

Van Tıp Derg 28(2): 280-287, 2021 DOI: 10.5505/vtd.2021.02259

Intraoperative Anesthesia-Related Mortality: A 10-

Year Survey in a Tertiary Teaching Hospital

İntraoperatif Anestezi İlişkili Mortalite: Bir Yükseköğretim Hastanesinde 10 Yıllık Bir Araştırma

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ÖZET

Amaç: Bu çalışmada Türkiye'de bir eğitim ve araştırma hastanesinde son 10 yılda anestezi ilişkili mortalite ve intraoperatif mortalite (IOM) insidansları ile birlikte ilişkili risk faktörlerinin belirlenmesi amaçlandı. Materyal ve Metod: 2010-2019 yıllarını içeren operasyonlar retrospektif olarak tarandı. Son 10 yılda anestezi uygulanan 351.930 hastadan 87 nin ex olduğu belirlendi. Ex olan her hasta hasta/durum ilişkili, cerrahi işlem ilişkili ya da anestezi ilişkili mortalite grubundan birine toplandı. Hasta özellikleri yaş, cinsiyet, ASA skoru ve komorbiditeler olarak belirlendi. Cerrahi işlemler minör/intermediate, major ve major kompleks olarak sınıflandırıldı. Anestezi tipi, cerrahi işlem süresi, vazopressor ihtiyacı, invazif monitorizasyon tipi belirlendi.

Bulgular: İntraoperatif mortalitenin genel insidansı 10.000 de 2,47 idi. Anestezi ilişkili mortalite insidansı 10.000 de 0,28 idi. IOM grubundaki hastalar mesai dışı çalışma, cerrahi aciliyet, uzun cerrahi süresi, yüksek komorbidite oranı, yüksek ASA skoru, yüksek komplekli cerrahilere, vp kullanımına, invazif monitorizasyon kullanımına sahipti. Çok yönlü lojistik regresyon modeli cerrahi aciliyeti (p:0,000), vp kullanımı (p:0,002) ve invazif monitörizasyonu (p:0,000) IOM nin bağımsız belirleyicileri olarak tanımladı. Anestezi ilişkili mortalite gelişen hastalarda ise yüksek kompleksli cerrahiler (p: 0.007), cerrahi aciliyet (p: 0.000), vp kullanımı (p: 0.002) ve invazif monitorizasyon (0.000) potansiyel olarak ilişkili özelliklerdi.

Sonuç: Mortalite oranları anestezi ilişkili 10.000 de 0.28, genel IOM 10.000 de 2,47 idi. Anestezi ilişkili mortalitenin havayolu yönetimi veya ilaç verilmesiyle ilişkili olması önleyici tedbirlerin gelişimi için önemlidir. Kötü ASA skoruna bağlı yüksek fatalite oranını azaltmada primer önleme kilit rol oynayabilir. Bu bulgular yüksek riskli ve acil hastalarda tıbbi perioperatif uygulamaları geliştirme ihtiyacını göstermektedir.

Anahtar Kelimeler: Anestezi, mortalite, insidans, ASA skoru

ABSTRACT

Purpose: This study aimed to determine anesthesiarelated mortality and intraoperative mortality (IOM) incidences and the associated risk factors. Material and Methods: The operations between the years of 2010-2019 were retrospectively reviewed. It was found that 87 of 351,930 patients who were anesthetized in the last 10 years died. Each patient who died was recruited into one of the patient/condition-related, surgical-related, or anesthesia-related mortality groups. Patient characteristics were determined as age, gender, ASA PS score, and comorbidities. Surgical procedures were classified as minor/intermediate, major, and major complex. Anesthesia type was recorded. Operative time, the requirement for vasopressor and the invasive monitoring were determined.

Results: The incidence of IOM and anesthesia-related mortality were 2.47 and 0.28 per 10,000 patients, respectively. The IOM group had a higher rate of out-ofhours work, surgical emergency, prolonged operative time, high comorbidity rate, high ASA PS score, major complex surgeries, use of VP, and invasive monitoring. Surgical emergency (p: 0.000), use of VP (p: 0.002), and invasive monitoring (p: 0.000) were independent determinants of IOM. Major complex surgeries (p: 0.007), surgical emergency (p: 0.000), use of VP (p: 0.002), and invasive monitoring (0.000) were potentially associated factors in anesthesia-related mortality. Conclusion: The incidence of IOM and anesthesia-related mortality were 2.47 and 0.28 per 10,000 patients, respectively. The fact that anesthesia-related mortality was associated with drug administration is important for the development of preventive measures. Primary prevention may play a key role in reducing the high fatality. These results indicate the need for improving medical perioperative practices in high-risk and emergency patients.

Key Words: Anesthesia, mortality, incidence, ASA PS

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Geliş Tarihi: 26.11.2020, Kabul Tarihi: 04.02.2021

Introduction

Perioperative cardiac arrest and mortality are the most important and feared complications of surgical operations (1) Not only anesthesia-related events, but also surgical technique and patient / condition-related events cause intraoperative mortality (IOM) (2). Most of IOM is unrelated to anesthesia (2, 3).

Anesthesia has the potential to induce physiological changes that can lead to morbidity and mortality and is widely considered a high-risk activity. However, many researchers have reported that anesthesia-related mortality has decreased for the last two decades. This reduction has been attributed to several safety developments, including improved monitoring techniques, the development and extensive use of practice guidelines, and other systematic approaches to reduce errors (4). Thus, the evaluation of intraoperative mortality enables us to know the quality of anesthesia management.

Anesthesia-related mortality is investigated in some countries (USA, France). Numerous publications on perioperative cardiac arrest have shown significant differences between countries. This heterogeneity stems from the definition of anesthesia-related mortality, age populations, surgical populations, time periods, and studies in different developing countries (5, 6). The evaluation of intraoperative mortality provides information on the quality of anesthesia management, enables preventive measures to be taken, and guides future research (1-3, 7). To our latest knowledge, the number of studies on anesthesia-related mortality in Turkey is limited.

This study aimed to determine anesthesia-related mortality and IOM incidences of a training and research hospital in Turkey in the last 10 years and the associated risk factors.

Materials and Methods

After obtaining the approval of the Non-Invasive Clinical Research Ethics Committee of Hatay Mustafa Kemal University (HMKU) numbered 27.02.2020/10, the operations of all clinics that were performed in the operating room of HMKU Research Hospital between the years of 2010 and 2019 were retrospectively reviewed. Cardiac, noncardiac and obstetric surgeries in all age groups were included in the study. The dead fetus in cesarean operation and the patients who came to the operating room with cardiopulmonary resuscitation and who did not undergo anesthesia and surgery were excluded from the study. Retrospective results were obtained from the Hospital Information Management System and the archives of the Department of Anesthesiology. HMKU Research Hospital is a hospital with 503 beds, 15 operating rooms including all surgical specialties, and 64 ICU beds. Anesthetic care is carried out by 7 anesthesiologist lecturers, 16 residents, and 43 anesthesia technicians. For the objective of the present study, the intraoperative period was defined as the time between the patient's arrival to the operating room and leaving the recovery room. Since patients who received anesthesia but did not die were required to determine the risk factors for mortality, for each patient who died, patients operated just before and after them in the same operating room on the same day were selected, if there were no patients, patients operated in the previous and next days were selected. Thus, 2 other patients who did not die were selected for each patient who died.

Based on the available literature, each patient who recruited into one of died was the patient/condition-related (P/C-IOM),surgical procedure-related (S-IOM), totally anesthesiarelated (TA-IOM), or partially anesthesia-related (PA-IOM) mortality groups. TA-IOM was defined as patients who developed arrest immediately after administering an anesthetic drug to a stable patient or who developed arrest due to all obvious adverse events in airway management. PA-IOM was defined as arrests that occurred in unstable patients (such as hemorrhagic shock) after the administration of an anesthetic induction agent. S-IOM was defined as mortality due to technical surgical problems alone or majorly. P/C-IOM was defined as mortality related to the patient's disease condition. Patient characteristics or were determined as age, gender, ASA PS score, and comorbidities. Surgical procedures were classified as minor/intermediate, major, and major complex depending on the severity of physiological stress, estimated blood loss, invasiveness, and operative time. Minor and intermediate surgical procedures included varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral prostate surgery, parathyroidectomy, and carpal tunnel. Major surgical procedures included craniotomy, colectomy, nephrectomy, bariatric surgery, and splenectomy. Major complex surgical procedures included coronary artery bypass grafting surgery, ruptured aortic aneurysm, radical cystoprostatectomy, mitral valve replacement.

					Patient /				
		Number	Anesthesia-	Surgery-	condition				P/C-
	Total	of	related	associated	related	T-IOM	A-IOM	S-IOM	IOM
Years	IOM	operation	IOM	IOM	IOM	incidence	incidence	incidence	incidence
2010	6	15153	1	0	5	3,95	0,65	0	3,29
2011	2	19732	0	1	1	1,01	0	0,5	0,5
2012	13	25941	1	2	10	5,01	0,38	0,77	3,85
2013	11	22848	1	2	8	4,81	0,43	0,87	3,5
2014	9	37303	0	2	7	2,41	0	0,53	1,87
2015	11	40538	2	2	7	2,71	0,49	0,49	1,72
2016	7	38772	1	2	4	1,8	0,25	0,51	0,98
2017	6	43149	0	3	3	1,39	0	0,69	0,69
2018	12	57535	3	4	5	2,08	0,52	0,69	0,86
2019	10	50959	1	4	5	1,96	0,19	0,78	0,98
Total	87	351930	10	22	55	2,47*	0,28*	0,62*	1,56*

Table 1. Classification, number and incidences of IOM

IOM: Intraoperative mortality; T-IOM: Total IOM; A-IOM: Anesthesia-related IOM; S-IOM: Surgery-related IOM; P/C-IOM: Patient/condition-related IOM;

* 10-year average incidence

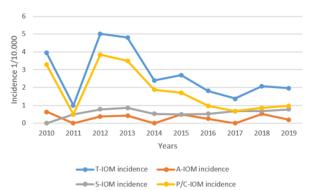


Fig.1. Annual incidences of IOM T-IOM: Total IOM; A-IOM: Anesthesia-related IOM; S-IOM: Surgery-related IOM; P/C-IOM: Patient/condition-related IOM

Anesthesia type was recorded as general, regional, sedoanalgesia, and monitored anesthesia care. In addition, operative time (min), hemodynamic stability, the requirement for vasopressor (VP), invasive monitoring type were determined. Primary ECG rhythm (Asystole, VF, PEA), time of cardiac arrest (induction, maintenance, awakening, recovery room), number of cardiac arrests during the same event, cardiac arrest time associated with standard working hours (08.00-16.00, 16.00-08.00, weekend)) were recorded to determine the etiology and time of the arrest.

Descriptive statistics for the continuous variables were presented as mean and standard deviation while categorical variables as count and percent. Student t test was performed to compare IOM and Non-IOM groups for the continuous variables. Pearson correlation analysis was carried out to examine linear relationships among these variables. In addition, Pearson Chi- square test was used to determine relationships between categorical variables. Multiple logistic regression was performed to determine effective variables on the mortality. Statistical significance level was considered as 5% and SPSS (ver: 23) statistical program was used for all statistical computations.

Results

Incidence of Mortality: During the 10-year course of the study, 351,930 patients were anesthetized at HMKU Research Hospital. A total of 87 patients died. The overall incidence of intraoperative mortality was 2.47 per 10,000 patients (Table 1). Ten patients who developed anesthesia-related mortality were identified (Table 2). One of them was neuraxial anesthesia-related, nine of them were partially anesthesia-related. The incidence of anesthesia-related mortality was 0.28 per 10,000 patients. The changes in incidence by years are shown in Figure 1. Of the patients who died, 36 were Syrian (refugee), 51 were citizens of the Republic of Turkey.

Analysis of mortality-related factors: The mean age of 87 patients who intraoperatively died was 47.16 years. Of these patients, 4 were newborns. One of them was operated for diaphragmatic hernia, one for omphalocele, one for atrial septal defect + patent ductus arteriosus (PDA), and the other for firearm injury (FAI) (craniotomy). Seven patients, excluding newborns, were under 18 years of age. A 1.5-year-old patient underwent laparotomy (Hypovolemic shock, Hirschprung disease, Electrolyte disorder). A 4-year-old patient

	1	,				
Patient n	Age	ASA PS	Arrest	Resuscitation	Time of arrest	Probable cause of mortality
(year)	(years)	class	type	time (minutes)		
1 (2010)	92	3E	VF	65	Post-surgery	Hypovolemic shock, Heart failure
2 (2012)	0	3E	VF	45	Induction	Neonatal respiratory failure, Diaphragmatic hernia
3 (2013)	63	4E	VF	60	Induction	Hypovolemic shock due to massive bleeding
4 (2015)	42	4E	Asistol	50	Induction	Cardiogenic shock following induction
5 (2015)	29	3E	VF	45	Induction	Hypovolemik shock, septic shock
6 (2016)	79	4E	Asistol	45	Induction	Hypovolemic shock, Aort dissection
7 (2018)	20	3E	PEA	45	Induction	Hypovolemic shock due to massive bleeding
8 (2018)	89	4E	Asistol	45	Post-NAA	Hypovolemic shock after spinal anesthesia *
9 (2018)	31	3E	PEA	45	Induction	Hypovolemic shock due to massive bleeding, gunshut injury, Post-CPR
10 (2019)	1,5	3E	Asistol	60	Induction	Hypovolemic shock, electrolyte imbalance, hirschsprung disease

Table 2. Intraoperative mortality related to anesthesia

ASA PS - American Society of Anesthesiology physical status; VF: Ventricular fibrilation; PEA: Pulseless electrical activity; NAA: Neuroaxial anesthesia; CPR: Cardiopulmonary resuscitation

* Totally-anesthesia related

underwent PDA closure with thoracotomy (Aortic Stenosis, Aortic Insufficiency, PDA). A 7-yearold patient from the Syrian civil war (FAI, Multiple Trauma) underwent craniotomy. An 8year-old patient who came from the Syrian civil war underwent thoracotomy and laparotomy (FAI, Post CPR, Multiple Trauma). A 9-year-old patient underwent limb lengthening implantation (Motor Mental Retardation, musculoskeletal deformity). A 12-year-old patient underwent laparotomy (acute abdomen, sepsis). А 12-year-old patient underwent arterial and venous repair (Arteriovenous malformation). Twenty patients, 17 of whom were from the Syrian civil war, were operated on for firearm injury and multiple trauma. Thirty-three patients underwent major complex cardiovascular surgery (CVS). Seven patients were operated on by obstetric surgery. Of the patients, 24.1% were elective and 75.9% were emergency cases.

Compared to the patients in the non-IOM group, the patients in the IOM group had higher rate of out-of-hours work (41.4% vs. 8.7%; p: 0.001), higher rate of surgical emergency (75.9% vs. 24.1%; p: 0.001), longer operative time (p: 0.001), higher rate of comorbidity (97.7% vs. 49.7%; p: 0.001), higher ASA PS score (97.7% vs. 32.4%; p: 0.001), higher rate of complicated surgery (p: 0.001), use of VP (89.7% vs. 20.3; p: 0.001), and higher invasive monitoring use (98.9% vs 33.1%; p: 0.001). There was no difference between the groups in terms of age and gender (Table 3). The multiple logistic regression model defined surgical emergency (p: 0.001), use of VP (p: 0.002), and invasive monitoring (p: 0.001) as independent determinants of IOM (Table 4).

Analysis of factors associated with the risk of anesthesia-related IOM: Major complex surgeries (p: 0.007), surgical emergency (p: 0.001), use of VP (p: 0.002), and invasive monitoring (0.001) were the potentially associated factors in patients who developed anesthesia-related mortality (A-IOM) (Table 5).

Discussion

Incidence of intraoperative mortality: It is difficult to compare the IOM rates in our study with the results of previous studies, as there are

	IOM cases	Non-IOM cases	Р
	(n=87) Count or n (%)	(n=173) Count or n (%)	
Nationalita			0.001*
Nationality Syria (refugee)	37 (42,5%) 50 (57,5%)	32 (20,5%) 124 (79,5%)	0,001*
Türkiye	50 (57,570)	124 (79,370)	
Age**	47,16 (24,630)	43,61 (19,533)	0,210
Gender	38 (43,7%)	78 (45,1%)	0,829
Female	49 (56,3%)	95 (54,9%)	•,•
Male			
Working hours	51 (58,6%)	157 (91,3%) 15	0,001*
Standard	36 (41,4%)	(8,7%)	
Non-standard		. ,	
ASA PS class	2 (2,3%)	117 (67,6%)	0,001*
ASA 1,2	85 (97,7%)	56 (32,4%)	
ASA 3,4,5			
Comorbidity	85 (97,7%)	86 (49,7%)	0,001*
Yes	2(2,3%)	87 (50,3%)	
No			
Urgency	21 (24,1%)	129 (74,6%)	0,001*
Elective	66 (75,9%)	44 (25,4%)	
Urgent			
Type of surgery	10 (11,5%)	73 (42,2%)	0,001*
Minor/intermediate	45 (51,7%)	60 (34,7%)	
Major	32(36,8%)	40 (23,1%)	
Major complex			
Type of anesthesia	83 (95,4%)	131 (75,7%)	
General	3 (3,4%)	27 (15,6%)	0,001*
Regional	1(1,1%)	15 (8,7%)	
Sedoanalgesia			
Duration of surgery**	157,92 (131,502)	103,96 (72,361)	0,001*
Use of vasopressors	78 (89,7%)	35 (20,3%)	0,001*
Yes	9 (10,3%)	137 (79,7%)	
No			
Use of arterial line and CVP monitor	86 (98,9%)	57 (33,1%)	0,001*
Yes	1(1,1%)	115 (66,9%)	
No			

Table 3. Characteristics of intraopetative mortality (IOM) cases and those in the non-IOM comparison group

n: number; ASA PS: American Society of Anesthesiology physical status; CVP: central venous pressure;

 \Box p values < 0.05;

**Mean (Standard Deviation)

significant differences between studies (3) in terms of method, surgical procedures, time periods, and patient population. Despite the differences in methodology, studies (2, 8, 9) have shown mortality rates between 2.4 and 3.5 per 10,000 patients (10, 11). Throughout the 10-year period, 351,930 patients received anesthesia in all surgical clinics of our institution. Over the 10-year period, the IOM rate was 2.47 per 10,000 patients. The A-IOM (TA-IOM + PA-IOM) rate was 0.28 per 10,000 patients (Table 1). These rates included refugee patients, CVS cases, and obstetric cases. In the study by Sobreira-Fernandes D et al. (2) the anesthesia-related mortality rate was 0.65 per 10,000 patients, and in their study in France, Lienhart et al. (12) found that it was 0.54 per 10,000 patients nationwide. There was only one TA-IOM over 10 years and its incidence was 0.028 per 10,000 patients. In the present study, the annual analysis of IOM showed an increase in the incidence due to the cases from the Syrian civil war in 2012-15 (Figure 1).

,		1	2			2	
	В	S.E.	Wald	Р	OR	95% C.I	l.for OR
						Lower	Upper
Urgency	-2,443	,529	21,331	0,000*	,087	,031	,245
Use of vasopressors	-2,042	,667	9,358	0,002*	,130	,035	,480
Invasive monitorizasyon	-4,901	1,325	13,677	0,000*	,007	,001	,100

Table 4. Multivariate analysis of the characteristics potentially associated with mortality

Table 5. Multivariate analysis of the characteristics potentially associated with anesthesia-related mortality

	В	S.E.	Wald	р	OR	95% C.I.:	for EXP(B)
						Lower	Upper
Type of surgery (major complex)	-2,753	1,013	7,393	0,007*	,064	,009	,464
Urgency	-2,443	,529	21,331	0,000*	,087	,031	,245
Use of vasopressors	2,042	,667	9,358	0,002*	7,703	2,082	28,492
Invasive monitorization	4,901	1,325	13,677	0,000*	134,393	10,009	1804,450

OR – odds ratio;

CI - confidence interval;

The incidence of P/C-IOM was higher than the incidence of anesthesia- and surgery-related mortality (Table 1, Figure 1). We can appreciate the significant contribution of the patient's illness to their outcome following perioperative cardiac arrest. This highlights the importance of adequate preoperative preparation in the process in which the anesthesiologist should have a leading role. Arbous et al. (7) mentioned that factors contributing to coma or death determined preventive measures to improve both quality and safety.

Factors associated with the risk of anesthesiarelated mortality: The characteristics of the developed anesthesia-related patients who mortality are shown in Table 2. IOM was not correlated with age and gender. There were no ASA 1, 2, or elective patients in A-IOM. All patients were ASA 3E or 4E. The potentially associated factors with A-IOM were major complex surgeries, surgical emergency, use of VP, and invasive monitoring (Table 5). The emergency of the surgery is a well-established preoperative predictive factor for A-IOM, as shown in our study and other studies (3, 13). In emergency surgeries, mortality risk depends on many factors such as the impossibility of adequate evaluation and preoperative patient preparation-optimization. Sobreira-Fernandes D et al.(2) found that anesthesia-related mortality was associated with medication with 44% and airway/ventilation with 44%. Sprung et al (14) reported these rates as

54.2% and 45.8%, and Newland et al.(5) reported these rates as 40% and 20%. In our study, there were no respiratory causes for A-IOM. In medication-related mortality, 8 patients had a relative overdose for the patient or an abnormal response to a standard dose. In a study designed to evaluate perioperative medication errors and adverse drug events, inappropriate medication doses were reported as the most common type of error. The most common drugs associated with this were reported as propofol, phenylephrine, and fentanyl (15). Sprung et al (14) reported that 37.5% of cardiac arrests developed due to the use of NMB agents. In our study, 8 of the PA-IOM developed during induction and due to relative overdose in unstable patients. Most of the PA-IOMs were associated with cardiovascular dysfunction, in line with the study of Sobreira-Fernandes D et al. (2). It has been shown that targeted fluid therapy reduces postoperative morbidity and mortality in patients with limited cardiovascular reserve (16). Arbous et al. (7) discovered that 52% of A-IOMs were associated with inadequate cardiovascular management and that the most critical period was induction and maintenance. In our study, we determined that 1 patient died after neuraxial anesthesia (NAA), 1 patient died after surgery, and the other 8 patients died during induction. However, no patient died during the maintenance period. One patient died after the administration of NAA. In the loss of sympathetic system-mediated vasoconstriction

 $[\]Box$ p values < 0.05.

after NAA, vascular resistance may be decreased and sympathetic system-mediated loss of cardiac tone can reduce both heart rate and stroke volume. Vasodilation causes peripheral blood to pool and a decrease in the end-diastolic volume (17).

Factors associated with the risk of intraoperative mortality: Factors associated with the risk of intraoperative mortality: Compared to patients in the non-IOM group, the patients in the IOM group (Table 3) had higher out-of-hours work, higher surgical emergency, longer operative time, higher comorbidity rate, higher ASA PS score, major complex surgery, use of VP, higher use of invasive monitoring. Sobreira-Fernandes D et al. (2), on the other hand, found advanced age, high ASA PS score, cardiac diseases, surgery type, and use of VP. In addition, high ASA PS scores, high comorbid diseases, and use of VP were determined as predictive factors. Newland et al. (5) also determined ASA PS, emergency surgery, thoracic and spinal surgery as predictive factors. The predictive factors in our study were a surgical emergency, use of VP, and invasive monitoring (Table 4).

The most important limitation of this study is that it represents only a tertiary research hospital. Another limitation is the lack of follow-up records of the cases from the postoperative period to discharge. Despite the limitations of this study, to our latest knowledge, it is the first retrospective observational study including all age groups and all surgical clinics in Turkey over a 10-year period. Multicenter and standardized studies can contribute to the development of universally acceptable strategies.

Conclusion: The majority of IOMs were caused by anesthesia-unrelated factors. The incidence of anesthesia-related mortality was 0.28 per 10,000 patients and the overall IOM incidence was 2.47 per 10,000 patients. There were no ASA 1, 2, and elective patients in any anesthesia-related mortality. All patients were ASA 3E and 4E. The fact that anesthesia-related mortality was associated with airway management or drug administration is important for the development of preventive measures. Primary prevention may play a key role in reducing the high fatality rate in surgical patients due to poor ASA PS scores. These results indicate the need for improving medical perioperative practices in high-risk and emergency patients.

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Van Tıp Derg Cilt:28, Sayı:2, Nisan/2021