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Impacts of major complications seen after ruptured abdominal aortic aneurysm repair surgery over mortality

Rüptüre aort anevrizma tamiri cerrahisi sonrası gelişen major komplikasyonların mortalite üzerine etkisi

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Abstract

Aim: To present our management approach, complications, and mortality-related risk factors in patients diagnosed with ruptured abdominal aortic aneurysm (RAAA) who underwent open surgery.

Materials and Methods: The charts of 39 patients with RAAA who underwent open surgery between September 2010 and August 2015 were reviewed retrospectively. Study population was divided into two groups; Group-1 (n=14) consisted of cases who died within 30 days after surgery and Group-2 (n=25) consisted of the survivors. Pre-, intra-, and postoperative factors related to mortality and morbidity were noted and statistically analyzed.

Results: Of the 39 patients with a mean age of 68.9±9.5 years, 37 (94.9%) were males. Twelve patients with hypovolemic shock (30.8%) were taken into operation; and 56.4% of all study participants had infrarenal aneurysms. A total of 69.2% of the patients developed at least one complication, while 38.5% developed two or more complications. Two patients (5.1%) died in the intraoperative period, whereas 12 (30.8%) died within 30 days after the operation. Intraoperative aortic cross-clamp time being over than 40 minutes, development of cardiac complications or acute renal failure, and sepsis were found to be independent risk factors related with mortality.

Conclusion: Our study results showed that preoperative hemodynamic regulation, shortening of aortic cross-clamp time and strict adherence to sterilization guidelines can reduce morbidity and mortality rates in cases with RAAA underwent repair surgery.

Keywords: Anesthesia, complication, mortality, renal failure, ruptured abdominal aorta aneurysm.

Öz

Amaç: *Rüptüre abdominal aort anevrizması (RAAA) tanısı alarak açık cerrahi uygulanan hastalarda uyguladığımız tedavi yaklaşımlarının, karşılaşılan komplikasyonlar ve mortalite ile ilişkili risk faktörlerinin sunulmasıdır.*

Gereç ve Yöntem: *Ekim 2010 ile Ağustos 2015 tarihleri arasında RAAA tanısı ile açık cerrahi uygulanan 39 hastanın verileri retrospektif olarak tarandı. Çalışma grubu ikiye ayrıldı; Grup-1 (n=14), cerrahi sonrası ilk 30 gün içerisinde kaybedilen olgulardan oluşurken, Grup-2 (n=25), halen hayatta olanlardan oluşmaktaydı. Mortalite ile ilişkili pre, intra ve postoperatif faktörler kaydedilerek istatistiksel olarak analiz edildi.*

Bulgular: *Ortalama yaşı 68.9±9.5 yıl olan toplam 39 olgunun 37'si (%94.9) erkekti. Oniki hasta (%30.8) hipovolemik şokta iken ameliyata alındı. Tüm olguların %56.4'ünde anevrizma infrarenal yerleşimliydi. Takip döneminde, çalışma olgularının %69.2'sinde en az bir komplikasyon saptanırken, %38.5'inde iki veya daha fazla komplikasyon gözlendi. İki olgu (%5.1) intraoperatif olarak, 12 hasta (%30.8) ise operasyon sonrası ilk 30 gün içinde kaybedildi. İntraoperatif aortik kross-klemp süresi 40 dakikanın üzerinde olması, kardiyak komplikasyonların ya da akut renal yetmezliğin gelişmesi ve sepsis varlığı, mortalite ile ilgili bağımsız risk faktörleri olarak bulundu.*

Sonuç: *Çalışmamızın sonuçları, preoperatif hemodinamik regulasyon, aortik kros-klemp süresinin kısaltılması ve sterilizasyon kılavuzlarına kesin uyum sağlanmasının tamir cerrahisi uygulanan RAAA hastalarında morbidite ve mortalite oranlarının düşürdüğünü göstermiştir.*

Anahtar Sözcükler: *Anestezi, böbrek yetmezliği, komplikasyon, mortalite, rüptüre abdominal aort anevrizması.*

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Introduction

Rupture abdominal aortic aneurysms (RAAAs) surgery has a high probability of serious complications directly linked to death. In elective abdominal aortic aneurysm surgeries, mortality rates are estimated as 5%, while these rates reach 60% in RAAAs (1). Despite the recent advancements in surgery and anesthesia techniques, as well as postoperative intensive care approaches, the mortality rate of RAAA surgery still remains unchanged over the past two decades (2). Several studies have shown that massive blood loss, cardiorespiratory dysfunction, and acute kidney failure are the main risk factors for RAAA-related mortality (3). In addition, several studies have reported that loss of consciousness, preoperative hemoglobin levels, pre- and intraoperative systolic blood pressure scores, intraoperative urine output, intraoperative blood loss, and the amount of transfusion following surgery are the main risk factors for mortality in open RAAA surgery (4,5).

Utilization of agents with minimal effect on patient hemodynamics, transfusing blood products before and after aortic cross-clamping, and adequate fluid replacement play a key role in the management of anesthesia. However, complications such as intestinal and renal ischemia, cardiac failure, sepsis, acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), requirement of massive blood transfusion, and prolonged intensive care unit (ICU) stay are frequent in early postoperative period (6). Herein, we aimed both to evaluate the major complications as well as mortality-related risk factors in patients with a RAAA who underwent open surgery, and to present our management approaches in such cases.

Materials and Methods

The study protocol was approved by the institutional Ethics Committee (15-11/2) and conducted in accordance with the principles of the Declaration of Helsinki. The charts of 39 patients with a diagnosis of RAAA who underwent an urgent open surgery between September 2010 and August 2015 were analyzed retrospectively. The patients were divided into two groups; Group-1 included 14 cases who died within the first month after the operation, and Group-2 included 25 survivors. Electrocardiogram, pulse oximeter, invasive arterial pressure (captured from radial or femoral artery), central venous pressure (captured with a 12F catheter), body temperature, urine output, and respiratory variables were monitored for all patients. Anesthesia induction was obtained with pentothal sodium (5 mg kg^{-1}) in hypertensive patients; with ketamine (1-2 mg kg^{-1}) and midazolam (30-50 μg kg^{-1}) in patients with hemodynamic shock. Rocuronium bromide (1 mg kg^{-1}) was used as a neuromuscular blocker. Anesthesia was maintained using bolus doses of ketamine, fentanyl, midazolam and rocuronium bromide, if required, and propofol (1-2 mg kg^{-1} h^{-1}), and volatile anesthetics (sevoflurane or desflurane 0.5-1 MAC). Aortic grafting interposition was placed by using cross-clamp with abdominal median incision. At the end of the operation, the patients were taken under mechanical ventilation in the cardiovascular ICU; where they were extubated when indicated.

Demographic and baseline characteristics of the patients including age, body weight, height, body mass index (BMI), blood pressure at referral, heart rate, mental status, comorbidities, and smoking habits were recorded for each participant. Intraoperative variables including diameter and localization of the aneurysm, anesthetic agents used, utilization of inotropes and blood products, as well as postoperative variables including mechanical ventilation time, length of stay in ICU, total duration of hospitalization, and postoperative complications were also recorded in all cases. Complications were defined as follows:

Renal complications: 0.3 mg dL^{-1} increase in creatinine levels compared to baseline values, 50% decrease in the calculated creatinine clearance rate, need for renal replacement treatment and dialysis

Cardiac complications: Postoperative myocardial infarction, right or left heart failure (more than two inotropic requirement), atrial or ventricular arrhythmias requiring *treatment*

Respiratory complications: Pneumonia, re-intubation, tracheotomy, and ARDS

Cerebrovascular events: Stroke, transient ischemic attack, cerebral hemorrhage and infarct

Gastrointestinal complications: Ileus, abdominal distention, and mesenteric ischemia

Sepsis: Presence of infection and concurrent systemic inflammatory response

MOF: Failure in two or more organs

Revision: The need for re-operation for any reason

Statistical analysis

Statistical analysis was performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed as mean ± standard deviation (SD), median (range), and percentage (%). The chi-square test and Fisher's exact test were used to analyze the differences between the groups, while independent t-test and Mann-Whitney U test were used for qualitative variables. The Shapiro-Wilk test was performed to analyze normality of the distributed data. Both simple and multiple logistic regression analyses were carried out to analyze pre-, intra-, and postoperative factors related to mortality. The total simple size studied was 39 patients (G*Power Software, Fisher's Exact Test, actual

power: 0.936, sample size Group-1: 14, sample size Group-2: 25). A p value of <0.05 was considered statistically significant.

Results

Of the 39 patients, 37 were males (94.9%). The mean age, body surface area, and BMI were 68.9±9.5 years (range: 46 to 89 years), 1.87±0.14 m^2 (range: 1.57 to 2.15 m^2), and 26.2±4.2 (range: 17.3 to 36), respectively. Twelve patients (30.8%) were taken into operation with hypovolemic shock (mean artery pressure of ≤50 mmHg with presence of confusion). Twelve patients (30.8%) had hypertension, five (12.8%) had coronary artery disease, three (7.7%) had diabetes mellitus, seven (17.9%) had chronic obstructive pulmonary disease, six (15.4%) had cerebrovascular disease, one (2.6%) had chronic renal failure history, and 26 (66.7%) were smokers. Anesthesia induction was carried out with pentothal sodium in 15 patients (38.5%) with hemodynamic stability, while ketamine and midazolam combination was used for the remaining patients. Despite this strategy, one patient (2.6%) developed cardiac arrest during anesthesia induction. Aneurysms were present at the infrarenal level in 56.4% of the patients (n=22) and suprarenal level in 43.6% (n=17). Pre- and postoperative variables of the patients are presented in tables 1 and 2.

Table-1. Demographic and Intraoperative Characteristics of Study Population.

	All Patients (n=39)	Non-Survivor (n=14)	Survivor (n=25)	p value
Age (year)	68.1±9.8	69.7±11.1	67±8.8	0.436
Sex (M/F)	37/2	13/1	24/1	0.766
Weight (kg)	75.8±12.4	74.1±12	76.9±12.9	0.520
Height (cm)	170.3±3.7	170.5±4.1	170.2±3.4	0.828
Smoking (pack-year^{-1})	30.8±28	35.9±30.7	27.4±26.2	0.561
MAP (mm Hg)	65.3±34.5	46.1±31.2	78.2±30.9	**0.005**
HR (bpm^{-1})	83.5±36.5	77.9±45.4	87.3±29.7	0.770
Aneurysm diameter (cm)	8.4±2.6	9±2.9	8±2.2	0.459
Preop Hb (mg dL^{-1})	10.2±2.4	10.2±2.5	10.2±2.5	0.928
Postop Hb (mg dL^{-1})	9.7 (7-13)	9.25 (7-12)	9.8 (8.5-13)	0.167
Preop creatinine (mg dL^{-1})	1.4±0.6	1.5±0.8	1.3±0.5	0.408
Postop Creatinine	1.25 (0.4-3.5)	1.73 (0.7-3.5)	1 (0.4-1.9)	**0.006**

F: female, Hb: Hemoglobin, HR: Heart rate, MAP: Mean arterial pressure, M: Male, Postop: Postoperative, Preop: Preoperative, SD: Standard deviation.
Data are expressed as mean± standard definition, median (min-max), and number of cases.

Table-2. Intraoperative and Postoperative Data of the Study Patients.

	All Patient (n=39)	Non-Survivor (n=14)	Survivor (n=25)	p value
Operative time (min)	220.3±47.2	241.3±43.6	207.8±45.7	**0.008**
Cross-clamp (min)	40.7±8.8	45±8.2	37.9±8.1	**0.006**
MV time (hour)	21 (4-672)	131 (8-672)	14.3 (4-200)	**0.001**
ICU time (hour)	85.5 (8-1128)	252 (8-1128)	85 (19.5-392)	0.321
Days in Hospital	10 (1-47)	11.5 (1-47)	10 (4-25)	0.970
Ketamine (mg)	72.4±76.3	85±91.4	65.8±68.8	0.529
Midazolam (mg)	2 (1-5)	2.5 (1-5)	2 (1-4)	0.316
Pentothal sodium (mg)	143±191	75±149	154±202	0.335
Fentanyl (µg)	125 (0-400)	150 (0-400)	100 (50-400)	0.880
Rocuronium (mg)	98.3±37.9	78±46.4	109±28.5	**0.034**
Intraop ES (Unit)	5.9±3.5	7.5±3.6	4.8±3	**0.027**
Intraop FFP (Unit)	2 (0-11)	4 (1-11)	1.5 (0-4)	**0.001**
Intraop Plt (Unit)	3.5±4.9	4.5±5.8	2.9±4.2	0.430

Cross-clamp: Aortic cross-clamp time, ES: Erythrocyte suspension, FFP: Fresh frozen plasma, ICU: Intensive care unit, Intraop: Intraoperative, MV: Mechanical ventilation, Plt: Random platelets.
Data are expressed as mean± standard definition, median (min-max).

A total of 69.2% patients (n=27) developed at least one complication, whereas 38.5% (n=15) had two or more complications. Respiratory complications were seen in 17 patients (43.6%), cardiac complications in 8 patients (20.5%), renal complications in 14 patients (35.9%); in which 7 patients (17.9%) were taken into hemodialysis, gastrointestinal complications in 7 patients (17.9%), hematological complications in 4 patients (10.3%), sepsis in 6 patients (15.4%), and MOF in 6 patients (15.4%). Two patients (5.1%) required revision surgery. In the simple linear regression analysis, a significant relationship was found between the complications and age (OR: 2.25, p=0.019), mean arterial pressure (OR: 0.93; p=0.006), erythrocyte suspension (ES) utilization (OR: 1.46; p=0.008), fresh frozen plasma (FFP) utilization (OR: 1.51; p=0.014), postoperative hemoglobin values (OR: 0.30; p=0.012), postoperative creatinine values (OR:8.75; p=0.013), and the total duration of surgery (OR: 8.44, p=0.017). However, multiple logistic regression analysis revealed no complication-related risk factor.

Two of the patients (5.1%) died in the intraoperative period, while 12 patients (30.8%) died within 30 days (30-day mortality 35.9%). One of 25 patients was discharged with tracheostomy, while the other one was discharged with hemodialysis dependent. The remaining 23 of 25 patients were discharged with full recovery. Having over 40 minutes of aortic cross clamp time as well as the presences of cardiac complications, acute renal failure, or sepsis were found to be independent risk factors associated with mortality (Table-3).

Table-3. Logistic Regression Analysis of Risk Factors Associated With Mortality.

	Univariate Models				Multivariate Models			
	OR	95% CI		p	OR	95% CI		p
		Low	High			Low	High	
MAP < 60 mmHg	7.2	1.66	31.3	**0.008**	5.9	1	35	0.053
Cross-clamp time >40 min	10.67	1.94	58.7	**0.007**	8.9	1.2	68	**0.034**
ES >5 package	14.1	1.59	124.6	**0.017**	9.7	0.77	122	0.078
Cardiac Complications	8.63	1.43	51.71	**0.018**	23	1.8	300	**0.017**
Acute Renal Failure	13.1	2.71	63.5	**0.001**	19.4	1.8	204	**0.014**
Sepsis	13.33	1.36	130.3	**0.026**	65.7	3.1	1403	**0.007**

ES: Erythrocyte suspension, MAP: Mean arterial pressure.

Discussion

Patients with the diagnosis of RAAA are often taken into operation urgently without a meticulous examination, since their hemodynamic status is highly susceptible for getting worse rapidly (such as cardiac arrest). Despite the recent advancements in intra- and postoperative intensive care and imaging studies, mortality rates still remain unchanged over the past two decades. Several studies have reported a mortality rate of 40 to 60% (2,5,7). In addition, the frequencies of ARDS or transfusion-related pulmonary injury, MOF, infection due to the need for allogenic blood products are still high. Older age, low hemoglobin levels, hypotension, syncope or cardiac arrest, and coagulation disorders have been reported as the major risk factors for mortality (1-6). Cho et al. (8) reported that the amount of intraoperative transfusion and renal failure with oliguria and increased serum creatinine levels (>2.0 mg dL^{-1}) are independent risk factors for mortality. Boyle et al. (9) also found that older age, presence of ischemic electrocardiograph changes, decreased hemoglobin and increased serum creatinine levels as well as loss of consciousness were the main preoperative risk factors for mortality. On the other hand, Grant et al. (10) showed that renal failure was the major predictive factor for mortality. Kim et al. (11) suggested that presence of preoperative shock, need for intraoperative inotropic support, and MOF development were independent risk factors for the postoperative two-day mortality; whereas prolonged aortic cross-clamp time, postoperative renal replacement, and postoperative MOF development were the main risk factors for postoperative 30-day mortality. In their study including a total of 168 patients, Mell et al. (12) estimated the mortality rate as 22.6%. Eleven of these patients died during surgery. The authors divided the study population into two groups, and found that mortality rate was lower in patients with the requirement of ES: FFP ≤2:1 (high FFP group) (39% vs 15%; p <0.03). In the low FFP group, the mortality rate was reported to be four-times higher. Hence, the authors concluded that the use of FFP to correct coagulopathy increased oncotic pressure and reduced mortality by regulating hypoperfusion. In another study including 151 patients, Kauvar et al. (7) recorded their mortality rate as being 44%. Approximately two third of their patients were given massive transfusion and autologous blood transfusion (ABT) was performed in 85 patients. The mortality rate was 34% in the patients with high ABT amounts (AT:ES≥1); whereas it was found to be 55% in the AT:ES <1 group. In the multiple variable analysis, age being >74 years, a preoperative systolic blood pressure of <90 mmHg, a blood loss of >6 L, and low ABT were found to be independent risk factors. In the ES:FFP ≤2 (high FFP) group, the mortality rate was 49%, while it was 40% in the ES:FFP >2 (low FFP) group. As a result, the authors concluded that the mean ES:FFP use was 2.7, and liberal FFP use had no contribution to mortality.

In the present study, 38.5% of the patients developed more than one complication. The most frequent complication was related to respiratory system. The use of inotropic agents, cardiac problems, use of blood products and fluid loading may be the cause of respiratory system complications. Similar to previous studies, it was found that mortality rates and independent risk factors were similar for mortality. Therefore, we suggest that hypovolemia and hypotension must be avoided till the patients are taken into operation, and aortic cross-clamp time must be shortened. Reduced systemic blood volume due to massive blood loss, reduced renal perfusion associated with hypotension, renal ischemic changes, utilization of contrast agents for imaging, and intraoperative suprarenal aortic cross-clamping may be the cause of renal failure in our study.

In addition, we found that the use of excessive amounts of intraoperative ES and FFP were found to be correlated with mortality. In general, ES and FFP were used at a ratio of 1:1 and hemoglobin value was attempted to be kept around 9 to 10 mg dL^{-1}. None of our patients were given ABT, as an ABT system is not available in our facility. Blood protection methods (i.e., ABT, acute normovolemic hemodilution) are applicable in hemodynamically stable patients and are considered

as an alternative, since they can reduce complications related to the use of blood products. Although the use of excessive blood products increased mortality and morbidity, it was not found to be an independent risk factor alone.

Furthermore, controlled hypotension is another anesthetic method and is applied in patients with sufficient intravenous volume (13). Until the aortic cross-clamp is placed, systolic blood pressure is attempted to be kept at 80 to 100 mmHg. The main goal of this method is to avoid blood loss due to high blood pressure and to establish resuscitation with fluid and high FFP as soon as the surgeon manages bleeding (13). In our study, 30.8% patients were taken into operation with hemodynamic instability (i.e., hypovolemic shock). Ketamine was given to such cases as an induction agent due to its tachycardia and hypertension-inducing effects, and the use of inotropic agents was rapidly required. In hypertensive patients, pentothal sodium was used as an induction agent, and nitroglycerin and propofol infusions were initiated to keep systolic arterial blood pressures at a level of 80 – 100 mmHg. Although etomidate is the agent that have minimal effects on patient hemodynamics, it could not be used as it did not exist in our hospital's pharmacy. However, we found no significant difference in the mortality rates between the patients who were taken into operation with hypertension and hypovolemic shock. This can be attributed to the successful resuscitation procedure until placing the aortic cross-clamp.

Conclusion

A RAAA surgery has a high mortality rate. Our study results showed that hypotensive patients, cases receiving excessive blood products, patients with longer aortic cross-clamp time, as well as those developed cardiac complications, acute renal failure and sepsis had higher mortality rates. Preoperative, intraoperative, and postoperative hemodynamic regulation can reduce morbidity and mortality rates in cases underwent open surgery for ruptured *abdominal aortic aneurysm* repair.

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