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REVIEW ARTICLE

Epidemiology of perioperative cardiac arrest and mortality in Brazil: a systematic review

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Abstract
Background and objectives: The perioperative cardiac arrest (CA) and mortality rates in Brazil, a developing country, are higher than in developed countries. The hypothesis of this review was that knowledge of the epidemiology of perioperative CA and mortality in Brazil enables the comparison with developed countries. The systematic review aimed to verify, in studies conducted in Brazil, the epidemiology of perioperative CA and mortality.
Method and results: A search strategy was carried out on different databases (PubMed, EMBASE, SciELO and LILACS) to identify observational studies that reported perioperative CA and/or mortality up to 48 hours postoperatively in Brazil. The primary outcomes were data on epidemiology of perioperative CA and mortality. In 8 Brazilian studies, there was a higher occurrence of perioperative CA and mortality in males; in extremes of age; in patients in worse physical status according to the American Society of Anesthesiologists (ASA); in emergency surgeries; in general anesthesia; and in cardiac, thoracic, vascular, abdominal and neurological surgeries. The patient's disease/condition was the main triggering factor, with sepsis and trauma as the main causes.
Conclusions: The epidemiology of both perioperative CA and mortality events reported in Brazilian studies does not show important differences and, in general, is similar to studies in developed countries. However, sepsis represents one of the major causes of perioperative CA and mortality in Brazilian studies, contrasting with studies in developed countries in which sepsis is a secondary cause.

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PALAVRAS-CHAVE
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Epidemiologia de parada cardíaca e de mortalidade perioperatória no Brasil: revisão sistemática

Resumo:
Justificativa e objetivos: As incidências de parada cardíaca (PC) e de mortalidade perioperatória no Brasil, um país em desenvolvimento, são mais elevadas em relação às dos países desenvolvidos. A hipótese desta revisão é que o conhecimento da epidemiologia de PC e de mortalidade perioperatória no Brasil possibilita sua comparação com a dos países desenvolvidos. A revisão sistemática teve como objetivo verificar, em estudos realizados no Brasil, a epidemiologia de PC e de mortalidade perioperatória.
Conteúdo: Realizou-se estratégia de busca em diferentes bases de dados (PubMed, EMBASE, SciELO e LILACS) para a identificação de estudos observacionais que reportaram PC e/ou mortalidade perioperatória até 48 horas pós-operatório no Brasil. Os desfechos primários foram dados de epidemiologia de PC e de mortalidade perioperatória. Em 8 estudos nacionais, identificou-se maior ocorrência de PC e de mortalidade perioperatória no sexo masculino, em extremos de idade, em pacientes em pior estado físico segundo a American Society of Anesthesiologists (ASA), em cirurgias de emergência, em anestesia geral, e em cirurgias cardíaca, torácica, vascular, abdominal e neurológica. A doença/condição do paciente foi o principal fator desencadeante, tendo como causas principais a sepse e o trauma.
Conclusões: Nos estudos nacionais, a epidemiologia dos eventos tanto de PC como de mortalidade perioperatória não apresenta diferenças importantes, e de maneira geral, é semelhante à de estudos de países desenvolvidos. Entretanto, a sepse, nos estudos nacionais, representa uma das principais causas de PC e de mortalidade perioperatória, diferenciando-se dos estudos de países desenvolvidos nos quais a sepse é causa secundária.

Background

Of all complications of surgical patients, cardiac arrest (CA) is one of the poorest outcomes, as it can precede sequelae, loss of function and, in the worst-case scenario, death.

Brazil is a developing country that, over the years, has found it very difficult to provide universal and adequate quality health care to its population. Review of studies developed in Brazil have found a reduction in the perioperative CA rates over the last 25 years, following the global trend.[1]

Studies performed in Brazil have shown that the poor preoperative physical status of patients is one of the most important factors for the occurrence of perioperative CA[2,3] and mortality,[2,4–7] with sepsis as the main cause of perioperative CA[2] and mortality.[2,7] On the other hand, studies conducted in the United States, a developed country, found that sepsis represents a secondary cause of these events.[8,9] Therefore, pre-anesthetic management of comorbidities is critical for minimizing perioperative complications.

Considering the major difference in pre-hospital and in-hospital care between developed and developing countries, and the higher perioperative CA and mortality rates in developing countries compared to developed countries,[10,11] our hypothesis for the current review was that better understanding of the epidemiology of perioperative CA and mortality in Brazil would allow the comparison with developed countries.

The systematic review aimed to scrutinize the epidemiology (risk factors, triggering factors, and causes) of perioperative CA and mortality in studies carried out in Brazil.

Method

As a systematic review, the study did not require approval from the Ethics in Research Committee.

Strategy for search and selection of studies

We performed the literature review complying with EQUATOR's instructions and with the methodological checklist for writing systematic reviews of observational studies (Meta-analysis Of Observational Studies in Epidemiology - MOOSE).[12] Databases were searched using a comprehensive search strategy for the identification of CA and perioperative mortality studies, using index terms (e.g., MeSH - MEDLINE), including a complete list of synonyms referring to the terms covered in the study: an(a)esthesia and cardiac arrest or mortality. The search strategy was adapted for each database in order to achieve greater sensitivity and identification of relevant studies.

Data were obtained from the following databases: US National Library of Medicine (MEDLINE via PubMed), Excerpta Medica Database (EMBASE), Scientific Electronics Library Online (SciELO) and Latin American and Caribbean Literature in Health Sciences (LILACS) for the identification of articles that reported perioperative CA or mortality in Brazil. The date of the last search was December 18, 2018.

Three reviewers (LGB, RS and ACM) made the initial selection of study titles and abstracts independently. The studies considered relevant were obtained in full and reviewed by two independent reviewers (LGB and ACM). Differences in results were discussed and solved. When there

was more than one study published on the same population group, data from the most recent and/or complete article were extracted.

Inclusion criteria for articles were observational studies that reported the epidemiology of CA and/or mortality up to 48 hours postoperatively in Brazil, in complete publications. We excluded articles with specific populations (e.g., children, older age), specific surgeries (e.g., cardiac surgery), a single type of anesthesia (e.g., regional anesthesia), a particular physical status (e.g., ASA physical status I) and case reports.

Data extraction and definition of outcomes

Two of the authors (LGB and ACM) independently identified the studies to be included in the review complying with inclusion criteria previously detailed. Dedicated standard forms were used to extract relevant data related to the epidemiology of perioperative CA or mortality: risk factors (sex, age, classification of patients' physical status according to the ASA physical status classification, type of surgical care, surgical specialty and type of anesthesia), triggering factors and their causes (patient's disease/condition, surgery or anesthesia), in addition to survival after CA. Discrepancies were solved after discussion with a third reviewer (JRCB). Data were extracted after defining the studies that would be included in the systematic review.

The primary outcomes assessed were data on epidemiology of perioperative CA and mortality.

Results

Selection of studies

We identified 14,132 citations in the databases and 3 citations through references. After reviewing titles and abstracts, we excluded 5,387 duplicate studies and 8,734 studies for lack of relevance. We identified 14 potentially relevant articles to undergo a more comprehensive assessment. Of these, we selected eight articles according to the inclusion criteria, with four studies on perioperative CA and eight studies on perioperative mortality (Fig. 1). The first study included was published in 1986, and the most recent in 2018. The description of perioperative CA and mortality studies included in the review is shown in Tables 1 and 2, respectively.

Risk factors for perioperative CA and mortality

Sex

A Brazilian study showed that there was no significant difference of perioperative CA rate in relation to sex in patients $\leq$ 17 years; however, there was a significantly higher perioperative CA rate in male patients $\geq$ 18 years compared to females; two other studies also found a higher proportion of perioperative CA in male patients.[3,13]

As for perioperative mortality, studies showed a higher proportion of events in males,[3,4,13,14] but in the only study in which statistical analysis was performed, no significant difference in rate was found between sexes.[5]

Age

Compared to the young adult age range (18–35 years), the extremes of age showed a significant higher perioperative CA and mortality rates. In neonates (0–30 days), the perioperative CA and mortality rates were 9.7 and 9.1 times higher, respectively; in children from 31 days to < 1 year, 3 and 9.3 times higher, respectively; and in the older patients $\geq$ 65 years, 4 and 5.9 times higher, respectively.[2,5]

ASA physical status classification

Patients presenting worse physical status (ASA III–V) had a higher perioperative CA[2,3] and mortality[4–7] rates compared to ASA I–II patients. Studies have shown 360 times higher CA[2] and 2,296 times higher perioperative mortality[5] rates in patients with ASA III–V physical status compared to ASA I–II.

Surgical procedures

Studies performed in Brazil unanimously found a higher perioperative CA[2,14] and mortality[4–7] rates during emergency surgeries compared to routine or urgent surgeries. Studies have shown CA[2] and perioperative mortality rates,[5] in emergency surgeries, 11 and 19 times higher, respectively, when compared to those in routine surgery.

Surgical specialty

Brazilian studies have shown a higher occurrence of perioperative CA[2,14] and mortality[4–6] in cardiac surgery, followed by vascular, thoracic, abdominal, neurological and orthopedic surgeries.

Type of anesthesia

The articles reported a higher occurrence of perioperative CA[2,3] and mortality[4,5,7] in surgical procedures performed under general anesthesia in comparison to neuroaxial anesthesia , in proportions 82 and 195 times higher, respectively.

Triggering factors for perioperative CA and mortality

In the 1980s, the first Brazilian study on perioperative CA rate showed that surgery was the main triggering factor (49.3%), followed by anesthesia (36.1%), patient's disease/condition (14.1%) and in one patient (0.5%) the CA eliciting factor could not be determined. Regarding mortality, surgery was the main factor (77.7%), followed by the patient's disease/condition (13.2%) and anesthesia (9.1%).[13]

More recent Brazilian studies have shown that the perioperative CA[2,3] and mortality[2,3,5,7] rates was lower due to the anesthetic factor, while the patient's disease/condition was the main factor, followed by surgery for both perioperative CA[2,3] and mortality.[2,3,5] Thus, a study[2] found proportions of perioperative CA and mortality, by patient disease/condition of 66% and 68%; by surgical factor of 25% and 27%; and by anesthetic factor of 9% and 5%. In only one Brazilian study, there was no mortality due to the anesthetic factor.[5]

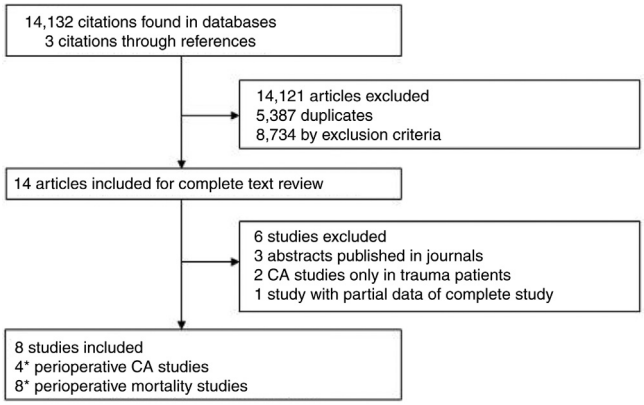

Fig. 1 Flowchart for selection of articles (CA, cardiac arrest; *Some studies were used in more than one category).

Table 1 Description of perioperative cardiac arrest studies.

Authors and year of publication	Data Source and period studied	Time of CA occurrence	Exclusion	Patients (n)
Ruiz Neto & Amaral, 1986[13]	Tertiary University Hospital Retrospective Medical Charts 1982–1984	OR	Cardiac Surgery	51,422
Braz et al., 1999[3]	Tertiary University Hospital Retrospective Database 1988–1996	OR and PACU	–	58,553
Braz et al., 2006[2]	Tertiary University Hospital Prospective Database 1996–2005	OR and PACU	–	53,718
Sebbag et al., 2013[14]	Tertiary University Hospital Prospective Database 2007	OR	Cardiac Surgery	40,379

CA, cardiac arrest; OR, operating room; PACU, Post-anesthesia care unit.

Causes of perioperative CA and mortality

Patient's disease/condition and/or surgery-related

The main causes of perioperative CA[6] and mortality[2,7] due to patient's disease/condition and/or surgery were: sepsis, trauma, hemorrhage in surgeries associated with primary disease (cancer), cardiac surgery and rupture of aortic aneurysm. The proportion of sepsis in relation to other causes of perioperative CA[2] and mortality[7] were 25% and 35%, respectively, while trauma was 18.4% and 24%.[2]

Anesthesia-related

In CA due to the anesthesia-related (factor), medication was considered as the main cause, followed by respiratory and airway complications in the first Brazilian study conducted in the 1980s.[13] In the most recent Brazilian studies, respiratory and airway complications have become the main cause of CA by anesthesia-related, followed by cardiovascular complications.[2,3]

Regarding mortality, one study showed pulmonary and airway complications as the main cause,[5] while another study showed cardiovascular complications as the main cause.[7]

Among the main pulmonary and airway events, we can highlight hypoxemia related to loss of airway, difficult tracheal intubation, orotracheal tube obstruction, pulmonary aspiration and complications related to double-lumen tube placement. Regarding cardiovascular complications, they were mainly associated with overdose of induction agents, high sympathetic block in neuraxial anesthesia, bradycardia, cardiac arrhythmias and anaphylactic shock.[2,5,7]

Perioperative CA survival

Brazilian studies have shown proportions of return of spontaneous circulation after perioperative CA varying from 32.6%

Table 2 Description of perioperative mortality studies.

Authors and year of publication	Data Source and period studied	Time of CA occurrence	Exclusion	Patients (n)
Ruiz Neto & Amaral, 1986[13]	Tertiary University Hospital Retrospective Medical Charts 1982–1984	OR	Cardiac Surgery	51,422
Cicarelli et al., 1998[6]	Tertiary University Hospital Retrospective Medical Charts 1995	OR up to 24 h postoperatively	Cardiac Surgery	25,926
Braz et al., 1999[3]	Tertiary University Hospital Retrospective Database 1988–1996	OR and PACU	–	58,553
Chan & Auler Jr, 2002[4]	Tertiary University Hospital Retrospective Medical Charts 1998–1999	OR up to 24 h postoperatively	–	82,641
Braz et al., 2006[2]	Tertiary University Hospital Prospective Database 1996–2005	OR and PACU	–	53,718
Sebbag et al., 2013[14]	Tertiary University Hospital Prospective Database 2007	OR up to 24 h postoperatively	Cardiac Surgery	40,379
Pignaton et al., 2016[5]	Tertiary University Hospital Retrospective Database 2005–2012	OR and PACU	–	55,002
Stefani et al., 2018[7]	Quaternary University Hospital Retrospective Database 2012–2013	OR up to 48 h postoperatively	–	11,562

CA, cardiac arrest; OR, operating room; PACU, Post-anesthesia care unit.

to 69%.[2,3,13,14] One study showed survival after CA of 69% intraoperatively, 38% up to 24 hours postoperatively, and 25% up to 30 postoperatively days, with 46% of surviving patients (25%) with a Glasgow scale $\geq$ 14.[14] In this same study, the authors found a significant relationship between the worst physical status (ASA IV–V), in which there was no survival, and the best physical status (ASA I–III), in which there was survival of 40% of the patients up to 30 days after surgery.

Discussion

This is the first systematic review of studies performed in Brazil on the epidemiology of CA and mortality in the perioperative period. The results showed a higher occurrence of perioperative CA and mortality in male patients, extremes of age, patients in worse physical status (ASA III–V), emergency surgery, general anesthesia, and cardiac, thoracic, vascular, abdominal and neurological surgery. Patient's disease/condition was the main triggering factor for perioperative CA and mortality, with sepsis and trauma as the main causes.

The results are not different from those found in the international literature. Compared to female patients, men are more predisposed to trauma, violence[15] and vascular diseases.[2] Consequently, studies from both developing[16,17] and developed countries[18–23] reported a higher occurrence of perioperative CA,[17–20,22] as well as mortality[16,21,23] in male patients.

Similar to Brazilian results, recent studies carried out in a developed country (the US) showed a significant higher perioperative CA[19,22] and mortality[22] rates in children under one year of age and in the older patients over 65. Therefore, extremes of age remain the age groups at higher risk for perioperative CA and mortality events and they should merit greater attention and care from the anesthesiologist.

Prematurity, congenital heart and neurological diseases and other congenital disorders in children, as well as clinical conditions associated with aging, are the factors that predispose both groups to a greater risk in comparison to young adults.[2,5,24–27]

A study carried out in a developed country showed that perioperative CA and mortality rates in patients with physical status ASA III–V, were 38 and 374 times higher, respectively, in comparison to patients with physical status ASA I–II.[22] In Brazilian studies perioperative CA[2] and mortality[2,5] rates in patients physical status ASA III–V compared to ASA I–II patients were 61 and 2,295 times higher, respectively. A study conducted in Brazil revealed that many older patients arrived to the operating room without optimizing their comorbidities, increasing the likelihood of anesthetic and surgical complications.[27]

Brazilian[2,4,7–14] and international studies[18,19,23] have revealed a higher risk of critical events, such as CA and death in emergency procedures compared to routine procedures. In emergency, the unfeasibility of ideal optimization of patients' pathophysiological conditions increases the occurrence of hemodynamic instability, surgical complications, such as profuse bleeding, infections and sepsis with multiple organ failure, in addition to thromboembolic phenomena.[17]

Studies performed in Brazil[2–5,7] and developed countries, such as Germany[19] and the United States,[22,23] have described a higher perioperative CA and mortality rates during general anesthesia compared to neuraxial blockade. Suitability of the anesthetic technique regarding physical status, comorbidities and type of surgery suggests general anesthesia as the technique of choice for critically ill patients and for higher risk surgeries, such as cardiac, thoracic and neurosurgery. Additionally, the introduction of new local anesthetics with less cardiac and central nervous system toxicity, associated with the introduction of ultrasound in anesthesiology, have enabled performing more accurate anesthesia blockades, and less likely blockade failures and systemic toxicity.[28]

In some surgery specialties, such as thoracic, neurological, vascular, but especially cardiac, Brazilian[2,4,5] and international[29,30] authors have shown a higher perioperative CA and mortality rates.

Trauma was reported as an important cause of perioperative CA and mortality in Brazil,[2,5,14,31] in other developing countries,[32] and also in developed countries.[8,9] Currently in Brazil, mortality due to trauma is the third cause of death, behind cardiovascular diseases and cancer. However, trauma due to external causes appears as the main cause in the 1 to 49 years age group, particularly in young men.[33] In Brazil, the main causes of perioperative CA in trauma were motor vehicle accidents (62.7%) and violence (29.4%).[15]

In Brazilian studies compared to other factors, sepsis represents a frequent cause of perioperative CA[2] and mortality,[7] 25% and 35%, respectively. The latter values are higher than in other developing countries (13.6%)[16] and contrast with a study performed in the US,[8] which found sepsis as a causal factor for only 4.9% and 7.1% of cases of perioperative CA and mortality, respectively. It should be highlighted that Brazil has one of the highest sepsis mortality rates worldwide.[34] The asymmetrical behavior of the causes of perioperative CA and mortality described in developing and developed countries demonstrates the great difference in healthcare among countries. In developing countries, such as Brazil, the inadequacy of primary and secondary care extends to tertiary care and is associated with insufficient number of beds (both in wards and in anesthesia and intensive care units)contributing to the maintenance of a high perioperative CA and mortality rates.[10,11,35,36]

Unlike Brazilian studies,[2,3] a recent study from a developed country (Germany) showed that cardiovascular complications overcome pulmonary and airway complications as the most important causes of CA events due to the anesthesia-related.[19]

More recent studies in developed countries have observed survival after perioperative CA in proportions similar to those obtained in Brazilian studies, from 42% to 62%.[19,22,37,38]

Perioperative CA has different characteristics from CA outside the operating room because it usually occurs in the presence of the medical team and, often, anticipated because the causal factors are, in most cases, already known.[39] Moreover, patients are monitored with venous access, and resuscitation equipment is readily available. These factors enable starting focused resuscitation fast, leading to possible reversal of CA.

It should be noted that there are some important limitations in Brazilian studies. In relation to perioperative CA and mortality events, there is still no objective definition of the period of time that should be considered. Some Brazilian studies have considered only events that occurred in operating room facilities (operating room and post-anesthesia care unit).[2,3,5,13,14] Others take into account the period in the operating room together with the postoperative period, ranging from the first 24 hours[4,6] or up to 48 hours postoperatively.[7] Considering that CA and death are very rare events in the perioperative period, the number of surgical patients included in the studies becomes very important for better analysis. The number of patients included in Brazilian studies is relatively low, always less than 100 thousand patients, whereas in many studies in developed countries the number exceeds 1 million patients.[22,40,41] Brazilian studies were carried out only in tertiary care university public institutions and there still are no multicenter studies. Another limitation is that some studies have excluded certain types of surgery, which generally have a high occurrence of critical events, such as cardiac surgery.[6,13,14] Thus, more studies are required to validate the results of the current review and to monitor any changes in the epidemiology of perioperative CA and mortality in patients in Brazil.

Conclusion

The epidemiology of both perioperative CA and mortality events reported in Brazilian studies does not show important differences and, in general, is similar to that of studies in developed countries. The main risk factors for CA and mortality events were neonates, children under one year of age, the older patients, male sex, physical status ASA $\geq$ III, emergency surgery, and general anesthesia in cardiac, thoracic, vascular, abdominal and neurological surgery. The clinical status of the patient is the main triggering factor for the occurrence of perioperative CA and mortality,

followed by surgery and, finally, anesthesia. Sepsis represents one of the main causes of perioperative CA and mortality in Brazilian studies, contrasting with the causes in studies in developed countries.

Conflicts of interest

The authors declare no conflicts of interest.

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