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REVIEW

A review of paediatric anaesthetic-related mortality, serious adverse events and critical incidents

L Cronjé[a*]

[a]*Discipline of Anaesthesiology and Critical Care, School of Clinical Medicine, College of Health Sciences, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa*
*Email: *larissa.cronje@kznhealth.gov.za*

Anaesthetists increasingly face questions from parents on the long-term outcomes of anaesthesia, and yet more immediate anaesthetic risks are not understood, nor explained to families. This review focused on paediatric anaesthetic-related mortality, cardiac arrest and anaesthetic-related serious adverse events and critical incidents during general anaesthesia, and within 24 hours of anaesthesia ending. Anaesthetic-related mortality is rare in the developed world, and is approximately 1 per 10 000 anaesthetics, but increases in high-risk children. Serious anaesthetic-related adverse events occur in 1.4 per 1 000 anaesthetics in the developed world. Data are lacking from the developing world but anaesthetic mortality is 2–3 times higher in middle-income countries and may be up to 100-fold greater in low-income countries. A critical incident occurs in 3–8% of anaesthetics and this figure is double that in low-income countries. Anaesthetic-related events are predominantly preventable. Brief recommendations on preventative strategies are made and research goals outlined.

Keywords: mortality, outcomes, paediatric anaesthesia, perioperative, risks

Introduction

The trend in perioperative outcome research is to focus on long-term, patient-centred outcomes, such as quality of life and disability-free recovery, rather than just survival.[1–7] The purpose of this review was to refocus on immediate clinical safety outcomes within 24 hours of anaesthesia ending.[8] There is a significant difference in outcome in developed and developing countries, and the contributory factors are highlighted in this regard. Challenges within the South African healthcare context are deliberated. Anaesthetic-related mortality and cardiac arrest are rare events, hence difficult to study.

Also, true anaesthetic-related mortality could be underestimated, and the effects of safety improvements that are made overestimated, because of methodological problems.[9,10]

The importance of studying anaesthetic-related mortality, cardiac arrest and serious adverse events

The most important perioperative trigger for cardiac arrest and morbidity and mortality is the child's disease or condition. Anaesthetic-related causes are conversely infrequent.[11,12] It may not be meaningful for patients to separate anaesthetic-related mortality and serious adverse events from other causes, yet the narrow-outcome focus remains important because:

- A baseline assessment of the safety of an anaesthesia service is provided by anaesthetic-related mortality and cardiac arrest.[13–16]
- High-risk patients are identified, which assists when making informed decisions on patient care.[2,17,18]
- Informed consent is enhanced when immediate anaesthetic-related risk is accurately communicated to families and patients.[13]
- System issues are identified which contribute to substandard anaesthetic care, especially in middle- and low-income countries.[18–21]
- Research is facilitated and can be appropriately directed to improving clinical anaesthetic safety.[22–26]

Definitions of "anaesthetic-related" mortality, cardiac arrest, serious adverse events and critical incidents

Event triggers or causes are divided into surgery related, patient disease or condition related, and anaesthesia related.[11,14] Standardised definitions do not exist with respect to the timeframe used, method of data acquisition or outcome definitions utilised.[23,27,28] Therefore, quoted incidences vary, making comparison between studies difficult, and resulting in potentially misleading conclusions.[12,16,23,27–29]

Anaesthetic-related mortality or cardiac arrest

Definitions (Table 1) may be considered to be either restrictive, inclusive or multiple. The contribution of anaesthesia may be underestimated when using restrictive definitions.[27,30,31] Thinking in "silos" is avoided with the use of inclusive definitions, while a wider range of cases relevant to anaesthetists is included.[16] Definitions in which multiple categories apply are complex, and are more likely to be subjective.[32] It has been proposed that researchers should adopt uniform, consensus definitions.[8,23,27] It is the opinion of the author that simple, but inclusive definitions, are appropriate to research in the developing world.[13,31]

Anaesthetic-related serious adverse events and critical incidents

Monitoring serious adverse events and critical incidents is a better indicator of safety advances, especially when mortality is low, and should incorporate feedback loops.[16,34] There is a fine

Table 1: Definitions of anaesthetic-related mortality or cardiac arrest

Source	Cardiac arrest deemed to be anaesthesic-related if
Flick et al[30] "Restrictive"	It occurred after the initiation of anaesthesia, in which anesthetic management was undoubtedly a cause for cardiac arrest, regardless of severe coexisting disease
POCA Registry[31,33] "Inclusive"	Anaesthesia personnel or the anaesthesia process played at least some role (ranging from minor to total) in the genesis of cardiac arrest
Source	**Death deemed to be anaesthesia-related if**
ANZCA Mortality Committee[13]	*Category 1:* It is reasonably certain that death was caused by the anaesthesia or other factors under the control of the anesthetist
"Multiple categories"	*Category 2:* There is some doubt as to whether or not the death was entirely attributable to the anaesthesia, or other factors under the control of the anesthetist *Category 3:* Death was caused by both the surgical and anaesthesia factors. This definition is applied regardless of the patient's condition before the procedure
Van der Griend et al[13] "Inclusive"	It is more likely than not that anaesthesia, or factors under the control of the anaesthesiologist, influenced the timing of death

ANZCA: Australian and New Zealand College of Anaesthetists, POCA: Pediatric Perioperative Cardiac Arrest

Table 2: Categories of serious adverse events and their definitions[14,16]

Serious adverse events	Category	Definition
Death	Death	Death during anaesthesia, or within 24 hours of anaesthesia
Life threatening	Airway event	Severe hypoxaemia or hypercapnia while receiving emergency intubation and medication during anaesthesia, or within 24 hours of anaesthesia
Life threatening	Cardiac arrest	Bradycardia or hypotension while receiving cardiac compressions during anaesthesia or within 24 hours of anaesthesia
Disability or incapacity	Awareness anaesthesia	Patient memory of events during general anaesthesia
Disability or incapacity	Musculoskeletal, joint and cutaneous injury	Injury to muscle, bone, joints, the skin or soft tissue from an anaesthesia care-limiting function, and requiring medical or surgical treatment (includes intravenous infiltration)
Disability or incapacity	Nervous system injury	Injury to the brain, spinal cord or peripheral nerves unrelated to a surgery - limiting function
Disability or incapacity	Visual system injury	Injury to the eye or visual pathway unrelated to surgery lasting beyond 24 hours of the anaesthesia
Disability or incapacity	Wrong surgery	The start of surgery or anaesthesia care on a body part for which consent for the procedure had not been given by the patient
Hospitalisation	Acute lung injury	New-onset impaired gas exchange with parenchyma signs which escalated the care
Hospitalisation or life threatening	Cardiovascular event	Unanticipated cardiovascular support during anaesthesia, or within 24 hours of the anaesthesia, which escalated the care
Hospitalisation	Care escalation	Fire, malignant hyperthermia, medication or an equipment error during anaesthesia care, which escalated the care

line between serious adverse events, which measure death, permanent disability and care escalation, and critical incidents. Critical incidents measure a wider variety of events, including "near misses" and have been defined as "any event that affected, or could have affected, the safety of the patient while under the care of an anaesthetist from the induction of anaesthesia until discharge from the post-anaesthesia care unit".[29] Discrimination is lacking with the use of adult reporting tools in paediatric events.[29] Paediatric-specific monitoring tools have been devised in the Wake Up Safe programme for serious adverse events (Table 2),[14,16] and by de Graff et al., for critical incidents.[29]

Data sources and their limitations

Information is gathered from three main sources, i.e. liability claims, incident-reporting systems (registries) and anaesthetic information systems (databases). Liability claims are subject to outcome bias, and are not always generalisable, but may reflect what families perceive to be unacceptable outcomes.[35,36] Incidence cannot be estimated using voluntary registries, which feature selective or inaccurate reporting bias, but can be the source of a large number of cases.[28,37–39] Valuable insight into trends and associations has been gained from these sources, and patient safety improved by routine respiratory monitoring and the reduction of preventable cardiac arrest from medication errors.[2,33,36,40]

Selection and reporting bias can be overcome with the use of databases and anaesthetic information systems featuring non-voluntary reporting. Large datasets with numerators and denominators for accurate incidence calculation are provided through such systems. Retrospective analysis may lead to inaccuracies, unless the database was designed for the outcome measures sought.[32] Comparative analysis is hampered with the use of a case mix and institutional audit with a small sample size.[2,27,28,41] Collaborative, prospective collection through paediatric-specific databases facilitates the accurate calculation of incidence, the elucidation of causality and the development of neonatal and paediatric perioperative risk models.[16,41–44]

Incidence and morbidity risks in paediatric operations

Because of changes in clinical practice and advances in anaesthetic care, data from a systematic review in 2011,[12] and from original studies not included in the review or published afterwards, are summarised in three eras (Table 3). A significant correlation exists between the Human Development Index (HDI)

Table 3: Twenty-four hour anaesthetic-related and 24-hour perioperative mortality per 10 000 anaesthetics

Era	24-hour anaesthetic related mortality			24-hour perioperative mortality		
Date of data	< 18 years	< 1 year	< 30 days	< 18 years	< 1 year	< 30 days
1947–1983						
High-income* (*n* = 47111)	1.57–2.9	NR	NR	4.9	NR	NR
1980–1999						
High-income* (*n* = 1374750)	0–0.42	NR	NR	1.23–3.8 or	6.63**	74.1–83.1**
Middle-income* (*n* = 37420)	NR	NR	NR	0.33–5.4	NR	NR
Low-income*	ND	ND	ND	ND	ND	ND
2000–2015						
High-income* (*n* = 1190486)	0–1.19	0–3.51**	0–0.8	0.41–13.4**	5.91–32.2	26.9–180.1
Middle-income* (*n* = 62519)	2.4–3.3***	3.7–4.7	NR	10.7–15.9***	18.5–65	76
Low-income* (*n* = 26057)	37–60	NR	NR	7.7****	NR	NR

n: number of cases recorded, ND: no data found, NR: data not recorded
*:Income categories are as per the World Bank classification
**:One study with operating room only data
***:Includes studies with data until post-anaesthesia recovery only
****:Data from an externally funded hospital

of a country and its 24-hour perioperative and anaesthetic-related mortality.[19] Hence, the data are further subdivided according to income categories, as defined by the World Bank.

Incidence of morbidity

Despite the methodological limitations presented, large volumes of paediatric data are available from high-income countries.[2,12,45] Since the first era, anaesthetic-related mortality has declined to approximately 1 in 10 000 anaesthetics.[12,13,46] Twenty-four hour perioperative mortality from any cause varies widely, and may relate to case mix.[12,13] This is evident in a study from Australia in which a higher-than-expected 24-hour perioperative mortality of 13.4 per 10 000 anaesthetics was reported, and which included cardiac and neurosurgery cases.[13] The mortality rate for complex cardiac operations may be up to 100-fold higher that of noncardiac surgery.[30]

There are relatively little paediatric data from developing countries, compared to those from high-income countries. Anaesthetic-related mortality in middle-income countries is 2–3 times higher than that in developed countries.[11,12,45,47–49] Perioperative mortality trends may initially increase in middle-income countries with increasing access to surgical care, the increased provision of surgery for unwell patients undergoing complex procedures, and more reliable data.[9,11,12,19,29] A 2014 study from Brazil demonstrated this, as 24-hour perioperative mortality increased when compared against the incidence of mortality reported in previous studies.[11,47,50]

Anaesthetic-related mortality increases by a factor of 50–100 in low-income countries, but may be 1 000-fold higher in certain poor countries.[11,18,19,21,47–55] Bainbridge reported a similar trend in adult patients.[19] Unlike the case in high HDI countries, anaesthetic-related mortality in low HDI countries has not declined. A reverse trend has been demonstrated, perhaps relating in part to improved data collection.[19]

Cardiac arrest from all causes during anaesthesia is approximately 20–30 per 10 000 anaesthetics, while anaesthetic-related cardiac arrest ranges from 1–5 per 10 000 anaesthetics.[11,42,47,56] Mortality following anaesthetic-related cardiac arrest is 30% in high-income countries, but far higher in low-income countries.[11,42,47,56–58]

Up to 75% of anaesthetic-related cardiac arrests and critical incidents are deemed to be preventable.[11,31,33,42,49,57,59]

Anaesthetic-related serious adverse event rates are 1.4 per 1 000 to 1.4 per 10 000 anaesthetics.[14,29] Anaesthetic-related critical incidents are three times more common in children, and occur in 3–8% of all anaesthetics, revealing high nonfatal event rates, even in high-income countries.[29,42,46,57] Limited data in low-income countries expose a critical incident rate double that of high- and middle-income countries.[60] More events are associated with infants and inexperienced practitioners,[59,60] and respiratory events involving ear, nose and throat surgery.[57]

Mortality and morbidity risks

Three high-risk categories for mortality and morbidity have emerged, and are consistent across developed and developing countries. These are age, i.e. neonates and infants aged ≤ 1 year, American Society of Anesthesiologists (ASA) status III-V, and emergency surgery.[12,29,33,42,45,55,57] The last two are the only factors that are predictive of death after a cardiac arrest.[12,31,33,45]

Emergency surgery

The increased risk of emergency surgery is calculated at an odds ratio of 2.8 (95% confidence interval: 1.3–5.9), (p 0.007).[33] Emergency surgeries are more common in developing countries.[12,20,45]

Age

On average, in comparison to older children, 24-hour perioperative mortality is 50-fold[45] greater in neonates, and approximately 20-fold[45] greater in infants, and may be higher depending on ASA status and surgical complexity.[13,30,45] Anaesthetic-related mortality is conversely low in high-risk age groups, indicating causes of cardiac arrest that predominantly relate to the patient's condition.[11,45] Low anaesthetic-related mortality may also be due to management by experienced anaesthetists at appropriate levels of care,[13,30,45,57] and the influence of a restrictive or inclusive definition.[13]

American Society of Anesthesiologists status

Anaesthetic-related mortality in ASA I and II children is not recorded in most studies from high- and middle-income countries. Although death from anaesthesia is not nonexistent, this confirms the inherent safety of anaesthesia in these patients.[11,29,30,33,36,45,57] However, the vulnerability of even healthy children anaesthetised with cardiac depressants and arrhythmogenic volatile agents[31] was demonstrated in the first Pediatric Perioperative Cardiac Arrest (POCA) Registry. A decrease in such arrests with the use of sevoflurane, in combination with the routine use of pulse oximetry to detect hypoxia, capnography to detect hypoventilation and hypercapnia, and advances in airway management, e.g. laryngeal masks, was established in subsequent studies and analysis.[28,33] An essential safety message for clinicians and health authorities is the use of safe agents, appropriate monitoring and the availability of airway equipment. ASA III–V patients account for the only mortalities in most studies, and such patients are consistently at increased risk of cardiac arrest and 24-hour mortality.[33,42,47]

The relationship between heart disease and mortality is complex.[61] Despite under-representation in studies, children with heart disease account for 80–100% of cardiac arrests and deaths, most during cardiac surgery or interventions.[13,30,40,62] A different pattern was found in the POCA Registry. Of 372 cases of cardiac arrest, heart disease was present in only 34%, and 54% cases of cardiac arrest occurred in the general operating room.[33,40] This may reflect selection and outcome bias. It was demonstrated through multivariate analysis, in a comparison of children without heart disease and those with heart disease, that although mortality was higher in children with heart disease, it did not differ when adjusted for ASA status.[40] It was shown in another study that approximately 7% of children presenting for noncardiac surgery had heart disease and increased mortality, and significantly so in the younger age groups and with increasing ASA status.[62] These findings suggest that heart disease is not an independent risk factor during noncardiac surgery. High-risk factors are patients with aortic stenosis lesions, cardiomyopathy,[40] pulmonary hypertension[13] and single ventricle physiology. However, the patient numbers are small.

Factors contributing to ongoing poor outcomes in low-income countries

Valuable insight into the problems experienced in delivering safe care can be gleaned from a small institutional audit or report by volunteer organisations. Such reports also highlight successful interventions.

Access and patient factors

Access to elective surgery is limited. Thus, patients present predominately for emergency or very basic surgery.[12,18,20,63] Important differences in patient demographics and disease patterns exist. Poor baseline health status, sepsis and trauma are greater contributors to perioperative mortality in the developing world.[21,53,58,64,65] Patients often present late or in extremis as lack of proximity to health facilities, transport problems and cultural mistrust of hospitals result in delays in seeking health care.[18,20,66]

Staff skills and resource factors

Hypoxaemia from hypoventilation and laryngospasm and bronchospasm are frequent anaesthetic-related events with good outcomes in high- and middle-income countries.[12,14,29,31,42,46,57,59,67] Data from parts of Africa show that respiratory monitoring by pulse oximetry or capnography, even when available, is not routinely used, delaying the detection of hypoxaemia, hypoventilation or hypercapnia. Pulse oximeter monitoring during an arrest in the operating room was performed in only 28% of patients in a university teaching hospital.[58] Outcomes from such arrests are poor. The majority die or have permanent disability.[58] Contributing factors are:

- Lack of medication, or the use of inappropriate medication, such as ketamine-only anaesthesia, cardiac depressants, arryhthmogenic volatile agents and long-acting, outdated neuromuscular blockers.
- Manual ventilation only, as ventilator equipment and oxygen is lacking in certain hospitals.
- Limited airway devices and airway skills training.
- Poor cardiopulmonary resuscitation (CPR) technique.[68]
- Inexperienced or untrained practitioners.[5,18,20,53,55,58,60,65,69]

Cardiac arrest and mortality, as a result of failing to recognise hypovolaemia, is common in developing and developed countries.[13,29,42,46,57,67] Hypovolaemia, from blood loss and sepsis in Africa, is poorly managed owing to a lack of blood or inappropriate fluid choices.[5,18,53,55,58,70] There is an established blood transfusion service in less than 30% of countries.[18]

Infrastructure, human resources and external support

Very few hospitals in low-income countries, even those that perform major operations, meet the World Health Organization (WHO) safety standards for essential surgery.[20,54,66,71] Problems with electricity, water, oxygen supply and lack of anaesthesia machines or pulse oximetry have been identified.[20,65,73] Staff shortages and surgical and anaesthesia services offered by non-specialist or non-physician practitioners are often the norm.[18,20] An in-theatre mortality rate of 7.7 per 10 000 anaesthetics was found in a study from Uganda with respect to paediatric surgery performed in mission and nongovernmental hospitals, despite the majority of the anaesthetics being delivered by non-physician anaesthetists.[54] This rate is comparable with that in middle-income countries. Although only basic surgery was offered, anaesthetic staff training, the availability of safe equipment and essential drugs, as well as externally funded surgeons, contributed to the good outcome.[54] Similar improvements have been demonstrated by volunteer organisations, especially when protocol-driven care is introduced, and even in conflict zones.[74]

Governance and data availability

Large datasets are lacking from low-income countries, partly because of poor governance, but also because of an inadequate information technology infrastructure and problems with patient follow-up, which make data collection difficult.[8,74] The creation of simple data tools, pragmatic reporting, the innovative use of cellular phone technology[75] and support from volunteer organisations and externally funded data platforms, have been shown to assist in the collection and reporting of data in low-income countries.[8,74,75]

South African health care

South Africa is classified as an upper- to middle-income country, and has a complex and fragmented healthcare system. There is a marked maldistribution of funding and quality of, and accessibility to, care, between the private and public health sectors.[76,77] Funding is almost equally divided between the sectors, yet private health care serves only 16% of the population, and is funded on par with Western Europe.[78–80]

By contrast, the public health sector serves 84% of the population, who have a greater need of health care, have poor health indicators and are at increased risk of adverse outcomes.[76,78,80]

The late presentation of paediatric surgical patients increases the complexity of surgery, and may result in poor outcomes.[81,82] While public academic and urban regional hospitals are generally well resourced and utilise skilled anaesthesia providers, problems such as staff shortages and equipment challenges have been identified.[83] Non-urban regional and district hospitals face similar challenges to those of low-income countries, including staff with minimal or no anaesthesia training,[83–85] equipment challenges, transport and referral problems and an inadequate supply of medication.[85,86] Blood shortages are reported in 54% of district hospitals.[86] Remedial interventions have been aimed predominately at obstetric anaesthesia. However, there isn't any published information on the safety of paediatric anaesthesia services or unmet needs for surgery.[15]

Discussion

Twenty-four hour anaesthetic-related mortality is low and almost negligible in ASA I and II patients in high-income countries, indicating the safety of the anaesthesia services. Well-established databases and incident monitoring now focus on further improving the quality of anaesthetic care and disability-free long-term outcomes.[14] Paediatric perioperative risk models can be generated from collaborative databases containing consensus definitions.[41,43] Research is appropriately directed at the potential toxicity of anaesthetic agents,[3,6,7] and at the significance of physiological parameters,[22,25] and will continue to advance the science of paediatric anaesthesia.

Large paediatric datasets have been provided by some middle- and low-middle income countries.[11,42,49] Anaesthetic-related mortality is still 2–3 times that of the developed world. As these countries develop, perioperative risk may initially increase because of increased surgical penetration rates and case complexity.[11,12] Health authorities must fund and provide support to these expanding services.[87,88] As an upper-middle income country, South Africa is conspicuous by its absence of data in this regard.

The high mortality rate in low-income countries indicates the scarcity of access to safe essential and emergency paediatric surgery and anaesthesia services.[54,66,73,87,88] Perioperative and anaesthetic outcomes in low-income countries are demonstrated in studies to be up to 100 times poorer than those in high-income countries, and the lack of data may potentially underestimate poor outcomes.[18,66,88] Outcomes reflect poorly on the state of health care in many low-income countries, but the willingness to report extremely poor outcomes demonstrates the effort that clinicians are making to improve safety.

External support and interventions by nongovernmental and volunteer organisations show that it is feasible to improve outcomes, even in resource-poor areas.[18,20,54,74] Programmes are most effective when simple sustainable changes are introduced and the support is ongoing, allowing for safe expansion of the services offered.[69,74] Cost-effective strategies include the introduction of pulse oximetry,[18,72] investment in staff training, especially airway skills and CPR, and the introduction of safety checklists[51,72] and protocol-driven care.[74] Safe care is further hampered by the nonavailability of basic infrastructure, equipment, medication, fluids, blood and human resources.

Conclusion

Perioperative mortality predominantly relates to patient condition or disease. However, anaesthesic related-mortality and morbidity is preventable in 75% of cases. The recognition of high-risk patients and identification of common precipitators of anaesthetic-related events may improve outcomes in both low- and high-income countries. Risk factors for mortality across developed and developing countries age, i.e. neonates and infants aged ≤ 1 year, ASA III–V status and those undergoing emergency surgery. Skilled anaesthesia providers and appropriate resources are required to anaesthetise such children, both of which are lacking in low-income countries.

The significant ongoing disparity in outcome between developed and developing countries is of concern. The majority of anaesthetic-related causes of death are highly preventable through basic interventions and investment in surgical and anaesthetic services in the developing world.[69] WHO initiatives have been introduced to address these issues,[89] but will fail if health system issues, governance and funding are not urgently addressed.[18,20,54,66]

Recommendations

Access to and the safety of surgery is key in addressing the unmet global burden of surgically treatable disease.[71,87] Simple metrics, such as 24-hour perioperative and anaesthetic-related mortality rates, are essential indicators of access and safety achieved, and must be reported on and monitored.[8] It is the author's opinion that the lack of large, prospective datasets from the developing world contribute to ongoing anaesthetic-related and perioperative mortality. It is essential that South Africa join such efforts to provide reliable data and establish the baseline safety of paediatric anaesthesia services and direct interventions accordingly. A pragmatic research agenda is required in these regions through the adoption of inclusive definitions and simple data collection tools.[8]

Once this has been carried out, information must be disseminated to clinicians to improve clinical safety practices, to families and patients for the purposes of obtaining informed consent, and most importantly, to healthcare funders to direct appropriate resources and strengthen systems for surgery and anaesthesia. Until this has been achieved, patients will continue to die from treatable surgical diseases and preventable events during anaesthesia.

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