

Retrospective study of perioperative cardiac arrest from a Chinese tertiary hospital

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Abstract

Studies on perioperative cardiac arrest in Chinese hospitals have rarely been retrieved from international journals. This survey evaluated the incidence, causes, and outcomes of perioperative cardiac arrests in a Chinese tertiary general hospital between July 2013 and December 2020. The incidence of cardiac arrest within 24 hours of anesthesia administration was retrospectively identified using an anesthesia database in Liaocheng People's Hospital. During the study period, there were 118,152 anesthetics. Data collected included patient characteristics, surgical procedures (elective or emergency), American Society of Anesthesiologists (ASA) physical status score, type of surgery, anesthesia technique, and outcome. Cardiac arrests were grouped into one of 3 groups: totally anesthesia-related, partially anesthesia-related, or anesthesia-unrelated. In total, 41 cardiac arrests (3.5:10,000) and 26 deaths (2.2:10,000) were found. Major risk factors for cardiac arrest were children under 1 year, adults between 19 and 65 years, and the elderly (>80 years) (P < .001), male patients (P = .02), emergency surgery (P < .001), and ASA grade V patients without anesthesia (P = .009). There were 19 anesthesia-related cardiac arrests (1.6:10,000) – 2 were totally related, and 17 were partially related to anesthesia. There were 9 anesthesia-related deaths (0.8:10,000), all of which were partially related to anesthesia. Perioperative cardiac arrests were correlated with age, gender, ASA grade and surgical procedures. The 2 most important patient factors leading to cardiac arrest were hemorrhagic shock from trauma and septic shock, respectively.

Abbreviation: ASA = American Society of Anesthesiologists.

Keywords: anesthesia, cardiac arrest, incidence, outcome

1. Introduction

Perioperative cardiac arrest is one of the worst events during surgery, as it is associated with high permanent brain damage or mortality. Data obtained from the National Anesthesia Clinical Outcomes Registry showed that intraoperative cardiac arrests occurred in 5.6 per 10,000 patients, with an associated mortality of 58.4%.^[1] The incidence and causes of anesthesia-related cardiac arrests in the perioperative period have been studied over the last 2 decades by many authors from different countries such as the United States,^[1,2] Germany,^[3] France,^[4] and Brazil.^[5]

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Data access statement: All relevant data are within the paper and its Supporting Information files.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Literature on perioperative cardiac arrests is scarce in Chinese tertiary hospitals, although more than 10% of surgical procedures worldwide are performed in China.^[6] This is because most Chinese data were published in domestic journals that are unknown to the international community because they were not indexed by the global databases. To date, we retrieved only 2 articles on perioperative cardiac arrest in Chinese hospitals, and 1 study reported that the incidence of cardiac arrest under regional anesthesia from 7 teaching hospitals was 0.9/10,000.^[7] The Third Affiliated Hospital of Sun Yat-sen University in Guangzhou found that the incidence and mortality rates of cardiac arrest were slightly lower than international standards.^[8]

Data on the incidence and causes of perioperative cardiac arrest and mortality are essential for understanding the medical status and can also be used for comparison with different countries. Comparative learning provides a high-quality indicator to improve patient safety and effectively reduce the incidence of unfavorable events.^[9] As the incidence of cardiac arrest within the 24 hours perioperative period is an important component of the anesthesia quality control index system published by the National Health and Family Planning Commission of the People's Republic of China in 2013, our database contains complete information on these patients.

This study reports all cardiac arrests that occurred in a surgical population during the 24 hours perioperative period over a 7year period in a Chinese general tertiary hospital and determined the incidence, causes, and outcomes.

2. Methods

This project was approved by the Medical Ethics Committee of Liaocheng People's Hospital (Ref: 2021011). Because of the retrospective and anonymous nature of this study, written informed consent was waived by the Medical Ethics Committee of Liaocheng People's Hospital. We analyzed all reported cardiac arrests in 118,152 consecutive anesthetics administered to all patients requiring anesthesia services at Liaocheng People's Hospital, a public tertiary teaching hospital, from July 2013 to December 2020.

Liaocheng People's Hospital, which was founded in 1949, is a 3200-bed public Class A tertiary comprehensive hospital performing more than 20,000 surgeries per year to all ages and provides care to the population of the Shanxi-Hebei-Lu-Henan region. It is the first provincial regional medical center in Shandong Province. The service scope of radiation is more than 20 million people. In our department, it is mandatory to record critical incidents, including cardiac arrest, that occur within 24 hours of anesthesia administration in an anesthesia database. This record was compiled and completed by the anesthesia team involved in the anesthetic cases.

We followed the preoperative visit regime. All patients were examined by an on-duty anesthetist immediately before emergency surgical procedures or the day before elective procedures. For regional and neuraxial anesthesia or sedation, we adopted basic safety monitoring in the operating room, including electrocardiogram display, automatic non-invasive blood pressure, and pulse oximetry. For general anesthesia, oxygen concentration, delivered anesthetic vapor concentration, endexpiratory carbon dioxide, ventilation parameters, anesthesia depth, and body temperature were also measured.

This is consistent with previous studies,^[3,5] cardiac arrest was defined as an event requiring cardiopulmonary resuscitation, which might involve closed or open chest compressions. Cardiac arrests and deaths occurring within 24 hours of anesthesia administration were prospectively identified from an anesthesia database that was developed using a quality assessment form as part of the mandatory documentation for each anesthetic procedure. The form contains basic characteristics of the patient (name, age, sex), surgical procedures (elective or emergency surgery) and area, American Society of Anesthesiologists (ASA) physical status classification, anesthetic technique (general anesthesia, regional anesthesia including epidural/spinal/caudal or plexus block, sedation), and a checklist of airway, respiratory, cardiocirculatory, neurological, renal, and miscellaneous events were obtained. The anesthetist responsible for each case was asked to review the case and provide a written summary for peer review. This procedure avoided a situation in which data collection forms were found to be incomplete.

The medical and anesthesia records, written summary, and when applicable, the autopsy reports were analyzed by the Anesthesia Cardiac Arrest Study Commission composed of 3

Table 1

senior anesthesiologists. Three members worked together to analyze cardiac arrest. There was unanimity in the event cause in the majority of cardiac arrests. Disagreements on the cause of cardiac arrest were resolved by discussion among the 3 members, and agreement or consensus was determined when at least 2 out of 3 members agreed on the cause of the event.

Following the classification system, all cardiac arrest events were assigned to one of 3 groups based on the contributory factor that caused the cardiac arrest: totally anesthesia-related group (anesthesia was the only or major contributing factor), partially anesthesiarelated group (both surgery and anesthesia were the contributing factors or there was some doubt whether cardiac arrest was entirely attributable to anesthesia), and anesthesia-unrelated group (surgery or other factors were the contributing factors) (Table 1).

Cheney et al^[10] suggested that the primary adverse events that occurred within 24 hours of anesthesia leading to cardiac arrest fall into the following categories: respiratory (inadequate ventilation/oxygenation, difficult intubation, esophageal intubation, premature extubation, aspiration, airway obstruction, endobronchial intubation, bronchospasm, and inadvertent extubation), cardiovascular (inadequate fluid therapy, stroke, hemorrhage, myocardial infarction, pulmonary embolism, multifactorial/miscellaneous events), medication-related, equipment-related, block-related, procedural, iatrogenic, and other not further classified incidents. In addition, for the cardiovascular category, arrhythmia and hypotension were involved in multifactorial miscellaneous events in circumstances where the primary event leading to cardiovascular system changes was not obvious. Surgical complications and patient conditions were also included in the multifactorial cardiovascular events.^[10]

The characteristics of anesthesia-related cardiac arrest cases and anesthesia-unrelated cardiac arrest cases were summarized and analyzed. We used the mean and standard deviation for continuous variables, and numbers and percentages for categorical variables. The χ^2 test and 2 independent samples *t* tests were used to compare categorical and continuous variables, respectively. The Tukey-type test for multiple comparisons among proportions^[11] was used for the incidence of cardiac arrests in the perioperative period, modeled as a function of various patient characteristics, including age, ASA physical status, surgical procedures, and anesthetic technique. Statistical analysis of all data was performed using SPSS software (version23, SPSS, Chicago, IL). Statistical significance was set at *P* < .05.

3. Results

Over the 7 years of the study (2013–2020), 118,152 patients received anesthesia care at Liaocheng People's Hospital. During

Group	Definition
Totally anesthesia-related	Where it is reasonably certain that CA was caused by the anesthesia or other factors under the control of the anesthetist
Partially anesthesia-related	1. Where there is some doubt whether CA was entirely attributable to the anesthesia or other factors under the control of the anesthetis 2. Where CA was caused by both surgical and anesthesia factors
Anesthesia-unrelated	 CA where the administration of the anesthesia did not contribute and surgical or other factors are implicated Inevitable CA, which would have occurred irrespective of anesthesia or surgical procedures Incidental CA, which could not reasonably be expected to have been foreseen by those looking after the patient, was not related to the indication for surgery and was not due to factors under the control of the anesthetist or surgeon Those that cannot be assessed despite considerable data but where the information is conflicting or key data are missing Cases that cannot be assessed because of inadequate data

Table 2	
The incidence of cardiac arrest according to age and gender.	

	Anesthetics Cardiac arres			rdiac arrests
	n	(%)	n	Incidence [*] (per 10,000)
Age group				
0—1 yr	1208	1.02	3	24.83 ^a
2–18 yr	16708	14.14	0	0 ^b
19–65 yr	78702	66.61	34	4.32 ^c
66–79 yr	18726	15.85	3	1.6 ^d
≥80 yr	2808	2.38	1	3.56
Gender				
Male	64380	54.49	30	4.66 ^e
Female	53772	45.51	11	2.05

For age letter "a" represents the comparison between the 0–1 yr group and other groups, P < .001. Letter "b" represents the comparison between the 2–18 yr group and other groups, P < .001. Letter "c" represents the comparison between the 19–65 yr group and 66–79 yr group, P < .001. Letter "d" represents the comparison between the 66–79 yr group and ≥80 yr group, P < .001. For the gender letter "e" represents the comparison between male and female group, P < .001. * Incidences followed by different letters are significantly different (P < .05).

this time period, 41 cardiac arrest events were identified within 24 hours of anesthesia administration from the anesthesia database, which meant that the cardiac arrest rate was 3.5/10,000. The overall mortality from cardiac arrest within 24 hours of anesthesia administration was 26 of 41 cardiac arrest events (2.2/10,000). Major risk factors were children below 1 year, adults between 19 and 65 years, and the elderly (P < .001) (Table 2); male patients (2.7:1 compared with female patients) (P = .02) (Table 2); patients with ASA V physical status (P = .009) (Table 3); emergency surgery (7.9:1 compared with elective surgery) (P < .001) (Table 3); and those who had not been anesthetized (P = .008) (Table 4).

Resuscitation was successful in all 2 cases of totally anesthesiarelated cardiac arrest, while for cardiac arrests that partially anesthesia-related or anesthesia-unrelated to, 9 (9/17, 52.9%) and 17 (17/22, 77.3%) patients died, respectively. The incidence of anesthesia-related cardiac arrest was 1.6/10,000, and the mortality was 0.8/10,000. Univariate analyses for risk factors were performed on anesthesia-related and anesthesia-unrelated teams. Differences were found between events related and

Table 3

The incidence of cardiac arrest according to ASA physical status and surgical procedure.

	Anesti	netics	Ca	rdiac arrests
	n	(%)	n	Incidence [*] (per 10,000)
ASA physical status				
1	28,185	23.85	1	0.35 ^a
I	77,128	65.28	8	1.04
III	11,556	9.78	7	6.06
IV	1114	0.94	20	179.53
V	169	0.15	5	295.86 ^a
Surgical procedures				
Elective	98,561	83.42	16	1.62 ^b
Emergency	19,591	16.58	25	12.76 ^b

Letter "a" represents the comparison between ASA I and ASA V groups, P=.009.

Letter "b" represents the comparison between the elective and emergency groups, P < .001. * Incidences followed by different letters are significantly different (P < .05).

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	Anest	hetics	Cardiac arrests		
Anesthetic technique	n	(%)	n	Incidence [*] (per 10,000)	
General anesthesia	80356	68.01	32	3.98	
Regional anesthesia	32970	27.90	4	1.21	
Epidural/spinal/caudal	22701	19.21	3	1.32	
Plexus blocks	10269	8.69	1	0.97 ^b	
Sedation	4773	4.04	0	0 ^a	
Others [†]	53	0.04	5	943.4	

Letter "a" represents the comparison between the sedation and others groups, P=.008Letter "b" represents the comparison between plexus blocks and the others group, P=.01 * Incidences followed by different letters are significantly different (P<.05).

[†] No anesthesia care in ASA V physical status patients.

unrelated to an esthesia with regard to surgical characteristics (P=.02) and mortality (P=.04) (Table 5).

Additional information on the 41 cardiac arrest cases attributable to patient disease/condition or surgery is shown in Table 6. The largest factor was hemorrhagic shock from trauma, followed by septic shock and electrolyte disturbances (hyperkalemia).

Adverse events in anesthesia-related cardiac arrests are summarized in Table 7. In these cases, 13 patients had significant underlying disease and consisted mostly of ASA physical status III or IV. The median age was 56 years (range, 1–79 years). Two patients with cardiac arrest were less than 1 year old, and both had failed resuscitation. Males comprised 68.4% of anesthesiarelated cardiac arrest cases. General anesthesia was used as the primary technique. Nine patients with anesthesia-related cardiac arrest died (47.4%). Cardiovascular adverse events were the major events contributing to cardiac arrest (n=14), which accounted for 73.7% of the cases. These included myocardial infarction, hypotension, septic shock with multiple organ failure, hyperkalemia, vagal response, and amniotic fluid embolism. In addition, medication and respiratory adverse events comprised the remaining cases.

Table 5

Univariate analysis for risk factors of patients with anesthesiarelated and anesthesia-unrelated cardiac arrest.

Cause	Anesthesia-related	Anesthesia-unrelated	P value
N	19	22	
Age (yr)	49.53 ± 20.03	47.67 ± 18.96	.762
Result			.047
Mortality	9 (47.37%)	17 (77.27%)	
Live	10 (52.63%)	5 (22.73%)	
Sex			.524
Female	6 (31.58%)	5 (22.73%)	
Male	13 (68.42%)	17 (77.27%)	
ASA			.166
<3	6 (31.58%)	3 (13.64%)	
≥3	13 (68.42%)	19 (86.36%)	
Anesthesia technique			.376
GA	16 (84.21%)	16 (72.73%)	
NGA	3 (15.79%)	6 (27.27%)	
Surgical characteristics			.021
Emergency	8 (42.11%)	18 (81.82%)	
Non-emergency	11 (57.89%)	4 (18.18%)	

Table 6

Cardiac arrests and deaths attributable to patient disease/condition, or surgical factors.

	Cardiac arrests		D		
Causes of cardiac arrest	n	% (No)	n	(%)	Mortality (%)
Trauma and hemorrhagic shock	11	26.83	11	42.31	100
Sepsis and multiple organ failure	6	14.63	5	19.23	83.33
Hyperkalemia	6	14.63	1	3.85	16.67
Perioperative myocardial infarction	3	7.32	3	11.54	100
Complication associated with cardiac surgery	3	7.32	3	11.54	100
Exsanguinating hemorrhage at operation	3	7.32	1	3.85	33.33
Respiratory obstruction	3	7.32	1	3.85	33.33
Narcotic reaction	2	4.88	0	0	0
Postpartum DIC	1	2.43	1	3.85	100
Surgical error	1	2.43	0	0	0
Vagus reflex	1	2.43	0	0	0
Hypersensitivity to blood products	1	2.43	0	0	0
Total	41		26		63.41

Medication-related problems accounted for 2 totally anesthesiarelated cardiac arrests. One patient received spinal anesthesia while intravenous administration of dexmedetomidine ($40 \mu g$ /hours). After 40 minutes, he felt pain and intravenous fentanyl (0.1 mg). His heart rate dropped sharply, and the other one occurred after induction with propofol, fentanyl, and cisatracurium. In both adult cases, they completely recovered. There were 3 cases of respiratory complications. Of these 3, 1 pediatric patient who had a cardiac arrest after arrival in the ward; unfortunately, the child was not resuscitated. The other 2 cases in an ASA physical status III adult patient were successfully resuscitated. anesthesiologists. From the 1990s to the 2000s, the global incidence of perioperative cardiac arrest ranged from 6.59/10,000 anesthetics in highly developed countries to 20.68/10,000 in less-developed countries.^[12] According to a meta-analysis,^[12,13] the incidence and mortality of perioperative cardiac arrest in developing countries are much higher than those in developed countries. This report provides insight into the origins and outcomes of 41 cardiac arrests in 118,152 anesthetic cases under current practices and conditions in a Chinese class A tertiary comprehensive hospital over a 7-year period. Our intraoperative cardiac arrest incidence (3.5:10,000 anesthetics) and mortality (2.2:10,000) were all lower than those in recent studies. This may be because China has experienced significant improvements in economic and human indicators in the last decades; however, the neurosurgery department of our hospital is an independent surgical-anesthesia system, and relevant data were not included in this study.

4. Discussion

Perioperative cardiac arrest and death were often the worst outcomes for patients and the most severe challenges for

Table 7

Adverse events in cardiac arrests related to anesthesia.

			ASA	Surgical		Anesthetics			
No	Age	Sex	status	procedure	Surgery	technique	Event leading cardiac arrest	Category	Outcome
1*	50 yr	Μ		Elective	Varicose veins in lower limbs	Spinal	Dexmedetomidine in combination with fentanyl	Medication	Full recovery
2*	56 yr	Μ	II	Elective	Adrenalectomy	General	Cardiovascular depression after induction	Medication	Full recovery
3†	63 yr	Μ	IV	Elective	Cardiac surgery	General	Hyperkalemia	Cardiovascular	Full recovery
4†	56 yr	Μ	III	Elective	Cardiac surgery	General	Hyperkalemia	Cardiovascular	Full recovery
5†	79 yr	F	IV	Elective	Femoral head replacement	Spinal	Myocardial infarction	Cardiovascular	Death
6^{\dagger}	61 yr	Μ		Elective	Electro-prostatectomy	Spinal	Vagal response followed by cardiovascular depression	Cardiovascular	Full recovery
7†	53 yr	F		Elective	Lower limb fracture	General	Intraoperative hemorrhage and hypotension	Cardiovascular	Full recovery
8†	52 yr	F	IV	Elective	Cardiac surgery	General	Hypotension after coronary artery bypass	Cardiovascular	Death
9†	41 yr	F	III	Emergency	Tracheotomy	General	Burns cause severe airway damage	Respiratory	Full recovery
10†	34 yr	F	IV	Emergency	Caesarean	General	Amniotic fluid embolism	Cardiovascular	Death
11†	1 yr	F	I	Elective	Retroperitoneal neoplasm	General	Intraoperative hemorrhage and hypotension	Cardiovascular	Death
12†	65 yr	М	Ш	Emergency	Lower limb fracture	General	hyperkalemia	Cardiovascular	Full recovery
13†	62 yr	М	Ш	Elective	Lower limb fracture	General	Myocardial infarction	Cardiovascular	Death
14†	60 yr	Μ	IV	Emergency	Biliary fistula after liver transplantation	General	Septic shock with multiple organ failure	Cardiovascular	Death
15 [†]	60 yr	Μ	IV	Emergency	Carcinoma of esophagus ruptured and perforated	General	Septic shock with multiple organ failure	Cardiovascular	Death
16^{+}	58 yr	М	IV	Emergency	Cerebral thrombosis	General	Myocardial infarction	Cardiovascular	Death
17†	54 yr	М	IV	Emergency	Liver transplantation	General	Hyperkalemia	Cardiovascular	Full recovery
18 [†]	35 yr	М	Ш	Elective	Pancreatoduodenectomy	General	Respiratory arrest 40 min after arrival in ward	Respiratory	Full recovery
19†	1 yr	M		Emergency	Hand trauma	General	Respiratory arrest 30 min after arrival in ward	Respiratory	Death

* Totally related to anesthesia.

[†] Partially related to anesthesia.

The analysis of these cardiac arrests is meaningful. In our study, as in other studies,^[14,15] the highest number of cardiac arrests was found in children under 1 year of age. Prematurity and congenital diseases place such patients at a higher anesthetic risk than older children and adults. Patients aged over 80 years also had a higher incidence of cardiac arrest, which is consistent with previous studies.^[16] Advanced age usually increases the risk of cardiac arrest during anesthesia 5 to 10 times.^[17] Surprisingly, there was no difference in the incidence of cardiac arrests between patients aged from19 to 65 years and those aged >80 years, possibly because patients in this age group (especially men) are more predisposed to trauma and violent events.^[18]

ASA physical status grade at least III, emergency surgery has been reported as a risk factor for anesthesia-related cardiac arrest,^[3,19] and is the only predictive factor of mortality after cardiac arrest. Our study also observed a 7.8-fold higher incidence of cardiac arrest in emergency surgery than in elective surgery and a 17.3-fold higher incidence in ASA III than ASA I patients, although there was no statistically significant difference, which may be due to our small sample size. Similarly, this may be the reason why there was no statistical difference between general anesthesia and regional block. There may be a bias towards general anesthesia in emergency settings or in patients with coexisting medical conditions.^[20] In our study, cardiac arrest frequency was 3.3-fold higher in general than regional anesthesia.

In this study, the incidence of anesthesia-related cardiac arrest (1.6/10,000) is similar to that in developed countries; however, all the events of cardiac arrest that were related to anesthesia were medication-related, rather than respiratory events.^[3,21] Pignaton et al^[11] indicated that respiratory events were the dominant factor for totally anesthesia-related events, accounting for 7% to 80%. Respiratory events were no longer the dominant factor for anesthesia-related cardiac arrest, which may be associated with the increasing use of respiratory monitors, such as pulse oximetry, capnography, disconnection alarms, and low-pressure alarms, which may be more helpful in preventing respiratory rather than cardiovascular events.^[10,22] In addition, advances in clinical practices, such as the adoption of standardized guidelines for the management of difficult airways, might also be helpful for reducing the incidence of cardiac events due to the airway.^[23]

A study based on data from the Pediatric Perioperative Cardiac Arrest Registry revealed that cardiovascular events, including hypovolemia due to blood loss and hyperkalemia from transfusion of stored blood, were the most common causes of anesthesia-related cardiac arrest (41% of all cardiac arrest patients).^[24] In the present study, hemorrhage resulting in hypotension and hyperkalemia was also the primary cause of cardiac arrest (35.3% of all partially anesthesia-related cardiac arrest of the events.

All trauma patients were middle-aged and young (<65 years old), mostly male, with a high mortality rate. In the United States and Brazil,^[18] the mortality rate of trauma is ranked third, second only to cardiovascular disease and cancer. However, trauma was a major factor in patients aged 1 to 49 years, especially in young men.

Notably, 2 anesthesia-related cardiac arrest events were due to regional block problems. The incidence of cardiac arrest after spinal anesthesia and neuraxial blockade was reported to range from 1.3 to 18 per 10,000 anesthetics.^[25] One varicose vein patient with ASA I grade experienced a sudden drop in heart rate after intravenous fentanyl (0.1 mg) with routine spinal anesthesia

and continuous intravenous infusion of dexmedetomidine (40 μ g/hours). This is considered to be due to excessive sedation and respiratory depression.^[20] Another patient who underwent transurethral resection of the prostate had a cardiac arrest caused by dilation of the urethra, which evoked the vagus nerve reflex,^[26] because the surgeon was eager to operate only 5 minutes after spinal anesthesia. Therefore, the anesthesiologist must fully understand the physiological changes and complications caused by spinal anesthesia and abide by routine work and strict monitoring.

There may have been some methodological weaknesses associated with our study. First, the retrospective nature of the present study is a great limitation; hence, a prospective study will help to clarify the findings. Second, the results of the present study were from a single-center study, and our data do not include anesthesia for neurosurgical procedures, which might not be generalizable. We hope to perform a multicenter prospective survey to reveal the incidence and risk factors of anesthesiarelated cardiac arrest.

5. Conclusions

In conclusion, there were 41 perioperative cardiac arrests (3.5:10,000) and 26 perioperative deaths (2.2:10,000) over a 7-year period in a public Class A tertiary comprehensive hospital in China. The incidence of anesthesia-related cardiac arrest was 1.6/10,000, and the mortality was 0.8/10,000. Perioperative cardiac arrests were correlated with age, gender, ASA grade and surgical procedures. The 2 most important patient factors leading to cardiac arrest were hemorrhagic shock from trauma and septic shock, respectively.

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Author contributions

Conceptualization: Zongwang Zhang, Huili Kan Data curation: Huili Kan, Shanshan Wu Formal analysis: Yonghong Ding Investigation: Huili Kan, Shanshan Wu Methodology: Zongwang Zhang, Huili Kan Project administration: Zongwang Zhang Resources: Shanshan Wu Supervision: Zongwang Zhang Validation: Huili Kan, Zongwang Zhang Writing – original draft: Huili Kan, Shanshan Wu Writing – review & editing: Huili Kan, Yonghong Ding

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