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ORIGINAL RESEARCH

Perioperative Cardiac Arrest: A 3-Year Prospective Study from a Tertiary Care University Hospital

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Purpose: Perioperative cardiac arrests (CAs) are a rare but catastrophic perioperative complication. Much about incidence, risk factors, and outcomes of such events are still unknown. This study investigated anesthesia-related CAs at a tertiary teaching hospital.

Methods: CA incidence within 24 hours of anesthesia administration was prospectively identified from May 1, 2016 to April 31, 2019. Each CA was matched by four other cases without CA receiving anesthesia on the same date and under similar operating conditions. The CA cases were reviewed and assigned to one of three groups: anesthesia-related, anesthesia-contributing, and anesthesia not related.

Results: A total of 58,303 patients underwent 73,557 procedures under anesthesia during the study period. In sum, 27 CAs were reported for incidence of 3.7 per 10,000 anesthesia administrations (95% CI 2.3–5.1). Eleven CA were anesthesia-related for incidence of 1.5 per 10,000 anesthesia administrations. Four CA cases were anesthesia-contributing for incidence of 0.5 per 10,000 anesthesia administrations, while 53% of the anesthesia-related and -contributing CAs were due to respiratory problems. American Society of Anesthesiologists (ASA) physical status score, cardiovascular surgery, emergency surgery, and increased duration of surgery were significantly correlated with CA incidents when compared to the control group. ASA physical status score is an independent risk factor of the occurrence of perioperative CA (OR 7.6, 95% CI 2.6–22.4; $P<0.001$).

Conclusion: Identifying factors associated with increased risk for anesthesia-related CA is of great importance in risk stratification for surgical patients. ASA physical status score was found to be a major factor in predicting perioperative CA, since patients with higher ASA scores had a statistically significant increased risk of CA. Therefore, extra precautions must be taken when dealing with unprepared patients who have uncontrolled medical illnesses, especially those who will be undergoing emergency surgery.

Keywords: anesthesia, cardiac arrests, surgery, incidence

Introduction

Perioperative cardiac arrest (CA) is a rare but catastrophic perioperative event. Its incidence has decreased over the last few years due to improvements in anesthesia technology, surgical equipment, and clinical practice.[1,2] During 1990–2000, the overall global perioperative CA rate was 7.9 per 10,000 anesthesia administrations,[3] while in recent decades this has decreased.[4–6]Although CA is rare in the perioperative period, it is still serious and catastrophic due to its high mortality.[7,8] Nevertheless, a report from the US in 2013 indicated that CA in the

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operating room and postanesthesia care unit had better survival than CA elsewhere.[9]

Several clinical studies have aimed to investigate risk factors for perioperative CA under different clinical settings.[10] For instance, a study conducted at a tertiary hospital in Brazil concluded that patients who are at increased risk of perioperative CA were neonates, children under the age of 1 year, elderly patients, adult male patients, patients with American Society of Anesthesiologists (ASA) physical status score of III or higher, patients undergoing emergency surgery, and general anesthesia in multiclinical and cardiac/thoracic surgery patients.[7] On the other hand, vascular injuries, blunt traumatic cardiac injuries, gunshot wounds, stab wounds, and multiple injuries were common risk factors of perioperative CA among trauma patients.[11]

Studies on CA within 24 hours in the perioperative period are still lacking in our hospital, as well as in the Middle East and North Africa. The reporting of perioperative CA incidents is important for anesthesia quality control. The main limitation of retrospective studies is underreporting and thus missing information. Therefore, the aim of this study was to prospectively investigate perioperative CA over 3 years for a large unselected group of patients at a tertiary teaching hospital. We sought to assess the incidence, risk factors, and outcome of anesthesia-related and other CA within 24 hours after anesthetic administration by comparing them with patients who received anesthesia under similar operating conditions and did not develop perioperative CA.

Methods

Study Design

This prospective observational study was approved by the scientific research committee of the medical school at the University of Jordan and the Institutional Review Board committee of Jordan University Hospital (2681/2016/6) on February 12, 2016, and was conducted in accordance with the Declaration of Helsinki[10] and Good Clinical Practice guidelines.[11] Informed consent was not required and was waived by the committee, since there was no intervention required. Patients were fully anonymized, and no identifying information was obtained. This investigation reports all CA events from the start of anesthesia until 24 hours postanesthesia[12] and whether patients were transferred to the postanesthesia care unit or intensive care unit (ICU) postoperatively from May 1, 2016 until 31st of April 31, 2019. Our hospital is a 600-bed public university tertiary hospital that serves more than 2 million people in our city and around the country. It includes ten ICU beds for children and 50 ICU beds for adults. It provides different surgical specialties, including cardiac surgery and obstetrics. In our hospital, >20,000 surgeries are performed under different types of anesthesia for patients of all ages every year. Anesthesia care is provided by full-time specialists in anesthesia and anesthesia residents.

Recruitment and Data Collection

All patients undergoing inpatient or outpatient diagnostic or surgical procedures, whether elective or emergency, during or outside working hours under sedation, general anesthesia (GA) with/without regional block, or regional anesthesia alone were included in the study. Recruitment ran from when patients arrived in the preoperative area until 24 hours postoperatively. In all sedated or anesthetized patients, standards of the ASA for monitoring were used: electrocardiography, pulse oximetry, blood pressure, temperature, and end-tidal carbon dioxide measurements. Critically ill patients or those who undergo major surgery are subjected to invasive blood-pressure measurements and central venous access. CA incidents were reported by anesthesia residents and consultants who were caring for each case. Information noted in CA registry comprised patient demographics, ASA physical status score, elective or emergency surgery, surgery type, time and type of anesthesia, events leading to CA, and outcomes.

All CA events were discussed in a departmental meeting, then these cases were reviewed and analyzed by three consultants in the department to assign them into categories according to the classification system of Hohn et al:[4] anesthesia-related CA, where it was reasonably certain that CA was caused by the anesthesia or factors under the control of the anesthesia; anesthesia-contributing CA, where there was some doubt as to whether CA was entirely attributable to the anesthesia, other factors under the control of the anesthetist, or where CA was caused by both surgical and anesthesia factors; CA unrelated to anesthesia for cases of CA where administration of the anesthesia did not contribute and surgical or other factors were implicated, inevitable CA that would have occurred irrespective of anesthesia or surgical procedures, incidental CA that 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 anesthesist or surgeon, unable to be assessed despite considerable data but information conflicting or key data missing, and cases that could not be assessed because of inadequate data. CA was defined as the absence of cardiac rhythm or chaotic cardiac rhythm requiring the initiation of any component of basic or advanced cardiac life support.[13] Primary events leading to CA in the perioperative period were also classified according to Cheney et al:[14] respiratory system, cardiovascular system, medication-related, equipment related, block-related, procedural, iatrogenic, and others not further classified.

Statistical Analysis

Each CA case was matched with four other cases without CA using the proximal convenience method described by Ellis et al,[12] where each CA was matched with one without CA receiving anesthesia on the same day and under similar operating conditions.[12] The ase group was defined as patients who developed perioperative CA, while the other comprised the control group. SPSS 25 was used to analyze the data. Means ± SD were used to represent age and duration of the procedure. Count with percentages were used for categorical variables. The number of intraoperative CAs per 10,000 cases with 95% CIs were calculated. Independent-sample *t*-tests were used to detect statistically significant differences between the case and control groups for age and duration of procedure. Fisher's exact and ?^{2} tests were used to detect significant differences between the two groups for sex, ASA score, type of anesthesia, surgical type, state of emergency of the case, and timing of surgery, followed by calculation of adjusted standardized residuals and post hoc analysis for ASA and surgical type. Univariate binary logistic regression analysis was applied, followed by multivariate binary logistic regression analysis for investigating factors independently associated with perioperative CA. We included age, sex, ASA, duration of surgery, anesthesia type, surgical type, emergency, and timing of operation in the aforementioned regression models. Regression coefficients are reported using ORs, *P*-values, and 95% CIs. All tests were two sided and statistical significance defined as $P<0.05$.

Results

Over the 3 years of the study, 58,303 patients received 73,557 anesthesia administrations at our university hospital for various types of surgery. A total of 27 CAs occurred from the start of anesthesia until 24 hours postoperatively. The overall incidence was 3.7 per 10,000 anesthesia administrations (95% CI 2.3–5.1). Five patients recovered completely from CA, giving a survival rate of 18.5% (0.7 per 10,000 anesthesia administrations), while 22 patients died, giving a death rate of 81.5% (3 per 10,000 anesthesia administrations). The mean age of the CA group was 47.4±23.8 years, ranging between 6 months and 85 years. Of the 27 patients who had CAs, 14 (51.9%) were male and 13 (48.1%) female.

The predominant anesthetic technique was GA (21 cases), while spinal anesthesia was used in five cases with CA incidents. Seven patients had an ASA physical status score of IV, while 7 patents had an ASA score of V. Eighteen cases were emergency surgeries, and nine were done outside working hours (Table 1). Eleven CA incidents were anesthesia-related, as shown in Table S1. With incidence of 1.5 per 10,000 anesthesia administrations, five patients with anesthesia-related CAs recovered, for mortality of 54.5% (0.8 per 10,000 anesthesia administrations). Of anesthesia-related CAs, six were related to the respiratory system (Table S1). All of the four CA cases in the anesthesia-contributing group died (Table S2). Only one patient recovered completely in the 12 cases of CA incidents where anesthesia was neither related nor contributing (Table S3).

Regarding the primary event leading to CA, eleven were related to the cardiovascular system and all these patients died, eight to the respiratory system with three recovering completely, four to spinal block with one recovering completely, two to medications with one recovering completely, one to inflation of abdominal gas during laparoscopic cholecystectomy (procedural) with this patient recovering completely, and one to allergy to cement of a partial hip replacement under spinal block and this patient died. Overall, five patients with CA recovered completely and were discharged home, while one recovered completely but died 5 days later due to complications of lymphoma. Ten of the patients who had recovered from CA died later from hypoxic brain damage. Eleven patients did not recover from CA and died on the table.

When CA cases were compared with the control group, ASA physical status score, cardiovascular surgery, emergency surgery, surgery outside working hours, and duration of surgery were found to be significant risk factors. Age, sex, type of anesthesia, and surgical type were not significant (Table 1). The rate of pediatric CA was 2.4 per

Table 1 Characteristics of cases and controls

		Controls (n=108)	Cases (n=27)	Total	*P*
Age (years)		42.1±24.9	47.4±23.8	43.2±24.6	0.323
Sex	Male	49 (45.4)	14 (51.9)	63 (46.7)	0.546
	Female	59 (54.6)	13 (48.1)	72 (53.3)	
ASA score	I	77 (71.3)	2 (7.4)	79 (53.3)	<0.001
	II	21 (19.4)	7 (25.9)	28 (20.7)	
	III	9 (8.3)	4 (14.8)	13 (9.6)	
	IV	1 (0.9)	7 (25.9)	8 (5.9)	
	V	0	7 (25.9)	7 (5.2)	
Type of anesthesia	GA	93 (86.1)	21 (77.8)	113 (84.4)	0.285
	Other modalities	15 (13.9)	6 (22.2)	21 (15.6)	
Surgery type	Cardiovascular	6 (5.5)	10 (37)	16	<0.001
	ENT	7 (6.5)	1 (3.7)	8	
	General	37 (34.3)	5 (18.5)	42	
	Neurosurgery	4 (3.7)	2 (7.4)	6	
	Obstetric and gynecology	14 (13)	1 (3.7)	15	
	Orthopedic	13 (12)	5 (18.5)	18	
	Pediatric	8 (7.4)	1 (3.7)	9	
	Plastic	6 (5.6)	2 (7.4)	6	
	Urology	13 (12)	0	13	
Emergency	Elective	92 (85.2)	16 (59.3)	108 (80)	0.003
	Emergency	16 (14.8)	11 (40.7)	27 (20)	
Timing	Daytime	94 (87)	18 (66.7)	112 (83)	0.012
	Outside hours	14 (13)	9 (33.3)	23 (17)	
Duration of surgery (minutes)		60.6±60.4	166.9±131.4	81.8±89.8	<0.001

Abbreviations: ASA, American Society of Anesthesiologists; GA, general anesthesia; ENT, ear, nose, and throat.

10,000 cases for age <18 years under GA, but when local and monitored anesthesia care were included, the rate was two per 10,000 cases. For GA, the CA rate in infants was 37.5 per 10,000 cases. When local and monitored anesthesia care were included, the rate was 15.9 per 10,000 cases. The rate of CA in neuraxial block was 3.6 per 10,000 cases and perioperative CA for GA 6.1 per 10,000 cases.

On univariate regression, we found that ASA score (OR 5.1, 95% CI 2.9–9.0; *P*<0.001), cardiothoracic surgery (OR 12.3, 95% CI 3.1–48.9; *P*=0.001), duration of surgery (OR 1, 95% CI 1–1; *P*<0.001), emergency surgery (OR 4.0, 95% CI 1.6–10.1; *P*=0.004), and surgery outside working hours (OR 3.4, 95% CI 1.3–8.9; *P*=0.015) were significantly associated with perioperative CAs. On multivariate regression (Table 2), only ASA score was found to be a statistically independent risk factor of CA (OR 7.6, 95% CI 2.6–22.4; *P*<0.001).

Discussion

In this 3-year prospective study, 27 perioperative CA incidents occurred in 58,303 patients who underwent 73,557

Table 2 Univariate and multivariate regression analysis for factors associated with perioperative CA

	Univariate			Multivariate		
	OR	**95% CI**	**P**	**OR**	**95% CI**	***P***
Age	1.01	0.99–1.03	0.321	1	0.96–1	0.849
Sex (male)	1.3	0.56–3.02	0.547	0.8	0.18–3.46	0.764
ASA score	5.08	2.87–9.02	<0.001	7.58	2.56–22.43	<0.001
Surgery type	—	—	0.027	—	—	0.517
Cardiovascular surgery[†]	12.33	3.11–48.88	<0.001	0.25	0.01–4.46	0.344
Duration	1.01	1.01–1.02	<0.001	1.01	1–1.02	0.085
Anesthesia (GA)	0.57	0.2–0.16	0.29	1.71	0.19–15.18	0.632
Emergency surgery	3.95	1.56–10.05	0.004	6.48	0.53–79.28	0.144
Timing (outside hours)	3.36	1.26–8.92	0.015	1.48	0.1–23.01	0.778

Note: [†]General surgery was used as a reference standard for all comparisons among surgery types.
Abbreviations: ASA, American Society of Anesthesiologists; GA, general anesthesia.

procedures under anesthesia (3.7 per 10,000 anesthesia administrations). The rate of anesthesia-related CA was 1.5 per 10,000 and aesthetic and anesthesia-contributing CA was 0.5 per 10,000 anesthesia administrations. To the best of our knowledge, this is the first study from our hospital and the Middle East in recent years on perioperative CA in a large sample of unselected patients. It is difficult to compare the perioperative CA rate in our study with other studies' results, due to differences in methods, patient population, time span, and the definition of perioperative CA. These factors have resulted in different rates of perioperative CA in the literature.[7,12,15–17]

In a systematic review by Koga et al,[18] in which they performed meta-regression and proportional meta-analysis, anesthesia-related and perioperative CA were 6.4- and 3.2-fold higher in countries with low Human Development Index (HDI) scores than countries with high HDI scores. In the current study, the incidence of anesthesia-related CA was 1.5 per 10,000 anesthesia administrations. In low-HDI countries, the incidence of anesthesia-related CA was 4.5 (95% CI 2.4–7.2) in the 1990s–2010s, while it was 0.7 (95% CI 0.5–1.0) in high-HDI countries. Our results in this study are also comparable to many results in this regard across developed countries.[4,10,12] The incidence of perioperative CA was 3.7 per 10,000 anesthesia administrations in our investigation, which is lower than those of low- and high-HDI countries in the review of Koga et al.[18] This can be explained by their use of a broader definition of perioperative CA, in which they included CA from any cause (patient disease/condition, surgery, and anesthesia) until the seventh day postoperatively. When comparing CA incidence with the control group, we could not find a significant difference based on sex, type of anesthesia, or age. Bras et al[7] found that male sex was a significant risk factor of perioperative CA due to trauma, but this was not found in our study.

Increasing age has been found by different authors to increase the rate of perioperative CA.[7,19] In our observation, ten CA incidents (37%) of all CAs occurred in those aged ≥60 years. Our results indicated that perioperative CA in pediatric patients <18 years old for GA was 2.4 per 10,000 anesthesia administrations and that for infants <1 year old for GA 37.5 per 10,000 anesthesia administrations. When local and monitored anesthesia care were included, the infant CA rate was 15.9 per 10,000 and that of pediatric patients aged <18 years 2.1 per 10,000 anesthesia administrations. However, the number of pediatric patients with CA was too small to compare with other studies, since we had only two cases of CA among infants <1 year of age, in addition to another two children less <18 years of age. Nevertheless, our results indicated that perioperative CA in children aged <1 year is high, as demonstrated by other studies.[4,20] Therefore, we recommend further studies be conducted at pediatric referral centers in order to stratify risk factors of perioperative CA.

Higher CA incidence was found among patients with ASA physical status classifications III–V (18 of 27, 66.7%

of all CA cases), in agreement with other studies.[10,16,21] Nunes et al found in their study that investigated ASA scores in an elderly population that patients with ASA physical status scores of III–V were more likely (14-fold) to suffer intraoperative CA than those with ASA physical status classifications I–II.[19] Ahmed et al[5] found no survival to discharge in patients with ASA scores of IV and V, and most studies in this regard have found increased risk of perioperative CA with increasing ASA grade.[4,21] In our survey, ASA physical status score was the only independent risk factor of CA (OR 7.6, 95% CI 2.6–22.4).

Emergency surgery in the current investigation was found to be a statistically significant risk factor of perioperative CA, and it is always said that working on unprepared patients outside working hours is the main explanation for the high rate of CA.[16,19,21] On multivariate regression, emergency surgery was not found to be a significant independent risk factor of the occurrence of perioperative CA. We found that surgery during working hours carried less risk of of CA and better survival when CA occurred than surgery outside working hours (28% survival rate for working hours versus 11% survival rate for outside working hours), similar to another investigation at a tertiary center.[8]

We found the incidence of perioperative CA for GA was 6.1 per 10,000 anesthesia administrations, while that for spinal block was 3.6 per 10,000 anesthesia administrations. Many studies have confirmed that the rate of perioperative CA with GA is more than that with spinal block.[7,8,22] In this study, there was no statistically significant difference between spinal block and GA. The rate of perioperative CA under spinal block has been reported to be 1.3–18 per 10,000 anesthesia administrations.[23] Although it is claimed that perioperative CA under spinal block is rare, it is not uncommon,[10] and this is explained by the fact that most critically ill, old, or unprepared patients undergo surgery mainly lower-abdomen and orthopedic surgery under spinal block. Another possible explanation for the occurrence of perioperative CA is the autonomic imbalance that results from spinal block, which leads to dilatation of blood vessels, severe bradycardia, and CA.[24,25]

Primary adverse events leading to anesthesia-related and anesthesia-contributing perioperative CA differ among studies. Our results indicated that 53% of anesthesia-related and anesthesia-contributing perioperative CAs were due to respiratory problems, but this rate has not been consistent among studies, with incidence of 7.9%–80%.[26] In a US study, 64% of anesthesia-related CAS were due to complications of airway management.[12] In our observation, only one (3.7%) perioperative CA in the anesthesia-related and -contributing group was due to a cardiovascular event, while Gong et al[10] reported 36.4% of all anesthesia-related CAs were due to cardiovascular problems. On the other hand, in our study 41% of all events leading to perioperative CA were due to cardiovascular problems. These diverse results for CA rates are due to the fact that this is a rare event, and any slight increase or decrease in the number of events will have a considerable impact on the rate reported. Therefore, future meta-analysis is highly encouraged in order to have more figures for the different causes of perioperative CA.

There are several limitations in our study. Firstly, although our department collected the data prospectively, there is the possibility that some data about our reported patients may have been missed.[27] Secondly, 3 years might be considered a relatively short study period. In the literature, the observational periods span 3–18 years.[6,7,17,28] There are several strengths in this study. Firstly, it was a prospective observational study. Secondly, our results of this study are comparable to those from developed countries, thoughfrom a single referral hospital in a developing country.

Conclusion

We found that 53% of anesthesia-related and -contributing CAs were due to respiratory events, 56% of all perioperative CAs were anesthesia-related and anesthesia-contributing, and 22% of all CAs were under spinal anesthesia. ASA physical status score, cardiothoracic surgery, duration of surgery, emergency surgery, and surgery outside working hours were statistically significant risk factors of the occurrence of perioperative CA. ASA physical status score was found to be a major factor in predicting perioperative CA, since patients with higher ASA scores were at significantly higher risk of CA. Based on these findings, we recommend extra precautions when dealing with unprepared patients who have uncontrolled illnesses, especially those who will be undergoing emergency surgery. Moreover, we recommend a national registry of cases of perioperative CA, which will enable to better understand risk factors of CA among patient groups, enabling us to address those risk factors and prevent the occurrence of CA in those patients.

Disclosure

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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