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REVIEW ARTICLE

Perioperative morbidity and mortality in the first year of life: a systematic review (1997–2012)

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Early mortality;
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Abstract
Background and objectives: Although many recognize that the first year of life and specifically the neonatal period are associated with increased risk of anesthetic morbidity and mortality, there are no studies directed to these pediatric subpopulations. This systematic review of the scientific literature including the last 15 years aimed to analyze the epidemiology of morbidity and mortality associated with general anesthesia and surgery in the first year of life and particularly in the neonatal (first month) period.
Content: The review was conducted by searching publications in Medline/PubMed databases, and the following outcomes were evaluated: early mortality in the first year of life (<1 year) and in subgroups of different vulnerability in this age group (0–30 days and 1–12 months) and the prevalence of cardiac arrest and perioperative critical/adverse events of various types in the same subgroups.
Conclusions: The current literature indicates great variability in mortality and morbidity in the age group under consideration and in its subgroups. However, despite the obvious methodological heterogeneity and absence of specific studies, epidemiological profiles of morbidity and mortality related to anesthesia in children in the first year of life show higher frequency of morbidity and mortality in this age group, with the highest peaks of incidence in the neonates' anesthesia.

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PALAVRAS-CHAVE
Mortalidade precoce;
Morbidade: parada cardíaca;
Eventos críticos e adversos perioperatórios;
Crianças de um ano/um mês de idade

Morbimortalidade perioperatória no primeiro ano de idade: revisão sistemática (1997-2012)

Resumo
Justificativa e objetivos: Embora muitos reconheçam que a idade inferior a um ano e especificamente o período neonatal estejam associados a maior risco de morbimortalidade anestésica, não existem estudos dirigidos a essas subpopulações pediátricas. Esta revisão sistemática das publicações científicas dos últimos 15 anos teve como objetivo analisar o perfil epidemiológico da morbimortalidade relacionada com a anestesia geral e cirurgia no primeiro ano de idade e em particular no período neonatal (primeiro mês de idade).
Conteúdo: A revisão foi conduzida por pesquisa de publicações nas bases de dados Medline/PubMed. Foram avaliados os seguintes desfechos: mortalidade precoce no primeiro ano de idade (<1A) e em subgrupos de diferente vulnerabilidade nesta faixa etária (0-30 dias e 1-12 meses) e prevalência de parada cardíaca e eventos críticos/adversos perioperatórios de diversos tipos nos mesmos subgrupos.
Conclusões: A literatura corrente indica grande variabilidade nos índices de mortalidade e morbidade na faixa etária em análise, bem como nos seus subgrupos. No entanto, apesar da óbvia heterogeneidade metodológica e da ausência de estudos específicos, os perfis epidemiológicos de morbimortalidade relacionada com a anestesia de crianças no primeiro ano de idade mostram frequência mais alta de morbimortalidade nessa faixa etária, com os maiores picos de incidência na anestesia de neonatos.

Introduction

Information on morbidity and mortality in pediatric anesthesia is abundant, but scattered. Although many recognize that age <1 year and specifically the neonatal period are associated with higher risk of anesthetic complications,[1,2] there are no studies aimed at this age group. Available data are scattered in studies that cover a wider range of ages, with reports differing from the results in these pediatric groups.

The improved survival in congenital pathologies, as well as the development of new surgical techniques in pediatrics, led to an increase in the number of surgeries performed in children under one year of age, many of which in extremely vulnerable infants.[3] The anesthesia of pediatric patients younger than 1 year has very specific characteristics, and the results of pediatric studies in older children are not necessarily applicable to them.

Although the risk of anesthetic complications is presumably associated with population characteristics, the study of morbidity and mortality related to anesthesia care in the pediatric population younger than one year has special relevance for its frequency and considerable impact on patients' health. The characterization of the epidemiological profile of morbidity and mortality in this age group, as an instrument of health care quality evaluation, can improve anesthesia in this group of very particular characteristics and provide a starting point for reducing morbidity and mortality.[1,4–6]

This systematic review of scientific studies published in the last 15 years aimed to analyze the epidemiological profile of morbidity and mortality related to general anesthesia in the first year of age, and particularly in the different vulnerable subgroups: first month and from one to 12 months.

Methods

We performed a systematic search of the studies published in Medline/Pubmed (http://www.ncbi.nlm.nih.gov/pubmed/) from 1 January 1997 to 31 October 2012 to find original articles on mortality or morbidity associated with the perioperative period of children under one year of age. The following keywords were used in the search: *anesthesia-related* and *mortality* and *anesthesia-related* and *morbidity*. From the title or abstract of the potentially relevant articles, we used the PubMed function *related articles*. Additional references from this research and relevant studies cited were included.

The search was limited to human studies and the last 15 years.

All titles, abstracts, and full texts of potentially relevant studies were evaluated for eligibility based on the inclusion or exclusion criteria previously determined.

Inclusion criteria were studies evaluating the incidence of early mortality or perioperative cardiac arrest or critical/adverse events of various types, as defined by different authors, with information regarding the specific subgroup of children under one year of age (group <1 Y). When ages 0–30 days and 1–12 months were specified, these data were also collected.

Exclusion criteria were studies limited to a single regional technique, surgical procedure, or pathology.

Data were collected independently by two authors of this study (DC and MFL).

Of each selected article, data on the type of study, geographic area, number of cases, number of anesthesia, type of surgery, and perioperative mortality and morbidity were collected. Regarding mortality, data on the mortality rate per 10,000 anesthesias were collected and the periods in which death occurred: in the operating room/post-anesthesia care unit or in the postoperative period at any time within 30 days. Regarding morbidity, data on the rate of perioperative cardiac arrest were collected. In addition to this critical event, we harvested information regarding critical/adverse events of various types (defined by the respective authors) whenever mentioned in the revised publication.

Results

The initial search for publications, limited to humans and the mentioned period, originated 104 and 144 articles for the *anesthesia-related* and *mortality* and *anesthesia-related* and *morbidity* combinations, respectively. After reading the title or abstract of these articles and other relevant surveyed by the *related articles* function and cited references, the selection included 20 articles reporting perioperative mortality or morbidity related to anesthesia in children under one year of age. Full analysis of these articles led to the exclusion of one systematic review.[1] Thus, our study data represent a compilation of information from 19 articles.[2,7–24] In 16 articles of incidence,[2,7–21] two reported series in which patients were also included in previous articles: the study by Braz 2006[17] included data from Braz 2004[18] and the study by Kawashima 2002[15] included data from Morita 2001.[7] These data analysis was made to complement the information, but not to duplicate. The remaining three publications[22–24] refer to multicenter database of reported cases. All studies are level B of scientific evidence, according to Oxford classification.[25]

Data on mortality are presented in Tables 1 and 2 and data on morbidity in Tables 3 and 4. Table 5 compiles mortality profiles and cardiac arrests in the different age subgroups within the first year of age.

Mortality in children in the first year of age

Mortality rates reported in the literature included in the study are presented in tables one and five. Five[10–14] of the eight studies in Table 1 have information on overall mortality per 10 thousand anesthesia in the first year of age (<1 Y or 0–12 M). There is a great variability, from 11.4 to 38.9 per 10,000 anesthesias during surgery and immediate postoperative period (an average of 30 deaths per 10,000 anesthesias, calculated on the basis of two series[10,12] that totaled 13,634 anesthesia) and 35.1 to 59.7 per 10,000 anesthesias up to the first 24 h after anesthesia (an average of 53 deaths per 10,000 anesthesias, calculated on the basis of two large series [1,141] that totaled 20,661 anesthesia). The mortality rate within the first two days of anesthesia, assessed in a study[13] involving pediatric patients up to 18 years of age and with 4863 anesthesias in the first year of age, was 18.5 per 10,000 anesthesias. In another study[14] involving pediatric patients up to 18 years and with 15,255 anesthesias in the first year of age, the mortality rate related to anesthesia at 30 days was 135 per 10,000 anesthesias.

The analysis of these results allows highlighting the following features:

1. The definition of death during the intraoperative and early postoperative periods or related to anesthesia has no consensus in the literature, but regardless of the criteria used, the studies involving multiple age groups found higher mortality rate in children under one year of age when compared to older children.
2. Data presented in Table 1 indicating very high mortality rates in the study by Chan et al.,[9] Van der Griend et al.,[14] and Flick et al.[10] should be read in this context of criteria variability, as it refer to the total anesthetized cases, including cardiac surgery, and, in the case of Chan et al.,[9] transplants. Van der Griend et al.[14] and Flick et al.[10] also report in their publications the mortality rate in non-cardiac surgery, which drops from 59.7 to 39.7/10,000 anesthesias in the first 24 hours in the study by Van der Griend et al.[14] and from 38.9 to 5/10,000 anesthesias in the study by Flick et al.[10]

Mortality in subgroups of children under the age of 1 year (0–30 days and 1–12 months)

Tables 1 and 5 have relevant data on mortality rate during the first month of age and from 1 to 12 months, and Table 2 shows the studies which indicate the cause of death.

Five[7–14] of the eight selected studies to evaluate the mortality rate contain data for analysis of this outcome in subgroups first month (0–30 days) and 12 months of age.

The death rates during surgery and postoperative period of anesthesias in neonates and children aged one to 12 months analyzed in a study[10] that involving children up to 18 years, with 1451 anesthesias in neonates and 7807 anesthesias in children aged one to 12 months were, respectively, 144.7 and 19.2 per 10,000 anesthesias. In the first 24 hours, the mortality rates presented in two studies[9,14] ranged from 180.1 to 288 per 10,000 anesthesias in neonates and from 32.2 to 129 per 10,000 anesthesias in children aged one to 12 months. Mortality rates in the first seven days analyzed in two studies[7,8] ranged from 26.94 to 74.10 and from 5.91 to 6.63 per 10,000 anesthesias, respectively, in neonates and children aged 1–12 months. In another study[14] involving pediatric patients up to 18 years of age and with 2831 anesthesias in neonates and 12,424 anesthesias in children aged 1–12 months, the 30 days mortality rates were, respectively, 367.4 and 82.1 per 10,000 anesthesias.

The following aspects are highlighted:

1. As in the analysis of mortality rate in the first year of age, the analysis of mortality rates in the two subgroups of this age group reveals the same methodological differences and the need for critical evaluation from the standpoint this variability. The analysis of these profiles shows that the peak risk of mortality is consistent in the anesthesia group of neonates, compared with the group of older infants.

Table 1 Incidence of intraoperative and early postoperative mortality in children under 1 year of age.

Author/s (year); type of publication; period of investigation and location	Deaths included in data collection	Number of procedures, maximum age	Overall mortality in the study/10,000 anesthesias	Subgroups under 1 year of age		
				Age	Number of anesthesias	Incidence/10,000 anesthesias
Morita et al. (2001)[7]; R-M; 1999; Japan	First 7 days	732,788 anesthesias at all ages	ND	0–30 d	3509	74.10
				1–12 M	13580	6.63
Morita et al. (2002)[8]; R-M; 2000; Japan	First 7 days	910,757 anesthesias at all ages	ND	0–30 d	ND	26.94
				1–12 M	ND	5.91
Chan e Auler (2002)[9]; R-1C; 1998–1999; Brazil	First 24 hours	82,641 anesthesias at all ages	51	0–30 d	ND	288
				1–12 M	ND	129
Flick et al. (2007)[10]; R-1C; 1988–2005; USA	OR and PACU	92,881 anesthesias in children under 18	6.8	0–30 d	1451	144.7
				1–12 M	7807	19.2
				Geral <1 Y	9258	38.9
Bunchungmongkol et al. (2007)[11]; P-M; 2003–2004; Thailand	First 24 h	25,098 anesthesias in children up to 15 years	15.9	0–12 M	5406	35.1
Ahmed et al. (2009)[12]; R-1C; 1992–2006; Pakistan	OR and PACU	20,216 anesthesias in children under 18	3.46	0–12 M	4376	11.4
Bharti et al. (2009)[13]; R-1C; 2003–2008; India	First 2 days	12,158 anesthesias in children under 18	10.7	0–12 M	4863	18.5
Van der Griend et al. (2011)[14]; R-1C; 2003–2008; Australia	First 24 hours	10.1855 anesthesias in children under 18	24 h: 13.4	24 h		
				0–30 d	2831	180.1
				1–12 M	12,424	32.2
				Geral <1 Y	15,255	59.7
			30 d: 34.5	30 d: 0–30 d	2831	367.4
				1–12 M	12,424	82.1
				Geral <1 Y	15,255	135.0

R-M, retrospective multicenter; R-1C, retrospective 1 center; ND, unavailable information; M, month; d, day; h, hour; OR, operating room; PACU, post-anesthesia care unit.

Table 2 Mortality context in children under 1 year of age reported in the literature over the last 15 years.

Author/s (year); type of publication	Age group	Number of deaths	Age/reported context
Reports concerning deaths related to anesthesia			
Kawashima et al. (2002)[15]; R-M	0–12 M	0	No deaths related to anesthesia
Bunchungmonkol et al. (2009)[2]; P-M	0–30 d	1	1 d/bradycardia after inadequate oxygenation due to pneumothorax on postoperative thoracotomy due to tracheoesophageal fistula
	1–12 M	1	6 M/bradycardia in the context of apparent hypovolemia in emerging craniotomy
Ahmed et al. (2009)[12]; R-1C	0–30 d	0	No deaths related to anesthesia
	1–12 M	1	8 M/inadequate ventilation after extubation
Van der Griend et al. (2011)[14]; R-1C	0–30 d	1	13 d/congenital heart disease
	1–12 M	2	4 M/ex-premature with trisomy 21 and congenital heart disease 4 M/degenerative neurological disease
Reports concerning overall intraoperative and early postoperative deaths			
Kawashima et al. (2002)[15]; R-M	0–12 M	26	ND/21 deaths related to preoperative complications (17 from cardiovascular events, including 11 congenital heart disease) ND/5 deaths related to surgery
Flick et al. (2007)[10] [a]; R-1C	0–30 d	4 (in 17 years)	2.11 and 25 d/massive bleeding 1 d/due to pericardial tamponade for central catheterization
	1–12 M	0	No death in non-cardiac surgery

R-M, retrospective multicenter; P-M, prospective multicenter; R-1C, retrospective 1 center; M, month; d, day; ND, unavailable information.

[a] Information regarding non-cardiac surgery.

2. In the data analysis of Kawashima et al.,[15] regarding the compilation and analysis of data presented by Morita et al.[7] for the annual study of mortality and morbidity in Japan in 1999, mortality was higher in children under one month of age. However, mortality in children aged between one and 12 months, even though higher than that of older children, has been superseded by that of individuals aged between 66 and 85 years or more.
3. Although several studies refers to the most frequent causes of death and risk factors, most of them does not contain or analyzes this data in different age groups; therefore, specific data for children under one year of age are rare and the existing data generally refer only to the anesthesia-related deaths. This information is compiled in Table 2.

Perioperative morbidity

Regarding perioperative morbidity, studies show great disparity between the available data. Some authors have chosen to analyze the cardiac arrests in the perioperative period (Table 3), while others evaluated a wider range of critical/adverse events (Table 4).

Perioperative morbidity in the first year of age

In Table 3, six[10–13,16,17] of the eight listed articles contain information on the rate of cardiac arrest per 10,000 anesthesias in the first year of age. Of these six articles, five refer to the operating room and post-anesthesia care unit and one to the first 24 h. Table 5 presents the profile of cardiac arrests in the different subgroups of first year of age.

It was noted that the rate of cardiac arrest per 10,000 anesthesias in the operating room and post-anesthesia care unit ranged from 8.9[16] to 87.1[17] (average of 38.6 cardiac arrests per 10,000 anesthesias, calculated based on five major series[10,12,13,16,17] totaling 25,392 anesthesias); and in one study[11] of the first 24 h, the rate was 48.1 per 10,000 anesthesias in a universe of 5406 anesthesias.

The rate of perioperative critical/adverse events of different types associated with anesthetic procedures (Table 4) ranged from 4.6% to 30.8%.

We highlight the following aspects of the critical analysis of Tables 3 and 4 and the related literature data:

1. As with mortality, the criteria used to calculate the incidence of cardiac arrest or critical/adverse events varied. There is therefore a discrepancy in the values presented that must be interpreted in its context. For example, the incidence of cardiac arrest reported by Flick et al.[10] is total, including cardiac surgery. In this study, in children under one year of age, the incidence of cardiac arrest considering only non-cardiac surgery was 8.7 per 10,000 anesthesias, one-fifth of the total incidence.
2. In all studies found, the incidence of cardiac arrest and critical/adverse events of various types was higher in children aged less than one year than in older children.[2,7,8,10–13,15–21]

Table 3 Incidence of perioperative cardiac arrest in children under 1 year of age.

Author/s (year); type of publication; period of investigation and location	Cardiac arrest	Number of procedures, maximum age	Overall incidence in the study/10,000 anesthesias	Subgroups under 1 year of age		
				Age	Number of anesthesias	Incidence/10,000 anesthesias
Morita et al. (2001)[7]; R-M; 1999; Japan	ND	732,788 anesthesias at all ages	ND	0–30 d 1–12 M	3509 13,580	54.1 8.8
Morita et al. (2002)[8]; R-M; 2000; Japan	ND	910,757 anesthesias at all ages	ND	0–30 d 1–12 M	ND ND	28.3 8.54
Murat et al. (2004)[16]; P-1C; 2000–2002; France	OR and PACU	24,165 anesthesias in children up to 15 years	3.3	<1 Y	3681	10.9
Braz et al. (2006)[17]; P-1C; 1996–2005; Brazil	OR and PACU	53,718 anesthesias at all ages	34.6	0–30 d 1–12 M Geral <1 Y	846 2368 3214	177.3 55.1 87.1
Flick et al. (2007)[10]; R-1C; 1988–2005; USA	OR and PACU	92,881 anesthesias in children up to 18 years	8.6	0–30 d 1–12 M Geral <1 Y	1451 7807 9258	158.5 23.1 44.3
Bunchungmongkol et al. (2007)[11]; P-M; 2003–2004; Thailand	First 24 hours	25,098 anesthesias in children up to 15 years	19.9	<1 Y	5406	48.1
Ahmed et al. (2009)[12]; R-1C; 1992–2006; Pakistan	OR and PACU	20,216 anesthesias in children up to 18 years[a]	4.95	<1 Y	4376	18.3
Bharti et al. (2009)[13]; R-1C; 2003–2008; India	OR and PACU	12,158 anesthesias in children up to 18 years	22.2	<1 Y	4863	35

R-M, A retrospective multicenter; P-1C, A prospective 1 center; R-1C, retrospective 1 center; P-M, A prospective multicenter; ND, unavailable information; OR, operating room; PACU, post-anesthesia care unit; d, days; M, months.

[a] Excluded cases of cardiac surgery.

Table 4 Incidence of perioperative critical/adverse events in children under 1 year of age.

Author/s (year); type of publication; period of investigation and location	Occurrence period	Number of procedures, maximum age	Overall incidence in the study	Subgroups under 1 year of age		
				Age	Number of anesthesias	Incidência
Tay et al. (2001) [19]; P-1C; 1997–1999; Singapore	ND	10,000 pediatric cases	2.78%	<1 Y	1022	8.6%
Morita et al. (2001)[7]; R-M; 1999; Japan	ND	732,788 anesthesias at all ages	ND	0–30 d 1–12 M	ND ND	1.68% 0.48%
Morita et al. (2002)[8]; R-M; 2000; Japan	ND	910,757 anesthesias at all ages	ND	0–30 d 1–12 M	ND ND	0.7% 0.42%
Murat et al. (2004)[16]; P-1C; 2000–2002; France	OR and PACU	24,165 anesthesias in children up to 15 years	3.1% at OR 4.8% at PACU	<1 Y	3681	3.6% at OR 1.47% at PACU
Edomwonyi et al. (2006)[20]; P-1C; 12 months, year unspecified; Nigeria	OR and PACU	270 anesthesias in children under 16 years	24%	0–30 d 1–12 M	15 69	26.7% 6%–8.7%
Bunchungmongkol et al. (2007)[11]; P-M; 2003–2004; Thailand	First 24 h	25,098 anesthesias in children up to 15 years	1.9%	<1 Y	5406	4.6%
Samaké et al. (2010)[21]; P-1C; Março-setembro 2004; Mali	ND	107 anesthesias in children up to 12 years	39%	<1 Y	107	30.8%

P-1C, prospective 1 center; R-M, retrospective multicenter; P-M, prospective multicenter; ND, unavailable information; OR, operating room; PACU, post-anesthesia care unit; Definition of critical event or adverse event, Ref.[19] – respiratory, cardiovascular, and related to the equipment, drugs, regional anesthesia, and others, including seizures, deaths, and dental injuries; Ref.[7,8] – cardiac arrest, severe hypotension, severe hypoxemia; Ref.[16] – cardiovascular, neurological, related to regional anesthesia and others, including anaphylaxis, malignant hyperthermia, dose error, prolonged neuromuscular blockade, hypo or hyperthermia, vomiting, postoperative hemorrhage, and equipment failure; Ref.[20] – cardiovascular, respiratory, neurological and gastrointestinal (postoperative nausea and vomiting); Ref.[11] – pulmonary aspiration, symptomatic esophageal intubation, desaturation for more than 3 minutes, reintubation, difficult intubation (more than 3 attempts or more than 10 minutes), intubation failure, coma/seizure, nerve damage, cardiac arrest, death, anaphylaxis, medication error, equipment failure; Ref.[21] – respiratory, cardiovascular, neurological (delay in waking), and gastrointestinal (postoperative vomiting).

Table 5 Epidemiological profiles of morbidity and mortality in subgroups under 1 year of age.

Age	Outcomes	Rate per 10,000 anesthesias	Number of studies for calculation (total number of anesthesias)	Variation per 10,000 anesthesias
Mortality				
<1 Y	OR/PACU	30	2 (13,634)	11.4–38.9
	First 24 h	53	2 (20,661)	35.1–59.7
	First 2 days	18.5	1 (4863)	18.5
	First 30 days	135	1 (15,255)	135
0–30 d	OR/PACU	144.7	1 (1451)	144.7
	First 7 days	ND	2 (ND)	26.94–74.10
	First 30 days	367.4	1 (2831)	367.4
1–12 M	OR/PACU	19.2	1 (7807)	19.2
	First 7 days	ND	2 (ND)	5.91–6.63
	First 30 days	82.1	1 (12,424)	82.1
Cardiac arrest				
<1 Y	OR/PACU	38.6	5 (25,392)	8.9–87.1
	First 24 h	48.1	1 (5406)	48.1
0–30 d	OR/PACU	165.4	2 (2297)	158.5–177.3
1–12 M	OR/PACU	30.5	2 (10,175)	23.1–55.1

OR, operating room; PACU, post-anesthesia care unit; d, day; M, month; ND, unavailable information.

3. The frequency of cardiac arrest at the age group referred to in our study is also relevant compared to older children. In the studies available, 50%–80% of cardiac arrests in children occurred in patients under one year of age.[10–13,16–18] Similarly, Morray et al.[22] in their study based on registration data from POCA (Pediatric Perioperative Cardiac Arrest Registry) stated that more than half of cardiac arrests reported between 1994 and 1997 at hospitals in the United States and Canada occurred in children under one year of age (169 per 289 children). In this study, age as an independent factor of the associated pathology was not predictive of mortality after cardiac arrest.
4. Bhananker et al.[23] showed in 2007 an update of the POCA Registry in which it is noticeable the relative percentage decrease of cardiac arrests reported in children under one year of age compared to data of previous years presented by Morray et al.[22] However, without information on the number of anesthesia performed in hospitals in question, it is not possible to calculate and compare incidences.
5. MacLennan et al.[24] identified 606 critical events reported in children between 2006 and 2008 in the United Kingdom, of which 102 (16.8%) in children under one year of age. As it is a compilation of reported cases of several hospitals, it is also not possible to calculate the incidence in this population.

Perioperative morbidity in subgroups of children under 1 year of age

In Table 3, four[7,8,10,17] of eight articles contain information regarding the rate of cardiac arrest per 10,000 anesthesias during the first month of age (0–30 days) and between one and 12 months. Table 5 shows the epidemiological profiles of cardiac arrest in subgroups 0–30 days and 1–12 months.

In the first month of age, the rate of cardiac arrest ranged from 28.3 to 177.3 per 10,000 anesthesias and in 1–12 months it varied from 8.54 to 55.1 per 10,000 anesthesias. In both studies[10,17] with complete data for the calculation of the number of cases of perioperative cardiac arrest, a mean of 165.4 cases of cardiac arrest occurred in the operating room and post-anesthesia care unity per 10,000 anesthesias in the first month of age, for a global universe of 2297 anesthesias, and a mean of 30.5 cases per 10,000 anesthesias in children 1–12 months, for a global universe of 10,175 anesthesias.

For the first month of age, the rate of critical/adverse events of various types (Table 4) ranged from 0.7 to 26.7% of anesthesias and for 1–12 months, it ranged from 0.42 to 8.7% of anesthesias.

The highlights of the critical analysis for data of Tables 3 and 4 and related literature are the following:

1. As for the group of children in the first year of age, the criteria used to calculate the incidence of cardiac arrest or critical/adverse events in subgroups of 0–30 days and 1–12 months varied. It was noticed discrepancy in the values, which must be interpreted in its context. For example, the incidence of cardiac arrest presented by Flick et al.[10] is total, including cardiac surgery. In this study, in children under one year of age, its incidence in cardiac surgery was much higher (434.8/10,000 anesthesias) than in non-cardiac surgery (39.4/10,000 anesthesias).
2. Bhananker et al.[23] found 93 cardiac arrests reported during anesthesia or in the immediate recovery in children

up to 18 years, of which 21 in neonates and 53 in children aged 1–12 months, in POCA Registry between 1998 and 2004.

Etiology and context of perioperative morbidity in children under 1 year of age

The etiology and context of cardiac arrests in children under one year of age are mostly specified only in cases related to anesthesia.

Thus, in the study of Ahmed et al.,[12] of the eight cardiac arrests in children under one year of age, three were attributed to anesthetic causes, notably by hypovolemia, inadequate ventilation (cited in the analysis of mortality), and bradycardia after succinylcholine administration. All were considered preventable.

In his study of 9 years, Braz et al.[17] reported that all cardiac arrests related to anesthesia in children under one year of age were due to inefficient ventilation and occurred in patients ASA III or IV. No death in the study was related to anesthesia and all cases of cardiac arrest due to respiratory event occurred in patients with significant associated pathology.

The seven cardiac arrests identified by Flick et al.[10] were due to hypoxemia ($n = 1$), massive bleeding ($n = 3$), possible air embolism ($n = 1$), complications related to central catheterization ($n = 2$), often in aggravating contexts as illustrated by the physical status ASA IV or V in five cases.

In the study by Bunchungmongkol et al.,[2] in addition to the two cases resulting in death previously described, caused by insufficient oxygenation and hypovolemia, the remaining five cardiac arrests related to anesthesia in children under one year of age were motivated by medication errors ($n = 3$) and inadequate oxygenation ($n = 2$).

In Japanese annual studies,[7,8,15] the incidence of cardiac arrest in children under one year of age (and more expressive in neonates) was mainly attributed to coexisting pathology. No cardiac arrest in neonates was associated with anesthesia. It is worth noting that in cases of 1999, following the occurrence of cardiac arrest, 80.8% of neonates died. This shows that cardiovascular resuscitation in this age group is exceptionally difficult.[15]

Regarding the various critical/adverse events in the population under one year of age, the literature data are once again widely dispersed, due to the wide range of data collected and because the population in studies is no restricted to that age group.

In the assessment of 1000 pediatric anesthesias, Tay et al.[19] found an incidence of 2.8% of laryngospasm in children under one year of age, significantly higher than in older children.

Murat et al.[16] and Edomwonyi et al.[20] reported in their studies a higher frequency of cardiac and respiratory events in children under one year of age either in the operating room or post-anesthesia care unit. The second study adds that adverse events occurred more frequently during anesthetic induction.

On the other hand, Bunchungmongkol et al.[11] report that in this age group critical events occurred more frequently during anesthesia. Desaturation was the most common event. In this study, children under one year of age had significantly higher incidence of delayed esophageal intubation detection (0.17%), desaturation (2.2%), reintubation (0.42%), cardiac arrest (0.65%), death (0.65%), and medication error (0.07%).

Discussion

In this systematic review, we emphasize the main findings: (1) the higher incidences of mortality and morbidity in children under one year of age undergoing general anesthesia compared with older children; (2) the increased risk in those incidences in children undergoing surgery in the neonatal period; (3) the high frequency of cardiac arrests in patients under one year of age among the total cardiac arrests in children; (4) the lack of studies centered in the neonatal period and first year of age; (5) the great variability of methodologies for the study of the same concepts.

Although there are several studies of morbidity and mortality in anesthetic-surgical setting with incidence data on pediatric population under one year of age and even neonatal, this systematic review allowed the compilation of several existing information that would allow both its joint analysis and comparison with pre-existing empirical knowledge and the identification of unanswered questions. Although the included studies were level B of scientific evidence, most of them included tens of thousands of anesthesias in their series.

Regarding the various studies methodology, a significant difference in the data collected definition is linked to the period in which the incident occurred: intraoperative, operating room and post-anesthesia care unit, the first 24 h, the first two days, the first postoperative week or month. On the other hand, there is no consensus in the literature regarding the definition of death and morbidity in the anesthetic/surgical context. Several authors report death related to anesthesia, but it is also determined in several ways: related to the anesthesiologist role or anesthetic technique, factors under the anesthesiologist control, and factors such as surgical and anesthetics, among others. Given its multifactorial nature, data analysis may be more informative if all factors are considered rather than just trying to emphasize the ones potentially related to anesthesia. Also, risk prevention is more likely if more importance is given to the occurrence of death and morbidity throughout the perioperative process, and not just to the risk of anesthesia in particular.[14]

Also, the discussion of causes and risk factors is often limited to a wide range of ages. Of data reported in the literature specifically related to children less than one year old, mortality and morbidity in the anesthetic context seem to be more related to cardiovascular and respiratory complications, which is consistent with the physiology of this age group. This trend seems to replace the deaths of older studies, mostly related to the anesthetic drug, often attributed to halothane, myocardial depressant drug especially in younger children with congenital heart disease, which, however, fell into disuse.[22,23,26] With the use of new and safer drugs, deaths began to be evidenced by bleeding, inadequate fluid therapy, and respiratory problems. Loss of vascular volume is often underestimated in young children.

Because the circulating volume is smaller, these patients are more sensitive to inadequate hydration, both excessive and insufficient. That age is a risk factor for respiratory complications for two main reasons: increased peripheral collapse trend due to increased chest wall compliance and increased vagal tone with quick response of apnea and laryngospasm to irritation of receptors present in the airways by secretions, tracheal intubation, and aspiration. The resulting hypoxia is at that age closely related to cardiac arrest.

In general, the pediatric series show an increased incidence of cardiac arrests, 1.4–4.6 per 10,000 anesthesias, compared with one case per 10,000 in adult series.[27] Within the first year, our study shows a much higher incidence, with a particularly high proportion of cases in the neonatal age (165.4 per 10,000 anesthesias).

The technical complications found related to central lines placement, although of unknown incidence in the perioperative setting, are well known in other settings, notably in pediatric intensive care studies, which are justified by the heart anatomy in the first months of life, with thinner walls more susceptible to trauma.[28] Some authors recommend the use of ultrasound to increase the technique safety.[28]

A common clinical implication to several studies in the literature, whether directed to pediatric anesthesia mortality or morbidity, is the guidance that pediatric anesthesia, especially for younger children, should be performed by anesthesiologists with experience in this age group.[1,4–6,12,14,22,29]

The global data analysis of pediatric cases of broader age groups is not necessarily applicable to anesthesia in the neonatal period and before the first year of age. Therefore, large multicenter randomized studies specific for these ages are needed, in order to minimize confounding factors and biases, and thus adjust the clinical practice more correctly to increase security.

Conflicts of interest

The authors declare no conflicts of interest.

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