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Best practice & research clinical anesthesiology: Safety and quality in perioperative anesthesia care. Update on safety in pediatric anesthesia

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Pediatric anesthesia is large part of anesthesia clinical practice. Children, parents and anesthesiologists fear anesthesia because of the risk of acute morbidity and mortality. Modern anesthesia in otherwise healthy children above 1 year of age in developed countries has become very safe due to recent advance in pharmacology, intensive education, and training as well as centralization of care. In contrast, anesthesia in these children in low-income countries is associated with a high risk of mortality due to lack of basic resources and adequate training of health care providers. Anesthesia for neonates and toddlers is associated with significant morbidity and mortality. Anesthesia-related (near) critical incidents occur in 5% of anesthetic procedures and are largely dependent on the skills and up-to-date knowledge of the whole perioperative team in the specific needs for children. An investment in continuous medical education of the perioperative staff is

Abbreviations: PPOG, Perioperative Outcomes Group; NACOR, National Anesthesia Clinical Outcomes Registry; PAP, physician anesthesia providers; NPAP, non-physician anesthesia providers; CME, continuous medical education.

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required and international standard operating protocols for common procedures and critical situations should be defined.

Introduction

Anesthesia in children is a common and a large part of daily clinical practice of the general anesthesiologist with almost 30% of all general anesthesia procedures provided in children less than 15 years of age [1]. Approximately, one out of seven children had at least one anesthetic procedure before the age of 4 years in high-income countries [2,3]. In children less than 8 years, most anesthetics are performed in American Society of Anesthesiologists (ASA)-physical status (PS) classes I (56%) and II (30%) patients, and are performed in a community hospital (57%) and surgical centers (22%) [4]. General anesthesia is the principle anesthetic technique (93%) and most anesthetics are provided for surgical procedures (79%). Diagnostic procedures (21%) are common in children, which is in stark contrast to adults [4].

Anesthesia in children is a safe procedure if performed by competent and well-trained health care providers within an organizational environment committed to provide suitable equipment and sufficient personnel for continuous perioperative monitoring and care. An overall very low incidence of anesthesia-related mortality has led to a new focus on reducing the risk of anesthesia-related morbidity over the past decade. However, this is not true on a global perspective. The World Health Organization (WHO) estimates that approximately 1.7 billion children and adolescents worldwide did not have access to surgical care in 2017. The majority of these patients originate from low- and middle-income countries in which children and adolescents make up a disproportionately large fraction of the population undergoing anesthesia. Lack of funding, education, and access to relevant human and technical resources are the primary causes for this divide.

This paper reviews the current trends and development in anesthesia-related morbidity and mortality, explores directions of improving anesthesia care in children, with special emphasis on education in perioperative anesthesia care.

Anesthesia-related mortality in children

Anesthesia-related mortality in children is uncommon in most industrialized nations. An elementary review of literature of anesthesia-related mortality shows that anesthesia-related mortality in children under 18 years declined from more than 10 per 10,000 in the 1950s to approximately 4 per 10,000 after the 1970s–1980s, and to less than 1 per 10,000 in the present century, particular in high-income countries (Fig. 1). This decline is commonly attributed to advances in diagnostics, medicine and surgery combined with the emergence of new and safe drugs, fluid and blood management protocols, and use of antibiotics [5].

Routine pulse oximetry and expiratory carbon dioxide (CO_2) monitoring was introduced in the 1980s. Subsequent research from closed claim projects of anesthesia malpractice from 1970 to 1990 demonstrated that the incidence of respiratory adverse events decreased from 51% to 23%, whereas cardiovascular events increased from 19% to 26% [6]. Data from the pediatric perioperative cardiac arrest (POCA) registry showed that the perioperative causes of cardiac arrests in children with ASA-PS class 1 and by medication was decreased significantly by the discontinuation of halothane as primary anesthetic and the use of newer anesthetics agents, in particular sevoflurane and propofol [7,8].

The continued decline in perioperative and anesthesia-related morbidity and mortality over the subsequent decades was achieved primarily by implementation of technological improvements and the introduction of standards for basic patient monitoring and widespread use of sevoflurane, propofol and sugammadex [9–11].

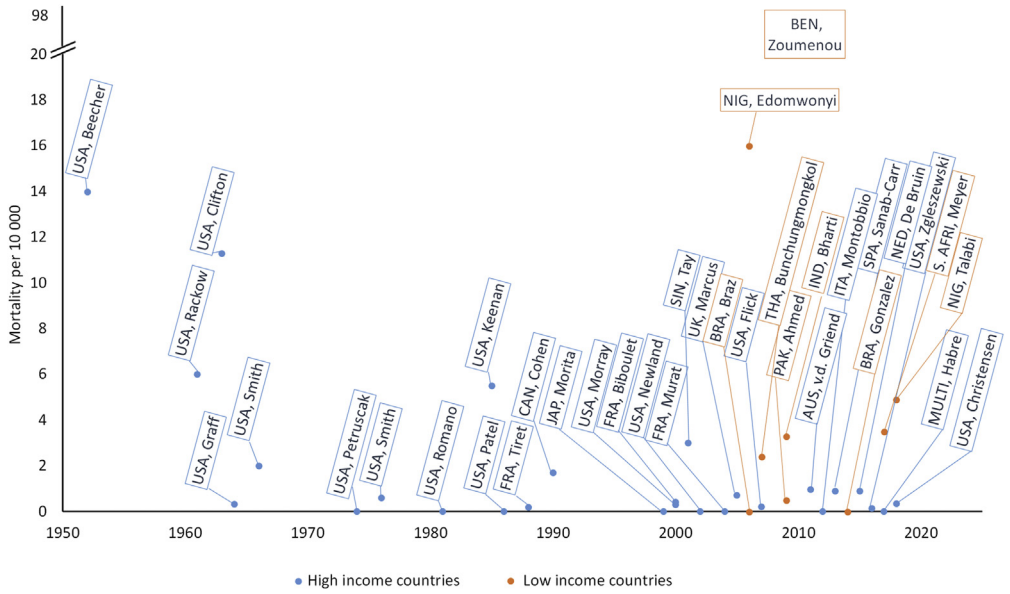

Fig. 1. Anesthesia-related mortality in time. **NIG**, Talabi [18]; **USA**, Christensen [35]; **S. AFRI**, Meyer [16]; **MULTI**, Habre [49]; **USA**, Zgleszewski [34]; **NED**, De Bruin [13]; **BRA**, Gonzalez [23]; **SPA**, Sanabria-Carretero [50]; **ITA**, Montobbio [51]; **AUS**, van der Griend [52]; **BEN**, Zoumenou [19]; **PAK**, Ahmed [53]; **IND**, Bharti [54]; **USA**, Flick [55]; **THA**, Bunchungmongkol [56]; **BRA**, Braz [57]; **NIG**, Edomwonyi [58]; **UK**, Marcus [59]; **FRA**, Murat [60]; **USA**, Newland [61]; **SIN**, Tay [62]; **USA**, Morray [7]; **FRA**, Biboulet [63]; **JAP**, Morita [64]; **CAN**, Cohen [65]; **FRA**, Tiret [66]; **USA**, Patel * [67]; **USA**, Keenan [68]; **USA**, Romano [69]; **USA**, Smith [70]; **USA**, Petruscak [71]; **USA**, Graff [72]; **USA**, Clifton [73]; **USA**, Rackow [74]; **USA**, Beecher [75].

In addition, the recognition of the importance of continuous medical education (CME) of health care providers and a change in organizational structures within the health care industry has led to standardization of treatment regimens with improved perioperative outcome.

At present, there is still some variance in the anesthesia-related mortality (Table 1). This variance is partly caused by the differences in definitions and registries. Mortality caused by anesthesia (or surgery) is best defined by van der Griend et al. as: “those cases for which all agreed that anesthesia (or surgery) or factors under the control of the anesthesiologist (or surgeon) more likely than not influenced the timing of death” [12]. Database studies in tertiary referral centers in Australia and the Netherlands showed a similar incidence of approximately 1 case per 10,000 anesthetics in which anesthesia contributed partly to the death of the patients (Table 1) [12,13].

In contrast to the figures of these tertiary referral centers, no anesthesia-related mortality was reported in the multi-center European APRICOT study [14]. This prospective cross-sectional cohort study recorded 31,127 anesthetic procedures in 30,874 children out of 261 centers among 33 European countries [14]. This low mortality is most likely due to the broad range of institution and the nature of the case load [14]. The safety of anesthesia in healthy patients is confirmed by the aforementioned tertiary referral centers, which show that anesthesia-related mortality was zero or close to zero in ASA-PS classes 1–3, and only occur in ASA-PS class 4 and higher [12,13]. Anesthesia in healthy children above 1 year of age has reached the level of safety which is comparable to anesthesia in adults, in which the risk for fatal adverse events is less than 1 in 100,000 general anesthesia procedures and much safer than road safety and comparable with the risk of charter flights [15].

The details of the anesthesia-related cause of death have been analyzed in 15 cases presented in studies by van der Griend [12] and de Bruin [13], and showed that mortality was caused by: cardiac ischemia because of hypotension ($n = 5$), cerebral ischemia because of hypotension ($n = 2$), pulmonary hypertension ($n = 5$), tension pneumothorax ($n = 1$), severe hypoglycemia ($n = 1$) and postoperative apnea ($n = 1$). Nine out of 15 patients were less than 1 year of age, and all patients were ASA-PS class 4

Table 1
Mortality after anesthesia.

Mortality	Zoumenou	Vd Griend	De Bruin	Habre
Published	*2010*	*2011*	2015	2017
Period database	*20*	2003–2008	2006–2012	2016
N	*512*	*101,885*	45,182	30,874
Type study	Mono-center	Mono-center	Mono-center	Multi-center
Type hospital	Tertiary	Tertiary	Tertiary	All type
Location	Benin	Australia	Netherlands	Europe
24-h mortality[a]	NR	13	13.1	0
24-h anesthesia-related[a]	98	0.7	0.7	0
30-d mortality overall[a]	NR	34.5	41.6	10
30-d anesthesia-related mortality overall[a]	NR	1.0	1.1	0
30-d mortality neonates	NR	367	387	NR
30-d mortality infants	NR	135	55.3	NR

[a] Death per 10,000 anesthetics (with 95%CI).

or higher. In most cases, the preexisting clinical condition contributed significantly to the cause of death (pulmonary hypertension, severe congenital cardiac malformation, etc.) [12,13].

Unfortunately, the decrease in anesthesia-related mortality in children is not universal. Whilst, anesthesia-related mortality declined to 1 per 10,000 in the last 50 years in high-income countries, recent studies in low-income countries continue to show a higher mortality of up to 7.4/10,000 (Fig. 1) [16–18]. Poverty, delayed diagnosis, and intervention, poor nutritional status and, in some areas, a lack of basic resources and lack of training contribute to numerous health care issues [19,20]. Fundamental resources for safe anesthesia, such as airway supplies and functional pulse oximetry, are absent in the majority (72%) of care facilities in low-income countries, and anesthesia machines and the capability to perform general anesthesia were unavailable in 56% of the hospitals [21]. The effect of facilities and adequate training is clearly illustrated in a study which has been performed in the main teaching referral center in Benin, Western Africa and has reviewed the anesthetic charts of 512 children operated in 2007. This study showed eight cases with POCA, of which five children died (Table 1). Hypoxemia, due to difficult intubation, laryngospasm and bronchospasm were the main causes of cardiac arrest, occurring at all stages of anesthesia [19]. Improvement in safety depends on the training of staff, and the hospital needs to review their practice of anesthesia in children.

Hospital mortality after anesthesia

The 30-day hospital mortality after anesthesia irrespective of the cause shows an increase in time (Fig. 2): However, the hospital mortality after anesthesia, especially in neonates and infants, has declined since 1985 but shows a large variance. This variance and increase are likely due to differences in inclusion criteria, setting (specialized referral center or general district hospital), definitions of mortality after anesthesia, database used (anesthesia, hospital, insurance and/or governmental birth, and death register). Remarkably, there is no clear difference reported in the hospital mortality after anesthesia between high-income country (Australia, USA, and the Netherlands) [12,13,22] and middle- and low-income countries (South Africa, Brazil, and Nigeria, Fig. 2) [16,18,23]. This is likely caused by the type of centers reporting these outcomes as most academic centers, including developing countries, report the highest mortality, whereas reported mortality is much lower in general hospitals with less complex patients. In addition, respective reports are also not available from low- and middle-income countries [14,24,25]. Notably, there is an increase of mortality in neonates to approximately 400 per 10,000 anesthetics over the past two decades which is independent of the economic situation of the country [12,13,16,18]. The cause of this increase is unknown, but may be related to the more detailed registration in the later years and/or more liberal indications for surgeries on higher risk patients, mostly very-low-birth-weight neonates [26]. Increasingly very-low-birth-weight neonates (from 20 weeks gestational age) are being treated also by surgical interventions (from 400 g), which is associated with a high mortality and morbidity [27,28].

The overall death in children from all causes within 30 days after anesthesia in Australia (2003–2008) was 34.5 per 10,000 anesthetics in a tertiary referral center, of which 13.4 per 10,000 died within 24 h [12]. Similar results in a comparable setting are reported over the period 2006–2012 in an academic center in the Netherlands (Table 1) [13]. Both studies showed that 30-day mortality after anesthesia in neonates and infants was much higher and varied between 367 and 387 per 10,000 for neonates and between 55 and 82 per 10,000 anesthetics for infants [12,13]. Furthermore, ASA-PS 3–5, emergency surgery and cardiothoracic surgery had a significantly higher 30-day mortality [13]. Younger age, emergency surgery, cardiothoracic surgery and number of anesthetic procedures were independent risk factors for 30-day hospital mortality after anesthesia [13].

The multi-center European APRICOT study reported a much lower 30-day hospital mortality (10 per 10,000), which is again much likely due to the different case mix [14]. In highly specialized tertiary referral centers, most children die after anesthesia due to the underlying disease, including congenital abnormalities, extreme prematurity, infection, immunocompromised, oncology, metabolic disease and (head) trauma [13]. These types of underlying disease are less common in a general hospital which also participated in the APRICOT study [14].

Near critical incidents

Low mortality rates and large variance in cohorts make it difficult to monitor and compare the quality of care. Near critical incidents and real incidents are much more common in pediatric anesthesia than mortality and are, therefore, a helpful quality indicator [29,30]. Accurate measurement and monitoring of critical incidents are crucial for patient safety and may indicate the quality of clinical practice and lead in future improvement. The registries and analysis of adverse events and the identifications of analogous causes may provide strategies to prevent adverse events in the perioperative care. Despite a possible underreporting, inhomogeneity of data, and the probable misclassification of manual reporting systems, results from these reports allow an insight into anesthesia-related critical incidents [29,31]. Recently, a group of anesthetists from all over the world has formed the Pediatric

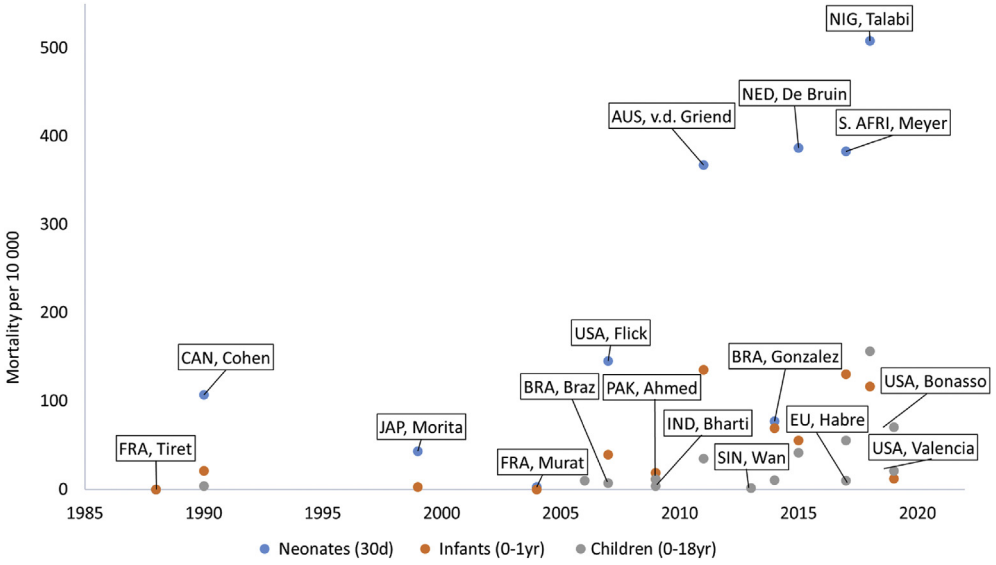

Fig. 2. 30-day hospital mortality after anesthesia in time. **USA,** Bonasso [76]; **USA,** Valencia [77]; **NIG**, Talabi [18]; **USA**, Christensen [35]; **S. AFRI**, Meyer [16]; **MULTI**, Habre [49]; **KOR**, Lee [78]; **USA**, Zgleszewski [34]; **NED**, De Bruin [13]; **BRA**, Gonzalez [23]; SIN, Wan [79]; **SPA**, Sanabria-Carretero [50]; **ITA**, Montobbio [51]; **AUS**, van der Griend [52]; **PAK**, Ahmed [53]; **IND**, Bharti [54]; **USA**, Flick [55]; **THA**, Bunchungmongkol [56]; **USA**, Bahanker [80]; **BRA**, Braz [57]; **NIG**, Edomwonyi [58]; **UK**, Marcus [59]; **FRA**, Murat [60]; **USA**, Newland [61]; **SIN**, Tay [62]; **USA**, Morray [7]; **FRA**, Biboulet [63]; **JAP**, Morita [64]; **CAN**, Cohen [65]; **FRA**, Tiret [66]; **KEN**, Newton [45].

Perioperative Outcomes Group (PPOG) which aims to standardize reporting of outcome measures in pediatric anesthesia by systematic approach [32,33]. A systematic review of available outcome measures, in combination with patient-centered outcomes identified through a stakeholder engagement will define a core outcome set for four specific age groups (neonates and former preterm infants, infants, toddlers and school age children, and adolescents) aiming to provide comparable outcome in scientific reporting [33].

Younger age, higher ASA-PS class status, emergency or multiple surgeries are risk factors for (near) critical incidents in multiple studies [14,30,31,34,35]. Age is the most important risk factor for both cardiovascular and respiratory incidents. Multiple studies illustrated that these incidents are twice as common in infants (below 1 year) than in toddlers and children (1–8 years, Fig. 3). This is also illustrated by retrospective analyses of the National Anesthesia Clinical Outcomes Registry (NACOR) database in 2013, which showed that cardiovascular arrests are over 10 times more frequent in children less than 1 year (35 per 10,000) than in older children (3 per 10.000), and five times more frequent than in patients over 80 years (10 per 10,000) [36].

Near critical incidents in pediatric anesthesia are mostly respiratory in origin. Respiratory incidents are more common in younger children because of their smaller respiratory reserve capacity, increased metabolic requirements and rapid heart rate compared with older children [37]. The Wake-Up-Safe registry reported 734 serious adverse events in more than 700,000 anesthetics (1.4 per 1000) with pharyngeal obstruction, laryngospasm or bronchospasm successfully treated before cardiac arrest [30]. The multi-center observational cohort study APRICOT showed that the incidence of severe cardiovascular and respiratory complications was 5.2%, with respiratory critical events accounting to 3.1% and an up to 20-fold variation among the participating countries [14]. Neonates are most at risk for respiratory incidents. Retrospective review of electronic registration in the operating room of a tertiary referral center showed that an SpO_2 below 90% and 80% for at least 1 min was registered in 56% and 26% of the neonates, respectively, and clearly declined with increasing age (Fig. 4) [38]. Here, the case load and clinical experience in delivering anesthesia to children is an important factor. In addition, years of experience of the anesthesiologist are related to the incidence of respiratory (1% reduction for each year experience) and cardiovascular events (2% reduction for each year experience) [14,39]. Furthermore, the annual number of days (less than annually 73 days) devoted to delivering anesthesia to children is a strong independent risk factor for the number of cardiac arrests at the operating and postoperative recovery room [34].

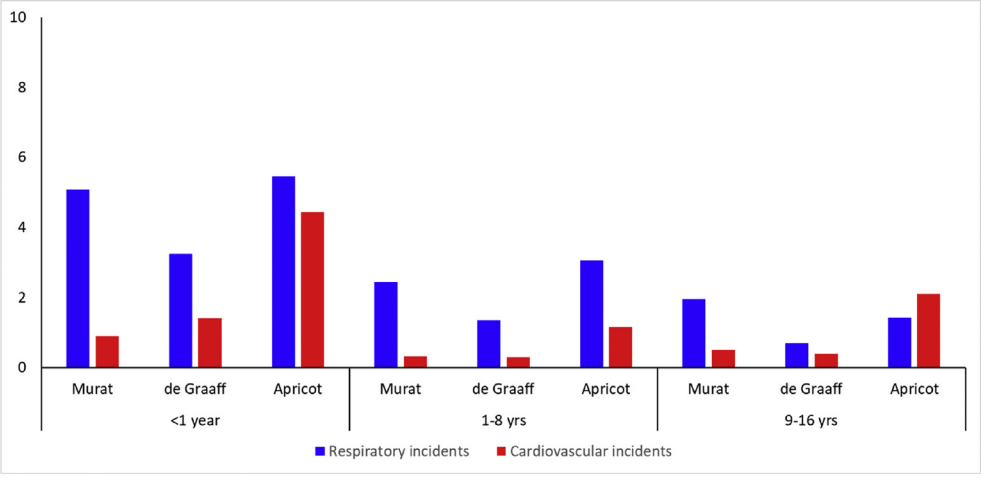

Fig. 3. Reported (near) critical incidents in relation to age. Percentage cases with (near) respiratory and cardiovascular critical incidents in relation to age group as reported prospectively in a tertiary referral center between 2000 and 2002 by Murat et al. [81], in a tertiary referral center between 2007 and 2013 by de Graaff et al. [31] and the multi-center Apricot study in 2016 [14].

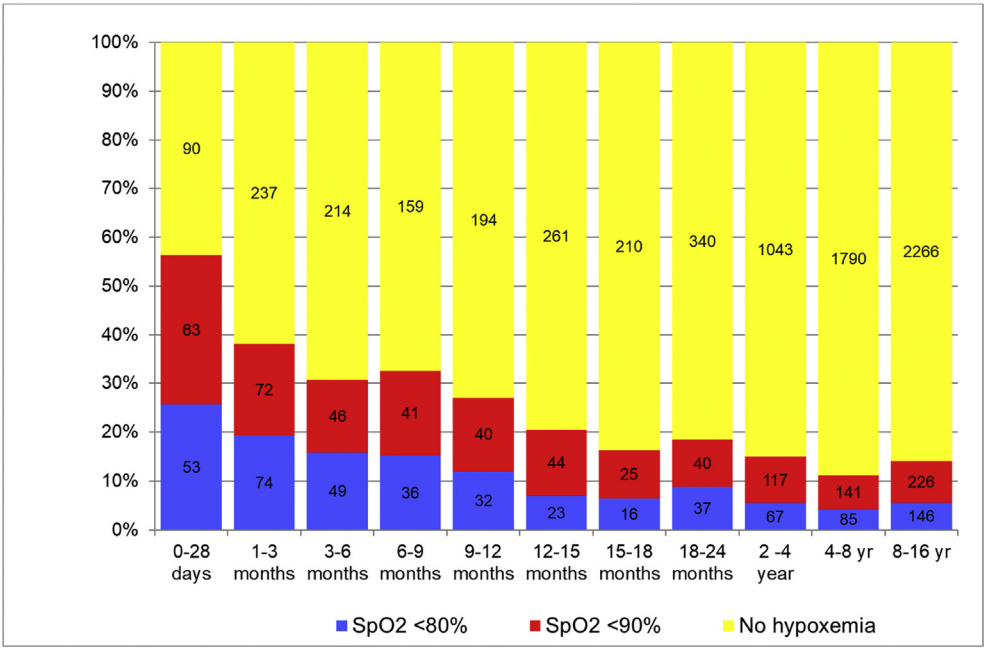

Fig. 4. Incidence of hypoxemia in children. Percentage of cases with at least 1 period of hypoxemia for at least 1 min in relation to age group in a retrospective cohort study. Modified from the work of de Graaff et al. [38]

Where and how to improve

There is a large variability in anesthesia-related morbidity and mortality among the countries in the world. Education and training are keys to reduce this variability in a suitable competent and resourced environment.

Improvement in low- and middle-income countries starts with investment in the structure which includes the facilities, technologies, staff and training to deliver clinical care [40]. Morbidity and mortality are caused by limited surgical and anesthetic specialized equipment and expertise and shortage of appropriate postoperative care. Well-functioning medical equipment is an elementary requirement for safe anesthesia in children. The basic requirements for anesthesia are described by the World Federation of Societies of Anesthesiologists (WFSA) and WHO [41,42]. Unfortunately, the basic infrastructure requirements, such as reliable availability of oxygen, electricity, and running water, and functioning anesthesia machine are frequently not present [43].

In addition, there is a serious shortage of well-trained anesthesia personnel. A survey from the WFSA showed that anesthesia is served by non-physician anesthesia providers (NPAP) in a large part of the world, especially in countries with limited resources. Furthermore, 70 countries (mostly middle African countries) had a total anesthesia (including NPAP) provider with a density of less than 5 per 100,000 [44]. The minimum density has been recommended for five physician anesthesia providers (PAP) per 100,000 populations, whereas Europe has a PAP density of 18.6, USA of 20.82, and in some countries, even higher (Germany: 31.0, Austria: 39.3). These differences are primarily related to the difference in capita income [44].

Morbidity and mortality are caused by limited surgical and anesthetic specialized equipment and expertise and shortage of appropriate postoperative care. In remote location, anesthesia is often administered by NPAP [45]. Recent reports have shown that quality improvement programs work by establishing a safety culture, resource allocation to meet needs, education and training of staff, standardization of care, improved communication and handoff, enhanced detection, recognition, and

response to adverse events and decrease of the incidence of respiratory events also in developing countries [46].

The low numbers of PAP and even NPAP in low-income countries indicate the big shortage in adequate investment in education and training of specialized medical staff. This includes not only staff to provide safe anesthesia during the procedure, but also after the procedure during recovery.

Neonates and infants, and patients with significant comorbidities (ASA-PS > 2) are still at a higher risk for critical and near critical incidents, and have significant risk for mortality and morbidity after anesthesia and surgery. Toddlers and preschool children have a higher risk for severe perioperative respiratory incidents. Therefore, all neonates and infants and all children with disabling comorbidities or healthy older children undergoing complex procedures should be treated by a specialized pediatric anesthetic and surgical team during their perioperative course. This includes preoperative anesthesiologic and surgical preparation, anesthetic and surgical management in the operating room, and postoperative care with adequate treatment of pain in hospital and at home.

Perioperative care

Improving patient outcome and ensuring low incidence of perioperative adverse events require not only a focus during the hours of anesthesia. A thorough preoperative evaluation of patient status, comorbidity, expected type and length of surgery as well as avoidance of postoperative pain and fear are key elements to ensure a continuous safe treatment with a low risk of morbidity and mortality. The volume and diversity of patients passing through the operating room often makes it difficult for the anesthesiologist to possess an in-depth knowledge in all cases. In 2014, the SAFETOTs initiative provided a simple matrix of clinical goals to improve the overall outcome during the anesthesia management of pediatric patients – the 10-N principles (Table 2) [47]. These principles, applied to simple as well as complex procedures, help to ensure the safe conduct of pediatric anesthesia through the maintenance of normal physiological homeostasis. Compliance with these simple and yet effective goals will ultimately result in optimal perfusion of vital organs, continuing energy supply, stable plasma osmolality, and avoidance of a negative impact on cellular function and body metabolism. Further, adding a stringent organizational structure, education, and focus on decreasing fear and pain related to hospital admission creates an overall framework for achieving the best perioperative outcome possible. Most industrialized countries possess the funds and structure to implement such a systematic approach to perioperative care. However, for developing countries, a lack of financial funding and access to educational resources and proper trained health care professionals is no doubt considered to be one of the greatest challenges. Addressing the known clinical risk factors by correct use of simple equipment (e.g., saturation probe, capnography, blood-pressure cuff, etc.) by trained personal is key.

Education

A result of exponential growth in surgical, medical, and research advancements during the past decade, combined with a worldwide lack of health care professionals, has imposed an even greater need for CME in order to provide the best and most safe patient-centered health care possible. 'State of the art' in pediatric anesthesia is frequently defined and propagated at scientific meetings, congresses and in literature in the form of expert lectures, opinions, and reviews. However, even in industrialized countries, economic pressures, time constraints, and demands of enhanced productivity conflict with the possibility of health care providers to attend up-to-date educational forums; a challenge which is only even more pronounced in the developing countries.

The digital technologies have revolutionized the educational infrastructure. Helping people learn in ways that are easier, faster, surer, and less expensive has led to a change in how we obtain and process information: moving away from the classic textbook and one-way classroom teaching towards a virtual learning environment. The internet has provided us with endless possibilities of self-education, such as podcasts, tutorial videos, e-learning modules and virtual reality medicine. Combining these educational possibilities with global online access provides the foundation for anywhere learning and

Table 2
The 10-Ns of Maintenance of physiological homeostasis is key for the Safe Conduct of Anesthesia in Children [47].

extended international CME. This is an essential digital resource with the potential of providing crucial educational, clinical, and research support to developing countries.

A group of specialist pediatric anesthesiologists with experience of working in low- and middle-income countries has developed a 3-day course for Safer Anesthesia From Education (SAFE) for pediatric anesthesia with free online training programs and instruction videos [48]. Large national and international pediatric anesthesia societies should take up the initiative to distribute the latest scientific knowledge for a wider audience. The latest switch from onsite specialist conferences to free online available conference because of the COVID-19 pandemic showed that there is great need of free available knowledge for low- and middle-income countries. The latest (2020) online and free of charge ESPA conference has reached over 200 attendees from South America and Middle East countries, whereas only a handful of attendees from these countries have previously attended onsite conferences (www.euroespa.com).

Demanding attention from regional and national societies to develop and implement strategies for quality improvement in pediatric anesthesia SAFETOTs have shed light to one of the most obvious and yet clinical and scientifically understated reasons for a poor perioperative outcome in young children – the "Who", "Where", "What", "When" and "How" [47]. The concept of an anesthetist is able to provide best care to all patients regardless of age and comorbidity and the idea that high-risk patients are equally treated in community vs. tertiary hospitals is outdated. The anesthetic management of children in inexperienced hands (<100 cases per year) results in a substantially higher morbidity rate compared with experienced operators (>200 cases per year) with the main difference being lack of training and continuous maintenance of required skills [14,39]. Acknowledging and rectifying this fact alone would enable the concentration of a high-risk population in specialized centers hence facilitating state of the art pediatric anesthesia, a continuous maintenance of skills and 1:1 consultant/fellow-resident supervision for achieving the best academic up-to-date education. To date, this systematic approach to assure and improve quality in pediatric anesthesia has become mandatory in some European countries; an initiative which should be propagated to not only includes Western industrialized countries, but also developing countries.

Based on best available scientific evidence we should strive to develop, implement and share standard operating protocols (SOPs) with our colleagues in developing countries. We should aim to define and describe not only what needs to be done, but also who is qualified to carry it out, and under what conditions the procedure can be performed reliably.

Conclusion

Mortality in anesthesia in ASA-PS I and II children has become very low in high-income countries. However, mortality after anesthesia in neonates and toddlers, children with severe comorbidities, and children in low-income countries remains unnecessarily high. In addition, the incidence of near critical, mostly respiratory, events in children is concerning. These incidents are typical for children (mostly laryngeal and bronchospasms) and require specific pediatric knowledge and skills in a timely manner. Concentration and specialization of care as well as continuing training of medical and non-medical staff involved in the operating and recovery phase is essential. Open access to online information, teaching seminars, e-conferences and registrations of onsite conferences should make it possible for all staff involved in the perioperative phase to acquire the specific knowledge of providing perioperative care in children. Furthermore, standardization of outcome measurements should allow international comparison between hospitals and countries to define optimal care which will be helpful to define standard operating procedures for perioperative care in children.

Practice points

- In high-income countries, anesthesia for children has become as safe as anesthesia for adults, whereas low-income countries significantly lag behind due to deficiencies in basic equipment and training of staff.
- Anesthesia-related mortality is mostly related to the underlying disease processes and occurs mostly in children below 1 year of age and in seriously ill children.
- Respiratory and cardiovascular critical incidents of critical events are very common and occur in 1 out of 20 anesthetics in children with neonates and infants particularly vulnerable.

Research and Education agenda

- Low-income countries need basic physical and training resources to increase the safety.
- Anesthesia-related mortality in healthy or mildly diseased children has become rare, and is mostly related to underlying disease and younger age.
- Education and training of those who provide anesthesia care to neonates and toddlers, since these are the children at highest risk.
- Free access to education and training for all staff involved in perioperative care is key to improve outcomes after anesthesia and surgery.
- Development of core outcome set of anesthesia specific mortality and morbidity are essential to allow a consistent comparison in research and evaluation of quality of care of centers and countries.

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Declaration of competing interest

JdG is President-elect of the European Society for Pediatric Anesthesiology.

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