



# Risk factors of cardiac arrest and failure to achieve return of spontaneous circulation during anesthesia: a 20-year retrospective observational study from a tertiary care university hospital

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## Abstract

**Purpose** There is still a lack of robust data on the epidemiology of cardiac arrest during anesthesia. We investigated the frequency and risk factors of cardiac arrest during anesthesia over the past two decades at a tertiary care university hospital in Japan.

**Methods** We retrospectively analyzed 111,851 anesthesia records of patients who underwent surgery under anesthesia between 2000 and 2019. Cardiac arrest cases were classified according to the patient's background, surgical status, main cause and initial rhythm of cardiac arrest, and the presence of the return of spontaneous circulation (ROSC). Univariate and multivariate logistic regression analyses were used to identify the risk factors of cardiac arrest and failure to achieve ROSC.

**Results** Ninety cardiac arrest cases during anesthesia were identified. The incidence of cardiac arrest was 8.05 per 10,000 anesthetics (95% CI, 6.54–9.90). There were 6 anesthesia-related cardiac arrests and 9 anesthesia-contributory cardiac arrests. The most common cause of cardiac arrest was blood loss. American Society of Anesthesiologists physical status 4–5, emergency surgery, and cardiovascular surgery were identified as independent risk factors of cardiac arrest. American Society of Anesthesiologists physical status 4–5, blood loss-induced cardiac arrest, and non-shockable rhythm were independently associated with failure to achieve ROSC.

**Conclusion** Blood loss was the most common cause of cardiac arrest and blood loss-induced cardiac arrest was independently associated with failure to achieve ROSC. Further improvements in treatment strategies for bleeding may reduce the future incidence of cardiac arrest and death during anesthesia.

**Keywords** Cardiac arrest · Anesthesia · Return of spontaneous circulation · Blood loss

## Introduction

Perioperative cardiac arrest is rare but is one of the most serious events in the management of anesthesia, and failure to resuscitate directly leads to perioperative death. The causes of cardiac arrest in the perioperative period are considered to be different from those in the non-perioperative period outside the hospital or elsewhere in the hospital [1]. In 2013, a study using a large database in the United States showed that patients with perioperative cardiac arrest had a

significantly higher survival rate than those with in-hospital non-perioperative cardiac arrest [2, 3]. In the past few decades, there have been many reports from around the world on the frequency and background of perioperative cardiac arrest and mortality. A meta-analysis for which results were published in 2012 showed that the frequency of perioperative cardiac arrest has been decreasing and that the incidence of cardiac arrest was 6.6 per 10,000 anesthetics in the 1990s–2000s in developed countries [4]. It was also reported that the incidence of anesthesia-related cardiac arrests in recent years in the United States and Germany were 0.52–0.74 per 10,000 anesthetics [5, 6]. Although, the causes and frequency of perioperative cardiac arrest might have varied depending on the time period, country, level of care and definition of the perioperative period (intra-anesthesia, postanesthesia care unit, 24 h postoperatively) [5–12]. To predict and prevent perioperative cardiac arrest

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and death, it is important to analyze not only overall information from large databases and meta-analyses but also detailed information from a single center. In Japan, Morimatsu et al. recently reported the frequency of perioperative accidents including cardiac arrest using the database of the Japanese Society of Anesthesiologists. However, the detailed background of cardiac arrest was not clarified [7]. In addition, there have been only a few studies in the world in which multivariate analyses of the risk factors of cardiac arrest and failure to achieve return of spontaneous circulation (ROSC) during anesthesia were performed.

The purpose of this study was to investigate cardiac arrest cases during anesthesia over a period of 20 years from 2000 to 2019 at a tertiary care university hospital with an advanced acute critical care and emergency center in Japan and to clarify risk factors of cardiac arrest and failure to achieve ROSC during anesthesia. Since data for a 20-year period were analyzed in detail in this study, this study has provided detailed information on cardiac arrest during anesthesia and information on changes in cardiac arrest rates over time.

## Materials and methods

This article adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. We retrospectively analyzed data from 111,851 anesthesia records of patients who underwent surgery under anesthesia from January 1, 2000 to December 31, 2019 at Sapporo Medical University Hospital (Japan). This retrospective observational study was approved by the Institutional Review Board of Sapporo Medical University (Sapporo, Japan; Chairperson Prof. K. Tsuchihashi; approval number 322–238; January 21, 2021). The requirement of informed consent was waived due to the retrospective and anonymous nature of this study.

Sapporo Medical University Hospital is a 938-bed tertiary care university hospital with an advanced critical care and emergency center and 16 operating rooms, in which approximately 6000 surgical cases per year are managed by anesthesiologists.

Information on surgical cases including anesthetic management is recorded in anesthesia records, which were stored in written form from January 2000 to March 2006 and in electronic form from April 2006 to March 2019. In this study, we retrospectively examined the anesthesia records and medical records and identified all cases of cardiac arrest during anesthesia.

## Data collection

Cardiac arrest cases during anesthesia were classified according to the patient's background (sex, age, American

Society of Anesthesiologists physical status (ASA-PS)), surgical status (department, anesthetic method, emergency or scheduled, on-time or off-time), main causes (blood loss, cardiac complications, hypoxia, dysfunction of the central nervous system, drug-induced, septic shock, hyperkalemia, vagal reflex, others), initial rhythm of cardiac arrest (pulseless ventricular tachycardia, ventricular fibrillation, pulseless electrical activity, or asystole), and presence of ROSC in the operating room. Moreover, to determine the risk factors of cardiac arrest, a non-cardiac arrest group was established by modifying to the "proximal convenience method" [6, 8]. Each case of cardiac arrest was matched to two other cases receiving anesthesia in a similar operating room. Although previous studies selected the cases "on the same day", we randomly selected cases from among three days; the day of cardiac arrest, the day before and the day after, to eliminate weekday and holiday bias. The ASA PS was based on the assessment of the anesthesiologist in charge at the time; we modified it according to the "ASA Physical Status Classification System" published by the ASA in 2014 and revised in 2020 [13]. Microsoft Excel (version 2019, Microsoft Corporation, Redmond, WA, USA) was used for random sampling. In the non-cardiac arrest group, we collected the same data for patient background and surgical status as in the cardiac arrest group.

## Definition and classification of cardiac arrest

We identified cases of cardiac arrest during anesthesia from 2000 to 2019. Cardiac arrest was defined as an absence of pulse requiring cardiopulmonary resuscitation with closed or open-chest cardiac compressions or defibrillation, which included pulseless ventricular tachycardia, ventricular fibrillation, pulseless electrical activity, or asystole. Patients who were already in cardiac arrest before induction of anesthesia were excluded. Two anesthesiologists (MM and NH) reviewed anesthesia records of suspected cardiac arrest to determine whether they matched the aforementioned criteria and then divided them into three categories according to their relationship to anesthesia: anesthesia-related, anesthesia-contributory, and unrelated to anesthesia. The association between cardiac arrest and anesthesia was based on the previously reported classification [5]. Anesthesia-related cardiac arrest was defined as cardiac arrest that was caused directly by anesthesia or other factors under the control of the anesthetist. Anesthesia-contributory cardiac arrest was defined as cardiac arrest caused by both surgical and anesthesiological factors or in which there was some doubt whether cardiac arrest was entirely attributable to anesthesia or other factors under the control of the anesthetist.

## Statistical analysis

A data analysis and statistical plan were written and filed with the Institutional Review Board of Sapporo Medical University before data were accessed. Between groups analysis (cardiac arrest vs. non-cardiac arrest, ROSC vs. non-ROSC) was performed by the unpaired t-test and chi-square test. Means and SDs were used for continuous variables, and numbers and percentages were used for categorical variables. Univariate and multivariate logistic regression analyses were used to identify the risk factors of cardiac arrest and failure to achieve ROSC. Results of logistic regression analysis were reported as odds ratios with 95% CI. The variables used in multivariate logistic regression analysis were based on previous studies, and those that were considered clinically important or showed significant differences in univariate analysis were also added. In the multivariable model with cardiac arrest as the dependent variable, we included age, sex, ASA-PS, and surgical status (department, anesthetic method, emergency or scheduled, time of day). The age cutoff was set at 65 years since several previous studies showed an increase in the incidence of cardiac arrest at over 65 years of age [9, 10, 14]. We also checked the logarithmic odds ratios between cardiac arrest and age categorized every 20 years to ensure that the cutoff was reasonable. In addition, we set another cutoff age of 3 years or younger to evaluate cardiac arrest in young children [5]. We also checked the logarithmic odds ratio between cardiac arrest and ASA-PS and classified the patients into ASA-PS 1–3 and ASA-PS 4–5. In the multivariate model with the presence of ROSC as the dependent variable, we included ASA-PS, emergency or scheduled surgery, main causes, and initial rhythm of cardiac arrest. To check for multicollinearity, we checked the cross-tabulation table between the independent variables. We also calculated the coefficient of association between them and confirmed that there was no relationship with phi coefficient  $\geq 0.8$ . Missing data were excluded from the analysis. The statistical analysis was performed using Statistical Package for Social Sciences (version 25; SPSS Inc., Chicago, IL, USA). P values  $< 0.05$  were considered statistically significant.

## Results

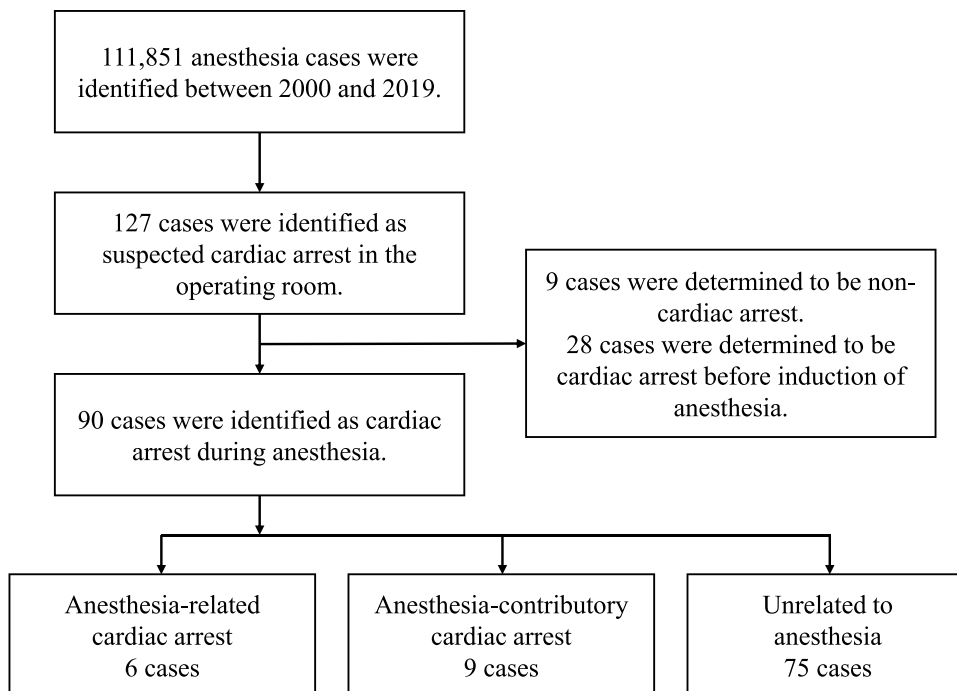
Between 2000 and 2019, 111,851 anesthetic procedures were performed at Sapporo Medical University Hospital, and 127 suspected cardiac arrests were identified during that period. Nine patients without cardiac arrest and 28 patients with cardiac arrest before induction of anesthesia were excluded, and 90 patients with cardiac arrest during anesthesia were identified. The incidence of cardiac arrest was 8.05 per 10,000 anesthetics (95% CI, 6.54–9.90). Of those cases, there were 6 anesthesia-related cardiac arrests with an incidence of 0.54 per 10,000 anesthetics (95% CI, 0.21–1.20). There

were 9 anesthesia-contributory cardiac arrests with an incidence of 0.80 per 10,000 anesthetics (95% CI, 0.40–1.56) (Fig. 1). The cardiac arrest rate per year is shown in Fig. 2. When the period was divided into decade, the incidence of cardiac arrest decreased markedly from 11.72 per 10,000 anesthetics (95% CI, 9.06–15.14) in 2000–2009 to 5.04 per 10,000 anesthetics (95% CI, 3.52–7.18) in 2010–2019. The incidences of anesthesia-related cardiac arrest were 0.60 per 10,000 anesthetics (95% CI, 0.11–1.84) in 2000–2009 and 0.49 per 10,000 anesthetics (95% CI, 0.09–1.51) in 2010–2019. The incidences of anesthesia-contributory cardiac arrest were 0.79 per 10,000 anesthetics (95% CI, 0.23–2.12) in 2000–2009 and 0.81 per 10,000 anesthetics (95% CI, 0.29–1.96) in 2010–2019. There was no significant difference between the incidence of anesthesia-related cardiac arrest or anesthesia-contributory cardiac arrest in the 2000s and the 2010s. The patient's background and surgical status during this period are shown in Online Resource 1. Patients were older ( $P < 0.001$ ) and the patient's severity assessed by ASA-PS was higher ( $P < 0.001$ ) in 2010–2019 than in 2000–2009. In contrast, the rates of emergency surgery and cardiovascular surgery were lower in 2010–2019 than in 2000–2009 ( $P < 0.001$  in both comparisons). The primary causes of cardiac arrest are shown in Fig. 3. The most common cause of cardiac arrest was blood loss ( $n = 39$ ) followed by cardiac complications ( $n = 25$ ).

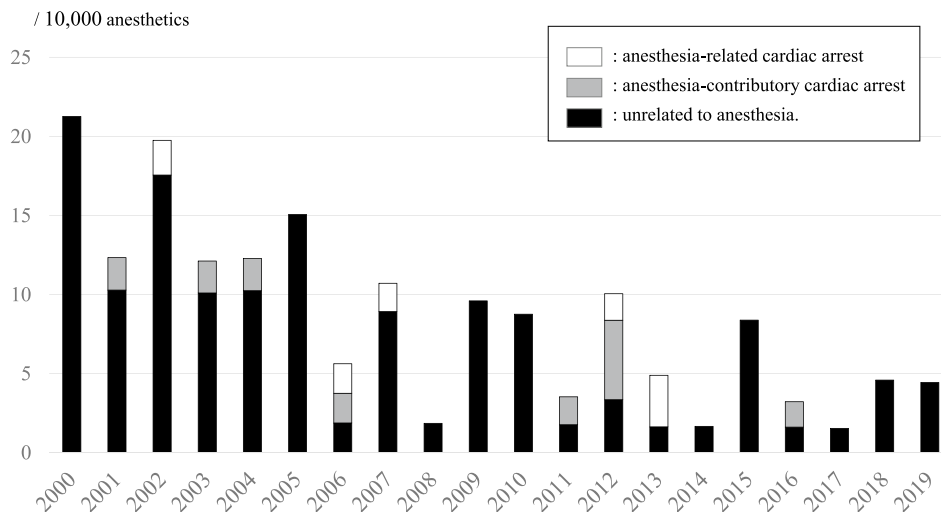
## Risk factors for cardiac arrest during anesthesia

The characteristics and risk factors of cardiac arrest during anesthesia are shown in Table 1. In addition, detailed information regarding the type of surgeries and age distribution is shown in Online Resource 2. There were 90 cardiac arrests, 2 of which were excluded from the table because of missing information on age. The mean age of patients in the cardiac arrest group was higher than that of patients in the non-cardiac arrest group ( $61.9 \pm 21.2$  vs.  $52.8 \pm 21.9$ , mean difference, 9.1, 95% CI, 3.4–14.6;  $P = 0.002$ ), and there was a particularly high proportion of patients over 65 years of age in the cardiac arrest group (48 of 88 [54.5%] vs. 64 of 176 [36.4%],  $P = 0.005$ ). The proportion of patients aged 3 years or younger was same in both groups (2 of 88 [2.3%] vs. 4 of 176 [2.3%]). The proportion of patients with ASA-PS 4–5 was only 2.8% (5 of 176) in the non-cardiac arrest group, whereas the proportion was 48.9% (43 of 88) in the cardiac arrest group ( $P < 0.001$ ). The ratios of cardiovascular surgery (45 of 88 [51.1%]), emergency surgery (57 of 88 [64.8%]), and off-time surgery (34 of 88 [40.0%]) in the cardiac arrest group were significantly higher than those in the non-cardiac arrest group (15 of 176 [8.5%], 20 of 176 [11.4%], 13 of 176 [7.2%], respectively,  $P < 0.001$  in all comparisons). Cardiovascular surgery, emergency surgery and ASA-PS 4–5 were identified as independent risk factors

**Fig. 1** Flow diagram of the review process to identify cardiac arrest during anesthesia and divide cardiac arrest cases into three categories, anesthesia-related, anesthesia-contributory and unrelated to anesthesia



**Fig. 2** Cardiac arrest rate from 2000 to 2019. White column; anesthesia-related cardiac arrest, gray column; anesthesia-contributory cardiac arrest, black column; unrelated to anesthesia



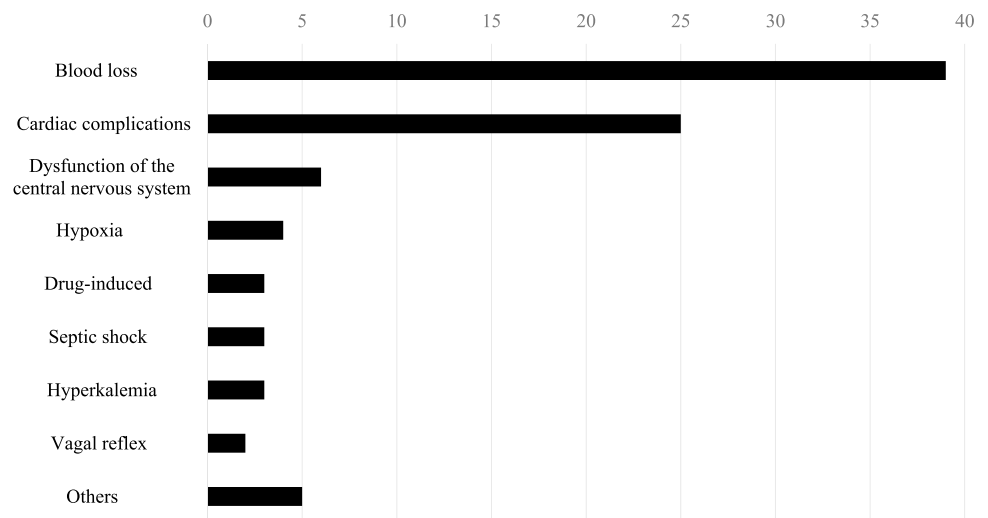
of cardiac arrest by multivariate logistic regression analysis (Table 1).

**Risk factors for failure to achieve ROSC**

The characteristics and risk factors of failure to achieve ROSC during anesthesia are shown in Table 2. There was no significant difference between the ROSC and non-ROSC groups in age or gender. The ratios of patients with ASA-PS 4–5, emergency surgery and blood loss-induced cardiac arrest in the non-ROSC group were significantly higher than those in the ROSC group (ASA-PS 4–5, 26 of 30 [86.7%] vs. 21 of 58 [36.2%],  $P < 0.001$ ; emergency surgery, 28 of 30

[93.3%] vs. 29 of 58 [50.0%],  $P < 0.001$ ; blood loss-induced cardiac arrest, 22 of 30 [73.3%] vs. 15 of 58 [25.9%],  $P < 0.001$ ). The ratio of patients with cardiac arrest unrelated to anesthesia in the cardiac arrest group was higher than that in the non-cardiac arrest group (29 of 30 [96.7%] vs. 44 of 58 [75.9%],  $P = 0.014$ ). Multivariate logistic regression analysis revealed that ASA-PS 4–5, blood loss that induced cardiac arrest, and non-shockable rhythm on the occurrence of cardiac arrest independently contributed to the failure to achieve ROSC.

**Fig. 3** Classification of the primary causes of cardiac arrest



**Table 1** Risk factors of cardiac arrest identified by univariate and multivariate analyses

	Cardiac arrest n (%) (n=88)	Non-cardiac arrest n (%) (n=176)	Odds ratio	95% CI		P value
<i>&lt; Univariate analysis &gt;</i>						
<i>Age</i>						
≤ 3 years	2 (2.3)	4 (2.3)	1.42	0.25	3.61	0.692
4–64 years	38 (43.2)	110 (58.5)				
≥ 65 years	48 (54.5)	64 (36.4)	2.13	1.26	3.61	0.005
<i>Sex</i>						
Male	57 (64.8)	93 (52.8)	1.61	0.97	2.78	0.065
Female	31 (35.2)	83 (47.2)				
<i>ASA physical status</i>						
1–3	41 (46.6)	167 (94.9)				
4–5	47 (53.4)	9 (5.1)	21.27	9.65	46.90	<0.001
<i>Emergency or scheduled</i>						
Emergency	57 (64.8)	20 (11.4)	14.34	7.57	27.17	<0.001
Scheduled	31 (35.2)	156 (88.6)				
<i>Department</i>						
Cardiovascular surgery	45 (51.1)	15 (8.5)	11.23	5.72	22.05	<0.001
Others	43 (48.9)	161 (91.5)				
<i>Anesthetic method</i>						
General anesthesia	88 (100)	160 (90.0)	–	–	–	0.004
Others	0 (0)	16 (9.1)				
<i>Time of day</i>						
Day (8:30–17:00)	54 (60.0)	163 (92.8)	7.90	3.88	16.05	<0.001
Night or Holiday	34 (40.0)	13 (7.2)				
<i>&lt; Multivariate analysis &gt;</i>						
Cardiovascular surgery			6.43	2.92	14.20	<0.001
Emergency			5.21	2.13	12.78	<0.001
ASA physical status 4–5			3.76	1.29	10.95	0.015

ASA american society of anesthesiologists

**Table 2** Risk factors of failure to achieve ROSC identified by the univariate and multivariate analyses

	ROSC <i>n</i> (%) ( <i>n</i> =58)	Non-ROSC <i>n</i> (%) ( <i>n</i> =30)	Odds ratio	95% CI		<i>P</i> value
<i>&lt; Univariate analysis &gt;</i>						
<i>Age</i>						
< 65 years	23 (39.7)	17 (56.7)				
≥ 65 years	35 (60.3)	13 (43.3)	0.50	0.21	1.23	0.129
<i>Sex</i>						
Male	34 (58.6)	23 (76.7)	2.32	0.86	6.27	0.106
Female	24 (41.4)	7 (23.3)				
<i>ASA physical status</i>						
1–3	37 (63.8)	4 (13.3)				
4–5	21 (36.2)	26 (86.7)	11.45	3.52	37.31	<0.001
<i>Emergency or scheduled</i>						
Emergency	29 (50.0)	28 (93.3)	14.00	3.05	64.27	<0.001
Scheduled	29 (50.0)	2 (6.7)				
<i>Department</i>						
Cardiovascular surgery	30 (51.7)	15 (50.0)	0.93	0.39	2.25	0.878
Others	28 (48.3)	15 (50.0)				
<i>Main cause</i>						
Blood loss	15 (25.9)	22 (73.3)	7.88	2.90	21.43	<0.001
Others	43 (74.1)	8 (26.7)				
<i>Anesthesia</i>						
Related or Contributory	14 (24.1)	1 (3.3)				
Non-related	44 (75.9)	29 (96.7)	9.23	1.15	74.02	0.014
<i>Rhythm</i>						
Shockable	30 (51.7)	5 (16.7)				
Non-shockable	28 (48.3)	25 (83.3)	5.36	1.80	15.93	0.001
<i>&lt; Multivariate analysis &gt;</i>						
ASA physical status 4–5			9.85	2.70	35.9	0.001
Blood loss			4.94	1.56	15.64	0.007
Non-shockable			4.31	1.20	15.43	0.025

ROSC return of spontaneous circulation, ASA american society of anesthesiologists

### Anesthesia-related cardiac arrest

Patient characteristics and adverse events leading to anesthesia-related cardiac arrest are shown in Table 3. Of the six anesthesia-related cardiac arrests, three were due to

hypoxia, two were due to vagal reflex, and one was due to an accidental bolus dose of remifentanyl. Although initial rhythm on the occurrence of cardiac arrest was non-shockable in all the patients with anesthesia-related cardiac arrest, ROSC was achieved during anesthesia in all patients. Patient

**Table 3** Patient characteristics and adverse events leading to anesthesia-related cardiac arrest

No	Age (years)	Sex	ASA-PS	Adverse event leading to cardiac arrest	Category	Rhythm	ROSC
1	57	Male	2	Cannot ventilate, cannot intubate due to laryngeal tumor	Hypoxia	PEA	Yes
2	65	Male	1	Hypoxia due to failure to replace the oral tracheal tube with the tracheostomy tube	Hypoxia	PEA	Yes
3	75	Male	2	Severe bradycardia due to accidental bolus of remifentanyl	Drug-induced	Asystole	Yes
4	85	Male	3	Vagal reflex during laryngoscope insertion	Vagal reflex	Asystole	Yes
5	68	Male	3	Vagal reflex during puncture of the right internal jugular vein	Vagal reflex	Asystole	Yes
6	25	Male	3E	During induction of anesthesia, hypoxia due to lead pipe phenomenon	Hypoxia	Asystole	Yes

ASA-PS american society of anesthesiologists physical status, PEA pulseless electrical activity, ROSC return of spontaneous circulation

**Table 4** Patient characteristics and adverse events leading to anesthesia-contributory cardiac arrest

No	Age (years)	Sex	ASA-PS	Adverse event leading to cardiac arrest	Category	Rhythm	ROSC
1	81	Female	2E	Inadequate treatment for hyperkalemia during massive blood transfusion	Hyperkalemia	PEA	Yes
2	80	Female	5E	Massive bleeding. Inadequate infusion of fluids due to IV leakage	Blood loss	PEA	No
3	63	Male	2	History of old myocardial infarction. Ventricular fibrillation due to hypotension after epidural anesthesia	Cardiac complications	Ventricular fibrillation	Yes
4	77	Male	2	History of sick sinus syndrome. Severe bradycardia after administration of anesthetics	Cardiac complications	Asystole	Yes
5	64	Male	2	After the operation, massive bleeding occurred when the patient was moved from lateral to supine position	Bleeding	PEA	Yes
6	71	Male	4E	Inadequate fluid infusion during peritonitis surgery	Septic shock	PEA	Yes
7	57	Male	2	History of syncope. Severe bradycardia after administration of anesthetics	Drug-induced	Asystole	Yes
8	87	Male	2	Severe bradycardia after administration of anesthetics. Preoperative electrocardiogram showed bifascicular block	Drug-induced	Asystole	Yes
9	62	Male	1	History of coronary spasmodic angina. Ventricular fibrillation after local injection of epinephrine-containing 1% lidocaine	Cardiac complications	Ventricular fibrillation	Yes

ASA-PS american society of anesthesiologists physical status, PEA pulseless electrical activity, ROSC Return of spontaneous circulation

characteristics and adverse events leading to anesthesia-contributory cardiac arrest are shown in Table 4. Although 7 of the 9 patients had non-shockable rhythm, ROSC was achieved in 8 of 9 patients.

## Discussion

In this study, we investigated cardiac arrest during anesthesia over a period of 20 years at a tertiary care university hospital with an advanced critical care and emergency center in Japan. We identified 90 cases of cardiac arrest during anesthesia that occurred during the two decades. We found that the incidence of cardiac arrest was 8.05 per 10,000 anesthetics (95% CI, 6.54–9.90) and that the incidence of anesthesia-related cardiac arrest was 0.54 per 10,000 anesthetics (95% CI, 0.21–1.20) and the incidence of anesthesia-contributory cardiac arrest was 0.80 per 10,000 anesthetics (95% CI, 0.40–1.56). A meta-analysis for which results were published in 2012 showed that perioperative cardiac arrest has been decreasing and that the incidence of cardiac arrests in developed countries was 6.6 per 10,000 anesthetics in the 1990s–2000s [4]. Since then, there have been several reports on perioperative cardiac arrest in all types of patients in the United States, Germany, Japan, China, and other countries, and the rate has been reported to be 2.63–6.8 per 10,000 anesthetics with variation by region and time period [5–11]. The variations are due to different regions, differences in the

levels of care, and different periods for collection of data on perioperative cardiac arrest (during anesthesia, until leaving the PACU, 24 h after surgery, and 48 h after surgery) [5–12]. In this study, we showed that the incidences of cardiac arrest during anesthesia were 8.05 per 10,000 anesthetics in 2000–2019 and 5.04 per 10,000 anesthetics in 2010–2019. Morimatsu et al. showed that the incidence of cardiac arrest was 2.63 per 10,000 anesthetics in Japan in a study published in 2021 using a database of data for more than 1000 hospitals [7]. The present study was conducted in a tertiary care hospital, in which major trauma, cardiovascular surgery, and critical care operations are more common, and therefore cardiac arrest may have been more frequent. The cardiac arrest rate was similar to the rates reported in recent years from tertiary hospitals in the US and Germany. Anesthesia-related cardiac arrest has been reported in recent years with a small variability of 0.52–0.74 per 10,000 anesthetics, and we reported a similar result [5, 6, 10]. Anesthesia-related cardiac arrest in our study was mainly due to airway, respiration, and drug administration as in previous studies, but our study is unique in that it included two cases of vagal reflex. In the both cases, although Holter electrocardiography and coronary artery examinations were performed postoperatively, there were no clinically significant findings. There are several case reports of cardiac arrest during laryngoscopy or tracheal intubation [15, 16]. Vagal reflex caused by stimulation of the larynx or carotid sinus combined with the effects of anesthetics seems to cause cardiac arrest. Although

it is rare, anesthesiologists should keep this possibility in mind. We identified cardiac arrest cases over a period of 20 years and showed that the cardiac arrest rate decreased from the 2000s to the 2010s. The reasons for the decrease in cardiac arrest rates by decade may include advancements in surgical practices and appropriate selection of patients for surgery as in a previous study [4]. Although the rates of anesthesia-related and anesthesia-contributory cardiac arrests did not decrease significantly, the use of new anesthetics and transfusion products and advances in monitoring may have indirectly reduced the incidence of cardiac arrest in the operating room.

### Risk factors for cardiac arrest during anesthesia

We performed univariate and multivariate logistic regression analyses of risk factors of cardiac arrest during anesthesia. In univariate analysis, several factors were associated with cardiac arrest during anesthesia as shown in Table 1. In multivariate analysis, ASA-PS 4–5, emergency surgery, and cardiovascular surgery were identified as independent factors. Previous studies have also shown ASA-PS and emergency surgery to be independent factors [5, 8], being consistent with our findings. Cardiovascular surgery may contribute to cardiac arrest due to arrhythmias related to cardiac manipulation and cardiovascular complications. Although the effect of age on cardiac arrest varies among studies, there is a consensus that cardiac arrest is more common in neonates and infants less than 1 year of age and patients aged 65 years or older [9, 10, 14]. In this study, the number of infants was too small to show significant results. Although patients aged 65 years or older had significantly more cardiac arrests in univariate analysis, there was no significant difference in multivariate analysis. This may be because the older patients had higher ASA-PS scores and were more likely to undergo cardiovascular surgery.

### Risk factors for failure to achieve ROSC

We also performed univariate and multivariate logistic regression analyses of risk factors of failure to achieve ROSC, and we identified ASA-PS 4–5, blood loss-induced cardiac arrest, and non-shockable rhythm as independent factors. When the cause of cardiac arrest was blood loss, the proportion of patients with non-ROSC increased in both univariate and multivariate analyses. This is similar to results of previous studies showing that in-hospital survival is reduced by bleeding [8, 12]. Carlucci et al. reported that trauma surgery was associated with more deaths after intraoperative cardiac arrest [17]. This relationship can be explained by the fact that trauma surgery often induces massive blood loss. Regarding the rhythm of cardiac arrest, shockable rhythm was more likely than non-shockable rhythm to result in

ROSC. On the other hand, in most of the anesthesia-related and anesthesia-contributory cardiac arrests, ROSC could be achieved despite non-shockable rhythm on the occurrence of cardiac arrest. The results are consistent with result of previous studies showing a better prognosis in patients with anesthesia-related cardiac arrest [8, 18]. ASA-PS 4–5 was identified as an independent risk factor for failure to achieve ROSC as well as a risk factor for cardiac arrest. In other words, high ASA-PS was associated with high mortality during anesthesia. Anesthesiologists should pay more attention to and perform careful anesthetic management in patients with high ASA-PS.

### Limitations

Our study has several limitations. First, because this study was a retrospective study and relied on anesthesia records for data collection, we could not rule out the possibility that cardiac arrest had been missed due to incomplete records. However, our study was limited to cardiac arrest during anesthesia, during which vitals were recorded every 5 min. It is also unlikely that anesthesiologists did not record cardiac arrest, which is the most critical event during anesthesia. Similarly, due to the study being a retrospective study, the cause of death and its relationship to anesthesia may also be inaccurate. Although cardiac arrest cases were evaluated by two anesthesiologists based on anesthesia records and medical records, a database should be established to review and record the details of each cardiac arrest. Secondly, because we collected data over a period of 20 years, some of the patient information, such as blood test data, were incomplete in older cases, and therefore detailed information was limited. Finally, because this study was a single-center study, the results of this study may not be generalizable. Sapporo Medical University Hospital is a tertiary care university hospital with an advanced critical care and emergency center. Moreover, Japan is a nation of almost a single race. There are biases in surgical procedures and patient backgrounds among countries and hospitals, which may not be generalizable to other hospitals.

In conclusion, we investigated cardiac arrest during anesthesia over a 20-year period and identified 90 cardiac arrests among 111,851 anesthetics. The overall cardiac arrest rate was 8.05 per 10,000 anesthetics, and there was a decrease in the rate from 11.72 per 10,000 anesthetics in the 2000s to 5.04 per 10,000 anesthetics in the 2010s. The incidence of anesthesia-related cardiac arrest was 0.54 per 10,000 anesthetics, and the incidence of anesthesia-contributory cardiac arrest was 0.80 per 10,000 anesthetics. Independent risk factors of cardiac arrest were identified by multivariate logistic regression analyses to be ASA-PS 4–5, emergency surgery, and cardiovascular surgery. Blood loss was the most common cause of cardiac arrest and blood loss-induced cardiac



arrest was independently associated with failure to achieve ROSC. Further improvements in treatment strategies for bleeding may reduce the future incidence of cardiac arrest and death during anesthesia.

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**Author contributions** All authors contributed to the study conception and design. Makishi Maeda and Naoyuki Hirata performed material preparation and data collection. Makishi Maeda, Naoyuki Hirata and Tomohiro Chaki performed data analysis. Michiaki Yamakage supervised the study. The first draft of the manuscript was written by Makishi Maeda and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## Declarations

**Conflict of interest** Not applicable.

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