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Risk Factors for Postoperative Complications after Open Infrarenal Abdominal Aortic Aneurysm Repair in Koreans

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Purpose: Open infrarenal abdominal aortic aneurysm (AAA) repair is performed without event in most cases. However, some patients suffer major morbidities such as renal failure, myocardial infarction, paraplegia, acute respiratory distress syndrome, or hepatic dysfunction. Predicting what kinds of patient populations are more prone to develop such complications may keep the clinicians more attentive to the patients, possibly leading to better prognoses. In this retrospective study, we searched the incidence of and risk factors for postoperative complications and their predictive equations in 162 patients who underwent open infrarenal AAA repair. **Materials and Methods:** Postoperative complications were observed within 30 days. Patient characteristics, types of aneurysm and surgery, and hemodynamic and metabolic variables during the periclamp period were analyzed in relation to postoperative complications using multiple logistic regression analysis. **Results:** Postoperative complications involved the cardiac (20%), pulmonary (14%), renal (13%), gastrointestinal (6%), hepatic (3.1%), and neurologic (2.5%) systems, and bleeding occurred in 1.2% of cases. The mortality rate was 5.6%. The risk factors were age [> 67 yrs, odds ratio (OR) 2.6], clamp duration (> 110 min, OR 4.7), volume of blood transfusion (> 1,280 mL, OR 4.4), emergency operation (OR 1.4), and vasopressor infusion during clamp (OR 1.4). The prediction model was: P(x) = exp(a)/[1 + exp(a)] a;-2.2 + 0.9 × age + 1.5 × clamp duration + 1.5 × transfusion + 0.3 × emergency + 0.4 × vasopressor infusion [insert 1 if risk factors exist, otherwise, insert 0 to each variable]. **Conclusion:** A significant number of complications occurred after infrarenal AAA repair. Therefore, creating a protocol to identify and monitor high risk patients would improve postoperative care.

Key Words: Complications, infrarenal aortic aneurysm, risk factors

INTRODUCTION

The prevalence of abdominal aortic aneurysm (AAA) among elderly people is high, approaching 8% and rising.[1] Infrarenal AAA is the most common type of aortic aneurysm, and approximately 40,000 patients undergo open repair of AAA each year in the United States.[2]

Most open infrarenal AAA operations are performed without event; however, some patients suffer hemodynamic and metabolic instability and major morbidities such as renal failure, myocardial infarction, paraplegia, acute respiratory distress syndrome, and hepatic dysfunction.

However, the incidence and risk factors for various complications have not been fully investigated, especially in Korea. Previous foreign reports on the morbidity and mortality of AAA surgery were based mainly on data from a multicenter questionnaire,[3] or included thoracic or suprarenal AAA.[4] Therefore, in the present study, we tried to find the incidence of postoperative complications and their risk factors, and to obtain a predictive equation from 162 Korean patients who had undergone open infrarenal AAA repair.

MATERIALS AND METHODS

This retrospective study assessed 211 consecutive patients undergoing elective or emergency open surgery for infrarenal AAA from 2000 to 2007. Forty-five patients were disqualified according to the exclusion criteria (aneurysms arising from arteritis associated with *de novo* mycotic or prosthetic graft infections and para-anastomotic aneurysms from prior bypasses), and four patients due to incomplete data (Fig. 1), leaving final enrollment at 162 patients. This study was approved by the institutional review board and the ethics committee of our hospital.

Anesthesia was induced by 4.0-5.0 mg/kg thiopental or 1.5-2.0 mg/kg propofol with muscle relaxant (1 mg/kg vecuronium or 0.6 mg/kg rocuronium) and maintained with isoflurane or sevoflurane carried by a 1 : 1 mixture of O_2 and medical air and an intermittent injection of 2 mg vecuronium. Invasive arterial pressure, central venous pressure (CVP), and urine output were measured in addition to basic monitoring of vital signs.

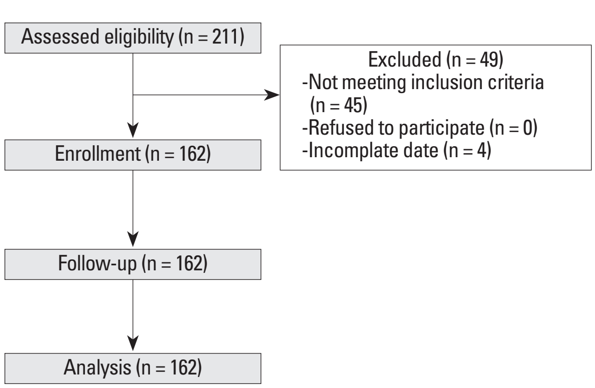

Fig. 1. Flow diagram of patient inclusion.

During the operation, hemodynamic variables were maintained within 20% of baseline values with inhaled anesthetics, drugs, or fluid administration under the attending anesthesiologist's discretion. Red blood cell transfusion was conducted when the patient's hemoglobin fell below 8 g/dL during operation.

Complications were recorded postoperatively for up to 30 days. Renal complications included acute renal failure or newly elevated serum creatinine > 2.0 mg/dL. Pulmonary complications were evaluated by radiologists blinded to the clinical condition of each patient and included pulmonary edema, pulmonary effusion, pneumonia, and atelectasis. Hepatic dysfunction included newly elevated aspartate aminotransferase (AST)(> 150 U/L), alanine aminotransferase (ALT)(> 150 U/L), or bilirubin (> 40 mg/dL) or ischemic hepatitis diagnosed by ultrasonography. Gastrointestinal complications included bowel necrosis and rupture, ileus and obstruction, and ulcer bleeding. Cardiac complications included myocardial infarction and sustained arrhythmia after surgery, which were diagnosed by laboratory tests, electrocardiogram (ECG), or echocardiography. Neurologic complications included cerebral infarction, paraplegia due to spinal cord ischemia, and peripheral neuropathy.

The analysis of the putative risk factors of postoperative complications included characteristics of both patients and surgery, and intraoperative hemodynamic and metabolic variables. Patient characteristic data included age, gender, body weight, height, and underlying disease (hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, cerebrovascular disease, or chronic renal failure). Surgery characteristics included aneurysm site and size, level and duration of aortic cross clamp, type of operation, volume and type of intravenous fluid, and volume of transfusion. Blood pressure, heart rate, CVP, events of decrease of more than 20 mmHg in systolic blood pressure from the baseline values, and amount of administration of dopamine, our main vasopressor during the periclamp period, were analyzed as hemodynamic characteristics. Blood electrolytes and acid-base state were analyzed as metabolic characteristics.

An equation for predicting complications was obtained by multivariate stepwise logistic regression with the five independent risk factors with the lowest p values.

Data analysis

Analysis of variables between patients who developed complications and those who did not was carried out by univariate testing using the Mann-Whitney test for continuous variables, and the Chi-square test for categorical variables with Bonferroni's correction. Cut-off values for each variable were obtained using the minimum p value approach. Independent prognostic factors were then evaluated by multivariate stepwise logistic regression and were reported as calculated odds ratios (OR) with 95% confidence intervals. An equation for prediction of complications was obtained and the area under the receiver operating characteristic (ROC) curve was assessed for discriminatory power in this predictive model.

RESULTS

Characteristics of both patients and surgeries are shown in Table 1.

The median blood loss was 1,300 mL (range: 200-25,000 mL). During surgery, 4,198 ± 2,385 mL of crystalloid, 892 ± 496 mL of colloid, and 640 mL (range: 0-16,000 mL) of red blood cell transfusion were administered. During clamp, 1,387 ± 994 mL of crystalloid, 531 ± 319 mL of colloid, and 457 ± 836 mL of red blood cells were administered. The transfused blood included cell salvage blood and homologous bank blood.

Twenty-nine percent of patients showed a decrease in systolic blood pressure of more than 20 mmHg after declamp; however, the overall mean hemodynamic changes during the periclamp period were not clinically significant (Fig. 2). The mean amount of dopamine administered was 5.1 ± 3.2 μg/kg/min.

During the clamp period, 31% of patients required vasodilator therapy (nitroglycerin or nitroprusside) and 26% required vasopressor infusion (dopamine). On the other hand, during the declamp period, 17% required vasodilator infusion and 41% required vasopressor infusion, respectively.

Changes in pH and electrolyte levels during surgery were not clinically significant (Table 2).

Elevated levels of lactate dehydorgenase (LDH) and creatine kinase (CK) indicate muscle injury and elevated creatine kinase isoenzyme (CKMB) indicates cardiac injury. At 24 hours after surgery, LDH was elevated from a median value of 372 IU/L (range: 51-1,441 IU/L) to 489 IU/L (range: 59-5,401 IU/L)($p < 0.05$), CK from a median value of 77.5 IU/L (range: 23-1,088 IU/L) to 120 IU/L (range: 23-10,570 IU/L)($p < 0.05$), and CKMB from a median value of 1.06 ng/ml (range: 0.03-48.5 ng/mL) to 1.32 ng/mL (range: 0.15-213.6 ng/mL) ($p < 0.05$), compared with preoperative levels. These levels of elevation were not considered clinically significant, but box plots showed that a few patients developed severe muscular or myocardiac injury (Fig. 3).

Renal function was not affected by surgery, as indicated by preoperative and postoperative levels of bilirubin (BUN) (18.2 ± 8.7 and 15.3 ± 10.3 mg/dL) and creatinine (1.2 ± 0.8 and 1.2 ± 0.8 mg/dL, respectively).

The overall incidence of postoperative complications during the first month was 34%. Cardiac complications were the most common (20%), followed by pulmonary (14%), renal (13%), gastrointestinal (6%), hepatic (3.1%), and neurologic (2.5%) complications, and bleeding (1.2%).

Table 1. Characteristics of Patients and Surgery

Age (yrs)	67.6 ± 9.3
Gender (M / F)	138 / 24 (85% / 15%)
Height (cm)	165.8 ± 7.1
Weight (kg)	65.9 ± 10.1
Underlying diseases	
Hypertension	112 (69%)
Coronary artery disease	45 (28%)
Diabetes mellitus	26 (16%)
Chronic obstructive pulmonary disease	16 (10%)
Cerebrovascular disease	13 (8%)
Chronic renal failure	10 (6%)
Emergency	21 (13%)
Aneurysmal Diameter (cm)	6.2 ± 1.6
Type of operation	
Aortoiliac bypass	
Unilateral	8 (5%)
Bilateral	84 (52%)
Primary repair	57 (35%)
Aortofemoral bypass	
Unilateral	4 (2%)
Bilateral	6 (4%)
Etc.	3 (2%)
Renal revascularization	6 (4%)
Clamp level	
Infrarenal	150 (93%)
Suprarenal	10 (6%)
Supravisceral	2 (1%)
Clamp duration (min)	89.4 ± 39.7
Operation time (min)	302 ± 106
ICU ventilation (hrs)	28.0 ± 152.7
ICU stay (days)	4.0 ± 7.2
Hospital stay (days)	16.6 ± 12.0

Values are expressed as mean ± SD or number of patients (%)

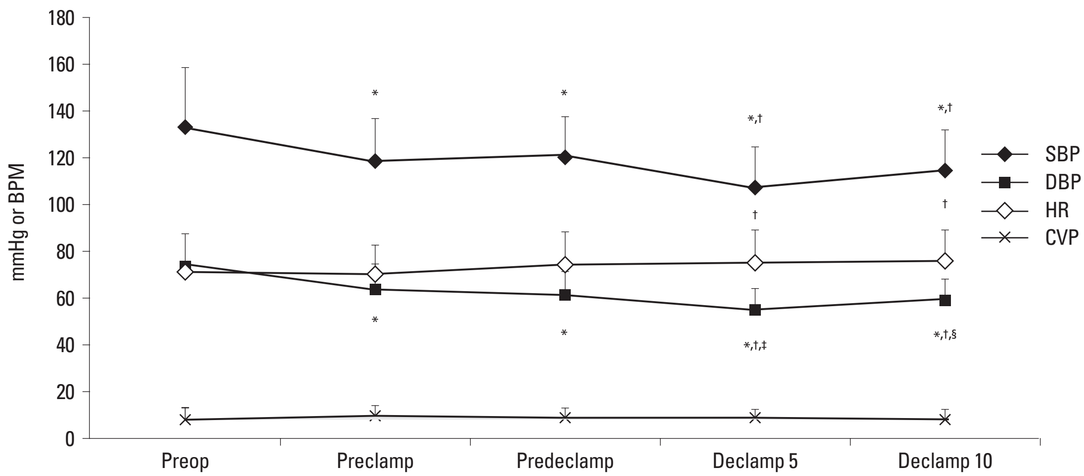

Fig. 2. Hemodynamic changes during the operation. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; CVP, central venous pressure; Declamp 5, 5 min after declamp; Declamp 10, 10 min after declamp; BPM, beat per minute. *$p < 0.05$ compared to Preop. †$p < 0.05$ compared to Preclamp. ‡$p < 0.05$ compared to Predeclamp. §$p < 0.05$ campared to Declamp 5.

Table 2. Changes in pH, Electrolyte Concentrations and Temperature During Operation

	Preop	Preclamp	Predeclamp	Declamp 5	Declamp 10
pH	7.41 ± 0.11	7.42 ± 0.07	7.37 ± 0.07*,†	7.33 ± 0.08*,†,‡	7.34 ± 0.07*,†,‡
Na^+ (mmol/L)	138.9 ± 4.8	138.6 ± 4.3	137.9 ± 4.5	137.6 ± 4.4	138.3 ± 4.3
K^+ (mmol/L)	3.8 ± 0.5	3.7 ± 0.4	3.7 ± 0.7	3.9 ± 0.6†,‡	3.9 ± 0.7†,‡
Ca^{++} (mmol/L)	0.95 ± 0.16	0.98 ± 0.19	0.88 ± 0.17†	0.92 ± 0.16	0.88 ± 0.16†
Temp (°C)	35.9 ± 0.7	35.7 ± 0.6	36.0 ± 0.4	36.0 ± 0.4	36.0 ± 0.4

Preop, preoperation; Declamp 5, 5 min after declamp; Declamp 10, 10 min after declamp.
Values are expressed as mean (SD).
*$p < 0.05$ compared to Preop.
†$p < 0.05$ compared to Preclamp.
‡$p < 0.05$ compared to Predeclamp.

The mortality rate was 5.6% (Table 3).

Risk factors for postoperative complications found by univariate analysis were age, emergency operation, duration of clamp and operation, the amount of transfusion during clamp and operation, the amount of crystalloid during clamp, blood loss and administration of dopamine during clamp (Table 4).

Multivariate logistic regression analysis showed that age, duration of clamp, volume of blood transfusion during the operation, emergency operation, and infusion of vasopressor during clamp were independent risk factors with the lowest p values. The cutoff values were 67 years for age, 110 minutes for clamp duration, and 1,280 mL for blood transfusion by the minimum p value approach (Table 5).

The prediction model was: P(x)=exp(a)/[1+ exp(a)]

a;-2.2 + 0.9 × age + 1.5 × clamp duration + 1.5 × transfusion + 0.3 × emergency + 0.4 × vasopressor infusion during clamp (Insert 1 to each variable when Age > 67 years old, clamp duration > 110 min, red cell transfusion > 1,280 mL, emergency, use of vasopressor infusion during clamp. Otherwise, insert 0 to each variable).

The AUC value was 0.78 [95% confidence interval (CI) 0.71-0.85] for this model (Fig. 4). For quick on-site risk evaluation for each patient, we have provided a simplified calculation table (Table 6).

Other variables such as the size of the aneurysm, gender, hemodynamic instability (decrease in systolic blood pressure of > 20 mmHg after declamp), metabolic instability (change in pH of > 0.2 and in K^+ of > 0.5 mmol/L after declamp), body mass index (BMI), and preoperative medical conditions did not affect the incidence of postoperative complications.

DISCUSSION

In previous reports, mortality rates for elective infrarenal AAA repair were 0%,[5] 2.5%,[6] and 3.1%.[7] If emergency cas-

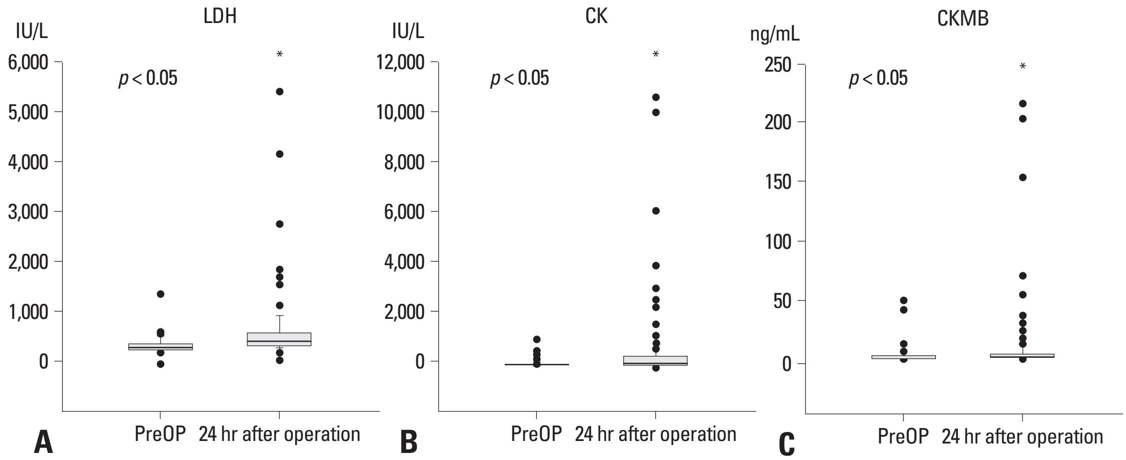

Fig. 3. Box plot of LDH, CK, and CKMB. *$p < 0.05$ compard to PreOP. LDH, lactate dehydorgenase; CK, creatine kinase; CKMB, creatine kinase isoenzyme.

Table 3. Incidence of Complications

Organ	Incidence	Disease entity	Number
Heart	33 (20%)	Infarction	24
		Arrythmia	7
		Heart failure	2
Lung	22 (14%)	Pleural effusion	5
		Pulmonary edema	7
		Atelectasis	2
		Pneumonia	8
Kidney	21 (13%)	Acute renal failure	9
		Cr > 2.0 mg/dL	12
Gastrointestinal	10 (6%)	Bowel edema	1
		Ileus	3
		Upper GI bleeding	2
		Ischemic colitis	1
		Bowel necrosis	3
Liver	5 (3.1%)	AST (> 150 U/L), ALT (> 150 U/L), or total bilirubin (> 40 mg/dL)	
Neurologic	4 (2.5%)	Subarachnoid hemorrhage	1
		Neuropathy	2
		Cerebral infarct	2
Bleeding	2 (1.2%)		
Death	9 (5.6%)	Multiorgan failure	7
		Subarachnoid hemorrhage	1
		Intraoperative cardiac arrest	1

Values are the number of patients. This result comes from one month of observation. Cr > 2.0 mg/dL: patients who showed Cr > 2.0 mg/dL without the need of hemodialysis. One patient showed peripheral polyneuropathy and cerebral infarct simultaneously.

es were included, as in ours, the mortality rate was 7.3 %.[3] Morbidity rates were reported as 37%[7] and 40%.[5] These results were in line with ours.

It is noteworthy that remote organs such as the lungs and intestines were relatively common targets for complications, occurring in 14% and 6% of patients, respectively. Except for direct postoperative complications such as pulmonary atelectasis, many cases of complications seem to be related to systemic inflammatory responses after lower limb ischemia and reperfusion following infrarenal aortic surgery.[8-13] Acute lung injury and acute respiratory distress syndrome (ARDS) as a remote sequela of severe lower torso ischemia-reperfusion have been demonstrated experimentally[8] and clinically.[9] The gastrointestinal system is also

Table 4. Risk factors for Postoperative Complications by Univariate Analysis

Variables	Odds ratio	95% CI	*p* value
Age (> 67 yrs)	2.9	1.4 - 6.1	0.03
Emergency operation	4.9	0.8 - 13.0	0.00
Duration of Clamp (> 110 min)	4.7	1.7 - 13.0	0.00
Duration of operation > 300 min	2.0	1.0 - 3.9	0.01
Crystalloid during clamp > 1,500	2.9	1.4 - 5.8	0.01
Red blood cell transfusion during clamp > 640 mL	4.2	1.8 - 9.8	0.00
Estimated blood loss > 2,000 mL	4.8	2.2 - 10.4	0.00
Red cell transfusion during operation > 1,280 mL	6.3	3.0 - 13.4	0.00
Dopamine during clamp	2.5	1.2 - 5.2	0.01

CI, confidence interval.
Duration of clamp and operation were related variables, so the duration of clamp that showed a lower *p* value was chosen for further multivariate evaluation. Crystalloid and red blood cell transfusion during clamp, estimated blood loss and red blood cell transfusion during operation were related variables, so red blood cell transfusion during the operation that showed the lowest *p* value was chosen for further multivariate analysis.

Table 5. Risk factors for Postoperative Complications by Multivariate Analysis

Variables	Odds ratio	95% CI
Age (> 67 yrs)	2.5	1.1 - 5.8
Duration of Clamp (> 110 min)	4.7	1.7 - 13.0
Transfusion during operation (>1,280 mL)	4.4	1.7 - 11.1
Emergency operation	1.4	0.6 - 3.4
Dopamine during clamp	1.4	0.4 - 4.8

CI, confidence interval.

Table 6. Simplified Calculation of Risk Prediction Model

	Risk factors	Risk (%)
Major risk factors	Age (> 67 yrs)	21
	Clamp duration (> 110 min)	33
	Transfusion during operation (> 1,280 mL)	33
Minor risk factors	Emergency operation; yes	13
	Vasopressor during clamp; yes	14
All 3 major risk factors		85
All 3 major risk factors with one or two minor risk factors		90

Two major risk factors can be simply added. Minor risk factors add 8%. For example, if age (> 67 yrs) and Clamp duration (> 110 min) co-exist, the sum of risks is 54% (21% + 33%) and if age (> 67 yrs) and emergency operation co-exist, the sum of the risks is 29% (21% + 8%).

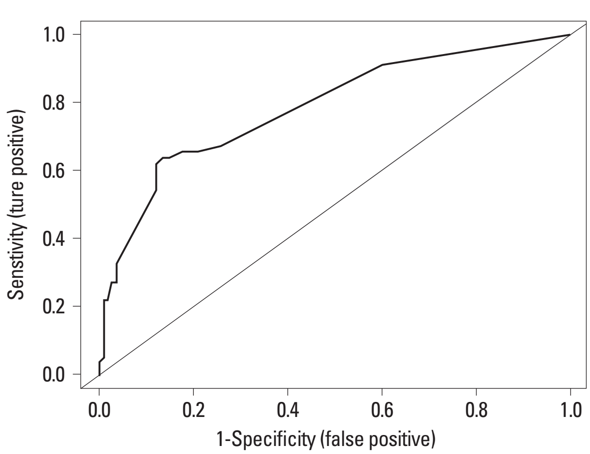

Fig. 4. The area under the receiver operating characteristic (ROC) curve. The AUC value was 0.78 (95% CI 0.71-0.85) for this model. AUC, area under the curve; CI, confidence interval.

commonly targeted for injury after ischemia-reperfusion below the infrarenal aorta.[11-13]

Renal complications were not rare (13%) despite the clamp position's location mostly below the renal artery. Therefore, maintaining adequate intravascular volume is important. However, embolization of atherosclerotic debris to the kidneys and surgical trauma to the renal arteries can also contribute to renal dysfunction.[14,15] Preoperative BUN and creatinine were not related to postoperative renal complications.

Neurologic complications such as paraplegia or paraparesis due to spinal cord ischemia have been reported in AAA surgery.[16,17] However, the lower extremity weakness in our patients were caused by femoral neuropathy, cerebral infarct, or polyneuropathy, rather than by spinal cord ischemia. We postulate that the risk of spinal cord ischemia might be minimal in infrarenal AAA surgery, and rather, traction injuries to lumbosacral nerve roots during the operation might have caused peripheral nerve injury, most commonly exhibited in our study as a femoral nerve deficit.[17]

There have been few studies on hemodynamic and metabolic changes during the periclamp period of infrarenal aneurysm repair. In our study, clamping at the infrarenal level was associated with minimal hemodynamic and metabolic changes. However, 29% of patients showed a decrease in systolic blood pressure of more than 20 mmHg after declamp. These patients, however, did not show a higher rate of postoperative morbidity.

In the present study, age, clamp duration, volume of blood transfusion during operation, emergency status, and vasopressor infusion during clamp were accepted as independent risk factors according to the multivariate analysis. In Bayly, et al's study,[3] a multicenter prospective audit of 177 hospitals, data were collected over a 4-month period by a questionnaire for patients undergoing elective or urgent surgery for infrarenal AAA or aortoiliac occlusive disease. Factors that increased the risk of death included: age over 74, urgent surgery, limited exercise capacity, a history of severe angina or cardiac failure. Another study of 130 patients over 6 consecutive years showed age, presence of heart failure, and chronic renal failure as risk factors.[7] However, a retrospective study of 100 patients treated by an open AAA repair at a single institution showed that complications were not predictable, but were related only to the presence of an excessive cumulative positive fluid balance on postoperative days 0 to 3.[5]

In our study, old age and emergency operation were major risk factors for morbidity, which is in line with a previous study.[3] Clamp duration, volume of transfusion, and vasopressor infusion during clamp were not shown to be risk factors in previous reports, possibly because these are intraoperative factors. However, these factors were more important than other variables such as patient's underlying diseases, fluid balance, aneurysmal or surgical factors in predicting postoperative complications.

Severe angina or heart failure, another risk factor identified in previous studies[3,7] was not observed in our study population. Instead, vasopressor infusion during clamp was a risk factor. We can assume that patients with potential coronary insufficiency or heart failure that is not apparent on routine preoperative evaluation were unable to withstand the increased left ventricular wall stress caused by clamping, and may have required vasopressor infusion during the clamping period.

A history of chronic renal disease, which was suggested as a risk factor in another study,[7] was not found to be related to morbidity, and postoperative renal function did not change significantly in our study.

We obtained a predictive equation for postoperative complications and have also provided a simplified risk table derived from the equation for quick on-site risk calculation for individual patients. In the simplified risk table, major risk factors were age, clamp duration, and blood transfusion. Minor risk factors were emergency and vasopressor infusion during clamp. Two major risk factors can be simply added together. Each minor risk factor adds 8% to other coexisting risks (Table 6). This on-site risk calculation can direct us regarding how intensively to monitor and how proactively to manage patients during the operation and intensive care unit (ICU) care.

One limitation of our study was the use of serum creatinine as a single parameter for renal complications, as it can estimate glomerular filtration rate (GFR) but is far from being accurate. Therefore, the incidence of renal complications (acute renal failure or newly elevated serum creatinine > 2.0 mg/dL) might have been under- or overestimated.

Prospective studies under standardized anesthesia and operation condition are needed to validate our prediction model.

In conclusions, open infrarenal AAA repair shows relatively stable hemodynamic and metabolic status during surgery; however, a significant number of complications occurred after operation. Our prediction model may help to identify patients at high risk for postoperative complications and to encourage surgeons to pay more attention to these patients.

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