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Quality of life outcomes in children born with duodenal atresia

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ABSTRACT

Purpose: The aim of this study was to determine long term quality of life (QoL) outcome for children who underwent surgery for duodenal atresia (DA).
Methods: Patients were identified from a prospective database of neonatal DA cases managed at a tertiary pediatric surgical centre. The QoL was measured using the validated PedsQL™ 4.0 core score and PedsQL™ gastrointestinal module; higher score equates to better QoL. Participants' scores were compared to published control cohorts, age-matching the core score. Trisomy 21 was identified a priori as a possible confounder, informing subgroup analyses for children with and without trisomy 21.
Results: Fifty-five families were invited to participate, with 38 surveys returned (39% male; median age 6.7y, range 2.7–17.3y). Seven participants had trisomy 21. There were no differences in QoL measures between all DA participants and controls. The PedsQL™ core score was significantly lower for DA participants with trisomy 21, but there was no accompanying difference in PedsQL™ gastrointestinal score.
Conclusions: Children undergoing DA surgery in the neonatal period typically grow up to have a QoL comparable to a healthy population. Children with DA and trisomy 21 were more likely to have reduced overall QoL, albeit without an associated difference in gastrointestinal QoL score.
Level of Evidence: Prognosis study – level II (prospective cohort study).

Duodenal atresia (DA) is a congenital abnormality of the duodenum with an incidence of 0.9 to 1.2 per 10,000 live births [1, 2]. Surgical repair of DA has been recognized as the mainstay of treatment since the introduction of the duodenojejunostomy [3] and duodenoduodenostomy [4] for successful surgical repair in the early and mid-1900s. DA has a well-recognized association with trisomy 21 (T21), with approximately 4% of T21 patients also having DA [5], whilst approximately 30% of DA patients are found to have T21 [2, 6].

Post-operative morbidity and prolonged hospitalization in neonates with DA has been attributed to associated anomalies, prematurity and low birth weight [7]. Late complications recognized in children undergoing surgical repair of DA include duodenal motility disorders, adhesive bowel obstruction and gastro-esophageal reflux disease [6, 7]. Although the morbidity and mortality associated with DA has been studied [7–9], the quality of life (QoL) of children born with DA after surgical management in early life has not been quantitated.

The aim of our study is to assess the QoL in children who underwent surgery duodenal atresia. Our primary outcome is to assess their QoL compared to a healthy cohort of children. Our secondary outcomes were to evaluate the QoL of children as rated by children compared to their parents, and to determine if there were other patient characteristics, such as type of duodenal atresia, had an impact on QoL.

1. Methods

1.1. Database

We have established an ethics-approved (#DB077) clinical database for all children managed with operatively confirmed DA at The Royal Children's Hospital, Melbourne since July 2000. This database includes information on demographics, antenatal history, delivery, postnatal case, associated anomalies, morphological type of DA, and operative details, including procedure performed and post-operative care.

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1.2. Quality of life outcome questionnaires

The Pediatric Quality of Life Inventory (PedsQL™) questionnaires are a collection of validated surveys that can be used to assess the quality of life of children with and without a breadth of medical conditions. The surveys have different versions that target different age groups but cover the same key themes but adjust their language and relevant activities to match the developmental age of the child. The PedsQL™ 4.0 core score is used to assess global quality of life and covers four domains: physical, emotional, social and school functioning. The first domain forms a physical subscale score, and the remaining domains form a psychosocial subscale score. For toddlers aged 2 to 4 years there is only a parent questionnaire containing 21 items. For the older age groups: young children (ages 5 to 7 years), children (ages 8 to 12 years) and teens (ages 13 to 17 years), there is an additional and separate questionnaire for the child to complete, with 23 items covering the same four domains. Irrespective of who completes the questionnaire, all questionnaires report on the child's quality of life.

The PedsQL™ gastrointestinal (GI) module is similar, in that there is only one parent questionnaire for toddlers aged 2 to 4 years, and a parent and child questionnaire for the other age brackets. However, each questionnaire contains 74 items over 14 domains covering a breadth of gastrointestinal symptoms the participant or parent may have encountered over the last 1 month.

Responses to the items in both questionnaires are given a score of 0 to 4. Items are then reverse scored and linearly transformed to give a score of 0 to 100. The PedsQL™ 4.0 physical and psychosocial subscale scores were similarly scored to give a result of 0 to 100. In both tools, a higher score equates to a better quality of life.

1.3. Survey Collection

DA patients 2 years or older as at the commencement of the study (May 30, 2018) were identified from the database, and their parents invited to participate. In accordance with local ethics committee recommendation, patients who had not visited our health service in the 5 years prior were first sent a tracing letter. Patients' families who responded to the tracing letter with current contact details, or who had been seen by our health services in the last 5 years, were then invited to participate and sent a PedsQL™ 4.0 generic core scale and PedsQL™ GI module questionnaire appropriate for the patient's age. Surveys were returned by provided, postage-paid envelopes. If no questionnaire was returned within 4 weeks of receipt, two attempts were then made to contact the parents via phone to return the survey or complete the survey over the phone.

1.4. Data analysis

Data presented is the results of the parental surveys, and are presented as means, median and standard deviations, unless otherwise stated. The results of the PedsQL™ scores were compared to published control groups [10, 11] using t-tests, with the core scores age matched. We could not identify any studies using the PedsQL™ score to examine quality of life in children with T21, thus we were unable to use a specific T21 only control cohort for this subgroup of patients. Matched parent and child results on the PedsQL™ scores were compared using Wilcoxin signed rank test. Categorical variables were compared using Fisher's exact test and numerical values were compared with Mann–Whitney U Test. Correlation between continuous variables were analyzed using regression analysis and quantitative variables between three or more categorical groups were compared using one-way analysis of variance (ANOVA).

In recognition of T21 as a possible confounder of QoL outcomes, a priori determined subgroup analyses were performed comparing healthy controls and DA participants with or without T21. Further, drop-out analysis was performed to address potential bias or differences between DA cases participating in the study and those not participating. Data were analyzed using SPSS Version 25.0 (Armonk, NY: IBM Corp); p value <0.05 was considered statistically significant for all tests.

1.5. Ethical considerations

Ethical approval for this study was obtained from The Royal Children's Hospital Human Research Ethics Committee (HREC 38054A).

2. Results

2.1. Participant characteristics

We identified 110 potential participants in our database who met our inclusion criteria. However of these, 12 children were deceased and 43 families were either not contactable by the tracing letter or had letters returned as not-deliverable. Thus, 55 families were contacted and invited to participate. Of these, 38 returned completed survey questionnaires, which correlates to a response rate of 69% (38/55). Twenty three children with DA were aged 5 years or older, and their families received *both* a parent *and* child survey questionnaires. Seventeen families returned the additional child survey questionnaire. Of the remaining six families who did not return additional child survey, five had children with DA and T21.

Median age at the time of the study was 6.7 years (2.7 to 17.3) and 39% were male. Further population type including type of DA, operation performed (including anastomosis type for cases managed by duodenoduodenostomy), incidence of T21 and other associated anomalies are displayed in Table 1.

Drop-out analysis to assess for possible bias between our participants (n = 38) and non-participants (n = 72) is also summarized in Table 1. The median age in the participant group (median = 6.7y) was a significantly younger than the non-participant group (median = 10.0y, U = 896, p = 0.02). Otherwise, there were no significant differences between our participant and non-participant groups with respect to morphological type of DA, operation performed, VACTERL association, CHARGE syndrome, cardiac abnormalities or genetic anomalies, including T21.

Table 1
Patient characteristics of duodenal atresia.

Characteristic	Participants (n = 38)	Non-participants (n = 72)
Age in years		
Median (range)	6.7 (2.7–17.3)	10.0 (2.5–17.9)
Sex, n (%)		
Male	15 (39)	39 (54)
Female	23 (61)	33 (46)
Type of DA, n (%)		
Type I	16 (42)	40 (56)
Type II	2 (5)	2 (3)
Type III	17 (45)	27 (38)
Not recorded	3 (8)	3 (4)
Operation, n (%)		
Duodenoplasty	5 (13)	8 (11)
Duodenoduonostomy	33 (87)	64 (89)
Diamond	26 (68)	50 (69)
Side-by-side	2 (5)	7 (10)
End-to-end	5 (13)	4 (6)
Not recorded	0 (0)	3 (4)
Additional anomalies, n (%)		
VACTERL (3+)	1 (3)	7 (10)
CHARGE	1 (3)	0 (0)
Cardiac		
Minor	10 (26)	17 (24)
Major	6 (16)	8 (11)
Genetic		
None	20 (53)	42 (58)
T21	7 (18)	14 (19)
Other	4 (11)	3 (4)
Not tested	7 (18)	14 (19)

2.2. Primary outcomes

Results of the PedsQL™ scores are summarized in Table 2. Overall, our results demonstrate that children undergoing surgical repair of DA as neonates have a similar quality of life compared to age-matched published controls [10] as measured by the PedsQL™ core score. On subgroup analysis however, participants with DA and T21 scored significantly lower than the control group ($p = 0.03$). This is likely due to participants with T21 scoring significantly lower than the control group in the social subscore ($p < 0.01$); Table 2. Gastrointestinal symptoms, as scored by the PedsQL™ GI score, were similar between our participants with DA and healthy controls [11] ($p = 0.35$). Further, in contrast to the core scores, subgroup analyses comparing PedsQL™ GI score in DA participants with or without T21 and the control group did not reveal any significant differences; Table 2.

2.3. Secondary outcomes

There was no difference between the parent reported and the child reported quality of life measured by the PedsQL™ core scores ($Z = 0.804$, $p = 0.421$). However, measuring gastrointestinal symptoms using the PedsQL™ GI score, parents reported fewer concerns and symptoms than their children (median = 93.2 vs 88.9, $Z = 2.05$, $p = 0.036$).

Age was not a significant factor in determining predicting a participants PedsQL™ core score ($r_s = -0.15$, $p = 0.36$) or PedsQL™ GI score ($r_s = -0.18$, $p = 0.28$). Similarly, morphological type of DA was not predictive of a participant's PedsQL™ core score ($F(2, 33) = 0.55$, $p = 0.59$) or of their PedsQL™ GI score ($F(2, 32) = 0.39$, $p = 0.68$).

3. Discussion

Despite requiring hospitalization and operative management early in life, this study shows children managed for DA have an overall QoL comparable with age-matched healthy controls. Furthermore, this positive outcome for DA patients is also seen when considering GI specific QoL parameters. The long term clinical outcomes of DA have been retrospectively examined [6], however, there is no published QoL data for patients with DA. This prospective QoL study offers new and positive insights into the long-term prognosis of this neonatal condition.

DA is among a number of surgical neonatal conditions for which survivors show QoL outcomes comparable with healthy controls. Neonatal conditions such as congenital diaphragmatic hernia, Hirschsprung Disease (HD), gastroschisis, omphalocele and esophageal atresia all have similar QoL outcomes to healthy children, as measured by the PedsQL™ generic core scores [12–15]. This is in contrast to neonatal conditions such as necrotizing enterocolitis, for which survivors do show worse QoL outcomes than heathy children [14]. When compared to children with chronic childhood gastrointestinal illnesses (both functional and organic), who score lower on PedsQL™ GI module as compared to healthy controls, children who have undergone surgery for DA have similar PedsQL™ GI module scores to healthy children [11, 16]. These findings will inform parent counseling by clinicians as to the expected long-term recovery of GI function in children with surgically-repaired DA.

In our study, age was not a predictive factor in determining QoL scores. However, in some congenital surgical conditions, such as HD, a downtrend in PedsQL™ core scores with age has been reported [12]. This distinction is likely related to the timing, and upper GI (DA) vs lower GI (HD) symptom implications of these two congenital conditions. Complications of DA surgical repair are likely to be maximal in the early postoperative course, i.e. neonatal period, and most likely within the index admission. Thereafter, long-term complications such as gastro-esophageal reflux are unlikely to worsen or gain renewed QoL importance with advancing age. This is in contrast to HD, where toilet training in the toddler years, constipation (or indeed fecal incontinence) in the early school years and psychosocial development while managing abnormal bowel habits in the later school years, each have explicable and negative effects on the QoL scores [12].

Our participants with T21 and DA had a significantly lower PedsQL™ core score compared to healthy controls, in distinction to the normal QoL for DA participants without T21. This T21-specific reduction in QoL was not evenly distributed in all domains, being limited to core score and social score, but not demonstrated in the PedsQL™ GI module. The normal GI symptom scores in children with both DA and T21, suggest that the QoL impairment otherwise evident in this subgroup may not be directly attributable to DA. The impact of T21 or QoL is however important in our patient group, and further assists clinicians and other healthcare professionals which patients and families may be in greatest need of support. For this reason, we consider future studies that examine the general QoL in congenital gastrointestinal conditions with a higher incidence of T21, e.g. HD, anorectal malformations and esophageal atresia, should undertake planned subanalysis of participants with T21 to address this as potential confounding factor biasing their results.

Prospectively collecting the clinical data in our study ensured we had almost complete data sets for all DA patients approached for inclusion in this study. However, in a small number of cases, the operation records did not specify DA morphological type and/or the specific type of anastomosis performed (i.e. diamond, side-by-side or end-to-end). Despite this potential limitation, our drop-out analysis of study participants and non-participants confirmed no difference in type of DA, comorbidities or type of surgery between the participants and non-participants. Given this consistency, disease-related factors do not appear to have influenced participation in this study. This notwithstanding, the participation or non-response bias may yet limit the applicability of our results, where families whose children have poor outcomes may consequently disengage from the opportunity to participate in such research. It could also be argued, that families of children with poor outcomes may seek out participation to make clear their child's plight, and so participation bias is not a given.

In conclusion, this study shows that children undergoing surgical repair of DA in early life typically have comparable QoL outcomes with

Table 2
Total PedsQL™ 4.0 Generic Core Scale and subscores, and PedsQL GIT module scores, for all participants (n = 38) with subanalysis of those with (n = 7) and without (n = 31) trisomy 21.

	Participants	Control	p-Value
PedsQL™, *mean (SD)*			
Overall	80.8 (19.5)	83.1 (14.7)	0.45
T21	62.6 (21.5)	82.8 (14.7)	**0.03**
Non-T21	84.9 (16.8)	86.5 (14.8)	0.59
Physical, *mean (SD)*			
Overall	85.6 (21.9)	85.0 (18.8)	0.86
T21	67.4 (30.2)	84.3 (18.8)	0.16
Non-T21	89.7 (17.7)	85.1 (18.9)	0.16
Psychosocial*, *mean (SD)*			
Overall	78.0 (19.7)	82.0 (14.6)	0.22
T21	60.6 (20.8)	81.8 (14.6)	**0.03**
Non-T21	82.0 (17.5)	82.1 (14.6)	0.98
Emotional, *mean (SD)*			
Overall	76.2 (20.4)	81.5 (16.2)	0.11
T21	72.9 (20.6)	81.2 (16.1)	0.29
Non-T21	76.9 (20.6)	81.6 (16.5)	0.22
Social, *mean (SD)*			
Overall	78.0 (26.9)	84.0 (18.8)	0.18
T21	46.3 (28.2)	84.3 (18.8)	<**0.01**
Non-T21	85.2 (21.2)	83.9 (18.4)	0.75
School, *mean (SD)*			
Overall	78.6 (24.4)	80.4 (18.5)	0.66
T21	56.4 (32.5)	80.1 (18.4)	0.11
Non-T21	83.9 (19.1)	80.5 (18.6)	0.39
Gastrointestinal Module, *mean (SD)*			
Overall	87.6 (15.6)	90.0 (12.7)	0.35
T21	84.2 (46.6)	90.0 (12.7)	0.37
Non-T21	88.3 (15.7)	90.0 (12.7)	0.57

* The psychosocial subscore is the average of all the items in the emotional, social and school subscores.

their healthy peers. Those children with T21 as well as DA represent an important subgroup, whose long-term needs may differ from other DA patients, even if not as a result of DA-related outcomes per se. Our study is the first to address such questions of QoL and specific gastrointestinal symptom QoL outcomes in DA patients utilizing validated PedsQL™ tools. The findings from this study may assist pediatric surgeons and other healthcare professionals, and improve the nature and relevance of counseling for families of children with DA when discussing long term outcomes, especially for those facing the challenges of both DA and T21.

Ethics

This study was approved by the Royal Children's Hospital (Melbourne) Human Research Ethics Committee (HREC 38054A).

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Disclosure

The authors have no conflicts of interest to declare.

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