Perianesthetic death: a 10-year retrospective observational study in a Japanese university hospital

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Abstract

Background: Studies reporting on perianesthetic death and anesthesia-related death are limited. The present study aimed to assess the incidence of perianesthetic death and its relation to anesthesia and to describe the patient characteristics and main events leading to death in cases of anesthesia-related death and anesthesia-contributory death.

Methods: We conducted a retrospective chart review of patients in whom anesthesia procedures were performed by anesthesiologists at a Japanese tertiary hospital between January 2008 and December 2017. Perianesthetic death was defined as death occurring within 48 h of an anesthetic, and it was divided into the following three categories: anesthesia-related death, anesthesia-contributory death, and nonanesthesia-related death. Patient demographics and perioperative factors were analyzed in cases of anesthesia-related death and anesthesia-contributory death.

Results: Among 46,378 patients who underwent anesthetics, 41 experienced perianesthetic death, with an incidence of 8.8/10,000 anesthetics (95% confidence interval [CI], 6.1–11.6). No patient experienced anesthesia-related death, whereas 10 experienced anesthesia-contributory death, with an incidence of 2.1/10,000 (95% CI, 0.69–3.6), and 31 experienced nonanesthesia-related death, with an incidence of 6.8/10,000 (95% CI, 4.2–9.1). The events leading to anesthesia-contributory death were hypovolemia, myocardial infarction, arrhythmia, and respiratory failure, and they occurred during anesthesia maintenance in 5 patients and after surgery in 5 patients.

Conclusions: The incidence of perianesthetic death was 8.8/10,000 anesthetics; however, anesthesia-related death was not detected. Ten patients experienced anesthesia-contributory death, and hypovolemia during or after surgery was most frequently associated with anesthesia-contributory death.

Keywords: Anesthesia, Mortality, Perioperative period

Introduction

Postoperative death, which is defined as death within 30 days of surgery, accounts for 7.7% of all deaths globally, and surgery is the third most common contributor to death [1]. In particular, death within 48 h of an anesthetic is defined as perianesthetic death, and it is a serious issue among anesthesiologists [2, 3].

Studies focusing on perioperative cardiac arrest have been published; however, studies focusing on perianesthetic death and anesthesia-related death are limited [3–9]. Two analyses of anesthesia-related death based on closed claims analysis and death certificates have been reported, but both analyses failed to provide denominators, making interpretation of the percentage of perianesthetic death difficult [8, 9]. One retrospective analysis of the quality assurance database of a community-based anesthesiology group practice revealed that the perianesthetic death rate and anesthesia-related death rate were 7.53/10,000 cases and 0.05/10,000 cases, respectively [3]. However, these rates vary depending on the institution and the study population, and limited information is available on the incidence of perianesthetic death and its relation to anesthesia in Japan.

Therefore, in the present study, we aimed to assess the incidence of perianesthetic death and its relation to
anesthesia at a Japanese tertiary hospital and to describe
the patient characteristics and main events leading to
death in cases of anesthesia-related death and
anesthesia-contributory death.

**Methods**

**Ethical approval**

This retrospective observational study was approved by
the Institutional Review Board of Nara Medical University (Kashiha, Nara, Japan; Chairperson Prof. M. Yoshi-
zumi; approval no. 2964; December 17, 2018). The
requirement of informed consent was waived because of
the retrospective nature of this study.

**Patient selection**

We included patients who underwent anesthetics per-
formed under general and local anesthesia managed by an-
esthesiologists at Nara Medical University between January
2008 and December 2017. We excluded patients who
underwent anesthesia procedures performed in the emer-
gency room or general ward without anesthesiologists.

Nara Medical University Hospital is a 992-bed tertiary
care referral center with 15 operation rooms, including 1
hybrid operation room. Anesthesia information was ob-
tained from our database, which had data provided by
each anesthesiologist. We reviewed both electronic med-
ical records and diagnosis procedure combination sys-
tems and extracted all patients who died by the first
discharge after surgery. Among these patients, we identi-
fied those who died within 48 h of anesthetics.

**Definition of perianesthetic death**

Perianesthetic death was defined as death within 48 h of
an anesthetic [2]. Perianesthetic death was divided into
the following three categories: anesthesia-related death
(death solely attributable to either the anesthesia
provider or the anesthetic technique), anesthesia-
contributory death (death in which the anesthesia role
could not be entirely excluded), and nonanesthesia-
related death [3]. In cases of anesthesia-related death
and anesthesia-contributory death, we identified the
pathophysiological processes that best described the se-
quence of events [8]. The classifications of death and
pathophysiological processes were performed independ-
ently by two researchers (MI and YN), and any disagree-
ment was resolved by discussion with another researcher
(MK).

**Explanatory variables**

Data on patient characteristics, including sex, age,
American Society of Anesthesiologists-Physical Status
(ASA-PS), surgery circumstance (elective or emergency),
surgery type, and anesthesia type, were collected. The
surgery type was categorized according to the classifica-
tion provided by the Japanese Society of Anesthesiolo-
gists. Burn surgery appears to be a high-risk procedure,
but it is difficult to classify with the existing classifica-
tion. Therefore, we added “burn surgery” to the existing
classification. The anesthesia type was categorized as fol-
loows: general anesthesia with inhalation anesthesia, gen-
eral anesthesia with total intravenous anesthesia, spinal
anesthesia, epidural anesthesia, combined spinal and ep-
dural anesthesia, and peripheral nerve block.

**Statistical analysis**

The details of patients who experienced anesthesia-
related death and anesthesia-contributory death are
summarized. The incidence rate is expressed as oc-
currence in 10,000 anesthetics. The Wilson method
was used to calculate 95% confidence interval (CI). In
patients who experienced perianesthetic death, ex-
planatory variables were analyzed using the Mann-
Whitney U test or Fisher's exact test. Patient age was
categorized as follows: < 1 year, 1 to < 3 years, 3 to < 6 years, 6 to < 20 years, 20 to < 65 years, 65 to < 75 years, and ≥ 75 years. All analyses were performed
using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). The level of statistical significance was set at a
*p value < 0.05.

Results
During the 10-year study period, 46,378 anesthetics were
performed in our hospital. Of 406 patients who died by the
first discharge after surgery, 41 experienced perianesthetic
death, with an incidence of 8.8/10,000 anesthetics (95% CI,
6.1–11.6) (Fig. 1, Table 1). As shown in Table 1, the rate of
perianesthetic death was high in the elderly, patients

| Table 1 Patients’ background of the patients’ experienced perianesthetic death or not |
|---------------------------------|---------------------------------|
| Age (years) | Perianesthetic death (−) (n = 46,337) | Perianesthetic death (+) (n = 41) |
| < 1 | 59.00 [36.00, 71.00] | 73.00 [59.00, 81.00] |
| 1 ≤ < 3 | 863 (1.9) | 2 (4.9) |
| 3 ≤ < 6 | 923 (2.0) | 0 (0.0) |
| 6 ≤ < 20 | 905 (2.0) | 0 (0.0) |
| 20 ≤ < 65 | 2822 (6.1) | 2 (4.9) |
| 65 ≤ < 75 | 22,403 (48.3) | 9 (22.0) |
| ≥ 75 | 7644 (16.5) | 17 (41.5) |
| Male | 21,597 (46.6) | 29 (70.7) |
| ASA-PS | | |
| I | 14,514 (31.3) | 0 (0.0) |
| II | 26,880 (58.0) | 0 (0.0) |
| III | 4628 (10.0) | 5 (12.2) |
| IV | 298 (0.6) | 12 (29.3) |
| V | 17 (0.0) | 24 (58.5) |
| Emergency surgery | 7475 (16.1) | 37 (90.2) |
| Type of surgery | | |
| Neuro | 4162 (9.0) | 10 (24.4) |
| Thoracic | 2247 (4.8) | 2 (4.9) |
| Cardiac | 1986 (4.3) | 12 (29.3) |
| Esophageal | 211 (0.5) | 1 (2.4) |
| Upper abdominal | 4216 (9.1) | 1 (2.4) |
| Lower abdominal | 9912 (21.4) | 11 (26.8) |
| Cesarean section | 3187 (6.9) | 1 (2.4) |
| Head, neck, pharyngeal, and laryngeal | 7137 (15.4) | 0 (0.0) |
| Chest wall abdominal wall and perineum | 2344 (5.1) | 0 (0.0) |
| Spine | 2113 (4.6) | 0 (0.0) |
| Hip joint and limbs | 6120 (13.2) | 1 (2.4) |
| Examination | 671 (1.4) | 0 (0.0) |
| Electroconvulsive therapy | 973 (2.1) | 0 (0.0) |
| Others | 724 (1.6) | 0 (0.0) |
| Burn | 361 (0.7) | 0 (0.0) |
| Cancel after anesthesia induction | 18 (0.0) | 2 (4.9) |
| Type of anesthesia | | |
| General anesthesia with inhalation anesthetics | 31,894 (68.8) | 41 (100) |
| General anesthesia with TIVA | 9720 (21.0) | 0 (0.0) |
| Spinal anesthesia | 4122 (8.9) | 0 (0.0) |
| Epidural anesthesia | 420 (0.9) | 0 (0.0) |
| Combined of spinal and epidural anesthesia | 142 (0.3) | 0 (0.0) |
| Peripheral nerve block | 39 (0.1) | 0 (0.0) |

ASA-PS American Society of Anesthesiologists-Physical Status, TIVA total intravenous anesthesia
Table 2 Backgrounds of patients who experienced nonanesthesia-related death and those who experienced anesthesia-contributory death

| Age (years)      | Nonanesthesia-related death (n = 31) | Anesthesia-contributory death (n = 10) | p value |
|------------------|--------------------------------------|---------------------------------------|---------|
| < 1              | 2 (6.5)                              | 0 (0.0)                               | 0.84    |
| 1 ≤ , < 3        | 0 (0.0)                              | 0 (0.0)                               |         |
| 3 ≤ , < 6        | 0 (0.0)                              | 0 (0.0)                               |         |
| 6 ≤ , < 20       | 1 (3.2)                              | 1 (10.0)                              |         |
| 20 ≤ , < 65      | 7 (22.6)                             | 2 (20.0)                              |         |
| 65 ≤ , < 75      | 9 (29.0)                             | 2 (20.0)                              |         |
| 75 ≤             | 12 (38.7)                            | 5 (50.0)                              |         |
| Male             | 22 (71.0)                            | 7 (70.0)                              | 1       |
| ASA-PS           |                                      |                                       |         |
| I                | 0 (0.0)                              | 0 (0.0)                               |         |
| II               | 0 (0.0)                              | 0 (0.0)                               |         |
| III              | 2 (6.5)                              | 3 (30.0)                              |         |
| IV               | 10 (32.3)                            | 2 (20.0)                              |         |
| V                | 19 (61.3)                            | 5 (50.0)                              |         |
| Emergency surgery| 30 (96.8)                            | 7 (70.0)                              | 0.04    |
| Type of surgery  |                                      |                                       | 0.57    |
| Neuro            | 10 (32.3)                            | 0 (0.0)                               |         |
| Thoracic         | 2 (6.5)                              | 0 (0.0)                               |         |
| Cardiac          | 7 (22.6)                             | 5 (50.0)                              |         |
| Esophageal       | 0 (0.0)                              | 1 (10.0)                              |         |
| Upper abdominal   | 0 (0.0)                              | 1 (10.0)                              |         |
| Lower abdominal   | 8 (25.8)                             | 3 (30.0)                              |         |
| Cesarean section | 1 (3.2)                              | 0 (0.0)                               |         |
| Head, neck, pharyngeal, and laryngeal | 0 (0.0) | 0 (0.0) | |
| Chest wall abdominal wall and perineum | 0 (0.0) | 0 (0.0) | |
| Spine            | 0 (0.0)                              | 0 (0.0)                               |         |
| Hip joint and limbs | 1 (3.4) | 0 (0.0) | |
| Examination      | 0 (0.0)                              | 0 (0.0)                               |         |
| Electroconvulsive therapy | 0 (0.0) | 0 (0.0) | |
| Others           | 0 (0.0)                              | 0 (0.0)                               |         |
| Burn             | 0 (0.0)                              | 0 (0.0)                               |         |
| Cancel after anesthesia induction | 2 (6.5) | 0 (0.0) | |
| Type of anesthesia|                                    |                                       |         |
| General anesthesia with inhalation anesthetics | 31 (100) | 10 (100) | |
| General anesthesia with TIVA | 0 (0.0) | 0 (0.0) | |
| Spinal anesthesia | 0 (0.0) | 0 (0.0) | |
| Epidural anesthesia | 0 (0.0) | 0 (0.0) | |
| Combination of spinal and epidural anesthesia | 0 (0.0) | 0 (0.0) | |
| Peripheral nerve block | 0 (0.0) | 0 (0.0) | |
| General anesthesia | 31 (100) | 10 (100) | |
| Pathophysiological process of death|                |                                       | 0.26    |
| Respiratory      | 1 (3.2)                              | 1 (10.0)                              |         |
| Arrhythmia       | 2 (6.5)                              | 1 (10.0)                              |         |
| Myocardial infarction | 4 (12.9) | 2 (20.0) | |
| Hypovolemia      | 13 (41.9)                            | 6 (60.0)                              |         |
| Central neurologic disorders | 11 (35.5) | 0 (0.0) | |

ASA-PS American Society of Anesthesiologists-Physical Status, TIVA total intravenous anesthesia
undergoing emergency surgery, and patients with a high ASA-PS. There was no anesthesia-related death. On the other hand, there were 10 anesthesia-contributory deaths, with an incidence of 2.1/10,000 anesthetics (95% CI, 0.69–3.6), and 31 nonanesthesia-related deaths, with an incidence of 6.8/10,000 anesthetics (95% CI, 4.2–9.1) (Table 2). Among the 41 patients, nonanesthesia-related death was more common in those undergoing emergency surgery ($\rho = 0.04$). Table 3 presents the details, including the pathophysiological mechanisms associated with the 10 anesthesia-contributory deaths. Overall, the events associated with anesthesia-contributory death were hypovolemia, myocardial infarction, arrhythmia, and respiratory failure. These events occurred during anesthesia maintenance in five and after surgery in 5 patients.

**Discussion**

In the present study, the overall incidence of perianesthetic death was 8.8/10,000 anesthetics (95% CI, 6.1–11.6), whereas anesthesia-related death was not detected. Additionally, the incidence of anesthesia-contributory death was 2.1/10,000 anesthetics (95% CI, 0.69–3.6), and it was associated with hypovolemia, cardiac infarction, arrhythmia, and respiratory failure and was more common in elective surgery.

Previous studies have reported perianesthetic mortality using different definitions. Kawashima et al. used the definition of mortality occurring in the operating room and within seven postoperative days with accompanying critical events during surgery, whereas Lagasse et al. and Pollard et al. used the definition of death occurring within 48 h of anesthesia induction [2, 3, 7]. Our study used the latter definition, and the incidence of perianesthetic death (8.8/10,000) was similar to that reported in a recent study (7.5/10,000) [3]. Furthermore, as expected, age, emergency surgery, and high ASA-PS were associated with perianesthetic death, and these findings are consistent with the findings of previous studies [3, 8, 10, 11].

Fortunately, there was no anesthesia-related death during the 10-year study period. This might be because our sample size was limited and there were no perianesthetic deaths associated with failed ventilation, aspiration of gastric contents, and accidental bolus of narcotics, which can lead to anesthesia-related death and anesthesia-related cardiac arrest [3–6].

In the present study, 10 patients experienced anesthesia-contributory death, with an incidence of 2.1/10,000 anesthetics, and this incidence is higher than that reported in a study from the USA (0.22/10,000) [3]. This difference might be associated with differences in the study populations, including a smaller denominator, and the definitions of anesthesia-related death and anesthesia-contributory death. In addition, there was no anesthesia-related death in the present study, resulting in an increase in the incidence of anesthesia-contributory death. Furthermore, the rate of emergency surgery was higher among patients who experienced nonanesthesia-related death than among those who experienced anesthesia-contributory death. This might be because patient status, such as preoperative

**Table 3** The pathophysiological mechanisms and details of patients who experienced anesthesia-contributory death

| Number | Age (year) | ASA-PS | Emergency | Sex | Period of the event leading to death | Pathophysiological process | Detailed description | Location of the event leading to death |
|--------|------------|--------|-----------|-----|-----------------------------------|---------------------------|----------------------|--------------------------------------|
| 1      | 78         | V      | Yes       | Male | Maintenance                        | Hypovolemia (hemorrhage)  | Ruptured abdominal aortic aneurysm; intraoperative massive hemorrhage and bradycardia | Operating room                 |
| 2      | 92         | IV     | No        | Female | Postoperative period               | Hypovolemia (true hypovolemia) | Bowel obstruction due to transverse colon cancer; atrial fibrillation with tachycardia and a large amount of intestinal solution | General ward                  |
| 3      | 75         | III    | No        | Male | Postoperative period               | Hypovolemia (true hypovolemia) | Hemodialysis; postoperative hyperkalemia; hemodialysis difficulty due to hypovolemia | General ward |
| 4      | 83         | V      | Yes       | Female | Postoperative period               | Hypovolemia (hemorrhage)    | Ruptured abdominal aortic aneurysm; hypotension shortly after anesthesia induction; massive hemorrhage | Intensive care unit |
| 5      | 48         | V      | Yes       | Male | Postoperative period               | Hypovolemia (sepsis)        | Multiple organ failure and hypotension after replacement of the ascending aorta | Intensive care unit |
| 6      | 70         | V      | Yes       | Male | Maintenance                        | Hypovolemia (hemorrhage)    | Ruptured abdominal aortic aneurysm; intraoperative massive hemorrhage | Operating room |
| 7      | 59         | III    | No        | Male | Maintenance                        | Myocardial infarction       | History of angina pectoris; intraoperative ventricular fibrillation following ST-elevation; possibility of cardiac ischemia | Operating room |
| 8      | 74         | V      | Yes       | Female | Maintenance                        | Myocardial infarction       | Aortic dissection with mitral valve regurgitation; low output syndrome; myocardial infarction on cardiology | Intensive care unit |
| 9      | 12         | III    | Yes       | Male | Maintenance                        | Arrhythmia                  | Perforation of a stress ulcer; burn; ventricular fibrillation caused by hyperkalemia after transfusion | Intensive care unit |
| 10     | 88         | IV     | Yes       | Male | Postoperative period               | Respiratory failure         | Bladder hemorrhage and anemia with multiple comorbidities; hypoxia after surgery | Operating room |

ASA-PS American Society of Anesthesiologists-Physical Status
comorbidity, has greater effects on death when compared with anesthesia.

Among the 10 patients who experienced anesthesia-contributory death, 4 pathophysiological processes were identified. Hypovolemia is one of the most common complications during anesthesia, and almost all cases are managed well. Hypovolemia caused by rapid massive hemorrhage and large leakage into the tissues can lead to serious consequences, although this is rare. Perioperative acute myocardial infarction rarely occurs in patients undergoing noncardiac surgery, but it has been shown to be strongly associated with in-hospital mortality [12]. One patient was suspected of ST-elevation myocardial infarction (case 7 in Table 3), and this patient had a history of angina pectoris. Another patient presented with acute myocardial infarction postoperatively (case 8 in Table 3), and this patient underwent aortic surgery owing to aortic dissection. Acute myocardial infarction might be caused by aortic dissection; however, this case was included in the anesthesia-contributory death group because we were unable to exclude inadequate oxygen delivery following perioperative low output syndrome. Arrhythmia caused by hyperkalemia after transfusion might be preventable with frequent blood analysis. The etiology of postoperative respiratory failure is unknown. However, it might be caused by preoperative multiple comorbidities, including anemia, heart failure, and kidney injury.

The limitations of this study include its representation of perianesthetic death from a single institution. Our institution is a 992-bed tertiary hospital and includes a trauma center, but there are no organ transplantation surgeries, except for kidney transplantsations. The rate of perianesthetic death can vary depending on the institution and study population. Additionally, the data were evaluated retrospectively, and thus, we experienced missing data and analyzed limited data. Moreover, death and pathophysiological processes were classified independently by two researchers, and they consulted with another researcher at the time of disagreement. The decisions might be different for other anesthesiologists.

Conclusion
The incidence of perianesthetic death in this study performed at a Japanese tertiary hospital over a period of 10 years was 8.8/10,000 anesthetics. Additionally, no patient experienced anesthesia-related death, 10 experienced anesthesia-contributory death, and 31 experienced nonanesthesia-related death. The most common event leading to anesthesia-contributory death was hypovolemia, followed by myocardial infarction, arrhythmia, and respiratory failure. In the future, a further study using a large database with exact information is required to analyze the epidemiology of perianesthetic death and reduce its rate.

Abbreviations
ASA-PS: American Society of Anesthesiologists-Physical Status; CI: Confidence interval

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None

Authors’ contributions
MS and YN collected the patients’ data. MI conducted the statistical analyses, drafted the manuscript, and obtained the approval from the Institutional Review Board. YN and MK revised and edited the manuscript. All authors contributed to and approved the final version of the manuscript.

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Availability of data and materials
They are available as a spreadsheet file upon reasonable request.

Ethics approval and consent to participate
This retrospective observational study was approved by the Institutional Review Board of Nara Medical University (Kashihara, Nara, Japan; Chairperson Prof. M. Yoshizumi; approval no. 2964; December 17, 2018). The requirement of informed consent was waived because of the retrospective nature of this study.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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