Section Editor: **Peter J. Davis**

CME

Postoperative Mortality in Children After 101,885 Anesthetics at a Tertiary Pediatric Hospital

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BACKGROUND: Mortality is a basic measure for quality and safety in anesthesia. There are few anesthesia-related mortality data available for pediatric practice. Our objective for this study was to determine the incidence of 24-hour and 30-day mortality after anesthesia and to determine the incidence and nature of anesthesia-related mortality in pediatric practice at a large tertiary institution.

METHODS: Children ≤18 years old who had an anesthetic between January 1, 2003, and August 30, 2008, at the Royal Children's Hospital, Melbourne, Australia, were included for this study. Data were analyzed by merging a database for every anesthetic performed with an accurate electronic record of mortality of children who had ever been a Royal Children's Hospital patient. Cases of children dying within 30 days and 24 hours of an anesthetic were identified and the patient history and anesthetic record examined. Anesthesia-related death was defined as those cases whereby a panel of 3 senior anesthesiologists all agreed that anesthesia or factors under the control of the anesthesiologist more likely than not influenced the timing of death.

RESULTS: During this 68-month period, 101,885 anesthetics were administered to 56,263 children. The overall 24-hour mortality from any cause after anesthesia was 13.4 per 10,000 anesthetics delivered and 30-day mortality was 34.5 per 10,000 anesthetics delivered. The incidence of death was highest in children ≤30 days old. Patients undergoing cardiac surgery had a higher incidence of 24-hour and 30-day mortality than did those undergoing noncardiac surgery. From 101,885 anesthetics there were 10 anesthesia-related deaths. The incidence of anesthesia-related death was 1 in 10,188 or 0.98 cases per 10,000 anesthetics performed (95% confidence interval, 0.5 to 1.8). In all 10 cases, preexisting medical conditions were identified as being a significant factor in the patient's death. Five of these cases (50%) involved children with pulmonary hypertension.

CONCLUSIONS: Anesthesia-related mortality is higher in children with heart disease and in particular those with pulmonary hypertension. The lack of anesthetic-related deaths in children who did not have major comorbidities reinforces the safety of pediatric anesthesia in healthy children. (Anesth Analg 2011;112:1440–7)

Mortality is a basic measure for quality and safety in anesthesia. Anesthesia-related mortality is infrequent[1–3] and there are few anesthesia-related mortality data available, particularly associated with pediatric practice. A better understanding of overall perioperative mortality rates, and in particular anesthesia-related mortality, may help anesthesiologists determine which patients are at higher risk, and guide planning, resourcing, and expert staffing for these high-risk cases. Defining risk of anesthesia-related mortality is also important to help inform preoperative discussion with families including informed consent for anesthesia.

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Accepted for publication January 21, 2011.

Funding: Hospital funded.

The authors declare no conflicts of interest.

Reprints will not be available from the authors.

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DOI: 10.1213/ANE.0b013e318213be52

In pediatric practice, published data suggest that death attributable to anesthesia ranges from 0.1 to 1.2 per 10,000 anesthetics delivered.[4–11] However, obstacles to obtaining more reliable information include the infrequent occurrence of perioperative deaths in children (studies require very large numbers of children), the lack of reliable and uniform methods of reporting deaths within a population (numerator), and difficulties in estimating the number of anesthetics actually delivered in a population (denominator). In particular, voluntary reporting may underestimate the true mortality rate, and relying on cardiac arrest as a trigger to data collection may miss cases in which an anesthesia-related death occurred postoperatively with no intraoperative cardiac arrest. Another problem with existing data is the subjective and variable definition of what is anesthesia-related mortality. In other words, deaths are often due to multiple factors, one of which may be the anesthetic.[12]

The objective of this study is to determine the incidence of overall mortality from any cause occurring within 24 hours and 30 days after the commencement of anesthesia and to then determine the incidence of anesthesia-related mortality. To attempt to generate a more accurate measure, we collected information from a single institution by merging 2 robust

Table 1. Age Groups and Distribution by Speciality Indicating Case Mix at the Royal Children's Hospital							
	0 to 30 days [neonates]	31 days to <1 year [infants]	Overall <1 year	1 to <4 years	4 to <10 years	10 to <18 years	Total, 0 days to <18 years
Number of children (*n*)	963	6,401	7364	14,201	18,693	16,005	56,263
Speciality:							
Anesthetics, *n* (%)	7 (0.7%)	79 (1.2%)	86 (1.2%)	49 (0.3%)	69 (0.4%)	139 (0.9%)	343 (0.6%)
Cardiac surgery, *n* (%)	302 (31.4%)	600 (9.4%)	902 (12.3%)	298 (2.1%)	312 (1.7%)	251 (1.6%)	1763 (3.1%)
Cardiology, *n* (%)	18 (1.9%)	101 (1.6%)	119 (1.6%)	221 (1.6%)	212 (1.1%)	185 (1.2%)	737 (1.3%)
Gastroenterology, *n* (%)	1 (0.1%)	156 (2.4%)	157 (2.1%)	712 (5.0%)	1280 (6.8%)	1995 (12.5%)	4144 (7.4%)
General surgery, *n* (%)	453 (47.0%)	2796 (43.7%)	3249 (44.1%)	3,061 (21.6%)	3526 (18.9%)	3135 (19.6%)	12,971 (23.1%)
Medical imaging, *n* (%)	23 (2.4%)	555 (8.7%)	578 (7.9%)	1,855 (13.1%)	1272 (6.8%)	470 (2.9%)	4175 (7.4%)
Neurosurgery, *n* (%)	21 (2.2%)	99 (1.6%)	120 (1.6%)	92 (0.7%)	211 (1.1%)	360 (2.3%)	783 (1.4%)
Orthopedic, *n* (%)	5 (0.5%)	268 (4.2%)	273 (3.7%)	743 (5.2%)	2243 (12.0%)	3161 (19.7%)	6420 (11.4%)
Otolaryngology, *n* (%)	26 (2.7%)	233 (3.6%)	259 (3.5%)	2409 (17.0%)	3540 (18.9%)	1355 (8.5%)	7563 (13.4%)
Plastic & maxillofacial, *n* (%)	11 (1.1%)	651 (10.2%)	662 (9.0%)	2119 (14.9%)	2402 (12.8%)	2655 (16.6%)	7838 (13.9%)
Urology, *n* (%)	75 (7.8%)	519 (8.1%)	594 (8.1%)	498 (3.5%)	585 (3.1%)	685 (4.3%)	2362 (4.2%)
Other, *n* (%)	21 (2.2%)	344 (5.4%)	365 (5.0%)	2144 (15.1%)	3041 (16.3%)	1614 (10.1%)	7164 (12.8%)

databases that do not rely on voluntary reporting and for which instances of death can be identified directly and accurately.

METHODS

The project was approved by the Royal Children's Hospital (RCH) Human Research Ethics Committee. Children ≤18 years old who had an anesthetic between January 1, 2003, and August 30, 2008, at the RCH were included for this study. The RCH is a large tertiary hospital with a catchment of approximately 6 million people, including approximately 1 million children. The RCH provides centralized medical care in the state of Victoria and surrounding areas. It provides surgical services in all areas except bowel transplantation and is the Australian national center for pediatric cardiac transplantation and other highly complex congenital heart diseases. It admits >35,000 patients per year, and approximately 20,000 anesthetics are performed annually. Approximately 45% of these anesthetics are performed as elective day-case patients.

The database used for this study was our Perioperative Management System (ORMIS—Operating Room Management Information System). This includes all procedures during which anesthesiologists provide anesthesia, sedation, or significant regional anesthesia anywhere in the hospital, including those in operating rooms (inpatient and outpatient surgery), medical imaging (magnetic resonance imaging [MRI] and computed tomography scans), and radiotherapy. ORMIS does not include cases not booked through this system, such as those receiving sedation without anesthesia staff involvement in areas such as the accident and emergency department, medical imaging, the wards, and the day medical unit. A small number of urgent cardiac surgical cases included in the database involved procedures performed in the intensive care unit (ICU) with anesthesia provided by intensive care physicians.

Retrospective data were collected by merging the ORMIS database with a second database provided by the hospital's "Health Information System," which is a highly accurate electronic record of children who attended the RCH who subsequently died at any location in Australia. This database is updated regularly from data provided by state and interstate government services (including the state coroner and the births, deaths, and marriages register) and referring health practitioners and hospitals (including hospitals from other states). Cases of children dying within 24 hours and 30 days of the commencement of anesthesia (the time that care is assumed by an anesthesia provider) were identified and data were retrieved, including date of birth, gender, admission date, diagnosis, date of surgery, anesthetic start and finish times, type of procedure, medical specialty team, discharge date (if applicable), and date of death. The data were merged for the period from January 1, 2003, to August 30, 2008: the time from when the electronic database was established to the time of analysis. Children were divided into 5 groups according to age: 0 to 30 days, 31 to 365 days, 1 to <4 years, 4 to <10 years, and older children 10 to <18 years.

The medical records of children who died within 30 days after anesthesia were examined and screened by the first author (B.V.). Those cases that resulted in intraoperative death and those cases whereby anesthesia or the anesthesiologist may have impacted in any way on the postoperative outcome were brought before a panel of 3 senior pediatric anesthesiologists and coauthors of this paper (I.M., N.M., and A.D.). Cases were discussed among the members of the panel, and anesthesia-related death was attributed by consensus. Anesthesia-related death was defined as those cases for which all agreed that anesthesia or factors under the control of the anesthesiologist more likely than not influenced the timing of death. Anesthesia for organ donation was excluded from the analyses.

Data analyses were conducted using Stata 10 (College Station, TX). Ninety-five percent confidence intervals (CI) were calculated using binomial exact method. In reporting the 95% CIs the risk is per anesthetic. Some children had more than 1 anesthetic. The reported 95% CIs around risk were not adjusted to account for the nonuniform risk introduced by children having multiple anesthetics.

RESULTS

Between January 1, 2003, and August 30, 2008, 101,885 anesthetics were administered to 56,263 individual children at RCH. We present all calculations as a proportion of the number of anesthetics performed, not as a proportion of the number of children who were anesthetized. Distribution of age groups and specialties is shown in Table 1. Of these

Table 2. Frequency of Reported Deaths Within 24 Hours of Anesthetics by Age

	Overall			Noncardiac surgery[a]			Cardiac surgery[a]		
Age	Anesthetics performed, *n*	Death within 24 hours, *n*	Deaths per 10,000 anesthetics	Anesthetics performed, *n*	Death within 24 hours, *n*	Deaths per 10,000 anesthetics	Anesthetics performed, *n*	Death within 24 hours, *n*	Deaths per 10,000 anesthetics
0 to 30 days [neonates]	2831	51	180.1	1541	26	168.7	1290	25	193.8
31 days to <1 year [infants]	12,424	40	32.2	11,047	24	21.7	1377	16	116.2
Overall <1 year	15,255	91	59.7	12,588	50	39.7	2667	41	153.7
1 year to <4 years	27,030	18	6.6	26,426	13	4.9	604	5	82.8
4 years to <10 years	32,409	11	3.4	31,784	7	2.2	625	4	64.0
10 years to <18 years	27,191	16	5.9	26,680	10	3.8	511	6	117.4
Total, 0 days to <18 years	101,855	136	13.4	97,478	80	8.2	4407	56	127.1

[a] Children were divided into 2 groups according to specialty, cardiac surgery, and noncardiac surgery.

Table 3. Frequency of Reported Deaths Within 30 Days of Anesthetics by Age, Including Deaths Within 24 Hours

	Overall			Noncardiac surgery[a]			Cardiac surgery[a]		
Age	Anesthetics performed, *n*	Death within 30 days, *n*	Deaths per 10,000 anesthetics	Anesthetics performed, *n*	Death within 30 days, *n*	Deaths per 10,000 anesthetics	Anesthetics performed, *n*	Death within 30 days, *n*	Deaths per 10,000 anesthetics
0 to 30 days [neonates]	2831	104	367.4	1541	54	350.4	1290	50	387.6
31 days to <1 year [infants]	12,424	102	82.1	11,047	62	56.1	1377	40	290.5
Overall <1 year	15,255	206	135.0	12,588	116	92.2	2667	90	337.5
1 year to <4 years	27,030	58	21.5	26,426	48	18.2	604	10	165.6
4 years to <10 years	32,409	42	13.0	31,784	33	10.4	625	9	144.0
10 years to <18 years	27,191	45	16.6	26,680	37	13.9	511	8	175.8
Total, 0 days to <18 years	101,855	351	34.5	97,478	234	24.0	4407	117	265.5

[a] Children were divided into 2 groups according to specialty, cardiac surgery, and noncardiac surgery.

anesthetic episodes, 13% were performed on children <1 year (1.7% on children ages 0 to 30 days and 11.4% on children ages 31 to 356 days). Overall, the most common type of surgery was general surgery (23%), followed by plastic and maxillofacial surgery (14%) and otolaryngology (13%). Cardiac surgery accounted for 3% of anesthetics given.

Deaths from All Causes Within 24 Hours

During this 68-month period, 136 deaths from any cause occurred within 24 hours of administration of anesthesia (13.4 deaths per 10,000 anesthetics; 95% CI 11.2 to 15.8). Of children who died within 24 hours, a large proportion were neonates (38%), and overall the highest rate was also in neonates (180 deaths per 10,000 anesthetics; 95% CI 134 to 236). In all age groups the rate of death was higher in cardiac than in noncardiac surgical groups (Table 2).

Of the 136 patients who died within 24 hours of their anesthetic, 39 of these cases (29%) involved initiation, adjustment, or withdrawal of extracorporeal life support (ECLS), including extracorporeal membranous oxygenation and ventricular assist devices. In 80 of the 136 patients who died within 24 hours of anesthesia (59%), the anesthetic was delivered outside of the operating rooms including the ICU on 43 occasions (32%), the neonatal ICU on 21 occasions (15%), and the MRI suite on 16 occasions (12%).

Deaths from All Causes Within 30 Days

During this 68-month period, 351 deaths from any cause occurred within 30 days of administration of anesthesia (overall 34.5 deaths per 10,000 anesthetics). Of children who died within 30 days, large proportions were neonates (30%) or of ages between 31 days and 1 year (29%). The overall highest rate was in neonates (367 deaths per 10,000 anesthetics; 95% CI 301 to 443). In all age groups the rate of death was higher in cardiac than in noncardiac surgical groups (Table 3).

Anesthesia-Related Death

Medical records were sought for review for all 351 deaths within 30 days of anesthesia. Of these 351 cases, 336 records (95.7%) were located and reviewed by the authors. For the 15 missing records, searching databases of diagnostic codes produced no information that indicated anesthesia was likely to have been a major contributor to the death. Of the 136 cases of death from any cause within 24 hours of anesthesia, all 136 medical and anesthetic records were reviewed.

There were 10 cases from 101,885 anesthetics of anesthesia-related death identified, that is, those cases whereby anesthesia or factors under the control of the anesthesiologist influenced the timing of death. Therefore, in this audit, the incidence rate of anesthetic-related death is 1 in 10,188 or 0.98 cases per 10,000 anesthetics performed (95% CI = 0.5–1.8).

Case 1

A 3-year-old with congenital heart disease (Ebstein's anomaly) and severe biventricular dysfunction presented for the surgical insertion of a central venous line. This child was listed for a possible cardiac transplantation and required continuing IV inotrope therapy. After induction of anesthesia with IV propofol, the child developed ventricular fibrillation requiring cardiac compression until established onto ECLS. Postoperatively, the child was transferred to the ICU where care was continued until further investigations demonstrated a severe hypoxic–ischemic brain injury and support was withdrawn.

Case 2

A 15-year-old autistic girl with severe primary pulmonary hypertension receiving maximal medical therapy required a surgically inserted IV line. Anesthesia for this procedure involved premedication with midazolam followed by further sedation with midazolam and remifentanil. Following the procedure, the patient developed an acute pulmonary hypertensive episode in recovery, which was managed with oxygen and nitric oxide. The condition settled and the patient was transferred to ICU before being discharged to the ward. However, that evening, the patient suffered a cardiac arrest and died despite attempts at resuscitation.

Case 3

A 4-year-old with a restrictive cardiomyopathy and pulmonary hypertension had anesthesia induced with IV ketamine and thiopental for cardiac catheterization. The patient's lungs were ventilated with a high-inspired concentration of oxygen with nitric oxide. During the procedure, there were several episodes of ST depression and arrhythmias on electrocardiogram. It was noted by the cardiologist that the patient's pulmonary artery pressure was at times suprasystemic. Towards the conclusion of the case, the patient developed further ST segment changes on electrocardiogram and ventricular fibrillation ensued. The patient was unable to be resuscitated.

Case 4

An 8-year-old with primary pulmonary hypertension required a surgically inserted IV line for further medical therapy. Anesthesia was induced with fentanyl and propofol and maintained with isoflurane with addition of nitric oxide. Approximately 60 minutes into the procedure, the patient developed bradycardia with pulseless electrical activity. Cardiac massage was commenced and continued for 45 minutes while the patient was established onto ECLS. ECLS was continued for 5 days; however, neurological testing was consistent with a poor outcome, and support was discontinued.

Case 5

A 1-year-old with a new diagnosis of primary pulmonary hypertension was referred for cardiac catheterization. Shortly after the induction of anesthesia with oxygen and sevoflurane, the patient suffered from a cardiac arrest. Despite attempts at resuscitation, the patient died in the operating room.

Case 6

A 3-year-old with a Chiari type 1 malformation and hydrocephalus presented with a ventriculoparietal shunt malfunction requiring revision. However, 3 days postoperatively the patient's condition deteriorated with increased intracranial pressure, and the patient underwent further surgery, including posterior cranial fossa decompression. The patient was hemodynamically unstable some hours postoperatively and was transferred for MRI under the care of the anesthetic team, and anesthesia was administered (isoflurane) during the scan. The patient sustained a cardiac arrest and, despite resuscitation attempts, died. The reviewing panel felt that it was likely that isoflurane contributed to hemodynamic instability and thus anesthesia impacted on the timing of cardiac arrest and death.

Case 7

A 4-month-old with an undiagnosed degenerative neurological condition associated with seizures and frequent apneas required fresh biopsies of the liver, muscle, and skin for diagnostic purposes. In consultation with the family, this patient was planned for palliation and no active resuscitation after the immediate recovery period. Some 7 hours after the operation the patient had an apneic event and died. The reviewing panel discussed this case and decided that anesthesia, more likely than not, influenced the timing of the apnoeic event and the patient's death.

Case 8

A 4-month-old ex 29-week preterm baby with Trisomy 21, chronic lung disease, congenital heart disease (atrioventricular septal defect), and pulmonary hypertension presented for cardiac surgery. The patient lost cardiac output during attempts to insert intra-arterial monitoring before surgery had commenced. Cardiac compressions were continued for 30 minutes until the patient was established on cardiopulmonary bypass. After surgery the patient required ECLS support. Postoperative care was complicated by sepsis and ECLS was withdrawn 12 days later.

Case 9

A 13-day-old with congenital heart disease (hypoplastic left heart syndrome) 8 days after Norwood procedure was referred for chest closure. There had been 2 previous failed attempts by the surgeons to close the chest, both attempts aborted because of profound hemodynamic changes. The final attempt was successful until the patient was being prepared by the anesthesiologist for transfer back to ICU when there was sudden hemodynamic collapse. The chest was reopened and external and internal cardiac massage was performed. However, after 45 minutes, resuscitation was stopped. After panel discussion and discussion with the anesthesiologist concerned, it was determined that the transfer of the patient and monitoring from the operating table to the cot (i.e., factors under the control of the anesthesiologist) influenced the timing of cardiac arrest.

Case 10

A 2-year-old with congenital heart disease (hypoplastic left heart syndrome) post bidirectional cavopulmonary shunt underwent anesthesia for gastroscopy and change of gastrostomy feeding tube. The procedure was uneventful and the patient was discharged home only to return to the hospital 2 days later with seizures. Computed tomography brain scan demonstrated multiple infarcts involving both cerebral hemispheres. Further investigation with MRI under anesthesia was organized. The patient was anesthetized with a gas induction and tracheally intubated. There were difficulties obtaining IV access. Bradycardia and loss of cardiac output ensued, and cardiopulmonary resuscitation was commenced and continued for approximately 4 to 5 minutes. An intraosseus needle was inserted and fluids and epinephrine administered. The patient died 5 days later when treatment was withdrawn because of poor neurological prognosis.

In all 10 cases, preexisting medical conditions were identified as being a significant factor in the patient's death. In 8 cases, cardiac arrest occurred while under the care of the anesthesia team. In 2 cases the children died on the ward without any cardiac arrest having occurred while under the care of the anesthesia team. Of the 8 children who had a cardiac arrest under the care of the anesthesia team, 2 occurred in the MRI facility, and the other 6 in the main operating complex, in the operating room, cardiac catheter room, or anesthesia induction room. Of the 10 cases, death occurred on the general ward in 2 cases, in the ICU in 4 cases, and in the operating room or MRI suite in the other 4 cases.

DISCUSSION

During this 68-month period, the overall 24-hour mortality rate from any cause after anesthesia at our tertiary pediatric hospital was 13.4 per 10,000 anesthetics delivered, and 30-day mortality rate was 34.5 per 10,000 anesthetics delivered. The 24-hour mortality rate and 30-day mortality rate give some indication that an appreciable number of anesthetics are given to children who are critically unwell. Patients undergoing cardiac surgery had a higher 24-hour mortality rate (127.1 per 10,000 anesthetics) and 30-day mortality rate (265.5 per 10,000 anesthetics) than did those undergoing noncardiac surgery (24-hour mortality rate of 8.2 per 10,000 anesthetics and 30-day mortality rate of 24 per 10,000 anesthetics). This is consistent with other studies.[5,13–16] The group of patients with the highest rate of postanesthetic mortality from any cause were neonates ($\leq$30 days old) undergoing cardiac surgery with a 24-hour mortality rate of 194 per 10,000 anesthetics and 30-day mortality rate of 388 per 10,000 anesthetics.

Perioperative mortality rate in a pediatric population has been stated to be as low as 0.2 per 10,000 procedures within 24 hours (including cardiovascular procedures) in a French study of 40,240 procedures performed (age <15 years) published in 1988.[7] Other published audits demonstrate higher incidences of mortality rate including 9.8 per 10,000 anesthetics (age <18 years) at a Brazilian tertiary teaching hospital (2006),[17] 10.7 per 10,000 procedures within 2 days of surgery from an Indian study that excludes cardiac surgery (2009),[10] and 22.6 per 10,000 cases from a multicenter audit published in Thailand (2007)[18] that includes cardiac surgery. In the United States, Flick et al. (2007)[5] described cardiac arrests and perioperative ("in the continuous care of the anesthesia team") mortality rate in a pediatric population (age <18 years) in a single tertiary referral center over a 17-year period (92,881 anesthetics). Their group published an overall mortality rate after perioperative cardiac arrest of 6.8 per 10,000 anesthetics delivered. The mortality rate (after perioperative cardiac arrest) associated with cardiac surgery was 115.5 per 10,000 anesthetics and 1.6 per 10,000 anesthetics for noncardiac surgery.[5] The results presented in our study demonstrate a high incidence rate of mortality in comparison with those in other studies; however, it is difficult to directly compare our 24-hour and 30-day mortality rates with other published data. Patient mix varies among centers. It is expected that hospitals treating a higher proportion of complex and acutely unwell children would have a higher mortality rate. Methodology and definitions also vary and, with the exception of Flick et al., many have relied on voluntary reporting.[4,6,7,9,10,14,15,17–21] Most data have been generated by identifying cardiac arrests within the perioperative (intraoperative and those in the postanesthetic care unit [PACU]) period rather than 24-hour and 30-day mortality.[5–7,9,14,15,17,18,20] When compared with previous studies that use data generated from identifying intraoperative cardiac arrests, our results would be expected to generate a higher rate of mortality because children may die in the postoperative period with no cardiac arrest in the operating room or PACU. Importantly in our study, 2 anesthesia-related deaths were in this category. Although it is unfortunate that direct comparisons cannot be made between our study and previous studies, overall it makes sense to assume that directly counting mortality is a more accurate and preferable measure of postoperative mortality than is relying on indirectly identifying cases through occurrence of intraoperative cardiac arrest, or relying on any system of voluntary reporting.

Anesthesia-Related Death

When performing this study it became apparent that there are few deaths totally attributable to anesthesia, but there were possibly more for which anesthesia may have contributed to the death. In these cases, attributing death to anesthesia is difficult and open to subjective interpretation of various definitions. The Australian and New Zealand College of Anesthetists Mortality Committee has defined anesthetic-related mortality by 3 categories. Those cases are designated *category 1* when it is reasonably certain that death was caused by the anesthesia or other factors under the control of the anesthetist; *category 2* when there is some doubt whether the death was entirely attributable to the anesthesia or other factors under the control of the anesthetist; and *category 3* when death was caused by both surgical and anesthesia factors. This definition is applied regardless of the patient's condition before the procedure.[1,2] Flick et al. defined anesthetic-attributed cardiac arrest as occurring after initiation of anesthesia in which anesthetic management was undoubtedly a cause for cardiac arrest regardless of severe coexisting disease.[5] The

North American Pediatric Perioperative Cardiac Arrest (POCA) registry attributed anesthesia-related cardiac arrest if anesthesia personnel or the anesthetic process played at least some role (ranging from minor to total) in the genesis of cardiac arrest.[6] Other audits do not define anesthetic-related cardiac arrest or death.[4,20,21] In the literature there is thus no standard or consistent way to define what is an anesthesia-related death. This makes any comparison with previous studies difficult.[12]

For the purposes of this study, the reviewing authors found it difficult to reach a consensus on possible anesthetic-related deaths using any previously published definitions, particularly for those cases whereby death was considered inevitable. In these cases, a number of factors were involved, and it was extremely difficult to determine whether anesthesia did in fact cause, or play some role in, death. We therefore have proposed a new definition of anesthesia-related death: those cases in which it is more likely than not that anesthesia or factors under the control of the anesthesiologist influences the timing of death. The authors found that it was simpler and more effective to define anesthesia-related death when observing that anesthesia impacted on the timing of death rather than being the cause of death. This definition does not imply that care was inadequate or negligent.

By applying this definition, we described an incidence rate of anesthesia-related death in our pediatric population of approximately 1 in 10,000 anesthetics delivered. This result is higher than the previously published rate of anesthetic-related death in Australian hospitals (0.19 per 10,000 anesthetics inclusive of adults and children)[1] and large audits in the United States including the POCA Registry (0.36 per 10,000),[6] both of which relied on voluntary reporting. Flick et al. reported an incidence rate of anesthesia-related death of 0.22 per 10,000 in a large audit of perioperative cardiac arrests at a single tertiary center (Mayo Clinic, Rochester, NY).[5] As outlined above, directly comparing studies is problematic. Our higher incidence rate of anesthesia-related death may be explained in part by identifying deaths directly rather than via incidence of cardiac arrest or voluntary reporting (as discussed above) and also possibly because of the different definition of anesthesia-related death. Realizing that opinions on what should be regarded as anesthesia-related death will inevitably vary, and to allow some comparison with previous studies, we have provided a brief synopsis of cases to help the reader interpret our findings.

Our series highlight several issues when deciding what is anesthesia-related death and what is not. For example, in case 2 it is possible that the crisis would have occurred without the anesthetic, and in case 7 the anesthetic may or may not have precipitated the apneic episode. Case 7 is complicated further by the possibility that had the child not been receiving supportive care only, then the postanesthetic apneic episode might not have resulted in death. Case 6 was also difficult because it could be argued that the child was already critically unwell and could have arrested and died during the scan even without anesthesia. Lastly, in case 9 the child had a cardiac arrest during transfer from operating table to bed. It is probable that moving the child precipitated the arrest, but although care during transport is the responsibility of the anesthesiologist it is perhaps semantic to say such an event is "anesthesia-related." There was no indication that care was in any way suboptimal. These cases illustrate the difficulty in trying to define exactly what an anesthesia-related death is. It is perhaps questionable that any method of defining anesthesia-related death is likely to be entirely clear-cut, and attempts to measure or compare anesthesia-related death will be inherently limited by the lack of clear definition.

Differences in case mix, variations in methods of data collection, and varying definitions of anesthesia related–death (along with the inherently subjective nature of deciding what role anesthesia played in many deaths) all mean that anesthesia mortality rates should be used cautiously. The literature should be looked at as a whole; comparisons between studies in different institutions may be of limited value, and any reports of absolute risk of anesthesia should perhaps avoid any emphasis on detailing actual numerical risk. Because death is often multifactorial, reporting perioperative mortality may be more informative if all factors are considered rather than just focusing on anesthesia-related factors. Preventing death may be more likely if more emphasis is placed on why deaths occurred in the whole perioperative care process rather than just trying to define the risk of anesthesia per se.

Finally, random variation must be considered when comparing incidence rates among studies; the reported incidence rates in some studies still lie within the breadth of the 95% CIs in others. Also when considering the 95% CIs the influence of nonuniform risk should be considered. In these studies children have more than 1 anesthetic. In general if children have more than 1 anesthetic, then the 95% CIs will be slightly wider than if each child only had 1 anesthetic (because the within-subject variation in risk will be less than the between-subjects variation in risk). It is however difficult to know exactly how much wider. As an extreme the interval cannot be wider than if one considered the risk per child rather than per anesthetic. In this case the risk of death per child receiving anesthetics in that period is 1.8 per 10,000 children with a 95% CI of 0.85 to 3.27, which is almost twice the 95% CI width when considering incidence of death per anesthetic with no adjustment for nonuniform risk.

Clinical Implications

It is important to note that in our study all cases of anesthesia-related death had significant life-threatening medical problems. With the advent of sophisticated extracorporeal cardiorespiratory support systems and improved and specific medical therapies for conditions such as pulmonary hypertension, patients with highly complex medical problems once considered "unfit for anesthesia" are increasingly presenting for surgery and other procedures including medical imaging. The implementation of some life-saving therapies may require potentially life-threatening anesthesia. Careful planning by the teams involved and detailed consultation with the family to provide realistic pictures of the risks and benefits are crucial to these situations. It is clear that the majority of the mortality we describe relate to such complex scenarios.

It has been shown that children with heart disease have an increased frequency of anesthesia-related cardiac arrests when undergoing cardiac surgery[22] and noncardiac surgery.[15] It is not surprising that a substantial proportion of anesthesia-related mortality in this series was in children with congenital heart disease. Of interest was that pulmonary hypertension was involved in 50% (5 cases) of anesthesia-related deaths. Three of these had primary pulmonary hypertension, and in 2 cases, pulmonary hypertension was secondary to heart disease. Previous publications have demonstrated an increased risk of perioperative morbidity and mortality in children with pulmonary hypertension.[23,24] Our audit, by describing a series of 5 anesthesia-related deaths that involved pulmonary hypertension, reaffirms that anesthesia for procedures in these children is very high risk. Anesthesia should only be performed in these children when there is a sound clinical justification, and if anesthesia is necessary, it should be performed with great care to avoid precipitating a pulmonary hypertensive crisis. Strategies must also be in place to treat such a crisis promptly and effectively if one occurs. It is also important to note that in these children, cardiac arrest occurred on induction of anesthesia, during the procedure, and in the PACU, highlighting the need for care during the entire perioperative period.

There were no anesthetic-related deaths in children without significant comorbidities. This would imply that when assessing quality of care in a tertiary pediatric hospital, the anesthesia-related death rate in healthy children should be very low. It may also imply that during routine consent for anesthesia, and when discussing anesthesia risk, it may not be appropriate to list risk of death for children who do not have significant comorbidities.

As well as the problem of definitions mentioned above, there are other limitations to this study. Institutions differ in their patient mix. This setting is a large referral center and certainly not representative of most practices in Australia. Only 45% of our cases are day cases (in which the child is admitted and discharged home on the same working day). Mortality in our hospital, which has a heavy cardiac load, may not be the same as in other tertiary institutions. Similarly, in our institution all our consultant anesthesiologists are trained pediatric anesthesiologists or trainees supervised by consultant pediatric anesthesiologists. Anesthesia-related mortality could be different from that at centers with fewer specifically trained staff. Although the results cannot be directly extrapolated to other clinical practices, it is nevertheless still instructive to know that there is an appreciable postoperative mortality in children with severe comorbidities. This audit was limited to identifying mortality within 30 days of anesthesia and therefore it is possible, although unlikely, that cases of anesthesia-related death beyond 30 days of anesthesia were missed. Cases of anesthesia-related death may also have been missed as a result of the small number of medical records that were not able to be located in our medical records department. However, the cause of death entered on the patient databases for these cases indicated that the probability of anesthesia-related death was low.

In conclusion, although the actual rate of anesthesia-related mortality was higher than was previously reported, differences in methodology and definition limit any conclusions that can be drawn from such comparisons. Of all postoperative deaths, few deaths were anesthesia-related, and this study highlights problems in defining what is anesthesia-related death. Importantly, in this study all anesthesia-related deaths were in children with highly complex medical problems, including congenital heart disease and in particular pulmonary hypertension; and no anesthesia-related deaths were identified in children with no or minor medical problems.

DISCLOSURES

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Attestation: Benjamin F. van der Griend has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
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