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PAEDIATRICS

Perioperative hospital mortality at a tertiary paediatric institution

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Abstract

Background: Research in postoperative mortality is scarce. Insight into mortality and cause of death might improve and innovate perioperative care. The objective for this study was to report the 24-hour and 30-day overall, and surgery and anaesthesia-related, in-hospital mortality at a tertiary paediatric hospital.

Methods: All patients <18 yr old who underwent anaesthesia with or without surgery between January 1, 2006, and December 31, 2012, at the Wilhelmina Children's Hospital, Utrecht, The Netherlands, were included in this retrospective cohort study. Causes of death within 30 days were identified and tabulated into four major categories according to principal cause.

Results: A total of 45 182 anaesthetics were administered during this 7-yr period. The all-cause 24-hour hospital mortality was 13.1 per 10 000 anaesthetics (95% CI: 9.9–16.8) and the all-cause 30-day in-hospital mortality was 41.6 per 10 000 anaesthetics (95% CI: 35.9–48.0). In total five patients were partially contributable to anaesthesia (30-day mortality: 1.1/10 000, 95% CI: 0.4–2.6) and four patients were partially contributable to surgery (30-day mortality: 0.9/10 000, 95% CI: 0.2–2.3). Mortality was higher in neonates and infants, children with ASA physical status III and IV, and emergency- and cardiothoracic surgery.

Conclusions: Neonates and infants, children with ASA physical status III or poorer, and emergency- and cardiothoracic surgery are associated with a higher postoperative mortality. Anaesthesia- or surgery-related complications contribute to mortality in only a small amount of the deaths, indicating the relative safety of paediatric surgical and anaesthetic procedures.

Key words: anaesthesia; child mortality; hospital mortality; infants, paediatrics, surgery

Mortality is a basic and objective measure for quality and safety in surgery. As a result of improvements in monitoring and patient care during the last decades, surgery and anaesthesia-related mortality has become infrequent.^{1 2} A better understanding of the aetiology of death after surgery and anaesthesia might improve perioperative care, by allowing better prediction and preemptive management of future problems. The analysis of

mortality may help caregivers to determine which patients are at higher risk, in order to guide planning, resourcing, and expert staffing for high-risk patients.

However, research in perioperative anaesthesia and surgery related mortality is scarce. As far as we know there have been no data published from Europe on post-surgical and anaesthesia mortality in children in specific groups recently. The incidence of

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Editor's key points

- Anaesthesia-related mortality is rare in paediatric practice but contributing factors offer insights to further improve care
- Electronic anaesthesia information systems enhance objective retrospective analysis of critical incidents
- There is a need for international standardization of terminology to evaluate anaesthesia-related mortality

perioperative cardiac arrests that occurred during procedures requiring anaesthesia services has been studied in a voluntary registry in a single institution in the USA.³ However, voluntary reports are likely to underestimate the true incidence. Another large study in a single tertiary institution in Australia also studied the incidence and nature of anaesthesia related 30-day mortality-voluntarily. Yet, they used hand-written anaesthesia charts which may be more inaccurate than electronic records.⁴

There is limited information about the risk of specific subgroups of patients [e.g. the risk differences between cardiac and non-cardiac surgeries and the variance among age-groups (neonates, toddlers and infants)] and about the incidence of the contribution of anaesthesia and surgical factors to short and long-term mortality. Electronic anaesthesia information systems (AIMS) and electronic patient charts are likely to reduce underreporting of intraoperative problems – for example, severe hypoxaemia or hypotension – and allow objective review of the anaesthesia charts to define the possible contribution of anaesthesia and surgery to perioperative deaths.

Therefore, the aim of this study was to determine the incidence and nature of mortality in paediatric practice occurring within 24 h, or 30 days after the termination of surgery and anaesthesia at a large tertiary institution, using AIMS and electronic patients charts to define the anaesthesia and surgery related contribution to death.

Methods

We retrospectively analysed the causes of 30-day postoperative in-hospital mortality of all children younger than 18 yr, who had been operated on in a tertiary paediatric university hospital (Wilhelmina Children's Hospital, University Medical Centre Utrecht, The Netherlands, 48.000 attendances per year, 220 beds) between January, 2006, and December, 2012. The institution provides surgical services in all areas, and one of the four national centres for paediatric congenital heart deformities in the Netherlands.

The study protocol has been reviewed by the Institutional Review Board of the University Medical Centre Utrecht, which waived the need for informed consent, as patients were not subjected to investigational actions (#13-627, November 25th, 2013). Patient confidentiality was guaranteed according to the Dutch law on personal data protection. Data were obtained from the Anaesthesia Information Management System (AIMS, AnStat®, Carepoint, Ede, The Netherlands) and the electronic hospital registration and billing administration (EZIS, Chipsoft®, The Netherlands) of the hospital. Anaesthetics performed outside locations might not be registered in AIMS. Therefore, additionally we coupled the hospital's general patient records and billing system to find the missing cases of children who underwent a surgical procedure outside the operation room or emergency department with anaesthesia by an anaesthesiologist. We excluded all deaths that occurred outside the hospital according to the definition of 'in hospital mortality'.

Surgical, anaesthetic and clinical charts of children who died within the hospital during administration - or within 30 days after the commencement - of the last procedure were reviewed. The characteristics of the patients, diagnosis, indications for surgery, ASA PS, type of operation, anaesthetic technique and duration, and the time, place and cause of death were recorded. Children were categorized into five groups according to age: neonates up to 30 days of age, infants from 31 days to 12 months of age, preschool children of one-to three yr of age, children aged four to nine yr and older children aged 10–17 yr. The principal causes of death were examined and tabulated into four major categories:

1. attributable to preoperative child condition or disease (when comorbidities were the only or the major contributory factor);
2. attributable to a preoperative trauma event (with subsequent surgery);
3. anaesthesia either fully or partially contributed to the death (when the child's disease or condition were primary factors but anaesthesia-related problems represented an additional factor);
4. the surgical procedure either fully or partially contributed to the death (when the child's disease or condition were primary factors but surgery-related problems represented an additional factor);

Categories 1 and 2 include all deaths in which the panel agreed that neither surgery nor the anaesthetic procedure contributed to death. Deaths where anaesthesia contributed were defined using the definition by Griend and colleagues⁴: patients for which the panel agreed that anaesthesia or factors under the responsibility of the anaesthetist contributed to death. The same panel-based assessment was applied to the category 'surgery-related death'. The medical records of children who died within 30 days after anaesthesia were examined by one author (L.B.), two paediatric anaesthetists (J.G. and D.W.) and two paediatric surgeons (F.H. and D.Z). Patients were discussed and anaesthesia- and surgery-related death was determined until consensus was reached by the entire team. Children receiving intraoperative care for organ donation were excluded.

Statistical methods

Mortality incidence is expressed per 10 000 procedures with 95% Confidence Interval (95% CI). In reporting the 95% CIs, the risk is per anaesthetic. The reported 95% CIs around risk were not adjusted to account for the non-uniform risk introduced by children having multiple procedures.⁴ We performed univariate and a multivariate logistic regression analyses to identify risk factors (age, gender, emergency status, surgical procedure) for 30-day in-hospital mortality. For children who had received multiple anaesthetics we included only the last anaesthetic, to reduce the potential unequal influence of repeated anaesthetics. All statistical analyses were performed using SPSS statistics version 20, (IBM, Chicago, IL, USA) with exception of the 95% CI's of risk differences which were calculated by Confidence Interval Analysis binomial exact method (Clopper-Pearson).

Results

A total of 45 182 anaesthetics in 26 436 patients were administered during a seven-yr period (Fig. 1). Hospital mortality within 24 h was 13.1 per 10 000, and 41.6 per 10 000 procedures within 30 days (Table 1). Most patients received a single anaesthetic (18 121/26 436; 68.5%). Approximately 17.1% received two anaesthetics

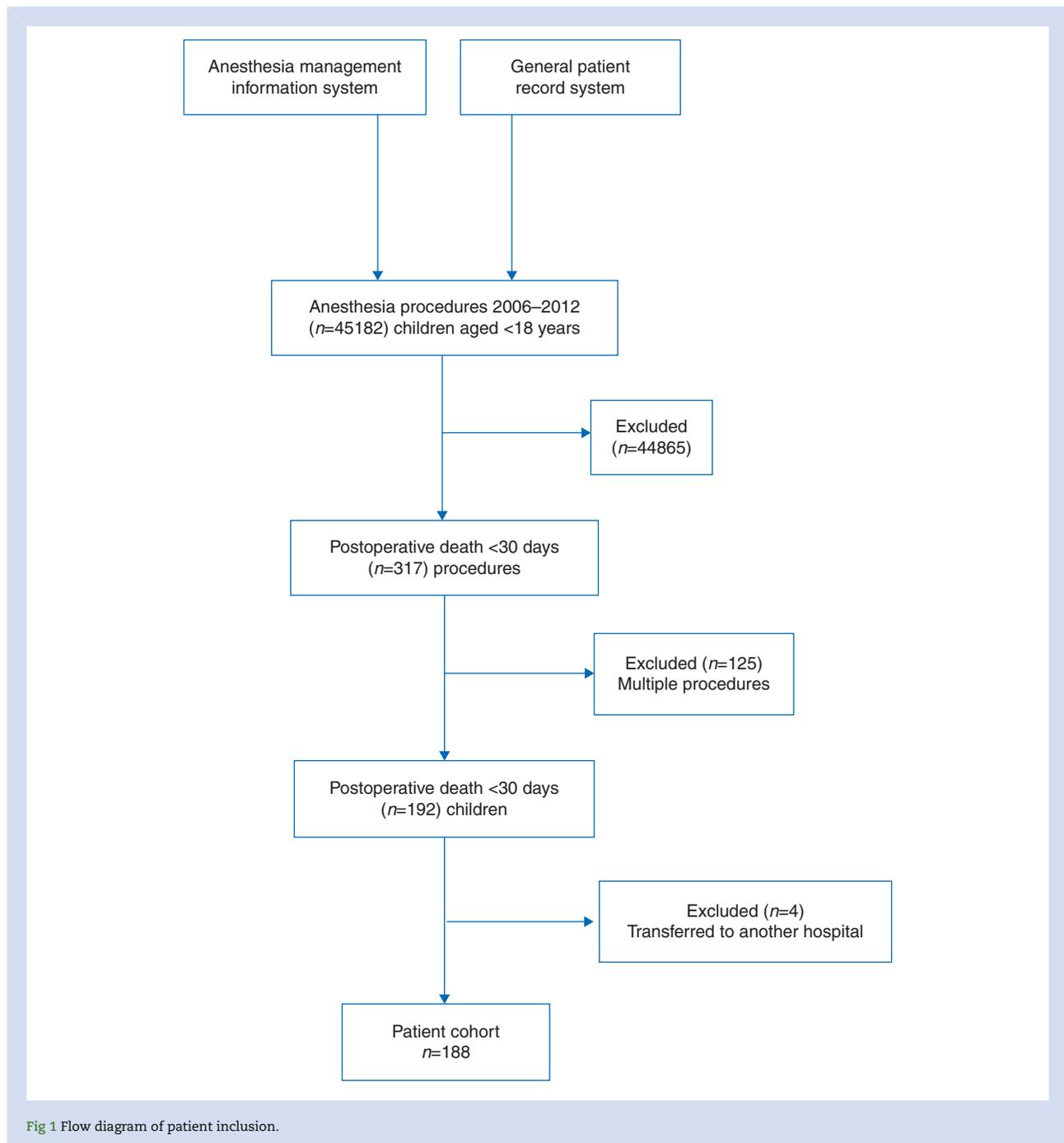


Fig 1 Flow diagram of patient inclusion.

(4534/26 436) or more (upper range 50 anaesthetics $n=1$). Mortality was 71.1 per 10,000 patients (95% CI: 61.3–82.0) irrespective of the number of anaesthetics. Only a minority of procedures were performed at Neonatal Intensive Care Unit (NICU) or Paediatric Intensive Care Unit (PICU) ($n=436$, 1.0%; 95% CI 0.8–1.1%) but a large proportion of these children who had been operated in the NICU or PICU died (1078 per 10 000 procedures, 95%: 802.9–1407.6 per 10 000 procedures).

Mortality in children older than one yr (21.2 per 10 000 procedures) was significantly lower than in children younger than one yr (124.4 per 10 000 procedures). Furthermore, mortality in relatively healthy children with ASA status I or II (6.8 per 10 000 procedures),

non-cardiothoracic (33.6 per 10 000 procedures) and elective surgery (23.1 per 10 000 procedures) was very low (Table 2).

There were a total of 188 death that occurred in children within 30 days of their procedure. Of the 59 patients that died in the first 24 h, 10 died in the operating room. The majority of the children died at the NICU (84%, Table 2). Most children died from their preoperative condition, disease or comorbidities, and a small number of children died from preoperative trauma (Table 3). In children who had received multiple anaesthetics the risk of death was six fold higher than in children who had received a single anaesthetic (Table 4). Univariate and multivariate logistic regression analyses identified younger age, emergency

Table 1 Number of anaesthetics and mortality according to calendar year. Mortality is per 10 000 procedures; CI, Confidence Intervals are for a proportion of the deaths relative to the procedures

Calendar Yr	Procedures, n	Death <24 h, n	Mortality (95% CI)	Death <30 days, n	Mortality (95% CI)
2006	6544	10	15.3 (7.3–28.1)	37	56.5 (39.1–77.8)
2007	6343	6	9.5 (3.5–20.6)	27	42.6 (28.1–61.9)
2008	6338	7	11.0 (4.4–22.7)	18	28.4 (16.8–44.8)
2009	6484	12	18.5 (9.6–32.3)	31	47.8 (32.5–67.8)
2010	6484	6	9.3 (3.4–20.1)	24	37.0 (23.7–55.0)
2011	6529	9	13.8 (6.3–26.2)	28	42.9 (28.5–61.9)
2012	6468	9	13.9 (6.4–26.4)	23	35.6 (22.6–53.3)
Total	45 182	59	13.1 (9.9–16.8)	188	41.6 (35.9–48.0)

Table 2 Patient characteristics and procedures 2006–2012. Mortality is per 10 000 procedures; CI, Confidence Intervals are for a proportion of the deaths relative to the procedures; (N)ICU, (Neonate) Intensive Care Unit, and P-values of differences between subgroups

Variables	Procedures, n	Death <30 days, n (% of 188)	Mortality (95% CI)	P-value
Total	45 182	188	41.6 (35.9–48.0)	
Sex				0.26
Male	26 655	104 (55)	39.0 (31.9–47.3)	
Female	18 527	84 (45)	45.3 (36.2–56.1)	
Age				<0.001
0–30 days (neonates)	1862	72 (38)	386.7 (303.8–484.5)	
31 days to <one yr (infants)	7052	39 (21)	55.3 (39.4–75.5)	
one to <four yr	11 036	25 (13)	22.7 (14.7–33.4)	
four to <10 yr	13 193	13 (7)	9.9 (5.2–16.8)	
10 to <18 yr	12 032	39 (21)	32.4 (23.1–44.3)	
Total <one yr	8921	111 (59)	124.4 (102.5–149.6)	
Total one <18 yr	36 261	77 (41)	21.2 (16.8–26.5)	
ASA status				<0.001
I	13 743	10 (5)	7.3 (3.5–13.4)	
II	8397	5 (3)	6.0 (1.9–13.9)	
Total <III	22 140	15 (8)	6.8 (3.8–11.2)	
III - IV	1544	134 (71)	867.9 (732.2–1019.5)	
Unknown	21 498	39 (21)	18.1 (12.9–24.8)	
Emergency				<0.001
Elective	39 040	90 (48)	23.1 (18.5–28.3)	
Emergency	6142	98 (52)	159.6 (129.7–194.1)	
Surgical procedures				<0.001
Cardiothoracic	3479	48 (26)	138.0 (101.9–182.5)	
Non-cardiothoracic	41 703	140 (74)	33.6 (28.2–39.6)	
Place of death				
Operation Room	–	10 (5)	2.2 (1.1–4.1)	
NICU/PICU	–	158 (84)	35.0 (29.7–40.9)	
Other in-hospital mortality	–	20 (11)	4.4 (2.7–6.8)	
Time of death				
Total <24 h		59 (31)	13.1 (9.9–16.8)	
24 h – 30 days		129 (67)	28.6 (23.8–33.9)	

surgery, cardiothoracic surgery and multiple anaesthetics as risk factors for mortality (Table 5). Anaesthetic or surgical procedure-related factors contributed to mortality in nine of the 188 patients. In none of these patients death could be attributed to anaesthesia or surgery alone; comorbidities played a substantial role in the aetiologies of all nine patients.

In five of these patients anaesthesia or factors under the control of the anaesthetist (in combination with the preoperative condition of the patient) contributed to death (Table 6). Three of these five children died within 24 h after the commencement of the procedure (24-h anaesthesia-related mortality: 0.7/10 000, 95% CI: 0.1–1.9).

In two children with severe congenital cardiac abnormalities, anaesthesia contributed to death because perioperative hypotension caused myocardial ischaemia. Child one was a six-week-old term infant admitted to the hospital because of a truncus arteriosus type II, with rapid increase of the brain natriuretic peptide (BNP), tachypnoea and cyanosis the day before operation. Immediately after induction of anaesthesia with ketamine and sufentanil, a self-limiting bradycardia and hypoxaemia occurred. After intubation the child developed a pulseless electrical activity, and despite adequate resuscitation the child died in the operating room (OR). The panel felt that coronary steal resulting in severe

Table 3 Deaths according to main cause. Mortality is per 10 000 procedures; CI, Confidence Intervals are for a proportion of the deaths relative to the total 45 182 procedures; NEC, Necrotizing Enterocolitis; SIRS, Systemic Inflammatory Response Syndrome

Cause of death	Death <30 days, n (% of 188)	Mortality (95% CI)
1. Preoperative condition	165 (88)	36.5 (31.2–42.5)
Congenital abnormalities	60	
Cardiac	37	
Neurologic	9	
Gastro-intestinal (e.g. oesophagus atresia)	4	
Combined	10	
Additional pulmonary hypertension	10	
Infection (e.g. sepsis, NEC)	48	
Immunocompromised (e.g. leukaemia)	30	
Oncology; solid tumor	7	
Metabolic disease	6	
Postnatal asphyxia	6	
Hypotension (e.g. capillary leak syndrome, SIRS)	3	
Coagulation disorder	3	
Postnatal intracranial bleeding	2	
2. Preoperative trauma event	14 (7)	3.1 (1.7–5.2)
Central nervous system derangement	6	
Haemodynamic instability	4	
Acute Respiratory Distress Syndrome	2	
Multi-organ failure	1	
Cardiac dysrhythmia	1	
3. Anaesthetic management +child condition	5 (3)	1.1 (0.4–2.6)
Cardiac ischaemia because of anaesthetic hypotension	2	
Cerebral ischaemia because of anaesthetic hypotension	1	
Tension-pneumothorax during tube changing	1	
Inadequate vigilance; severe hypoglycaemia	1	
4. Surgical procedure+child condition	4 (2)	0.9 (0.2–2.3)
Spinal cord damage; distributive neurologic shock	1	
Tracheal damage; hypoxemia	1	
Endocardial damage; cardiac tamponade	1	
Corpus alienum (catheter tip) left behind	1	

myocardial ischaemia was the most likely underlying cause of death.

Child two was a four-month-old girl diagnosed with the Williams Beuren syndrome and a mid-aortic syndrome. On arrival at the cardiac catheterization room the child looked pale

Table 4 30 Day mortality per 10 000 anaesthetics, grouped by total number of anaesthetics per patient; CI, Confidence Intervals are for a proportion of the deaths relative to the procedures

Number of procedures per patient	Number of patients	Death <30 days	Mortality
one	18 121	87	48.0 (38.5–59.2)
two– five	7290	75	102.9 (81.0–128.8)
six–10	640	20	312.5 (191.9–478.5)
>11	197	6	304.6 (112.6–651.1)

and repolarization disorders were seen on the ECG. After induction and right heart catheterization, a very high right ventricular end-diastolic pressure and a poor right ventricular function were observed, possibly caused by myocardial ischaemia as a result of anaesthetic-induced decrease of diastolic blood pressure in the presence of coronary stenosis. The infant died despite cardiac resuscitation for 20 min with intraventricular pacing. Autopsy showed severe stenosis of the descending aorta and biventricular hypertrophy.

Child three was an 18-day-old term with Robin sequence who was referred to our hospital for jaw distraction because of several episodes of airway obstruction before her procedure.⁵ After jaw distraction she developed right-sided focal seizures, which progressed to epileptic status at 21 h postoperatively. She died 16 days postoperatively from the effects of cerebral ischaemia and haemorrhage. In retrospect, the reviewing panel argued that the most likely cause was a relative hypotension during the procedure, in combination with preoperative severe respiratory problems.

Child four was a six-weeks-old premature (born 24 weeks, 645 g) who had to be intubated because of grade III infant respiratory distress syndrome. She was brought into OR for intubation because of previous difficult intubations at the NICU. During tube change from 2.5 to 3.0 using a bougie, a tension pneumothorax arose. Two thorax drains were placed in position. However, despite high frequency oscillation ventilation and nitric oxide ventilation the child died 29 h later because of severe respiratory insufficiency.

Child five was a 10 month-old infant who was transferred from a secondary hospital with clinical signs of a fulminant circulatory shock treated with high dose dopamine and noradrenalin, lactate acidosis (lactate 55 mmol litre⁻¹), anuria, and compartment syndrome of arms and legs. An emergency laparotomy did not show an abdominal focus. The circulatory shock resulted in a pulseless electrical activity, which was adequately treated with adrenalin and volume therapy. After a fasciotomy of all extremities the boy died 14 h postoperatively as a result of a resuscitation relapse. Retrospective analysis showed severe perioperative hypoglycaemia of 1.2 mmol litre⁻¹ which was not detected during laparotomy. The panel deemed that it was likely that the missed hypoglycaemia had accelerated an inevitable death.

In four of these patients, surgery or factors under the control of the surgeon (in combination with the preoperative condition of the patient) contributed to death (Table 6). Two of the four children died within 24 h after the commencement of the surgical procedure (24-hour surgery-related mortality: 0.4/10 000, 95% CI: 0.1–1.6).

Three of the patients concerned tissue damage (spinal cord, tracheal-, and endocardial damage Table 6). Child six was a nine yr old girl with spina bifida with myeloschisis and microcephaly, who underwent an anterior and posterior spinal fusion

Table 5 Covariates defining 30-day in hospital mortality. OR, Odds Ratio; CI, Confidence Interval

	OR; univariate model (95% CI)	P-value; univariate model	OR; multivariate model (95% CI)	P-value; multivariate model
Gender (male)	0.85 (0.64–1.13)	0.26	–	–
Age (yr)	0.88 (0.85–0.91)	<0.001	0.92 (0.90–0.95)	<0.001
Emergency surgery	10.15 (7.50–13.72)	<0.001	9.86 (7.23–13.45)	<0.001
Cardiothoracic surgery	4.31 (3.06–6.08)	<0.001	3.20 (2.23–4.59)	<0.001
Number of anaesthetics	1.19 (0.96–1.26)	0.19	1.19 (1.03–1.38)	<0.001

for progressive scoliosis which was complicated by a dura tear. Postoperatively at the PICU a non-treatable circulatory shock progressed (bradycardia and hypotension), most likely caused by spinal cord injury and acute progression of Arnold Chiari syndrome, caused by CSF leakage with brain stem compression.

Child seven was a preterm (born at 27 weeks, 850 g) with oesophageal atresia who underwent a thoracoscopic correction at day three, which was complicated by inoperable rupture of the trachea ligature causing respiratory problems with circulatory arrest. After 45 min of cardiac massage and surgical efforts to close the tracheal rupture the procedure was aborted and the boy died shortly after arrival at the NICU.

Child eight was a preterm (born 25 weeks, 800 g) who was operated at the NICU at day 36 because of an unstable respiratory condition for a diaphragmatic hernia after patent ductus arteriosus ligation. Preoperative insertion of a central venous catheter in the right subclavian vein was complicated by a pericardial tamponade and cardiopulmonary resuscitation, which was successfully treated by thoracotomy. However, the child died five days after the incident because of severe acute respiratory distress syndrome. The panel argued that the pericardial tamponade and subsequent thoracotomy might have worsened the respiratory problems.

Child nine was a seven yr old child with acute lymphoblastic leukaemia and sepsis who was referred from another hospital for percutaneous evacuation of a retained catheter-tip in the right atrium, after removing a port-a-cath. The cardiologist was unable to remove the catheter tip because of thrombus formation around the tip. The child died six days later as a result of severe sepsis with veno-occlusive disease at ICU.

Discussion

In the current report, 30-day hospital mortality after anaesthesia and surgery in a specialized paediatric hospital was 41.6 per 10 000 procedures performed (95% CI: 35.9–48.0) and the 24-hour mortality was 13.1 per 10 000 (95% CI: 9.9–16.8). Both rates are consistent with a previous study from a tertiary centre in Melbourne, Australia.⁴ The authors reported a 30-day hospital mortality of 34.5 (95% CI: 31.1–38.3) and a 24-hour mortality of 13.4 (95% CI: 11.3–15.8). The 24-hour hospital mortality rate in the present study is higher than a study from Rochester, Minnesota, USA, by Flick and colleagues³ who reported a single-centre mortality of 6.8/10 000 (95% CI: 5.2–8.7) in the OR and at the Post-Anaesthetic Care Unit (PACU). This latter difference might have been caused by a shorter follow-up period being set as the PACU, regardless if the duration of stay was <24 h. Furthermore, the partially anaesthesia-related mortality 1.1/10 000 (95% CI: 0.4–2.6) within 30 days and 0.7/10 000 within 24-hours (95% CI: 0.1–1.9) is comparable with Van der Griend and colleagues (1.0 and 0.7 respectively).⁴ The partially anaesthesia-related mortality within 24-hours in the present study is lower than in the

study by Flick and colleagues (0.2/10 000) and the North American Paediatric Perioperative Cardiac Arrest (POCA) Registry (0.4/10 000),^{6,7} which might be explained by a stricter definition of anaesthesia-related death ('if the anaesthetic management was undoubtedly a cause').⁸ The incidence of paediatric perioperative deaths attributable to anaesthesia in previous studies of developed countries between 2000 and 2011 ranges from 0.0 to 1.2 per 10 000 procedures delivered depending on the definitions and postoperative time-window used.^{3,4,6,7,9–15} Differences in mortality incidences may be attributed to substantial variations in study design and population. The design can affect a study's incidence rates, for example by the way in how anaesthesia-related mortality is defined, the method of data collection, the length of the postoperative time-window, the age range of the children included, and the cohort size. The term anaesthesia-related mortality is not yet validated; there is an urge for international standardization of terminology in order to make study comparison and large-scale multicentre research possible.¹⁶

Differences in study populations and healthcare systems may also impede comparison of study results. Rates will be generally lower when including primary and/or secondary centres in a nation-wide cohort^{6,9,10,17} compared with a single tertiary institutional environment with a higher concentration of high-risk patients (as the present study).^{3,4} Besides, inclusion of cardiac surgery is of great importance as these patients and interventions have the highest mortality.^{12,14,18}

In the initial analysis of mortality we did not correct for repeated anaesthetics; children undergoing >1 anaesthetic will have a slightly wider 95% CI than in a situation whereby each child only had one anaesthetic.⁴ Including only the last anaesthetic in the analysis almost doubled the overall mortality from 41.6 (95% CI 35.9–48.0) per 10 000 anaesthetics to 71.1 (95% CI: 61.3–82.0) per 10 000 patients. We included only the last anaesthetic in the regression analyses to define risk factors for a higher mortality to reduce bias. The present study shows that perioperative mortality from any cause is increased in neonates and infants, compared with older children, an observation which is consistent with previous studies.^{3,4,9,10,18} The 30-day mortality from any cause in children older than one yr varies between 9.9 and 32 per 10 000 procedures. Other risk factors for mortality are ASA physical status \geq III, emergency surgery and cardiac surgery.^{3,4,7,13,17,19–21} Furthermore, the present study shows for the first time that mortality where anaesthesia or surgery was deemed to be a contributing factor, is low in young age groups (1–6 per 10 000 procedures) and extremely low in patients aged one yr and older, ASA I or II, elective – and non-cardiothoracic surgery (Tables 2 and 6).

Determining when death is partially caused or influenced by surgery- or anaesthesia-related factors is debatable. We did not find any patient in which the cause of death was solely related to anaesthesia or surgery (Table 3). The determination of

Table 6 Number of death (with mortality per 10 000 anaesthesia's, and 95% confidence interval) in which the anaesthesia or surgery, or factors under the control of the anaesthesiologist or surgeon (in combination with the preoperative condition of the patient) are more likely than not, influenced the timing of death.

	Total	Cardiac surgery	Non-cardiac surgery	0–30 days neonate	31 day <1 yr infant	1 <4 yr	4–10 yr	10–18 yr
Anaesthesia related death	5 (1.1; 0.4–2.6)	2 (5.7; 0.5–20.8)	3 (0.7; 0.1–2.1)	1 (5.4; 0.1–29.9)	4 (5.7; 1.5–14.5)	0 (0; 0–3.3)	0 (0; 0–2.8)	0 (0; 0–3.1)
Surgery related death	4 (0.9; 0.2–2.3)	1 (2.9; 0.1–16.0)	3 (0.7; 0.1–2.1)	1 (5.4; 0.1–29.9)	1 (1.4; 0–7.9)	0 (0; 0–3.3)	2 (1.5; 0.4–5.5)	0 (0; 0–3.1)
Total	9 (0.2; 0.9–3.8)	3479	41 703	1862	7052	11 036	13 193	12 032

causality relies on subjective interpretations and the interpretations can be applied on various existing definitions. There is no consensus in the literature regarding the definition of deaths in which anaesthesia was the primary cause or a contributing factor¹⁶ and thence definitions varied widely among research groups. The POCA Registry classifies cardiac arrest and its mortality as anaesthesia-related 'if anaesthesia personnel or the anaesthetic process played at least some role (ranging from minor to minor) in the cause of the cardiac arrest'.^{6 7} Flick and colleagues defined anaesthesia-related as 'occurring after initiation of anaesthesia in which anaesthetic management was undoubtedly a cause for cardiac arrest, regardless of severe coexisting disease'.¹³ We used the definition of Van der Griend and colleagues: 'those cases for which all agreed that anaesthesia (or surgery) or factors under the control of the anaesthesiologist more likely than not influenced the timing of death'⁴ because we share their opinion that anaesthesia should be considered as a contributing factor, instead of being a cause, within the aetiology of death. The comorbidities of the patients in categories three and four were such that it is difficult to totally attribute the cause of death to either surgical or anaesthetic complications. All children in categories three and four suffered from major comorbidities, which emphasized the approach that complications in anaesthesia or surgery contribute rather than cause death.

The use of an electronic AIMS allows objective retrospective analyses of the perioperative physiologic measurements. As it is known that anaesthetists and surgeons voluntarily report only a small part of adverse events occurring during procedures,^{20 22 23} electronic registration of vital signs minimizes potential selection bias by preventing completion of the charts left to the discretion of the attending anaesthetist and surgeon. Electronic registration increases objective registration of physiologic variables and might improve to define the role of anaesthesia and surgery in the cause of death retrospectively.

A large proportion (10%) of the patients who had been operated at NICU and PICU died within 30 days. Unfortunately, the use of our AIMS does not include all hospital procedures (e.g. procedures performed at PICU and NICU). The surgical procedures performed at the NICU of our hospital were only registered in the general patient record system and not in the AIMS (47 out of 188 deaths; 25%). Some of the anaesthesia data concerning these procedures are missing and therefore a surgery- or anaesthesia-related death might have been missed. We also were not able to check the mortality outside the hospital as by the citizen registration. Therefore, the total 30 day mortality might be underestimated. Furthermore, data were reviewed retrospectively by the authors who were not directly involved in the patient, which could introduce imprecision in the interpretation.

In conclusion, this study confirms previous reports from other developed countries that perioperative mortality is extremely rare in healthy children more than one yr of age. Risk factors for mortality are very young age (neonates and infants), children with ASA physical status III and IV, emergency- and cardiothoracic interventions and repeated anaesthetics - representing the more severe primary conditions. Importantly, the contribution of anaesthesia or surgery-related problems to mortality was negligible, indicating the relative safety of paediatric procedures.

Authors' contributions

Study design/planning: J.C.G.

Study conduct: L.B., W.P., J.C.G.

Data analysis: L.B., D.B.M.W., T.A.N.J., F.H., D.C.Z., J.C.G.

Writing paper: L.B., W.P., D.B.M.W., T.A.N.J., F.H., D.C.Z., L.W., J.C.G.

Revising paper: all authors

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Declaration of interest

None declared.

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References

1. Lagasse RS. Anesthesia safety: model or myth? A review of the published literature and analysis of current original data. *Anesthesiology* 2002; **97**: 1609–17
2. Gibbs N. *A Review of Anaesthesia- Related Mortality Reporting in Australia and New Zealand 2003–2005*. Melbourne: Australian and New Zealand College of Anaesthetists, 2009
3. Flick RP, Sprung J, Harrison TE, et al. Perioperative cardiac arrests in children between 1988 and 2005 at a tertiary referral center: a study of 92,881 patients. *Anesthesiology* 2007; **106**: 226–37
4. van der Griend BF, Lister NA, McKenzie IM, et al. Postoperative mortality in children after 101,885 anaesthetics at a tertiary paediatric hospital. *Anesth Analg* 2011; **112**: 1440–7
5. McCann ME, Schouten AN, Dobija N, et al. Infantile post-operative encephalopathy: perioperative factors as a cause for concern. *Pediatrics* 2014; **133**: e751–7
6. Morray JP, Geiduschek JM, Ramamoorthy C, et al. Anesthesia-related cardiac arrest in children: initial findings of the Pediatric Perioperative Cardiac Arrest (POCA) Registry. *Anesthesiology* 2000; **93**: 6–14
7. Bhananker SM, Ramamoorthy C, Geiduschek JM, et al. Anesthesia-related cardiac arrest in children: update from the Pediatric Perioperative Cardiac Arrest Registry. *Anesth Analg* 2007; **105**: 344–50
8. Flick RP, Katusic SK, Colligan RC, et al. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. *Pediatrics* 2011; **128**: e1053–61
9. Morita K, Kawashima Y, Irita K, Iwao Y, Seo N, Tsuzaki K. [Perioperative mortality and morbidity in the year 2000 in 520 certified training hospitals of Japanese Society of Anesthesiologists: with a special reference to age—report of Japanese Society of Anesthesiologists Committee on Operating Room Safety]. *Masui* 2002; **51**: 1285–96
10. Kawashima Y, Takahashi S, Suzuki M, et al. Anesthesia-related mortality and morbidity over a 5-year period in 2,363,038 patients in Japan. *Acta Anaesthesiol Scand* 2003; **47**: 809–17
11. Tay CL, Tan GM, Ng SB. Critical incidents in paediatric anaesthesia: an audit of 10 000 anaesthetics in Singapore. *Paediatr Anaesth* 2001; **11**: 711–8
12. Murat I, Constant I, Maud'huy H. Perioperative anaesthetic morbidity in children: a database of 24,165 anaesthetics over a 30-month period. *Paediatr Anaesth* 2004; **14**: 158–66
13. Gobbo BL, Braz JR, Modolo NS, do NP, Brushi BA, Raquel de CL. Perioperative cardiac arrest and its mortality in children. A 9-year survey in a Brazilian tertiary teaching hospital. *Paediatr Anaesth* 2006; **16**: 860–6
14. Ahmed A, Ali M, Khan M, Khan F. Perioperative cardiac arrests in children at a university teaching hospital of a developing country over 15 years. *Paediatr Anaesth* 2009; **19**: 581–6
15. Hoffman GM. Outcomes of pediatric anesthesia. *Semin Pediatr Surg* 2008; **17**: 141–51
16. Deshpande JK. Cause and effect or conjecture? A call for consensus on defining 'anesthesia-related mortality'. *Anesth Analg* 2011; **112**: 1259–61
17. Tiret L, Nivoche Y, Hatton F, Desmots JM, Vourc'h G. Complications related to anaesthesia in infants and children. A prospective survey of 40240 anaesthetics. *Br J Anaesth* 1988; **61**: 263–9
18. Bharti N, Batra YK, Kaur H. Paediatric perioperative cardiac arrest and its mortality: database of a 60-month period from a tertiary care paediatric centre. *Eur J Anaesthesiol* 2009; **26**: 490–5
19. Gonzalez LP, Pignaton W, Kusano PS, Modolo NS, Braz JR, Braz LG. Anesthesia-related mortality in pediatric patients: a systematic review. *Clinics (Sao Paulo)* 2012; **67**: 381–7
20. de Graaff JC, Sarfo MC, van WL, van der Werff DB, Schouten AN. Anesthesia-related critical incidents in the perioperative period in children; a proposal for an anesthesia-related reporting system for critical incidents in children. *Paediatr Anaesth* 2015; **0**: 0
21. Baum VC, Barton DM, Gutgesell HP. Influence of congenital heart disease on mortality after noncardiac surgery in hospitalized children. *Pediatrics* 2000; **105**: 332–5
22. de Graaff JC, Bijker JB, Kappen TH, van WL, Zuithoff NP, Kalkman CJ. Incidence of intraoperative hypoxemia in children in relation to age. *Anesth Analg* 2013; **117**: 169–75
23. Staender S. Incident reporting in anaesthesiology. *Best Pract Res Clin Anaesthesiol* 2011; **25**: 207–14

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