Motor-function and exercise capacity in children with major anatomical congenital anomalies: An evaluation at 5 years of age

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ABSTRACT

Background
Children with major anatomical congenital anomalies (CA) often need prolonged hospitalization with surgical interventions in the neonatal period and thereafter. Better intensive care treatment has reduced mortality rates, but at the cost of more morbidity.

Aim
To study motor-function and exercise capacity in five-year-old children born with CA, and to determine whether motor-function and exercise capacity differ according to primary diagnosis.

Study design
Descriptive study.

Subjects
One hundred and two children with the following CA: congenital diaphragmatic hernia (CDH) n = 24, esophageal atresia (EA) n = 29, small intestinal anomalies (SIA) n = 25, and abdominal wall defects (AWD) n = 24.

Outcome measures
Overall and subtest percentile scores of the Movement Assessment Battery for Children (MABC) were used to measure motor skills. Endurance time on the Bruce treadmill test was used to determine maximal exercise capacity.

Results
Motor-function: Seventy-three children (71.6%) had an overall percentile score within the normal range, 18 (17.6%) were classified as borderline, and 11 (10.8%) had a motor problem. This distribution was different from that in the reference population (Chi-square: p = 0.001). Most problems were encountered in children with CDH and EA (p = 0.001 and 0.013, respectively). Ball skills and balance were most affected.
Exercise capacity: Mean standard deviation score (SDS) endurance time = -0.5 (SD: 1.3); p = 0.001; due to poor exercise performance in CDH and EA patients.

Conclusions
Children with major anatomical CA and especially those with CDH and EA are at risk for delayed motor-function and disturbed exercise capacity.

INTRODUCTION

Annually some 5,500 newborns (about 3% of all births) in the Netherlands present with major anatomical congenital anomalies (CA).[1] Children with major anatomical CA often need prolonged hospitalization with (multiple) surgical interventions in the neonatal period and thereafter. Better intensive care treatment has reduced mortality rates, but at the cost of more morbidity. It is therefore that the department of Pediatric Surgery of our tertiary hospital started in 1999 a multidisciplinary follow-up program for children born with CA and their families.[2] The aim of the program is to evaluate and to reduce the overall morbidity associated with the malformations of the children. Within this follow-up program, children with CA are tested at fixed time points. We have recently shown that children with major CA suffer from psychomotor developmental delay within the first two years of life.[2] And, a recent evaluation of persistent respiratory morbidity in children born with esophageal atresia (EA) and congenital diaphragmatic hernia (CDH) revealed disturbed exercise capacity in 5-year-old-survivors.[3] Further standardized assessment of motor-function and exercise capacity in school-aged children with major CA other than cardiac malformations has hardly been published.[4,5] Early identification of children with motor impairments however, is important to provide support and intervention for the child as early as necessary, since motor problems do not disappear spontaneously.[6]

The aim of the present study was to determine whether 5-year-old children with different major CA are at risk for impaired motor-function and reduced exercise capacity, and to determine whether motor-function and exercise capacity differ according to primary diagnosis. We evaluated four different groups of CA patients: children born with CDH, EA, small intestinal anomalies (SIA), and abdominal wall defects (AWD).

METHODS

Participants

Between January 1999 and December 2003, 204 newborns with CDH, EA, SIA or AWD were admitted to our pediatric surgical intensive care unit within seven days of birth. As twenty-six of these babies died (CDH n = 14; EA n = 5; SIA n = 5; AWD n = 2), 178 were eligible for follow-up. The parents of 35 children declined to participate. By the age of five years, 15 children had not been assessed for logistic reasons. Twenty-six children were not testable and thus excluded from analysis: 19 with syndromal or chromosomal disorders (CDH n = 3; EA n = 4; SIA n = 10; AWD n = 2), six with neurological impairments (CDH n = 2; EA n = 1; SIA n = 1; AWD n = 2), and one child (with AWD) with behavior problems. Finally, 102 of 178 eligible children (57.3%) participated in this study (Figure 1). The Medical Ethical Review Board approved the follow-up program, and written parental informed consent was obtained.

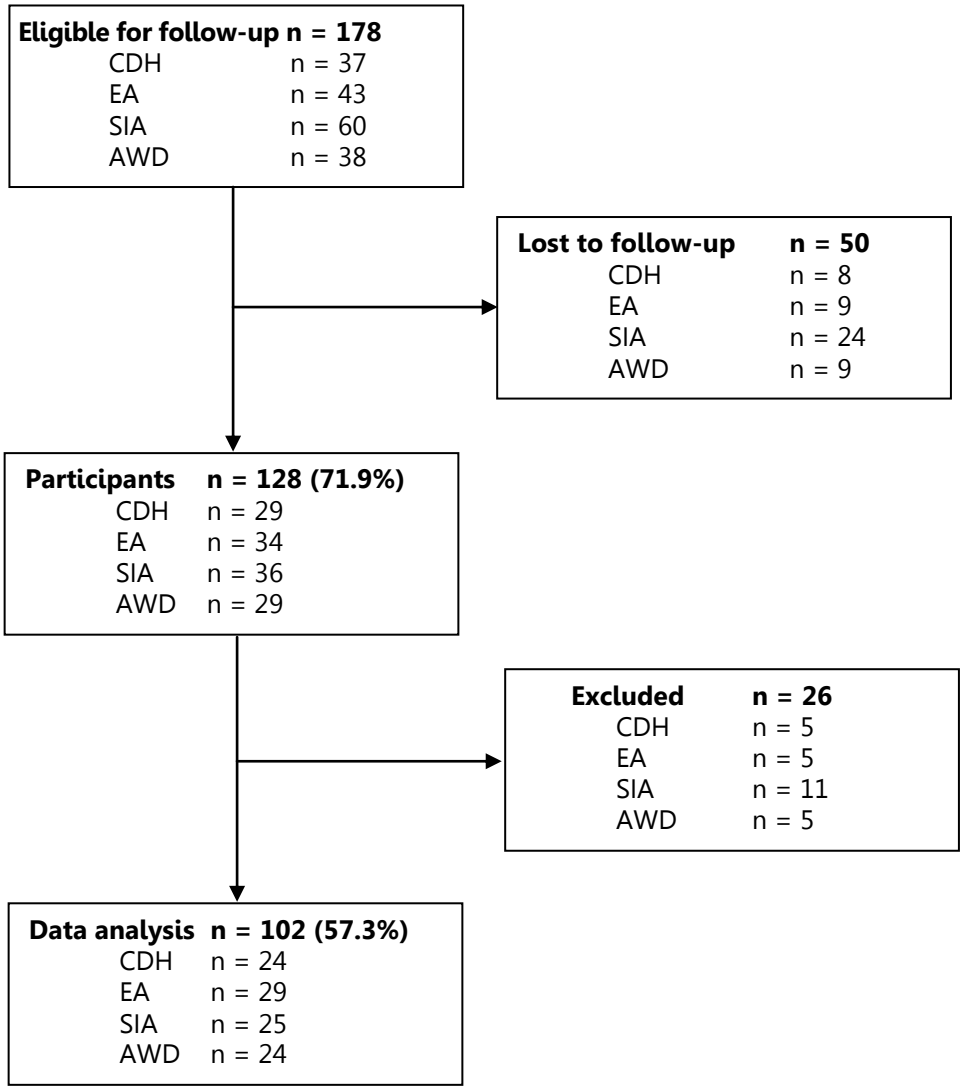

Figure 1 *flow chart*

Procedure

General

Since 1999, the multidisciplinary team has prospectively performed follow-up for neonates with major CA treated in the pediatric surgical department at our tertiary children's hospital. The following data were collected prospectively: gestational age, birth weight, major CA, duration of artificial ventilation, number and duration of hospital admissions, and number of surgical interventions. Small for gestational age (SGA) was defined as birth weight < -2SD for gestational age. These baseline data were also retrieved for 50 children who were lost to follow-up. Major chromosomal, syndromal and cerebral abnormalities were routinely evaluated. From the medical records we retrieved data on results of cerebral ultrasound examinations and MR-imaging of the brain.

By protocol the children were seen at ages 6, 12 and 24 months, corrected for gestational age, and at 5 years.[2] The evaluation at age 5 years refers to evaluation between 5 and 6.5 years of age (mean age 5.7 years). A pediatrician performed a physical examination, including neurological examination and measurement of height and weight. Previously published data on growth for the Dutch population[7,8] served as reference values, and we calculated standard deviation scores (SDS) for height, weight, and body mass index (BMI) using Growth Analyzer version 3.5 (Dutch Growth Foundation). The existence of visual impairment, physical abnormalities interfering with motor-function, and treatment by physiotherapist was recorded.

Motor-function assessment

The MABC was used to evaluate the children's motor skills. The test evaluates motor-function in daily life and is suitable for children without neurological impairments who can understand and act on instructions. A Dutch standardization study has shown that the original norm scores and cut off points can also be applied to Dutch children.[9] Good validity and reliability have been demonstrated.[10] Because all children were younger than 7 years tasks from age band I (4 - 6 years) were used. The MABC consists of eight items: three manual dexterity items; two ball-skill items; and three balance items. Scores for each item were provided; these ranged from good (0) to very poor (5). A profile of the child's motor performance for each domain of the test was obtained by summing the relevant item scores. Summation of all item scores produces the total impairment score (TIS). The three subtest scores and the TIS can be interpreted using age-related normative data tables. The range between the 100th and 16th percentile is regarded as "normal"; between the 15th to 6th percentile as "borderline". The 5th percentile and below is regarded as a "definite motor problem".[9,11] All tests were administered by an experienced pediatric physiotherapist.

Exercise capacity

The children performed a graded, maximum exercise test using a motor-driven treadmill (En Mill, Enraf Nonius, Rotterdam, the Netherlands) programmed for increases in angle of inclination and speed according to the Bruce protocol.[12,13] The children were encouraged to perform to voluntary exhaustion. The maximal endurance time (in minutes, one decimal) served as criterion of exercise capacity. Before and during the test heart rate and transcutaneous oxygen saturation were monitored with a pulse Oximeter (motion artifact system, type 2001, Respironics Novametrics, Murrysville, PA, USA). Maximal performance was indicated by a HR of ≥ 185 beats per minute (bpm) or loss of coordination.[14] The SDS of the maximal endurance time was calculated using recently age-related established reference values for healthy Dutch children.[12,13]

Statistical analysis

Unless stated otherwise, data are presented as mean (SD). One-sample t-tests were used to test whether the SDS of growth parameters and the maximal endurance time were different from those of the norm population. Non-parametric tests were used to perform group comparisons. A Chi-square test was applied to test whether the distribution of motor performance scores in our population differed significantly from that in the normative population. Spearman Rank correlation coefficients (r_s) were calculated to evaluate the association between motor performance scores on the one hand and baseline variables, and growth data on the other hand. The Kruskal Wallis test was used to measure group differences. Statistical significance was accepted at a 5% level. Analyses were performed using SPSS 15.0.

RESULTS

Cerebral ultrasound examinations performed within the first weeks of life were abnormal in 4 patients: hyperdense lesions reflecting perinatal asphyxia were seen in 2 CDH and 1 SIA patient and 1 EA patient had benign hydrocephalus. In addition, another EA patient had signs of delayed myelinisation on MRI at 4 months. Baseline characteristics for participants are shown in Table 1. From the 10 children with cardiac malformation 4 needed cardiac surgical intervention (coarctation of the aorta n = 3 (2 of them with additional septal defects); atrial septal defect n = 1). The other 6 patients with septal defects (n = 4) and mild coarctation of the aorta (n = 2) were not operated on.

Participating CDH patients were hospitalized longer in the first 6 months after birth and had more hospital admissions between 6 and 24 months ($p = 0.002$ and $p = 0.037$ respectively) than children who were lost to follow-up. Participating children had more often Dutch parents than the children in the missing group ($p < 0.001$). All other baseline characteristics in participants and missing patients were not significantly different (data not shown).

The characteristics at age 5 are presented in Table 2. Two patients suffered from seizures after the neonatal period; subsequent MR-imaging of the brain was normal. Prior to the evaluation of motor skills, a pediatrician performed a physical examination, including neurological examination. Six children were found to have minor neurological dysfunction, varying from mild mental retardation (n = 3), amyotrophic shoulder neuralgia (n = 1), and mild hypotony (n = 1).

Table 1 *Baseline characteristics*

	CDH	**EA**	**SIA**	**AWD**
	n = 24	n = 29	n = 25	n = 24
Boys, n (%)	13 (54.2)	16 (66.7)	13 (52.0)	10(41.7)
Gestational age, wk	39.4 (36 - 41.4)	38.4 (28.6 - 42.0)	36.9 (29.6 - 41.7)	38 (33.6 - 41.9)
Birth weight, kg	3.2 (1.8 - 4.0)	2.9 (0.8 - 4.5)	2.8 (1.6 - 3.6)	2.5 (2.1 - 4.4)
SGA, n (%)	0 (0)	4 (13.8)	0 (0)	4 (16.7)
Patients with ≥ 1 additional major CA, n (%)	5 (20.8)	9 (31.0)	4 (16.0)	6 (25.0)
Dutch parents, n (%)	21 (87.5)	26 (89.7)	23 (92.0)	22 (91.7)
Cardiac malformation, n (%)	1 (4.2)	4 (13.8)	4 (16.0)	1 (4.2)
Ventilatory support, days*	21 (2 - 62)	3 (1 - 44)	2 (0 - 18)	2 (0 - 192)
Hospital admission first 6 months, days	53.5 (14 - 167)	50 (11 - 168)	29 (6 - 184)	33 (7 - 182)
Hospital admission between 6 and 24 months, days	1 (0 - 31)	3 (0 - 93)	0 (0 - 23)	0 (0 - 29)
Hospital admission 24 months to 5 years*, days	0 (0 - 18)	0 (0 - 31)	0 (0)	0 (0 - 47)
Surgical interventions in 24 months*	3 (1 - 7)	6 (1 - 18)	2 (1 - 5)	1.5 (1 - 6)
ECMO, n (%)*	11 (45.8)	0 (0)	0 (0)	0 (0)

Presented are the baseline characteristics of the group of 102 children available for analysis
SGA = small for gestational age; ECMO = extracorporeal membrane oxygenation; Data are presented as number (%) of patients or median (range);
** p < 0.01 Kruskal Wallis (differences between groups)*

Table 2 *Characteristics of the study group at 5 years of age*

	CDH	EA	SIA	AWD
	n = 24	n = 29	n = 25	n = 24
Age in years	5.7 (0.4)	5.9 (0.5)	5.9 (0.4)	5.6 (0.3)
Weight SD score[#]	-1.3 (1.0)*	-0.5 (0.9)*	-0.6 (1.0)*	-1.0 (1.3)*
Height SD score	-0.8 (1.4)[§]	-0.6 (1.1)*	-0.3 (1.1)	-0.8 (1.2)*
BMI SD score[†]	-1.2 (0.8)*	-0.2 (0.9)	-0.4 (0.9)[§]	-0.6 (1.0)*
Physiotherapy at age 5, n (%)	3 (12.5)	7 (24.1)	4 (16.0)	0 (0)

Data are presented as number (%) of patients or mean (SD)
[#] *p < 0.05 Kruskal Wallis (differences between groups)*
* *p < 0.01 one sample t-test (SDS significant below zero)*
[§] *p < 0.05 one sample t-test (SDS significant below zero)*
[†] *p < 0.01 Kruskal Wallis (differences between groups)*

All 102 children were tested using the MABC (Table 3 and Figure 2). Seventy-three children (71.6% vs 85.0% expected) had a TIS within the normal range, eighteen children (17.6% vs 10.0% expected) were classified as borderline, and another eleven (10.8% vs 5.0% expected) as having a motor problem. This distribution is significantly different from reference values (Chi square p = 0.001). The six children with neurological impairments due to cerebral palsy were excluded and not tested. When added to the eleven children with a percentile score representing a definite motor problem, 17 of 108 (15.7%) had a definite motor problem.

Most problems were encountered with ball skills (Chi square p < 0.001) and balance (Chi square p < 0.001) but not with manual dexterity. TIS of the children with CDH and EA differed significantly from the reference population (p = 0.001 and 0.013, respectively). Ball skills were impaired in CDH and EA patients; children with EA also had problems with balance (Figure 2).

Maximal exercise performance data were analyzed for 82 (80.4%) children because 20 children did not reach maximal performance according to our pre-defined criteria (CDH n = 2, EA n = 7, SIA n = 6, AWD n = 5). Overall, these 82 children performed worse than the reference population: mean SDS endurance time = -0.49; p = 0.001, due to poor maximal exercise performance in CDH and EA patients (Table 3).

The percentile score on the MABC correlated negatively with the total number of major CA (r_s = -0.27, p = 0.007), and positively with the SDS of the maximal endurance time (r_s = 0.33; p = 0.002). A significant negative correlation was also found with duration of hospitalization and number of surgical interventions (r_s = -0.29; p = 0.003 and r_s = -0.27; p = 0.006). No significant correlation was found between the MABC score and growth parameters.

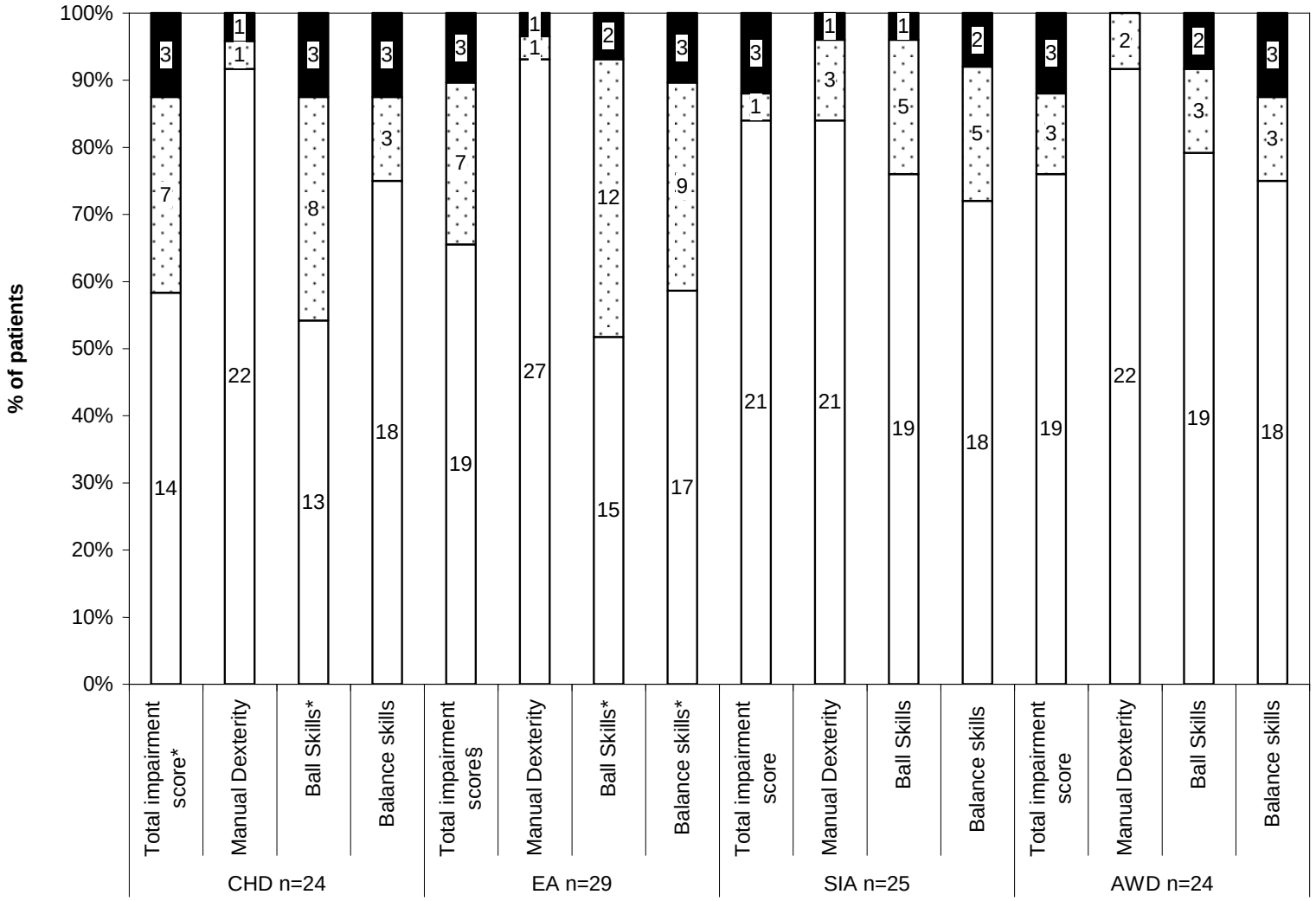

Figure 2 *MABC scores for different groups; For each group TIS and sub-scores are shown.*
Normal range (> P 15, open bar); Borderline range (P 6 - P 15, stippled bar); Definitive motor problem (≤ P 5, black bar)
** p < 0.01 chi square (difference from norm values)*
§ p < 0.05 chi square (difference from norm values)

Table 3 *Overall results of motor-function performance and maximal exercise capacity*

	CDH	EA	SIA	AWD	Total
	n = 24	n = 29	n = 25	n = 24	n = 102
MABC overall percentile score, n (%)					
≥ P 16 normal	14 (58.3)*	19 (65.5)†	21 (84.0)	19 (79.2)	73 (71.6)*
P 6-P 15 borderline	7 (29.2)	7 (24.1)	1 (4.0)	3 (12.5)	18 (17.6)
≤ P 5 motor problem	3 (12.5)	3 (10.3)	3 (12.0)	2 (8.3)	11 (10.8)
Bruce SDS endurance time, mean (SD)§	(n = 22) -0.9 (1.3)#	(n = 22) -0.8 (1.1)#	(n = 19) 0.2 (1.3)	(n = 19) -0.3 (1.3)	(n = 82) -0.5 (1.3)#
Advise pediatric physiotherapy at home, n (%)	5 (20.8)	8 (27.6)	4 (16.0)	1 (4.2)	18 (17.6)

** Chi Square: p < 0.01 (comparison to the percentage expected)*
† Chi Square: p < 0.05 (comparison to the percentage expected)
§ Kruskal Wallis: p < 0.05 (difference between groups)
 # One sample Test : p < 0.01 (SDS significant below zero)

Only one EA-patient with a ventricular septal defect was classified as having a definite motor problem, the other nine children with cardiac malformations performed within the normal range.

Fourteen of the 102 tested children (13.7%) received pediatric physiotherapy (CDH n = 3, EA n = 7, SIA n = 4). Seven of them scored < P5, one between P5 and P15, and the other six scored within normal range. For 18 patients it was thought advisable to start (n = 6) or to continue (n = 12) pediatric physiotherapy at home. These 18 children scored significantly worse on the MABC than did the other 84 children ($p < 0.001$).

DISCUSSION

This study describes standardized motor-function assessment and assessment of exercise capacity in 5-year-old children born with major anatomical congenital anomalies (CA). Motor-function was found normal for 73 of the 102 tested children (71.6%). This proportion is significantly lower than expected from the normative scores. We identified differences in the sub-scores of the MABC depending on primary diagnosis. Children with EA have more problems with ball skills and balance; those with CDH have problems with ball skills. The higher the number of additional congenital anomalies, the greater the impairment of motor-function performance is. Exercise capacity was analyzed in 82 children; they performed worse than expected on the basis of normative scores. Poor performance in CDH and EA patients was responsible for this outcome.

We excluded patients with syndromal abnormalities, and those with neurological impairment. Although neurological evaluation did not reveal serious problems in the

remaining study population and cerebral ultrasound examination within the first months showed slight abnormalities in the minority of patients (n = 4), minor neurological dysfunction with clumsy motor behavior may be present and explain –at least to some extent– our results. Children with major anatomical CA are at risk for several perinatal risk factors reported to be associated with minor neurological dysfunction: intrauterine growth retardation, mild to moderate perinatal asphyxia, and prenatal stress resulting from psychological stress of the mother.[15]

Holm et al[4] showed that eight-year-olds born with a complex congenital heart disease have lower MABC TIS and sub-scores than their healthy age- and sex-matched controls. The proportion of children with cardiac malformations in our study was low, and the majority of these malformations were not complex. This may explain that we found higher scores than in Holm's paper.

Next to TIS and sub-test scores of the MABC, maximal exercise performance was also assessed. Maximal exercise capacity was impaired in patients with CDH and EA. This is in line with previous studies by Zaccara et al. in CDH patients and in patients who were operated for tracheoesophageal fistulas.[16,17] Several authors have reported on the relationship between exercise capacity and motor competence. Haga et al.[18] established exercise capacity in 9- and 10-year-old children, showing a significant correlation between the TIS of the MABC and exercise capacity. This may be explained by physical activity levels; exercise capacity results from the degree and intensity of a child's physical activity over time.[19] In the same vein, one can also argue that motor competence is a consequence of the level of physical activity, e.g. the more time spent practicing motor skills, the more opportunity there is for better motor performance. We assume that CDH and EA patients, with high respiratory and gastrointestinal morbidity during the first years, get little physical activity and have few opportunities to practice gross motor skills. This may explain the lower percentile scores in these groups, and the differences in motor-function profiles (poorer ball skills and balance, but good performance at manual dexterity). As their physical activity is lower and their gross motor-function is impaired they are at risk for decreased maximal exercise tolerance. And, in a study of Majaesic et al., especially children with CDH, and those treated with ECMO had poor pulmonary outcome at 8 years of age. These authors assume that respiratory morbidity impairs maximal exercise tolerance.[20] Most children with SIA and AWD have few problems beyond the first few months of life,[21] and may have more opportunities for physical activity and hence for improving motor competence. In addition, undetectable neurological damage, perhaps secondary to minor neurovascular problems during surgery or veno-arterial ECMO-treatment cannot be ruled out. This assumption is supported by the fact that EA patients underwent the highest number of surgical interventions and only CDH patients were treated with ECMO.

Another factor that may contribute to decreased physical activity is parental reluctance to stimulate their child too much of fear for physical problems. CDH and EA patients both suffer from pulmonary morbidity and respiratory distress may easily occur after physical activity. Holm and Bjarnason[4,5] reported a similar parental protection in children with cardiac malformations.

A limitation of our study is that in this single centre study, per subgroup, the number of subjects studied was small, which makes it difficult to draw hard conclusions. Comparison of baseline characteristics of patients who were lost to follow-up with the participants revealed that only for CDH patients a possible selection bias might have occurred because participants were hospitalized longer. However, there were no differences regarding the need for extracorporeal membrane oxygenation (ECMO) and duration of ventilatory support. Other possible limitations are the lacking of more detailed neurological examination focused on minor coordination and balance dysfunctions, and a potential selection bias because of the fact that more children of non-Dutch origin were lost to follow-up. However, in children with CA motor-function development up till 2 years was not influenced by ethnic origin.[2]

Early identification of children at risk for developmental motor problems is very important. Predictive models as recently presented for preterms may be of great interest.[22] Studies in children born prematurely have shown that assessment of motor development by a pediatrician alone is insufficient and that standardized tests are needed.[23] Since motor problems do not disappear spontaneously[6] and may be associated with learning disabilities and behavioral problems[15] long-term multidisciplinary follow-up and adequate intervention when necessary are important. The use of validated standardized assessment instruments is of great help in this respect.

In addition, adequate and repeated instructions about positive effects of physical activity may help parents to be less overprotective.

CONCLUSION

Children with CA are at risk for delayed motor-function performance and exercise capacity, especially those with CDH and EA and those with additional anomalies associated with longer hospitalizations and multiple surgical interventions.

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REFERENCES

1. Anthony S, Schönbeck Y, Jacobusse GW, van der Pal-de Bruin KM. Aangeboren afwijkingen in Nederland 1996-2004. Leiden: TNO kwaliteit van leven, 2006.
2. Gischler SJ, Mazer P, Duivenvoorden HJ, van Dijk M, Bax NM, Hazebroek FW, et al. Interdisciplinary structural follow-up of surgical newborns: a prospective evaluation. J Pediatr Surg, 2009;44:1382-1389.
3. Gischler SJ, van der Cammen-van Zijp MH, Mazer P, Madern GC, Bax NM, de Jongste JC, et al. A prospective comparative evaluation of persistent respiratory morbidity in esophageal atresia and congenital diaphragmatic hernia survivors. J Pediatr Surg, 2009;44:1683-1690.
4. Holm I, Fredriksen PM, Fosdahl MA, Olstad M, Vollestad N. Impaired motor competence in school-aged children with complex congenital heart disease. Arch Pediatr Adolesc Med, 2007;161:945-950.
5. Bjarnason-Wehrens B, Dordel S, Schickendantz S, Krumm C, Bott D, Sreeram N, et al. Motor development in children with congenital cardiac diseases compared to their healthy peers. Cardiol Young, 2007;17:487-498.
6. Pless M, Carlsson M, Sundelin C, Persson K. Preschool children with developmental coordination disorder: a short-term follow-up of motor status at seven to eight years of age. Acta Paediatr, 2002;91:521-528.
7. Fredriks AM, van Buuren S, Burgmeijer RJ, Meulmeester JF, Beuker RJ, Brugman E, et al. Continuing positive secular growth change in The Netherlands 1955-1997. Pediatr Res, 2000;47:316-323.
8. Fredriks AM, van Buuren S, Wit JM, Verloove-Vanhorick SP. Body index measurements in 1996-1997 compared with 1980. Arch Dis Child, 2000;82:107-112.
9. Smits-Engelsman BCM. Dutch manual Movement Assessment Battery for Children. Lisse: Swets en Zeitlinger, 1998.
10. Smits-Engelsman BC, Fiers MJ, Henderson SE, Henderson L. Interrater reliability of the Movement Assessment Battery for Children. Phys Ther, 2008;88:286-294.
11. Henderson SE, Sugden DA. The Movement Assessment Battery for Children: manual. The Psychological Corporation, 1992.
12. van der Cammen-van Zijp MH, IJsselstijn H, Takken T, Willemsen SP, Tibboel D, Stam HJ, et al. Exercise testing of pre-school children using the Bruce treadmill protocol: new reference values. Eur J Appl Physiol, 2010;108:393-399.
13. van der Cammen-van Zijp MH, van den Berg-Emons RJ, Willemsen SP, Stam HJ, Tibboel D, IJsselstijn H. Exercise capacity in Dutch children: new reference values for the Bruce treadmill protocol. Scand J Med Sci Sports, 2010;20:e130-e136.
14. Karila C, de Blic J, Waernessyckle S, Benoist MR, Scheinmann P. Cardiopulmonary exercise testing in children: an individualized protocol for workload increase. Chest, 2001;120:81-87.
15. Hadders-Algra M. Developmental coordination disorder: is clumsy motor behavior caused by a lesion of the brain at early age? Neural Plast, 2003;10:39-50.
16. Zaccara A, Felici F, Turchetta A, Calzolari A, Lucchetti MC, Rivosecchi M, et al. Physical fitness testing in children operated on for tracheoesophageal fistula. J Pediatr Surg, 1995;30:1334-1337.
17. Zaccara A, Turchetta A, Calzolari A, Iacobelli B, Nahom A, Lucchetti MC, et al. Maximal oxygen consumption and stress performance in children operated on for congenital diaphragmatic hernia. J Pediatr Surg, 1996;31:1092-1094.
18. Haga M, Pedersen AV, Sigmundsson H. Interrelationship among selected measures of motor skills. Child Care Health Dev, 2008;34:245-248.
19. Blair SN, Cheng Y, Holder JS. Is physical activity or physical fitness more important in defining health benefits? Medicine and science in sports and exercise, 2001;33:S379-399.

20. Majaesic CM, Jones R, Dinu IA, Montgomery MD, Sauve RS, Robertson CM. Clinical correlations and pulmonary function at 8 years of age after severe neonatal respiratory failure. Pediatr Pulmonol, 2007;42:829-837.

21. Lindham S. Long-term results in children with omphalocele and gastroschisis-a follow-up study. Z Kinderchir, 1984;39:164-167.

22. Janssen AJ, Nijhuis-van der Sanden MW, Akkermans RP, Tissingh J, Oostendorp RA, Kollee LA. A model to predict motor performance in preterm infants at 5 years. Early Hum Dev, 2009;85:599-604.

23. de Kleine MJ, den Ouden AL, Kollee LA, Nijhuis-van der Sanden MW, Sondaar M, van Kessel-Feddema BJ, et al. Development and evaluation of a follow-up assessment of preterm infants at 5 years of age. Arch Dis Child, 2003;88:870-875.