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Major Abdominal Surgery, Neurosurgery, Orthopedic Surgery in Children aged between 10 and 18 years and Postoperative Outcome

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Research Article

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Abstract

Background

In a previously conducted monocentric retrospective study, predictors of postoperative outcome in children included American Society of Anesthesiologists score, transfusion, emergency interventions, surgery and age. A study has been undertaken to describe postoperative outcome in patients aged between 10 and 18 years included in the initial study in abdominal surgery, neurosurgery and orthopedics.

<u>Aims</u>

To describe postoperative outcome in children aged between 10 and 18 years.

Methods

Secondary analysis of postoperative outcome in children aged between 10 and 18 years included retrospectively in the initial study of 594 patients. The study was approved by the Ethics Committee.

Results

There were 221 children with a mean age of 165.5±24.3 months in abdominal surgery, neurosurgery and orthopedics.16.3% patients had intra-operative or postoperative complications. Intra-operatively, 3.2% had hemorrhagic shock, 0.45% anaphylaxis and 0.45% respiratory failure. Postoperatively, 3.2% had neurologic failure, 2.3% respiratory failure, 0.45% cardio-circulatory failure, 0.45% endocrinal failure, 0.45% had hepatic failure, 0.45% multiple organ failure, and 0.45% had renal failure. In-hospital mortality rate was 0.45%.

Conclusion

These results emphasize the importance of optimizing intra-operative management in critically ill patients in major surgery with goal directed therapies in order to improve postoperative outcome.

Keynotes

Postoperative outcome is multifactorial in surgical patients. Intra-operative goal directed fluid and hemodynamic therapy to optimize patient management with validated tools in children is one of the main aims of goal directed therapies which have the objective to improve postoperative outcome in surgical patients. It is time to integrate goal directed therapies in our routine practice for intra-

operative management to improve postoperative outcome in children.

Introduction

A monocentric retrospective study was conducted in 594 patients with a mean age of 90.86±71.80 months with the objective to determine predictors of postoperative outcome in abdominal surgery, neurosurgery and orthopedics (1). Postoperative outcome predictors in this study were American Society of Anesthesiologists status (ASA), transfusion, emergency, surgery and age. A similar analysis in different surgical settings was undertaken and conducted to the same conclusions (2, 3, 4). Postoperative outcome was defined as organ failure, infections, re-operations, length of stay in the intensive care unit, length of hospital stay, total length of hospital stay and length of mechanical ventilation. Meta-analyses in patients under 18 years revealed that intra-operative goal directed fluid and hemodynamic therapy is not a routine generalized practice, that non optimal intra-operative hemodynamic parameters were predictors of adverse postoperative outcome in terms of morbidity and mortality, that transfusion goal directed therapy with point of care tests reduced fresh frozen plasma transfusion and length of hospital stay and that enhanced recovery after surgery applied in surgical settings reduced postoperative complications (5, 6, 7).

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was conducted with the objective to describe in detail with regard to age, postoperative evolution in children aged between 10 and 18 years included in the initial retrospective study (1). Similar secondary analyses have been conducted in pre-terms, infants less than 1 year old, children aged between 1 and 3 years, children from 3 to 6 years old and children from 6 to 10 years with the objective to describe postoperative outcome with consideration to age since age has been revealed to be an independent predictor of postoperative outcome (1, 2, 3, 4).

Methods And Materials

Secondary analysis of children between 10 and 18 years old included in the initial study (1). The study was declared to the CNIL, National Commission for Computer Science and Liberties on 21 February 2017 under the registration number 2028257 v0. The Ethics Committee of Necker approved the study on 21 March 2017 under the registration number 2017-CK-5-R1. Patients were included retrospectively from 1 January 2014 to 17 May 2017. Inclusion criteria were children aged between 10 and 18 years old. Exclusion criteria were children aged less than 10 years old and older than 18 years. Statistics were analyzed with XLSTAT 2020.4.1 software. Continuous variables were described in means ± standard deviation or medians with interquartile ranges. Categorial variables were described in proportions.

Results

Table 1 illustrates general characteristics.

There were 221 children with a mean age of 165.5±24.3 months.

There were 38 patients (17.2%) in abdominal surgery, 65 (29.4%) in neurosurgery and 118 (53.4%) in

orthopedics. 25 patients (11.3%) had an emergency surgery. 121 patients (54.8%) were ASA 3 and 19

(8.6%) were ASA 4.

Table 2 illustrates types of surgery.

The most common surgical interventions were scoliosis in 86 patients (39.9%), intracerebral tumor

resection in 28 patients (12.7%), limb tumor resection in 19 patients (8.6%), pelvic tumor in 10

patients (4.5%), renal transplantation in 8 patients (3.6%), epileptogenic lesion resection in 7

(2.3%), femoral osteotomy in 5 patients (2.3%), Chiari's malformation in 4 patients (1.8%), liver

transplantation in 4 patients (1.8%), ventriculostomy in 4 patients (1.8%) and limb amputation in 3

patients (1.4%).

36 patients (16.3%) had intra-operative and or postoperative complications (organ failure or sepsis).

7 patients (3.2%) had intra-operative hemorrhagic shock, 1(0.45%) had intra-operative anaphylaxis

and 1 (0.45%) had intra-operative respiratory failure. 7 patients (3.2%) had postoperative neurologic

failure, 5(2.3%) had postoperative respiratory failure, 1 (0.45%) had postoperative cardio-circulatory

failure, 1 (0.45%) had postoperative endocrinal failure, 1 (0.45%) had postoperative hepatic failure,

1(0.45%) had postoperative multiple organ failure, and 1(0.45%) had postoperative renal failure. The

most common postoperative infections were surgical wound sepsis in 7 patients (3.2%), abdominal

sepsis in 5 (2.3%), septicemia in 3 (1.4%), urinary sepsis in 3 (1.4%), neuro-meningeal sepsis in 1

(0.45%) and pulmonary sepsis in 1(0.45%).

15 patients (6.8%) had re-operations.

83 patients (37.6%) had intra-operative transfusion. Mean preoperative and postoperative

hemoglobin levels were 12.4±1.7 g/dL and 11.4±1.7 g/dL respectively.

In-hospital mortality rate was 0.45% in 1 trauma patient who underwent a decompressive

craniectomy and presented postoperative multiple organ failure and died on postoperative day 7

(table 3).

Median total length of hospital stay was 9 days[5-18].

Table 4 illustrates outcomes per surgery.

Table 5 illustrates co-morbidities.

The most common co-morbidities were intracerebral tumor in 27 patients (12.2%), cerebral anoxic

lesions 19 patients (8.6%), epilepsy 14 patients (6.3%), Ewing's sarcoma 12 patients (5.4%), cancer 9

patients (4.1%), neurofibromatosis 8 patients (3.6%), chronic renal failure 8 patients (3.6%), Chiari's

malformation 6 patients (2.7%), hepatic failure 5 patients (2.2%) and psychomotor deficiency 4

patients (1.8%).

Discussion And Conclusion

In this cohort of 221 patients aged between 10 and 18 years in major abdominal surgery, neurosurgery and orthopedic surgery, 16.3% of the patients presented with intra-operative and or postoperative complications and most were ASA grade \geq 3. The most common intra-operative complication was hemorrhagic shock and 37.6% were transfused intra-operatively. Transfusion goal directed protocols with point of care tests should be integrated in intra-operative management in hemorrhagic surgery with the aim to optimize patient blood administration in children. A recent meta-analysis in children aged less than 18 years old in hemorrhagic settings revealed that transfusion guided with point care tests reduced fresh frozen plasma administration and length of hospital stay (5). Since transfusion is one of the predictors of postoperative outcome (1, 2, 3, 4) it is mandatory to have patient blood management protocols in hemorrhagic surgery since these protocols are not yet a routine generalized practice in our Hospital. Length of hospital stay as well as hospital costs were significantly higher in transfused patients than in non-transfused patients (8). The rate of patients with postoperative complications in this study emphasizes the importance of optimizing intra-operative patient management in critically ill patients in major surgery (5, 6, 7, 8, 9, 10, 11, 12, 13, 14). Optimizing intra-operative patient management with goal directed therapies is not a routine generalized practice in our Hospital. Intra-operative goal directed therapies include goal directed fluid and hemodynamic therapy with validated tools in children, transfusion goal directed protocols with point of care tests and enhanced recovery after surgery

(5, 6, 7, 8, 9, 10, 11, 12, 13, 14). The aim of goal directed therapies is to optimize patient intra-operative

management with the objective to improve postoperative outcome which depends on multiple

factors. Non optimal intra-operative hemodynamic parameters have been correlated to adverse

postoperative outcome in surgical pediatric patients (6). Considering the results of previous studies

there is enough evidence to integrate goal directed therapies for intra-operative patient

management in pediatric surgical patients to optimize postoperative outcome (1, 2, 3, 4, 5, 6, 7, 8).

Declarations

Conflicts of Interest The author declared no conflicts of interest.

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Tables

Table 1 General characteristics

ristics	N=221
in months±standard deviation	165.5 ± 24.3
d surgery n (%)	38(17.2)
gery n (%)	65(29.4)
ic surgery n (%)	118(53.4)
urgery n (%)	196(88.7)
y surgery n (%)	25(11.3)
y n (%)	15(6.8)
vith intra-operative and or postoperative complications (organ failure or sepsis) n (%)	36(16.3)
rative hemorrhagic shock n (%)	7(3.2)
rative anaphylaxis n (%)	1(0.45)
rative respiratory failure n (%)	1(0.45)
tive neurologic failure n (%)	7(3.2)
tive respiratory failure n (%)	5(2.3)
tive cardio-circulatory failure n (%)	1(0.45)
tive endocrinal failure n (%)	1(0.45)
tive hepatic failure n (%)	1(0.45)
tive renal failure n (%)	1(0.45)
tive multi-organ failure n (%)	1(0.45)
tive surgical wound sepsis n (%)	7(3.2)
tive abdominal sepsis n (%)	5(2.3)
tive septicemia n (%)	3(1.4)
tive urinary sepsis n (%)	3(1.4)
tive neuro-meningeal sepsis n (%)	1(0.45)
tive pulmonary sepsis n (%)	1(0.45)
ıl Mortality n (%)	1(0.45)
on n (%)	83(37.6)
operative hemoglobin levels± standard deviation g/dL	12.4±1.7
toperative hemoglobin levels ± standard deviation g/dL	11.4±1.7
%)	7(3.2)
(%)	73(33)
(%)	121(54.8)
(%)	19(8.6)
(%)	1(0.45)
ngth of intensive care unit stay in days [interquartile range]	3[1-5]
ngth of hospital stay in days [interquartile range]	5[3-11]
tal length of hospital stay in days [interquartile range]	9[5-18]
ingth of mechanical ventilation (invasive or non-invasive) in days [interguartile range]	0[0-0]

Table 2 Surgery

Surgery	Number of patients (%)
Ano-rectal malformation	1(0.45)
Attached/Fixed spinal cord	1(0.45)
Cerebral cavernoma	1(0.45)
Chiari's malformation	4(1.8)
Cranioplasty	1(0.45)
Craniosynostosis	5(2.3)
Cysto-ureterectomy	1(0.45)
Decompressive craniectomy	5(2.3)
Epileptogenic lesion resection	7(3.2)
Exploratory laparotomy	1(0.45)
Femoral osteotomy	5(2.3)
Femoral prothesis	1(0.45)
Gastrectomy	1(0.45)
Gastroscopy	1(0.45)
Hepatic tumor	2(0.9)
Interscapular thoracic desarticulation	1(0.45)
Intestinal resection	2(0.9)
Intracerebral biopsy	3(1.4)
Intracerebral tumor resection	28(12.7)
Intraventricular stenting	1(0.45)
Laparotomy for volvulus	1(0.45)
Lefort III	1(0.45)
Limb amputation	3(1.4)
Limb tumor resection	19(8.6)
Liver transplantation	4(1.8)
Mediastinal ganglioneuroma	1(0.45)
Nissen gastrostomy	1(0.45)
Orbital tumor	1(0.45)
Pancreatectomy	1(0.45)
Pelvic tumor	10(4.5)
Polytrauma	1(0.45)
Renal transplantation	8(3.6)
Revascularisation/by-pass	1(0.45)
Scoliosis	86(38.9)
Spinal cord tumor resection	1(0.45)
Splenectomy	2(0.9)
Sterno-cleido mastoidian tenotomy	1(0.45)
Ventriculostomy	4(1.8)
Vertebral laminectomy/Arthrodesis	2(0.9)
Extradural hematoma drainage	1(0.45)

Table 3 patient with fatal outcome

	Age months	ASA score	Co- morbidities	Intra-operative complications	Postoperative outcome	Delay of in-hospital mortality in days	Emergency	Transfusion
sive	168	5	Polytrauma	0	Multiple organ failure	7	Yes	No

Table 4 outcomes per surgery

	number of cases	Intra- operative anaphylaxis	Intra- operative hemorrhagic shock	Intra- operative respiratory failure	Postoperative cardio- circulatory failure	Postoperative endocrinal failure	Postoperative hepatic failure	Postoperative multiple organ failure	Postoperative neurologic failure	Postoperative renal failure	Postoperative respiratory failure	Postoperative abdominal sepsis	Postoperative neuro- meningeal sepsis	Postoperative pulmonary sepsis	Postoperative	Postoperative Surgical wound sepsis	Postoperative urinary sepsis	Re-
ation	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
nal	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
a	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ion	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
y	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	
	5	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	
	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
omy	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	5	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	
icic	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
,	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	
- v	3	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	
r	-																	
	28	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	
enting	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
vulus	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ion	19	0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	
m	4	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
У	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	
	10	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	1	
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ion	8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
by-	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	86	1	2	1	1	0	0	0	4	1	3	2	0	0	0	7	2	
											-							
	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	
	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
oidian	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
odesis	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
ша	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	

Table 5 Co-morbidities

Apert syndrome1(0.45)Arachnoid cyst1(0.45)Arachnoid cyst1(0.45)Arathritis3(1.4)Asthma1(0.45)Brain trauma1(0.45)Cancer9(4.1)Central core myopathy1(0.45)Cerebral anoxic lesions19(8.6)Chiari's malformation6(2.7)Chronic renal failure8(3.6)Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome2(0.9)Immune deficiency1(0.45)Intracerebral tumor27(12.2)Intussuception1(0.45)Lowe syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Veroderma Pigmentosum1(0.45)Veroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polymalformative syndrome2(0.9)Polymalformative syndrome2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina limuscular amyotrophy1(0.45)Spina bifida2(0.9) <t< th=""><th>Co-morbidity</th><th>Number of cases(%)</th></t<>	Co-morbidity	Number of cases(%)
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Brain trauma1(0.45)Cancer9(4.1)Central core myopathy1(0.45)Cerebral anoxic lesions19(8.6)Chiari's malformation6(2.7)Chronic renal failure8(3.6)Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome1(0.45)Intestinal pseudo-occlusion1(0.45)Intestinal pseudo-occlusion1(0.45)Lowe syndrome1(0.45)Lowe syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Veroderma Pigmentosum1(0.45)Veroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polymalformative syndrome2(0.9)Polymalformative syndrome1(0.45)Preder Wili syndrome1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Synhome1(0.45)Spina bifida2(0.9)Synhome1(0.45)Spina bifida2(0.9) <td>Asthma</td> <td>1(0.45)</td>	Asthma	1(0.45)
Cancer9(4.1)Central core myopathy1(0.45)Cerebral anoxic lesions19(8.6)Chiari's malformation6(2.7)Chronic renal failure8(3.6)Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intestinal pseudo-occlusion1(0.45)Lowe syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Veroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)Stroke1(0.45)	Brain trauma	1(0.45)
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Chiari's malformation6(2.7)Chronic renal failure8(3.6)Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intestinal pseudo-occlusion1(0.45)Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Varoderma Pigmentosum1(0.45)Varoderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)Kest syndrome1(0.45)	Cerebral anoxic lesions	19(8.6)
Chronic renal failure8(3.6)Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intracerebral tumor27(12.2)Intracerebral tumor1(0.45)Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome2(0.9)Polymalformative syndrome2(0.9)Polynalformative syndrome1(0.45)Pospisi1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)Kest syndrome1(0.45)	Chiari's malformation	6(2.7)
Congenital heart disease2(0.9)Convulsive encephalopathy1(0.45)Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intestinal pseudo-occlusion1(0.45)Loeys-Dietz syndrome1(0.45)Mediastinal tumor1(0.45)Mucular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spina bifida2(0.9)Syna bifida2(0.9)Syna bifida2(0.9)Syna bifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Chronic renal failure	8(3.6)
Convulsive encephalopathy1(0.45)Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intussuception1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Spina huscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Congenital heart disease	2(0.9)
Crouzon syndrome1(0.45)Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome1(0.45)Intracerebral tumor27(12.2)Intracerebral tumor1(0.45)Loeys-Dietz syndrome1(0.45)Loeys-Dietz syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytaruma3(1.4)Pierre Robin syndrome1(0.45)Scoliosis1(0.45)Sepsis1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Stroke1(0.45)Stroke1(0.45)West syndrome1(0.45)	Convulsive encephalopathy	1(0.45)
Di George syndrome2(0.9)Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intusception1(0.45)Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Sepisis1(0.45)Spina bifida2(0.9)Synab ifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Crouzon syndrome	1(0.45)
Epilepsy14(6.3)Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intracerebral tumor1(0.45)Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Mediastinal tumor1(0.45)Myelomeningocele1(0.45)Neurofhbromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Varoderma Pigmentosum1(0.45)Polytrauma3(1.4)Prader Will syndrome2(0.9)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Di George syndrome	2(0.9)
Ewing's sarcoma12(5.4)Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intracerebral tumor27(12.2)Intracerebral tumor1(0.45)Loeys-Dietz syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofhormatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polynalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Epilepsy	14(6.3)
Former pre-term with sequelae2(0.9)Goldenhar syndrome1(0.45)Gorlin's syndrome3(1.4)Hepatic failure5(2.2)Hurler's syndrome2(0.9)Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intussuception1(0.45)Lowe syndrome1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Spina huscular amyotrophy1(0.45)Stroke1(0.45)	Ewing's sarcoma	12(5.4)
Goldenhar syndrome 1(0.45) Gorlin's syndrome 3(1.4) Hepatic failure 5(2.2) Hurler's syndrome 2(0.9) Immune deficiency 1(0.45) Intestinal pseudo-occlusion 1(0.45) Intracerebral tumor 27(12.2) Intussuception 1(0.45) Loeys-Dietz syndrome 1(0.45) Mediastinal tumor 1(0.45) Mediastinal tumor 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 1(0.45) Xeroderma Pigmentosum 1(0.45) Polytrauma 3(1.4) Prader Wili syndrome 1(0.45) Psychomotor deficiency 4(1.8) Scoliosis 1(0.45) Spina bifida 2(0.9) Spina bifida 2(0.9) Stroke 1(0.45)	Former pre-term with sequelae	2(0.9)
Gorlin's syndrome 3(1.4) Hepatic failure 5(2.2) Hurler's syndrome 2(0.9) Immune deficiency 1(0.45) Intestinal pseudo-occlusion 1(0.45) Intracerebral tumor 27(12.2) Intussuception 1(0.45) Loeys-Dietz syndrome 1(0.45) Low syndrome 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 2(0.9) Polytrauma 3(1.4) Prader Will syndrome 2(0.9) Polytrauma 3(1.4) Prader Will syndrome 1(0.45) Sepisi 1(0.45) Spina bifida 2(0.9) Spina bifida 2(0.9) Stroke 1(0.45) Stroke 1(0.45)	Goldenhar syndrome	1(0.45)
Hepatic failure 5(2.2) Hurler's syndrome 2(0.9) Immune deficiency 1(0.45) Intestinal pseudo-occlusion 1(0.45) Intracerebral tumor 27(12.2) Intusception 1(0.45) Loeys-Dietz syndrome 1(0.45) Lowe syndrome 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 2(0.9) Polytrauma 3(1.4) Prader Wili syndrome 1(0.45) Scoliosis 1(0.45) Spina bifida 2(0.9) Spina bifida 2(0.9) Stroke 1(0.45) Stroke 1(0.45)	Gorlin's syndrome	3(1.4)
Hurler's syndrome 2(0.9) Immune deficiency 1(0.45) Intestinal pseudo-occlusion 1(0.45) Intracerebral tumor 27(12.2) Intuscerebral tumor 1(0.45) Loeys-Dietz syndrome 1(0.45) Lowe syndrome 1(0.45) Mediastinal tumor 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 2(0.9) Polytrauma 3(1.4) Prader Wili syndrome 1(0.45) Scoliosis 1(0.45) Spspis 1(0.45) Spina bifida 2(0.9) Spina bifida 2(0.9) Stroke 1(0.45) Stroke 1(0.45)	Hepatic failure	5(2.2)
Immune deficiency1(0.45)Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intussuception1(0.45)Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome2(0.9)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spina bifida2(0.9)Spina huscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Hurler's syndrome	2(0.9)
Intestinal pseudo-occlusion1(0.45)Intracerebral tumor27(12.2)Intussuception1(0.45)Lovesy-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spinal bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)West syndrome1(0.45)Storke1(0.45)	Immune deficiency	1(0.45)
Intracerebral tumor 27(12.2) Intussuception 1(0.45) Loeys-Dietz syndrome 1(0.45) Lowe syndrome 1(0.45) Mediastinal tumor 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 1(0.45) Xeroderma Pigmentosum 1(0.45) Polymalformative syndrome 2(0.9) Polytrauma 3(1.4) Prader Wili syndrome 1(0.45) Psychomotor deficiency 4(1.8) Scoliosis 1(0.45) Sepsis 1(0.45) Spina bifida 2(0.9) Spina hifida 2(0.9) Stroke 1(0.45) West syndrome 1(0.45)	Intestinal pseudo-occlusion	1(0.45)
Intussuception 1(0.45) Loeys-Dietz syndrome 1(0.45) Lowe syndrome 1(0.45) Mediastinal tumor 1(0.45) Muscular dystrophy 2(0.9) Myelomeningocele 1(0.45) Neurofibromatosis 8(3.6) Osteogenesis imperfecta 3(1.4) Pierre Robin syndrome 1(0.45) Xeroderma Pigmentosum 1(0.45) Polytnauma 3(1.4) Prader Wili syndrome 1(0.45) Psychomotor deficiency 4(1.8) Scoliosis 1(0.45) Spina bifida 2(0.9) Spina bifida 2(0.9) Stroke 1(0.45) Stroke 1(0.45)	Intracerebral tumor	27(12.2)
Loeys-Dietz syndrome1(0.45)Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Scoliosis1(0.45)Spiss1(0.45)Spina bifida2(0.9)Synah muscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Intussuception	1(0.45)
Lowe syndrome1(0.45)Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofhromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Scoliosis1(0.45)Spiss1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Loeys-Dietz syndrome	1(0.45)
Mediastinal tumor1(0.45)Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Spina bifida2(0.9)Spina bifida2(0.9)Stroke1(0.45)Stroke1(0.45)	Lowe syndrome	1(0.45)
Muscular dystrophy2(0.9)Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Sepsis1(0.45)Spina hifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Mediastinal tumor	1(0.45)
Myelomeningocele1(0.45)Neurofibromatosis8(3.6)Osteogenesis imperfecta3(1.4)Pierre Robin syndrome1(0.45)Xeroderma Pigmentosum1(0.45)Polymalformative syndrome2(0.9)Polytrauma3(1.4)Prader Wili syndrome1(0.45)Psychomotor deficiency4(1.8)Scoliosis1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Spina hifida2(0.9)Stroke1(0.45)West syndrome1(0.45)	Muscular dystrophy	2(0.9)
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Psychomotor deficiency4(1.8)Scoliosis1(0.45)Sepsis1(0.45)Spina bifida2(0.9)Spinal muscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Prader Wili syndrome	1(0.45)
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Sepsis1(0.45)Spina bifida2(0.9)Spinal muscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Scoliosis	1(0.45)
Spina bifida2(0.9)Spinal muscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Sepsis	1(0.45)
Spinal muscular amyotrophy1(0.45)Stroke1(0.45)West syndrome1(0.45)	Spina bifida	2(0.9)
Stroke 1(0.45) West syndrome 1(0.45)	Spinal muscular amyotrophy	1(0.45)
West syndrome 1(0.45)	Stroke	1(0.45)
	West syndrome	1(0.45)
Wiliams syndrome 1(0.45)	Wiliams syndrome	1(0.45)