Intraoperative cardiac arrest
A 10-year study of patients undergoing tumorous surgery in a tertiary referral cancer center in China

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Abstract
Intraoperative cardiac arrest (IOCA) is a lethal complication of noncardiac surgery. According to several reports, immediate survival after IOCA is approximately 50%. In this study, a retrospective case analysis was performed to determine the incidence of IOCA, the potential causes of cardiac arrest, and the risk factors of no resuscitation in patients undergoing tumorous surgery.

The medical records of surgery patients who experienced cardiac arrest during the intraoperative period between 2005 and 2014 were reviewed. The general conditions of the patients with IOCA were compared between the successfully resuscitated group and the unresuscitated group.

Fifteen patients with IOCA among 142,853 patients undergoing tumorous surgery were reviewed during the study period. Immediate survival after IOCA was 60%. Hospital survival was 46.7%. The incidence of IOCA decreased during 2010 to 2014 when compared with the rate during 2005 to 2009 (P < .05). The risk factors affecting the success of resuscitation after IOCA included American Society of Anesthesiologists Physical Status (ASA PS) classification ≥ III (P < .05) and preoperative tachycardia (heart rate ≥ 100/min, P < .05). The methods of anesthesia had no effects on the results of resuscitation.

The incidence of IOCA in patients undergoing tumorous surgery was 1.05 per 10,000 anesthesia. The overall mortality of IOCA was 0.56/10,000. The frequency of IOCA decreased within 10 years. There was no cardiac arrest primarily attributable to anesthesia over this study period. The risk factors leading to unsuccessful resuscitation after IOCA were ASA PS classification ≥ III and preoperative tachycardia.

Abbreviations: ASA PS = American Society of Anesthesiologists Physical Status, CPR = cardiopulmonary resuscitation, ECG = electrocardiogram, HR = heart rate, IOCA = intraoperative cardiac arrest, MAP = mean arterial pressure.

Keywords: anesthesia, cardiac arrest, intraoperative, IOCA, resuscitation

1. Introduction
The number of patients undergoing surgery has increased quickly over the past several decades. Approximately 2.5 million major surgical procedures are performed worldwide annually.[1] Intraoperative cardiac arrest (IOCA) in patients undergoing noncardiac surgery is a rare but potentially catastrophic event that is associated with high mortality. Although many anesthesiologists believe that the incidence of IOCA is decreasing, the morbidity and mortality of IOCA has not been well studied. The incidence of IOCA is heterogeneous in different hospitals and countries. The results of clinical studies demonstrated that the incidence rate of IOCA was 1.1 per 10,000 anesthesia to 34.6 per 10,000 anesthesia and the survival was 35% to 46.6%.[2–7] IOCA occurs due to complex reasons, including cardiac causes, loss of blood, severe hypotension, hypoxia, acidosis, electrolyte disturbance, nerve reflex, drug usage, and anesthesia and operation.[2–4]

In this study, a retrospective analysis of 10-year IOCA occurrence were performed to determine the incidence of IOCA, the immediate resuscitation rate, the in-hospital survival, the main factors leading to IOCA, and the risk factors of unsuccessful resuscitation in patients undergoing tumorous surgery. The results of this study may supply anesthesiologists and surgeons evidence for the prevention and treatment of IOCA during clinical anesthesia and operation.

2. Methods
This study was approved by the Ethics Committee of the Cancer Center (a tertiary referral center) of Harbin Medical University. All patients with records of IOCA during anesthesia in the central
operating room of the Cancer Center, Harbin Medical University, were reviewed in this study during a period of 10 years between January 1, 2005 and December 31, 2014. IOCA was identified from an anesthesia database, which was developed from a quality assessment form that was included with each anesthesia record as mandatory documentation of every anesthesia. The forms were completed by anesthesia staff, residents, and nurse anesthetists responsible for the anesthesia. The quality assessment forms were collected along with a copy of the anesthesia record and reviewed for completeness by one of the authors. IOCA was defined as cardiac arrest occurring in the operating room from the induction of anesthesia until the termination of anesthesia. Events that occurred outside the operating rooms, such as postoperative transportation to the recovery room or Intensive Care Unit, were not included. No case was included if the anesthesia team became involved only during resuscitation efforts in patients. Cardiac arrest was defined as an event requiring cardiopulmonary resuscitation (CPR) with either closed-chest cardiac compression or open cardiac massage. The basis for the judgment of cardiac arrest was whether the electrocardiogram (ECG) showed ventricular fibrillation, sudden disappearance of direct arterial blood pressure, and reduction of mean arterial pressure (MAP) to less than 20 mmHg. Successful resuscitation of patients was defined as achieving a return of spontaneous circulation and MAP > 60 mmHg for more than 1 hour.

All patients with IOCA were divided into the resuscitated group and the unresuscitated group according to the results of the resuscitation. The baseline and demographic characteristics of the patients, including age, sex, body weight, the American Society of Anesthesiologists Physical Status (ASA PS), preoperative MAP and heart rate (HR), the medical history and history of anesthesia and surgery, preoperative laboratory examinations, preoperative ECG examination, preoperative concomitant diseases of vital organs, preoperative diagnosis, methods of anesthesia, the type of operation, the time from anesthesia initiation to cardiac arrest, the main causes of cardiac arrest, the specific steps, medication, the duration of CPR, and the prognosis of the patients, were evaluated and compared between the resuscitated group and the unresuscitated group. The causes of cardiac arrest were identified according to the records of the case discussion after events. All unclear data from the records remained open. The final judgment of its significance was made by consensus with all of the authors.

2.1. Statistical analysis

Data were presented as the mean ± standard deviation or median (quartile). A Student t test was performed to compare the means of the resuscitated group and unresuscitated group for continuous data of normal distribution. Wilcoxon rank-sum test was used for continuous data of non-normal distribution. The Fisher Exact test was performed to compare qualitative data between the 2 groups. Logistic regression was used to determine factors that independently predict the risk of unsuccessful resuscitation. SPSS 17.0 for Windows (SPSS Inc., Chicago, IL) was used for the statistical analysis, and P < .05 was considered statistically significant.

3. Results

There were 142,853 patients who had records of anesthesia in the central operating room between 2005 and 2014.
3.2. Characteristics of patients with IOCA

Characteristics of patients with IOCA, including age, sex, ASA PS, preoperative diagnosis, coexisting diseases, preoperative ECG diagnosis, anesthesia methods, the time from anesthesia initiation to cardiac arrest, the duration of CPR, and causes of IOCA, are shown in Table 1. No IOCA occurred during induction of anesthesia or anesthesia emergence. All IOCA occurred during the maintenance of anesthesia. No IOCA were directly related to anesthesia. Among the 15 patients with IOCA, there were 8 men and 7 women ranging in age from 30 to 83 years old (mean 58.7 ± 14.1 years). General anesthesia was performed on 2 patients, 4 patients underwent epidural anesthesia, and 9 patients received epidural combined with general anesthesia. Intraoperative hemorrhage was the most common cause of IOCA (33.3%, 5/15), with a resuscitation rate of 60%. Other reasons were thromboembolic events (13.3%), hypokalemia/hyperkalemia (13.3%), parasympathetic reflex (6.7%), myocardial infarction (6.7%), and bronchial asthma attack (6.7%). No patients of IOCA with thromboembolic events or myocardial infarction were successfully resuscitated. In addition, the causes of IOCA in 3 patients remained unidentified.

3.3. Risk factors affecting resuscitation

There were no significant differences in age, sex, and body weight of patients with IOCA between the resuscitated group and the unresuscitated group (Table 2). There were no significant differences in preoperative MAP, blood glucose, plasma ions (potassium, sodium, calcium, and magnesium), and hemoglobin concentration between the resuscitated group and the unresuscitated group. There was no significant difference in the methods of anesthesia between the resuscitated group and the

| No. | Age (y) | Gender | ASA PS | Preoperative diagnosis coexisting diseases | Preoperative ECG | Anesthesia methods | T1 (min) | Causes of IOCA | T2 (min) | ROSC |
|-----|---------|--------|--------|--------------------------------------------|-----------------|-------------------|----------|----------------|----------|------|
| 1   | 61      | M      | III    | Left lung neoplasms Chronic bronchitis Anemia pectoris Diabetes mellitus | Atroventricular block | EA + GA | 200 | Pulmonary embolism | 80 | No |
| 2   | 30      | F      | II     | Right kidney neoplasms Left lung inflammation | Sinus tachycardia ST segment changes | EA | 80 | Pulmonary embolism | 40 | No |
| 3   | 36      | F      | II     | Cavitas pelvis neoplasms | Sinus tachycardia Limb lead low tension Occasional premature Ventricular contractions | EA + GA | 240 | Hemorrhage | 50 | No |
| 4   | 69      | F      | III    | Rectal cancer vaginal fistula | Sinus tachycardia Limb lead low tension ST segment changes | EA | 125 | Hemorrhage | 150 | No |
| 5   | 68      | M      | II     | Cancer of colon | ST segment changes | EA + GA | 180 | Low potassium | 180 | No |
| 6   | 73      | M      | III    | Hydrothorax | Sinus tachycardia | EA + GA | 60 | Extensive anterior wall acute myocardial infarction | 105 | No |
| 7   | 69      | F      | II     | Right kidney and bladder neoplasms Anemia | ST segment changes | EA | 210 | Hemorrhage | — | Yes |
| 8   | 49      | F      | I      | Left lung neoplasms | Premature beat | Normal | EA + GA | 120 | Hemorrhage | 20 | Yes |
| 9   | 48      | F      | I      | Gynecal cancer Bronchial asthma | Normal | Normal | EA + GA | 210 | Bronchial asthma attack | 17 | Yes |
| 10  | 73      | M      | II     | Duodenal neoplasms History of myocardial infarction | Obsolete cardiac muscle infarction ST segment changes | EA + GA | — | Unidentified | — | Yes |
| 11  | 58      | M      | II     | Rectal cancer History of hypertension | Atrial premature beat | Normal | EA + GA | 180 | Unidentified | 7 | Yes |
| 12  | 55      | M      | II     | Rectal cancer | Normal | EA + GA | 95 | Parasympathetic reflex | 35 | Yes |
| 13  | 83      | M      | II     | Meningioma History of hypertension Diabetes mellitus | Normal | GA | 255 | Hemorrhage | 45 | Yes |
| 14  | 60      | M      | II     | Rectal cancer | Complete right bundle branch block | EA + GA | 255 | Unidentified | 120 | Yes |
| 15  | 48      | F      | II     | Meningioma | Sinus bradycardia ST segment changes | GA | 135 | High potassium | 135 | Yes |

ASA = American Society of Anesthesiologists Physical Status, EA = epidural anesthesia, ECG = electrocardiogram, F = female, GA = general anesthesia, “—” = no exact record, IOCA = intraoperative cardiac arrest, M = male, ROSC = return of spontaneous circulation, T1 = the time from anesthesia initiation to cardiac arrest, T2 = the duration of CPR.
unresuscitated group. There was no significant difference in the time from the initiation of anesthesia to the occurrence of IOCA between the resuscitated group and the unresuscitated group. There was no significant difference in the volume of intraoperative bleeding between the resuscitated group and the unresuscitated group. Last recorded MAP before cardiac arrest showed no significant difference between the resuscitated group and the unresuscitated group. Eleven out of 15 patients with IOCA presented preoperative abnormal ECG. Five out of 11 (45.5%) patients with normal ECG were successfully resuscitated. Four patients (100%) with normal ECG were all successfully resuscitated. However, there were no statistically significant differences on the ECG between the resuscitated group and the unresuscitated group.

Among 15 IOCA, 8 out of 10 patients with an ASA PS classification < III were successfully resuscitated compared with 1 out of 5 patients with an ASA PS classification ≥ III (odds ratio, 16.000, 95% CI, 1.093–234.243, P = .043, Fig. 4), which indicated that patients with an ASA PS classification ≥ III was one of the risk factors of unsuccessful resuscitation. There was significant difference (P = .011) in preoperative tachycardia (defined as HR ≥100/min) between the resuscitated group (0 of 9) and the unresuscitated group (4 of 6). Preoperative tachycardia was one of the risk factors of unsuccessful resuscitation.

### 4. Discussion

In this study, we examined the frequency and outcome of IOCA in 142,853 patients who underwent tumorous surgery between 2005 and 2014. The incidence of IOCA was 1.05 per 10,000 anesthesia and decreased within 10 years. The immediate survival in patients with IOCA was 60.0%, and the hospital survival was 46.7%. The hospital mortality of IOCA was 0.56/10,000. No IOCA was primarily caused by anesthesia. Intraoperative hemorrhage was the most common cause of IOCA. The risk factors affecting the success of resuscitation after IOCA were ASA PS classification ≥ III and preoperative HR > 100/min. The methods of anesthesia did not affect the results of resuscitation.

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**Figure 4.** The effect of ASA on ROSC when intraoperative cardiac arrest occurred. ASA = American Society of Anesthesiologists Physical Status; ROSC = return of spontaneous circulation. *, P < .05.
4.1. Incidence of IOCA

Numerous studies examined IOCA. However, the incidence of IOCA for noncardiac surgery varies largely from 1.1/10,000 to 34.6/10,000. The principle reason for the lack of consistency of the incidence of IOCA is that the occurrence of IOCA decreased with improved technology and clinical practices.\(^\text{[10]}\) The incidence of IOCA also varies in different countries during similar periods based on the quality and availability of health care.\(^\text{[9]}\) In addition, some studies have reported the incidence of IOCA as only during surgery, while other studies included the period of 24 hours after surgery including the stay in a postanesthesia care unit and intensive care unit.\(^\text{[2,3,10–13]}\) Furthermore, the incidence of IOCA may be correlated to the age of the patients. Children younger than 1 month had a high incidence of cardiac arrest (54.2/10,000) and mortality (43.0/10,000).\(^\text{[14]}\) Numes et al\(^\text{[15]}\) identified a high incidence (54.4/10,000 cardiac surgery included) of IOCA with high mortality (37.0/10,000) in older patients. Finally, the incidence and mortality of IOCA may be dependent on the surgical types. Some studies have reviewed all types of surgery,\(^\text{[16–18]}\) while others exclude cardiac surgery,\(^\text{[3,19]}\) or obstetrical surgery.\(^\text{[20]}\) Thus, the variability makes comparisons among different studies difficult.

Although the incidence of IOCA varies, the decrease in IOCA correlates with the development of clinical technology and practices. Sprung et al\(^\text{[3]}\) reported a declining incidence of IOCA from 1990 to 2000 in a single center study. From our data, there was a trend of decreasing incidence of IOCA during the 10 years included in our study. The incidence of IOCA decreased from a rate of 2.18/10,000 during the first 5 years to a rate of 0.43/10,000 during the following 5 years. Considering that our data were obtained using a consistent methodology in a single center, the decrease in the frequency of IOCA may indicate a significant improvement in patient care over this period.

4.2. Causes of IOCA

Massive hemorrhage, myocardial infarction, severe arrhythmia, and pulmonary embolism comprised the major causes of IOCA.\(^\text{[3,21]}\) Sprung et al\(^\text{[3]}\) found that 43.9% of cardiac arrests were related to cardiac events, and 35.0% were related to bleeding. An et al\(^\text{[2]}\) reported that causes of IOCA among 218,274 noncardiac surgical procedures included intraoperative bleeding (52.2%), end-stage organ disease (21.7%), thromboembolic events (17.4%), cardiac events (13.0%), sepsis (8.7%), and anesthesia (4.3%).

The incidence of IOCA attributed to nonanesthetic reasons was much higher compared with anesthesia-related causes.\(^\text{[2,3,8,12,19]}\) Some studies have shown that the main risk factors contributing to IOCA included the preoperative characteristics of patients and concurrent diseases.\(^\text{[3,6]}\) Braz et al\(^\text{[6]}\) analyzed 53,718 consecutive anesthetics over a 9-year period. Ninety-two percent of patients experiencing IOCA had an ASA PS classification $\geq$ III. Newland et al\(^\text{[2]}\) obtained a similar conclusion that 96% of patients experiencing IOCA had an ASA PS classification $\geq$ III by analyzing data obtained from 72,959 consecutive anesthetics over a 10-year period. Interestingly, in our study, 33% of patients experiencing IOCA had an ASA PS classification $\geq$ III. This finding was lower than those obtained in previous reports.\(^\text{[2,6]}\) It indicated that except for patients, other factors such as intraoperative hemorrhage and surgery were also main causes of IOCA. Approximately, 26% of IOCA was attributed to the surgical operation.\(^\text{[22]}\) The operation of heart and large vessels was accompanied with the highest incidence of cardiac arrest, followed by combined thoracoabdominal operation, thoracotomy, laparotomy, craniotomy, spinal operation, and limbs operation.\(^\text{[23]}\) On the basis of our data, intraoperative massive blood loss was the leading cause of IOCA (33.3%). Reducing intraoperative hemorrhage became an important factor to improve the success rate of resuscitation and to reduce the occurrence of IOCA.\(^\text{[3,4]}\) The urgency of surgery is a well-established preoperative risk factor for IOCA.\(^\text{[3,24]}\) The increased risk of IOCA in an emergency operation is likely due to multiple factors. Patients who required high-risk emergency surgeries always had higher preoperative cardiac complications or may have experienced substantial intraoperative fluctuation in volume status, HR, and blood pressure. In addition, it was difficult to evaluate and optimize the preoperative status of patients, such as perforated or ischemic viscus, ruptured aortic aneurysms, ischemic limb, or trauma.

Over the past several decades, the incidence of cardiac arrest due to anesthesia-related factors appeared to decline. It has been reported that the frequency of cardiac arrest associated with anesthesia decreased significantly over time from 2.1/10,000 anesthetics (1969–1978) to 0.05/10,000 anesthetics (1989–2001).\(^\text{[7–24]}\) The incidence of cardiac arrest was higher during general anesthesia (5.5/10,000) than during regional anesthesia (1.5/10,000) or monitored anesthesia care (0.7/10,000).\(^\text{[3,15,26]}\) However, this finding may be related to the fact that many high-risk surgeries were performed under general anesthesia. In the current study, we did not observe anesthesia-related IOCA. The effect of an improvement in monitoring and clinical practices over time may have resulted in the declining trend of anesthesia-related cardiac arrest, such as airway misadventures or medication-related events.

4.3. Analysis of risk factors affecting the success of resuscitation for IOCA

The factors affecting the results of resuscitation in patients were complex. Most studies have an insufficient number of cases to perform multivariate analysis that would identify independent factors predicting outcome. The risk factors affecting the success of resuscitation were associated with the composite factors of preoperative patient condition. Higher ASA PS scores and urgent surgical procedures were predictors of both a higher incidence of IOCA and mortality.\(^\text{[2,10,11,15,19,27,28]}\) In our study, 80% of patients of ASA PS $\geq$ III were not resuscitated. However, 80% of patients of ASA PS $< $ III were successfully resuscitated. ASA PS $< $ III was a significant predictor of the success of resuscitation after IOCA. In a study performed by Sprung et al,\(^\text{[3]}\) patients with ASA PS $\geq$ III were the risk factor for the failure of resuscitation after IOCA, which were similar to our data. Infants and elderly patients also reported a higher incidence of both IOCA and mortality.\(^\text{[2,10,14,19]}\) Sex was not a predictor of IOCA or mortality in elderly patients.\(^\text{[13]}\) Nevertheless, it was reported to be a significant risk factor for perioperative CA and mortality in young men suffering from trauma.\(^\text{[6]}\)

Ten patients with IOCA have preoperative abnormal ECG from our data with 60% unresuscitation. However, 5 patients with preoperative normal ECG were 100% successfully resuscitated. These findings indicated that preoperative cardiovascular diseases in patients were an important factor of IOCA and death. Similar to our data, studies from Thailand found that cardiovascular disease was correlated with high mortality.\(^\text{[29–31]}\) Siriphuwanun et al\(^\text{[32]}\) also suggested that cardiovascular disease was related to cardiac arrest, particularly arrhythmias prior to cardiac arrest. Furthermore, they demonstrated that patients with
precardiopulmonary comorbidity had 3 times higher mortality compared with the other patients. It has been reported that the presence of hypotension or hemodynamic instability of patients prior to IOCA is a predictor of low survival. A study from Thailand found that actively bleeding patients with uncontrolled hemodynamic shock had a high mortality rate.[11,12] Sriphuwathan et al.[12] demonstrated that shock prior to cardiac arrest yielded a 6 times higher mortality rate. In patients who required continuous intraoperative infusion of vasopressors before arrest, the immediate survival and hospital survival were 28.8% and 13.7%, respectively, which were significantly lower than patients with stable circulation.[13] In this study, patients with a relatively lower preoperative MAP and a higher preoperative HR (>100/min) were predictors for the failure of resuscitation after IOCA. A lower preoperative MAP and a higher preoperative HR (>100/min) of patients may be easier to present hypotension or hemodynamic instability prior to IOCA.

A previous study demonstrated that a duration of CPR of more than 30 minutes was one risk factor of cardiac arrest mortality.[13] Many studies have found that a duration of CPR ranging from 10 to 20 minutes increases the chance of initial survival.[14–16] Sriphuwathan et al.[12] also found that onset time to start CPR within 1 minute was 9-fold higher in return of spontaneous circulation than the response time after 1 minute. The time of initial CPR is an important factor for the success of resuscitation.

5. Limitations
The current study has some specific limitations. The fact that the study has been carried out in a cancer center precludes any generalization of the findings. Since patients may present with specific preoperative comorbidities and other conditions that differ from general hospital patients. The data of patients with IOCA were collected and analyzed, but no data of patients without IOCA were available. Thus, it was not possible to compare patients with IOCA with patients without IOCA. In addition, it is not possible to perform statistical analysis on some factors due to the absence of data, such as the time interval between IOCA and the initiation of CPR, as well as the exact times for defibrillation.

6. Conclusions
The overall incidence of IOCA in patients undergoing tumors surgery was 1.05 per 10,000 anesthesia between 2005 and 2014. The incidence of IOCA decreased within 10 years. No IOCA was primarily attributed to anesthesia. The immediate survival in patients with IOCA was 60.0% and hospital survival was 46.7%. The overall mortality was 0.56 per 10,000 anesthesia. Intraoperative hemorrhage was the most common cause of IOCA. The methods of anesthesia did not affect the results of resuscitation. The risk factors leading to unsuccessful resuscitation after IOCA were ASA-PS classification ≥III and preoperative tachycardia.

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