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ORIGINAL ARTICLE

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Oesophageal atresia: what has changed in the last 3 decades?

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Abstract The aim of the study was to analyse the outcomes of children born with oesophageal atresia over the last 3 decades. The records of 104 patients born between 1973 and 1999 were reviewed retrospectively. To evaluate changes over time, the analysis was done for three consecutive time periods: 1973–79, 1980–89, and 1990–99. Mean birth weight was 2553 g (SD 640), and mean gestational age was 39 weeks (SD 4). Forty-two newborns (40%) had one or more associated congenital malformations, and 30% had associated cardiac malformations. There was no change in incidence of associated anomalies over the three time periods studied. Mortality of patients decreased from 33% to 14% ($p = 0.048$). There was a significant association between the presence of a major cardiac malformation and survival (survival: 88% vs. 57%, $p = 0.004$). Analysing the three different time periods separately reveals that cardiac disease was not a significant risk factor in the first period but became significant in the period from 1980–99 (relative risk: 6.76, 95% CI 1.44–31.77). Birth weight was significantly higher in infants who survived (2626 g, SD 642) compared with those who died (2290, SD 570, $p = 0.028$). This effect, however, is mainly based on the difference during the first period and is lost later. Early and late postoperative complications occurred in 44/102 patients. Strictures developed in 33/91 patients who survived the first month of life (33%). The rate of symptomatic strictures decreased significantly over the three time periods, from 50% to 23% ($p = 0.022$). In summary, this study shows no significant change in patient characteristics over the last 3 decades, but mortality and postoperative complication rates decreased, and associated cardiac anomalies became the far most important risk factor for mortality.

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Introduction

Since the first correction of an oesophageal atresia more than 50 years ago, many things have changed in regard to treatment and outcome. Over the decades, the overall survival rate has steadily improved because of advances in surgical techniques and in preoperative and postoperative medical care [5,8]. In addition, some studies also showed a change in patient characteristics [3,4]. The purposes of this study were to review these changes in characteristics and management of patients born with oesophageal atresia and the impact of these changes on mortality and postoperative results. To do this, we analysed the data from a series of infants with oesophageal atresia treated in our institution since 1973.

Patients and methods

The case records of all infants with oesophageal atresia and/or tracheo-oesophageal fistula admitted to the University Children's Hospital in Bern between November 1973 and December 1999 were reviewed. Data recorded included birth weight, duration of pregnancy, presence of cardiac defects and other associated anomalies (VACTERL association), surgical interventions, complications, and outcome. A major cardiac anomaly was defined as either cyanotic congenital heart disease that required surgery or noncyanotic congenital heart disease that required medical or surgical treatment for cardiac failure. This definition excluded patent ductus arteriosus unless it required surgical ligation. A diagnosis of VACTERL syndrome was made if three or more components of the association were present.

To critically evaluate changes over time, the patients were analysed over three consecutive time periods: 1973–1979, 1980–1989, and 1990–1999. Statistical analysis was

performed using a commercial statistics package (StatView 4.0, Abacus Concepts, Berkeley, CA, USA). For continuous data, differences between groups were assessed using an unpaired student's *t*-test or one-way analysis of variance (ANOVA). Chi-square analysis was employed for categorical data. Instead of odds ratio, relative risk was calculated because the outcome of interest was not considered rare. Differences were considered significant at a probability level of $p < 0.05$.

Results

Patient characteristics

During the 27-year period, 104 patients were treated for oesophageal atresia. Mean followup was 12 years (SD 9). The mean birth weight was 2553 g (SD 640), and seven patients (7%) had a birth weight < 1500 g. The mean gestational age was 39 weeks (SD 4), with 28 patients (27%) having a gestational age < 37 weeks. Table 1 shows the distribution of the types of atresia. Over the three time periods, mean birth weight or mean gestational age did not change significantly (Table 2).

Comorbidity

Forty-two newborns (40%) had one or more associated congenital malformations: vertebral malforation in 11 patients, anorectal in five, cardiac in 30, renal in 10, limb in four, duodenal atresia in two, and chromosomal abnormalities in seven. There was no increase in associated malformations over the observed time period. The percentage of associated cardiac malformations was 30% and remained stable as well (Table 2). A VACTERL association was diagnosed in 13/104 patients (13%).

Table 1 Types of atresia in 104 patients from 1973–1999 (*OA* oesophageal atresia, *TOF* tracheo-oesophageal fistula)

Type	1973–1979	1980–1989	1990–1999	Total
	n (%)	*n* (%)	*n* (%)	*n* (%)
OA and distal TOF	34 (87)	27 (93)	25 (70)	86 (86)
OA and proximal TOF	–	–	2 (6)	2 (2)
OA and proximal and distal TOF	2 (5)	1 (3)	3 (8)	6 (6)
OA without TOF	1 (3)	1 (3)	4 (11)	6 (6)
H-type TOF	2 (5)	–	2 (6)	4 (4)

Operations

Simple fistula ligation was performed in all four children with an H-type fistula. A primary anastomosis was performed in 84/94 (91%) patients with atresia and fistula, a delayed primary repair in three (3%) patients, and a staged repair in four (4%) patients. Two patients with trisomy 18 did not undergo operation, and in one patient with a massive intracerebral haemorrhage, only a gastrostomy was performed. Six neonates had pure oesophageal atresia without tracheo-oesophageal fistula. Of these, five patients underwent colonic interposition, and one patient had gastric transposition. In regard to operative management, there were no gross changes during the observed 3 decades.

Outcome

Overall mortality was 22% (22/104). Mortality decreased significantly from 31% in period 1, between 1973 and 1979, to 14% in period 2, and remained stable thereafter (Table 3). There was a significant association between the presence of a major cardiac malformation and survival (survival without vs. with cardiac malformations: 88% vs. 57%, $p = 0.004$) but not with the presence of VACTERL syndrome and survival ($p = 0.36$). The relative mortality risk for major cardiac disease was 3.57 (95% CI 1.69–7.5). Analysing the three different time periods separately reveals that cardiac disease was not a significant risk factor in the period from 1973–1979 (relative risk: 2.63, 95% CI 0.24–6.13), whereas the relative mortality risk for major cardiac malformations was significantly increased in the period from 1980–1999 (6.76, 95% CI 1.44–31.77). This finding reflects the fact that in the 1970s, death in the neonatal period was very often related to respiratory failure, sepsis/multiorgan failure, or both (7/13 neonates who died), in contrast to the period from 1980–1999, when no neonate in this study died due to these sorts of problems. From 1980–1999, 2/9 deaths occurred owing to trisomy 18 (no operation), one to massive perinatal ventricular haemorrhage, and one to sudden infant death (trisomy 21). All others were associated with major cardiac

Table 2 Patient characteristics

Variable	1973–1979 ($n = 39$)	1980–1989 ($n = 29$)	1990–1999 ($n = 36$)	All patients ($n = 104$)	p
	n (SD or %)	*n* (SD or %)	*n* (SD or %)	*n* (SD or %)	1973–1979 vs. 1990–1999
Gestational age	39 (4)	39 (3)	38 (4)	39 (4)	0.648
Birth weight	2590 (597)	2688 (577)	2409 (715)	2553 (640)	0.24
Associated anomalies	15 (38%)	14 (48%)	13 (36%)	42 (40%)	0.94
Major cardiac defects	12 (31%)	7 (24%)	11 (31%)	30 (29%)	0.98
Chromosomal abnormalities	2 (5%)	2 (7%)	3 (8%)	7 (7%)	0.66

Table 3 Outcomes 1973–1999 (*TOF* tracheo-oesophageal fistula)

Variable	1973–1979 ($n = 39$)	1980–1989 ($n = 29$)	1990–1999 ($n = 36$)	Total ($n = 104$)	p
	n (%)	n (%)	n (%)	n (%)	1973–1979 vs. 1990–1999
Mortality	13 (33%)	4 (14%)	5 (14%)	22 (22%)	0.048
Anastomotic leak	2 (5%)	2 (7%)	3 (8%)	7 (7%)	0.57
Stricture requiring dilatation[a]	15/30 (50%)	10/26 (38%)	8/35 (23%)	33/91 (36%)	0.022
No. dilatations per patient (range)	3.5 (1–9)	3.6 (1–9)	3.8 (1–14)	3.6 (1–14)	0.87
Recurrent TOF	5 (17%)	1 (4%)	1 (3%)	7 (7%)	0.055
Fundoplication	10 (26%)	5 (17%)	5 (14%)	20 (19%)	0.41

[a]Patients surviving the 1st month of life

Table 4 Survival related to birth weight (*BW*) and major congenital heart disease (*CHD*) (1980–1999, $n = 65$)

Group		n	Mortality	Survival rate (%)
I	BW >= 1500 g and no major CHD	44	3	93
II	BW <1500 g or major CHD	19	5	74
III	BW <1500 g and major CHD	2	1	50

anomalies; in 2/5, the anomalies were in combination with trisomy 21.

Birth weight was significantly higher in infants who survived (2626 g, SD 642) compared with those who died (2290, SD 570, $p = 0.028$). This effect, however, is mainly based on the difference during the period from 1973–1979 (2732 g, SD 577, vs. 2327, SD 562, $p = 0.047$, mean difference 404 g), analysing the last period between 1990 and 1999 separately, the difference did not reach significance (2452 g, SD 706, vs. 2142 g, SD 794, $p = 0.15$, mean difference 310 g). Overall, gestational age was significantly greater in infants who survived compared with those who died (39 weeks, SD 3, vs. 37 weeks, SD 4, $p = 0.035$). From 1990–1999, however, the difference was not significant (38 weeks, SD 4, vs. 37 weeks, SD 5, $p = 0.60$).

Outcomes of children between 1980 and 1999 with respect to Spitz's classification are shown in Table 4. The three patients in group 1 died of trisomy 18, massive perinatal ventricular haemorrhage, and sudden infant death at the age of 3 months.

Early and late postoperative complications occurred in 44/102 patients (Table 3). An anastomotic leak (symptomatic or observed on routine postoperative oesophagography) was reported in seven patients (7%). Two of these patients developed a recurrent fistula that required a second intervention. The incidence of anastomotic leaks did not change over time. Spontaneous resolution of the leak was observed in 5/7 patients. There were no strictures as a consequence of an anastomotic leak. Recurrent fistulas developed in a total of seven patients (7%), with a relevant decrease in incidence over the last decades. Strictures occurred in 33/91 patients who survived the first month of life (33%). The strictures were successfully treated by dilatations in all but two patients, in whom a resection of the stricture was necessary. Strictures resolved after one or two dilatations in 19 patients (58%); in 14 patients more than two sessions were needed. The mean number of dilatations performed was 3.6 (range 1–14) per patient. The number of patients who had to undergo dilatations because of strictures decreased significantly over the three time periods, from 50% to 23% (Table 3). Either a primary or secondary Nissen fundoplication was performed in 20 patients (20%; primary, 7; secondary, 13). A re-do fundoplication was necessary in one patient. No aortopexy was performed.

Comment

The mortality of patients studied decreased from 33% to 14% since 1973. In recent years there was a strong association between mortality and major cardiac anomalies. Postoperative complications such as stricture formation and recurrent tracheo-oesophageal fistulas decreased significantly over the studied time period. The percentage of children born with associated anomalies did not change over time.

Several risk factors are well established for adverse outcome after correction for oesophageal atresia, including birth weight and the presence of associated anomalies [11, 12, 13]. There is some evidence that the risk profile of children born with oesophageal atresia (that is, the expression or incidence of these risk factors) has changed over time. Deruloo et al. reported a decrease in mean gestational age and birth weight of patients born with oesophageal atresia over the last 5 decades [3]. In addition, they reported an increased rate of associated anomalies, a finding confirmed by Driver et al. [4]. Our patients treated nowadays are born earlier and weigh less than those treated 30 years ago, too; however, the difference did not reach significance. This might be due to the smaller number of patients. But in contrast to the previously mentioned studies [3, 4], we found no increase in the frequency of associated

malformations over the last 3 decades in our population. The percentage of children with any type of associated malformation, as well as the percentage of children with cardiac defect as the only associated malformation, did not change over the observed period. Therefore, we can assume that the risk profile of the patients treated today is not much different from that of the patients treated at the beginning of the study period.

In regard to mortality, two things changed. First, as reported by other authors [3, 5, 8, 10, 11], mortality decreased drastically. Second, there is some evidence that the predictors for adverse outcome changed, with cardiac anomalies becoming the most important risk factor [2, 3, 7, 11]. This change seems to be mainly due to improved preoperative and postoperative care. Between 1973 and 1979, more than half of the patients died in the first 30 days of life due to respiratory failure, sepsis/multiorgan failure, or both. Since that time, only one patient who underwent corrective surgery died during the neonatal period, in this case as a consequence of major cardiac defects. Improvements in neonatal intensive care have contributed to an increased survival rate of even very premature, high-risk infants, thereby attenuating the influence of gestational age and birth weight on outcome. In our study population, the mean differences in birth weight and gestational age between neonates who survived and those who did not decreased from 404 g and 1.6 weeks in the first period to 310 g and 1 week in the last period. The fact that birth weight might not be a powerful predictor is underlined by findings of a large recent study that did not show a difference in survival in patients with birth weights <1500 g when compared with patients with birth weights >1500 g [2]. In the Montreal experience, birth weight did not affect survival, either [12].

The relevance of associated cardiac malformations as a risk factor for mortality, however, gained more and more importance in our study population over the years. This observation is in accordance with several other reports [2, 3, 7] and was one of the reasons for Spitz et al. to propose a new classification for predicting outcome [11]. In the 1970s, associated cardiac anomalies were not a significant risk factor for mortality, whereas from 1990–1999, the relative mortality risk was more than six times higher in patients with associated cardiac disease. In the last decade, death was associated with major cardiac defects in all but one patient, who had trisomy 18. Other associated malformations such as the VACTERL association had no impact on mortality. Of interest is the fact that none of the patients with trisomy 21 survived. Although the small number of patients with Down syndrome precludes definite conclusions, it might indicate that outcomes in children with associated trisomy 21 are different from those without trisomy 21, a finding also observed by others [1, 2].

Not only improvements in intensive care management but also improvements in surgical skills led to a significant decrease in postoperative complications in the study patients over the last 3 decades. Whether this is due to a more delicate tissue handling, to improved suture material, or to other surgical factors cannot be established. In any case, the incidence of recurrent fistula formation and the formation of symptomatic strictures necessitating dilatations decreased significantly. In the 1970s, 50% of patients needed one or more dilatations because of anastomotic stricture formation, compared with only 23% in the last decade. The mean number of dilatations per patient remained unchanged. In more than half of the patients, strictures resolved after one or two dilatations. The low incidence of stricture formation and the fact that more than half of the patients needed not more than one or two dilatations may call into question the usefulness of routine dilatations after oesophageal atresia repair, an observation confirmed by a recent study [6]. For unknown reasons, the number of anastomotic leaks did not change and remained between 5% and 8% in the three periods observed. As reported elsewhere, there was no association between anastomotic leaks and stricture formation [9]. None of our patients with an anastomotic leak developed a symptomatic stricture on followup.

In summary, this study shows no significant change in patient characteristics over the last 3 decades. Mortality rates and postoperative complication rates decreased, and associated cardiac anomalies became the far most important risk factor for mortality in children born with oesophageal atresia.

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