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Gastro-intestinal function and quality of life are favorable in adolescent and adult gastroschisis patients

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ABSTRACT

Background and aims: Studies on long-term sequelae of gastroschisis are scarce. The limited data suggest increased abdominal complaints in young children. To provide proper counseling for both parents and patients, more information on long-term outcome is needed. This study aims to evaluate long-term outcome regarding GI function, gastroesophageal reflux (GER), health-related quality of life (HRQoL) and cosmetic satisfaction.

Methods: An observational longitudinal cohort study was performed. All patients ($N = 43$) born between 1982 and 2008 with gastroschisis that were admitted to the University Medical Centre Utrecht, Wilhelmina Children's Hospital were invited to fill in a survey. Data of included patients were compared to validated Dutch reference standards.

Results: Fourteen patients responded to the survey. The median follow-up was 18 years. Abdominal pain on weekly basis was present in two patients (14%) and feeding difficulties were present in one patient. Presence of a complication during gastroschisis treatment led to more GI symptoms (80% versus 22%). One patient experienced moderate complaints of regurgitation or dyspepsia. Although the overall HRQoL was lower in teenage gastroschisis patients as compared to healthy controls (73/100 versus 83/100, respectively), we found no relevant difference in overall HRQoL in the other age groups. Seven patients (50%) were satisfied with the cosmetic result of the scar.

Conclusions: GI function and HRQoL in gastroschisis patients seem similar to healthy controls at adolescent and adult age. Complications during gastroschisis treatment led to an increase of abdominal complaints later in life. The surgical technique had no significant effect on the cosmetic results.

1. Introduction

Gastroschisis is a congenital abdominal wall defect that is mostly located at the right side of the umbilical cord and causes herniation of the abdominal organs in newborns. The condition needs rapid surgical intervention (< 24 h after birth) and during the first period (weeks-months) of life, total parenteral nutrition (TPN) is needed. More than half of the infants with gastroschisis need additional surgical procedures later in life [1]. Several studies have shown that this condition and the subsequent interventions had an impact on neurodevelopment and gastrointestinal function in young children, such as verbal

intelligence and global executive functioning [1–3]. Harris et al. published that twenty-one (41%) of fifty young gastroschisis patients (age 5–17) reported abdominal pain on a weekly basis [3]. Unfortunately, long-term follow-up regarding gastro-intestinal (GI) function has never been investigated in gastroschisis patients beyond middle school age.

Another problem that can occur after surgical repair of gastroschisis is gastroesophageal reflux (GER). Only a few studies on gastroschisis and GER have been published and reported an increased incidence of GER in gastroschisis patients. This increase may be allocated to secondary complications of gastroschisis, such as bowel resection or hiatal hernia. These studies are, however, scarce and the association between

Abbreviations: BMI, body mass index; GER, gastroesophageal reflux; GERD, gastroesophageal reflux disease; GI, gastro-intestinal; HRQoL, health-related quality of life; PedsQL™, Pediatric Quality of Life Inventory; RDQ, Reflux Disease Questionnaire; TNP, total parenteral nutrition

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GER related to gastroschisis remains indistinct [4,5]. Despite the higher incidence of GER at a young age, data on GER at later age is lacking completely.

Gastroschisis is commonly associated with intra-uterine growth retardation and/or prematurity, resulting in lower birthweight in babies born with gastroschisis. Growth retardation has been described in gastroschisis patients up until the age of two [6]. Previous studies have shown that gastroschisis patients seem to catch up this growth retardation after two to 15 years compared to their peers [2,7–9]. Studies on height and weight at adult age after gastroschisis repair are, however, not available.

Contrary to what may be expected, the few studies on health-related quality of life (HRQoL) in young children have shown no significant difference in quality of life (QoL) in gastroschisis patients compared to healthy controls [8–12]. Only two studies have published data on long-term QoL in patients with abdominal wall defects. However, these studies included both gastroschisis as well as omphalocele patients without separating these two different types of abdominal wall defects [13,14].

Only a few studies have described cosmetic satisfaction with the scar. These studies were also limited to young children [8,15]. There is no data available on the cosmetic end result in adults after gastroschisis repair.

In short, data on long-term follow up beyond middle school age regarding GI function, HRQoL and cosmetic result is limited in gastroschisis patients. Therefore, this study aims to evaluate GI function, GER, growth, health-related quality of life and cosmetic satisfaction at adolescent and adult age.

2. Materials and methods

All patients born with gastroschisis between 1982 and 2008 that were admitted to the Wilhelmina Children's Hospital, UMC Utrecht, were considered for participation in this observational cohort study. Patients that passed away, moved abroad or patients that were not found were excluded from the study.

2.1. Ethical approval and informed consent

This study was approved by the UMCU Ethics Committee (EC, number 17–665/C). Informed consent was obtained from the patients and/or their parents (when under 16 years old).

2.2. Surgical procedure

Surgical closure of the abdominal wall defect under general anesthesia was performed in all patients. All procedures were performed or supervised by an experienced pediatric surgeon. In most patients, the defect could be closed primarily within hours after birth. The herniated abdominal organs were repositioned into the abdomen and the abdominal fascia and skin were closed using absorbable sutures. When primary closure was not possible due to risk of pulmonary and/or hemodynamic difficulties, a silicone bag (silo) was placed underneath the fascia of the defect in order to gradually reposition the herniated abdominal organs into the abdominal cavity. Within seven to 10 days, the herniated intestinal organs lay intra-abdominally and the fascia and skin could be closed. There were no relevant changes or innovations in the surgical procedure during the study period (1986–2008).

2.3. Clinical assessment

The following patient characteristics and medical history were derived from the electronic patient records.

2.3.1. Gastrointestinal function

Patients were asked to fill out a nutrition diary for 7 days and a questionnaire on the presence and frequency of gastrointestinal symptoms, including abdominal pain, gas bloat, and difficulties with completing a meal and GI complaints after meal.

2.3.2. Reflux disease

The Reflux Disease Questionnaire (RDQ) was used to determine the presence and severity of reflux disease. The RDQ is a self-administered questionnaire that consists of twelve items and assesses the frequency and severity of gastrointestinal symptoms in the past 7 days. The scores were converted into three subscales: heartburn, regurgitation and dyspepsia. The heartburn and regurgitation subscales were combined into a GERD (gastroesophageal reflux disease) dimension [16]. A Dutch translation of RDQ was used for this study. Reflux symptoms were divided in no symptoms, mild symptoms (mild symptoms on weekly basis), moderate symptoms (mild symptoms on daily basis or severe symptoms on weekly basis) and severe symptoms (severe symptoms on daily basis).

2.3.3. Growth

Height and weight were assessed and used to calculate Z-scores for weight-for-length and height-for-age, based on the Netherlands Organization for Applied Scientific Research (TNO) growth standards [17]. Z-scores were expressed as standard deviations from the reference mean.

2.3.4. Quality of life

The Pediatric Quality of Life Inventory (PedsQL™) 4.0 Generic Core Scales was used to assess the HRQoL in the study patients. The PedsQL™ is a self-administered questionnaire that consists of 23 items related to four domains, including health and activities, feelings, social relations and work or school. The scores were linearly transformed into a 0–100 scale, where higher scores indicate better HRQoL. Validated Dutch translations of the PedsQL™ for adults, young adults (18–25 years old), teenagers (13–17 years old) and children (8–12 years old) were used for this study. Validated Dutch PedsQL™ questionnaires for the patients' parents were used for children under 13 years old. The HRQoL scores were compared to Dutch reference standards for different age groups [18,19]. Only one young adult (18–25 years) was included in this study, consequently this age group was excluded from the analysis on HRQoL.

2.3.5. Cosmetic result

Satisfaction with the cosmetic result of the scar was assessed by a questionnaire (Appendix A). The questionnaire consisted of two questions; the first question addressed satisfaction with the scar and the second question addressed overall satisfaction with the appearance of the abdomen. The questions could be answered with 'satisfied', 'minimal satisfaction' or 'not satisfied'.

2.4. Statistical analysis

Continuous data with normal distributions were presented as mean and non-normal distributed continuous data were presented as median.

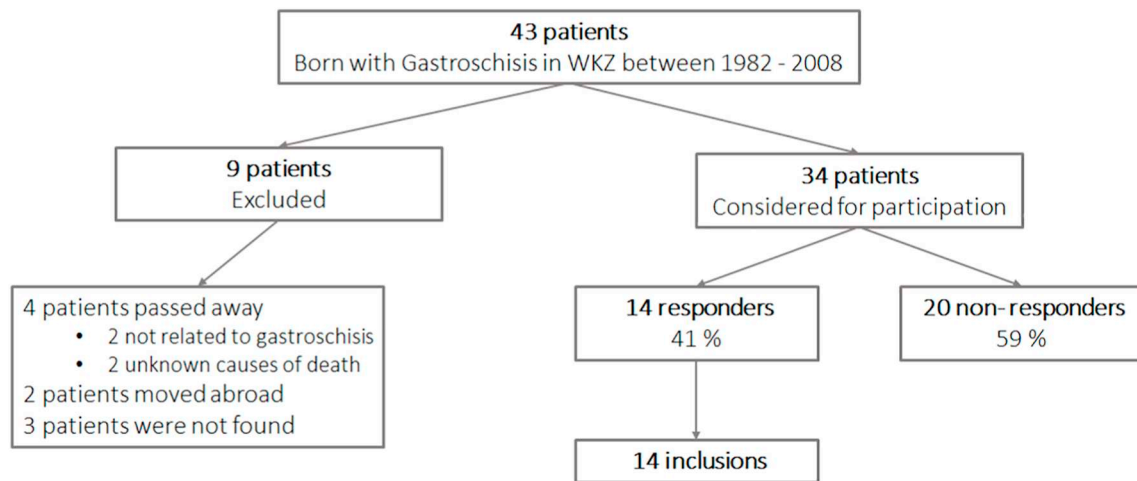


Fig. 1. Flowchart of inclusions.

Table 1
Baseline characteristics of responders and non-responders.

	Responders n = 14	Non-responders n = 23
Age (mean, SD)	18.0 (8.0)	19.0 (6.1)
Age (n, %)		
Children (8–12 years old)	5 (35.7)	3 (13.0)
Teens (13–17 years old)	4 (28.6)	7 (30.4)
Young adults (18–25 years old)	1 (7.1)	8 (34.8)
Adults (> 25 years old)	4 (28.6)	5 (21.7)
Gender (n,%)		
Male	6 (42.9)	14 (60.9)
Female	8 (57.1)	9 (39.1)
Gestational age (mean, SD)	255.2 (2.5)	251.9 (3.2)
Prematurity (n,%)		
Yes	10 (71.4)	14 (60.9)
No	4 (28.6)	8 (34.8)
Unknown	0	1 (4.3)
Surgery (n,%)		
Primary closure	7 (50.0)	11 (47.8)
Silo	6 (42.9)	11 (47.8)
Patch	0	1 (4.3)
Unknown	1 (7.1)	0
Number of surgical corrections (n, %)		
1	7 (50.0)	9 (39.1)
2	6 (42.9)	9 (39.1)
3–5	1 (7.1)	2 (8.7)
> 5	0	3 (13.0)
Complication after surgery (n, %)		
Yes	5 (35.7)	13 (56.5)
No	9 (64.3)	10 (43.5)
Days of TPN (mean, SD)	9 (5)	19 (14)
Discharge with enteral feeding (n, %)		
Yes	11 (78.6)	20 (87.0)
No	2 (14.3)	1 (4.3)
Unknown	1 (7.1)	2 (8.7)

Categorical data and scores were presented as numbers and percentages (n,%). Means were presented as mean \pm standard deviation (SD) or as mean \pm 95% confidence interval (CI). Medians were presented as median \pm interquartile range (IQR). Fisher's exact tests and independent sample *t*-tests were used where appropriate. An alpha of 0.05 was considered significant. There were no missing data.

3. Results

3.1. Patient characteristics

In total, 43 patients had been treated at the Wilhelmina Children's Hospital for gastroschisis. Of these patients, two patients emigrated, and three patients could not be tracked (Fig. 1). Four patients were deceased, of which two causes of death were not related to gastroschisis and two causes of death were unknown. Thirty-four patients were considered for participation and twenty patients did not respond. Fourteen patients responded and were included in the study. The mean age of the participants was 18 years. Patient characteristics of both responders and non-responders are shown in Table 1.

3.2. GI function

3.2.1. Bowel symptoms

One patient experienced abdominal pain and 5 patients (36%) experienced symptoms of gas bloat (Table 2a). Three patients (21%) had difficulties with completing meals and one patient (7%) experienced abdominal pain after meals. Patients with complications during gastroschisis treatment had more abdominal symptoms as compared to patients with an uncomplicated treatment course (80% versus 22% respectively). There was no relation between feeding methods in the neonatal period (the amount of days on TPN and the feeding method at discharge) and the reported bowel symptoms.

3.2.2. Reflux symptoms

Six patients (43%) reported reflux symptoms (Table 2b). Sixty percent of the patients with complications during gastroschisis treatment (per example ileus or reoperation) experienced reflux symptoms, whereas only 33% of the patients without complications had reflux symptoms ($p = .60$).

3.3. Growth

The mean z-score for weight-for-length was 1.16 (95% CI 0.16–1.58) in adult patients and -0.63 (95% CI -1.15 – -0.20) in children (Table 3). The mean z-score for height-for-age was -0.82 (95% CI

Table 2a
GI symptoms.

n = 14	< 1/week	1 ×/week	2–3 days a week	4–6 days a week	Daily
Abdominal pain (n,%)	12 (85.7)	1 (7.1)	0	0	1 (7.1)
Gas bloat (n,%)	9 (64.3)	1 (7.1)	2 (14.3)	1 (7.1)	1 (7.1)
Difficulties with completing a meal (n,%)	11 (78.6)	1 (7.1)	1 (7.1)	0	1 (7.1)
GI complaints after meal (n,%)	13 (92.9)	0	0	0	1 (7.1)

Table 2b

RDQ score.

Reflux symptoms (n, %)	n = 14
None	8 (57.1)
Mild	5 (35.7)
Moderate	1 (7.1)
Severe	0

Higher scores indicate more symptoms.

Table 3
Growth.

	n = 14
Mean weight-for-length z-score	
Children (95%, CI)	−0.63 (−1.15, 0.20)
Adults (95%, CI)	1.16 (0.16, 1.58)
Mean height-for-age z-score	
Children (95%, CI)	−0.16 (−1.07, 0.76)
	−0.82 (−1.89, 0.25)

−1.89–0.25) in adults and −0.16 (95% CI −1.07–0.76) in children, which indicates a low mean length and a high mean BMI in adult gastroschisis patients. The length and BMI for premature and full-term patients were similar.

3.4. Quality of life

The mean score for physical functioning was significantly higher for children (8–12 years) after gastroschisis correction compared to healthy controls (98 vs 85, $p = .002$) (Fig. 2a–c). In teenagers (13–17 years) and adults after gastroschisis correction, physical functioning was significantly lower compared to healthy controls (70 vs 87, $p = .002$, 73 vs 89, $p = 0.025$). Emotional functioning was significantly lower in children after gastroschisis correction (62 vs 77, $p = .023$) compared to healthy controls. No significant differences were found in the other age groups. Social functioning showed no significant differences between patients after gastroschisis correction and healthy controls. School functioning was significantly lower in children after gastroschisis correction compared to healthy controls (56 vs 79, $p < .001$). No significant differences were found in school or work functioning in the other two age groups. The overall HRQoL was significantly lower in teenagers after gastroschisis correction as compared to healthy controls (73 vs 83, $p = .04$). There were no significant differences in overall HRQoL in the other two age groups. There was no association between complications during gastroschisis treatment and reported HRQoL. As only one young adult (18–25 years) was included in this study, this age group was excluded from the analysis on HRQoL.

3.5. Cosmetic result

Seven patients (50%) were satisfied with the cosmetic result and five patients (36%) were not satisfied with the cosmetic result of the scar (Table 4). Cosmetic satisfaction with the scar seems associated with satisfaction with the overall appearance of the abdomen, as twelve patients (86%) reported equal satisfaction for cosmetic result of the scar and overall appearance of the abdomen. Males seemed less satisfied with the cosmetic result of the scar and the overall appearance of the abdomen; however, this was not statistically significant. There was a difference in cosmetic satisfaction after the different surgical procedures, as 57% of the patients with primary closure was satisfied about the cosmetic result and only 33% of the patients with secondary closure was satisfied.

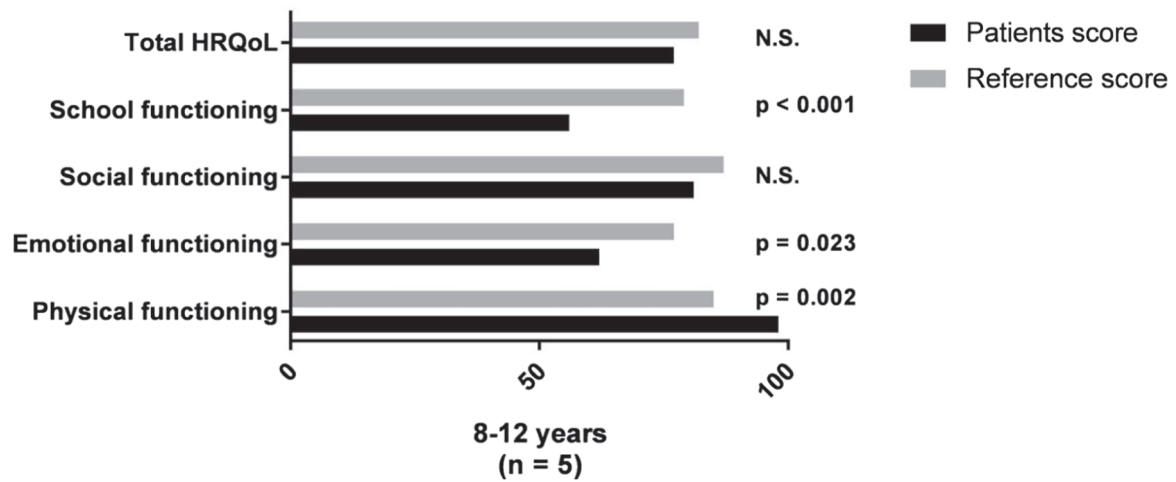
4. Discussion

This study suggests that only a small portion of the gastroschisis patients experienced GI problems at adolescent or adult age. Gastroschisis patients seem to have a normal height and weight at adult age. The overall health related quality of life may be equal for gastroschisis patients as compared to healthy controls and gastroschisis patients seem satisfied with the cosmetic result of the gastroschisis surgery.

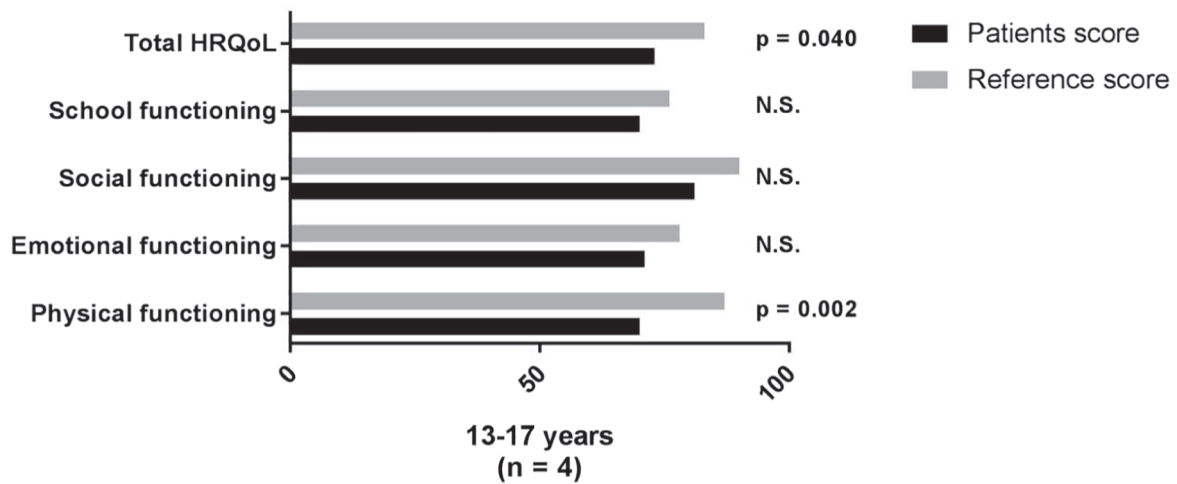
Similar to our findings, Swartz et al. reported no residual bowel symptoms in gastroschisis patients at adolescent age [2]. Harris et al. studied abdominal pain in gastroschisis patients at young age and showed that 41% of their fifty participants reported abdominal pain on a weekly basis [3]. This difference can be explained by the higher age in our study sample. Our study found that very few patients had trouble with completing a meal or GI complaints after a meal. This is in line with the results of Harris et al. Marseglia et al. found that there is an increased incidence of GER in gastroschisis patients at young age [4]. The results of our study indicate that this does not apply to adolescent and adult patients, as only one patient experienced moderate reflux symptoms. Our study is the first to evaluate gastrointestinal function, HRQoL and cosmetic satisfaction in gastroschisis patients at adolescent and adult age. This could explain the differences in the existing evidence and the results of this study, as there were no earlier studies with this long-term follow-up.

Frybova et al. found that gastroschisis patients follow a normal growth curve at young age [8]. As this study found that gastroschisis patients have a normal height when grown up, it confirms the hypothesis that growth of gastroschisis patients catches up at higher age. However, this study found that adult patients with a history of gastroschisis have a significantly higher BMI as compared to reference values corrected for age. This could be explained by social status, as this has a strong inverse relationship with obesity [20,21]. Gastroschisis patients have below average socio-economic status, which predisposes

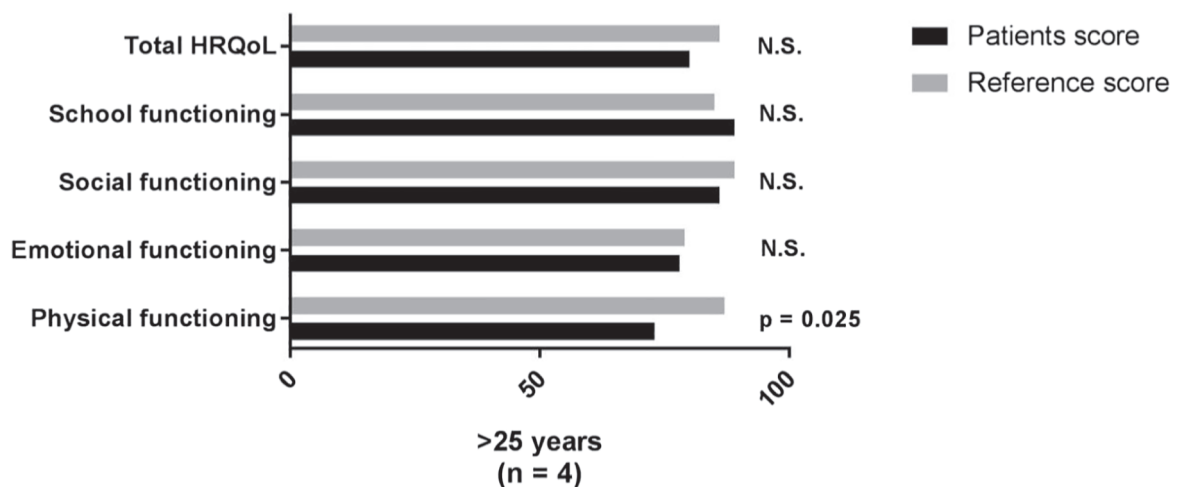
a HRQoL 8-12 years



b HRQoL 13-17 years



c HRQoL >25 years



(caption on next page)

Fig. 2. a. HRQoL 8–12 years.
b. HRQoL 13–17 years.
c. HRQoL > 25 years.

Table 4

Cosmetic satisfaction.

n = 14 Females n = 8 Males n = 6	Not satisfied	Minimal satisfaction	Satisfied
Cosmetic satisfaction of operational scar (n,%)	5 (35.7)	2 (14.3)	7 (50)
Females	2 (25)	2 (25)	4 (50)
Males	3 (50)	0	3 (50)
Overall satisfaction of the appearance of the abdomen (n,%)	5 (35.7)	2 (14.3)	7 (50)
Females	2 (25)	1 (12.5)	5 (62.5)
Males	3 (50)	1 (16.7)	2 (33.3)

for developing overweight and obesity [22,23].

Earlier studies have shown no significant differences in QoL outcomes in gastroschisis patients at long-term follow-up [8–12]. This study confirms this, as most patients reported equal HRQoL as compared to healthy controls of the same age. HRQoL regarding school and emotional functioning was reported lower in children (8–12 years) after gastroschisis. However, teenagers and adults after gastroschisis function on the same level as healthy controls in school or work. This could indicate that time and education diminishes the adverse consequence of gastroschisis and its treatment on this aspects.

Previous studies have reported good cosmetic results in gastroschisis patients up until 10 years old, as 80–92% of the patients and parents were satisfied with the cosmetic result after gastroschisis repair [8,15]. This study found different results for adolescent and adult patients, as only half of the patients was satisfied with the cosmetic end result after gastroschisis repair. Cosmetic satisfaction with the scar was directly related to satisfaction with the overall appearance of the abdomen. This illustrates the importance of this outcome regarding self-confidence about physical appearance. There was a considerable difference in cosmetic satisfaction between the different surgical methods, suggesting more favorable results after primary closure. As we included only a small study population, more extensive research on cosmetic outcomes after different closing techniques is recommended.

There are several important limitations in our study. The first limitation is the small study population, as gastroschisis is a rare disorder

Appendix A

A.1. Questionnaire cosmetic results

A.1.1. How satisfied are you about the scar of the gastroschisis surgery?

- Not satisfied.
 A little satisfied.
 Satisfied.
 Very satisfied.

A.1.2. How satisfied are you about the overall appearance of your abdomen?

- Not satisfied.
 A little satisfied.
 Satisfied.
 Very satisfied

and the population of gastroschisis patients in this hospital is small. Another limitation is the low response rate (41%). This could have initiated selection bias, as patient characteristics from responders can differ from patient characteristics of non-responders. Non-responders underwent more surgical procedures and had more complications after surgery (Table 1). This may have caused underreporting of clinical symptoms, as it seems that more complicated cases of gastroschisis were less likely to respond to the survey. If these persons were included, it could have resulted in poorer GI outcomes and HRQoL. Furthermore, it is striking that only one out of nine young adults (18–25 years) responded to the survey. This causes a hiatus in the results for this age group. The small response rate in this age group can be explained by the survey mode, as it is known that young adults are less likely to respond to a mailed survey and prefer online surveys [22]. A possible explanation for the small response rate in all age groups is intelligence and social status of the patients, as it is known that gastroschisis patients often have a lower intelligence and socio-economic status compared to the average population [23,24].

5. Conclusion

This study found that gastroschisis patients experience few GI problems at adolescent or adult age, though patients with complications during gastroschisis treatment are more likely to develop abdominal complaints later in life. Adolescents and adults with a history of gastroschisis experience a HRQoL that is comparable to healthy persons. Only half of the patients is satisfied with the scar and the overall appearance of the abdomen. The surgical closing method had no significant influence on the long-term cosmetic results. As the numbers in this study are small, multicenter studies on the topic are warranted.

Financial disclosure

The authors have no financial relationship relevant to this article to disclose.

Declaration of competing interest

The authors have no conflicts of interest to disclose

Appendix B. PedsQL™ score

	8–12 years n = 5		13–17 years n = 4		18–25 years n = 1		> 25 years n = 4		
	Patients	Reference value [18] p-Value	Parents ^a	Patients	Reference value [18] p-Value	Patients	Reference value [19] p-Value	Patients	Reference value [19] p-Value
Physical functioning ^b (mean, 95% CI)	98 (94.28–100)	85.25 (84.00–86.51) 0.002	99 (1)	70 (4.76–100)	86.76 (85.26–88.26) 0.002	97	90.20 (88.81–91.59)	73 (44.36–100)	88.68 (86.77–90.59) 0.025
Emotional functioning (mean, 95% CI)	62 (19.78–100)	76.85 (74.89–78.81) 0.023	57 (33)	71 (34.40–100)	77.53 (75.09–79.97) N.S.	100	78.42 (76.44–80.40)	78 (58.91–97.09)	78.74 (76.36–81.12) N.S.
Social functioning (mean, 95% CI)	81 (57.41–100)	86.51 (84.77–88.25) N.S.	78 (20)	81 (31.67–100)	90.14 (88.29–92.00) N.S.	95	88.44 (86.91–89.97)	86 (68.50–100)	89.31 (87.54–91.08) N.S.
School functioning (mean, 95% CI)	56 (32.41–79.60)	78.88 (77.19–80.57) < 0.001	56 (20)	70 (38.18–100)	75.95 (73.89–78.01) N.S.	90	83.95 (82.36–85.54)	89 (71.50–100)	84.98 (82.95–87.00) N.S.
Total HRQoL (mean, 95% CI)	77 (59.62–94.38)	82.31 (81.05–83.57) N.S.	76 (15)	73 (25.26–100)	83.14 (81.68–84.60) 0.040	96	85.90 (84.65–87.15)	80 (60.91–99.09)	85.85 (84.20–87.50) N.S.

^a Parent scores were not included in the analysis.

^b Scores 0–100; higher scores indicate better HRQoL.

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