Perioperative and Anesthesia-Related Mortality
An 8-Year Observational Survey From a Tertiary Teaching Hospital

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Abstract: In 2006, a previous study at our institution reported high perioperative and anesthesia-related mortality rates of 21.97 and 1.12 per 10,000 anesthetics, respectively. Since then, changes in surgical practices may have decreased these rates. However, the actual perioperative and anesthesia-related mortality rates in Brazil remains unknown. The study aimed to reexamine perioperative and anesthesia-related mortality rates in one Brazilian tertiary teaching hospital.

In this observational study, deaths occurring in the operation room and postanesthesia care unit between April 2005 and December 2012 were identified from an anesthesia database. The data included patient characteristics, surgical procedures, American Society of Anesthesiologists (ASA) physical status, and medical specialty teams, as well as the types of surgery and anesthesia. All deaths were reviewed and grouped by into 1 of 4 triggering factors groups: totally anesthesia-related, partially anesthesia-related, surgery-related, or disease/condition-related. The mortality rates are expressed per 10,000 anesthetics with 95% confidence intervals (CIs).

A total of 55,002 anesthetics and 88 deaths were reviewed, representing an overall mortality rate of 16.0 per 10,000 anesthetics (95% CI: 13.0–19.7). There were no anesthesia-related deaths. The major causes of mortality were patient disease/condition-related (13.8, 95% CI: 10.7–16.9) followed by surgery-related (2.2, 95% CI: 1.0–3.4). The major risks of perioperative mortality were children younger than 1-year-old, older patients, patients with poor ASA physical status (III–V), emergency, cardiac or vascular surgeries, and multiple surgeries performed under the same anesthesia technique (P < 0.0001).

There were no anesthesia-related deaths. However, the high mortality rate caused by the poor physical conditions of some patients suggests that primary prevention might be the key to reducing perioperative mortality. These findings demonstrate the need to improve medical perioperative practices for high-risk patients in under-resourced settings.

INTRODUCTION

Safety is a routine concern in anesthesiology. Although cardiac arrest and death rarely occur during the perioperative period, these events represent the worst patient outcomes. A past study of our institution, a general tertiary teaching hospital in Brazil, which is considered a high human development country according to the Human Development Index (HDI) set by the United Nations Development Programme, reported overall and anesthesia-related mortality rates of 21.97 and 1.12 per 10,000 anesthetics, respectively. Furthermore, our previous perioperative and anesthesia-related mortality rates were higher than those reported in studies from very high human development countries (ranging from 3.44 to 18.9 per 10,000 anesthetics and 0.10 to 0.95 per 10,000 anesthetics, respectively) that were published during the same period; these discrepancies were partially attributable to methodology disparities, but decreased access to healthcare is also a factor in our country.

In the last decade, Brazil has experienced significant improvements in economy and human indicators, thereby decreasing the inequality in relation to very high human development countries. In addition, in the last 10 years, our institution has developed initiatives to improve the care of surgical patients, including installing anesthesia workstations with ventilators in operating rooms (ORs); monitoring oxygen, carbon dioxide, nitrous oxide, and inhaled anesthetic concentrations; monitoring ventilation, to enable adequate ventilation and anesthesia control; acquiring devices for adequate core temperature control; and increasing the number of staff anesthesiologists and adult intensive care beds. However, the actual perioperative and anesthesia-related mortality rate in Brazil remains unknown.

We hypothesized that identifying and controlling risk factors and improving healthcare conditions following broadly defined institutional initiatives would improve anesthesia care and, consequently, improve surgical patients outcomes.

To address the lack of available information concerning perioperative and anesthesia-related mortality, the aim of this study was to reexamine the rates, causes and triggering factors of deaths occurring during anesthesia and in the postanesthesia care unit (PACU) over an 8-year period in a surgical population at a single Brazilian tertiary teaching hospital.
METHODS

The study was approved by the Botucatu Medical School Human Research Ethics Committee (protocol number 3160-2009), which waived the requirement for written informed consent.

In this observational study, we analyzed all reported perioperative deaths that occurred in the OR and PACU (short stay) in 55,002 consecutive anesthetized patients at the hospital of the School of Medicine, Universidade Estadual Paulista (UNESP) from April 1, 2005 to December 31, 2012. UNESP hospital is a public tertiary teaching hospital with 450-beds with a catchment of 2 million people that perform approximately 7000 surgeries per year on people of all age groups. The patient mix includes all surgical areas, as well as, high-risk obstetric and newborn patients. The hospital has 15-bed neonatal, 10-bed pediatric, and 37-bed adult intensive care units. Anesthesia care is provided by full-time faculty anesthesiologists, staff anesthesiologists, and anesthesia residents.

All patients were examined by an anesthesiologist immediately before all emergency and urgent surgical procedures or the day before all elective procedures. Continuous ECG monitoring and automatic noninvasive blood pressure and pulse oximetry measurements were utilized as a basic safety measure in the OR during regional and neuraxial anesthesia and sedation. For general anesthesia, the following parameters were also measured: oxygen concentration, capnography, delivered anesthetic vapor concentration, ventilation, and core temperature. Critically ill patients received direct invasive blood pressure and central venous monitoring.

Cardiac arrest was defined as the cessation of cardiac mechanical activity, with the loss of effective circulation, as determined by the absence of a palpable central pulse. Resuscitation was performed according to the interventions and protocols of the Advanced Cardiovascular Life Support guidelines. Patient deaths were identified from an anesthesia database, which was developed using a quality assessment form, which was part of the mandatory documentation for each anesthetic procedure. This database includes all procedures performed in the OR and PACU. The recorded data included the date and location (OR or PACU), patient characteristics, surgical procedures (elective, urgent, or emergency surgery), American Society of Anesthesiologists (ASA) physical status classification, medical specialty team, surgery type, anesthesia type, anesthesia provider information and a 95-item checklist of airway, respiratory, cardiovascular, neurological, renal, and miscellaneous events. When regional and general anesthesia were combined, general anesthesia was considered to be the technique used. In the cases of perioperative mortality, the anesthesiologist responsible for each case was asked to review the case and to provide a written summary for peer review.

Medical and anesthesia record data, written summaries, and, when applicable, the necropsy records of the patients who died during anesthesia or in the PACU were analyzed by the Anesthesia Cardiac Arrest and Mortality Study Commission, which is composed of 3 of the authors, who are faculty members in the Department of Anesthesiology (JR CB, NSPM, and LGB). The deaths were independently analyzed by all 3 board members in early 2014 and in early 2015 (final review) for a more detailed analysis. The triggering factors leading to mortality were assigned to 1 of 4 groups: totally related to anesthesia (ie, anesthesia was the only or major contributory factor); partially related to anesthesia (ie, the patient disease/condition or surgical procedure was a contributory factor, but the anesthesia represented an additional factor); totally related to surgery; or totally related in the to the patient’s disease or condition. For the majority of the deaths, there was unanimity regarding the cause of the event. After the final review, disagreements among the 3 members were resolved by discussion; in all cases, an agreement or consensus was reached when at least 2 of the 3 members agreed on the event’s cause.

Statistical Analysis

The mortality rates (expressed per 10,000 anesthetics) and 95% confidence intervals (CIs) were compared with χ² test (ie, sex) or Tukey’s test for multiple comparisons among proportions (ie, age group, ASA physical status, surgical procedure, anesthesia technique, and triggering factors). The factors predicting perioperative mortality (ie, age group, ASA physical status, surgical procedure, and surgery type) were analyzed with multivariate forward stepwise logistic regression, with odds ratios and 95% CIs. Data were considered to be significant when P < 0.05. The statistical analyses were performed using SPSS software, version 17.1 (SPSS Inc., Chicago, IL).

RESULTS

During the 8-year study period, 55,002 consecutive patients were anesthetized. Eighty-eight deaths (16.0 per 10,000 anesthetics; 95% CI: 13.0–19.7) representing all triggering factors were identified during the perioperative period in the OR and PACU. The majority of deaths occurred in the OR (96.6%) compared with the PACU (3.4%).

The highest estimated mortality rates occurred in children younger than 1 year of age, patients aged 65 years and older, and patients aged between 51 and 64 years, but mortality rates were not different between males and females (Table 1). Mortality rates also varied according to ASA physical status, surgery procedures, and type of anesthesia (Tables 2–3). In addition, the highest estimated mortality rates occurred in multiple surgeries performed under the same anesthetic technique (507.2 per 10,000 anesthetics; 95% CI: 141.1–873.3), cardiac (206.3 per 10,000 anesthetics; 95% CI: 114.5–298.1), vascular (108.4 per 10,000 anesthetics; 95% CI: 69.8–147.0), neurological (24.2 per 10,000 anesthetics; 95% CI: 6.3–42.1), gastroenterological (19.8 per 10,000 anesthetics; 95% CI: 9.8–29.8), and pediatric surgeries (16.8 per 10,000 anesthetics; 95% CI: 3.3–30.3).

After adjustment, higher mortality rates were identified in children younger than 1 year of age and patients aged 65 years and older, compared with children between 1 and 17 years of age; patients with ASA physical status III–IV compared with I–II; emergency compared with nonemergency surgery; cardiac or vascular surgeries compared with other types of surgery; and multiple surgeries during the sampling period compared with one surgery (Table 4).

The patient’s disease or condition was the most important triggering factor for mortality (86.4% of the perioperative deaths), followed by surgery-related (13.6%) (P = 0.02). No cases of anesthesia-related mortality were recorded (Table 5).

Table 6 provides additional information concerning the 88 deaths attributable to patient disease/condition or surgery-related factors. The most frequent causes were ruptured aneu- rysm, followed by complications associated with cardiac surgery (including the inability to wean the patients from cardiopulmonary bypass and complications associated with congenital
TABLE 1. Perioperative Mortality Rates in 55,002 Anesthetics According to Age and Sex

| Age group | N | % | N | Rate per 10,000 Anesthetics | 95% CI |
|-----------|---|---|---|-----------------------------|-------|
| 0 to 30 d | 494 | 0.9 | 3 | 60.7	extsuperscript{a} | 0.0–129.2 |
| 31 d to <1 yr | 960 | 1.7 | 6 | 62.5	extsuperscript{a} | 12.6–112.4 |
| 1 to ≤12 yr | 9074 | 16.5 | 3 | 3.3	extsuperscript{c} | 0.0–7.0 |
| 13 to ≤17yr | 2802 | 5.1 | 1 | 3.5	extsuperscript{c} | 0.0–10.4 |
| 18 to ≤35 yr | 13,441 | 24.4 | 9 | 6.7	extsuperscript{c} | 2.3–11.1 |
| 36 to ≤50 yr | 10,535 | 19.1 | 11 | 10.4	extsuperscript{c} | 4.2–16.1 |
| 51 to ≤64 yr | 9476 | 17.2 | 25 | 26.3	extsuperscript{b} | 16.6–36.6 |
| 65 to ≤79 yr | 6646 | 12.2 | 23 | 34.6	extsuperscript{b} | 20.5–48.7 |
| ≥80 yr | 1574 | 2.9 | 7 | 44.4	extsuperscript{b} | 11.6–77.2 |

| Sex | N | % | N | Rate per 10,000 Anesthetics | 95% CI |
|-----|---|---|---|-----------------------------|-------|
| Male | 27,095 | 49.3 | 50 | 18.4	extsuperscript{a} | 13.3–23.5 |
| Female | 27,907 | 50.7 | 38 | 13.6	extsuperscript{c} | 9.3–17.9 |

CI = confidence interval, d = days, yr = years.
	extsuperscript{a} Incidence followed by different superscript letters are statistically significant different; age group, \( P = 0.02; \) sex, \( P = 0.16.\)

There was no perioperative death in patient with ASA I physical status. However, there were 2 perioperative deaths in patients with ASA II physical status. The first 1 was an obstetric patient who had a hydatiform mole and underwent uterine curettage under general anesthesia during the early postpartum period. During the procedure, the patient developed sudden severe hypoxemia, followed by cardiovascular collapse and cardiac arrest. This patient passed away in the OR. The necropsy report revealed an amniotic fluid embolism. The second case was an elderly patient who underwent cholecystectomy under general anesthesia. During the surgical procedure, it was observed an abnormal neovascularization in the gallbladder and hepatic hilum, there was an excessive bleeding and the patient passed away in the OR.

TABLE 2. Perioperative Mortality Rates in 55,002 Anesthetics According to the ASA Physical Status and Surgical Procedures

| ASA physical status | N | % | N | Rate per 10,000 Anesthetics | 95% CI |
|---------------------|---|---|---|-----------------------------|-------|
| I | 23,972 | 43.5 | 0 | 0.0	extsuperscript{d} | 0.0–0.0 |
| II | 22,414 | 40.7 | 2 | 0.8	extsuperscript{d} | 0.0–1.6 |
| III | 6391 | 11.6 | 21 | 32.8	extsuperscript{a} | 18.8–46.8 |
| IV | 2064 | 3.7 | 39 | 188.9	extsuperscript{b} | 126.1–242.1 |
| V | 161 | 0.3 | 26 | 1614.9	extsuperscript{a} | 1,046.5–2,183.3 |

| Surgical procedures | N | % | N | Rate per 10,000 Anesthetics | 95% CI |
|---------------------|---|---|---|-----------------------------|-------|
| Elective | 33,631 | 61.1 | 19 | 5.6	extsuperscript{b} | 3.1–8.1 |
| Urgent | 15,455 | 28.1 | 5 | 3.2	extsuperscript{c} | 0.4–6.0 |
| Emergency | 5916 | 10.8 | 64 | 108.1	extsuperscript{a} | 81.7–134.5 |

ASA = American Society of Anesthesiologists, CI = confidence interval.

	extsuperscript{a} Incidence followed by different superscript letters are statistically significant different; ASA physical status, \( P = 0.001; \) surgical procedures, \( P = 0.03.\)

DISCUSSION

Compared with our previous study, the main findings in this study were as follows: the current perioperative mortality rates (16.0 per 10,000 anesthetics) were lower than those from the 1996 to 2005 period (21.97 per 10,000 anesthetics; 95% CI: 18.3–26.3); the current anesthesia-related (zero per 10,000 anesthetics; 95% CI: 0.0–0.0) and surgery-related (2.2 per 10,000 anesthetics; 95% CI: 0.5–2.4) mortality rates were lower than those previously reported (ie, 1.12 per 10,000 anesthetics; 95% CI: 1.0–3.4) mortality rates were lower than those previously reported (ie, 1.12 per 10,000 anesthetics; 95% CI: 1.0–3.4) mortality rates were lower than those previously reported (ie, 1.12 per 10,000 anesthetics; 95% CI: 1.0–3.4). The current anesthesia-related mortality rates were lower than those previously reported (ie, 1.12 per 10,000 anesthetics; 95% CI: 1.0–3.4). The current anesthesia-related mortality rates were lower than those previously reported (ie, 1.12 per 10,000 anesthetics; 95% CI: 1.0–3.4). Other methods and patients populations among these studies. Some perioperative and anesthesia-related mortality studies excluded patients with ASA V physical status, as well as cardiac11,12,14 and transplant surgeries.12 The inclusion of all types of surgeries and patients with poorer ASA physical status certainly influenced our mortality rates. Preexisting morbidities, such as traumatic injury and sepsis, which have high incidences and mortality rates in Brazil, also influenced our perioperative mortality rates.
In studies that included children, the perioperative mortality rates are higher in cardiac surgery compared with noncardiac surgery.\cite{7,18} Cardiac surgery had a perioperative mortality risk factor that was 42-fold higher than noncardiac surgeries in patients younger than 18 years old.\cite{17} The current study revealed that cardiac surgery exhibited a greater risk of perioperative mortality compared with noncardiac surgery (11.8-fold), as well as cardiac or vascular surgeries compared with noncardiac and vascular surgery (14.2-fold) and multiple surgeries compared with no multiple surgeries (32-fold).

In our study, many surgical patients arrived at the OR without optimization of their disease management. For some of these patients, intraoperative mortality might have been prevented by adequate primary care and preoperative assessments. These findings demonstrate a persistent need to improve the quantity and quality of resource utilization and healthcare access, which are still inadequate in Brazil\cite{19} and other low and middle human development countries.\cite{20} In addition, to initiate multidisciplinary discussions of adverse effects and to optimize a patient before surgical emergencies, especially in cases of a ruptured aortic aneurysm or severe trauma.\cite{15}

A meta-analysis\cite{24} revealed that the baseline risk status of perioperative and anesthesia-related mortality have declined significantly over the past 50 years being the greatest and most consistent decline in developed countries compared with developing countries. According to the authors, these results suggest continuous safety improvements for surgical patients, specially in developed countries.

Patient disease/condition remained the major triggering factor for perioperative mortality, followed by surgery. The mortality risk conferred by surgery in the current study was 2.7-fold lower compared with the previous study.\cite{3} Advances in medical practices favor best outcomes but may result in a greater number of procedures in patients with more comorbidities, as well as older and high risk patients. Patients with highly complex diseases who were once considered unfit for anesthesia are increasingly undergoing surgery.\cite{18}

Despite methodology differences, most studies published in the last decade\cite{3,5,10,25,27} and from 2010 to present\cite{11,28} have reported anesthesia-related mortality rates in surgical patients of <1.0 per 10,000 anesthetics (from 0.0 to 0.95 per

### TABLE 4. Multivariate Analysis of Predictors of Perioperative Mortality in Surgical Patients

| Factors                        | Odds Ratio | 95% CI     | Estimated Coefficient | P Value |
|--------------------------------|------------|------------|-----------------------|---------|
| Age group                      |            |            |                       |         |
| <1 yr                          | 11.6       | 3.5–38.4   | 0.611                 | <0.0001 |
| 1 to ≤17 yr                    | 1.0 (Reference) |          |                       |         |
| ≥65 yr                         | 8.8        | 3.0–25.2   | 0.535                 | <0.0001 |
| ASA physical status            |            |            |                       |         |
| I–II                           | 1.0 (Reference) |          |                       |         |
| III–V                          | 107.0      | 31.8–360.2 | 4.673                 | <0.0001 |
| Surgical procedures            |            |            |                       |         |
| Nonemergency                   | 1.0 (Reference) |          |                       |         |
| Emergency                      | 8.7        | 5.3–14.2   | 2.161                 | <0.0001 |
| Surgery type                   |            |            |                       |         |
| Noncardiac surgery             | 1.0 (Reference) |          |                       |         |
| Cardiac surgery                | 11.8       | 7.0–20.0   | 2.71                  | <0.0001 |
| Noncardiac and nonvascular     | 1.0 (Reference) |          |                       |         |
| surgeries                      | 14.2       | 9.1–22.1   | 2.653                 | <0.0001 |
| Cardiac or vascular surgeries  | 1.0 (Reference) |          |                       |         |
| Not multiple surgeries         | 32.0       | 14.3–71.8  | 3.468                 | <0.0001 |
| Multiple surgeries             |            |            |                       |         |

ASA = American Society of Anesthesiologists, CI = confidence interval, yr = years.

### TABLE 5. Triggering Factors Contributing to Mortality in 55,002 Anesthetics

| Triggering Factors | Deaths | Rate Per 10,000 Anesthetics | 95% CI |
|--------------------|--------|-----------------------------|--------|
| Patient disease/condition | 76    | 13.8<sup>a</sup> | 10.7–16.9 |
| Surgery            | 12    | 2.2<sup>b</sup> | 1.0–3.4 |
| Anesthesia         | 0     | 0.0<sup>c</sup> | 0.0–0.0 |

CI = confidence interval.

<sup>a</sup> Incidence followed by different superscript letters are statistically significant different; triggering factors, P = 0.02.
10,000 anesthetics), which represents a 2- or 3-fold improvement compared with studies performed in the 1980s.29,30 Our study confirmed this trend (ie, zero anesthesia-related deaths per 10,000 anesthetics). Two recent studies from our institution highlighted the lack of anesthesia-related mortality in children31 and older patients between 2006 and 2010.32 In the literature, only 2 studies have reported no anesthesia-related deaths.1,33 Both studies excluded cardiac surgeries11,33 and one of the studies excluded patients younger than 20 years old.11 Thus, our study is the first to report no anesthesia-related deaths without excluding any patients.

The influence of age on perioperative mortality rates has been demonstrated by some studies, which have cited the subpopulations of neonates, infants, and older patients as those at higher risk.1,3,11,34 Immaturity and congenital diseases in neonates and infants and chronic disease (eg, cancer, cardiovascular disease) contribute decisively to the high-risk status of these populations.18,31,32,35 Thus, in our study, a ruptured aneurysm was the first important cause of perioperative mortality in older patients, whereas complications associated with cardiac surgery were an important cause of mortality in children and older patients.

Despite the healthy trend of higher life expectancy of the women36 and some reports of male predisposing to cardiac arrest and death in perioperative period,4,28 our findings corroborated with other studies6,11,12 demonstrated no evidence of sex predisposing perioperative death.

The higher frequency of perioperative mortality in patients receiving general anesthesia does not necessarily imply that general anesthesia is less safe. Instead, this correlation may reflect the fact that many high-risk surgeries (eg, cardiac, thoracic, gastroenterological, and neurological) were performed under general anesthesia. Another possible confounding factor in this case is that the anesthesiologist often prefers to give general anesthesia to the most fragile patients, independent of the type of surgery.

There may have been some methodological weaknesses in the present study. First, the data are derived from adverse event reports. Underreporting is likely in this situation, although in each case, it was mandatory to complete the form. To minimize the risk of underreporting a death, the information was crosschecked with the operating theatre records and hospital administration records. Second, this study is representative of the experience of a single hospital. Certain practices specific to our institution may have influenced our results. However, our institution is a public tertiary hospital similar to many other public hospitals from our country. Thus, the findings may represent the entire spectrum of the general surgical Brazilian population.

Global measurements of patient safety, including the main outcomes of anesthesia, such as cardiac arrest37 and mortality24 should be provided more consistently in all countries, but especially in those with low, medium, and high human development countries due to the lack of available data in the literature.

In conclusion, this observational study demonstrates that despite the improvements achieved in patient anesthesia safety (ie, no anesthesia-related death and an important reduction in the surgery-related deaths rate), the perioperative mortality rate of 16.0 per 10,000 anesthetics (while lower compared with a previous study) is higher than the rates in developed countries. Significant predictors of perioperative mortality included ASA, age (with neonates, infants, and older patients at a greater mortality risk), and emergency, cardiac or vascular surgeries, and multiple surgeries. The high perioperative mortality rate in surgical patients due to poor physical status suggests that primary prevention may be important in reducing perioperative mortality. These findings demonstrate the need to improve medical perioperative practices for high-risk patients in under-resourced settings.

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TABLE 6. Causes of Perioperative Mortality Related to Patient Disease/Condition or Surgery Factors in 55,002 Anesthetized Patients

| Causes | Mortality |
|--------|-----------|
|        | N  | %  | 95% CI          |
| Ruptured aneurysm: abdominal, thoracic, or cerebral | 23 | 26.1 | 16.9–35.3 |
| Sepsis and multiple organ failure | 15 | 17.1 | 9.2–25.0 |
| Trauma: motor vehicle accident, gunshot wound, or stab wound | 15 | 17.1 | 9.2–25.0 |
| Unable to wean from cardiopulmonary bypass | 11 | 12.5 | 5.6–19.4 |
| Exsanguinating hemorrhage at surgery associated with primary disease | 9 | 10.2 | 3.9–16.5 |
| Complications associated with congenital heart defect | 3 | 3.4 | 0.0–7.2 |
| Technical surgical complications | 3 | 3.4 | 0.0–7.2 |
| Myocardial infarction | 3 | 3.4 | 0.0–7.2 |
| Complications associated with cardiac surgery | 2 | 2.3 | 0.0–5.4 |
| Complication associated with radical cancer surgery | 2 | 2.3 | 0.0–5.4 |
| Pulmonary embolism | 1 | 1.1 | 0.0–3.3 |
| Amniotic fluid embolism | 1 | 1.1 | 0.0–3.3 |

CI = confidence interval.
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