Male/Female:7/5	2.36	NA	NA	8
			Ligation: 12	34.66	Male/Female:6/6	2.22	NA	NA	

RCT, randomized controlled trial; NA, not available; JS, Jadad score.

meeting the inclusion criteria were ultimately included in the final analyses (5, 8, 10, 11). Table 1 summarizes the baseline characteristics and Jadad scores of these four studies. A total of 286 patients were assigned to the preservation group (n = 164) or the ligation group (n = 122). Table 2 reports the exact case numbers of each outcome in each study. There was no evidence of obvious publication bias in each analysis, based on funnel-plot symmetry.

Operative time

Although all four records reported the average operative time (5, 8, 10, 11), only one record reported the average operative time with standard deviation (10). The results of three studies found a longer mean operative time in the preservation group than in the ligation group, (8, 10, 11) ranging from 0 to 10 min, while one study showed a longer mean operative time in the ligation group than in the preservation group (5).

TABLE 2 Summary of the outcomes of included studies.

Study	Sample size	Anastomotic leakage	Mortality	Mean operative time (min)
Upadhyaya et al. (8)	Preservation: 25	4 (16.00%)	4 (16.00%)	80
	Ligation: 25	5 (20.00%)	4 (16.00%)	70
Sharma et al. (5)	Preservation: 46	3 (6.52%)	5 (10.87%)	60
	Ligation: 50	10 (20.00%)	14 (28.00%)	64
Rashid et al. (11)	Preservation: 81	10 (12.35%)	9 (11.11%)	63
	Ligation: 35	7 (20.00%)	8 (22.85%)	60
Fathi et al. (10)	Preservation: 12	0 (0.00%)	NA	60
	Ligation: 12	0 (0.00%)	NA	60

NA, not available.

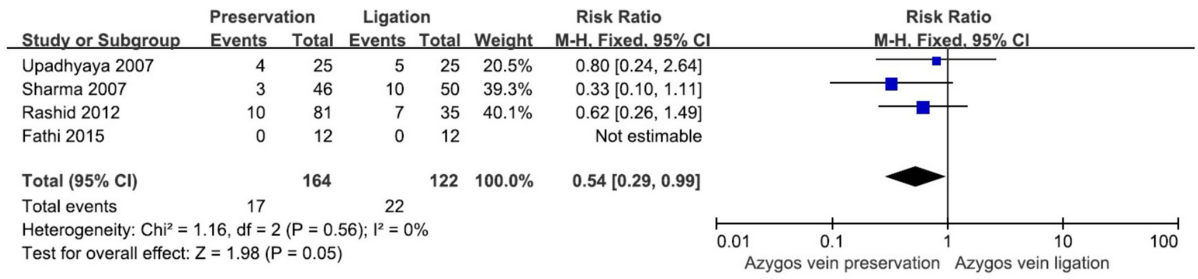

FIGURE 2
Forest plot showing the risk ratio for the occurrence of anastomotic leakage in the two groups.

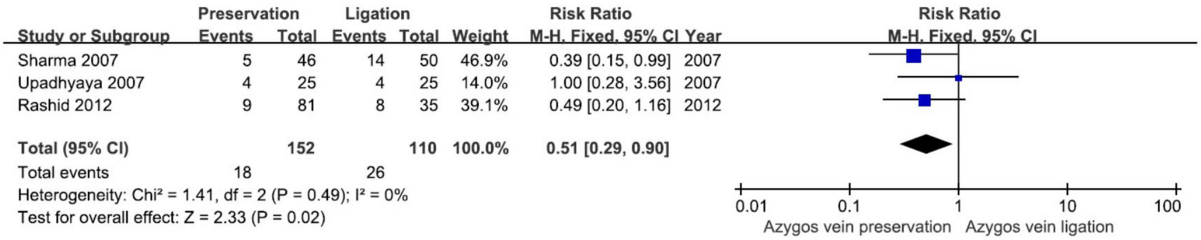

FIGURE 3
Forest plot showing the risk ratio for the occurrence of mortality in two groups.

Anastomotic leakage

All four studies reported the incidence of anastomotic leakage as an outcome in pediatric patients with EA/TEF (5, 8, 10, 11). The incidence of anastomotic leakage was 10.37% (17, $n = 164$) in the preservation group and 18.03% (22, $n = 122$) in the ligation group. No detectable heterogeneity was examined among the four studies ($I^2 = 0\%$). The results of the meta-analysis indicated that there was a perceptible discrepancy in the incidence of anatomic leakage between the two groups, with a pooled RR of 0.54 (95% CI 0.29–0.99, $P = 0.05$) (Figure 2). The preservation group had a lower risk of anastomotic leakage than the ligation group.

Mortality

Three out of four studies investigated mortality in EA/TEF patients (5, 8, 11). In total, there were 18 deaths in the preservation group ($n = 152$) and 26 deaths in the ligation group ($n = 110$). There was no observable heterogeneity among these studies ($I^2 = 0\%$). A significant difference in mortality was detected between the two groups, and the ligation group had a

higher risk of mortality (RR 0.51, 95% CI 0.29–0.90; $P = 0.02$) (Figure 3).

Discussion

EA is the most frequent congenital malformation of the esophagus, which is supposed to emerge as a consequence of the abnormal development of the foregut (16). The first successful end-to-end anastomosis and fistula ligation to treat EA/TEF was presented in 1941, (17) and currently, surgery is considered to be inevitable to save life.

In the standard operation procedure of repair surgery of EA/TEF, the azygos vein would be ligated and divided to provide a clear operation field and facilitate identification of the distal esophagus and fistula to conduct esophageal anastomosis. It was worrisome whether preservation of the azygos vein would prolong operative time. A longer duration of surgery means a longer duration of general anesthesia. Some studies have indicated that prolonged anesthesia might affect neurodevelopmental outcomes (18). Harmsen et al. reported that the duration of anesthetic exposure was negatively correlated with motor developmental outcome in patients with EA (19). Our study found that the preservation group might not need a longer operative time than the ligation group. The results of four studies were not consistent. The differences in the mean operative times in the two groups were small. Further large trials are needed to clarify this question.

The azygos vein drains deoxygenated blood from the ascending lumbar veins and the right subcostal veins into the superior vena cava, which means that the azygos vein also drains the esophagus and bronchus. Compared with ligation of the azygos vein, preservation of the azygos vein possibly lowered the degree of esophageal anastomotic edema and postoperative congestion of the lung. It might be reasonably deduced that preservation of the azygos vein could reduce the risks of anastomotic complications and pneumonias.

Anastomotic leak was a main early postoperative complication in EA patients, with an estimated prevalence of 20% (20). Patients with long gap EA had a higher risk of anastomotic leakage, which might be attributed to high tension on the anastomosis (20, 21). Minor leaks might heal spontaneously by managing conservatively with drainage. Nevertheless, major leakage might be life-threatening, and reoperation may be needed. Some researchers supposed that ligation of the azygos vein would aggravate postoperative edema at the anastomosis and consequently increase the risk of anastomotic leakage in patients (8). Our study demonstrated that preservation of the azygos vein could reduce the prevalence of anastomotic leakage. Nevertheless, whether the decrease in anastomotic leakage is related to the relief of postoperative edema by draining blood remains to be clarified.

Although mortality after EA repair remarkably dropped from 81% in the 1940s to 9% in the 2010s with the development of equipment and perioperative management 26, death is still a threat to patients with EA. In this study, we found that preservation of the azygos vein could significantly lower mortality. Approximately half of patients with EA have associated anomalies (3, 22). Cardiac defects were the most common associated anomaly, with a prevalence of 26.7% (22). It was reported that cardiac defects were related to mortality (22, 23). Preservation of the azygos vein might have less of an effect on the circulatory system than ligation of the azygos vein. In addition, preservation of the azygos vein was able to reduce the risk of postoperative pneumonitis (8, 11). These advantages might contribute to the lower mortality.

Some limitations should be noted in this study. Although only RCTs were included in this meta-analysis, which maximally reduced potential biases, the number of included studies was limited. Many postoperative complications, including anastomotic stricture, recurrent TEF and gastroesophageal reflux disease, were not compared owing to a lack of relevant data. Thus, we were not able to evaluate the preservation of azygos veins in all aspects, and more studies are needed to assess the preservation of azygos veins in those aspects to provide a further understanding.

Conclusions

This study offers distinguished evidence regarding the safety and benefit of preservation of the azygos vein in patients with EA/TEF. Our research demonstrates that preservation of the azygos vein is able to reduce the prevalence of anastomotic leakage and mortality compared with ligation of the azygos vein. Further studies are needed to evaluate the preservation of the azygos vein in other aspects, including anastomotic stricture, recurrent TEF and gastroesophageal reflux disease.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

XM contributed to the design of the study. CW and JZ performed the literature search and extracted the data. XM and CW analyzed the data and interpreted the statistical analysis.

XM, CW, and JZ drafted the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Is endoscopy beneficial in pediatric laparoscopic gastrostomy insertion; A 9-year comparative study

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Objectives: Advancements in pediatric percutaneous endoscopic gastrostomy placement (PEG), laparoscopic-assisted gastrostomy (LAG) technique, and laparoscopic-assisted percutaneous endoscopic gastrostomy (LAPEG) procedure have opened up new options for gastrostomy tube placement. LAPEG utilizes endoscopy and laparoscopy for gastrostomy insertion. This review compares the outcomes and complications of LAG and LAPEG techniques in children.

Methods: All LAG and LAPEG gastrostomy tube placements in children from September 2010 to September 2019 were reviewed retrospectively. Patient demographic, along with procedural and 1-year complication data, were collected.

Results: In total, 92/181 of gastrostomies were LAG and 89/181 were LAPEG. The mean age, weight and patient characteristics were comparable. Conversion rate was 1% in both groups (p = 0.74), there was no peritoneal leak in either group, a minor serosal injury to the stomach was seen in 1 patient in LAG with no bowel injury in LAPEG cohort (p = 0.51), need for re-operation was 1 and 2% in LAG and LAPEG, respectively (p = 0.49), early tube dislodgement was in 8 (9%) patients in LAG and 7 (6%) in LAPEG (p = 0.53) and wound infection was 13/92 in LAG and 11/89 in LAPEG (p = 0.8). The median operative time for LAPEG was less than LAG ($p < 0.001$) by 11 min but the median length of hospital stay was not significantly different ($p < 0.096$).

Conclusion: Both LAG and LAPEG techniques in children are safe with comparable complication rates and length of hospital stay, the addition of endoscopy to LAG allowed for shorter operative time in the LAPEG technique.

KEYWORDS

gastrostomy, percutaneous endoscopic gastrostomy, laparoscopic-assisted gastrostomy, laparoscopic-assisted percutaneous endoscopic gastrostomy, pediatric

What is known

- Laparoscopic-assisted percutaneous endoscopic gastrostomy (LAPEG) was introduced in 1993 as a gastrostomy placement technique that utilizes both endoscopy and laparoscopy.
- LAPEG can be used when percutaneous endoscopic gastrostomy (PEG) is contraindicated or carries increased complication risk.
- Case reports and case series have demonstrated the high safety profile of LAPEG.
- There is only one comparative study comparing laparoscopic-assisted gastrostomy (LAG) to LAPEG in adults (1).

What is new

- This is the first study comparing LAPEG and LAG in children.
- LAPEG and LAG are both safe with minimal complication rate.
- The addition of endoscopy in LAG makes the procedure shorter.

Introduction

Gastrostomy tube insertion is a routinely performed procedure in children who require long-term enteral feeding support (2). Gastrostomy is performed in children with underlying oncological disorders, metabolic, renal disorders, neurological pathologies, and congenital or acquired gastrointestinal tract conditions in which oral intake is hindered. Several technical approaches are used for gastrostomy insertion, including percutaneous endoscopic gastrostomy (PEG), percutaneous image guided gastrostomy (PIG), laparoscopic-assisted gastrostomy (LAG), and laparoscopic-assisted percutaneous endoscopic gastrostomy (LAPEG) (3). LAPEG, the most recently introduced technique, simultaneously utilizes both laparoscopic and endoscopic guidance for better visualization during the procedure (4). Typically, one gastrostomy insertion approach is favored over another based on the clinical scenario, facilities, and the clinician's expertise (5).

Our institution has traditionally used open techniques for gastrostomy placement and very few patients received percutaneous endoscopic gastrostomies due to our concern about risk of possible organ injury associated with PEG. Gastrostomies were inserted for patients who required prolonged tube enteral nutrition (EN) secondary to gastrointestinal and surgical bowel abnormalities, neurological disorders, syndromic disease, increased nutritional requirement from renal, cardiac, and respiratory disease and for metabolic patients who require specialized feeding. Over the past 10 years, we have shifted our clinical practice to lesser invasive techniques, including LAG and LAPEG. Although recent studies have sought to compare outcomes between different modalities and confirmed the safety of laparoscopic techniques (6), the benefit of incorporating endoscopy with laparoscopy, as seen in LAPEG, has not been previously evaluated in children. Therefore, this study aims to compare outcomes and major complications between LAG and LAPEG in the pediatric population.

Materials and methods

We performed a retrospective analysis of the LAG and LAPEG procedures performed on children over a 9-year period from September 2010 to September 2019 at the Sheikh Khalifa Medical City, the main tertiary-care pediatric hospital in the United Arab Emirates. Approval was obtained from the Institutional Review Board for Research and Ethics Committee. All children under the age of 16 who underwent LAG or LAPEG tube placement during the study period were included in the study. Patients who had an open gastrostomy, percutaneous interventional radiologic gastrostomy (PIRG), and gastrostomy insertion with fundoplication were not included in the study. The minimum follow-up was 1 year. All the procedures were performed after obtaining informed consent from the patients' parents or legal guardians. The decision for LAPEG and LAG insertion was based on primary physician specialty referral. If the primary physician referred the patient to pediatric gastroenterology, then the patient underwent LAPEG, however, if the patient was referred to the pediatric surgeons, then the patient would undergo LAG. Factors such as obesity, patient weight and previous abdominal surgery did in influence the choice of gastrostomy insertion technique. We have four pediatric gastroenterologists and four pediatric surgeons within our institution and they all were involved in the gastrostomy placement.

A list of all patients undergoing LAG and LAPEG under 16 years was obtained from the operating room electronic record. Data including patient demographics (age, gender, and weight), significant past medical history for cardiac disease or abdominal surgery, pre-operative location of the patient in Pediatric Intensive Care Unit (PICU) or general ward and American Society of Anesthesia (ASA) score were collected from the electronic medical patient records. The primary outcome points were success of the procedure, operative time, length of stay (LOS), rate of surgical site infection, procedure-related complications, and mortality rate. The operative time was calculated only for the patients who underwent isolated

gastrostomy insertion, children who underwent another surgical procedure at the time of gastrostomy insertion were excluded when calculating the operative time. Children were discharged when they were deemed clinically stable and after they had achieved the feeding goal set by the pediatric dietician as per the patient needs. Only elective LAG and LAPEG cases were included in the LOS analysis, elective cases included the cases who were planned for gastrostomy insertion through clinic and were not chronic inpatients at the time of the gastrostomy insertion. Patients who were in hospital for prolonged medical or surgical management unrelated to gastrostomy care were excluded. Procedure complications were sub-grouped into intraoperative and postoperative. Intraoperative complications included adjacent bowel injury, intraperitoneal leak and conversion from the planned technique to an alternative gastrostomy placement method. Postoperative complications included re-intervention under general anesthesia, surgical site infection, and early tube dislodgement. Re-intervention under anesthesia was defined as any procedure undertaken under general anesthesia that was performed in relation to a gastrostomy related complication within the first 6 weeks of insertion. Surgical site infection was identified as erythema, induration, exudate, or purulent secretion at the surgical gastrostomy site within 30 days of the procedure (7). A wound culture was obtained any time considered necessary and treatment with antibiotics was prescribed when considered indicated, which was at the surgeon or gastroenterologists' discretion. Early tube dislodgement was characterized as dislodgement of the feeding tube within 6 weeks of insertion.

The continuous variables are expressed as mean and standard deviations, whereas all the categorical variables are calculated as frequencies and percentages. Median operative time and length of hospital stay were calculated for both procedures because the data were not normally distributed. Statistical analyses were performed utilizing Fisher's exact test for categorical variables and Student's *t*-test for all continuous variables. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS version 22.0 for Windows.

Operative technique

Laparoscopic-assisted percutaneous endoscopic gastrostomy

All LAPEG procedures were performed under general anesthesia. We used the push technique to insert a balloon gastrostomy device with the aid of laparoscopy. Since the procedure required the deployment of both endoscopic and laparoscopic techniques, both a pediatric gastroenterologist and a pediatric surgeon were involved.

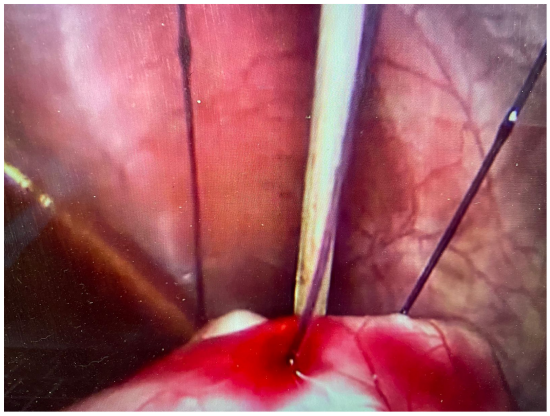

FIGURE 1
The stomach fixed to the abdominal wall under laparoscopic visualisation.

An initial incision was made at the umbilicus to place a 5-mm optical trocar for the laparoscope. Pneumoperitoneum was achieved at a pressure of 8–12 mmHg. In few cases where adhesions secondary to previous abdominal surgeries such as necrotizing enterocolitis, bowel surgery, diaphragmatic hernia repair or peritoneal catheter insertion, additional ports were placed for better visualization. Once the stomach was identified, an upper endoscopy was performed using a flexible gastroscope. The appropriate site for the gastrostomy insertion was chosen by direct visualization and external finger indentation after insufflating the stomach. The stomach was routinely fixed to the abdominal wall using trans-abdominal trans-gastric tuckers under direct laparoscopic and endoscopic visualization (**Figures 1**, **2**). After fixing the stomach to the abdominal wall, a balloon-type gastrostomy tube was inserted in the gastric lumen with the help of a guidewire (**Figure 2**) through modified Seldinger technique using a gastrostomy introduction kit. The gastrostomy tube used was either 12 or 14 French depending on patient size. The gastrostomy balloon was finally inflated, and the gastrostomy tube was fixed to the skin at an appropriate length.

Laparoscopic-assisted gastrostomy

In patients who underwent LAG, the first camera port was inserted by open technique and pneumoperitoneum is sustained at 8–12 mm Hg, with a tendency to use less pressure in smaller children and patients with selected cardiac complications. A 5-mm 30° laparoscope was placed through the umbilical port, and quick abdominal inspection was performed before choosing the appropriate site for gastrostomy tube insertion to avoid creating excessive tension on the gastric wall. With the help of a 3-mm grasping clamp inserted through the planned gastrostomy site, the stomach was grasped along the greater curvature

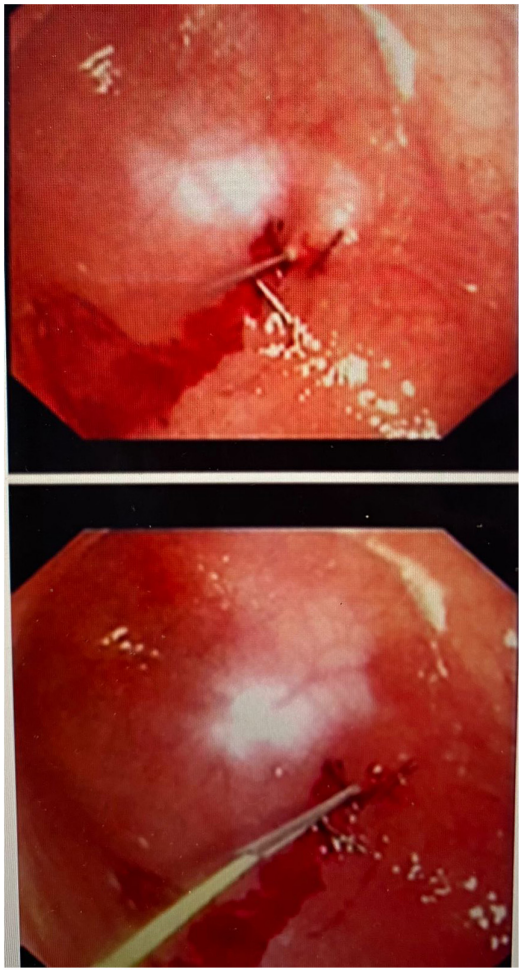

FIGURE 2
Tuckers placed and guide-wire inserted under endoscopic visualisation.

and fixed to the abdominal wall. A guidewire was introduced into the stomach through an 18-G cannula; the passage was subsequently dilated by means of fascial dilators of increasing caliber until a caliber that was wider than the gastrostomy tube to be inserted. The gastrostomy was inserted into the gastric cavity through the push technique, and the balloon was subsequently filled with saline solution. The correct positioning of the gastrostomy was checked by infusing and aspirating methylene blue saline solution.

In both techniques, patients received prophylactic intravenous co-amoxiclav in theater at time of gastrostomy insertion and remained on antibiotics for 24 h. The patients are started on oral rehydration solution on the day following the gastrostomy insertion for 2 h, if the patient tolerated the oral rehydration solution, they will then be started on milk feeds. The patient is generally put on the same milk feed that he was taking prior to gastrostomy insertion. A feeding plan to achieve the target feeding goal is made by a pediatric dietician. Over time we have shifted from next day feeding to feeding on same day the gastrostomy is inserted. The T fastener would normal dissolve spontaneously within a month of insertion. However, if the patient remains hospitalized for more than 5 days, we would cut the tuckers.

Replacement of the gastrostomy tube into a button device occurred 6 weeks after primary insertion.

Results

In total, 181 children fulfilled the inclusion criteria and underwent either LAG or LAPEG procedure. In total, 92/181 (51%) underwent LAG and 89/181 (49%) underwent LAPEG. The majority of gastrostomies in our series were inserted for patients with neurological disorders 45% such as cerebral palsy, spinal muscular atrophy, hydrocephalus, and lissencephaly. In total, 15% of patients had complex congenital heart disease and some had congenital heart disease as part of a syndrome such as Down's syndrome, Noonan syndrome, and Di George syndrome. Other less common indications included; 10% had GT insertion following abdominal bowel surgery for necrotizing enterocolitis, bowel atresia, and diaphragmatic hernia, 10% had syndromes with or without swallowing impairment, 8% had metabolic disorders such as glycogen storage disease and urea cycle defects, 4% had chronic lung disease, 4% had renal disorders, and 3% had immune deficiency with associated failure to thrive.

There were no statistically significant differences in patient demographics and patient characteristics between the two groups (**Table 1**). The youngest patient who underwent LAG was 1 month old, compared to the LAPEG group, where the youngest patient was 3 months old. Most patients (148/181) had an ASA score of 3, 9 patients had a score of 2, 23 patients had a score of 4, and only one patient had a score of 5. In total, 34/92 patient who underwent LAG had previous abdominal surgery such as necrotizing enterocolitis, nephrectomy, peritoneal catheter insertion, ventriculoperitoneal catheter insertion, perforated appendix, midgut volvulus, intestinal atresia, intestinal perforation, diaphragmatic hernia, and exomphalos repair. In total, 29/89 patients who underwent LAPEG had previous abdominal surgery for necrotizing enterocolitis, ventriculoperitoneal shunt insertion, peritoneal catheter insertion, nephrectomy, diaphragmatic hernia, adhesiolysis and fenestration of peritoneal cyst, omphalocele repair, omentectomy, and ligation of patent processes vaginalis. The procedures were elective (outpatients attending for gastrostomy insertion) in 107 patients, including 54 (59%) in the LAG group and 53 (60%) in the LAPEG group. The rest of the patients were in hospital patients requiring prolonged hospital stay for complex and multiple medical disorders and required gastrostomy insertion as part of their overall medical care.

TABLE 1 Patient demographics and characteristics.

	LAG ($n = 92$)	LAPEG ($n = 89$)	*P*-Value
Female	43 (46.7)	40 (45)	1.0
Mean age (years)	2.8 (0.08–16)	2.5 (0.25–14)	0.1
Mean weight (kg)	10.3 (2.6–48.4)	10.6 (2.8–33.9)	0.4
Mean American Society of Anesthesiology (ASA) score	3	3	1.0
Previous abdominal surgery	34 (37%)	29 (33%)	0.64
Cardiac disease	19 (21%)	19 (21%)	1.0
Elective cases	54 (59%)	53 (60%)	0.65
PICU patients prior to surgery	37 (40%)	30 (34%)	0.44

TABLE 2 Surgical outcomes and complications.

	LAG ($n = 92$)	LAPEG ($n = 89$)	*P*-Value
Successful completion	91 (99%)	88 (99%)	>0.99
Conversion	1 (1%)	1 (1%)	0.74
Adjacent bowel/organ injury	1 (1%)	0 (0%)	0.51
Intraperitoneal leak	0 (0%)	0 (0%)	
Early tube dislodgement	8 (9%)	7 (6%)	0.53
Repeated early intervention under general anesthesia	1 (1%)	2 (2%)	0.49
Wound infection	13 (13%)	11 (12%)	0.8
Total	29 (32%)	23 (26%)	0.14

Both LAG and LAPEG were performed successfully for patients with no significant complications and no perioperative mortality (Table 2). However, due to poor surgical visibility and limited working space, one patient in each procedure group was converted to open gastrostomy. Only one patient in the LAG group developed a minor serosal injury of the stomach which did not require any surgical intervention. There were no intraperitoneal leaks in either group.

Review of the postoperative complications revealed no difference in early tube dislodgement in either group ($p = 0.53$). A total of 15 patients had early tube dislodgement, the earliest tube dislodgement occurred 15 and 10 days following LAG and LAPEG placement, respectively. Only one patient from the LAG and two patients from the LAPEG tube required a second operation under general anesthesia for tube replacement within 15 days of the initial gastrostomy tube insertion. The remaining patients had their gastrostomy tubes replaced successfully at bedside, with no need for additional surgical intervention. In total, 24 (13 LAG and 11 LAPEG) patients had surgical site infection requiring treatment with oral antibiotics. Surgical site infection was identified as erythema, induration, exudate, or purulent secretion at the surgical gastrostomy site within 30 days of the procedure (7). A wound culture was obtained any time considered necessary and treatment with antibiotics was prescribed when considered indicated, which was at the surgeon or gastroenterologists' discretion. Empiric oral co-amoxiclav was started until the swab result with antibiotic sensitivities were obtained. Antibiotics were changed if the surgical site infection was caused by an organism that is not sensitive to co-amoxiclav. No patient with stoma infection required hospital admission or intravenous antibiotics, there was no deep-seated infection and all patient improved with oral antibiotics. Although there was a trend toward an increased rate of overall surgical complication rate in the LAG group (32%) compared to LAPEG (26%), this result did not achieve statistical significance ($p = 0.14$).

TABLE 3 Comparison of median length of stay and operative time.

	LAG	LAPEG	*P*-Value
Median length of hospital stay (days)	6	5	0.096
Median surgery duration (minutes)	38	27	<0.001
LAG/LAPEG performed with another procedure	32 (35%)	40 (45%)	0.36

Excluding patients who had a concurrent other surgical procedure (32 LAGs and 40 LAPEGs), the median total operating time was 38 (range 18–66) min in the LAG group and 27 (range 21–74) min in the LAPEG group ($p < 0.001$) (Table 3). The median postoperative hospital stay was 6 days (range 2–20) in the LAG group and 5 days (range 2–16) in the LAPEG group. There was no difference in the LOS between both the groups ($p = 0.096$). Only elective cases were considered while calculating the median length of hospital stay to remove any possible confounders. A total of 74 (41%) patients were transferred to rehabilitation centers for long-term care due to the nature of their underlying comorbidities.

Discussion

Gastrostomy tube insertion is a well-established procedure for pediatric patients which can be placed using various techniques. Gastrostomy insertion is indicated when patients have insufficient nutritional or medical intake for a period of >2–3 weeks, or when the need for additional enteral feeding (e.g., through a nasogastric tube) is expected to exceed >3 months (7). Our patients had a variety of medical diseases requiring prolonged enteral tube feeding or specialized feeds for metabolic disorders. The choice of insertion method should be decided after careful consideration of each patient's clinical scenario, available equipment and local clinicians' expertise (8). It is important to select the procedure that is associated with the least complications and best outcome for each patient. The two gastrostomy insertion techniques compared in our study are similar with addition of endoscopy to the LAG procedure. In some patients with distorted anatomy traditional

PEG insertion can be impossible, these patients will benefit from LAG or LAPEG. Hermanowicz et al. reported twelve patients with cerebral palsy, spastic quadriparesis, severe kyphoscoliosis, and interposed organs who required EN. For these patients PEG placement was deemed impossible. In all patients LAPEG was performed with no complications in the perioperative period (9).

Gastrostomy insertion is associated with a number of complications which can be divided into major and minor complications (10). Major complications include failure of the procedure with the need for conversion to another technique, gastrostomy peritoneal leak causing peritonitis, tube dislodgement, adjacent bowel injury, and gastrocolocutaneous fistula formation. Laparoscopic technique have been demonstrated to be safer than percutaneous endoscopic technique because laparoscopy allows for direct visualization of the peritoneal cavity thereby enabling early detection and avoidance of inadvertent complications of viscus injury during gastropexy and fixation of the stomach to the anterior abdominal wall (11, 12, 13). This apparent advantage thereby minimizes the risks of the serious intra and postoperative complications that require re-operation. Therefore, it is expected that the addition of endoscopy in our study will not demonstrate significant reduction in operative and postoperative surgical complications in the LAPEG group. A meta-analysis reviewing major complications in children after LAG and PEG insertion demonstrated the LAG technique to be associated with 1% compared to 5.4% in the PEG technique. The risk of major complications was higher in PEG than in LAG 3.86 (95% confidence interval 1.9–7.81; $p < 0.0002$) (10). Our study results demonstrated similar findings of low major complication rate in both laparoscopic procedure; LAG and LAPEG. It has been mentioned in previous studies that patients with higher BMI may not be good candidates for LAG procedure because of the technical difficulty in fixation of the stomach through the thicker abdominal wall and possible excessive traction which may potentially result in unrecognized gastric injury (14). In addition, in children with foregut dysmotility and a relatively immobile stomach, attaching the insufflated stomach to the abdominal wall may be challenging (15). We did not specifically review the association between obesity, increased BMI and foregut dysmotility and difficulty in gastrostomy insertion in our group. These unique patient groups may need to be evaluated separately in future studies.

We observe a significantly reduced median operative time for LAPEG compared to LAG by 11 min (p-value < 0.001). This can be explained by the fact that endoscopy provided additional visibility of the stomach, allowing for a more confident approach and hence a faster LAPEG procedure. In addition, omitting the step of methylene blue injection to confirm tube placement in LAG may have also contributed to the reduced operative time in the LAPEG group. The median time for LAPEG insertion in our cohort was 27 min, which is similar to previous published data of 20 min (16, 17). However, the median time for LAG in our study is 38 min compared to 75 min as reported by Wragg et al. (18). This added operative time benefit needs to be carefully considered in busy and high-volume centers with prolonged patient waiting time for gastrostomy insertion.

Whilst the median length of hospital stay was shorter by 1 day for patients undergoing LAPEG compared to LAG, this difference was not statistically significant. Some patients in our cohort who had cardiac disease and complex respiratory status require to be transferred to pediatric intensive care following gastrostomy insertion for stabilization for 1–2 days prior to transfer to the ward. We believe that the late introduction of feeds in our patients and the need for stabilization of some patients in pediatric intensive care prior to discharge may explain the prolonged overall hospital stay in both groups. We have recently adopted an enhanced early gastrostomy feeding protocol which will further shorten our hospital post-operative LOS. The cost implication related to increased length of procedure time and increased hospital stay in LAG still needs to be assessed against the need for two clinicians, a surgeon and endoscopist to perform the LAPEG procedure. However, good coordination and harmony between the surgeon and endoscopist is key to achieving a shortened operative time and smooth procedure.

The authors recognize a few limitations to this study. Firstly, this is a retrospective study and as such may be limited by inaccurate documentation. Secondly, since the patients were followed up to 1 year, any major complication beyond the follow-up year had not been accounted for. However, most clinically relevant procedure-related complications associated with gastrostomy insertions are usually identified within a year of initial procedure completion. Thirdly, non-randomization of patients to LAG or LAPEG may have influence the results. Finally, although this study represents the largest review of LAPEG and LAG in children, the authors appreciate that this is still a relatively small sample size which may limit the power of conclusions drawn from this study.

We conclude that this is the first study comparing LAPEG to LAG placement in children. Although, both LAG and LAPEG are safe without significant reported complications, the addition of gastroscopy to the laparoscopic technique in LAPEG allowed for better visualization and eventually a significantly reduced operative time. A larger multi-center randomized controlled trial is required to provide a more comprehensive comparison of LAPEG and LAG in children.

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Institutional Review Board for Research and Ethics Committee, Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates. Written informed consent to participate in this study was provided by the participants' or their legal guardian/next of kin.

Author contributions

RB and SA contributed to the conception and design of the work, analysis, interpretation of data, drafting, writing up the work, and revisiting it critically. AS contributed to the design of the work, acquisition, analysis, interpretation of data, and revisiting it critically. AA and MM contributed to the design of the work, interpretation of data, and revisiting it critically. DR and MH contributed to the design of the work, analysis, interpretation of data, and revisiting it critically. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Modified conjoint fascial sheath suspension for the correction of severe congenital blepharoptosis in pediatric patients at different ages

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Objective: To evaluate the surgical outcomes of modified combined fascia sheath (CFS) and levator muscle (LM) complex suspension for the correction of severe congenital blepharoptosis in pediatric patients.

Methods: Pediatric patients with severe congenital blepharoptosis were enrolled form July 2017 to July 2021. All patients were divided into two groups according to their age (group A ≤ 7 years; group B > 7 years) and received CFS + LM suspension surgery. Main surgical outcome indexes include margin reflex distance 1 (MRD1) and MRD1 regression. Postoperative complications such as lagophthalmos (LAG), conjunctival prolapse, exposure keratopathy and trichiasis were documented.

Results: Fifty patients (60 eyes) were enrolled, including 17 patients (18 eyes) in group A and 33 patients (42 eyes) in group B. The MRD1 in group A was 3.06 ± 0.64 mm at 6 months after the operation, and the MRD1 in group B was 2.64 ± 0.69 mm 6 months postoperatively which is significantly lower than that of group A ($P = 0.044$). At the last visit, however, the MRD1 in group A was 3.00 ± 0.69 mm and the MRD1 in group B was 2.64 ± 0.70 mm. There was no significant difference in MRD1 between two groups in long term ($P = 0.255$). Additionally, there were a variety of degrees of MRD1 regression, especially in the first month after the operation in both groups (both $P < 0.001$). Moreover, there were 9 cases of postoperative complications in group A and 13 cases in group B. The overall occurrence of postoperative complications in group A was significantly lower than that in groups B ($\chi^2 = 4.413$, $P = 0.036$).

Conclusions: CFS + LM suspension, a modified CFS-based surgery, is an effective treatment for severe congenital blepharoptosis in pediatric patients. Moreover, CFS + LM suspension demonstrate excellent long-term outcomes, including good movement of the eyelid, satisfied eyelid closure and fewer postoperative complications.

Abbreviations
CFS, conjoint facial sheath; LM, levator muscle; MRD1, margin reflex distance 1; LAG, lagophthalmos

KEYWORDS

general anesthesia, pediatric blepharoptosis, conjoint fascial sheath (CFS), severe congenital blepharoptosis, levator muscle

Key messages

1. Congenital blepharoptosis is very common in clinical practice, and surgery is the only effective treatment at present.
2. Modified conjoint fascial sheath suspension has shown good results for the treatment of severe blepharoptosis.
3. The purpose of this study was to analyze the applicability of this technique in pediatric patients.
4. The operations, which were performed under general anesthesia, were found to be more challenging.

Introduction

Congenital blepharoptosis is mostly caused by dysplasia of the oculomotor nucleus or levator muscle (LM), and patients mainly show partial or complete blepharoptosis. It has been estimated that levator function is poor in 71.8% of eyes with congenital blepharoptosis, and unilateral cases account for 64.7%–75.0% (1, 2). Patients with congenital blepharoptosis, especially unilateral cases, are more susceptible to the development of amblyopia, usually due to convergent strabismus, high astigmatism, or anisometropia (3). Blepharoptosis can be cosmetically, functionally, and psychosocially problematic for children. This disease can be divided into 3 grades: mild, moderate, and severe. In mild cases, the upper eyelid margin is located on the upper edge of the pupil, and the amount of blepharoptosis is 1–2 mm; in moderate cases, the upper eyelid margin covers 1/3 of the pupil, and the amount of blepharoptosis is 3–4 mm; in severe cases, the upper eyelid margin covers 1/2 of the pupil, and the amount of blepharoptosis is >4 mm (4).

In the past, frontalis muscle flap suspension was used for the surgical treatment of severe blepharoptosis (5). Postoperative complications such as poor ocular mobility, subcutaneous hematoma and obvious lagophthalmos are often troublesome for surgeons. Since 2002, conjoint fascial sheath suspension (CFS) has been applied to correct congenital blepharoptosis (6). This procedure has a satisfactory curative effect in mild or moderate blepharoptosis, however, the effect of the surgery on severe ptosis was not ideal (6, 7). Over the past few years, CFS + LM complex suspension, a modified CFS-based surgery, has shown good results for the treatment of severe blepharoptosis (7–9). Many anatomical and histological studies have also provided helpful information (9, 10). Recent research has confirmed that the CFS is rich in collagen fibers and elastic fibers (11). Additionally, our previous study confirmed that the CFS and LM are rich in elastic fibers and elastin in pediatric patients, and CFS-based suspension is effective to cure severe congenital blepharoptosis in pediatric patients (9). In the present study, we performed CFS + LM suspension to treat severe congenital blepharoptosis in pediatric patients in different age groups and evaluated the efficacy and safety of this procedure.

Materials and methods

Patients

Pediatric patients with severe congenital blepharoptosis from July 2017 to July 2021 were included in this study. Patients were divided into group A (≤7 years old) and group B (>7 years old). All patients underwent CFS + LM suspension, a modified CFS-based surgery, under general anesthesia performed by one experienced surgeon (P.B.). The inclusion criteria included patients older than 3 years old and younger than 15 years old; clinically diagnosed severe congenital blepharoptosis; normal ocular movement on preoperative examination; no serious autoimmune diseases or connective tissue diseases; no other contraindications for eyelid surgery; capability of attending follow-up visits for at least 6 months after treatment. The exclusion criteria included patients with contraindications for eyelid surgical intervention, patients with oculomotor nerve palsy, patients with immune diseases or connective tissue diseases, patients with systemic diseases, and patients with psychosis history. This study was consistent with the Declaration of Helsinki, and it was approved by the Ethics Committee of Hebei Provincial Eye Hospital. Written informed consent forms were obtained from the parents of all patients.

CFS + LM suspension technique

All CFS + LM suspension surgeries were under general anesthesia performed by the same surgeon (P.B.) using the same technique (9). The surgical incision consisted of a double eyelid line incision and its course was marked with methylene blue preoperatively. The upper lid was anesthetized using ropivacaine plus 1:10,000 epinephrine. Initially, the skin was cut along the marked line, and the subcutaneous tissue was separated. Then, the orbicularis oculi was cut at a width

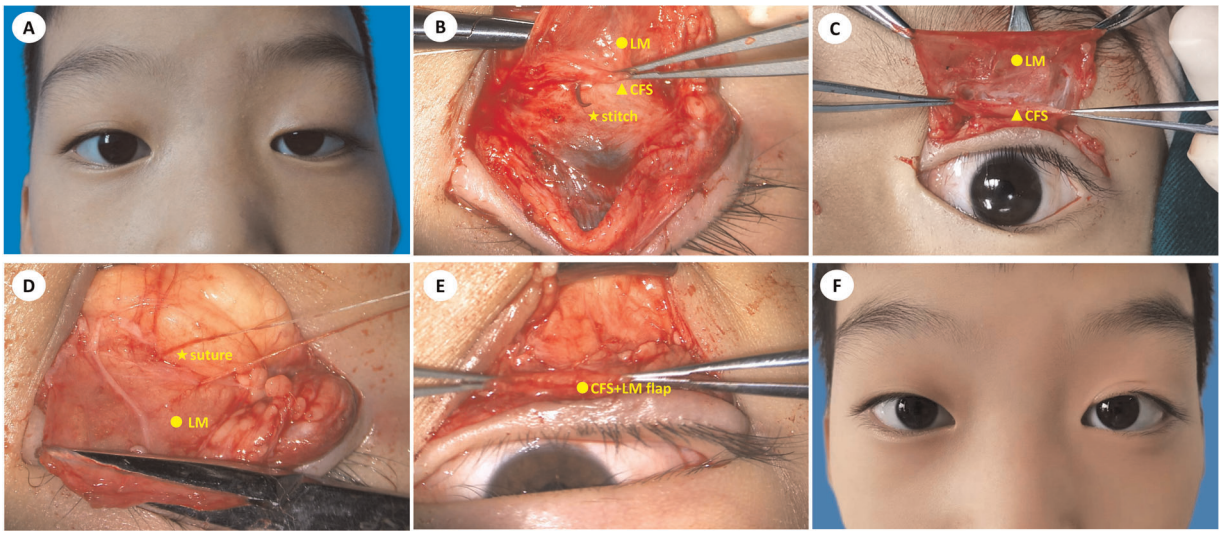

FIGURE 1
An 8-year-old boy with congenital ptosis (OS) treated by modified CFS suspension under general anesthesia. (**A**) preoperative image; (**B**) suturing CFS and LM with 5-0 absorbable stitches; (**C**) exposure of CFS and LM; (**D**) using mattress sutures to fix CFS + LM complex flap onto the tarsus; (**E**) exposure of the CFS + LM complex flap; (**F**) twelve months after CFS + LM suspension.

of 2 mm before the tarsal plate. The aponeurosis of the levator was cut to the same length as the incision parallel to the margin of the tarsal plate. The levator aponeurosis was carefully separated from the Müller muscle, leaving the Müller muscle and conjunctiva intact. The levator aponeurosis was detached from the Müller muscle and pulled approximately 4–5 mm over the fornix to expose the CFS. As shown in **Figure 1**, the CFS is a sheath-like connective tissue whose thickness varies among individuals. The upper margin of the tarsus was suspended and fixed to the CFS + LM complex at a certain length according to patients' margin reflex distance 1 (MRD1). With reference to the position of the tarsus and pupil, U-shaped stitches of 5-0 absorbable thread were applied at the outer, intermediate, and inner positions. Then adjust the upper eyelid height to a satisfactory position, and the skin incision was closed with 5-0 nylon stitches, which were removed one week after surgery.

Postoperative evaluation

On the second day after surgery, the bandage was removed, and the skin incision was wiped with iodophor daily. Sodium hyaluronate eye drops were given 4 times a day, and erythromycin eye ointment was administered once every night. Eyelid sutures were removed on the seventh day after surgery. The follow-up time points were preoperative, 1 week after the operation, 1 month after the operation, 3 months after the operation, 6 months after the operation, and the last follow-up. The MRD1, lagophthalmos (LAG), and complications after the operation were recorded and analyzed by experienced ophthalmologists (R.P. and J.Y.). MRD1 was determined by the ophthalmologist and patient aligning at the same level. During the examination, the patient was instructed to gaze in the primary position, after which a light is directed at the patient's eyes and the distance between the light reflex on the patient's cornea to the upper-eyelid margin was measured in millimeters with a ruler. LAG is the inability to close the eyelids completely on attempted closure. During the test, the patient was instructed to look down and gently close both eyes, and the distance between the upper and lower eyelid margins was measured with a ruler in millimeters. In terms of cosmetic evaluation, the symmetry of lid height, lid contour, and lid crease were recorded.

The upper eyelid located 1–2 mm below the upper corneal margin was considered to be well corrected; the upper eyelid located at or above the upper corneal margin was considered to be overcorrected; and the upper eyelid located >2 mm below the upper corneal margin was considered to be undercorrected (12).

Statistical analysis

Statistical analysis was performed using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA). A normality test was performed for each continuous variable, and two independent sample *t* tests were performed for normally distributed data, while *rank sum* tests were performed for nonnormally distributed data. The *chi-square* test was used for the comparison of

categorical variables between groups. Measurement values are presented as the mean ± standard deviation. A *P*-value <0.05 was considered statistically significant. GraphPad Prism 8.0 was used for drawing.

Results

Fifty pediatric patients (60 eyes) undergoing modified CFS suspension for severe congenital blepharoptosis were included in the study. The demographic characteristics of the study population were summarized in **Table 1**. There were 17 patients (18 eyes) in group A (12 males and 5 females), with an average age of 5.76 ± 1.15 years and an average preoperative MRD1 of −1.17 ± 1.20 mm. The average LF was 1.50 ± 1.29 mm. There were 33 patients (42 eyes) in group B (26 males and 7 females), with an average age of 10.09 ± 1.67 years and an average preoperative MRD1 of −0.99 ± 0.77 mm. The average LF was 1.98 ± 1.39 mm. All patients had normal ocular movement on preoperative examination and were followed up for at least 6 months after surgery. There was no difference in general data between the two groups ($P > 0.05$).

Corrective effects

In group A, 4 eyes were overcorrected within 1 week after the operation; 14 eyes were well corrected and 4 eyes were undercorrected after the operation at the last visit. In group B, 4 eyes were overcorrected and 2 eyes were undercorrected within 1 week after the operation; 27 eyes were well corrected and 15 eyes were undercorrected after the operation at the last visit. The correction rate was not significantly different between group A and group B at the last follow-up visit (**Figure 2**).

TABLE 1 Preoperative patient data.

Characteristics	Group A	Group B	*P*-value
n	17	33	
Sex, *n*			0.769[a]
Female	5	7	
Male	12	26	
Laterality, *n*			0.156[a]
Unilateral	16	24	
Bilateral	1	9	
Age (years)	5.76 ± 1.15	10.09 ± 1.67	
Preoperative			
MRD1, mm	−1.17 ± 1.20	0.76 ± 1.16	0.166[b]
LF, mm	1.50 ± 1.29	1.98 ± 1.39	0.289[b]

MRD1, margin-to-reflex distance; LF, levator function.
[a]χ^2.
[b]Rank sum test.

Postoperative MRD1

The MRD1 results in group A and group B at different follow-up points were listed in **Table 2**. The MRD1 in group A was 3.06 ± 0.64 mm at 6 months after the operation, and the MRD1 in group B was 2.64 ± 0.69 mm 6 months postoperatively which is significantly lower than that of group A ($P = 0.044$). As is shown in **Figure 3**, however, the MRD1 in group A at the last visit was 3.00 ± 0.69 mm and the MRD1 in group B was 2.64 ± 0.70 mm. There was no significant difference in MRD1 between two groups in long term ($P = 0.255$).

Upper eyelid regression

The intraoperative palpebral fissure height (PFH) was set at 8 mm, and the measurement of MRD1 was made in each patient within 1 week after the operation. However, the upper eyelid regressed gradually in group A and group B. MRD1 regression was most evident during the first month and gradually stabilized after the third month in both group A and group B (**Figure 4**). It was suggested that the first month after the operation was the key period of this treatment.

Postoperative complications

All patients had early incomplete eyelid closure, which resolved at 1 month after surgery. Two patients presented exposure keratopathy in the follow-up period. The number of eyes with lagophthalmos greater than 2 mm after the operation at the last visit was recorded. Nine patients (9 eyes) showed conjunctival prolapse within 1 week after surgery, and one patient showed conjunctival prolapse 10 days after surgery among these 50 patients (60 eyes), including 4 patients (4 eyes) in group A and 6 patients (6 eyes) in group B. Among them, 7 patients recovered after fixation of the conjunctival fornix with deep sutures, and the remaining 3 patients with mild conjunctival prolapse recovered after conservative treatment, such as eye drops and bandaging. There were fewer postoperative complications in group B than in group A ($P < 0.05$), as shown in **Table 3**.

Discussion

Congenital blepharoptosis is very common in clinical practice, and surgery is the only effective treatment at present. Pediatric blepharoptosis is more challenging than adult

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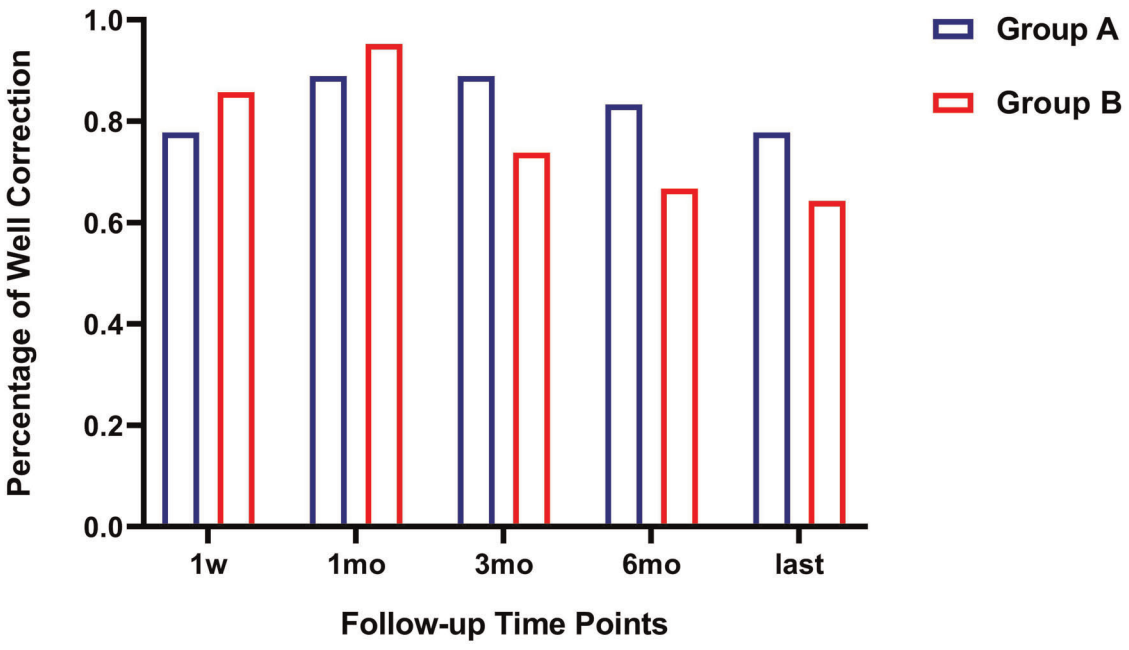

FIGURE 2
Comparison of corrective effect between two groups at different follow-up points.

TABLE 2 MRD1 results (mm) in two groups at different follow-up points.

	preoperative	1 week	1 month	3 months	6 months	Last follow-up
Group A	−1.17 ± 1.20	4.89 ± 0.76	3.89 ± 0.90	3.17 ± 0.62	3.06 ± 0.64	3.00 ± 0.69
Group B	−0.76 ± 1.16	4.52 ± 0.99	3.60 ± 0.80	2.79 ± 0.68	2.64 ± 0.69	2.62 ± 0.70
P	0.166	0.256	0.248	0.050	0.044	0.255

blepharoptosis because of extra considerations such as the risk of amblyopia, difficulty of examination, need for general anesthesia, and the age at which the surgery should be performed (13). LF and severity of blepharoptosis determine the choice of surgical treatment for congenital blepharoptosis (14). For severe blepharoptosis with poor LF, frontalis suspension is generally considered to be the most effective method and is especially recommended for patients with unilateral congenital blepharoptosis (15). In previous studies, frontalis suspension was used to treat unilateral severe blepharoptosis with a success rate of 77.0%–95.0% (16). Many different materials used in frontalis suspension surgery are readily available and can shorten operative times, but they can also lead to the recurrence of blepharoptosis or complications related to allogeneic materials such as infection, graft exposure, rejection and granuloma formation. Lid lag on downward gaze after frontalis suspension has also been reported in up to 90% of cases (17). Unilateral frontalis suspension may show less satisfactory outcomes, which result from ipsilateral nondominant eye amblyopia and failure to elevate the forehead (18). Mild-to-moderate exposure keratopathy can develop in all patients after the correction of severe congenital blepharoptosis, regardless of the procedure (19). Entropion or eyelash inversion occurs in 5.4%–11.9% of cases after correction of severe congenital blepharoptosis, which is associated with increased posterior lamella vertical tension (16, 20). In recent years, CFS suspension has been used to correct severe blepharoptosis, and the therapy has been widely recognized by clinicians. CFS suspension has achieved good results in the treatment of severe blepharoptosis (7). CFS is the fusion of fascia between the levator muscle and the superior rectus muscle, and its efficacy derives from the combined strength of the muscle belly of the levator muscle and the Tenon capsule. Numerous histological studies of CFS were published many years ago. The previous reports on the efficacy of CFS suspension mainly focused on adults (21), while congenital blepharoptosis was found to be more common in children. In this study, 50 patients (60 eyes) ranging from 4 years to 14 years with severe congenital

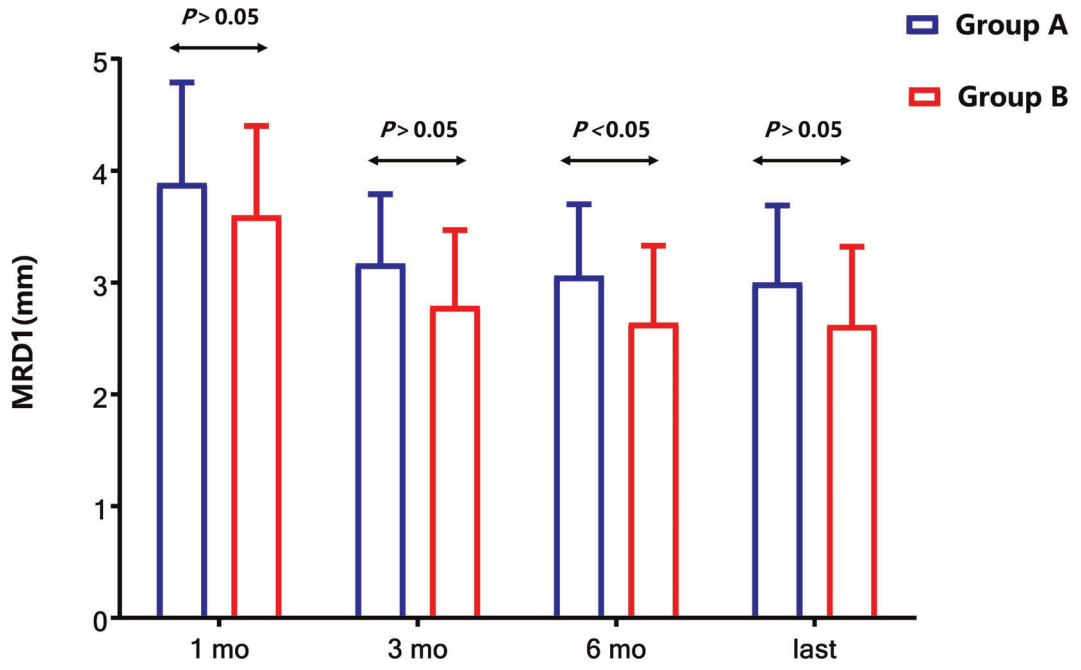

FIGURE 3
Comparison of MRD1 between two groups after surgery. Compared with the MRD1 values in group B, the values of MRD1 at 6 months after the operation were elevated significantly ($P < 0.05$), but those at the last follow-up were not significantly elevated ($P > 0.05$).

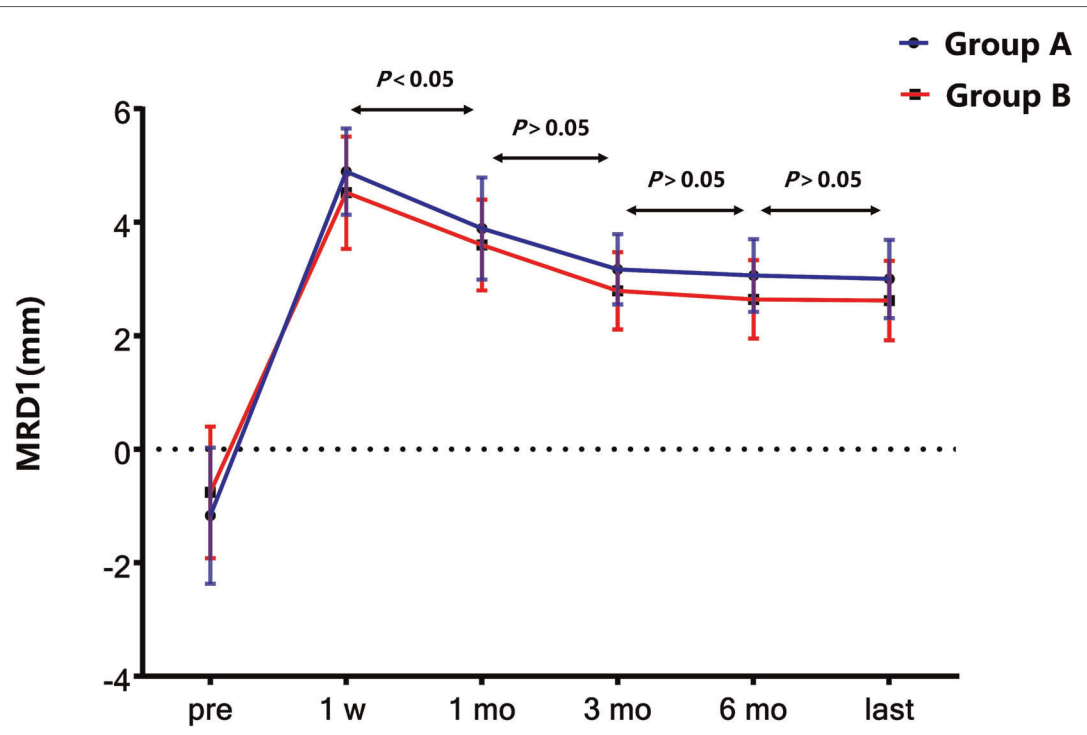

FIGURE 4
MRD1 regression in two groups at different follow-up points.

TABLE 3 Comparison of postoperative complications between two groups.

Complication	Group A	Group B	χ^2	*P*
Lagophthalmos greater than 2 mm	4 (4/18)	6 (6/42)		
Conjunctival prolapse	4 (4/18)	6 (6/42)		
Exposure keratopathy	1 (1/18)	1 (1/42)		
Trichiasis	0 (0/18)	0 (0/42)		
Total incidence rate	9 (9/18)	13 (13/42)	4.413	0.036

blepharoptosis were recruited to analyze and compare the applicability of this technique in pediatric patients at different ages.

In 2002, Holmström and Santanelli found abundant collagen fibers and elastic fibers in a histological study of CFS (10) Our previous study confirmed that CFS contains abundant collagen fibers and elastic fibers (9). The appearance of CFS tissue in children is yellowish and whitish with varying thickness, which is not obviously different in appearance and elasticity compared with those in adults. Traditional CFS suspension has a high rate of upper eyelid retraction and blepharoptosis recurrence (7). The CFS + LM suspension can strengthen the longitudinal and upward traction force, and maintains the original physiological structure of the upper eyelid. It is thus easier to achieve a natural and beautiful radian of the eyelid margin in children, and to avoid deformities of the eyelid margin in the long term. Motility is obviously more consistent with the physiological structure, and good blinking function can be maintained to a certain extent. Meanwhile, CFS + LM suspension also prevents upper eyelid hypertrophy and scarring and does not depend on eyebrow elevation when opening the eyes, unlike frontalis suspension.

Previous reports on CFS surgery focused on adult patients who could tolerate local anesthesia, and the position between the upper eyelid margin and the upper corneal margin could be observed in the sitting position during the operation to achieve better surgical results. It is unable to make precise designed before the CFS + LM suspension, which was a major challenge for doctors treating pediatric patients; consequently, the upper eyelid margin was adjusted to 0–1 mm from the upper corneal margin during general anesthesia. However, depending on the depth of general anesthesia, the position of the cornea can also change during the operation. Therefore, in addition to referring to the upper corneal margin, we also paid attention to the size of the palpebral fissure, which was set to 8 mm. In this study, good surgical results were achieved

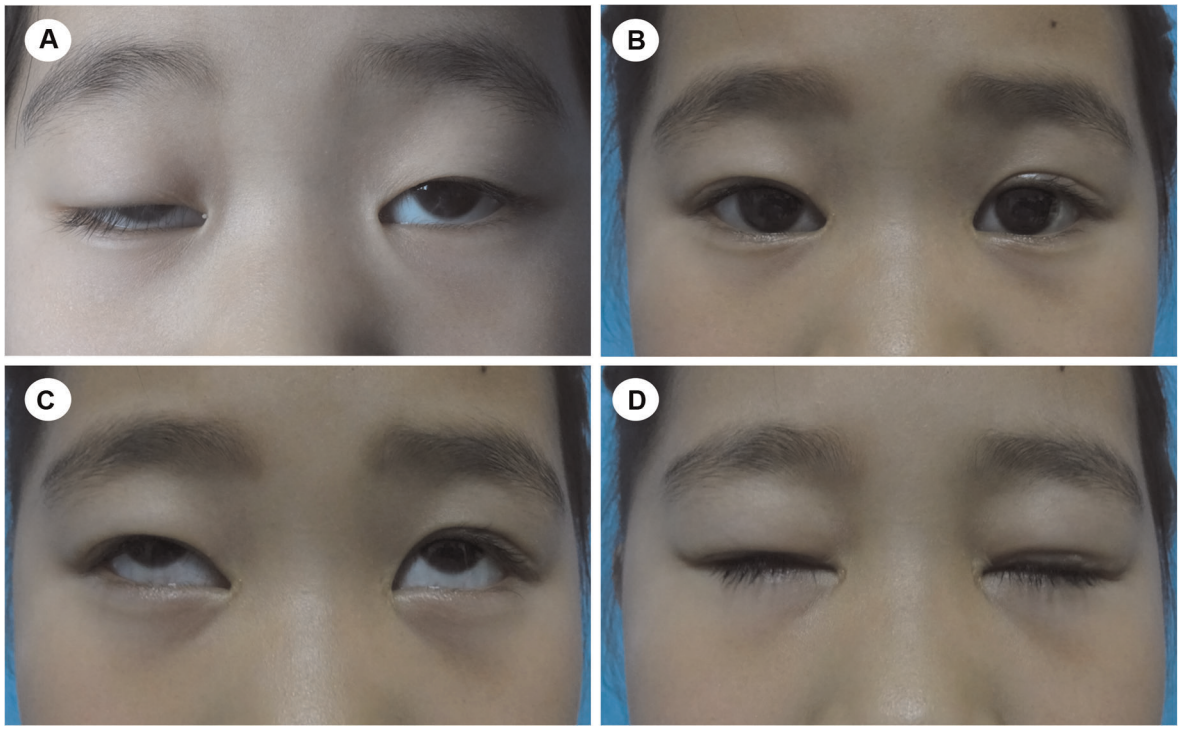

FIGURE 5
A 6-year-old girl with congenital blepharoptosis OU. (A) preoperative appearance; (B) image of the patient eight months after CFS + LM suspension; (C,D) eye movement was normal and lagophthalmos was relieved.

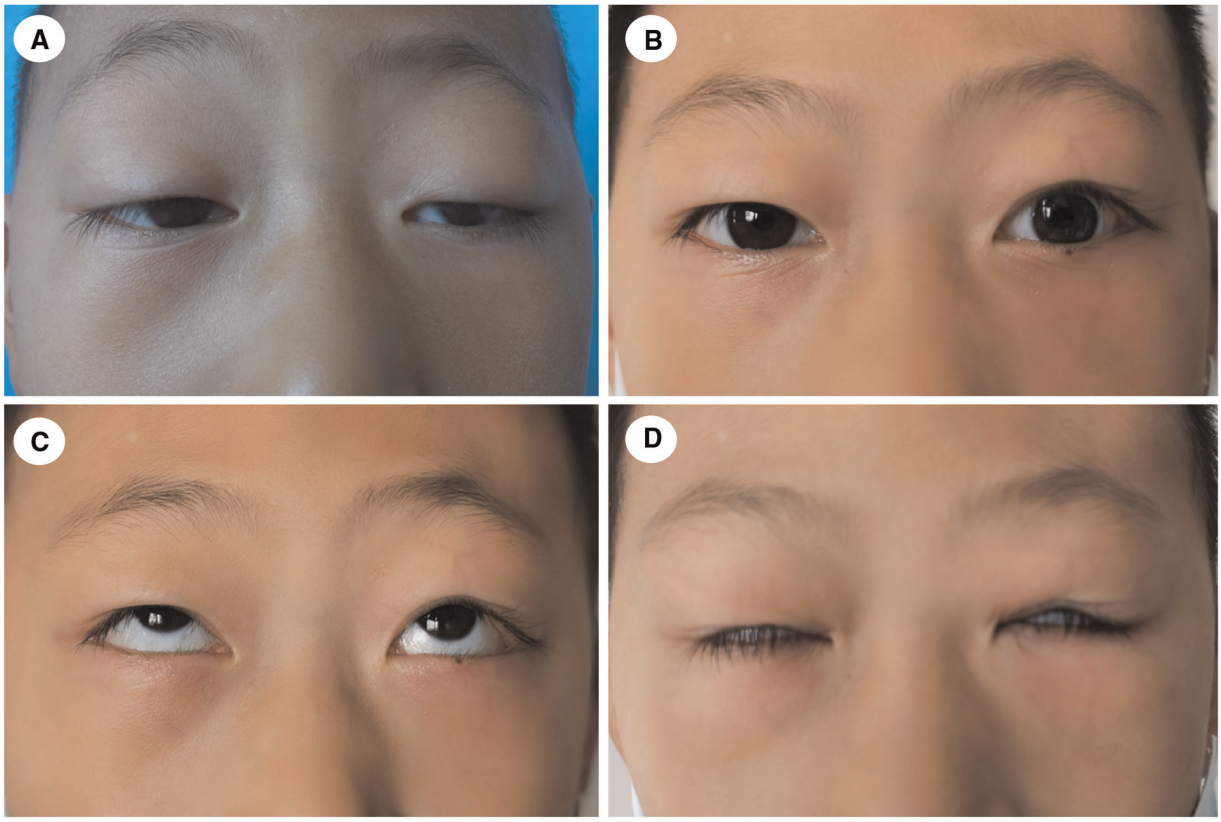

FIGURE 6
A 9-year-old boy with congenital blepharoptosis OU. (A) preoperative appearance; (B) twelve months after CFS + LM suspension; (C,D) eye movement was normal and lagophthalmos was relieved.

after surgery in both group A and group B. The mean MRD1 of group A at the last visit was 3.00 ± 0.69 mm, which approximates the result of 3.10 ± 0.22 (22). The corrective effect was 77.78% at the last visit in group A, which is better than the result of 67.92% in a previous report (23). In view of the long-term outcomes after the operation, there was no significant difference between group A and group B. Therefore, modified CFS suspension under general anesthesia is safe and effective for the correction of severe congenital blepharoptosis in pediatric patients and is worth applying in clinical practice. In **Figures 1**, **5**, **6**, we listed three successful cases of congenital blepharoptosis who received CFS + LM suspension.

Moreover, we divided the patients into two groups depending on age to explore whether age affects the outcomes of the surgery. The upper eyelid suspension support system is a complex system composed of muscles, aponeurosis and other tissue. Various components have synergistic or buffer effects. The orbital wall of children develops rapidly, reaching 90% of the adult volume by the age of 5 and, before the age of 7, reaching a state similar to that in adults (24). The eyelid soft tissue also changes rapidly. In our study, there was a statistically significant difference in MRD1 between group A and group B at 6 months after the operation ($P < 0.05$) but not at the last visit ($P > 0.05$). Additionally, there were varying degrees of regression after suspension, especially 3 months after the operation, which was confirmed in a previous report. This result suggested that the third month after the operation was the key period of this treatment.

All patients had early incomplete eyelid closure, which resolved at 1 month after surgery, and the eyelid closure improved over time, which was not bothersome for the patients or their parents. The lower the occurrence of lagophthalmos greater than 2 mm, the lower was the occurrence of exposure keratopathy after surgery. Only two patients presented exposure keratopathy in the follow-up period. Postoperative conjunctival prolapse was found in both group A and group B, which was considered related to the young age of patients and to postoperative conjunctival edema. The edematous conjunctiva fell below the upper edge of the eyelid due to gravity, and conjunctival prolapse recovered as the edema subsided. For severe conjunctival prolapse that could not recover, fixation of the conjunctival fornix with deep sutures was performed. The sutures were removed 10 days later, and the conjunctival prolapse recovered well. Attention should be given to the following

points to prevent complications: ① During the operation, it is easy to damage the conjunctiva when separating the Muller's muscle and upper eyelid conjunctiva in the direction of the upper eyelid fornix, leading to postoperative conjunctiva perforation or aggravating postoperative edema. Therefore, the maneuvers should be performed gently to minimize stimulation of the conjunctiva. ② Surgical separation above the fornix may cause varying degrees of conjunctival prolapse or even blepharon prolapse and reversal if the anatomical operation is not skillfully conducted (25). The dissection area above the fornix was not too large, and the CFS was sutured appropriately. Once conjunctival prolapse occurs during the operation, the conjunctiva can be fixed on the aponeurosis of the upper eyelid by 5-0 absorbable sutures before the incision is stitched. If the incision has been sutured, the suture can be ligated on the skin surface under the eyebrow. Early postoperative conjunctival prolapse can be treated under topical anesthesia with instruments to retrieve the conjunctival prolapse, and eye ointment can be administered, along with bandaging of the affected eye. If the prolapse of the conjunctiva cannot recover 1 month after edema revolution by the abovementioned method, the prolapsed conjunctiva needs to be excised surgically. There were fewer postoperative complications, including LAG, exposure keratopathy and conjunctival prolapse, in group B than in group A ($P < 0.05$). Younger patients tended to have unsatisfied compliance due to ocular pain, swelling and other reasons in the first month after surgery.

In conclusion, CFS + LM suspension, a modified CFS-based surgery, is an effective treatment for severe congenital blepharoptosis in pediatric patients with excellent long-term outcomes. Although the upper eyelid position slightly retracts after the operation, it is still safe and feasible for correcting severe congenital blepharoptosis in pediatric patients under general anesthesia. This procedure maintains relatively normal functioning of the levator muscle, which results in better movement of the eyelid, good eyelid closure and fewer complications, which is worthy of further clinical application to cure severe congenital blepharoptosis in pediatric patients.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Hebei Eye Hospital ethics committee. (No. 2020KY013). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

PB, ZL and HW were primarily responsible for the experimental concept and design. HW, ZL, LS, RP and JY performed the data acquisition and analysis. HW and ZL drafted and edited of the manuscript. PB performed all operations. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Laparoscopic surgery versus robot-assisted surgery for choledochal cyst excision: A systematic review and meta-analysis

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The aim of this following study is to systematically review and analyze the published data comparing laparoscopic surgery and robotic assisted surgery for choledochal cyst excisions through the metrics of operative time, length of hospital stay and postoperative outcome. PubMed, Web of Science, Embase, Ovid, and the Cochrane Library databases were combed through and data was retrieved from the timespan between January 1995 and October 2021. The primary measures included operative time, intraoperative bleeding, hospital stay, and postoperative complications. Quality and risk of bias were assessed using the Newcastle-Ottawa Quality Assessment Scale. Making use of random-effects models, we pooled the odds ratios (ORs) and mean differences (MDs) with 95% confidence intervals (95% CIs). Six studies comprising a total 484 patients who had undergone either laparoscopic surgery [307 (63.43%) patients] or robot-assisted surgery [177 (36.57%) patients] were included in this analysis. Three of the articles involved adults while the other three involved children. All of the studies were published after 2018 and were retrospective case–control studies. Patients undergoing robotic surgery had a shorter hospital stay (MD, 0.95; 95% CI, 0.56 to 1.35; $p < 0.00001$) and a longer operative time (MD, −57.52; 95% CI, −67.17 to −47.87; $p < 0.00001$). And there was no significant discrepancy in complications between the two groups. Compared to laparoscopic surgery, robot-assisted surgery is associated with a shorter hospital stay, scores highly in terms of both safety and feasibility, however it also results in a longer operative time. And the two procedures have the same short- and long-term results.

KEYWORDS

choledochal cyst excision, laparoscopic surgery, robot-assisted surgery, systematic review, meta-analysis

Introduction

Choledochal cysts (CCs) are extremely rare malformations found in bile ducts involving dilatation and pancreaticobiliary maljunction (1). They often lead to symptoms such as abdominal pain, vomiting, jaundice, and fever (2). Without effective treatment, patients with choledochal cysts may experience cyst perforation,

recurrent pancreatitis, canceration, and even severe cholestasis, which itself eventually results in liver cirrhosis, portal hypertension, and ultimately liver failure (3).

The main treatments for choledochal cysts are the complete resection of the cyst, cholecystectomy and Roux-en-Y choledochojejunostomy, which traditionally have been performed as open procedures (1–3). The laparoscopic approach towards treating choledochal cysts has gradually joined these previously mentioned procedures as a mainstream method over the last decade, ever since Farello et al. executed the very first laparoscopic choledochal cyst resection with a hepaticoenterostomy successfully on a girl of the age of six in 1995 (4). However, due to their intense technical demands laparoscopic approaches have still not achieved widespread usage, especially the hepaticoenterostomy which requires a certain learning curve. At the same time, robotic assisted surgery has been suggested as an alternative method for pediatric choledochal cyst excision, as the first robot-assisted choledochal cyst resection in children was reported by Woo et al. in 2006 (5, 6). Robot-assisted surgery has several features that give it an advantage. Examples of these include its operability and accuracy being enhanced relative to laparoscopic surgery due to its three-dimensional imaging and the flexible design of its simulation manipulator (7).

To our knowledge few systematic review or meta-analysis has as of yet been published comparing laparoscopic surgery and robotic assisted surgery for choledochal cyst excisions to determine which is the preferential treatment. The aim of the present study is to systematically review and analyze the published data comparing laparoscopic surgery and robotic assisted surgery for choledochal cyst excision regarding operative times, length of hospital stay and postoperative outcomes.

Methods

Information source and search strategy

This systematic review/meta-analysis was performed using Medline, PubMed, Web of Science, Embase, Ovid, and the Cochrane Library databases with articles within the time period from January 1995 to October 2021 being sought after. The search terms were: "choledochal cyst or congenital biliary dilatation", "laparoscopy", "robot or da Vinci". The search was limited to the English language only. Furthermore, reference lists of relevant papers were also explored for any other studies of interest. The study was registered with the PROSPERO database (CRD42021283740).

Inclusion and exclusion criteria

Studies were considered eligible for inclusion as long as they met the following criteria: (1) they conducted a comparative study of laparoscopic surgery and robot-assisted surgery that were definitely done to treat a choledochal cyst; (2) the outcome data reported was available, and (3) the study format was full text only; editorials, case reports, abstracts, and conference presentations were left out. If studies did not meet the inclusion criteria, they were not included.

Study selection and data collection

All of the study titles and abstracts selected for further study were cross-checked by the two independent authors (KZ and XXL). Eligible studies that met the inclusion criteria were then retrieved. The relevant data from the included studies—specifically their study characteristics and outcomes—was then extracted by those two authors separately. Complete agreement was necessary at each stage of the study selection process and if a discrepancy occurred, a third investigator would step in to resolve the matter (DFZ).

In each of the studies, the following information was deemed notable: the lead author's name, country, year of publication, study type, follow-up time, mean age and number of patients in each group, cystic diameter, and outcomes (e.g., operative time, enteral feeding time, length of hospital stay, as well as postoperative complications including bile leaking, adhesive intestinal obstruction, bleeding, cholangitis, bile reflux/gastritis, and reoperation rates). Throughout the course of this study, if there was missing data like the standard deviation, it would be calculated based on formulas from the Cochrane handbook.

Quality assessment

In order to assess the quality attributes and to help eliminate any risk of bias in the nonrandomized studies chosen in this meta-analysis, the Newcastle-Ottawa Quality Assessment Scale (NOS) was employed. Each study was assessed according to three criteria in a sort of "star system": selection, comparability, and ascertainment of exposure. Eight items were covered in this scale: four points could be scored for selection; two points, for comparability; and three points, for exposure. A maximum of one star for each numbered item within the selection and exposure categories could be awarded to each study. For the comparability categories, there was a maximum of two stars which could be rewarded. The higher the score was, the higher the quality of the study. Studies with

1–3 stars were deemed to be "low quality," while with 4–6 stars ones were considered of "moderate quality," and studies with 6–9 stars "high quality" respectively.

Statistical analysis

To pool all of the data the RevMan 5.4 statistical software, which was updated by the Cochrane Library for Systematic Reviews, was employed. This produced forest plots, funnel plots, pooled odds ratio (OR), pooled the mean difference (MD), and confidence intervals (CIs) found in this study. Regarding the dichotomous variables, the Mantel–Haenszel method assisted in computing the OR. As to the continuous variables however, the inverse variance method assisted in the calculation of the MD. The CI was set at 95%, and a value of $p < 0.05$ was considered statistically significant. In order to assess the heterogeneity of the study, the I^2 statistic—representing the percentage of between-study variation—was measured. In the case that the total number of publications included for each outcome exceeded 10, funnel plots were established so as to attempt to indicate any evidence of potential.

Results

Altogether, there was a total of seventy-nine articles identified, and these included two studies which were manually drawn from the references found in other studies. Seventy-three articles were left out due to either lack of relevance or a failure to meet the inclusion criteria set out. The six remaining studies

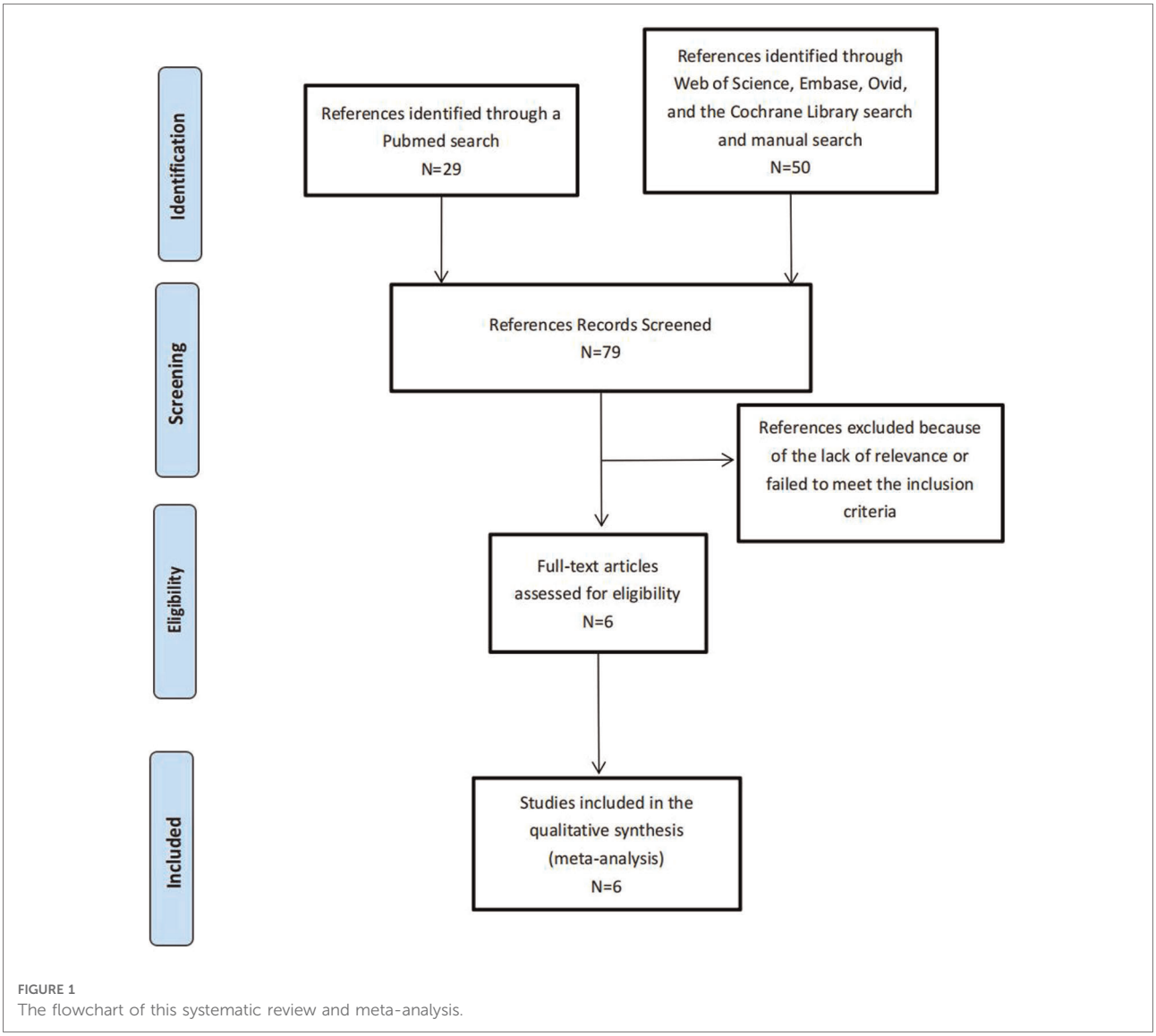

FIGURE 1
The flowchart of this systematic review and meta-analysis.

TABLE 1 Basic characteristics of the enrolled studies.

	Year	Country	Design of study	Year of publication	Total number of patients (LG/RG)	Women, No. (%) (LG/RG)
Hongeun Lee	2018	Korea	Retrospective	2004–2016	67 (49/18)	43 (87.8%)/18 (100%)
Jang Hun Han	2018	Korea	Retrospective	2014–2017	56 (34/22)	27 (79.4%)/22 (100%)
Hiroyuki Koga	2019	Japan	Retrospective	2017–2019	37 (27/10)	-
Xiaolong Xie	2020	China	Retrospective	2015–2018	145 (104/41)	79 (75.96%)/31 (75.61%)
Jong Hwi Yoon	2021	Korea	Retrospective	2005–2018	39 (23/16)	20 (87.0%)/13 (81.3%)
Shui-qing Chi	2021	China	Retrospective	2014–2019	140 (70/70)	48 (68.57%)/48 (68.57%)
	Age (years) mean (SD) (LG/RG)		Cystic diameter (cm) (LG/RG)		Follow up (months) (LG/RG)	Primary outcomes
Hongeun Lee	36.57 ± 10.84/36.17 ± 13.33		-		-	Duration of surgery, LOS, Complications
Jang Hun Han	37.5 ± 11.6/35.3 ± 11.05		3.14*5.23/3.14*5.04		5–100/5–100	Duration of surgery, LOS, Complications
Hiroyuki Koga	5.2 ± 3.8/5.6 ± 3.4		-		36/20	Duration of surgery, LOS, Complications
Xiaolong Xie	2.33 (0.73–4.42)/4.0 (2.54–6.46)		3.78 ± 2.39/3.18 ± 1.65		-	Duration of surgery, LOS, Complications
Jong Hwi Yoon	34.3 ± 11.2/37.0 ± 10.7		0.98 ± 0.19/1.15 ± 0.43		-	Duration of surgery, LOS, Complications
Shui-qing Chi	36.21 ± 32.80/34.00 ± 27.71		-		-	Duration of surgery, LOS, Complications

LG, laparoscopic procedures group; RG, robot-assisted procedures group; LOS, length of hospital stay; SD, standard deviation.

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included a total of 484 patients, of which 307 underwent laparoscopic surgery (63.43%) and 177 underwent robot-assisted surgery (36.57%), and were included in the analysis (8–13) (**Figure 1**). The characteristics of the included studies are summarized in **Table 1**. Five studies all used robots to complete cyst resection and choledochojejunostomy while Koga H et al. completed cyst resection by laparoscopic procedures and choledochojunostomy by robotic procedures (10). Three of the articles involved adults (8, 9, 12) and the other three involved children (10, 11, 13). All of the studies were published after 2018 and were retrospective case–control studies (8–13). The NOS scale was used to assess study quality among the six studies: all six studies were deemed to be of high quality and no study was of low quality.

Operative time

Six studies reported on the operative time with the mean operative time and standard deviation (8–13), while three were excluded following heterogeneity analysis (9–11). The three remaining studies included a total of 246 patients, and of these 142 underwent laparoscopic surgery and 104 underwent robot-assisted surgery (8, 12, 14). The pooled mean difference showed that the operative time of robot-assisted surgery was longer than the laparoscopic surgery and that the difference was statistically significant (MD, −57.52; 95% CI, −67.17 to −47.87; $p < 0.00001$) (**Figure 2**).

Intraoperative bleeding

Five studies provided data on the intraoperative bleeding (8, 10, 11–13), however two of these articles were excluded following heterogeneity analysis (8, 13). The three remaining studies included 221 patients, of which 154 underwent laparoscopic surgery and 67 underwent robot-assisted surgery (10–12). The difference was not statistically significant between these two groups (MD, 1.49; 95% CI, −1.49 to 4.47; $p = 0.33$) (**Figure 3**).

Bile leakage

Six studies provided data on bile leakage (8–13), while one article was excluded following heterogeneity analysis (12). As reported in the five remaining studies with a total of 445 patients (8–11, 13), 12 (4.23%) of the 284 patients in the laparoscopic group and 1 (0.62%) of the 161 patients in the robotic group experienced bile leakage. No statistically significant difference existed between the two groups, but the results favored the robotic group (OR, 1.92; 95% CI, 0.48 to 7.68; $p = 0.36$) (**Figure 4**).

Wound infection

Two studies provided data on wound infection (8, 13). Wound infection occurred in 2 (1.68%) of the 119 patients in

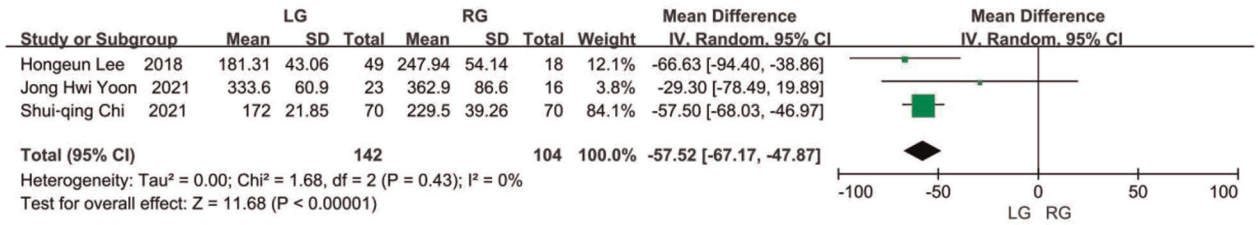

FIGURE 2
Operative time.

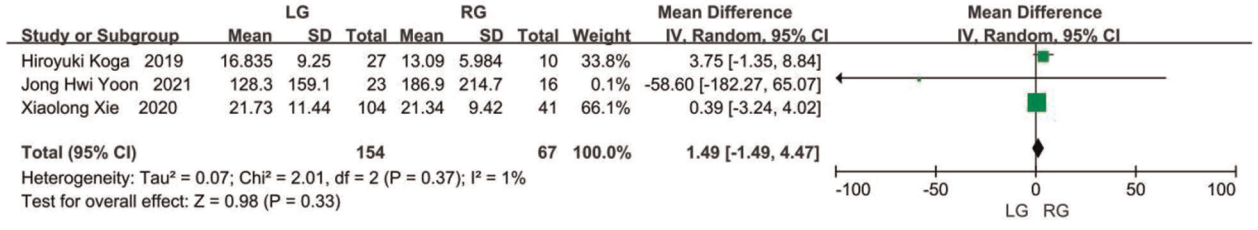

FIGURE 3
Intraoperative bleeding.

the laparoscopic group and none of the 88 patients in the robotic group. The pooled results showed that no difference was statistically significant between the two groups, but the results favored the robotic group (OR, 1.87; 95% CI, 0.19 to 18.41; $p = 0.59$) (**Figure 5**).

Hospital stay and analgesia treatment

Six of the studies delivered data regarding the length of hospital stay (8–13), while 3 articles were excluded following the heterogeneity analysis (10–12). The 3 remaining studies included 263 patients, and of these there were 153 who underwent laparoscopic surgery and 110 who underwent robot-assisted surgery (8, 9, 13). The pooled results showed that the hospital stay of robot-assisted surgery was shorter than that of laparoscopic surgery and the difference was considered statistically noteworthy (MD, 0.95; 95% CI, 0.56 to 1.35; $p < 0.00001$) (**Figure 6**). Only one of the six studies described analgesia treatment after surgery and the results showed that postoperative pain medication usage was signifcantly lower in robotic surgery than in laparoscopic surgery ($p < 0.001$) (11).

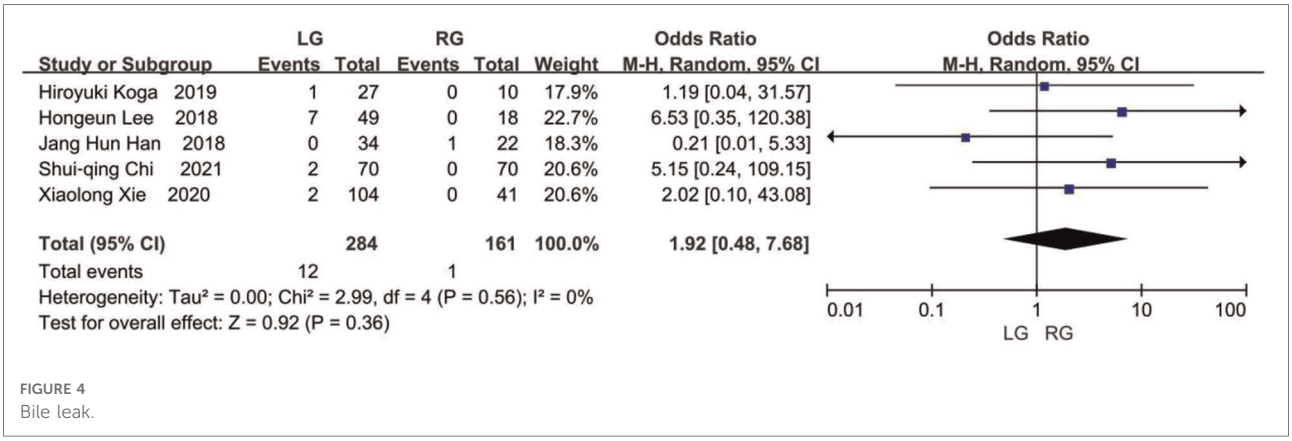

FIGURE 4
Bile leak.

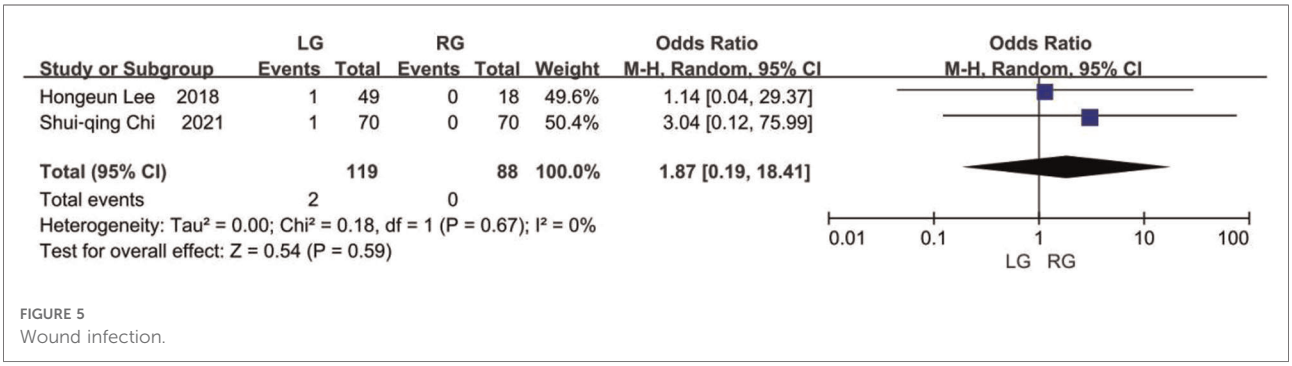

FIGURE 5
Wound infection.

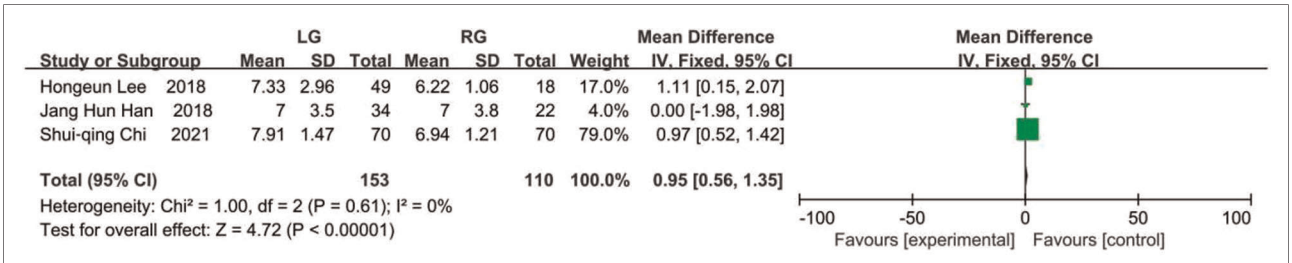

FIGURE 6
Hospital stay.

Bleeding

Four studies delivered data regarding the number of patients suffering from bleeding, and this occurred in 4 (1.56%) of the 257 patients in the laparoscopic group and 1 (0.66%) of the 151 patients in the robotic group (8, 9, 11, 13). The difference was not statistically significant between these two groups and the results favored the robotic group (OR, 1.17; 95% CI, 0.25 to 5.54; $p = 0.84$) (**Figure 7**).

Cholangitis

Two studies reported on the incidence of cholangitis after biliary reconstruction (9, 13). In these two studies, 2 (2.17%) of the 92 patients in the robotic group and none of the 104 patients in the laparoscopic group experienced cholangitis. No significant difference existed between the groups, but the results favored the laparoscopic group (OR, 0.26; 95% CI, 0.03 to 2.57; $p = 0.25$) (**Figure 8**).

Anastomotic stricture

Occurrences of anastomotic stricture were reported on in five studies (8, 9, 11–13). Anastomotic stricture occurred in 8 (2.86%) of the 280 patients in the laparoscopic group and 3 (1.80%) of the 167 patients in the robotic group. There was no significant statistical deviation between the two groups, but the results favored the robotic group (OR, 1.10; 95% CI, 0.32 to 3.73; $p = 0.88$) (**Figure 9**).

Adhesive intestinal obstruction

Four studies assessed the rate of occurrence of adhesive intestinal obstruction (8, 9, 11, 12), and this took place in 4 (1.90%) of the 210 patients in the laparoscopic group and 2 (2.06%) of the 97 patients in the robotic group. The pooled OR indicated that there was no statistical difference found in adhesive intestinal obstruction among these two groups, but that the results favored the laparoscopic group (OR, 0.78; 95% CI: 0.17 to 3.51; $p = 0.74$) (**Figure 10**).

Residual cysts

Two studies reported on the incidence of residual cysts after the choledochal cyst excision procedure (12, 13). In the two studies, 2 (1.15%) of the 174 patients in the laparoscopic group and none of the 111 patients in the robotic group experienced residual cysts. No significant difference existed

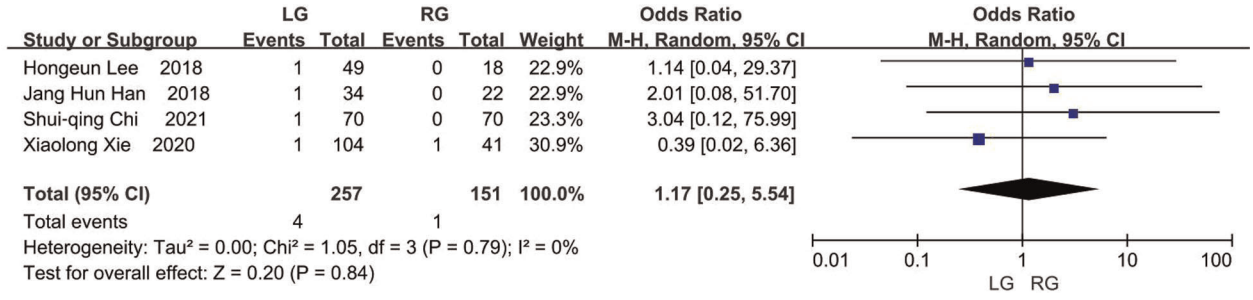

FIGURE 7
Bleeding.

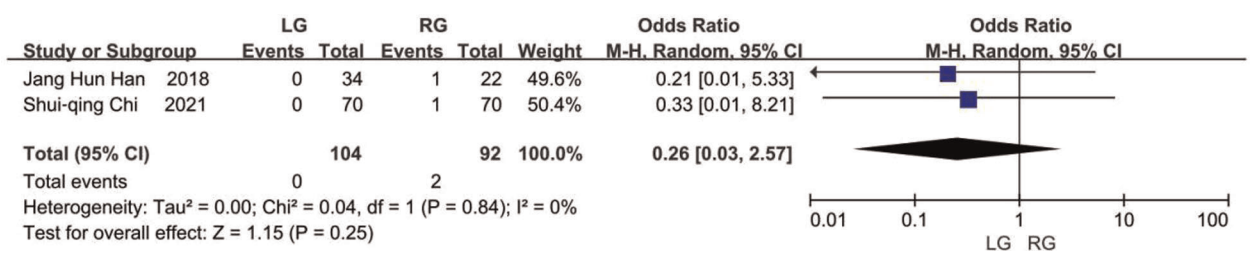

FIGURE 8
Cholangitis.

between the laparoscopic and robotic groups, but the results favored the robotic group (OR, 1.91; 95% CI, 0.20 to 18.65; $p = 0.58$) (**Figure 11**).

Biliary stones

Four studies reported on the incidence of biliary stones (8, 9, 11, 13). Biliary stones occurred in 7 (2.72%) of the 257 patients in the laparoscopic group and none of the 151 patients in the robotic group. No significant statistical difference was found between these two groups, but the results favored the robotic group (OR, 2.47; 95% CI, 0.52 to 11.80; $p = 0.26$) (**Figure 12**).

Reoperation rates

Two studies reported on the need for secondary operation rates (9, 11). In the laparoscopic group, 11 (7.97%) of the 138 patients needed reoperation surgery, compared to 2 (3.17%) of the 63 patients in the robotic group. There was no statistically significant difference, as revealed by the meta-analysis (OR, 3.01; 95% CI, 0.64 to 14.10; $p = 0.16$) (**Figure 13**).

There were two additional articles which reported on enteral feeding time and hospitalization expenses respectively, but these were excluded following the heterogeneity analysis.

Discussion

The most common method of treatment for choledochal cysts tends to be the complete resection of the cyst using a Roux-en-Y hepaticojejunostomy, and this has been traditionally performed as an open procedure (1). Along with the increasing focus on aesthetic considerations when considering treatment, laparoscopic approaches in hepatobiliary surgery have become the inevitable result. From when the first laparoscopic choledochal cyst excision took place in 1995 (4), studies on this approach have consistently reported that laparoscopic surgery scores highly both in terms of safety and feasibility in the treating of choledochal cysts. As laparoscopy is minimally invasive, leading to a cosmetically enhanced recovery as well as providing better vision of the deep anatomic structures compared with open approaches, it

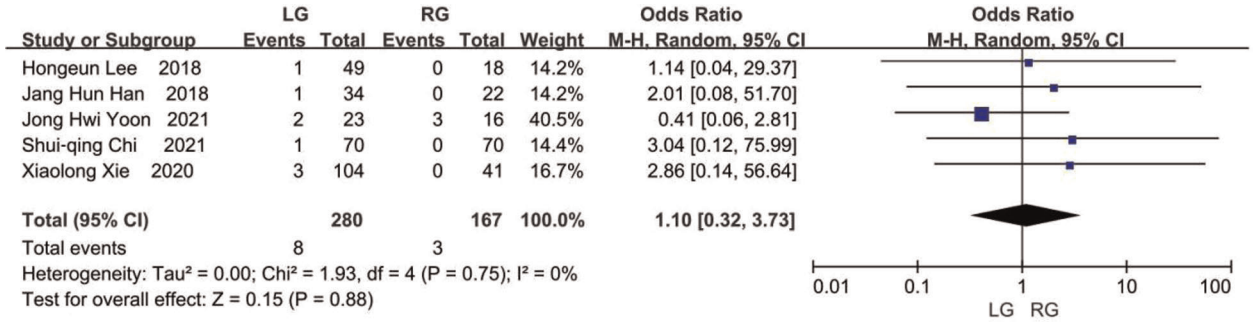

FIGURE 9
Anastomotic stricture.

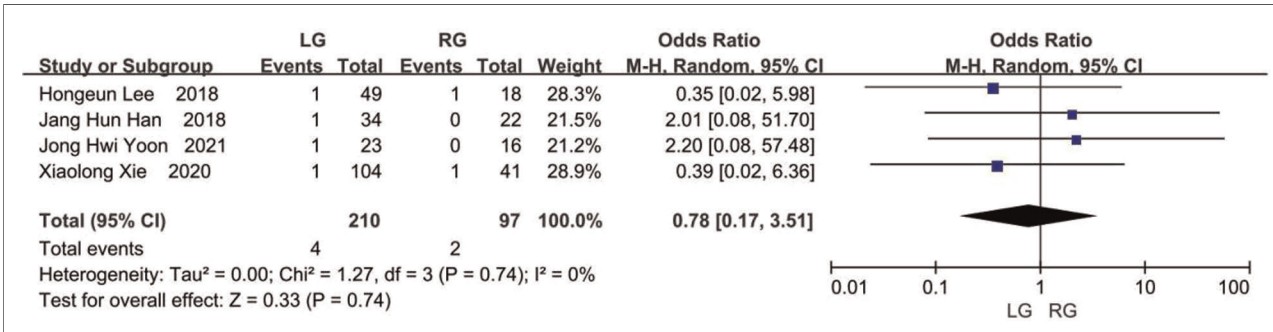

FIGURE 10
Adhesive intestinal obstruction.

possesses significant advantages (14). However, the drive towards using laparoscopic approaches to perform choledochal cyst excisions has been sluggish, mainly due to the technical complexities of these procedures. They require a considerable learning curve, with hepaticojejunostomy being a notable example of this. In addition to this, there are several other limitations, such as: necessary usage of straight rigid instruments within a tight working space, a limited degree of freedom to work within, instability of the camera platform with two-dimensional imaging, and non-ergonomic instruments. Robot-assisted surgery though offers several technical advantages over laparoscopic surgery, and these include: high-quality three-dimensional imaging, free-moving multi-joint forceps and image stabilization. As a result, laparoscopic surgery's learning curve can be shortened. Despite this, a serious lack of data and large-scale sample cases which compare the safety and effectiveness of these two surgical methods for choledochal cyst excisions, remains an ever-present issue.

This systematic review and meta-analysis compares the outcomes of laparoscopic surgery and robot-assisted surgery, using studies in the literature as a basis for review. It was

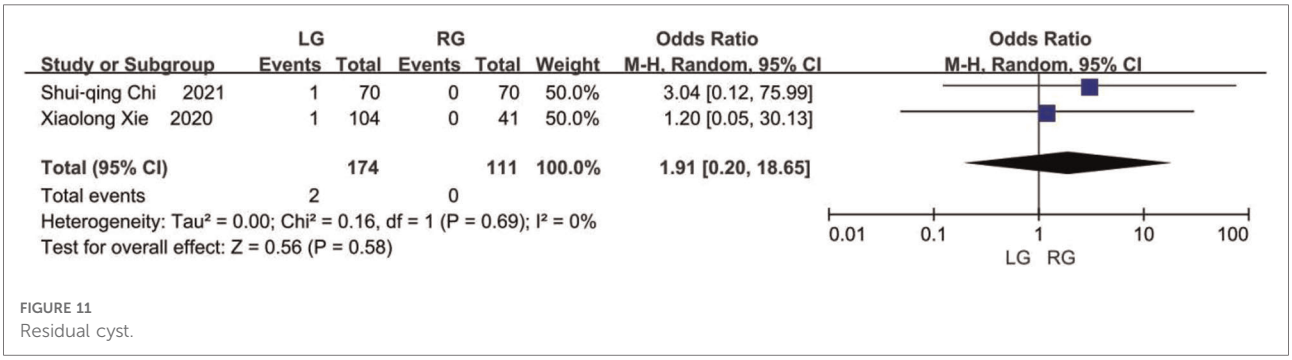

FIGURE 11
Residual cyst.

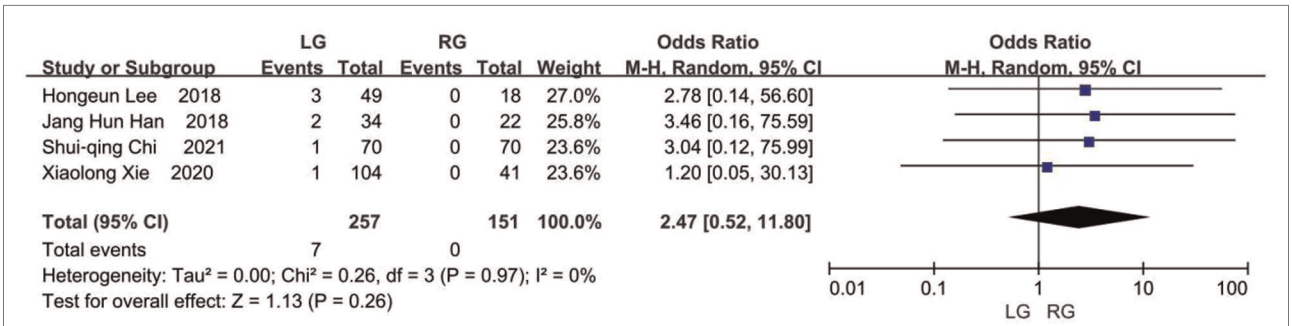

FIGURE 12
Biliary stones.

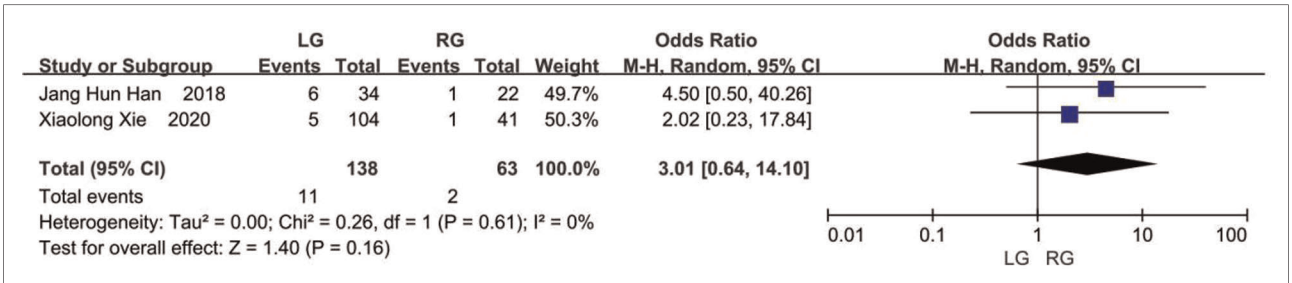

FIGURE 13
Reoperation rates.

indicated by the findings that robot-assisted surgery resulted in a hospital stay of shorter duration and longer operative time. One possible reason why the operative time of robotic surgery is significantly longer than that of laparoscopic surgery is that the operative time in robotic surgery includes both the docking time and instruments replacement time. Xie et al. reported on the learning curve for the robot-assisted choledochal cyst excision and Roux-en-Y hepaticojejunostomy with the da Vinci surgical system methods and came to the conclusion that it was 14 cases (15). With improvement in the learning curve, the installation time decreases gradually. A few studies also reported that robotic surgery takes less time than laparoscopic surgery (9–11). What's more, robot-assisted approaches result in a shorter hospital stay, which might be caused by the substantial improvements in visibility and manipulation through the use of 3D imaging, tremor filters, and articulated instruments (16). The imaging of 3D can more clearly reveal the deep anatomical structure and the doctors can adjust the lens depth and angle according to their own habits and requirements. The simulation manipulator of the robotic surgery is highly flexible, simulating the translation, bending, opening and closing, rotation and other operations of the human hand. It can even rotate 540° to accurately grasp, free, cut and sew. It also has the functions of eliminating vibration and motion calibration. Each step of the robotic surgery has less interference on the intestine leading to less interference. As for the enteral feeding time, only two of the six articles included reported on this, but these were excluded following heterogeneity analysis. Thus more reports are needed to verify the impact of these two methods on postoperative enteral feeding time.

The reports on complications after laparoscopic or robotic choledochal cyst resections yielded differing results. Xie et al. reported that complications found in laparoscopic procedures were of a higher rate than those found in the robot-assisted procedures, but also that there was no meaningful difference found between the two groups overall (11). And robotic surgery can remove the tissue of cyst to the maximum extent which the distal end of cyst can be finely dissected down to the pancreatic segment and the proximal end is closed to the hilar bile duct. Hiroyuki et al. discovered that robotic surgery was positively correlated with enhanced postoperative outcomes when compared with laparoscopic surgery, such as less estimated blood loss, less time needed for the drainage tube insertion and a shorter duration for bowel sound return (10). Markar et al. undertook a systematic review and demonstrated that the occurence of anastomotic stricture in the robotic Roux-en-Y gastric bypass procedure within the laparoscopic group was a significantly reduced (17). Shui-qing Chi et al. reported that robotic surgery had obvious advantages for cyst excision and could provide a clearer view of hepatic duct anatomy which had encountered difculties in cyst dissection and was related to enhanced intraoperative and short-term postoperative outcomes in comparison to laparoscopic-assisted surgery (13). Robot surgery was not a single link that improves the quality of choledochal cyst excision which was improved as a whole with the help of the clarity, flexibility and stability of the robot operating system. The sharp cutting of the curvature of the electric shear protected the blood supply of the bile duct and intestinal to be anastomosed, reduced the damage to the blood supply of the bile duct and intestinal and improves the healing ability of the anastomosis. The mucosa to endothelium and small diameter of hepaticojejunostomy could be completed without difficulty. Abnormal blood vessels and bile ducts could also be clearly found and easier and more accurate to be dissected. In this systematic review and meta-analysis, laparoscopic surgery was found comparable to that of robot-assisted surgery as relates to common postoperative outcomes (e.g., cholangitis, bile leak, anastomotic stricture, bleeding, and reoperation rates). Despite there being no difference in postoperative complications found between laparoscopic and robotic surgery, Shui-qing Chi et al. reported that enhanced clarity of the hepatic duct anatomy was provided by the robotic system compared to traditional laparoscopy. A clear surgical field of vision assists surgeons in treating the lesions in a more accurate and thorough way, and can help to avoid or at least limit complications associated with surgical procedures to a certain degree (13).

At the same time, robotic surgery certainly also has its share of defects. Firstly, in general the cost of robotic procedures is significantly higher than that of other techniques. In fact, in China the cost of robotic surgery is approximately 20–40 thousand RMB (3,094–6,188 US dollars, according to the exchange rate in October 2021) and this is higher compared with open and laparoscopic methods. Two of the six articles included in this review reported on hospitalization expenses, but were excluded following heterogeneity analysis. Besides this, the da Vinci surgical system lacks a function providing tactile feedback, and as such the operator cannot directly feel the mechanical feedback when separating, suturing, and knotting. However, with improvements in the learning curve, visual feedback through hand-eye coordination will eventually make up for this absence in tactile feedback.

This study has some notable limitations. First, all included articles were retrospective analyses. Second, the amount articles were relatively small in number. Future large and multicenter prospective studies consisting of a greater population of patients and follow-ups over a longer-term are needed to further assess and compare the safety and feasibility of laparoscopic and robotic surgery. However, this review make use of meta-analysis in systematically reviewing and analyzing the published data comparing laparoscopic surgery and robotic assisted surgery for choledochal cyst excisions in terms of clinical outcomes.

Conclusion

Compared to laparoscopic surgery, robot-assisted surgery is associated with a shorter hospital stay, scores highly in terms of both safety and feasibility, however it also results in a longer operative time. And the two procedures have the same short- and long-term results.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

BX: study conception and design, analysis and data interpretation, critical revision. WW: study conception and design, analysis and data interpretation, critical revision. KZ: study concept and design, data analysis, drafting of the manuscript and critical revision of the manuscript. DZ: study conception, data collection and analysis. XX: data collection, conducting a research and investigation process. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Treatment of postoperative intestinal dysfunction of hirschsprung's disease based on the principle of "anorectal balance"

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Purpose: Radical surgery is the most effective treatment for Hirschsprung's disease. However, some children still have symptoms of intestinal dysfunction such as constipation, abdominal distension, and recurrent enterocolitis after operation. The purpose of this study was to evaluate treatment outcomes of postoperative intestinal dysfunction in children with Hirschsprung's disease by using the principle of "anorectal balance".

Methods: The clinical data of postoperative intestinal dysfunction in children with Hirschsprung's disease in the single treatment group from July 2019 to July 2021 were retrospectively analyzed. All the enrolled children underwent botulinum toxin injection (2.5 U/kg); 3 to 6 months later, the injection was performed again; the children who had received more than two botulinum toxin injections underwent the internal sphincter myectomy. Anorectal manometry was performed routinely after operation, and abdominal distension and defecation were recorded.

Results: A total of thirty children with postoperative intestinal dysfunction underwent radical surgery for Hirschsprung's disease were included in this study. Symptoms of constipation, abdominal distension and enterocolitis were improved after botulinum toxin injections in most children compared to before surgery ($P < 0.01$). After re-injection of botulinum toxin in twelve children, the frequency of defecation increased, the anal resting pressure decreased, and the clinical symptoms were relieved again ($P < 0.05$). Eleven children underwent internal sphincter myectomy, and the symptoms of constipation, abdominal distension and enterocolitis were significantly improved after the operation ($P < 0.01$).

Conclusion: Botulinum toxin injection and internal sphincter myectomy based on the principle of "anorectal balance" can effectively reduce the resting pressure of the anus and relieve intestinal dysfunction, and have satisfactory clinical effect.

KEYWORDS

anorectal balance, hirschsprung's disease, intestinal dysfunction, botulinum toxin, internal anal sphincter

Introduction

Hirschsprung's disease (HSCR) is a developmental disorder characterized by the absence of ganglion cells in the distal bowel, leading to chronic functional obstruction (1). The ultimate goal of surgical treatment is to remove the non-ganglion segment of the intestine and anastomose the innervated proximal intestine with the anus, so that the patients can defecate normally after operation.

Radical surgery is the most effective treatment for HSCR (2, 3). Although the bowel function of most children can be significantly improved after operation, some children still have symptoms such as constipation, abdominal distension, and recurrent enterocolitis after operation (4, 5). Some scholars defined this postoperative anal defecation dysfunction as anal outlet obstruction. We recently conducted a systematic study of clinical data from these children and found that their symptoms might be due to weaker proximal bowel function and greater anal resistance to defecation. When the defecation force was weaker than the resistance of the anus to hinder the excretion of stool, it would lead to poor defecation and manifest as symptoms of intestinal dysfunction. In other words, the bowel function did not match the anal function and stool was retained. The essence of the physiological behavior of defecation was that the force of the intestines and the body (the pressure formed by the diaphragm and abdominal muscles) to promote defecation exceeds the force formed by the anal sphincter to hinder defecation.

Therefore, we proposed the principle of "anorectal balance": anorectal function was a dynamic balance system, when the intestinal propulsion and anal resistance reached a dynamic balance, which was what we called "anorectal balance", normal defecation could be achieved. For some children with HSCR who have undergone radical surgery but could not receive further bowel resection, reducing anal resistance to achieve a balance between the bowel and anus – "anorectal balance" – might be a breakthrough point in clinical diagnosis and treatment.

Methods and materials

Case collection

From July 2019 to July 2021, the clinical data of children with intestinal dysfunction after radical resection of HSCR in the department of pediatric surgery of Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology were collected, including general conditions, past surgery history, number of bowel movements per day, preoperative anal resting pressure.

Inclusion and exclusion criteria

Patients with HSCR who presented with symptoms of intestinal dysfunction after radical resection, such as constipation, abdominal distension and enterocolitis, or who did not respond to anal dilation and drug treatment, were selected for inclusion in this study. Patients with non-HSCR who presented with constipation, abdominal distension and enterocolitis after surgery were not considered to be candidates for this study.

Treatment procedures

All patients routinely received colonic barium angiography, anorectal manometry, and rectal mucosal acetylcholinesterase staining before surgery (**Supplementary Figures S1,S2**).

All operations in this study were performed by a fixed surgical team. Botulinum toxin injections were performed as follows: the patient was placed on an operation table in the lithotomy position and was under anesthesia; the anal canal was repeatedly disinfected 3 times with 0.5% vital iodine; botulinum toxin was (Botulinum toxin type A for injection, trade name: Botox; manufacturer: Allergan Pharmaceuticals Ireland; import drug registration number: S2017005) injected into the internal sphincter at the 1, 5, 6, 7, and 11 o'clock directions near the dentate line, respectively, at a dose of 0.5 U/kg/point. One week after the operation, all patients received anorectal manometry again, and the number of defecation, abdominal distension, and enterocolitis were recorded. For those patients who experienced constipation, abdominal distension, and enterocolitis about 3 months after the first botulinum toxin injection, repeat botulinum toxin injection was performed.

According to the principle of "anorectal balance", if receiving a second dose of botulinum toxin was effective, but the patient developed symptoms again after 3 months, the internal sphincter myectomy was performed. The patient was placed in the lithotomy position. The skin was incised in an arc at the intersphincteric groove behind the anal verge, the internal and external sphincter muscles were separated, and about a 1.5 cm-long internal sphincter strip was removed from the anal verge to the lower edge of the dentate line (**Figure 1**). The boundary between the internal and external anal sphincter was determined by the following criteria: (1) The external anal sphincter contracts in response to electrocautery stimulation, while the internal anal sphincter does not have this response. (2) The external anal sphincter is pink and the internal anal sphincter is white. (3) There is a layer of connective tissue between the internal and external anal sphincter muscles (6). The patients started with fluid diet on postoperative 3 day and normal diet from postoperative 5

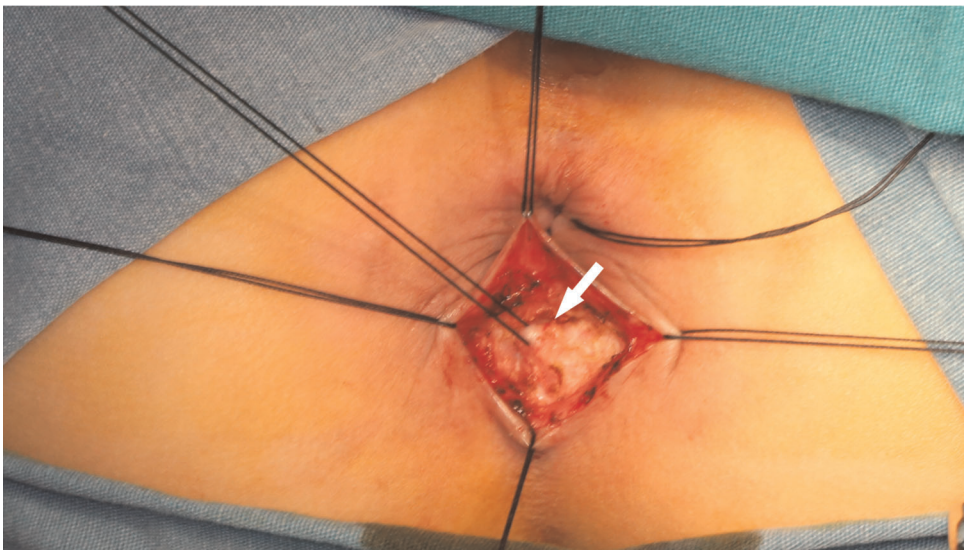

FIGURE 1
Intraoperative picture of internal sphincter myectomy. White arrow: internal anal sphincter.

days onwards. Anal dilatation was started from two weeks for 3 to 6 months postoperatively.

Follow up

All patients were followed up for 3–6 months. Follow-up data were obtained by review of medical records and telephone interviews. Constipation is diagnosed by the appearance of small, pebble-like, hard stools after at least two weeks in most cases; or two or fewer stools per week (7). Abdominal distention is defined as a full abdomen with an abdominal wall higher than the line between the xiphoid process and the pubic symphysis, with or without symptoms such as vomiting and belching. Hirschsprung's disease-associated enterocolitis is defined as a patient with symptoms such as fever, diarrhea, and vomiting, and a large amount of foul-smelling stool can be excreted by digital rectal examination (1).

Statistical methods

SPSS 22.0 software was used for statistical analysis. Measurement data were expressed as mean ± standard deviation, and enumeration data were expressed as frequency. The t test was used for measurement data, and the chi-square test and Fisher's exact test were used for enumeration data. $P < 0.05$ was statistically significant.

Results

Patient demographics

A total of 30 patients with HSCR were admitted to our department in the period between July 2019 and July 2021. Mean age at follow-up was 2.4 ± 1.02, and male-to-Female ratio was 1.73: 1. The main clinical manifestations of these children were abdominal distension, constipation and enterocolitis. All the enrolled children had a history of colectomy, of which 25 (83.3%) underwent subtotal colectomy and 5 (16.7%) underwent total colectomy. The primary operation had been Soave-type pull-through in 26/30 (86.7%) patients and Duhamel in 4/30 (13.3%) patients. Among them, 7 (23.3%) patients received their primary operations in our hospital, and 23 (76.7%) patients received their primary operations in other hospitals. Basic information of these children was summarized in **Table 1**.

Outcomes after the first botulinum toxin injection

In the present study, we first compared changes in the number of bowel movements, resting anal pressure, and clinical symptoms in the enrolled children after the first injection of botulinum toxin. The results showed that after receiving botulinum toxin injection, the frequency of defecation in these children increased, the anal resting pressure was lower than that before the operation, and the clinical symptoms were significantly relieved. These

TABLE 1 Demographic data and clinical characteristics ($N = 30$).

Gender	
Male, *n* (%)	19 (63.3)
Female, *n* (%)	11 (36.7)
Age, $\bar{X} \pm s$, years	2.4 ± 1.02
Clinical symptoms	
Abdominal distension, *n* (%)	21 (70.0)
Constipation, *n* (%)	28 (93.3)
Enterocolitis, *n* (%)	23 (76.7)
Previous operation	
Soave, *n* (%)	26 (86.7)
Duhamel, *n* (%)	4 (13.3)
Extent of resection	
Subtotal colectomy, *n* (%)	25 (83.3)
Total colectomy, *n* (%)	5 (16.7)

TABLE 2 Outcomes after the first botulinum toxin injection ($N = 30$).

Clinical indicators	Preoperative	Postoperative	*P*	t/χ^2
Number of bowel movements ($\bar{X} \pm s$)	1.1 ± 0.6	5.4 ± 1.1	<0.001	18.80
Anal resting pressure ($\bar{X} \pm s$, mmHg)	62.1 ± 9.1	27.3 ± 5.4	<0.001	18.01
Clinical symptoms				
Abdominal distension, *n* (%)	21 (70.0)	4 (13.3)	<0.001	19.82
Constipation, *n* (%)	28 (93.3)	3 (10.0)	<0.001	41.71
Enterocolitis, *n* (%)	23 (76.7)	3 (10.0)	<0.001	27.15

differences were statistically significant (Table 2). The results suggested that botulinum toxin injection could effectively reduce anal resting pressure, thereby relieving symptoms such as abdominal distension, constipation, and enterocolitis.

Outcomes after second botox injection

It is important to note that the effects of Botox last for about 3 months. Therefore, some children will experience abdominal distension, constipation or enterocolitis again after the effect of the drug wears off. Next, we further compared the clinical parameters of 12 children who received a second botulinum toxin injection. The results showed that after receiving the second injection, the number of bowel movements increased, the anal resting pressure decreased, and the clinical symptoms were relieved again (Table 3). The results further demonstrated the effectiveness of botulinum toxin injections.

TABLE 3 Outcomes after second botulinum toxin injection ($N = 12$).

Clinical indicators	Preoperative	Postoperative	*P*	t/χ^2
Number of bowel movements ($\bar{X} \pm s$)	1.2 ± 0.7	4.7 ± 1.2	<0.001	8.73
Anal resting pressure ($\bar{X} \pm s$, mmHg)	49.2 ± 6.3	23.4 ± 4.4	<0.001	11.63
Clinical symptoms				
Abdominal distension, *n* (%)	12 (100.0)	1 (8.3)	<0.001	20.31
Constipation, *n* (%)	11 (91.7)	3 (25.0)	<0.001	10.97
Enterocolitis, *n* (%)	9 (75.0)	3 (25.0)	<0.001	6.00

Outcomes after internal anal sphincter myectomy

We performed internal anal sphincter myectomy for children who had received botulinum toxin injections twice but had recurring symptoms of abdominal distension, constipation, and enterocolitis. We found that the frequency of defecation, anal resting pressure and clinical symptoms of these children after operation were significantly improved compared with those before operation, and the difference was statistically significant (Table 4).

Discussion

Surgical treatment for HSCR has been performed for over 65 years and has an overall good outcome. Nonetheless, some children complained of persistent postoperative symptoms, such as constipation, abdominal distension, and recurrent enterocolitis.

This postoperative anal defecation dysfunction has been defined as anal outlet obstruction (8). However, this definition was only a general description of symptoms and did not emphasize the function and innervation of the anal sphincter. Furthermore, the definition did not distinguish obstruction from other causes. In this study, we refered to these symptoms

TABLE 4 Outcomes after internal sphincter myectomy ($N = 11$).

Clinical indicators	Preoperative	Postoperative	*P*	t/χ^2
Number of bowel movements ($\bar{X} \pm s$)	0.9 ± 0.1	5.7 ± 1.6	<0.001	9.93
Anal resting pressure ($\bar{X} \pm s$, mmHg)	51.4 ± 3.7	17.2 ± 3.2	<0.001	23.19
Clinical symptoms				
Abdominal distension, *n* (%)	10 (90.9)	2 (18.2)	<0.001	11.73
Constipation, *n* (%)	11 (100.0)	2 (18.2)	<0.001	15.23
Enterocolitis, *n* (%)	9 (81.8)	1 (9.1)	<0.001	11.73

as postoperative bowel dysfunction. In fact, we found that some children who have undergone subtotal colectomy or total colectomy still have the above-mentioned manifestations of intestinal dysfunction, which may be due to the imbalance between the force of the bowel to promote defecation and the resistance formed by the internal anal sphincter. Therefore, we used botulinum toxin injection to relieve symptoms in some children, and performed internal anal sphincter myectomy for children who received re-injection but had exceeded the duration of the drug effect. The results show that the above treatments have achieved good clinical outcomes. Excitingly, our work is consistent with several previous studies demonstrating that botulinum toxin injections and internal sphincter myectomy can be used to treat the obstructive symptoms of patients with HSCR after pull-through surgery (4, 9).

Of note, postoperative bowel dysfunction described in this study should be differentiated from internal anal sphincter achalasia. Internal anal sphincter achalasia was also one of the causes of constipation, which was considered to be ultrashort-segment megacolon (10, 11). However, recent studies have found that internal anal sphincter achalasia was different from HSCR in clinical manifestations, pathophysiology and treatment (12, 13). The diagnostic of internal anal sphincter achalasia is determined by the following criteria: anorectal inhibitory reflex is negative, the internal anal sphincter has ganglion cells, the rectal mucosa is negative for acetylcholinesterase staining, and no surgical treatment is performed (11, 14). Although the clinical manifestations of postoperative intestinal dysfunction of children with HSCR are similar to internal anal sphincter achalasia, it is essentially a mismatch between intestinal function and anal function, that is, "anorectal imbalance".

The essence of human defecation control is that under the control of the nervous system, the driving force of the intestine and the force of the body to promote defecation (such as the pressure formed by the diaphragm and abdominal muscles) exceed the force of the anal system to hinder defecation (such as the sphincter, pelvic floor muscles, anal pad). The internal anal sphincter provides 50% to 80% of the anal resting pressure to prevent fecal discharge (15, 16). The anorectal function is a dynamic balance system, which controls the defecation process under the coordination of the pelvic floor anal canal receptors, the primary center of the lumbosacral spinal cord and the cerebral cortex (17). Under normal circumstances, the anal resistance exceeds the defecation motivation, there is no fecal incontinence. When the feces in the intestines accumulate to a certain extent, the urge to defecate is triggered. Under the coordination of the nervous system, the force that promotes defecation exceeds the force that hinders defecation, then the feces can be discharged. In short, when the pushing force is greater than the resistance, defecation is possible; when the resistance is greater than the pushing force, defecation cannot be performed. Based on this, we propose the concept of "anorectal balance", that is, when a dynamic balance is achieved between the intestinal propulsion and anal resistance, defecation can be achieved. In fact, the essence of treatment for children with HSCR is to remove the diseased bowel and anastomosis of the proximal normal bowel with the anus to achieve "anorectal balance".

Some children with HSCR have symptoms such as constipation, abdominal distension, and recurrent enterocolitis because of "anorectal dysfunction": their proximal bowel function is weaker than that of normal children, and the anal sphincter is well developed. So these children have relatively greater anal resistance. In the case of inability to further resection of the bowel with reduced function (such as subtotal colectomy or total colectomy), it is a reasonable and feasible option for clinical treatment to achieve "anorectal balance" by reducing anal resistance. In addition, we also observed that some children with HSCR had smooth bowel movements in the early postoperative period (about half a year), but gradually developed a series of symptoms such as constipation and enterocolitis 1 to 2 years after the operation. The reason may be that the initial operation will lead different degrees of damage to the anus, and the resistance of the anal sphincter will decrease in a short period of time; when the anal function is restored, the resistance formed by the sphincter will gradually increase, resulting in defecation dysfunction. Some surgeons are less disruptive to the anus during surgery based on functional protection and surgical techniques. However, it is more likely to lead to recurrence of postoperative constipation or enteritis. This further supports the applicability of the principle of "anorectal balance".

Based on the above clues and principles, we used botulinum toxin injection and internal anal sphincter myectomy to treat postoperative intestinal dysfunction in children with HSCR, which had good clinical effect. Botulinum toxin can block the release of peripheral acetylcholine by cleaving SNAP-25 in the anterior membrane of cholinergic nerve endings, thereby leading to the relaxation of neuromuscular junctions and reducing the resistance formed by sphincter (14, 18, 19). This method has the advantages of simplicity, safety, effectiveness and repeatability. After the first injection of botulinum toxin, most of the children's symptoms were significantly relieved and no further injection was required. However, the effects of botulinum toxin only last for about 3–6 months. When the effect of the drug wore off, some children had symptoms again. Therefore, according to the principle of "anorectal balance", botulinum toxin injection was performed again on 12 children. The results showed that while some children's symptoms disappeared within 3 months after the injection, they reappeared as the drug effects wore off. Therefore, the internal sphincter myectomy is an option reoperation when the effectiveness of botulinum toxin injection has been proven. Its essence is to achieve "anorectal balance" in anatomy and relieve the symptoms of constipation. After careful evaluation of the data of these children, we found that: (1) according to the principle of "anorectal balance", the use of botulinum toxin

injection could relieve the symptoms, suggesting that these children have high postoperative anal resistance and need to reduce the anal resting pressure to achieve the purpose of treatment; (2) the reason of some children underwent repeat botulinum toxin injections rather than direct internal anal sphincter myectomy was that the latter might lead to complications (e.g., possible fecal incontinence). Re-injection of botulinum toxin could not only further confirm the effectiveness of reducing anal resistance, but also provided a clinical basis for the implementation of internal sphincter myectomy. Recently, the author performed botulinum toxin injection and internal anal sphincter myectomy on a patient with HSCR who had recurrent enteritis and severe malnutrition after total colectomy and entero-anastomosis. About four weeks later, the child's weight increased significantly, and the symptoms were significantly relieved.

It should be noted that this study has certain limitations. On the one hand, the sample size of this study is limited, and large-scale prospective observations are still needed. On the other hand, internal anal sphincter myectomy may lead to complications such as fecal incontinence, wound infection, and prolonged healing time. Therefore, this operation needs to be performed by an experienced and skilled surgeon.

The essence of defecation control is a process in which the lower center and cerebral cortex coordinate the dynamic balance between the power of the intestine and the resistance formed by the anal sphincter. In this study, the principle of "anorectal balance" was proposed, and botulinum toxin injection and internal anal sphincter myectomy were used to treat postoperative intestinal dysfunction in children with HSCR. It can effectively reduce the anal resting pressure and relieve the clinical symptoms of the children. This may bring new ideas for the treatment of HSCR.

Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Tongji Hospital Affiliated to Tongji Medical College of Huazhong University of Science and Technology (No. 2019S108). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

TL: Conducted the study, collected, analyzed and interpreted the data, and wrote the manuscript. MCS, DZD, ZTQ, ZX and HY: collected and analyzed the data. WMF and FJX: review and editing the manuscript. YDH: performed the surgery, and conceptualisation, study design and supervision. All authors contributed to the article and approved the submitted version.

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Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2022.996455/full#supplementary-material.

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Treatment for complete bilateral duplex kidneys with severe hydronephrosis and ureterectasis of the upper moiety in a child: A case report and literature review

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Aim: To explore the treatment experience of the duplex kidney.
Method: A case of the complete bilateral duplex kidney with severe hydronephrosis and ureterectasis in the upper moiety of the kidney diagnosed in the Department of Urology of Kunming Children's Hospital from 2021 to 2022 was retrospectively analyzed and relevant literature was reviewed.
Results: A 2-month-old baby girl was admitted to the hospital because of hydronephrosis of bilateral kidneys found by prenatal ultrasound for 3 months and fever for 3 days. After being given the relevant examinations, the girl was diagnosed with complete bilateral duplex kidneys with severe hydronephrosis and ureterectasis in the upper moiety, and urinary tract infection. The patient's urinary tract infection was poorly controlled after positive anti-infective therapy, so a bilateral ureterostomy was performed. After the surgery, urinary tract infection was soon cured. A bilateral ureteroureterostomy was performed 13 months later, and the patient recovered after 7 days.
Conclusion: Cutaneous ureterostomy combined with late ureteroureterostomy for children with complete bilateral duplex kidneys with severe hydronephrosis in the upper moiety and ureter are not only beneficial to caregivers' nursing after the operation, but also have significance for salvaging renal function.

KEYWORDS
child, duplex kidney, renal malformation, ureterostomy, ureteroureterostomy

Background

Duplex kidney is a common disease in pediatric urology. There are many controversies due to the children's deformities and treatment methods are diverse and complicated (1). We report a case of severe hydronephrosis and ureterectasis in the upper moiety of bilateral duplex kidney with ectopic ureter on the left side and ureterocele on the right side, and summarize the characteristics of the disease for improving the understanding of pediatricians of the disease.

Clinical material

Patient information

The patient's parents informed and agreed to this case report: A 2-month-old baby girl was admitted to the hospital because of hydronephrosis of bilateral kidneys found by prenatal ultrasound for 3 months and had a fever for 3 days. The child was found to have bilateral hydronephrosis in her mother's late pregnancy, and ultrasound was not regularly performed after birth. The child had a fever for 3 days without an obvious cause, and the highest temperature was 39°C. After treatment in a local hospital, the child still had a recurrent high fever. After being referred to Kunming Children's Hospital, the child was given relevant examinations.

Physical examination

No positive signs were found.

Laboratory examination

Urine test revealed white blood cell: +++, white blood cell enzyme (+), nitrite (+). Urine culture: *Escherichia coli*.

Imaging examination

Ultrasound of urinary system showed bilateral duplex kidney (**Figure 1**). Severe hydronephrosis and ureterectasis were found in the bilateral upper moiety. Intravenous pyelography (IVP) showed there was an ureterocele in the bladder (**Figure 2**). Computerized tomography (CT) revealed severe hydronephrosis and ureterectasis of bilateral upper moiety, left ureteral opening was ectopic in location, and the right ureterocele was found (**Figure 3**).

After discussion, cystoscopy and bilateral cutaneous ureterostomy was performed for the patient (**Figure 4**). In cystoscopy, ectopic insertion of lift upper moiety ureter and ureterocele of right upper moiety ureter were found. The patient's urinary tract infection (UTI) was cured soon after bilateral cutaneous ureterostomy, and she was discharged 5 days later (**Figure 5**).

No UTI a **Figure 5** fever occurred in the patient during discharge. The results of routine urine examination were normal, and ultrasound indicated that bilateral hydronephrosis was relieved obviously. 13 months after the ureterostomy, the child was returned to the hospital for further surgery. IVP showed no hydronephrosis in bilateral duplex kidney (**Figure 6**). Voiding cystourethrography (VCU) showed mild vesicoureteral reflux (VUR) on the right lower moiety ureter (**Figure 7**). The patient recovered and was discharged on the 7th day after bilateral ureteroureterostomy. The D-J tubes were removed 1 month after operation (**Figure 8**).

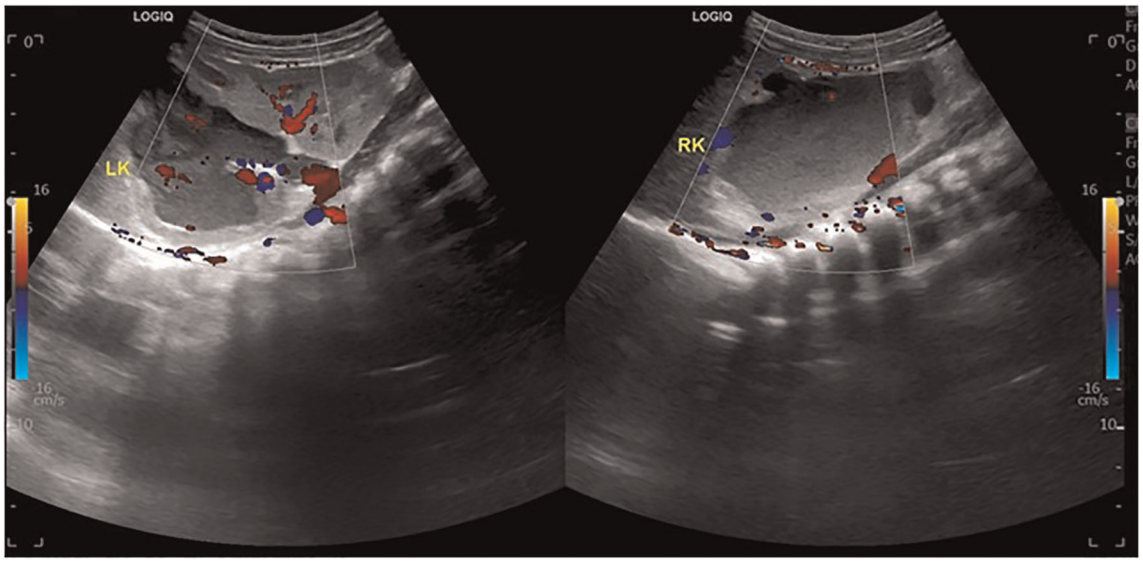

FIGURE 1
Preoperative ultrasound showed severe hydronephrosis and ureterectasis of bilateral upper moiety.

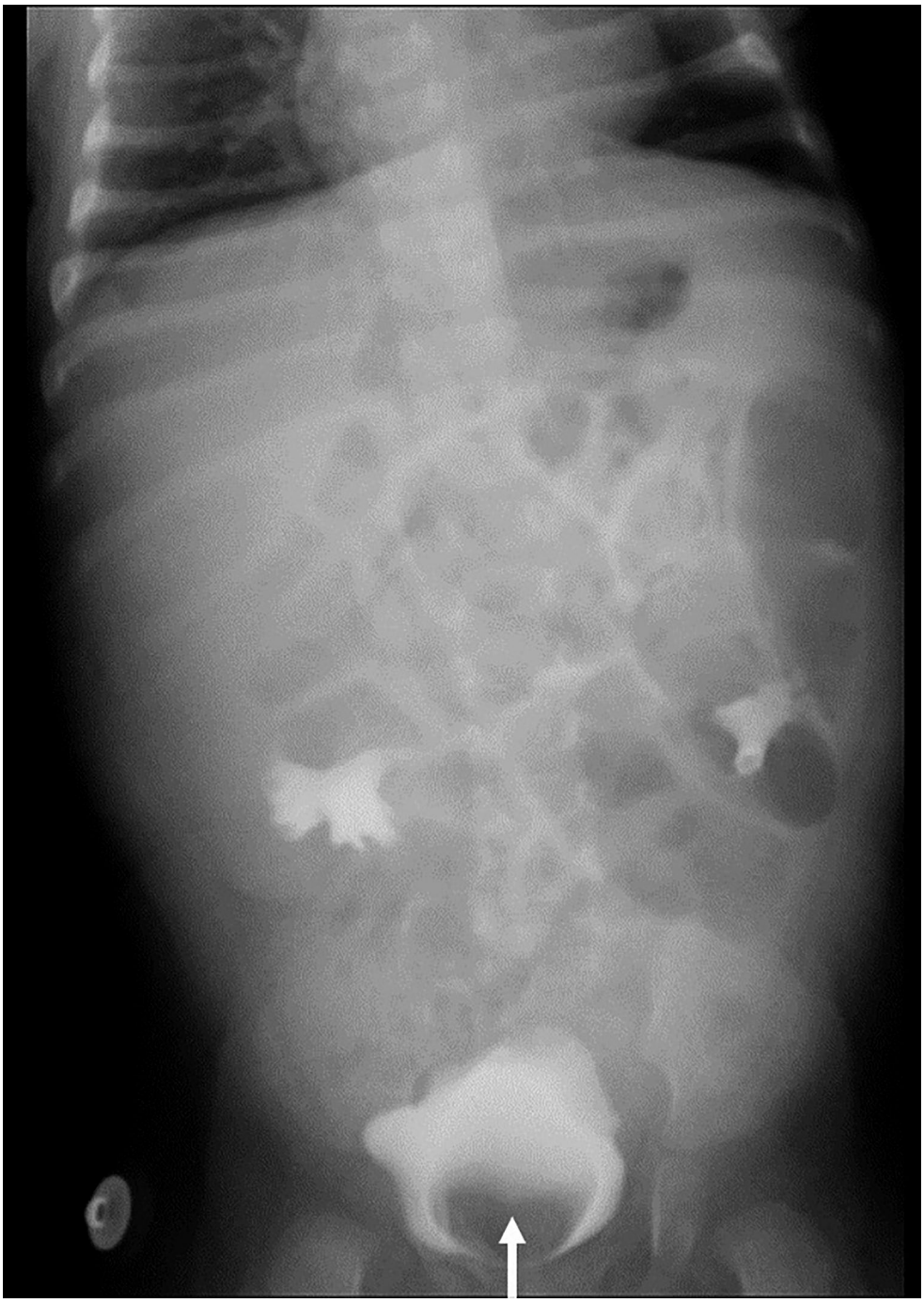

FIGURE 2
Preoperative IVP showed an ureterocele in the bladder (↑).

Discussion

Prenatal ultrasound is necessary for both pregnant and fetus. With the continuous development and maturity of ultrasound technology, it not only helpful for diagnosing an obstruction of the urinary tract in pregnancies, but also meaningful for permitting the prenatal anatomical assessment of most congenital anomalies of the kidney and urinary tract during the second or third trimester (2, 3). The incidence of duplex kidney malformation is about 0.8% and it is common

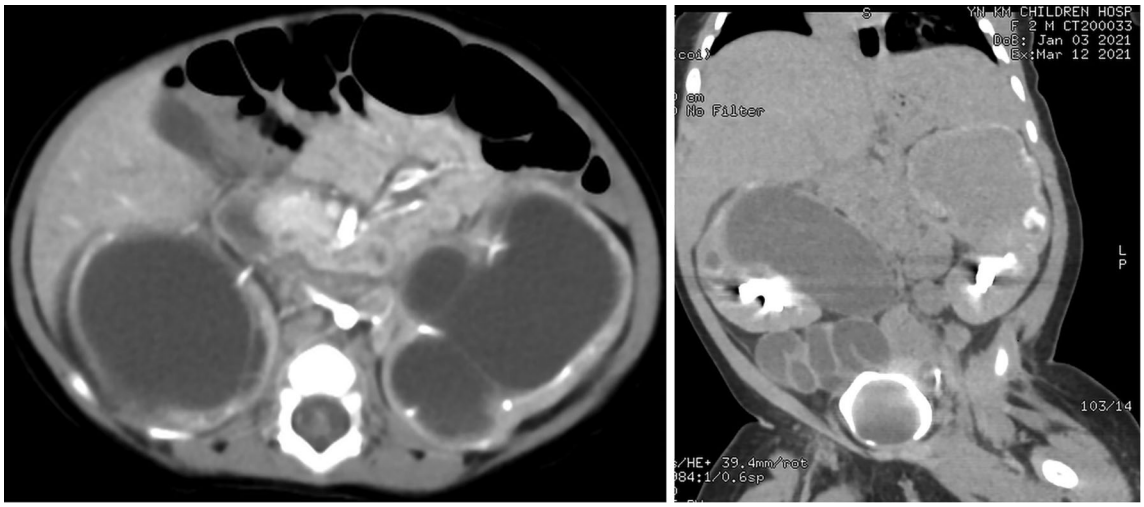

FIGURE 3
Results of preoperative CT showed severe hydronephrosis and ureterectasis of bilateral upper moiety, left ureteral opening, and the right ureterocele.

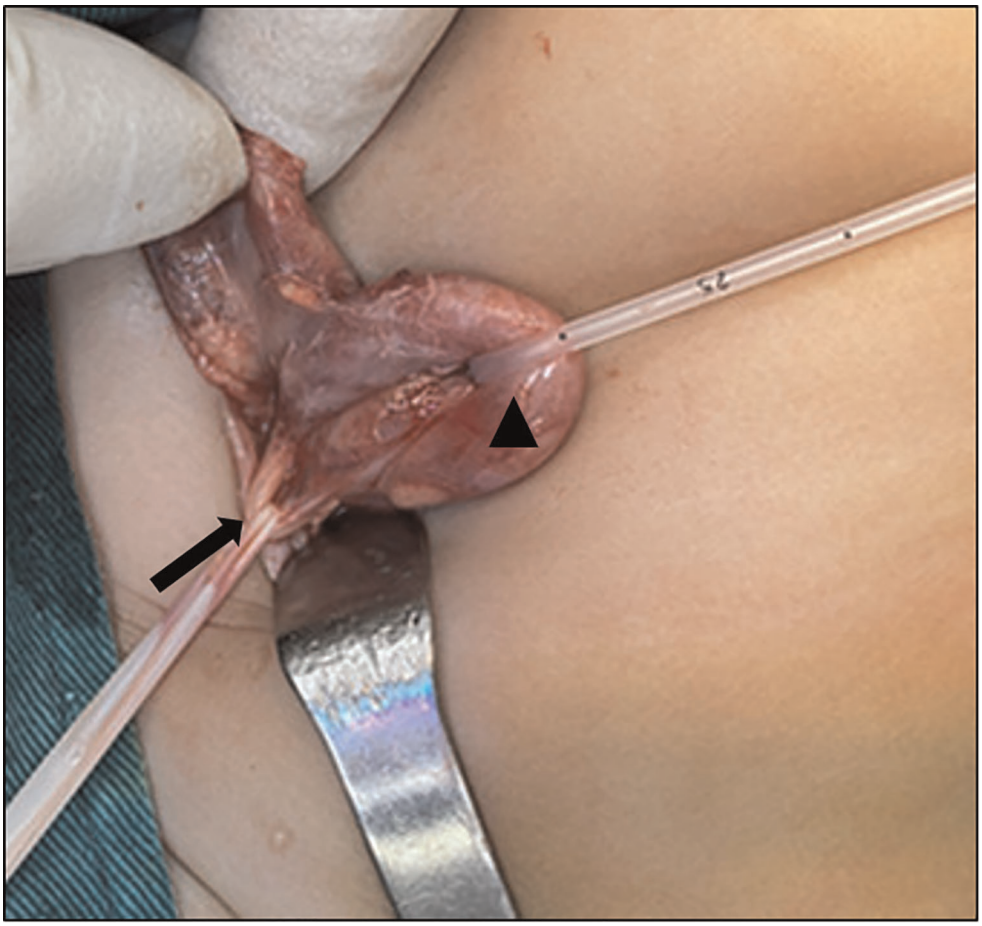

FIGURE 4
▲: Upper moiety ureter, ↑: lower moiety urtter.

FIGURE 5
Patient's situation after bilateral cutaneous ureterostomy.

to women (4, 5). Among children diagnosed with hydronephrosis before birth, 5%–7% are due to duplex kidney (6). The duplex kidney can be divided into incomplete type (Y type) and complete type. The incidence of complete ureteral deformity is about 0.2% (7). According to Weigert-Meyer-Rule, the upper pole is normally seen as ectopic and therefore dysplastic due to obstruction, whereas the lower pole is related to vesicoureteral reflux (8–10).

Fetal interventions include ultrasound-guided bladder puncture and drainage and transurethral incision of ureterocele under fetal cystoscope. Although the decompression effect is good, there are risks of premature rupture of membranes, premature delivery, infection, bleeding, and fetal death, which need to be carefully evaluated and considered (11, 12). Nearly 60% of patients with duplex kidney are asymptomatic and need no treatment after birth. Patients with ectopic ureteral opening, ureteroceles, hydronephrosis, calcuil, urinary tract infection, or non-functional need surgical treatment (13). Treatment for duplex kidney needs to be individualized, and hemi-nephroureterectomy is the earliest technique used in duplex kidney therapy. If the duplex kidney function is good and there is no dysplasia, the upper moiety can be reserved. Common surgical methods include ureteric reimplantation, ureteroureterostomy, pelopureteroplasty, etc. (14). The objective of treatment is to prevent urinary tract infection, and renal damage and to achieve urinary continence (15).

The surgical indication for hemi-nephroureterectomy is upper renal function <10% due to recurrent urinary tract infection with vesicoureteral reflux, or severe obstruction (16, 17). And most scholars agree that upper moiety resection should be performed in patients with recurrent urinary tract infection and ipsilateral abdominal pain (18). However, it is controversial whether the operation should be performed in patients with renal function <10% and no relevant clinical symptom. Proponents believe that surgical removal of non-functional or dysplasia renal tissue and ureters can prevent the long-term occurrence of hypertension or pyelonephritis (1, 19). On the contrary, the possibility of long-term hypertension and pyelonephritis in the non-functional kidney is low, and the operation will easily affect the blood supply and function of the lower kidney, leading to kidney loss (15, 20, 21).

Ureteroureterostomy is usually performed at the level of the iliac vessels to avoid dissociation of the colon, interference with the nerves and vessels of the bladder, and extensive dissociation of the ureter (22). The procedure is not only easier than common sheath ureteral reimplantation but also can protect bladder function from damage. Anastomotic fistula, anastomotic stenosis, and ureteral stump complications are the main postoperative complications of this procedure, and the overall incidence is similar to that of common sheath ureteral bladder replantation (23).

In duplicated ureters with VUR, without obstruction, and with the preserved function of both renal moieties, the gold standard surgical intervention is ureteral reimplantation. However, the incidence of surgical complications is as high as

FIGURE 6
Result of IVP after ureterostomy showed no hydronephrosis in bilateral duplex kidney.

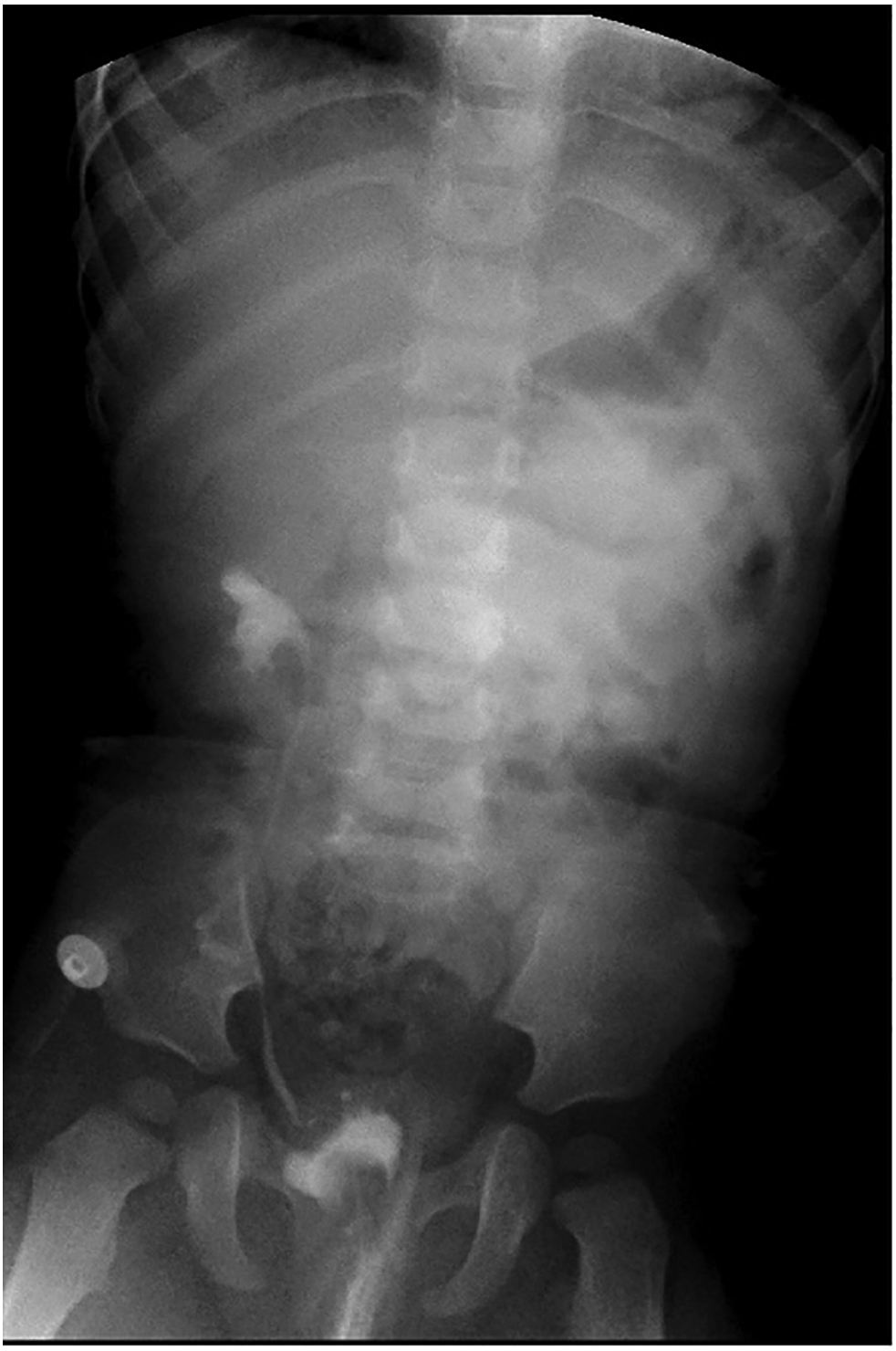

FIGURE 7
Result of VCU before ureteroureterostomy showed mild vesicoureteral reflux (VUR) on the right lower moiety ureter.

10%–12.5%, and bladder function will inevitably be disturbed. Studies showed that about 10% of patients require a second surgery (21, 24).

For patients with severe hydronephrosis combined with severe urinary tract infection and sepsis, timely removal of obstruction and urine drainage are beneficial to the recovery

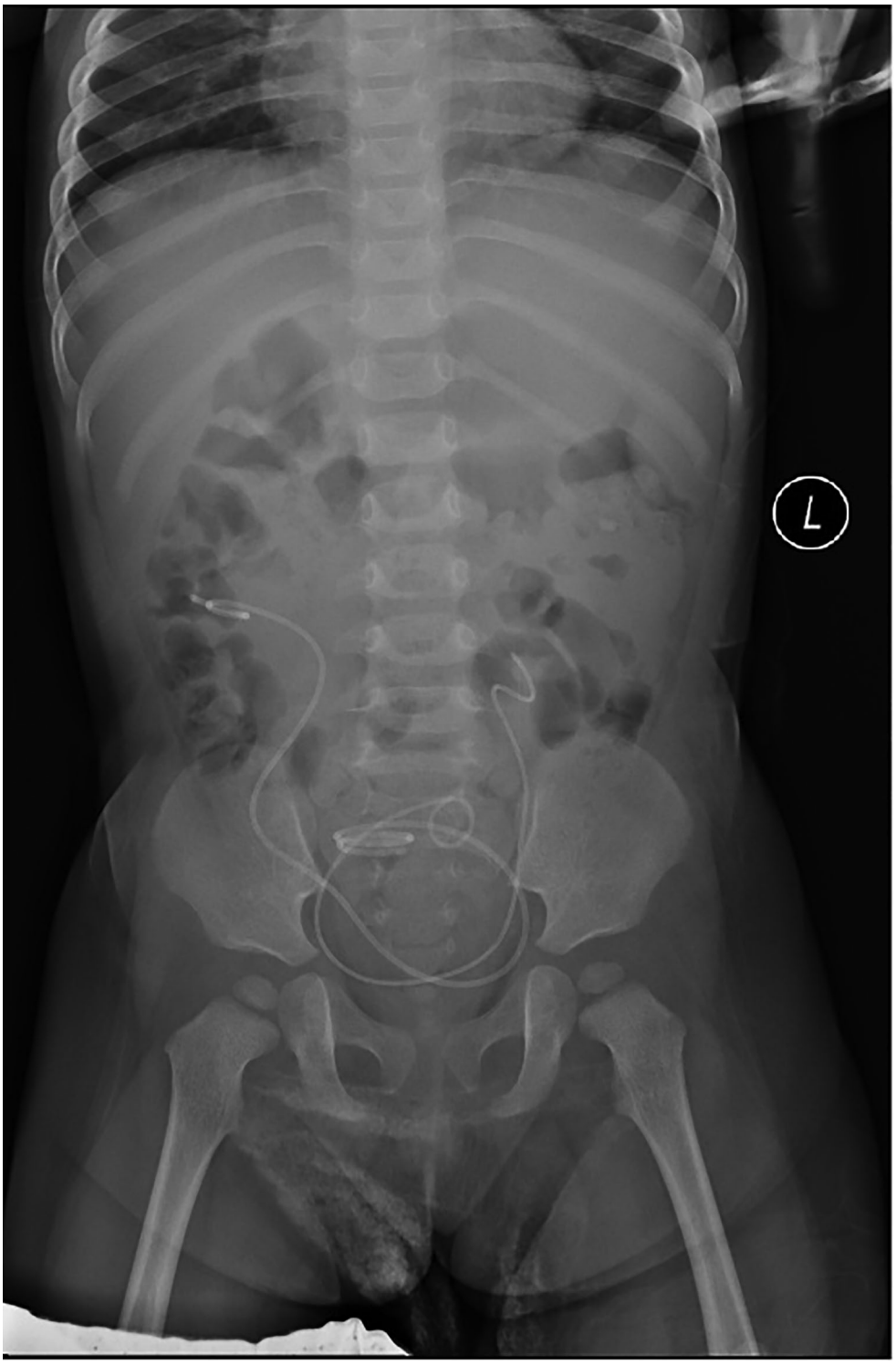

FIGURE 8
Postoperative situation of the D-J tubes.

of duplex kidney function and the retention of the kidney (25, 26). Common urine drainage methods include ① Pyelostomy: This method is simple and effective. But it requires indent and regular replacement of external drainage tube, and later nursing is relatively tough for patients with troublesome for the caregivers. ② Transurethral incision of

ureterocele (TIU): TUI has an invasive, cosmetic, and no external drainage surgical effect. However, this method has secondary or aggravating risks of VUR on the affected side, and patients with large cysts may also have postoperative cyst wall prolapse in the urethra. ③ Cutaneous ureterostomy: This operation has a definite curative effect, no external drainage after the operation, and postoperative nursing of infants is relatively convenient.

In this case, considering that both external renal drainage tubes should be placed after pyelostomy, and unilateral TIU has no definite significance for the relief of obstruction on the other side, so bilateral ureterostomy was performed in this case. The patient's hydronephrosis was significantly relieved after cutaneous ureterostomy, and IVP showed that the development of both kidneys was normal after 13 months. It indicated that timely relief of obstruction was of significance to salvage renal function.

At present, it is still controversial whether ureteral bladder reimplantation should be performed for duplex kidney with lower moiety VUR. Due to the low grade of reflux, ureteric reimplantation was not performed in our case for the following reasons: On the one hand, mild reflux has the possibility of self-healing. On the other hand, if the patient's grade of VUR is aggravated or recurrent urinary tract infection occurs, only a single ureteral bladder reimplantation will be required in the future. Compare with common sheath ureteral reimplantation, it requires a smaller bladder capacity, ureter diameter, and bladder mucosal tunnel length, which is not only beneficial to reduce surgical trauma and bladder disturbance, but also has a higher surgical success rate (24).

When indicated, the type of surgery for children with the complicated duplex renal anomaly is based on renal moiety function and lower tract anatomy, and sequential treatment is meaningful to reduce bladder disturbance, reduce surgical trauma and improve the success rate of surgery.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

CW and FJ performed the surgery and drafted the original manuscript. HZ and ZY collected data and participated in to amend the manuscript. BY and LL designed the operation scheme and amended the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Delayed vs. early enteral feeding after repair of congenital recto-vestibular fistula: The effect on perineal wound healing

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Introduction: congenital Recto vestibular fistula represents the commonest type of anorectal malformation in females. The treatment of this anomaly is mainly approached either through anterior or posterior sagittal ano-rectoplasty approach. Several perioperative factors may affect the outcome. One of major postoperative complications is the occurrence of wound infection. We aimed to study the effect of delayed vs. early enteral feeding on the occurrence of perineal wound infection (PWI) after repair of congenital recto vestibular fistula.

Patients and methods: Fifty-five infants with recto-vestibular fistula were included. They were managed by single stage anterior sagittal anorectoplasty (ASARP) at an age ≥3 months. Groups A and B included infants who started oral intake on the 6th and 2nd postoperative days respectively. Group A infants were kept on peripheral parenteral nutrition (PPN) during the fasting period.

Results: Superficial wound infection occurred in three cases in group A while it developed in seven cases in group B. Deep perineal infection occurred in two and five cases in group A and group B respectively. The mean hospital stay was 8 days in group A vs. 13 days in group B when PWI developed.

Conclusion: Delayed enteral feeding with PPN keeps the perineal wound less contaminated with stool. This promoted proper and fast healing with lower incidence of PWI. Also, PPN compensates the catabolic effects of both surgical trauma and fasting during the postoperative period and ensures maintenance of normal levels of essential nutrients that allow for proper healing.

KEYWORDS

rectovestibular fistula, perineal wound infection, anterior sagittal anorectoplasty, enteral nutrition, peripheral introduced central line

Introduction

Congenital recto-vestibular fistula in females is a common variant of anorectal malformation. This anomaly has the potential for favorable prognosis regarding post-repair sphincter function (1).

There are two options for the management of recto-vestibular fistula, which include posterior sagittal anorectoplasty (PSARP) or anterior sagittal anorectoplasty (ASARP). Also, some surgeons perform a covering colostomy before definitive management, while others perform single-stage repair. Some surgeons plan to repair this anomaly during the neonatal period while other plan to repair the condition after the age of 3 months. Irrespective of the technique used or the timing of repair, good prognosis and functional outcome are anticipated (2–4).

Several perioperative factors may have a potential effect on the prognosis of the repair of recto-vestibular fistula. These factors included antibiotic prophylaxis, mechanical bowel preparation, and nutritional regime. They are characterized by being individually assisted and practiced by surgeons (5).

Nutritional status and regime influence the prognosis of repair of recto-vestibular fistula. Early initiation of enteral feeding is one of the principles of enhanced recovery protocols (ERP) of colorectal surgery in the pediatric age group. However, some surgeons postpone the start of oral intake for 1–2 weeks especially during single stage repair of rectovestibular fistula to avoid local soiling of the perineal wound with stool and to decrease the incidence of wound infection (6).

Perineal wound infection (PWI) is a serious complication. It may lead to failure of the reconstructive surgery, weakness or even degeneration of the sphincter complex and ends in faecal incontinence. Moreover, its healing by fibrosis may lead to stenosis of the new anal opening and massive rectal dilatation that affects bowel evacuation. As a result of this complication the functional outcome will be poor with a bad prognosis. This exerts a psychological burden on parents (7).

We aimed to study the effect of early versus late enteral post-repair feeding on the development of PWI in cases of single stage repair of recto-vestibular fistula.

Methods

Study design

This was a randomized control trial. The study included 55 female infants diagnosed with congenital rectovestibular fistula during the period from January 2015 to March 2022. The patients were randomly divided into two groups A and B using opaque sealed envelopes and randomly generated tables. Group A included patients who had delayed initiation of oral intake for 5 days postoperatively. Group B included patients who started oral intake on the 2nd postoperative day and gradually increased as tolerated by the patient. We excluded premature infants, cases with a plan of staged repair and cases with poor nutritional status (their mean level of albumin was 3 gm/dl ± 0.2). All participants were operated on at the age of 3 months or older.

The study was approved by the ethics committee of our institution and assigned code 35054/11/21.

The study was conducted in compliance with COSORT criteria of randomized control trials (**Figure 1**).

Preoperative management in both groups

Infants in both groups were subjected to regular dilatation of the fistula with Hegar's dilators twice daily from birth till the time of the operation. The diameter of the dilator gradually increased with the growth of the infant and usually reached size 13 or 14 by the infant's age of 3 months. All infants were admitted to hospital 2 days preoperative. They had mechanical bowel preparation (warm normal saline enema), prophylactic antibiotics, and oral intake of clear fluids. Oral intake was stopped 24 h before surgery and intravenous fluid was initiated. In group A all patients had peripherally introduced central lines (PICL) to be nourished with total parenteral nutrition (TPN) during the first postoperative 5 days.

Operative management

Infants of both groups had single stage ASARP as definitive treatment. The sphincter saving technique was applied in both groups. Complete urinary diversion using Folly's catheter (size 6 F) was planned in both groups for 5 days postoperatively. The procedures were performed by the expert consultants (author No 1 and author No. 6).

Postoperative management

Patients of group A were maintained as nothing per os (NPO) for 5 days postoperatively. They were nourished *via* PICL with daily energy requirement provided by TPN. To maintain the efficacy and safety of the PICL, we used the three lumen one and every lumen was identified to a certain medication. Local wound care was performed using local antibiotic cream three times daily. Broad spectrum antibiotic (third generation cephalosporin 100 mg/kg/day intravenous) was administered for 3–5 days. Enteral intake was initiated on the 6th day postoperatively and gradually increased as tolerated by the infant. All infants were followed up every week for the next 6 months.

Patients of group B started oral intake as early as possible according to the protocols of enhanced recovery after colorectal surgery in the pediatric age group. They initiated oral intake on the 2nd postoperative day. These infants started

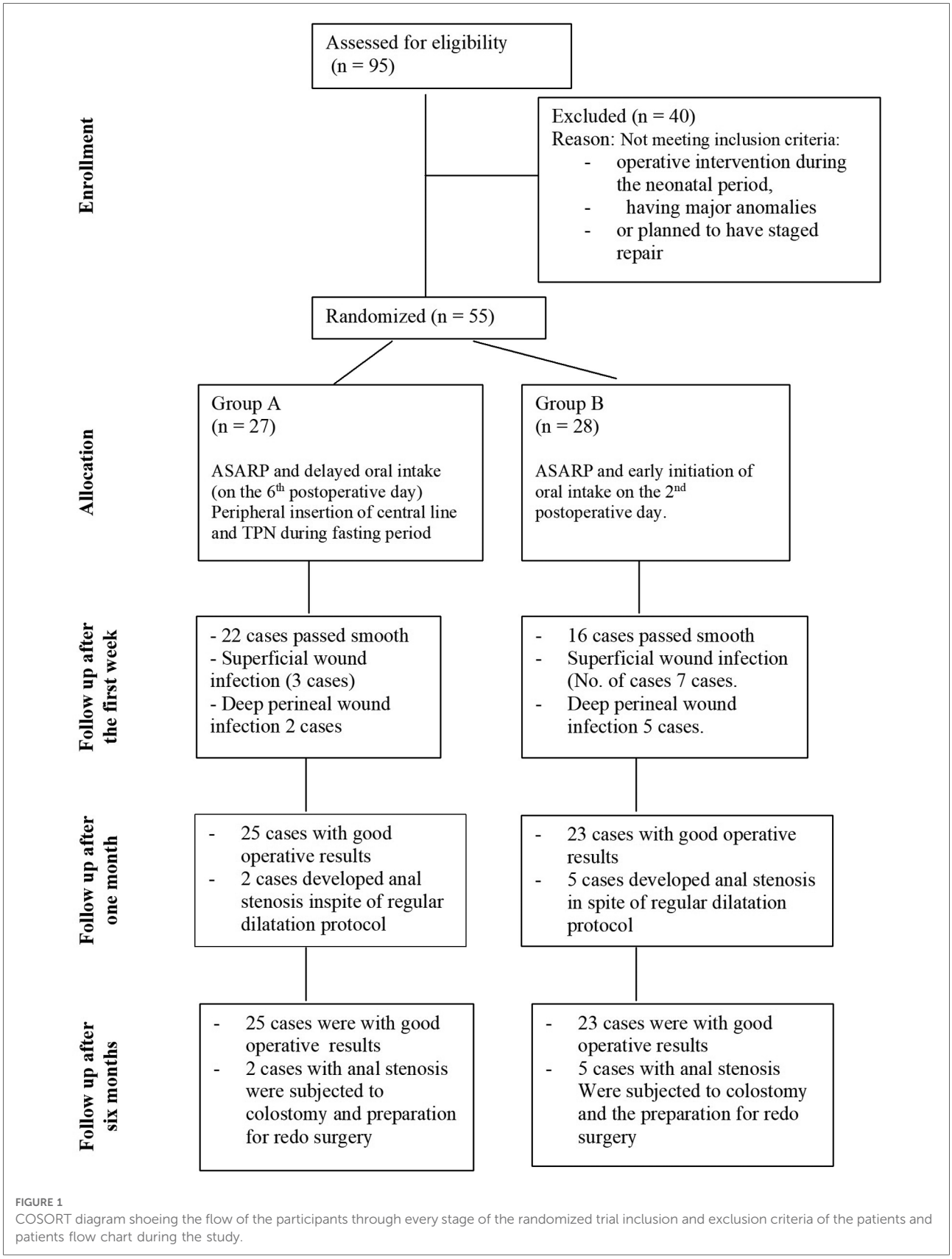

FIGURE 1
COSORT diagram shoeing the flow of the participants through every stage of the randomized trial inclusion and exclusion criteria of the patients and patients flow chart during the study.

feeding with breast feeding or formula in small amounts and frequent periods, then both the amounts and frequency of periods were increased as the infant tolerated. Local wound care and systemic antibiotics were the same as in group A. The patients were discharged on the sixth day postoperatively. They were followed up according to the same regimen of group A.

Outcome

The patients were followed up for the development of a PWI. Daily inspection of the wound was performed to detect the signs of PWI. These signs included redness, tenderness, discharge of pus, tender swelling in the wound line and wound dehiscence. The occurrence of some or all these signs in patients of group A or group B, oral intake was restricted and the patient. No complications related to PICL was reported in patients of group A.

Follow up

All our infants were followed up daily during the first week. The infants who developed PWI continued their treatment in the hospital. Then, there was a regular schedule of follow up every month till 6 months for all cases. We didn't have any cases missed follow-up schedule.

Statistical analysis

Statistical analysis was conducted using SPSS™ statistical package v. 21 (IBM SPSS, NY, USA). Numerical data were compared using an independent sample t-test, while categorical data were compared using the chi-square test. p-values < 0.05 were considered statistically significant. The epidemiologic and characteristic differences between the two study groups were analyzed using chi square.

An *a priori* power analysis was conducted using G*Power version 3.1.9.7 to determine the minimum sample size required to test the study hypothesis. Results indicated the required sample size to achieve 80% power for detecting a medium effect, at a significance criterion of $\alpha = 0.05$, was $N = 50$ for using independent t test and chi square to test the hypothesis.

Results

During the period of study, 95 females with recto-vestibular fistula were admitted for ASARP. Forty cases were excluded due to either having had operative intervention during the neonatal period, having major anomalies or having plans for staged repair. Fifty-five cases met our inclusion criteria.

Inclusion and exclusion criteria of the patients are presented in Figure 1.

Group A included 27 patients who had delayed initiation of oral intake for 5 days postoperatively. Group B included 28 patients who had started oral intake on the 2nd postoperative day and gradually increased in accordance with patient tolerance.

Preoperative and operative results

There were no significant differences between both groups regarding the mean age at operation (in months), the mean body weight (in kg), and the mean level of albumin (gm/dl) (Table 1).

Both groups were operated on using the ASARP approach. No significant differences were found with the regard to the mean operative time (Table 1).

Postoperative results

Oral intake was initiated in patients of group A on the sixth postoperative day (if there was no PWI) which was statistically significant when correlated to the early initiation of the oral intake in patients of group B.

Superficial wound infection (the infection was limited to the skin and subcutaneous tissue only) developed in three (11%) patients in group A while it developed in seven (25%) patients in group B (Figure 2).

Deep wound infection (the infection extended to the perineal muscles and sphincter with complete disruption of the wound) developed in two (7%) patients in group A while it occurred in five (17.8%) patients in group B and attained statistical significance (p value < 0.05) (Figure 3).

In both groups the onset of PWI occurred on the 3rd and 2nd postoperative day respectively, however, the incidence was

TABLE 1 Preoperative and operative data in both groups.

	Group A ($N = 27$)	Group B ($N = 28$)	p
Age (mean in months)	3.5 (±0.2)	3.7 (±0.4)	0.472
Weight at the operation (mean in kg)	11.3 (±1.3)	10.4 (±1.1)	0.352
Median size of Hegar dilator at the operation	14 (12–15)	13.5 (12–15)	0.463
Albumin level (mean in g/dl)	4.2 (±0.5)	4.3 (±0.4)	0.254
Operative time (mean in minutes)	90 (±15.3)	88 (13.4)	0.138

p value is significant if <0.05.

FIGURE 2
Superficial perineal wound infection.

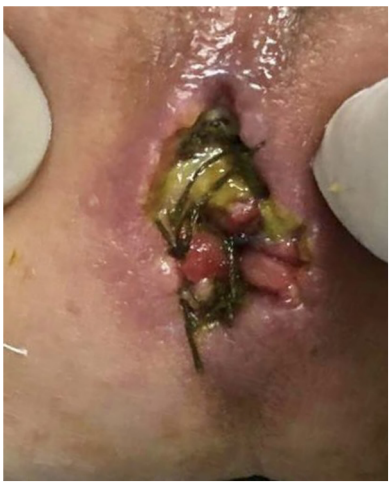

FIGURE 3
Deep perineal wound infection.

significantly lower in group A. Superficial wound infection responded to conservative measures such as stop oral intake, swaps for culture and sensitivity, and daily wound care twice using local antibiotics (Garamicin or Fusidine).

The same principles were followed during the management of deep PWI. In group A healing occurred by the eighth day (±2 days) while in group B two cases responded to the conservative measures and healed by the thirteenth day (±2.5 days). This was statistically significant where the p value was <0.05. Two cases in group A needed a covering colostomy versus five cases in group B to control PWI that did not respond to the conservative treatment.

During the management of post operative PWI, the mean level of serum albumin in complicated cases of group A was 3.9 gm/dl (±0.3) while it was 3.3 gm/dl (±0.5) in complicated cases of group B. This result was statistically significant (p value was <0.05). The mean levels of serum prealbumin in group A was 22 mg/dl (±5 mg/dl) and it was 18 mg/dl (±7 mg/dl) in group B. This was of statistical significance and the p value was <0.05 (**Table 2**).

Follow up

In group A regular dilatation with Hegar dilators for 3 months was performed. Two cases developed stenosis. In group B the same protocol was followed but for 5 months and 5 cases remained with stenosis despite the regular dilatation (**Table 3**).

Redo surgery was planned in two cases (Group A) versus five cases (Group B) (**Table 3**).

Discussion

PWI is a serious complication that causes several problems. Apart from affecting the sphincter mechanism and worsening the prognosis post repair of congenital recto-vestibular fistula, it also adds a psychological burden on the parents and increases the cost of hospitalization (8).

The actual incidence of PWI after surgical repair of a rectovaginal fistula is unclear. Several factors may have a direct impact on its development such as poor surgical technique, inadequate preoperative preparation, and improper postoperative care. Some patient factors such as nutritional status and the age of the patient at the time of operation might also contribute (9).

One of the major causes for the development of PWI is the continuous passage of stool over the wound during the early postoperative period. Even with meticulous cleaning and care of the wound, there may be some micro debris of faecal matter that sticks to the sutures and acts as a suitable media for the development of a wound infection.

To avoid this some paediatric surgeons, prefer to operate on females with recto-vestibular fistula during the early hours of an infant's life. The rationale behind this strategy is that the meconium is sterile, thus reducing the incidence of infection. However, this strategy carries the additional risk of early exposure to the anaesthesia and does not allow for proper pre-operative preparation and investigations to detect if other associated anomalies are present (10).

Some pediatric surgeons plan for regular dilatation of the fistula track to avoid ballooning of the rectum and the subsequent discrepancy between the diameter of the pulled through rectum and the future anal opening. This plan allows

TABLE 2 Postoperative data in both groups.

	Group A ($N = 27$)	Group B ($N = 28$)	p value
Superficial wound infection (No. of cases)	3 (11%)	7 (25%)	0.03*
Deep perineal wound infection	2 (7%)	5 (17.8%)	0.05*
Time of onset of PWI (mean in days ± SD)	3 ± 1	2 ± 1	0.347
Mean serum of albumin in complicated cases	3.9 gm/dl (±0.3)	3.3 gm/dl (±0.5)	0.05*
Mean serum of prealbumin in complicated	22 mg/dl (±5 mg)	18 mg/dl (±7 mg)	0.05*
Hospital stay in uncomplicated cases (mean in days)	7days (±1.2 days)	3 days (±1.1)	0.05*
Readmission to treat PWI (No. of cases)	2 cases (7%)	5 cases (17.8%)	0.03*
Mean hospital stay after readmission (days)	8 days	13 days (±2.5 days)	0.05*

PWI, perineal wound dehiscence and infection. p value is significant if <0.05.
*Significant.

TABLE 3 Long term follow-up in both groups.

	Group A ($N = 27$)	Group B ($N = 28$)	p value
Stenosis	2 (7%)	5 (17.8%)	0.05*
Colostomy	2 (7%)	5 case (17.8%)	0.05*
Mean duration of dilatation (months)	3 ± 0.5	5 ± 0.5	0.05*
Redo surgery	2 (7%)	5 cases (17.8%)	0.05*

p value is significant if <0.05.
*Significant.

for the proper assessment of the infant for further associated anomalies, avoids anesthesia-associated-troubles during the early hours of life, and promotes weight gain.

Optimum timing for the initiation of oral intake after ASARP of recto vestibular fistula remains a subject of debate. At present, most centers have their own policy regarding when to initiate the oral feeding. Few reports have discussed this issue either as a case series or in the form of prospective studies. The debate about whether long fasting or early oral intake may be associated with better wound healing is still unsettled (11, 12).

According to the available data, this study represents the first randomized control trial to assess the impact of time of initiation of oral intake in patients with recto-vestibular fistula after ASARP.

In group A, infants were supported by TPN (during the fasting period which lasted 5 days post operatively) supplied through the PICL with the aim of providing adequate calories to overcome the catabolic effect of fasting and surgical trauma and maintain their nutritional status at a proper level to promote healing. We called this procedure "TPN colostomy", as it helped reduce both the frequency and the volume of intestinal fluids passing over the perineal wound during the early postoperative days. Another advantage of TPN during the early postoperative period was maintaining normal serum levels of albumin, and prealbumin which are required for proper wound healing. The synthesis of these proteins may have been impaired in patients of group B due to inadequate enteral feeding because of pain or as a side effect of drugs in the gastrointestinal tract. There was a decrease in the serum levels of both albumin and prealbumin in patients who developed wound infection in group B. This result attained statistical significance in relation to group A.

The perineal wound was complicated either by superficial or by deep infection. Deep PWI leads to complete perineal dehiscence. PWI developed on the second postoperative day in both groups, with an incidence of 18% in group A and a significantly higher incidence of 42% in group B. This difference may reflect the effect of delayed initiation of oral intake.

The incidence of wound complications in infants in whom early oral intake was initiated ranged from 1% to 27%. Previous studies were either case series or retrospective studies and enrolled only patients that were continuously followed-up at the clinic, including those that were either with ASARP or posterior sagittal anorectoplasty. They also included patients who had colostomies and were operated on either in the neonatal period or in the early infancy. The inclusion of these variables may have been limitations to reach a proper conclusion about the optimal timing of initiation of oral intake (13–15).

The incidence of post operative wound complications reported in previous studies after prolonged fasting ranged from 0% to 22%. These infants were operated on in single stage operations. Moreover, the perioperative variables were not matched in all cases. During the fasting period, the infants were supplied with the daily requirement of fluid and electrolytes and not by TPN (16, 17).

The standards of enhanced recovery protocol after colorectal surgery in children are still evolving. These measures included insurance of early oral intake following

colorectal surgery. However, all studies were limited to an age ranging from 2 to 18 years (18).

The main advantage of early initiation of oral intake was the significantly shorter hospital stay seen in group B. However, this was offset by a significantly longer duration of hospital stay on readmission due to PWI in the early post operative period in group B.

In group A, duration of hospital stay was similar to that reported by Menon et al., but another study by Okada et al. reported 4 weeks hospital stay on average (10, 17).

In group B the mean duration of hospital stay was 3 days, which was similar to the duration reported by Upadhyaya et al. and Kulshrestha et al. They documented an average of 2 days in hospital with a range from 2 to 5 days (15, 19).

The sequalae of PWI can cause significant morbidity in infants. The first is healing of the wound by secondary intention and formation of excessive fibrosis that would affect the functioning of both the new anus and the sphincter complex. The new anus may become stenotic if frequent dilatation to overcome this tightness is not carried out. Retention with massive dilatation of the rectum might also develop, necessitating an anoplasty later in their lives. The fibrosis may also affect the sphincter control causing infants to experience a variable degree of soiling. Another complication of PWI is complete dehiscence of the wound with development of an intractable infection that may endanger the sphincter complex. This may result in the need for a colostomy to divert the stool away from the perineum to allow for infection control and healing.

According to our data, stenosis developed in two cases (7%) in group A versus five (17.8%) cases in group B. This result was statistically significant. Two cases in group A underwent colostomy to control infection, while five cases in group B required this type of intervention. The mean duration of dilatation required in group A was 3 months versus a mean of 5 months in group B. This reflected the need for more frequent dilatation in group B to overcome the stenosis after healing of PWI. Due to perineal wound dehiscence and the need of colostomy, two cases in group A required redo surgery versus five cases in group B.

Redo surgery was planned in 3.9%–5.7% in the case series reported by Wakhlu et al. and Kuijper et al. respectively. These were related to the early initiation of oral intake in these patients (13, 20).

On contrary, redo surgery was planned in 0%–2.4% in the series of Menon et al. and Kumar et al. respectively. These patients were managed on the basis of long postoperative fasting period (10, 21).

Limitations

The small sample size, and the lack of multicenter data are the main limitations. Therefore, a large-scale multicenter study with long-term follow-up is needed to substantiate our proposal.

Conclusion

Delayed post operative enteral feeding versus early postoperative enteral feeding after ASARP in females with congenital recto-vestibular fistula remains a debated issue. We concluded that delayed enteral feeding with nutritional support by TPN *via* a PICL keeps the perineal wound less contaminated with stool. This promoted proper and fast healing with lower incidence of PWI when compared with infants who were started on oral intake during the early postoperative period. TPN also compensates for the catabolic effect of the surgical trauma and fasting during the postoperative period and ensures the supply of essential nutrients that are necessary for proper healing.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The study was approved by the ethics committee of our institution and assigned code 35054/11/21. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

MGK and MK designed the study and operated the cases ME, AM assisted the operators and followed up cases HA, MB cared cases in the intensive care units, inserted the peripheral introduced central line MGK and MK performed the statistical analysis MGK edited the manuscript. MK revised the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Comparison of clinical features and prognosis between ultrashort-segment and short-segment hirschsprung disease

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Objective: To compare the differences in clinical features, postoperative complications, and long-term bowel function outcomes of ultrashort-segment Hirschsprung disease (USHD) and short-segment Hirschsprung disease (SHD).

Methods: A retrospective study was conducted to compare patients with USHD or SHD who underwent transanal endorectal pull-through (TEPT) at Beijing Children's Hospital between January 2014 and June 2021. Clinical details were collected from medical records. A long-term bowel function questionnaire (age > 4 years old) was completed by the patients' parents.

Results: A total of 84 patients (USHD = 15, SHD = 69) were included. Age at diagnosis and radical surgery in the USHD group were significantly older than the SHD group (46 [38, 66] vs. 34 [6, 55] months, $p = 0.002$; 51 [39, 68] vs. 37 [10, 68] months, $p = 0.001$, respectively). Compared with the SHD group, patients with USHD are more likely to suffer anastomosis leakage and postoperative enterocolitis after TEPT ([3/15, 33.3%] vs. [1/69, 1.4%], $p = 0.017$; [5/15, 33.3%] vs. [6/69, 8.7%], $p = 0.023$). In addition, patients in the USHD group are inclined to suffer lower bowel function scores (12.0 [7.5, 18.3] vs. 17 [15, 19], $p = 0.018$).Patients in the USHD group were more likely to suffer poorer ability to hold back defecation ($p = 0.023$), soiling ($p = 0.011$), fecal accidents ($p = 0.004$), and social problems ($p = 0.004$).

Conclusion: Compared with patients with SHD, patients with USHD are diagnosed and performed TEPT at an older age. and they are inclined to suffer postoperative enterocolitis, anastomosis leakage, and poorer long-term bowel function following TEPT.

KEYWORDS

ultrashort-segment hirschsprung disease, transanal endorectal pullthrough, complications, bowel function outcomes, clinical features

Highlights

- Compared with short-segment Hirschsprung disease (SHD), ultrashort-segment Hirschsprung disease (USHD) was diagnosed and performed radical surgery at an older age.

- USHD are inclined to suffer anastomosis leakage and enterocolitis after TEPT.
- USHD are inclined to suffer anastomosis leakage and enterocolitis after TEPT.

Introduction

Hirschsprung disease (HD), known as aganglionosis, is one of the most common congenital malformations, with an incidence of 1 in 5,000 live births (1, 2). More than 80% of HD patients had aganglionosis restricted to the rectum and sigmoid colon. However, there is minimal knowledge concerning ultrashort-segment HD (USHD), a rare variant of HD (3). So far, there has been no universally accepted definition for USHD. Some scholars considered USHD and internal anal sphincter achalasia (IASA) as the same entity, which could be alleviated by sphincter myotomy or botulinum toxin (4, 5). A recent study proposed that they were utterly different diseases (6, 7). IASA was characterized by normal ganglion cells in the rectal mucosal biopsy but the absence of nitrergic innervation or defective innervation of the neuromuscular junction, resulting in motility dysfunction. Anal sphincter myotomy or botulinum toxin might be the primary treatment (4, 7, 8). However, USHD, presenting as a suddenly dilated bowel without an obvious transition zone on barium enema, is characterized by aganglionosis extending proximal to the distal rectum, and transanal endorectal pull-through (TEPT) might be required (3, 7, 9). In our study, we chose the latter to define USHD.

In recent years, postoperative complications and long-term bowel function recovery of HD has become gradually attracted attention (10, 11). Previous studies had revealed the postoperative complications and long-term bowel function operated by Soave, Duhamel, or Swenson (12, 13). However, few studies were concerned about the treatment and prognosis of different types of HD, especially for patients with USHD. This study was designed to compare the differences in clinical features, postoperative complications, and long-term bowel function outcomes between USHD and SHD following TEPT, aiming to provide guidance for the diagnosis and treatment of USHD.

Materials and methods

Patient selection

Approved by the Ethics Committee of Beijing Children's Hospital, we reviewed the medical records of 84 consecutive patients with rectosigmoid HD who underwent primary TEPT at Beijing Children's Hospital, National Center for Children's Health, between January 2014 and June 2021. The operation was performed by either totally transanal performed TEPT (TTEPT) or laparoscopic/laparotomy-assisted TEPT (LTEPT). All patients underwent Soave TEPT without a stoma by the same surgeon team. Patients who underwent radical surgery in other hospitals or patients without a completely preoperative radiography examination were excluded. Rectal biopsies and postoperative histopathological examination verified the diagnosis of HD. Contrast enemas was used to estimate the extension of the aganglionosis segment in all patients.

Study design

Considering the significant imaging differences between USHD and SHD, the USHD was defined as presenting a suddenly dilated bowel without an obvious transition zone on preoperative barium enema based on the absence of ganglion cells 3–4 cm above the pectinate line by rectal mucosal biopsy. To distinguish the presence of a transitional zone, all preoperative radiographs of HD were independently and randomly reviewed by an experienced pediatric radiologist and two practiced doctors. For the disputed imaging results, these radiography examinations were reviewed again to detect the presence of a transitional zone. Rectosigmoid HD was divided into two groups according to whether a transition zone presented on barium enema: the USHD group was defined as presenting a suddenly dilated bowel without an obvious transition zone (**Figures 1A,B**), and the short-segment (SHD) group as aganglionosis extending proximal to the rectum and sigmoid with a transition zone (**Figures 1C,D**). A comparative study was performed to analyze the difference in clinical manifestations, postoperative complications, and long-term bowel function outcomes between the two groups.

Acquisition of data

The patient's characteristics and clinical details were recorded retrospectively from medical records, including gender, birth weight, gestational age, congenital malformations, age at diagnosis, presenting symptoms, surgical details, and postoperative complications.

Bowel function outcome was evaluated by a bowel function score (BFS) questionnaire established by 7-item scoring systems with a maximum score of 20 (**Table 1**). Patients' parents filled out all the questionnaires. The BFS was only assessed when the children were older than 4 years old. Patients were also inquired about the history of enterocolitis and other postoperative complications following TEPT. Enterocolitis was diagnosed when patients presented with clinical signs of bowel inflammation, such as abdominal distension, diarrhea, fever, or lethargy.

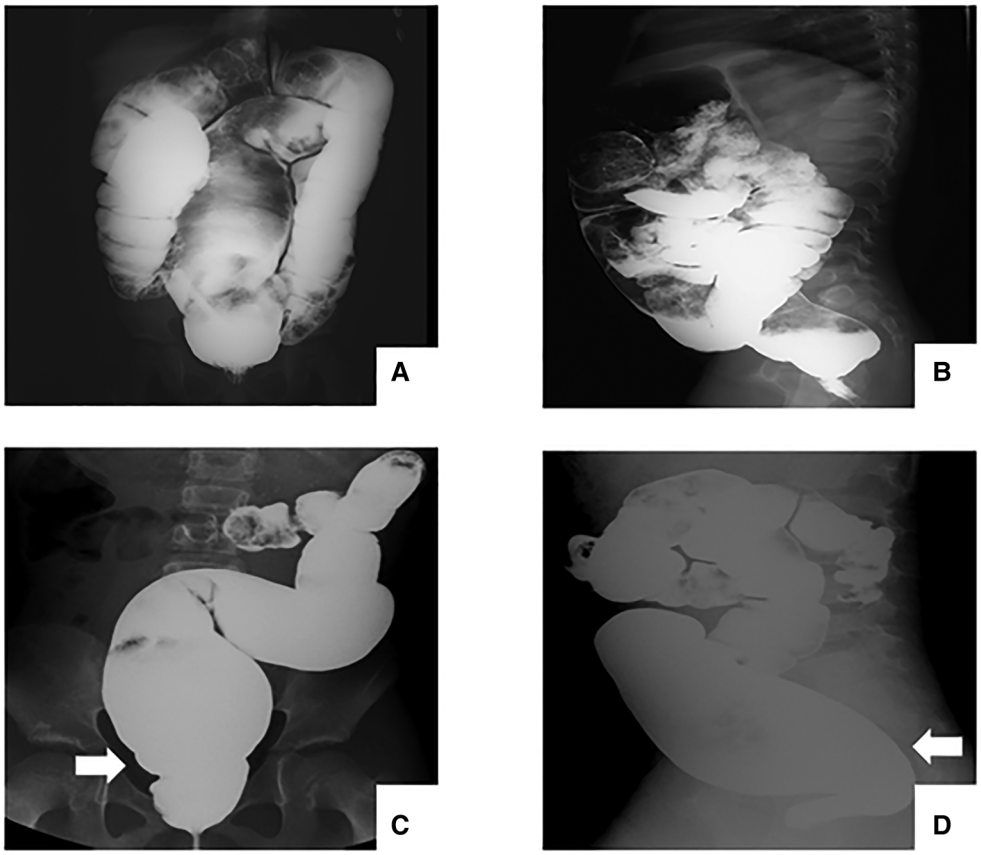

FIGURE 1
Radiography examination before TEPT. (A-B) patients with USHD shows a suddenly dilated bowel without an obvious transition zone. (C-D) patients with SHD shows a clear transition zone.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics for Statistics ver. 26.0 Software. Data were presented as frequency (percentage) for qualitative variables and median and interquartile range (IQR) for continuous variables. All the statistical tests were two-sided, with a significant level of $p < 0.05$. Continuous Chi-squared tests or Fisher's exact tests (Fisher's exact if >25% of cell have expected counts less than 5) were applied for categorical variables. Independent sample t-test or Mann-Whitney U test (Mann-Whitney if the data did not meet normal distribution) for continuous variables.

Results

Patient characteristics

A total of 84 patients were enrolled in our study, including 15 patients with USHD and 69 with SHD. The clinical manifestations of all patients before admission are presented in Figure 2. No significant difference was observed between the two groups. Abdominal pain, constipation, and delayed meconium were the predominant clinical manifestations.

The baseline characteristics of all patients are presented in Table 2. The age at diagnosing HD, age at radical surgery, and weight at radical surgery in the USHD group were significantly higher than in the SHD group, respectively (age at diagnosis, 46 [38, 66] vs. 34 [6, 55] months, $p = 0.002$; age at surgery, 51 [39, 68] vs. 37 [10, 68] months, $p = 0.001$; weight at surgery, 15 [14, 18] vs. 12 [9, 17] Kg, $p < 0.001$). The frequency of TTEPT or LTEPT was similar in both groups. However, there were significantly prolonged hospital days following TEPT in the USHD group despite no statistically significant differences in operation time, blood loss, oral intake time, and hospital days.

Postoperative complications

Table 3 shows postoperative complications between the two groups. All the patients were followed up for more than

TABLE 1 Bowel function score questionnaire (>4 years old).

Evaluation of bowel control	Score
Ability to hold back defecation, *n* (%)	
Always	3
Problems less than 1/week	2
Weekly problems	1
No voluntary control	0
Feels/reports the urge to defecate, *n* (%)	
Always	3
Most of the time	2
Uncertain	1
Absent	0
Frequency of defecation, *n* (%)	
Every other day to twice a day	2
More than	1
Less than	1
Soiling, *n* (%)	
Never	3
Staining < 1/week, no change of underwear required	2
Frequent staining, change of underwear often required	1
Daily soiling, requires protective aids	0
Fecal accidents, *n* (%)	
Never	3
Fewer 1/week	2
Weekly, requires protective aids	1
Daily, requires protective aid day and night	0
Constipation, *n* (%)	
No constipation	3
Manageable with diet	2
Manageable with laxatives	1
Manageable with enemas	0
Social problems, *n* (%)	
No social problems	3
Sometimes	2
Problems restricting social life	1
Severe social/psychosocial problems	0

one year with a median follow-up time of 5.3 years (4.9 [3.1, 6.4] vs. 5.4 [2.9, 6.9], $p = 0.691$). Postoperative complications included anastomotic leakage or stricture, postoperative enterocolitis, and residual transitional zone. Compared with the SHD group, anastomosis leakage after TEPT was more likely to occur in the USHD group ([3/15, 33.3%] vs. [1/69, 1.4%], $p = 0.017$). These patients with anastomosis leakage often presented fever, abdominal pain, abdominal distention, blood stool, and severe infection, and ileostomies and anastomotic resuturing were performed. In addition, the frequency of postoperative enterocolitis in the USHD group was significantly higher than in the SHD group ([5/15, 33.3%] vs. [6/69, 8.7%], $p = 0.023$). No significant difference in both groups was observed in terms of residual transitional zone.

Long-term bowel function outcomes

Table 4 presents the results of the BFS questionnaire completed by patients' parents. There was no statistically significant difference between the two groups in terms of follow-up age (8.7 [7.3, 11.9] vs. 7.8 [5.9, 9.4] years, $p = 0.119$). As shown in Figure 3, the median total bowel function score in the USHD group was significantly lower than the SHD group (12.0 [7.5, 18.3] vs. 17 [15, 19], $p = 0.018$). Besides, the percentage of poorer bowel function in the USHD group was significantly higher than SHD group ($p = 0.01$). Further, compared with the SHD group, we found that patients in the USHD group were more likely to suffer poorer ability to hold back defecation ($p = 0.023$), daily soiling ($p = 0.011$), fecal accidents ($p = 0.004$), and social problems ($p = 0.004$). There was no statistically significant difference between the two groups regarding feeling the urge to defecate, frequency of defecation, and constipation.

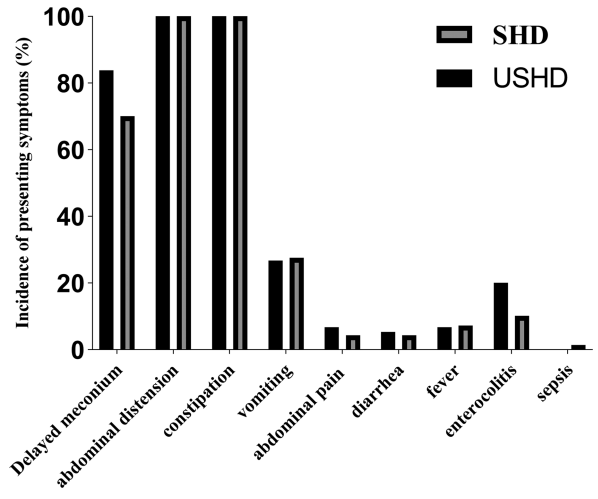

FIGURE 2
Difference in clinical mainfestaions between USHD and SHD group before admission.

TABLE 2 Patient characteristics.

Characteristics	USHD ($n = 15$)	SHD ($n = 69$)	p-Value
Sex			
Male	15 (100)	57 (82.6)	0.113
Female	0 (0.0)	12 (17.4)	
Gestational age			
Preterm (<37 weeks)	2 (13.3)	3 (4.3)	0.216
Term (>37 weeks)	13 (86.7)	66 (95.7)	
Birthweight in kilograms, mean (SD)	3.40 ± 0.54	3.25 ± 0.48	0.274
Congenital malformation			
Yes	1 (6.7)	4 (5.8)	>0.999
No	14 (93.3)	65 (94.2)	
Age at diagnosis, months	46 [38, 66]	34 [6, 55]	0.002
Age at radical surgery, months	51 [39, 68]	37 [10, 68]	0.001
Weight at radical surgery, kilogram	15 [14, 18]	12 [9, 17]	<0.001
Surgical approach			
Transanal only	12 (80.0)	51 (73.9)	0.374
Open surgery + transanal	1 (6.7)	13 (18.8)	
Laparoscopic + transanal	2 (13.3)	5 (7.2)	
Operation time, min	130 [98, 240]	108 [80, 154]	0.170
Blood loss, ml	2 [2, 10]	5 [2, 5]	0.929
Oral intake time, days	3 [3, 5]	3 [3, 4]	0.142
Hospital stays in days	12 [9, 15]	14 [9, 20]	0.337
Total length of hospital stays after surgery, days	11 [7, 15]	8 [7, 10]	0.015

Data are presented as median [IQR, interquartile range] and frequency (%).

Discussion

This is the first single-center retrospective study to show that patients with USHD were diagnosed and performed

TABLE 3 Postoperative complications.

	USHD ($n = 15$)	SHD ($n = 69$)	p-Value
Mean follow-up time, years	4.6 [3.1, 6.4]	5.4 [2.9, 6.9]	0.691
Anastomosis leakage, n (%)	3 (20.0)	1 (1.4)	0.017
Enterocolitis, n (%)	5 (33.3)	6 (8.7)	0.023
Residual transitional zone, n (%)	0 (0.0)	1 (1.4)	>0.999

Data are presented as median [IQR, interquartile range] and frequency (%).

TABLE 4 Bowel function score (>4 years old).

Evaluation of bowel control	Score	USHD[a] ($n = 14$)	SHD[b] ($n = 52$)	p-Value
Mean follow-up age, years		8.7 [7.3, 11.7]	7.8 [5.9, 9.4]	0.119
Ability to hold back defecation, n (%)				
Always	3	5 (35.7)	31 (59.6)	0.023
Problems less than 1/week	2	1 (7.1)	12 (23.1)	
Weekly problems	1	3 (21.4)	4 (7.7)	
No voluntary control	0	5 (35.7)	5 (9.6)	
Feels/reports the urge to defecate, n (%)				
Always	3	5 (35.7)	28 (52.8)	0.089
Most of the time	2	3 (21.4)	16 (30.2)	
Uncertain	1	2 (14.3)	6 (11.3)	
Absent	0	4 (28.6)	3 (5.7)	
Frequency of defecation, n (%)				
Every other day to twice a day	2	10 (71.4)	34 (65.4)	>0.999
More than	1	3 (21.4)	14 (26.9)	
Less than	1	1 (7.1)	4 (7.7)	
Soiling, n (%)				
Never	3	2 (14.3)	17 (32.7)	0.011
Staining < 1/week, no change of underwear required	2	3 (21.4)	17 (32.7)	
Frequent staining, change of underwear often required	1	3 (21.4)	15 (28.8)	
Daily soiling, requires protective aids	0	6 (42.9)	3 (5.8)	
Fecal accidents, n (%)				
Never	3	5 (35.7)	39 (75.0)	0.004
Fewer 1/week	2	1 (7.1)	7 (13.5)	
Weekly, requires protective aids	1	6 (42.9)	4 (7.7)	
Daily, requires protective aid day and night	0	2 (14.3)	2 (3.8)	
Constipation, n (%)				
No constipation	3	11 (78.6)	44 (84.6)	0.053
Manageable with diet	2	0 (0.0)	6 (11.5)	

(*continued*)

TABLE 4 Continued

Evaluation of bowel control	Score	USHD[a] ($n = 14$)	SHD[b] ($n = 52$)	p-Value
Manageable with laxatives	1	3 (21.4)	2 (3.8)	
Manageable with enemas	0	0 (0.0)	0 (0.0)	
Social problems, *n* (%)				
No social problems	3	8 (57.1)	44 (84.6)	0.004
Sometimes	2	5 (35.7)	3 (5.8)	
Problems restricting social life	1	0 (0.0)	3 (9.6)	
Severe social/ psychosocial problems	0	1 (7.1)	0 (0.0)	
Total BFS, *n* (%)				
Good bowel function	≥17	5 (35.7)	30 (57.7)	0.010
Moderate bowel function	12–16	2 (14.3)	16 (30.8)	
Poor bowel function	<12	7 (50.0)	6 (11.5)	

Data are presented as median [IQR, interquartile range] and frequency (%).
[a]USHD: one patient was excluded due to the loss of follow-up (1/15, 6.7%).
[b]SHD: seventeen patients were excluded due to the loss of follow-up (11/69, 15.9%) and less than 4 years old at follow-up (6/69, 8.7%).

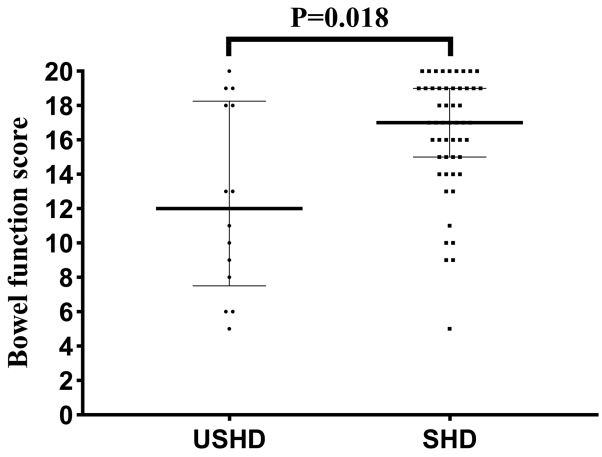

FIGURE 3
BFS for each patient in the USHD group and the SHD group.

TEPT at an older age, mainly related to non-specific symptoms. We have also shown that anastomosis leakage and postoperative enterocolitis are more likely to occur in the USHD group rather than SHD group after TEPT. In addition, our results suggest that compared with SHD, a higher proportion of patients with USHD may be predisposed to suffering long-term bowel functional defects.

Our study found that the age at diagnosis and radical surgery in both groups was significantly higher than in previous literature reports (14, 15). It might be related to the fact that most patients with HD in our study did not initially develop serious clinical symptoms, and most of them improved after conservative treatments (glycerine enema, polyethylene glycol, et al.) at local hospitals. Most of them would not be transferred to our center for radical surgery until presenting more severe symptoms. Moreover, the age at diagnosing HD and performing radical surgery in the USHD group was significantly older than in the SHD group. This condition was mainly due to the fact that patients with shorter-segment aganglionosis were more likely to relieve the obstructive symptoms by conservation treatment (3, 9, 16). However, the older age at performing radical surgery was an important factor for more severe dilated colon, leading to a higher frequency of early postoperative complications, which could also explain prolonged hospitalization following TEPT in the USHD group (17, 18).

Regarding postoperative complications, the most striking difference in terms of short-term postoperative complications between the USHD group and the SHD group was the incidence of anastomotic leakage. The frequency of anastomosis leakage in the USHD group (20%) was significantly higher than in the SHD group (1.4%). A plausible explanation for this phenomenon might be related to problems of a severely dilated distal rectum (17, 19). It could significantly contribute to the difficulty in dissection during the dissociation above the dentate line and hemodynamic disorder in the distal bowel, leading to a high incidence of anastomosis leakage (17, 20, 21). Some studies even recommended a preoperative stroma to decompress the distal colon to prevent anastomosis leakage (17, 18). Unlike previous studies, our study did not observe anastomotic stricture following TEPT, which might be related to regular anal dilatation two weeks after radical surgery (22, 23). Enterocolitis is the most common postoperative complication. The incidence of postoperative enterocolitis ranged from 10% to 44% based on heterogeneity in case definitions and geographical differences (24–26). However, the incidence of postoperative HAEC in the USHD group (33.3%) was significantly higher than in the SHD group (8.7%). A possible explanation was related to the higher preoperative enterocolitis frequency in the USHD group (26.7% vs. 13.0%) (15, 26). Preoperative enterocolitis episodes could change the gut microbial system, making patients susceptible to the development of further episodes of enterocolitis (27, 28).

Compared with the SHD group, the patients in the USHD group were inclined to suffer lower bowel function scores, and the percentage of poor bowel function in the USHD group (50%) was significantly higher than in the SHD group (11.5%). After careful analysis of the bowel function of these patients with low scores, we found that fecal incontinence was the main reason for poorer bowel function outcomes. Fecal incontinence, which refers to the poor ability to hold back

defecation, daily soiling, and fecal accidents, is the most common problem following pull-through, predisposing children to impaired social functioning and emotional psychosocial well-being (11, 29, 30). The reason could explain the high frequency of fecal incontinence that more prolonged and extensive anal dilatation was required due to a severely dilated bowel below the peritoneal reflection, resulting in excessive stretching of the sphincter during TEPT (29, 31–33). To minimize the damage to the anal sphincter, some studies also advocated LTEPT as the primary treatment for HD rather than TTEPT (11, 29, 33). A previous study found internal anal sphincter defects occurred more often following TEPT by endosonography (32). However, recent studies did not find a significant difference in long-term bowel function outcomes between the two surgical approaches (34,35). In our study, three patients in the USHD group who underwent laparoscopic/laparotomic-assisted TEPT did not achieve good long-term bowel function. The reason was that the dissection of the severely dilated distal rectum was equally tricky whether choosing LTEPT or TTEPT.

It was the first study to identify that USHD was prone to suffering anastomosis leakage, postoperative enterocolitis, and poorer long-term bowel function outcomes than SHD. In addition, all the TEPT procedures were performed by the same surgeon, avoiding deviation due to the discrepancy in surgical details. However, this study has some limitations. First and foremost, there is no universally accepted definition for USHD. In our study, the USHD was defined as s presenting a suddenly dilated bowel without an obvious transition zone without transitional zone on preoperative barium enema based on the absence of ganglion cells of the distal rectum by rectal mucosal biopsy and postoperative histopathology examination. Second, a small number of cases of the USHD group might lead to a potential selection bias. Third, this study was retrospective in nature and included patients treated at a single center, leading to a particular deviation. Last but not least, despite a dropout of 16.7%, it remained unknown whether their bowel function result differed in those who completed and those who did not.

Conclusion

In conclusion, our study suggests that compared with SHD, USHD presenting as a suddenly dilated bowel without an obvious transition zone on barium enema has a greater delay in the age of diagnosis and radical surgery. After TEPT, USHD is more likely to suffer anastomosis leakage, enterocolitis, and poor long-term bowel function outcome, which was related to the problem of a severely distal dilated rectum. For USHD, it is a therapeutic challenge for pediatric surgeons to enhance earlier diagnosis rates and improve long-term bowel function following TEPT.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by 2021-E-132-R. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

All authors read and confirmed the final manuscript. CPX and JYY participated the data collections, data analysis, and drafting the article; CPX and GJL contributed to the data collections; YKL contributed to revising the article. YJC was the major surgeon who conducted the surgery and contributed to reviewing and drafting the article. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Testing the circulation of expanded flaps—prevention of necrosis of expanded flaps (a clinic study)

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Background: Expanded flaps are commonly used in plastic surgery. Although expanded flaps are more resistant to hypoxia than unexpanded flaps, flap necrosis can sometimes occur, particularly with skin incisions of regular proportion. Distal skin necrosis of the expansion flap can be avoided by careful design; however, the utilization rate of the expansion flap decreases. Consequently, successfully avoiding distal skin flap necrosis remains a challenge. In this study, we designed a device for testing the circulation of the expanded flap that can decrease the risk of expanded flap necrosis, thus maximizing the use of an expanded flap.
Methods: A total of 128 patients who underwent surgical repair between 2011 and 2019 and were retrospectively examined with the device for testing the circulation of the expanded flap were included in the study. The procedure included (1) making a device for testing the circulation, (2) implanting a skin expander, (3) injecting normal saline into the skin expander, (4) testing the circulation of the expanded flap, and (5) transferring the expanded flap to repair the defect.
Results: One hundred forty-eight expanded flaps were implanted in 128 patients. The expanded flap that was transferred to repair the defect had no necrosis or infection. None of the expanded flaps with separated blood supply, which could be observed during operations, revealed complications. The survival rates of the expanded flap were increased by testing the circulation of the expanded flap. Expanded flaps designed by this method showed no swelling or paleness and no obvious temperature changes. In addition, the length-to-width ratio could be extended to 3:1.
Conclusions: Our proposed method resulted in an effective surgical procedure for the repair of tissue defects. This approach could effectively change the direction of the blood vessel of the expanded skin flap and prevent necrosis of the expanded flap, thus representing a practical way to increase the use of expanded flaps and the flap survival rate, making the whole expanded flap transfer procedure more convenient.

KEYWORDS

testing the circulation, expanded flap, flap necrosis, children, blood supply

Introduction

Conventional skin reconstruction methods contain skin grafts and transfer of skin flaps. Skin grafts can produce an inconsistent skin change color, while the transfer of skin flaps can produce necrosis of transferred skin flaps. Filatov wrote the first paper on tubed pedicle formation in 1917. The method provided a technology for neovascularization and skin reconstruction. However, there was extensive scarring in the tubed region.

Tissue expansion is a technology of skin reconstruction. In 1984, Mander et al. (1) reported the expansion of adjacent tissue for scar resurfacing. Its advantage was repairing skin defects with neighboring skin, which was similar in color and texture and could avoid secondary damage to the donor site. Yet, in some cases, the utilization rate of the expanded skin flap is not high, along with flap necrosis. Namd found that flap necrosis easily occurs, and the width

of the expander must be twofold larger than that of the defect. Necrosis of the skin flap was also reported in other papers (2, 3).

We have noted that partial flap necrosis still occurs in our practice (**Figure 1**). Flap necrosis is extremely undesirable for patients, particularly on the face and limbs. Many surgeons would prefer to choose conventional graft skin rather than resolve these issues. It was also reported that surgical delay could prevent flap necrosis, which has been proven reliable for increasing the vascularity of a random flap (4). Thus, the main problems we have to solve are increasing the blood supply and maximizing the usage of the expanded flap.

Testing the circulation is an old technology of training skin blood flow for tube flap. In this study, we designed a device for testing the circulation of the expanded flap that can decrease the risk of expanded flap necrosis, thus maximizing the use of an expanded flap.

Patients and methods

Patients

A total of 128 patients who underwent surgical repair between 2011 and 2019 were retrospectively examined with a testing circulation device. There were 66 men and 62 women patients, with an average age of 38 months. There were 88 cases with scars, 22 cases associated with a congenital giant nevus, and 18 cases of body surface tumors (neurofibroma, hemangioma, fibromatosis, melanoma). One hundred forty-eight expanded flaps were implanted in 128 patients. Evaluation results were recorded.

Device for testing the circulation

The device for testing the circulation consisted of a tourniquet and a bridge of vascular pedicle pass. The tourniquet was made of a general rubber strip. The bridge was made of a plastic plate and covered the vascular pedicle. The vascular pedicle pass was made into the corresponding size according to the bridge's height (**Figures 2**, **3**).

Operation technique and testing the circulation of the expanded flap

All patients with implanted expanders underwent surgical repair followed by standard general anesthesia and received one dose of intravenous antibiotic coverage half an hour before the procedure.

Expander implantation

The incision was carefully performed at the edge of the defect, with the expander package forming below the superficial fascia. The size of the expander ranged from 100 to 400 ml. The expander package was at least 1–2 cm larger than the expander in each dimension. The tissue expander was implanted into the prepared package, while the filling port was placed in a performed cavity with no potential pressure next to the expander site. In all cases, we only used remote internal filling ports and base tissue expander and made sure to smoothen the connection between filling ports and expander. After the insertion of the expander, the package was closed with three layers of sutures. The inner layer was sutured by a 4-0 absorbable stitch, while subcutaneous tissue was sutured by a 6-0 absorbable stitch. A 7-0 nylon stitch was used to suture the skin. We did not place any drainage in any expander package.

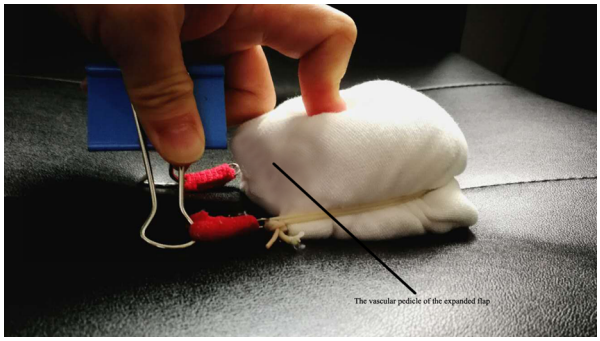

FIGURE 2
Device for testing the circulation of the expanded flap.

FIGURE 1
Necrosis of the flap tip.

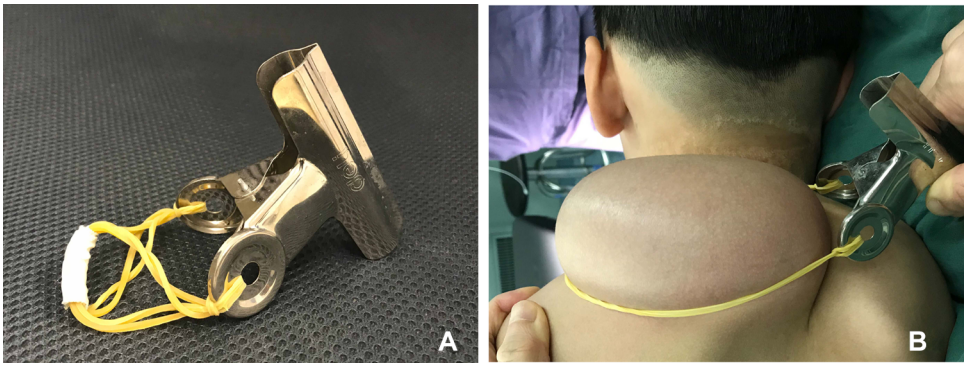

FIGURE 3
Testing the circulation of the expanded flap. (A) Device for testing the circulation. (B) Testing the circulation of the expanded flap.

Expander inflation

The expander inflation process started on the seventh day after surgery. Saline was injected every 3 days, and the final volume of injection was decided based on the size of the expander. The injecting volume each time was 5%–10% of the designed volume of the expander. The skin color was carefully observed, capillaries were refilled, and expander palpation was performed before and after injection.

Testing the circulation of the expanded flap

The patients were ready to undergo testing of the circulation of the expanded flap 1 month after the expansion was completed. First, the rubber strip was clamped to block the blood supply for 10 min. If there was no color change of the expanded flap skin, the clamping time could gradually be extended, and the clamping could be performed 4–6 times daily. Finally, when the clamping time could last 8 h and the expanded flap's skin showed no swelling or paleness and no obvious temperature change, the promotion of blood circulation was considered successful, and the expanded flap was ready for repair surgery (Figure 4). To facilitate patients to finish circulation testing by themselves, online video tutorials were performed during postoperative follow-up.

Design and rotation of the expanded flap

According to the newly reformed circulation by our technique and defect shape, we designed the shape of the rotation flap. A skin incision was made along the designed line, and the length-to-width ratio was 3:1 (Figure 5).

Results

One hundred forty-eight expanders were implanted in 128 patients. No hematoma, no expander exposure, and no infection were reported. All expended flaps were randomly rotated without any necrosis. There were two cases of distal skin cyanosis, which eventually improved and finally healed after repeated wound dressing changes. There was no obvious scarring in any of the cases after repair surgery.

FIGURE 4
Expanded flap being ready for repair surgery.

Case 1

The patient was a 5-year-old boy with a 15 × 30 cm congenital nevus on his left upper limb. He was implanted with one reniform-shaped tissue expander (200 ml) between the subcutaneous tissue and fascia below the nevus. Then, 20 ml of normal saline was injected into each expander every 3 days until it was inflated to 400 ml in volume over 2 months (Figure 6A). We started testing the circulation of the expended flap from 10 min to 1 h for the first 2 days and extended the duration to 2 h from the fourth day onward. The clamping was performed 4–6 times each day. Finally, when the clamping time was more than 8 h, we transferred the expanded flap to repair the defect after the nevus was removed, and the flap survived without necrosis (Figure 6B–D).

Case 2

A 6-year-old girl presented with a scar on the right shoulder she had since birth. A 400-ml reniform-shaped

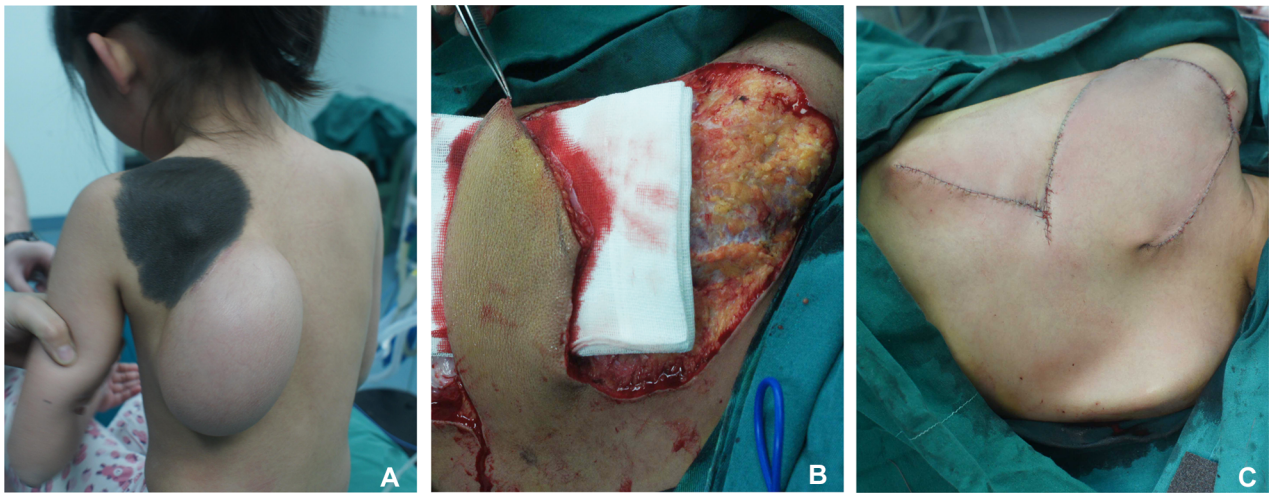

FIGURE 5
Skin incision was made along the designed line on the expanded flap, and length-to-width ratio of the flap was 1:3. (A) Preoperative appearance. (B) Length-to-width ratio of the flap was 3:1. (C) Immediate postoperative appearance.

FIGURE 6
Case 1. (A) Upper limb moles. (B) Preoperative appearance of the expanded flap. (C) Flap resection during operation. (D) Postoperative appearance at follow-up.

tissue expander was implanted between the subcutaneous tissue and the superficial muscular aponeurotic system in the shoulder. The expender was serially inflated with saline to 800 ml in volume over 3 months. We started testing the circulation of the expended flap following our protocol and rotated the flap to repair the defect after the vascular malformation was removed. The flap was not affected by necrosis (**Figure 7**).

Case 3

A 3-year-old girl who presented with an 18 × 22 cm scar on her left lower limb was referred to our center. A reniform-shaped tissue expander (200 ml) was implanted between the subcutaneous tissue and fascia above the scar, while another expander was implanted below the scar. We inflated the expander to 400 ml over 3 months and performed testing of the circulation of the expanded flap

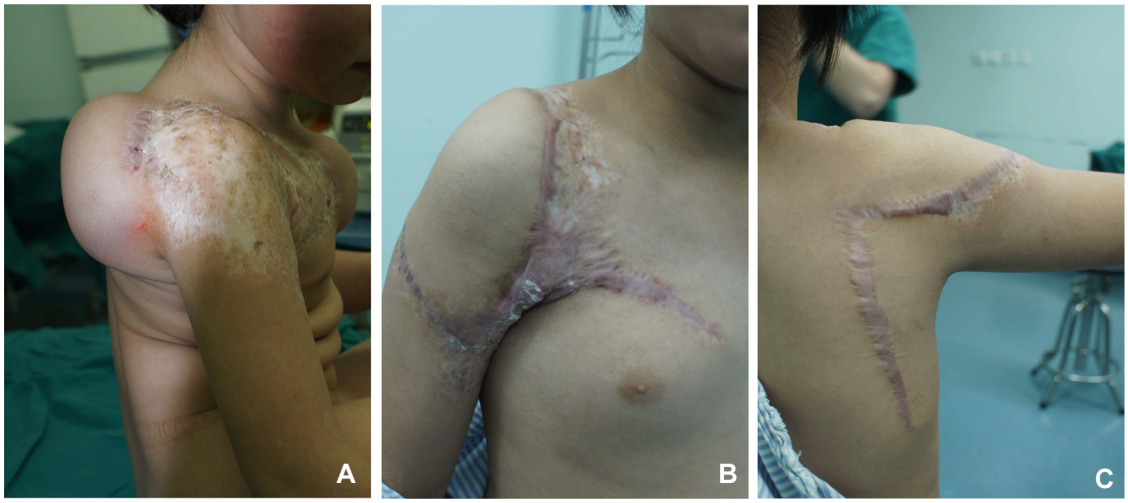

FIGURE 7
Case 2. (A) Preoperative appearance of the expanded flap. (B) Anterior view at postoperative follow-up. (C) Posterior view at postoperative follow-up.

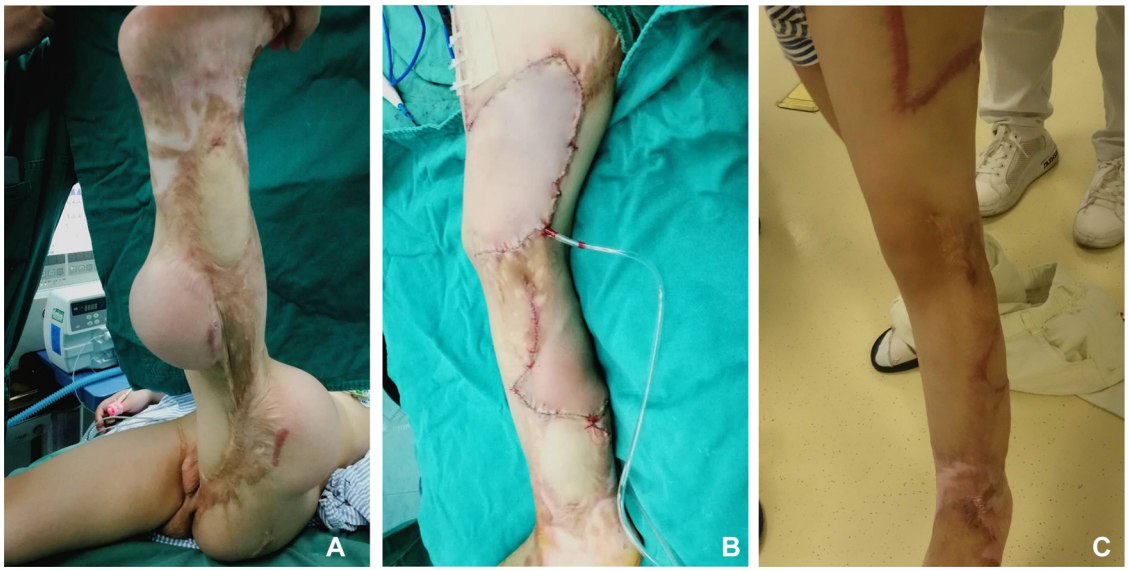

FIGURE 8
Case 3. (A) Preoperative appearance of the expanded flap. (B) Immediate postoperative appearance. (C) Postoperative appearance at follow-up.

following our protocol (**Figure 8A**). The flap was randomly rotated to repair the defect with a good outcome (**Figure 8B,C**).

Discussion

Skin soft-tissue expansion first began in 1976, and over a period of 40 years, it has become widely used in various fields of plastic surgery. It has become one of the basic plastic technologies highly used for tissue repair, skin grafting, and skin flap transfer (5).

Skin soft-tissue expansion is a method that involves implanting the expander under normal skin and soft tissue and increasing the pressure on local skin by inflating the expender in volume, thus creating the new "extra" skin and transferring it to repair the defect. Skin soft-tissue expansion is widely used in repairing skin or soft tissue defects induced by various causes, such as incision of congenital giant nevus, scars, tumors, and skin defects after trauma. Following the wide application of expanders, numerous studies have reported an increasing number of expanded skin flap uses (6–8). However, the use of a flap has also been associated with some complications such as necrosis, infection, and hematoma. Hu et al. (9) suggested that the necrosis of the expanded flap was related to its length-to-width ratio and the presence or absence of well-known arteries. Moreover, Chen and colleagues (10) argued that changing the blood flow of the expanded flap could prevent the necrosis of the flap. Therefore,

increasing the blood supply, maximizing the usage of the expanded flap, and preventing necrosis after flap rotation surgery are challenging issues that our proposed method can successfully overcome.

By testing the circulation of the expanded flap, we can change the vascular distribution of the skin and achieve blood vessel axial development. Applying this kind of skin flap can exceed the normal ratio (11, 12) and evaluate vascular redistribution (13). Yet, Hainan et al. (14) reported on using prefabricated expanded skin flaps, revealing a significantly lower rate of necrosis after flap rotation surgery. This provided a new approach for preventing the expended flap from necrosis; however, further research on axial pattern skin flaps is still urgently needed. With vascular transformation emerging in the tube flap through surgery or blood supply training, we can get similar outcomes to the tube flap if we perform blood supply training on the expended skin flap using the principle of the tube flap. Our research showed that vascular transformation occurs in an expended flap after long-term blood supply training with our testing circulation device. The direction of a blood vessel on the expended flap can change as the designed position of the vascular pedicle pass. We could design flap transfer in the way of an axial pattern skin flap, which in turn could increase the use of expanded flaps and the flap survival rate, making flap transfer surgery more convenient. In our experience, if there is no necrosis as the elasticity of the tourniquet increases to the maximum for 6 to 8 h, the expended flap will survive without necrosis after flap transfer surgery. Future experimental research is needed to further verify whether the elasticity of the tourniquet may block the blood supply of the expended flap.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Children's Hospital of Nanjing Medical University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

Author contributions

WS: reviewed and revised the manuscript. JC and HC: performed the surgery and conducted data analysis. JC: performed postoperative follow-up. TH: wrote a draft of the article and edited the figures. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Single-site laparoscopic ligation of the hernia sac in infants with congenital Morgagni hernia

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Background: Congenital Morgagni hernia (CMH) is a rare midline defect involving herniation of abdominal viscera into the thoracic cavity through triangular parasternal gaps in the diaphragm.
Methods: The medical records of three patients with CMH admitted to the Department of Pediatric Surgery at the Affiliated Hospital of Zunyi Medical University between 2018 and 2022 were retrospectively reviewed. Pre-operative diagnosis was based on chest x-ray, chest computerized tomography, and barium enema. All patients were treated with single-site laparoscopic ligation of the hernia sac.
Results: Hernia repair was successful in all patients (males; age: 14 months, 30 months, 48 months). The average operative time for repair of a unilateral hernia was 20 ± 5 min. Volume of surgical blood loss was 2–3 ml. There was no damage to organs such as the liver or intestines, or to tissues such as the pericardium or the phrenic nerve. Patients were allowed a fluid diet 6–8 h after surgery, and remained on bed rest until 16 h after surgery. No postoperative complications occurred, and patients were discharged on postoperative Day 2 or 3. No symptoms or complications were noted during the 1–48 months of follow-up. Aesthetic outcomes were satisfactory.
Conclusions: Single-site laparoscopic ligation of the hernia sac provides pediatric surgeons a safe and effective technique for repair of CMH in infants and children. The procedure is straightforward, operative time and surgical blood loss are minimal, recurrence is unlikely, and aesthetic outcomes are satisfactory.

KEYWORDS
congenital morgagni hernia, hernia sac high ligation, infants, single site laparoscopic, CMH

Background

Congenital Morgagni hernia (CMH), also known as Morgagni-Larrey hernia, is a rare midline defect involving herniation of abdominal viscera into the thoracic cavity through triangular parasternal gaps in the diaphragm. CMH, first described by Morgagni in 1761 (1), comprises 3%–5% of all types of congenital diaphragmatic herniae (2) and occurs in 1 in 4,800 live births (3). The etiology of CMH is multifactorial (4), and may include environmental exposures, genetic factors, malnutrition, Down syndrome and congenital heart disease (5) (6). CMH has no typical clinical symptoms and may be misdiagnosed. In some cases, CMH may present with respiratory and gastrointestinal symptoms, including acute respiratory distress in infancy (7) and acute or chronic intestinal obstruction, or intestinal perforation in adults. Surgical repair is the only treatment for

Abbreviations
CMH, congenital Morgagni hernia; CT, chest computerized tomography; MRI, magnetic resonance imaging.

CMH. Traditional approaches comprise laparotomy and open thoracic surgery (8). More recently, minimally invasive repairs of CMH in infants and children have used endoscopic and laparoscopic techniques (9), including the use of "U"-shaped stitches that transverse the abdominal wall, hernia sac, and the posterior rim of the diaphragmatic defect, and are secured in the subcutaneous tissue (10). Here, we describe a novel approach to the treatment of CMH, and describe our clinical experience in three cases that had satisfactory outcomes.

Methods

The medical records of three patients with CMH admitted to the Department of Pediatric Surgery at the Affiliated Hospital of Zunyi Medical University between 2018 and 2022 were retrospectively reviewed. The patients were three males aged 14 months, 30 months, and 48 months. One patient presented with clinical symptoms of recurrent upper respiratory tract infection. One case was discovered incidentally when the patient was being treated for car accident injury. One case was discovered incidentally during investigations for chest deformity. Preoperatively, routine blood tests were normal in all patients. Routine chest x-rays were normal in two patients and showed increased density in the left lung field and a left sided pericardial mediastinal shadow in one patient (**Figure 1A**). In this patient, chest computerized tomography (CT) showed a bowel loop projecting into the anterior mediastinum, part of the left lobe of the liver and the colon projecting into the thoracic cavity, and cardiac compression (**Figures 1B,C**), and barium enema showed that a loop of the transverse colon was behind the sternum (**Figure 1D**). Angiography for upper gastrointestinal bleeding was negative and cardiac color ultrasound showed no abnormalities in all patients. The preoperative diagnosis was CMH. One patient had mild pectus carinatum that did not require surgical correction. The other two patients had no comorbidities. All patients were treated with single-site laparoscopic ligation of the hernia sac. Informed consent for the surgery was obtained from the parents of each infant.This study was approved by the ethics committee of our hospital.

General endotracheal anesthesia was administered with the patient in the supine position. A 0.5 cm incision was made at the left and right edge of the umbilicus. A 0.5 cm trocar was placed through the incision, and the abdominal pressure was adjusted to 7–8 mmHg. A left trocar was placed in the incision as an observation hole, followed by insertion of a 30°lenses. A right trocar was used as the operating hole (**Figure 2A**). A U-shaped defect was found in all patients. This was confirmed as CMH, consistent with the preoperative diagnosis. One patient had a left-sided CMH, with the transverse colon and greater omentum forming the contents of the hernia sac. There was a 4 cm × 6 cm diaphragmatic defect. One patient had a bilateral CMH, with the

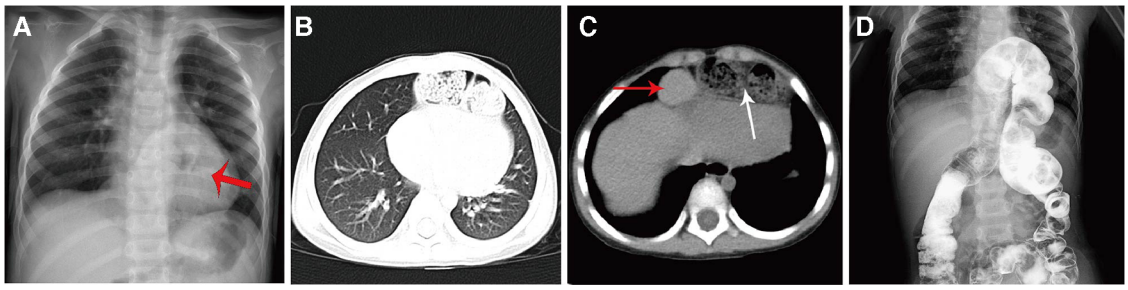

FIGURE 1
Preoperative imaging of a patient with a bilateral CMH. (A) Routine chest x-ray showing a left sided pericardial mediastinal shadow (red arrow); (B) Chest CT showing a shadow behind the sternum; (C) Chest CT showing partial herniation of the left lobe of the liver into the thoracic cavity, and herniation of the intestine into the thoracic cavity; (D) Barium enema showing herniation of the transverse colon above the diaphragm into the thoracic cavity.

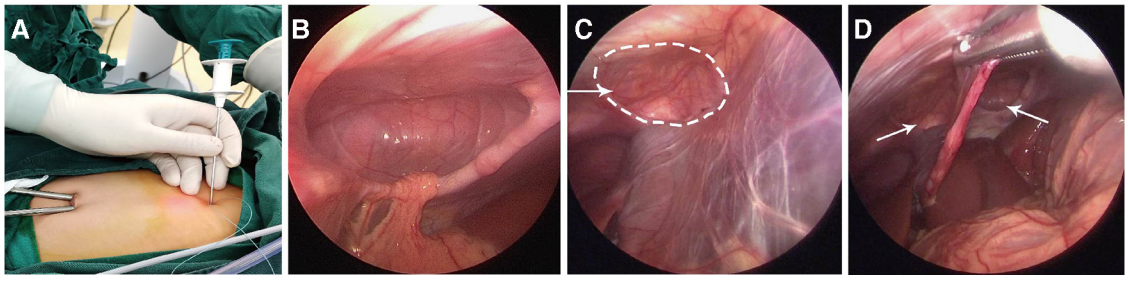

FIGURE 2
Single-site laparoscopic ligation of the hernia sac. (A) A left trocar was placed in the incision as an observation hole, followed by insertion of a 30°lenses. A right trocar was used as the operating hole. (B) Left side of the bilateral CMH, with the greater omentum forming the contents of the hernia sac. (C) The right side of the bilateral CMH was smaller than the left side (D) The bilateral CMH was behind the falciform ligament of the liver.

greater omentum forming the contents of the hernia sac on the left side but not on the right side (Figures 2B–D). There was a 4 cm × 5 cm left diaphragmatic defect and a 3 × 4 cm right diaphragmatic defect. One patient had a right-sided CMH, and the hernia sac had no obvious contents. There was a 3 cm × 4 cm diaphragmatic defect.

The hernia sac contents were reduced. A needle holding threads of non-absorbable sutures (2–0 Ethibond) was inserted at the midpoint of the diaphragmatic defect, introduced into the peritoneal space, and passed through the diaphragm into the abdominal cavity. The suture curved from the midpoint around the rim of the hernia sac. The needle was pulled out of the abdominal cavity leaving the suture inside (Figure 3A). The needle was reintroduced and a second suture was curved in the opposite direction until it met the first suture at the midpoint of the posterior wall of the hernia sac (Figure 3B). The sutures were pulled out of the patient (Figure 3C), tightened to ligate the hernia sac, and extracorporeal knots were tied (Figure 3D). In the patient with a bilateral CMH, ligation was used to repair both sides of the hernia sac.

Results

Hernia repair was successful in all patients. Ligation was a reliable technique, with no need for Optilene mesh. The average operative time for repair of a unilateral hernia was 20 ± 5 min. Volume of surgical blood loss was 2–3 ml. There was no damage to organs such as the liver or intestines, or to tissues such as the pericardium or the phrenic nerve. Resection of the falciform ligament of the liver was not required. The intestine was not pulled or compressed during surgery; therefore, patients were allowed a fluid diet 6–8 h after surgery, and remained on bed rest until 16 h after surgery. No postoperative complications occurred, and the patients were discharged on postoperative Day 2 or 3 (Table 1). No symptoms or complications were noted during the 1–48 months of follow-up. Chest CT showed no recurrence (Figure 4). There was no aggravation of the pectus carinatum in the affected patient. Aesthetic outcomes were satisfactory.

Discussion

CMH occurs due to a failure of fusion or muscularization of the pars sternalis and pars costalis during development of the diaphragm, resulting in a triangular parasternal gap. An estimated 90% of CMH occurs on the right side; however, CMH may be left sided or bilateral (11, 12). In the present study, one patient had a right-sided CMH, one patient had a left-sided CMH, and one patient had a bilateral CMH.

CMH often lacks typical clinical manifestations and is prone to misdiagnosis and delayed diagnosis (7). Respiratory and gastrointestinal symptoms may be caused by an increase in intra-abdominal pressure and herniation of the abdominal contents into the chest cavity; therefore, symptoms may be precipitated by chronic constipation, chronic cough, trauma, pregnancy, and obesity (13). Hernia sac contents can include the colon, omentum, stomach, small intestine, or liver. Infants with CMH often present with respiratory distress syndrome (12). Late diagnosis in adults may occur in patients presenting with chest pain, acute or chronic intestinal obstruction, or intestinal perforation (6, 14, 15).

Most CHM are found incidentally, but CMH may be suspected in patients with recurrent respiratory infections, gastrointestinal symptoms or Down syndrome, with a diagnosis made radiologically. In the present study, one patient presented with clinical symptoms of recurrent upper respiratory tract infection. One case was discovered incidentally when the patient was being

TABLE 1 Surgical outcomes for three patients with CMH.

Characteristic	Patient #1	Patient #2	Patient #3
Sex	Male	Male	Male
Age	14 months	30 months	48 months
Type of defect	Right	Left	Bilateral
Operative time	15 m	18 m	25 m
Volume of surgical blood loss	1 ml	2 ml	3 ml
Time to ingestion of solid food	7.5 h	6 h	8 h
Time on postoperative bed rest	16 h	16 h	16 h
Time to discharge	3 day	2 day	3 day

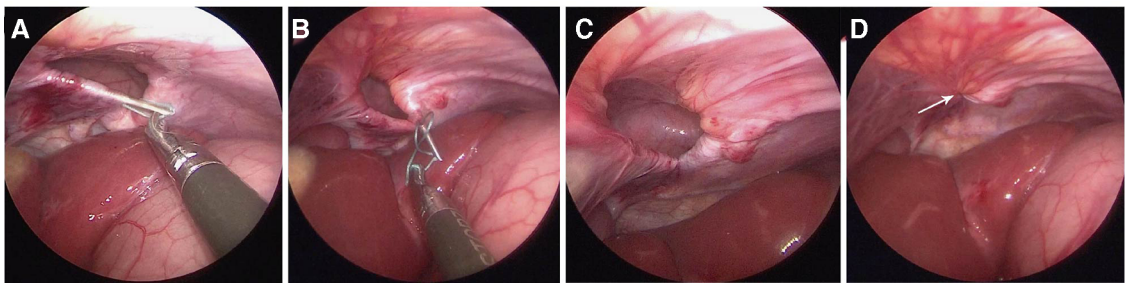

FIGURE 3
Operative procedure. (A) A needle holding threads of non-absorbable sutures (2–0 ethibond) was inserted at the midpoint of the diaphragmatic defect, introduced into the peritoneal space, and passed through the diaphragm into the abdominal cavity. One suture curved from the midpoint around the rim of the hernia sac. The needle was pulled out of the abdominal cavity leaving the suture inside; (B) The needle was reintroduced and a suture was curved in the opposite direction until it met the first suture at the midpoint of the posterior wall of the hernia sac; (C) The sutures were pulled out of the patient; (D) The sutures were tightened to ligate the hernia sac, and extracorporeal knots were tied (arrows).

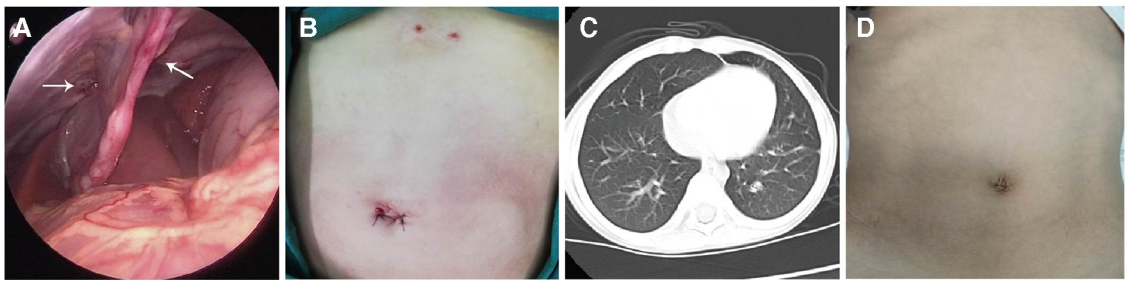

FIGURE 4
Postoperative outcomes. (**A**) Ligation of the bilateral hernia sac: ligation was firm and did not leave any gaps; (**B**) Abdominal incisions: the umbilical incision was small, and the extracorporeal knots were located under the xiphoid process; (**C**) Chest CT 15 months after the operation: the shadow behind the sternum had disappeared, and there was no aggravation of the pectus carinatum; (**D**) Aesthetic outcomes were satisfactory 15 months after the operation.

treated for car accident injury. One case was discovered incidentally during investigations for mild pectus carinatum; however, existing evidence suggests an association between pectus carinatum and CMH is unlikely. CMH may be seen on chest x-ray as an anterior mediastinal shadow on the lateral view. Chest CT may be required to confirm the diagnosis, as this can show a diaphragm defect and a retrosternal mass of fat density or an air-containing viscus when the omentum or bowel, respectively, have herniated into the chest cavity. Differential diagnosis includes a hiatus hernia, which can be excluded by upper gastrointestinal barium examination. Magnetic resonance imaging (MRI) may be employed, but the cost is usually prohibitive.

CMH should be treated surgically due to the risk of acute strangulation, volvulus, or incarceration. Open laparotomy or minimally invasive laparoscopy may be used (16). There is controversy over removal of the hernia sac. Resection of the hernia sac is technically challenging and can increase operative time and the risk of phrenic nerve injury, pneumothorax, pericardial injury, hemorrhage, and postoperative mediastinal emphysema (17). Mesh may be used in larger hernias and adults (18), but is not usually applicable in infants as the diaphragmatic defects are small and abdominal pressure is low.

Two main surgical methods are often used for repair of CMH: laparoscopic-assisted intralobular suture repair of the hernia sac (16) or percutaneous transperitoneal needle suture under laparoscopic surveillance (10, 14, 19, 20). Laparoscopic-assisted intralobular suture repair of the hernia sac is technically demanding and requires the insertion of 3 trocars in the abdominal wall, which may affect aesthetics. If the diaphragm at the anterior wall of the hernia sac lacks a firm edge, the diaphragm must be stitched to the abdominal wall, which is associated with a risk of recurrence. In percutaneous transperitoneal needle suture under laparoscopic surveillance (10, 14, 19, 20), such as U-stitches and mattress sutures, sutures of non-absorbable thread are placed through the abdominal wall into the peritoneal cavity, under the peritoneum and through the posterior edge of the hernia. The sutures are tied in the subcutaneous tissue to form a safe, effective and solid repair of the diaphragmatic defect. However, this approach requires several sutures placed through the full thickness of the abdominal wall, the technique is relatively complicated, and operative time is long. More recently, CMH has been successfully repaired using single-incision laparoscopic surgery and a suture-assisting needle (20), but this approach may not be cost-effective. In the present study, we used single-site laparoscopic ligation of the hernia sac, which was inspired by laparoscopic repair of infant and children with indirect inginal hernia. The technique does not require special instruments, the abdominal wall is punctured once, aesthetic outcomes are satisfactory, and the ligation is secure. The procedure is straightforward and can be performed by surgeons with experience treating indirect inguinal hernia in infants. If there is no adhesion between the hernia sac and the viscera, the operation may be completed by one experienced surgeon with one hole. If there is adhesion between the hernia sac and the omentum or intestine, an electric hook can be used to separate the adhesions. Operative time and surgical blood loss are minimal and no recurrence was detected with the longest follow-up time of 48 months.

Conclusions

Single-site laparoscopic ligation of the hernia sac provides pediatric surgeons with a safe and effective technique for repair of CMH in infants and children. The procedure is straightforward, operative time and surgical blood loss are minimal, recurrence is unlikely, and aesthetic outcomes are satisfactory.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the ethics committee of Affiliated Hospital of Zunyi Medical University. Written informed consent to

participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

Author contributions

CW: Data curation; Formal analysis; Methodology; Software; Writing—original draft. XL, GZ: Formal analysis; Investigation; Software. ZS: Data curation; Formal analysis. JY: Data curation; Investigation. ZL: Resources; Supervision. GZ: Resources. BL: Methodology; Resources; Supervision; Writing—review & editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Predictors for the clinical prognosis of sylvian arachnoid cysts in children

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Objectives: To investigate the potential factors affecting the clinical prognosis of intracranial sylvian arachnoid cysts(IAC) in children.
Methods: All patients with IAC admitted to our department from January, 1, 2015 to December, 31, 2016, were retrospectively reviewed. Patients were grouped based on surgical treatment (surgery cohort vs non-surgery cohort). The clinical and image outcome of the patients were followed routinely. The clinical characteristics and the prognosis of the patients were compared in different cohorts. Binary logistic regression analysis was applied to analyze the potential factors which may post an influence on the prognosis of the patients.
Results: Of 500 patients admitted to our department for IAC, 424 patients had good prognosis and 76 had poor prognosis, with no deaths occurred during the follow-ups. 68 patients had IAC related complications and 91 patients developed new symptoms during the follow-ups. There were significant differences ($P < 0.05$) between the 2 cohorts in below aspects: age, gender, Galassi subtype, whether the mother was a unipara, the maximum diameter of the cysts at the first visit and the last follow-up, headache, head circumference, temporal bulge, new symptoms, cysts rupture and hemorrhage, subdural effusion, and IAC disappearance. The mean changes in the maximum diameter of the IAC for the patients were marginally higher for the surgery cohort than for the non-surgery cohort ($P < 0.01$). Binary logistic regression analysis suggested that the number of symptom, no new symptoms during follow-up, surgical treatment, age, maximum diameter of cysts at first diagnosis were independent risk factors affecting the prognosis of patients ($P < 0.05$).
Conclusions: Patients older than 22.5 months, with the maximum diameter of IAC greater than 5.75 cm, who have multiple symptoms, born prematurely, develope new symptoms during the follow-ups and obvious symptoms after trauma need to conduct necessary surgical treatment in time. Patients with complications such as cysts rupture with hemorrhage and subdural effusion will acquire good prognosis after timely surgical treatment. IAC complete disappearance warrants no such important attention for the good prognosis.

KEYWORDS
intracranial sylvian arachnoid cysts, prognosis, children, surgery, predictors

Introduction

IAC is a benign intracranial lesion in children with an overall prevalence of 0.3%–2.6%, which is the most common place among different kinds of pediatric intracranial arachnoid cysts (1, 2).The main surgical treatment options include microscopic fenestration (3, 4), neuroendoscopic fenestration (5, 6) and cystoperitoneal shunt (CP shunt) (7). The CP shunt has been gradually replaced by the former 2 methods for the reason of series complication (8). Nowadays, the standard principle of surgical treatment made by surgeon has not reached a consensus. Previous studies suggest that asymptomatic patients should be followed up regardless of the size

of the IAC, which do not need early surgical treatment (2).Other studies put forward the opposite theory that aggressive surgical treatment should be conservatively considered for the association between IAC and symptoms is still not clear (9).The objective of this study is to present the clinical characteristic of the IAC and discuss the potential prognosis factors of children with IAC between the 2 cohorts,which may provide reference for the standardized treatment of children IAC.

Material and methods

Clinical materials

The study population comprised patients who admitted to our department from January 01, 2015, to December 31, 2016, as shown in the **Figure 1**.

Inclusion criteria: IAC confirmed by preoperative imaging examination; age at first diagnosis ≤18 years;a solitary cyst without concomitant arachnoid cysts in other sites.

Exclusion criteria: comorbidity with other severe metabolic disorders, genetic syndromes and other conditions affecting brain growth and development; incomplete medical record; intracranial hemorrhage history; comorbidity with other intracranial disorders or conditions; recurrence or failure of IAC surgical treatment history.

The data of the patients and their mothers, including: age, gender, birth weight, gestational weeks, whether the children's mothers were primiparas, were obtained through the electronic medical record system and telephone follow-ups.

All children underwent regular head CT or MRI examinations. CT plain scan showed that the IAC were round or round-like homogeneous low-density lesion with clear boundaries, which was the same as the density of cerebrospinal fluid. MRI plain scan showed that the IAC showed long T1 and long T2 signals, which were consistent with the signal of cerebrospinal fluid, and there was no edema in the surrounding brain tissue. IAC enhanced scan showed no enhancement of the wall and contents.

Criteria for good prognosis: (1) The patient's clinical symptoms basically disappear and adapt well to life; (2) There is no intellectual disability related to the development or treatment of IAC; (3) There are no complications associated with IAC or the complications disappear after treatment.; If all the criteria for the good prognosis are not fully met, the prognosis is identified as poor.

The ethical standards followed in this study were in accordance with the World Medical Association Declaration of Helsinki. Patient consent was not required for the retrospective nature of the study.

Follow-up assessment

Head circumference was measured in children with increased head circumference by taking the circumference from the upper edge of the eyebrow against the scalp to the occipital tuberosity. Then, we would compare the head circumference with the normal range for children of the same age.

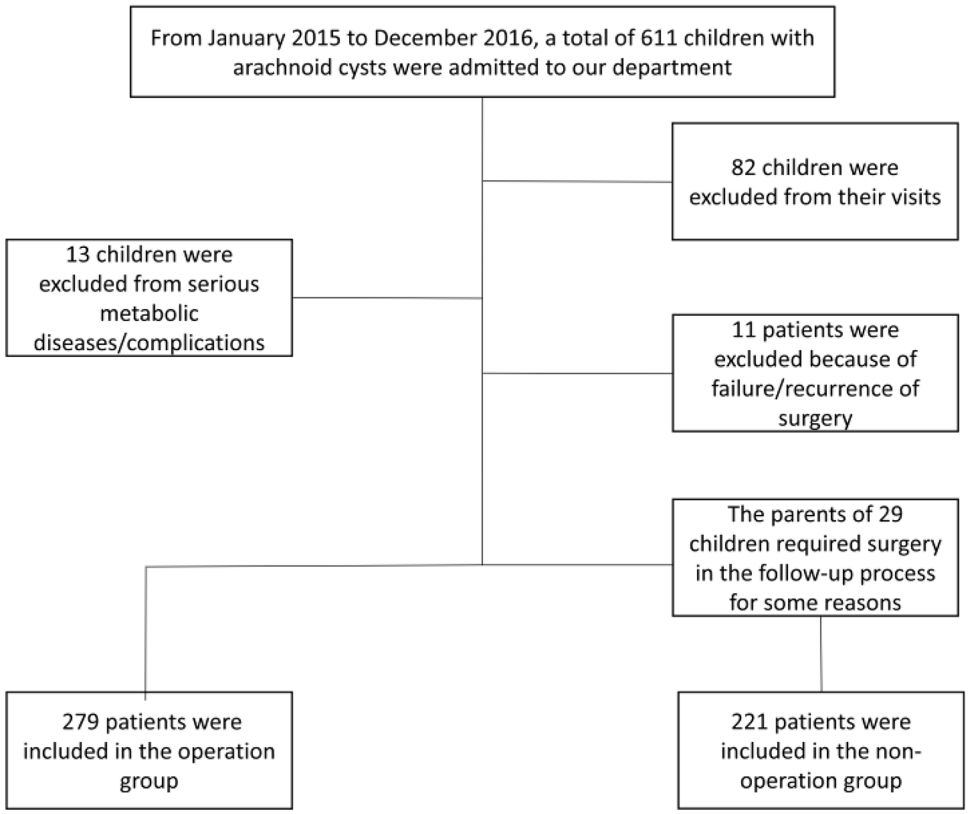


FIGURE 1
Shows the flow chart for patients with IAC included in this study.

Seizures, abnormal behavior, irritability, headache and other symptoms need to be referred to the relevant hospital department, which should be determined by the specialist physician after systematic evaluations.

Developmental retardation need to be evaluated by the child health care physician according to the relevant assessment scales. Subsequently, the patients would be regularly reviewed and evaluated during the follow-ups by the child health care department.

Children with ophthalmic symptoms underwent a comprehensive ophthalmic assessment, including the assessment of eye alignment (strabismus or nystagmus) and examination of the anterior bulbous area and fundus), in order to exclude related eye diseases.

Temporal bone bulge should be examined by physical examination combined with head CT examination, in order to exclude self-related diseases or related syndromes of the temporal bone. Regarding the comparison of IAC during the follow-ups, CT examinations were regularly performed.

Patients with endocrine abnormalities were included in the study after excluding other endocrine diseases and the related endocrine hormone indicators should be regularly monitored for the comparison.

According to the data of image examination, the maximum diameter of cysts were measured at the first visit. Besides, the variations in the maximum diameter of cysts were measured and recorded during the follow-ups. The above monitoring data were routinely evaluated and recorded by 2 pediatric neurosurgeons before and after surgery treatment.

Based on the shape of the cysts and the malformation of adjacent brain structures, the patients were divided into convex and non-convex cohorts (10).

During the follow-ups, subdural effusion, IAC rupture and hemorrhage, hydrocephalus and other conditions were comprehensively evaluated by CT/MRI to determine whether the above complication were related to the IAC.

Tada formula (11) was used to determine the approximate volume of hemorrhage and effusion. Evans index >0.30 (12) was used to confirmed the presence of hydrocephalus.

According to Galassi classification, IAC could be divided into 3 types (13).

Type I: The cysts were small, spindle-shaped and confined to the anterior temporal fossa;

Type II: The cysts are intermediate in size, occupying mainly the anterior middle of the temporal fossa, and may develop along the lateral fissure;

Type III: The cysts are large, occupy essentially the entire middle cranial fossa position, and locally compress the occipital or parietal lobes.

Statistical analysis

All statistical analysis were conducted by using the SPSS software (version 10.0, SPSS Inc., Chicago, Illinois).Continuous variables with normal distribution were expressed as mean ± 1 standard deviation or median and interquartile range. Comparison between cohorts was analyzed using the independent sample T test. Continuous variables which were not following normal distribution were represented as M (P25, P75), and comparison between cohorts was analyzed using the Mann-Whitney U test. Categorical variables were expressed as the number of cases or percentage composition ratio, and comparison between cohorts was analyzed using the chi-square test or Fisher exact probability. Potential factors showed significant ($P < 0.15$) in univariate analysis and reported significant in clinical practice or previous literature were analyzed by binary logistic regression analysis in which we used the forward stepwise regression method to determine the risk factors which may affect the prognosis of patients. $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

500 patients were enrolled in the study, including 279 patients in the surgery cohort and 221 patients in the non-surgery cohort. The

TABLE 1 Baseline characteristics.

Baseline Characteristics	Surgery	No-surgery	*P* value
Age (Mean ± SD)	56.00 ± 36.33	65.67 ± 39.38	0.003
Age (*n*, %)			<0.001
1–6 years	156 (55.91)	79 (35.74)	
Others	123 (44.09)	142 (64.26)	
Sex (*n*, %)			0.032
Female	46 (16.49)	54 (24.43)	
Male	233 (83.51)	167 (75.57)	
Galassi (*n*, %)			0.015
2	141 (50.54)	136 (61.54)	
3	138 (49.46)	85 (38.46)	
Side (*n*, %)			0.340
Left	192 (68.82)	143 (64.71)	
Right	87 (31.18)	78 (35.29)	
Convex (*n*, %)			0.577
C	177 (63.44)	134 (60.63)	
NC	102 (36.56)	87 (39.37)	
Premature infant (*n*, %)			0.119
Yes	26 (9.31)	31 (14.03)	
No	253 (90.69)	190 (85.97)	
Low-birth weight infant (*n*, %)			0.319
Yes	12 (4.30)	14 (6.33)	
No	267 (95.70)	207 (93.67)	
Unipara (*n*, %)			0.040
Yes	165 (59.14)	151 (68.33)	
No	114 (40.86)	70 (31.67)	
The first visit	6.14 ± 2.48	4.98 ± 1.22	<0.001
The last follow-up	1.79 ± 1.50	4.11 ± 1.72	<0.001
Change	4.00 (3.20–5.10)	0.50 (0.20–1.10)	<0.001
Follow-up time (Mean ± SD)	76.99 ± 7.89	73.06 ± 7.61	–

outcomes compromised 400 males and 100 females, with a male to female ratio of 4 : 1. Table 1 presents the basic characteristics of the whole cohort. The average age of the surgery cohort was 56.00 ± 36.33 months, which in the non-surgery cohort was 65.67 ± 39.38 months. Patients aged 1–6 years were divided into a single cohort, and 265 patients of other ages were divided into the other cohort. Of all the Galassi classification IAC patients, there were 277 type II and 223 type III. 335 patients were on the left side and 165 cases were on the right side. Convexity cysts were observed in 311 patients and non-convexity cysts were observed in 189 patients.

Preterm infants were confirmed in 57 patients, with 26 low birth weight infants and 316 primiparas in the cohort. The maximum diameter of cysts in the surgery cohort and the non-surgery cohort were 6.14 ± 2.48 cm and 4.98 ± 1.22 cm, respectively, and the maximum diameters of cysts at the last follow-up were 1.79 ± 1.50 cm and 4.11 ± 1.72 cm, with the mean follow-up time were 76.99 ± 7.89 months and 73.06 ± 7.61 months, respectively. Significant differences between the 2 cohorts were identified in age, gender, Galassi classification, whether they were premature infants, whether their mothers were primiparas, the maximum diameter of the cysts at the first and last visit, and the variation in the maximum diameter of the cysts ($P < 0.05$). We have not confirmed the significant difference between the 2 cohorts in cysts location (left/right), cysts shape (convexity/non-convexity) and low birth weight ($P > 0.05$). Figure 2 shows the OR value and the P value of the above seven factors.

Figure 3 shows that in the ROC curve analysis, the best sensitivity of age ≥ 22.5 months to predict the prognosis of children was 86.3%, and the specificity was 63.2%, [area under the curve (AUC) = 0.618; 95%CI: 0.544–0.691]. The maximum diameter of cysts ≥ 5.75 cm had the best sensitivity of 66.0% and specificity of 56.6% in predicting the prognosis of children [area under the curve (AUC) = 0.622; 95%CI: 0.544–0.691].

Clinical presentation

The most common symptom was headache (221 cases), followed by seizures (90 cases), developmental delay (31 cases), increased head circumference (28 cases), temporal bone protuberances (17 cases), behavioral abnormalities (11 cases), irritability (11 cases), bulging eyeball (6 cases), and endocrine abnormalities (5 cases). 186 children visited the hospital for the reason of head trauma

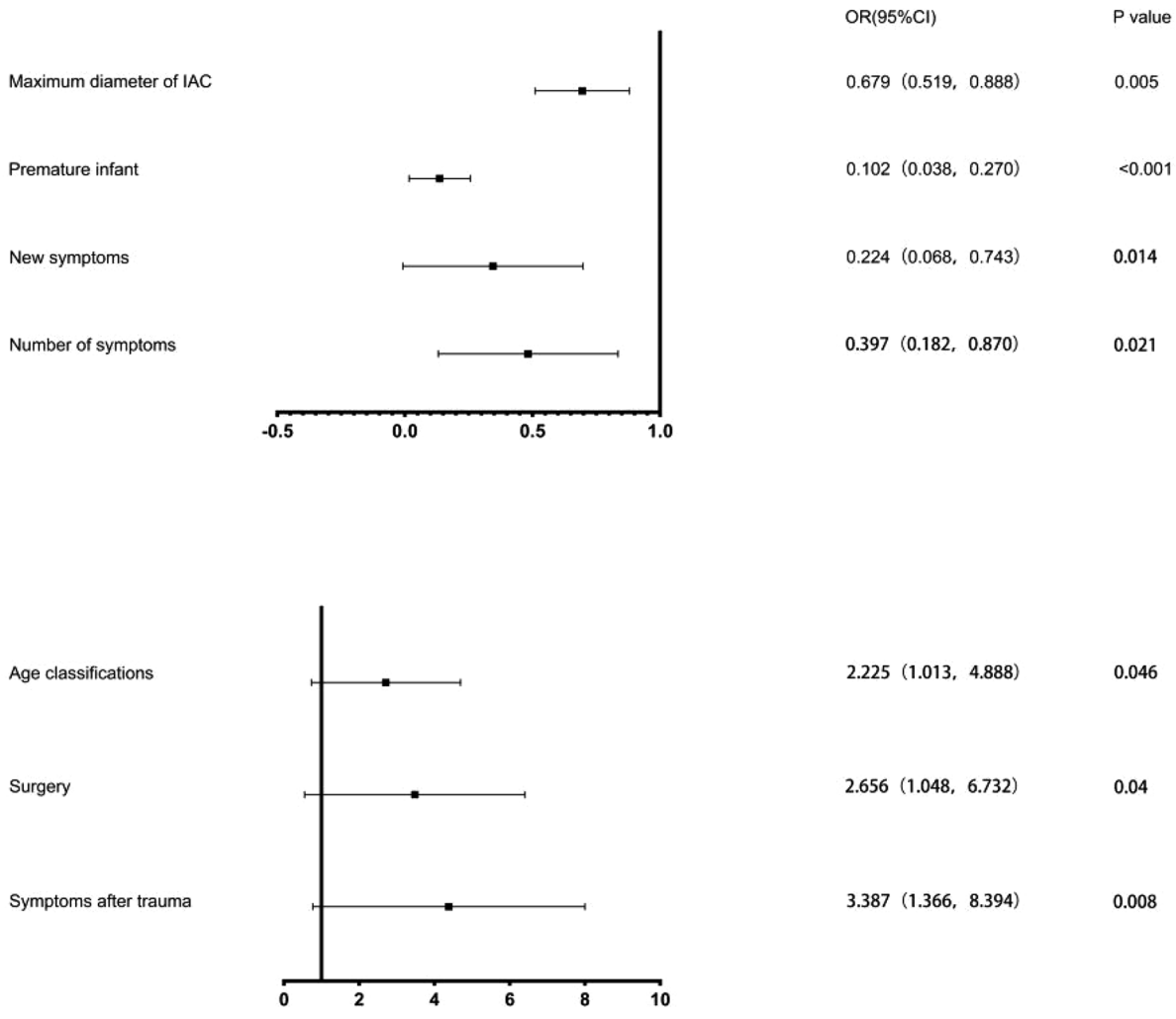
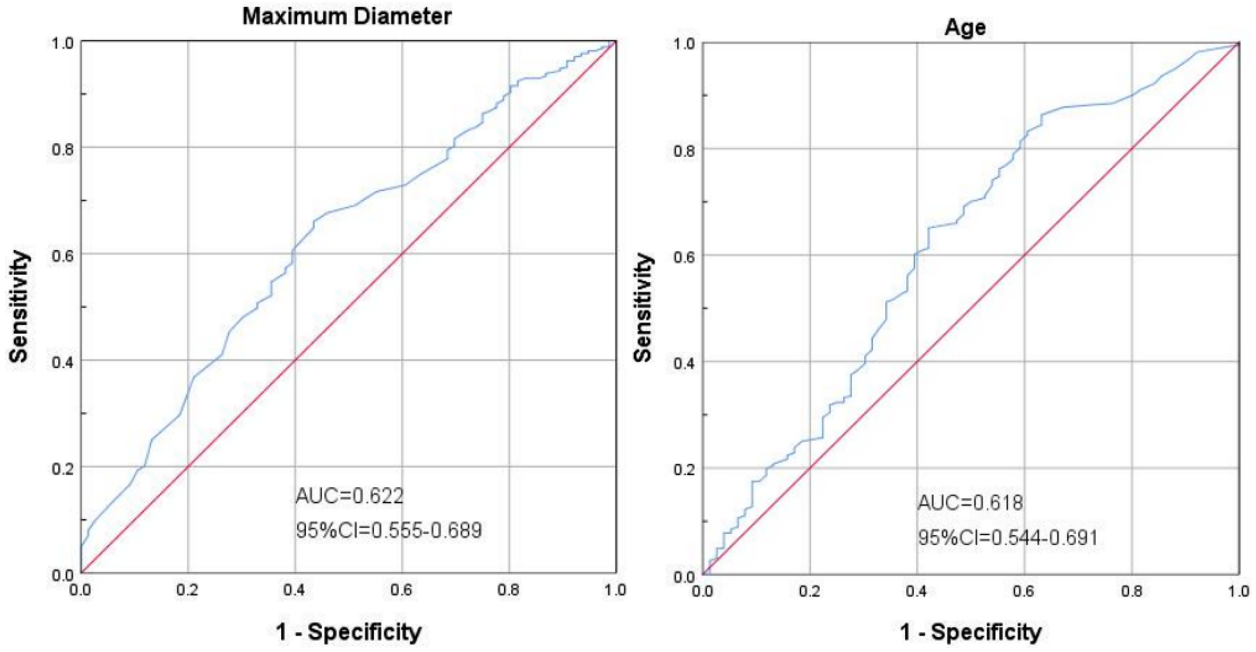


FIGURE 2
Results of Binary logistic regression analysis. The black squares indicate the OR values, the error bars represent 95% CIs, and $P < 0.05$.



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Shows that in the ROC curve analysis, the best sensitivity of age ≥22.5 months to predict the prognosis of children was 86.3%, and the specificity was 63.2%, [area under the curve (AUC) = 0.618; 95%CI: 0.544-0.691]. The maximum diameter of cysts ≥5.75 cm had the best sensitivity of 66.0% and specificity of 56.6% in predicting the prognosis of children [area under the curve (AUC) = 0.622; 95%CI: 0.544-0.691].

associated symptoms. 248 patients with one symptom were observed and 152 patients with more than one symptom were identified during the entire follow-up period.

30 patients visited the hospital for the reason of IAC rupture, while 38 patients were identified as subdural effusion before the surgical treatment. There were 32 patients who have hydrocephalus before operation and 70 patients whose IAC completely disappeared during the follow-ups.

11 patients with cysts rupture and hemorrhage were included. Patients with a small amount of hemorrhage and no obvious symptoms recovered well after hemostatic treatment. 18 patients underwent surgical evacuation of hematoma and external drainage operation for the reason of obvious symptoms and large amount of hemorrhage, 2 of whom underwent VP shunt due to the persistent symptomatic hydrocephalus after operation, with relieved symptoms at the end.

38 children had subdural effusion, 3 of whom existed obvious symptoms and underwent external drainage operation, with 1 patient underwent subdural-peritoneal shunt operation. The subdural effusion of the other patients disappeared during the follow-ups. **Table 2** shows the basic data related to the clinical characteristics of the cohort. The last follow-up of 500 patients manifested that 424 patients had good prognosis, while 76 patients had poor prognosis.

Independent factors of a good prognosis

Independent factors associated with a good prognosis were the number of symptoms (1 symptom), disappearance of new symptoms during follow-ups, surgery treatment, age group (1–6 years), and maximum cysts diameter at first diagnosis (the maximum diameter <5 cm) (**Table 3**).

Discussion

Dominant results

(1) The maximum diameter of the IAC ≥ 5.75 cm was the best indicator to predict the prognosis, with a sensitivity of 66.0% and a specificity of 56.6%.
(2) The age of patients with IAC ≥ 22.5 months was the best predictor of prognosis, with a sensitivity of 86.3% and a specificity of 63.2%.
(3) The independent potential factors of good prognosis of IAC shows as follow: number of symptoms (1 symptom); no new symptoms during follow-ups; timely surgical treatment;age group (1–6 years old); maximum diameter of IAC at first diagnosis (<5 cm).

Previous literature suggests that when the maximum diameter of type II and III IAC patients are greater than 5 cm (14, 15), the optimal option towards IAC should be surgical treatment. Prevention of IAC rupture is the primary purpose of the above proposal. Our study demonstrated that IAC patients with the maximum diameter greater than 5.75 cm could obtained a good prognosis between the cohorts after timely surgical treatment, in which the difference was significant ($P < 0.05$). Indeed, the maximum diameter of the IAC reflects the effect of the cysts volume. Larger IAC volume reflects more unstable situation, which may have an association with the more obvious symptoms and

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TABLE 2 Clinical presentation.

Clinical presentation	Surgery	Non-surgery	*P* value
Headache (*n*, %)			0.002
Yes	141 (50.54)	80 (36.20)	
No	138 (49.46)	141 (63.80)	
Epileptic seizure (*n*, %)			0.483
Yes	47 (16.85)	43 (19.46)	
No	232 (83.15)	178 (80.54)	
Developmental retardation (*n*, %)			1.000
Yes	17 (6.09)	14 (6.33)	
No	262 (93.91)	207 (93.67)	
Increase head circumference (*n*, %)			<0.001
Yes	25 (8.96)	3 (1.36)	
No	254 (91.04)	218 (98.64)	
Abnormal behavior (*n*, %)			0.123
Yes	9 (3.23)	2 (0.90)	
No	270 (96.77)	219 (99.10)	
Irritability (*n*, %)			1.000
Yes	6 (2.15)	5 (2.26)	
No	273 (97.85)	216 (97.74)	
Eyes bulge (*n*, %)			0.235
Yes	5 (1.79)	1 (0.45)	
No	274 (98.21)	220 (99.55)	
Cryptorrbea (*n*, %)			0.476
Yes	3 (1.08)	5 (2.26)	
No	276 (98.92)	216 (97.74)	
Temporal bone bulge (*n*, %)			0.026
Yes	14 (5.02)	3 (1.36)	
No	265 (94.98)	218 (98.64)	
Symptoms after trauma (*n*, %)			0.113
Yes	95 (34.05)	91 (41.18)	
No	184 (65.95)	130 (58.82)	
Number of symptoms (*n*, %)			0.379
Yes	199 (71.33)	149 (67.42)	
No	80 (28.67)	72 (32.58)	
New symptoms (*n*, %)			<0.001
Yes	83 (29.75)	8 (3.62)	
No	196 (70.25)	213 (96.38)	
Hydrocephalus (*n*, %)			0.716
Yes	19 (6.81)	13 (5.88)	
No	260 (93.19)	208 (94.12)	
Cyst rupture and hemorrhage (*n*, %)			<0.001
Yes	29 (10.39)	1 (0.45)	
No	250 (89.61)	220 (99.55)	
Subdural effusion (*n*, %)			<0.001
Yes	34 (12.19)	4 (1.81)	
No	245 (87.81)	217 (98.19)	
Cyst disappear (*n*, %)			<0.001
Yes	61 (21.86)	9 (4.07)	
No	218 (78.14)	212 (95.93)	
Prognosis (*n*, %)			0.099
Good	230 (82.44)	194 (87.78)	
Poor	49 (17.56)	27 (12.22)	

develop new symptoms. Meantime, the larger size of the IAC, the compression of the brain tissue is severer, which may lead to more cases of developmental delay. In addition, larger IAC may lead to more complication related to IAC rupture, which indicates the poor prognosis. Previous literature reported that subdural hemorrhage accounted for 71.5% of the complications of cysts rupture (16). Our results suggest that patients with lager IAC (the maximum diameter ≥5.75 cm) should be considered to take operation.

0–6 years period lies an important place across the children's brain development, the Karolinska Institute study corroborated the cognitive decline on the neuropsychological tests (17). Research from the School of Medicine at the University of Haukeland in Norway also found that IAC in the dominant hemisphere indeed affected the language development (18, 19). The compression of brain tissue by IAC may lead to the delay or abnormality of brain development, which then cause the developmental and cognitive retardation. We consider the early surgical treatment may lead to a higher frequency of subdural effusion among the patients under 1 year old because the vigorous secretion of arachnoid cysts granules (20).Therefore, in this study, we divided patients aged 1–6 years into a separate cohort. Binary regression analysis showed that surgical treatment performed at the age of 1–6 years could significantly improve the good prognosis. Our study demonstrated that surgical treatment at the patients whose age ≥ 22.5 months was associated with a related better prognosis.

Our results suggest that the maximum diameter of cysts in the non-surgery cohort keeping stable during the follow-ups, which is consistent with the previous literature reported that the volume of most IAC remained stable during the follow-ups (2). The average maximum diameter of IAC at the first visit were significant higher than that at the last visit in the surgery cohort. The results demonstrated that the surgical treatment could achieve ideal results in terms of IAC volume. Furthermore, the complete disappearance ratio of IAC in the surgical cohort is significant greater than that in the non-surgical cohort in the long-term follow-ups ($P < 0.001$), which proves the effectiveness of surgical treatment for eliminating IAC to achieve a good prognosis.

The complications mainly include IAC rupture and hemorrhage and subdural effusion, which contribute a higher occurrence rate in surgical cohort than that in non-surgical cohort. However, our study demonstrate that cysts rupture and subdural effusion were not

TABLE 3 Results of Binary logistic regression analysis.

	OR	95%CI	*P* value
Symptoms after trauma	3.387	(1.366, 8.394)	0.008
Number of symptoms	0.397	(0.182, 0.870)	0.021
New symptoms	0.224	(0.068, 0.743)	0.014
Surgery	2.656	(1.048, 6.732)	0.040
Age classifications	2.225	(1.013, 4.888)	0.046
Premature infant	0.102	(0.038, 0.270)	<0.001
Maximum diameter of IAC	0.679	(0.519, 0.888)	0.005

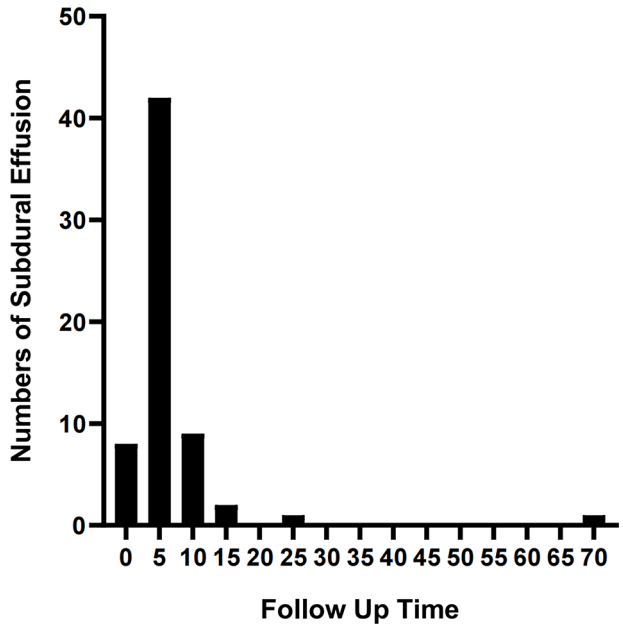

FIGURE 4
Shows the recovery time of IAC patients with subdural effusion.

independent risk factors for good prognosis in the multivariate analysis. Our study also suggests that temporary cysts rupture and hemorrhage and subdural effusion during the treatment of the IAC, a satisfactory clinical prognosis can still be obtained after timely and reasonable treatment, as shown in the Figures 4–8. As we shows in the Figure 4, of 63 patients with subdural effusion in our study, most of which disappeared in 25 months after operation. Meanwhile, our study also indicate that IAC related complications are mostly associated with head trauma during follow-ups. Therefore, the prevention of head trauma for the IAC patients is warranted to reduce the potential occurrence of complications.

Previous reports showed that most patients with IAC had no obvious symptoms at the first visit of hospital, which were mainly diagnosed accidentally after trauma (2, 21). We included patients who visited our hospital for the reason of head trauma with obvious uncomfortable symptoms in the study. Multivariate analysis showed that patients with uncomfortable symptoms after trauma had a better prognosis than that without uncomfortable symptoms after trauma. The uncomfortable symptoms associated with trauma may indicate the instability of the IAC pressure or the severe compression to the surrounding brain tissue, which will result in significant uncomfortable symptoms in IAC patients even with minor trauma.

Patients who had single symptom or developed no additional new symptoms during follow-ups were independent risk factors about the good prognosis. Multiple symptoms at the first visit or the occurrence of additional symptoms during follow-ups may indicate that the IAC influence on the surrounding brain tissue was grievous and continuous. Thus, our study suggests timely surgical treatment should be considered about the above situation.

Previous reports suggest that the formation of IAC has association with embryonic development (22), so we include the follow risk factors: the birth weight of the child, whether the

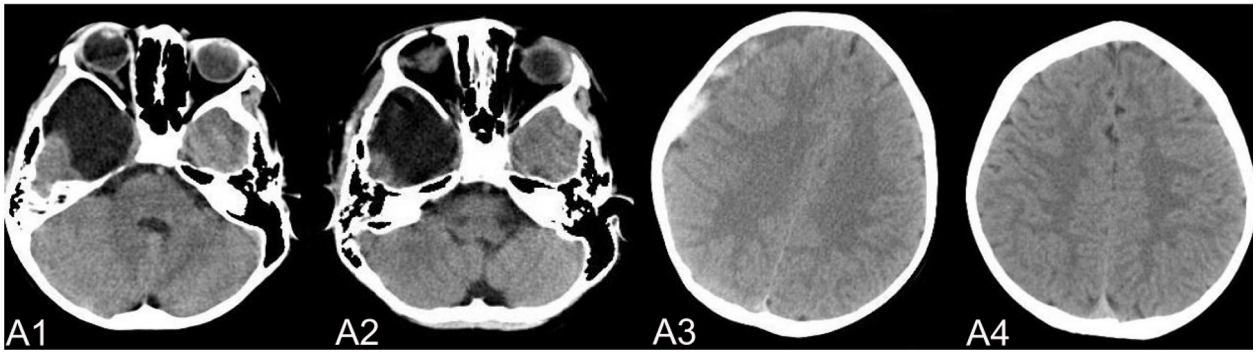

FIGURE 5
(A) shows a patient,who had a subdural hemorrhage during the follow-up time after operation. A1 and A2 shows the IAC CT images before and after operation. A3 shows the IAC hemorrhage after head trauma during the follow-ups. A4 shows the IAC hemorrhage disappeared after hemostasis treatment.

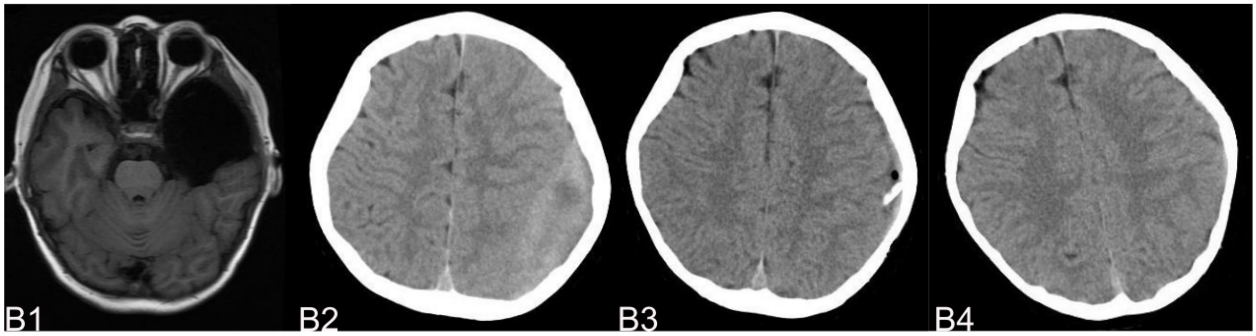

FIGURE 6
(B) shows a typical patient, who had a subdural hemorrhage during the follow-up time after operation. B1 shows the IAC MRI image before operation. B2 demonstrates the IAC hemorrhage after head trauma 2 months after operation. B3 shows the surgical treatment towards the hematoma. B4 shows the recovery of the subdural hemorrhage after the surgical treatment.

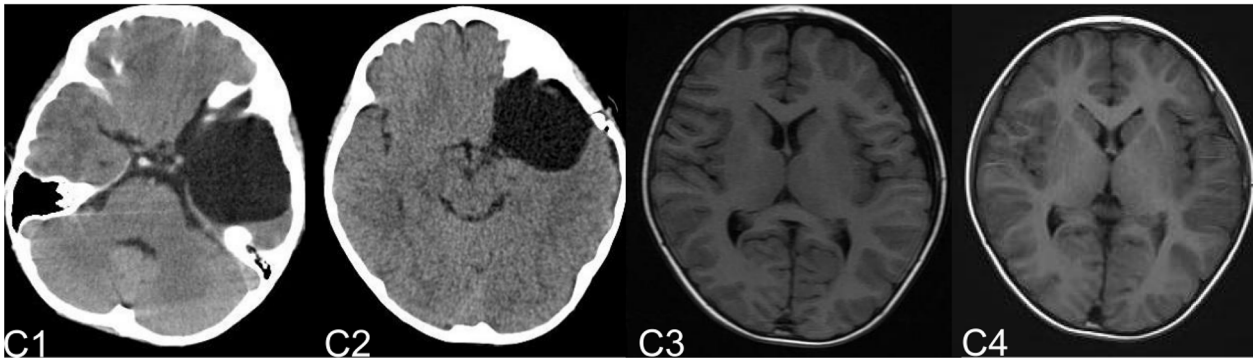

FIGURE 7
(C) shows the patient, who had subdural effusion after IAC operation during the follow-ups. C1 and C2 shows the CT images before and after operation. C3 shows the subdural effusion 2 months after the operation. C4 shows the recovery of the subdural effusion with the treatment of follow up observation after 5 month.

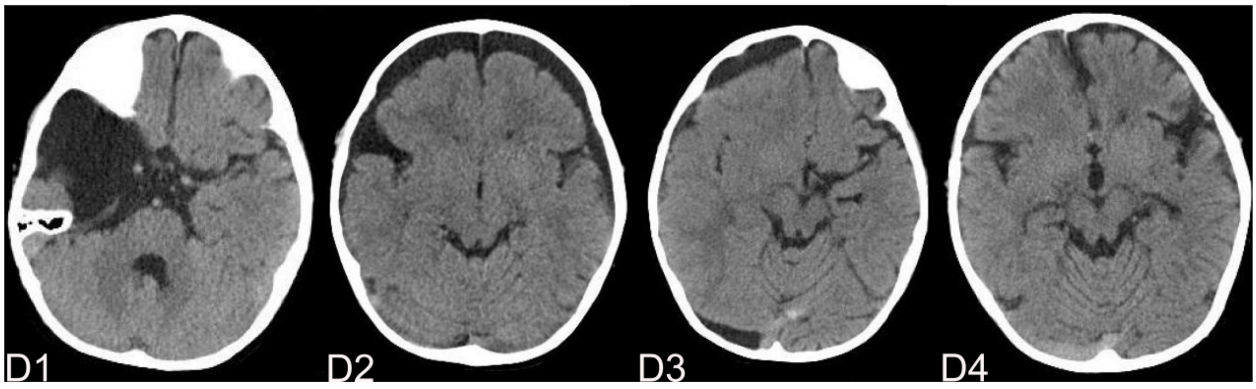

FIGURE 8
(D) shows the patient, who had subdural effusion after IAC operation during the follow-ups. D1 shows the CT image of IAC before operation. C2 shows the subdural effusion 3 month after operation. C3 shows the subdural effusion which decreases after the surgical treatment. C4 shows the disappearance of the subdural effusion 6 months latter.

child was premature, and whether the child's mother was a primipara. Multivariate analysis suggested that preterm birth is an independent risk factor for prognosis ($P < 0.001$).Previous reports point out the differences in the membrane of the arachnoid cysts wall, which can be divided into transparent/thin and pale/tenacious cohorts (23). Preterm birth may affect the composition of the texture of the cysts wall as well ad the compression degree of brain tissue. Therefore, a prospective

study of IAC embryo correlation is warranted in future studies to observe more details.

Limitations

This study was a single-center retrospective study, and the multicenter study were needed in the future. At the same time, we have not systematically studied the prenatal embryological factors and pathogenesis of IAC combined with clinical data. In future studies, the mechanism related to prenatal IAC can be further studied on the basis of prospective study.

Conclusion

Patient with the below situation: age $\geq$ 22.5 months, the maximum diameter of IAC $\geq$ 5.75 cm, multiple symptoms, additional symptoms during the follow-ups, born prematurely, obvious uncomfortable symptoms after trauma, we recommend that the necessary surgical treatment should be performed in time. Complications such as cysts rupture with hemorrhage and subdural effusion during the follow-ups will not have a significant effect on the prognosis of patients after timely treatment. Meanwhile, IAC disappearance is not necessary for good prognosis.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by HZ, WX, LC, ZN, BW and JM. The first draft of the manuscript was written by HZ. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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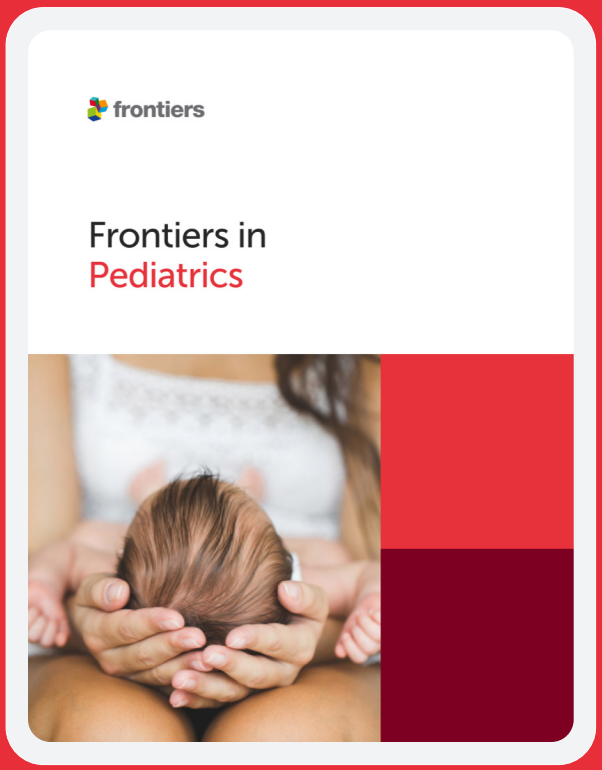

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