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Factors affecting short-term neurodevelopmental outcome in children operated on for major congenital anomalies

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ABSTRACT

Purpose: Identify clinical and socio-demographic risk-factors affecting short-term neurodevelopmental outcome (NDO) in children operated on for abdominal and thoracic congenital anomalies (CA).
Methods: Prospective cohort observational study on newborns operated on for non-cardiac major CA. Evaluations were conducted at 6 and 12 months of age. Univariate linear regression and multivariate regression were conducted to analyze the impact on NDO of clinical and sociodemographic variables. Infants were evaluated with the Bayley Scales of Infant and Toddler Development—3rd Edition.
Results: One-hundred-fifty-five children were enrolled. They were affected by the following anomalies: Esophageal Atresia (N = 41), Congenital Diaphragmatic Hernia (N = 42), Midgut Malformations (N = 34), Abdominal Wall Defects (N = 18), Colorectal Malformations (N = 20). There were no statistically significant differences among the five groups of CA as to NDO. Variables which reached statistical significance at multivariate regression ($p \leq 0.001$) at 6 and 12 months as to cognitive and motor development were: ventilatory time, associated malformations, medical appliances for feeding, number of surgery and length of hospital stay.
Conclusions: On the average, children born with CA show a NDO within normal range. The identified risk-factors could prompt health care professionals to conduct a close surveillance on most vulnerable children giving them the best chance to reach their full potential.

Over the past decades, novel surgical techniques, advances in intensive care and medical therapies have significantly lowered mortality rate in children with non cardiac surgical malformation requiring surgery at birth [1].

Due to the improving success rate of surgical intervention, outcome studies in congenital malformation have shifted from survival to short- and long-term morbidity [2]. Available data suggest that survivors, regardless type of malformation, may show considerable morbidity and may face neurodevelopmental delay [3–5].

Despite documented risk of neurodevelopmental delay in this patient population, no guidelines currently exist for surveillance, screening and evaluation. To the same extent, clinical and socio-demographic risk-factors affecting neurodevelopmental outcome are still to be established.

1. Material and methods

A longitudinal study was set up including all infants seen at our Institution with major anomalies requiring surgery in the neonatal period from 2008 to 2012. Infants underwent a comprehensive evaluation by pediatrician, surgeon and psychologist at pre-set time frames: 6 and 12 months of age. Children were affected by thoracic and abdominal anomalies while those with urological, brain and cardiac anomalies were excluded since they were cared for by other services. Five groups of anomalies were considered: 1. Esophageal Atresia; 2. Congenital Diaphragmatic Hernia; 3. Midgut Malformations (intestinal atresia, intestinal duplication, volvolus); 4. Abdominal Wall Defects (omphalocele and gastroschisis); 5. Colorectal Malformations (imperforate anus and Hirschsprung's disease). Preterm infants (G.A. < 33 weeks) and infants with a genetic syndrome, chromosomic anomaly or central nervous system anomalies known to be associated with neurodevelopmental delay, were excluded as well as those operated on in other Institutions. Over the study period, ECMO was not performed in our Institution. Clinical data of the child and socio-demographic data of the parents were collected during hospitalization. Socioeconomic status was classified according to European Socio-Economic Classification into: salariat, intermediate, working class, unemployed [6]. Reasons of unemployment were not investigated.

At follow-up, infants were evaluated with the Bayley Scales of Infant and Toddler Development — 3rd Edition (BSID-III) [7]. The BSID-III is an internationally recognized clinician administered tool designed to

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assess the development in very young children (1–42 months). It consists of three scales of which we used cognitive and motor ones. The Cognitive Scale is made up of largely non verbal activities involving memory, problem solving, and manipulation. The Motor Scale is composed of the fine motor subtest, which measures visual-motor integration, visual spatial, and motor control skills of the hands, and gross motor subtest, which measures large body complex movements and mobility.

This standardized test of infant development is age normed to have a mean of 100 and standard deviation of 15. Infants with a standard score between 84 and 70 were considered moderately delayed; those with a standard score <70 were considered very delayed.

Univariate linear regression was conducted to analyze the impact on NDO of the following variables: gender, gestational age, birth-weight, head circumference, type of malformation, associated anomalies requiring surgery, number of major surgeries during first hospitalization, length of stay (LOS, expressed in number of days), ventilatory time, medical appliances at discharge (for feeding and/or respiratory and/or stomas), number of major surgeries at 6 and 12 months, number of general anesthesia at 6 and 12 months, number of hospitalization at 6 and 12 months, LOS at 6 and 12 months, medical appliances (for feeding and/or respiratory and/or stomas) at 6 and 12 months, weight <5° percentile (based on Italian growth charts) at 6 and 12 months, maternal and paternal age, educational level and nationality and SES. Multivariate regression was conducted on those variables which reached a significance of 0.02. Written Parents' Informed Consent was obtained. The study was IRB approved.

2. Results

One-hundred-ninety-three patients met the aforementioned criteria. Of these, children attending both follow-up appointments were 155 (80.3%) and they form the object of the study. We have no data on reasons for not attending follow-up appointments. No statistical significant differences on base-line characteristics were observed between respondent and not-respondent in the considered group. Diagnoses were equally distributed between the participating and non participating groups.

Clinical data of children at birth are reported in Table 1, at first admission in Table 2, at 6 months follow-up in Table 3 and at 12 months follow-up in Table 4.

None of our patients had intra-cranial hemorrhage. Associated malformations requiring surgery were: 7 children had a congenital heart disease (2 in the EA group, 2 in the CDH group, 1 in the MM group, 1 in the AWD group and 1 in the CM group), 3 children had the VACTERL association and were in EA group, 2 children with EA had also CM, 1 children with CDH had also AWD. Mortality rate was less than 5% in all considered malformations with the exception of CDH in which it was 29%.

Median interquartile range (IQR) maternal and paternal ages were 33 (30–38) and 36 (31–40), respectively. Eighty-nine percent of mothers and fathers were Italian. As to educational level: primary school 0 mother and 1 father; secondary school 23 mothers and 30 fathers; high school 100 mothers and 96 fathers; degree 42 mothers and 28 fathers. Regarding Socio-Economic-Status 12 mothers and 23 fathers were in class 1, 67 mothers and 64 fathers were in class 2, 65 mothers and 22 fathers were in class 3, 54 mothers and 3 fathers were in class 4.

Mean (SD) Mental and Motor scores were stratified by type of CA and reported in Table 5. There were no statistically significant differences among the five groups of CA as to neurodevelopmental outcome. Considering total sample, children with a cognitive development < 85 were 27 (17.41%) at 6 months and 14 (9.03%) at 12 months, respectively; children with a motor development < 85 were 32 (20.64%) at 6 months and 29 (18.71%) at 12 months, respectively. Motor and Cognitive performances improved significantly from 6 to 12 months ($p = 0.000$; $p = 0.02$).

Results of linear regression and multivariate regression at 6 and 12 months as to cognitive and motor development are reported in Table 6.

3. Discussion

Although thoracic and abdominal anomalies account for a significant percentage of neonatal surgery, there appears to be little consensus in the literature regarding which neonatal factors are significant predictors of neurodevelopmental outcome in this patient population. Guidelines for surveillance and screening of NDO as well as risk factors for neurodevelopmental delay have been actually established among children requiring surgery for congenital heart diseases [8]. At present, outcome research in the area of neonatal surgery is still making efforts to clarify the role played by patient-specific risk factors, surgical and perioperative management strategies, post-discharge events, sociodemographic variables in the pathogenesis of neurodevelopmental dysfunction.

As previously mentioned, in our population cognitive and motor development at 6 and 12 months on the average fell within normal range and this happened regardless of type of malformation. In particular, percentage of children with a moderate delay is comparable with that of normative data. This finding is consistent with what was reported by Gishler et al. and Bevilacqua et al. in similar populations of surgical newborns [1,9]. In contrast, Mazer et al. and Laing et al. found more dysfunctional motor development than children in the general population

Table 1
Clinical data of children at birth.

	Total	EA[a]	CDH[b]	MM[c]	AWD[d]	CM[e]
	(n = 155)	(n = 41)	(n = 42)	(n = 34)	(n = 18)	(n = 20)
Clinical data at birth						
Male N (%)	99 (63.9)	25 (61.0)	31 (73.8)	18 (52.9)	10 (55.6)	15 (75.0)
Gestational age median (IQR)	38 (36–39)	38 (37–39)	38 (37–39)	37 (36–39)	36.5 (36–38)	39 (38–40)
Weight median (IQR)	2870 (2437–3258)	2650 (2380–3100)	3025 (2600–3300)	2780 (2325–3187)	2645 (2225–2980)	3305 (2807–3582)
Head circumference	34 (33–35)	34 (32–34.5)	35 (34–35.9)	34 (33–35)	33.25 (32.25–34)	34.75 (33.375–35)
Prenatal diagnosis N (%)	75 (48.4)	5 (12.2)	32 (76.2)	18 (52.9)	16 (88.9)	4 (20.0)
Associated anomalies						
None N (%)	139 (89.7)	31 (75.6)	39 (92.8)	33 (97.1)	17 (94.4)	19 (95.0)
One N (%)	11 (7.0)	6 (14.6)	2 (4.8)	1 (2.9)	1 (5.6)	1 (5.0)
Two or more N (%)	5 (3.3)	4 (9.8)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)

[a] EA: Esophageal Atresia.
[b] CDH: Congenital Diaphragmatic Hernia.
[c] MM: Midgut Malformation.
[d] AWD: Abdominal Wall Defects.
[e] CM: Colorectal Malformation.