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Original Article

Treatment Outcomes and Risk Factors for In-Hospital Mortality in Patients with Acute Aortic Occlusion

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Purpose: The aims of the present study are to determine the outcomes after acute aortic occlusion (AAO) and analyze the risk factors for in-hospital mortality.

Materials and Methods: We retrospectively analyzed 24 patients who were diagnosed with AAO from 2002 to 2017 in our registered data. Demographic and radiologic characteristics of AAOs were retrospectively collected. Perioperative treatment outcomes including in-hospital mortality were also assessed and the risk factors of in-hospital mortality were analyzed.

Results: The median symptom duration was 21 hours. Five patients had complete paraplegia and 10 patients (41.7%) were initially evaluated for central nervous system disorders instead of acute arterial occlusion. The etiology was determined to be aortoiliac thrombosis in 17 patients (70.8%) and embolic occlusion in 7. Surgical revascularization was performed in 23 patients, and one patient did not receive any treatment. The overall in-hospital mortality was 34.8% (8/23) and 30-day mortality was 26.1%. In the univariate analysis, age (P=0.040), preoperative renal insufficiency (serum creatinine over 1.5 mg/dL at the time of presentation) (P=0.008), postoperative acute kidney injury (need for dialysis or an increase in serum creatinine of >50.0% within 48 hours) (P=0.006), combined external iliac artery occlusion (P=0.019) and combined bilateral internal iliac artery occlusion (P=0.039) were associated with in-hospital mortality.

Conclusion: A substantial number of AAO patients were initially evaluated for a central nervous system lesion, which led to a delay in diagnosis. Thus, vascular examinations should always be performed in every patient presenting with lower limb neurologic deficits. Age, perioperative renal function, and combined iliac artery occlusion were associated with the prognosis of AAOs.

Key Words: Abdominal aorta, Thrombosis, Embolism, Mortality, Risk factors

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INTRODUCTION

Acute aortic occlusion (AAO) is an infrequent clinical entity but is considered as devastating condition with significant morbidity and mortality. It may result from aortic saddle embolism, in situ thrombosis of a previously atherosclerotic abdominal or iliac arteries, sudden thrombosis of an aortic aneurysms, or a traumatic distal aortic intimal flap. Even with successful revascularization, the reported 30-day mortality ranges from 20.0% to 75.0% due to vari-

ous reasons including reperfusion injury [1-6]. The common clinical presentations of patients with AAO include sudden onset lower extremity pain, paralysis with altered sensation, and mottled discoloration of the skin. In some cases, paraplegia of lower extremities can be identified at the first presentation, and occasionally, the diagnosis may be delayed due to initial evaluation for a central nervous system lesion [7,8].

Due to the rarity of this condition, the characteristics and clinical findings of AAOs are largely based on case series and reports from several decades ago. Additionally, the risk factors associated with in-hospital mortality are not well understood.

The purpose of this study was to investigate the characteristics of concurrent series of AAOs, evaluate the therapeutic outcomes of patients with AAOs, and identify possible risk factors for in-hospital mortality in AAO patients.

MATERIALS AND METHODS

Between January 2002 and December 2017, 24 consecutive patients presenting with AAOs at a single major tertiary hospital in South Korea were eligible for inclusion in the study. The present study was initiated after obtaining approval from the Institutional Review Board at Kyungpook National University Hospital. Informed consent for review of the medical records was exempted by the board because this was a retrospective study. Patients with AAOs suffering from arterial trauma and dissection and those with AAOs secondary to graft occlusion were excluded from this study. Of the note, during the study period, there was one patient with acute graft occlusion after an abdominal aortic aneurysm repair and two patients with AAOs secondary to traumatic dissection of the abdominal aorta. These three patients were not included in the analysis.

Twenty-three patients were admitted through the emergency department with acute onset symptoms, including a loss of sensation, weakness, pain, paleness, and lack of a pulse, and the remaining 1 patient was referred to our department after admission for another disease. “Acute” was defined as symptoms being present for less than 2 weeks.

The diagnosis of aortic occlusion was made by contrast enhanced computed tomography (CT) in all patients. Information regarding demographics, preoperative laboratory findings and images, operative and postoperative characteristics, and the necessity for fasciotomy and amputation were collected from the electronic medical records. Congestive heart failure, coronary artery disease, arrhythmias, valvular heart disease, peripheral artery disease, cerebrovascular accidents/transient ischemic attacks, and chronic renal insufficiency were considered present if these were documented in the electronic medical record. Hyperlipidemia, diabetes, and hypertension were determined by documentation in the electronic medical record or by the documented use of medications used to treat these conditions. In our series, all the patients underwent preoperative CT scan. The extent of the occlusion, the presence of combined visceral and lower extremity arterial occlusive disease, and the occurrence of combined aneurysms was also reviewed.

The general treatment protocol for treatment included intravenous heparin (3,000 to 5,000 IU as bolus injection) administered at the time of diagnosis and emergent surgery, involving either bypass surgery or thromboembolectomy. The decision to perform bypass surgery or thromboembolectomy was determined based on the CT findings, such as suspected chronic arterial occlusive patterns of the aortoiliac arteries, and the clinical history, such as the presence of claudication.

Preoperative renal insufficiency was defined as a serum creatinine greater than 1.5 mg/dL at the time of presentation. Postoperative acute kidney injury (AKI) was defined as a need for dialysis or an increase in serum creatinine of >50.0% within 48 hours. Postoperative laboratory tests including aspartate aminotransferase, serum myoglobin, and creatinine kinase were usually monitored for 3 days after surgery.

After surgery, the patients were admitted to the intensive care unit and received general care to maintain blood pressure and urine output. In patients who developed acute renal failure despite of postoperative supportive care, such as fluid resuscitation, diuretics and urine alkalinization, continuous renal replacement therapy (CRRT) or hemodialysis (HD) was performed. Beginning in 2012, a femoral dual lumen catheter for dialysis was inserted intraoperatively in patients suspected of developing acute renal failure. Postoperative hypotension was defined as systolic blood pressure that remained below 80 mmHg despite of intravenous inotropic agent.

The outcomes of interest included the clinical and radiologic characteristics of AAOs, suspected causes, early outcomes including in-hospital mortality, and suspected risk factors for in-hospital mortality. Clinical history at the time of presentation, physical examination, CT findings, postoperative echocardiography, and operative findings were used to classify the etiology of AAOs as thrombotic or embolic.

A univariate analysis was performed to identify the risk factors for postoperative in-hospital mortality. Categorical variables were subjected to the chi-square test (for adequately sized samples) or Fisher’s exact test (for smaller samples). For continuous variables with a normal distribution, the data were subjected to Student’s independent t-tests. Given the potential for skewing, group comparisons

of age were based on the nonparametric Mann-Whitney U-test. Kaplan-Meier plots were used to assess survival rates. A multivariate analysis could not be performed because of the small sample size. All the calculations were performed with PASW Statistics ver. 20.0 software (IBM Co., Armonk, NY, USA), with statistical significance set at $P<0.05$.

RESULTS

1) Patient characteristics and suspected causes of AAOs

The median patient age was 70 years (range, 31-86 years), and 17 patients (70.8%) were male. Detailed clinical characteristics are described in Table 1. The median symptom duration was 21 hours (range, 2-240 hours). At initial presentation, lower extremity motor/sensory deficits were present in 22 patients (91.7%), and 5 patients (20.8%) had complete paraplegia. Eighteen patients (75.0%) complained of resting pain on at least one side of their lower extremities. Aortoiliac thrombosis was felt to account for 17 patients (70.8%) of the AAO patients and embolic occlusion in seven patients including one patient caused by cardiac myxoma.

2) Diagnostic methods and imaging findings at initial presentation

During the initial diagnostic process at emergency department, 10 patients (41.7%) were mistakenly evaluated for a central nervous system lesion. Without evaluation for acute arterial occlusion, these patients were examined by a neurologist or neurosurgeon to assess the central nervous system disorders. These 10 patients initially received a spinal X-ray and five patients underwent magnetic resonance imaging of the spine.

Contrast enhanced CT was performed as a part of the diagnostic evaluation in all patients. The level of aortic occlusion was in the infrarenal abdominal aorta (below the renal arteries) in 23 patients and at the aortic bifurcation level (below the inferior mesenteric artery [IMA]) in 13 patients. One patient presented with aortic occlusion that extended above the renal artery but below the superior mesenteric artery. With respect to the iliac arteries, all the occlusions involved at least the bilateral common iliac arteries. Eleven patients had bilateral external iliac artery (EIA) occlusion, five patients had unilateral EIA occlusion, and eight patients had patent bilateral external iliac arteries. Infrainguinal femoropopliteal arterial occlusion also occurred in 19 patients, and bilateral femoropopliteal occlusion was present in 4 patients. The detailed findings from the CT

Table 1. Clinical characteristics of the patients

Characteristic	Patients (n=24)
Age (y)	70±14
Male	17 (70.8)
Symptom duration (h)	21 (2-240)
Coexisting medical condition	
Hypertension	12 (50.0)
Diabetes mellitus	8 (33.3)
Coronary artery disease	7 (29.2)
Congestive heart failure	5 (20.8)
Dyslipidemia	15 (62.5)
Atrial fibrillation	10 (41.7)
Cerebrovascular accident	6 (25.0)
Chronic obstructive pulmonary disease	2 (8.3)
Current smoker	5 (20.8)
Preoperative renal failure	5 (20.8)

Values are presented as median±standard deviation, number (%), or median (range).

Table 2. Radiological findings in acute aortic occlusion patients

Radiological finding	Patients (n=24)
Level of aortic occlusion	
Suprarenal aorta	1 (4.2)
Infrarenal aorta (between the renal artery and the IMA)	10 (41.7)
Aortic bifurcation (below the IMA)	13 (54.2)
Level of combined iliac artery occlusion	
Bilateral common iliac arteries	24 (100.0)
Unilateral external iliac artery	5 (20.8)
Bilateral external iliac arteries	11 (45.8)
Unilateral internal iliac artery	10 (41.7)
Bilateral internal iliac arteries	10 (41.7)
Combined common femoral artery occlusion	6 (25.0)
Bilateral	1 (4.2)
Unilateral	5 (20.8)
Combined infrainguinal arterial occlusion	19 (79.2)
Unilateral FPA	15 (62.5)
Bilateral FPA	4 (16.7)
Combined visceral infarction	
Renal infarction	5 (20.8)
Splenic infarction	1 (4.2)
Combined aneurysm	
Descending thoracic aortic aneurysm	1 (4.2)
Abdominal aortic aneurysm	2 (8.3)

Values are presented as number (%).
IMA, inferior mesenteric artery; FPA, femoropopliteal artery.

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scans are described in Table 2.

3) Surgical details

One patient did not receive any treatment and died 4 days after diagnosis. Besides one patient, 23 patients underwent surgical treatment. Ten patients underwent bypass surgery including aortobifemoral bypass in 8 patients and axillobifemoral bypass in 2 patients. The remaining 13 patients underwent thromboembolectomy. Thromboembolectomy was performed via a bilateral femoral approach in 11 patients and a bilateral femoral and transabdominal approach in 2 patients. Among 10 patients who underwent bypass surgery, 7 adjunctive procedures were also performed in 5 patients: thromboembolectomy of the lower extremity in 3 cases, thromboembolectomy of the renal artery in 1, femoropopliteal bypass in 1, and reimplantation of the IMA to the aortic graft in 2 cases. Among 13 patients who underwent thromboembolectomy for AAO, 11 adjunctive procedures were also performed in 10 patients: throm-

Table 3. Univariate analysis of possible risk factors for postoperative in-hospital mortality in acute aortic occlusion patients

Characteristic	Mortality (n=8)	Survivor (n=15)	P-value
Age (y)	78.5 (31-86)	66.0 (40-85)	0.040
Male	7 (87.5)	9 (60.0)	0.345
Symptom duration (h)	51.0 (2-210)	54.9 (2-240)	0.910
Paraplegia	3 (37.5)	2 (13.3)	0.297
Coexisting medical condition			
Atrial fibrillation	3 (37.5)	6 (40.0)	1.000
Hypertension	5 (62.5)	7 (46.7)	0.667
Diabetes mellitus	4 (50.0)	4 (26.7)	0.371
Hyperlipidemia	4 (50.0)	10 (66.7)	0.657
Ischemic heart disease	3 (37.5)	4 (26.7)	0.657
Congestive heart failure	2 (25.0)	3 (20.0)	1.000
Cerebral infarction	3 (37.5)	3 (20.0)	0.621
Preoperative renal insufficiency (serum creatinine >1.5 mg/dL)	4 (50.0)	0 (0)	0.008
Radiologic findings			
Thrombotic occlusion	7 (87.5)	9 (60.0)	0.345
Embolic occlusion	1 (12.5)	6 (40.0)	0.345
Occlusion above the inferior mesenteric artery	4 (50.0)	6 (40.0)	0.657
External iliac artery occlusion	8 (100.0)	7 (46.7)	0.019
Unilateral	3 (37.5)	2 (13.3)	0.297
Bilateral	5 (62.5)	5 (33.3)	0.221
Internal iliac artery occlusion	8 (100.0)	11 (73.3)	0.257
Unilateral	2 (25.0)	7 (46.7)	0.400
Bilateral	6 (75.0)	4 (26.7)	0.039
Combined femoropopliteal artery occlusion	8 (100.0)	10 (66.7)	0.122
Abdominal aortic aneurysm	2 (25.0)	0 (0)	0.111
Combined visceral thromboembolism	1 (12.5)	4 (26.7)	0.621
Surgical details			
Bypass surgery	6 (75.0)	4 (26.7)	0.039
Postoperative complications			
Postoperative hypotension[a]	6 (75.0)	0 (0)	0.000
Postoperative acute kidney injury	7 (87.5)	3 (20.0)	0.006
Pneumonia	2 (25.0)	2 (13.3)	0.589
Myocardial infarction	2 (25.0)	0 (0)	0.111

Values are presented as median (range) or number (%).
[a]Postoperative hypotension was defined as systolic blood pressure that remained below 80 mmHg despite of intravenous inotropic agent.

boembolectomy of the lower extremity in 9 cases, stent placement in the iliac artery in 1, and patch angioplasty of the femoral artery in 1 case. No patients were treated with thrombolytic therapy in our series.

4) Early outcomes and risk factors for in-hospital mortality

As local complications after surgery, a fasciotomy was performed in 5 patients (21.7%) because of compartment syndrome causing severe leg swelling and pain, and a major amputation was performed in 2 patients (8.7%). Both of the major amputations were above-knee amputations due to irreversible ischemic tissue damage and performed on the 7th and 35th days after the aortic surgery. A lymphocele in the groin and a retroperitoneal hematoma were treated with conservative management in one patient each. Vascular complications, including one instance of retrograde aortic dissection and one instance of left common iliac artery dissection, occurred in patients who underwent thromboembolectomy. Both of these dissections were managed conservatively.

In terms of systemic complications during index admission period, 4 patients suffered from pneumonia, and 2 patients developed acute myocardial infarction, and 1 patient had a cerebral infarction. Postoperative AKI developed in 10 patients (43.4%), and temporary HD or CRRT was necessary in 4 patients, after consultation with a nephrologist. However, 2 of these 4 patients declined to undergo temporary HD or CRRT, and both of them died postoperatively.

After the exclusion of a patient who did not undergo surgery, the overall in-hospital mortality was 34.8% (8/23), with a 30-day mortality rate of 26.1% (6/23). The cause of death in 6 patients with 30-day mortality was a multiorgan failure due to myonephropathic metabolic syndrome with reperfusion injury, and the median interval between surgery and death was 3 days. During the index admission period, one patient died 50 days after the initial surgery due to pneumonia, and another patient died 61 days postoperatively due to massive gastrointestinal bleeding. In the univariate analysis, some factors were associated with in-hospital mortality (Table 3). Patients with in-hospital mortality were significantly older than the survivors (P=0.040). Combined external iliac arterial occlusion and bilateral internal iliac artery occlusion were more frequent in patients with in-hospital mortality compared with survivors (100.0% vs. 46.7%, P=0.019; 75.0% vs. 26.7%, P=0.039). The rate of preoperative renal insufficiency and postoperative AKI was significantly higher in patients with in-hospital mortality than in survivors (50.0% vs. 0%, P=0.008; 87.5% vs. 20.0%, P=0.006). Postoperative hypotension was also more common in patients with in-hospital mortality (75.0% vs. 0%, P=0.000). The in-hospital mortality rate was higher in patients who underwent bypass surgery than in those who underwent thromboembolectomy (60.0% for bypass vs. 15.0% for thromboembolectomy, P=0.039).

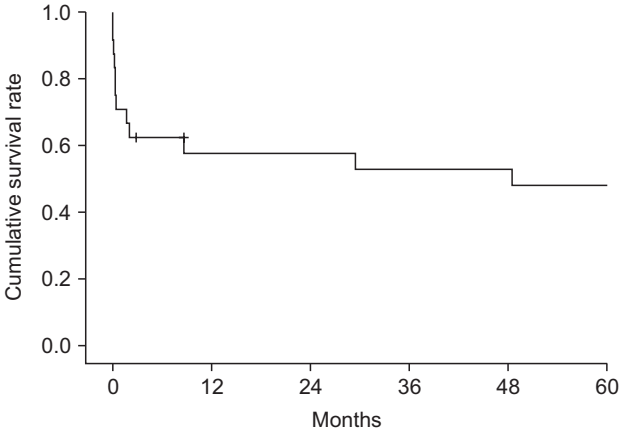
5) Long-term follow-up results

The mean follow-up duration was 44.6 months (median, 19.0 months; range, 0-142 months). Six additional deaths occurred during follow-up and the causes of 6 additional deaths were as follows: recurred thromboembolism in 2 patients (recurred aortic occlusion and superior mesenteric artery embolism), acute myocardial infarction in 1, cerebral infarction in 1, acute renal failure in 1, and an unknown cause in 1 patient. The overall survival rates were 58.0% at 1 year, 53.0% at 3 years, and 48.0% at 5 years (Fig. 1).

DISCUSSION

AAO is an uncommon clinical entity, and most of reports are small series over extended time periods or case reports. However, the general consensus regarding AAO is that the prognosis is devastating due to the high mortality caused by reperfusion injury [5,6,9-11]. Our series is a relatively large series about AAO, and we determined the prognosis and risk factors associated with mortality.

Due to the rarity of AAOs, the diagnosis of AAO is difficult, and this disease entity can easily go unrecognized, which results in prolonged ischemia. In addition, patients with AAOs usually had varying degrees of motor/sensory deficits on presentation. Patients are often referred to a



Months	0	12	24	36	48	60
No. at risk	24	12	12	11	11	10

Fig. 1. Overall survival rate of patients with acute aortic occlusion.

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neurologist or neurosurgeon, particularly patients with flaccid paraplegia, even if a physical finding of absent femoral pulses is identified, leading to misdiagnosis and a loss of valuable time. Meagher et al. [7] reported that 4 of the 8 patients with AAOs were referred for neurologic evaluation at the time of presentation, and Babu et al. [12] reported a delay of over 10 hours in 29.2% (14/48) of patients who presented with clinical signs other than limb ischemia, such as neurologic deficits, abdominal pain and acute hypertension. These findings are similar to our series, in which 41.7% (10/24) of patients were initially evaluated for neurologic problems at presentation due to varying degrees of motor/sensory deficits.

In our series, the level of aortic occlusion was infrarenal in the majority of patients and only 1 patient presented with suprarenal aortic occlusion below the superior mesenteric artery. However, 20.8% (5/24) of patients presented with complete paraplegia, which is similar to a study by Crawford et al. [13], in which 27.6% (8/29) of patients with AAOs presented with complete paraplegia. The principle radicular artery is known as the greater radicular artery of Adamkiewicz, and it most commonly arises from the left intercostal artery between T9 and T12 [14]. Occlusion of this artery can result in acute spinal cord infarction. Aortic dissection and reparative vascular surgery are well established causes of spinal cord ischemia. In contrast, there are few reports in the literature concerning paraplegia associated with acute infrarenal aortic occlusion [7,8]. Currently, translational research has developed a collateral network concept, which is a model for understanding and optimizing spinal cord perfusion during and after thoracic aortic surgery [15]. This concept emphasizes the important contribution of collaterals to the net spinal cord blood supply, which includes vascular territories supplied by the intercostal, lumbar, subclavian, and hypogastric arteries. In addition, the abovementioned radicular artery is occasionally discontinuous or stenotic in patients with AAOs due to preexisting atherosclerosis [15]. In these patients, acute paraplegia may occur after acute infrarenal aortic occlusion due to the sudden occlusion of the lumbar collaterals and hypogastric perfusion, which act as major sources of blood supply to the spinal cord. Therefore, AAO may initially present as complete paraplegia, and this may obscure the classic signs of arterial occlusion. Thus, vascular examinations should always be performed in every patient presenting with lower limb neurologic deficits, and treating physicians should be on alert for this entity, particularly in patients with a clinical history of peripheral vascular disease.

Currently, the etiology of AAO is changing, and the frequency of thrombotic AAO has increased over the last few decades. In a report by Dossa et al. [3] on a 40-year experience of AAOs from 1953 to 1993, the frequency of thrombotic AAOs was 35.0%, and embolic occlusion accounted for 65.0% of cases. However, in accordance with a recent series by Crawford et al. [13] that evaluated 29 patients, the etiology was aortoiliac thrombosis in 22 cases, embolic occlusion in 2 cases, and indeterminate in 5 cases. The authors concluded that the dominant etiology of AAOs is now thrombotic occlusion. In our series, thrombotic occlusion was considered the primary cause of AAO similar to recent series.

However, the association between the etiology of AAO and postoperative mortality is controversial. In their series, Surowiec et al. [16] reported that the postoperative mortality of patients with embolic occlusion was higher than that of patients with thrombotic occlusion. Similarly, in a recent series by Crawford et al. [13], the post-procedural 30-day mortality of a group of patients with a large proportion of thrombotic AAOs was 15.0%; the authors suggested that this may have been the result of improved critical care or the high number of thrombotic occlusions in their series. The reason for lower postoperative mortality in patients with thrombotic AAOs than in those with embolic AAOs may be because these patients have had the advantage of forming collaterals and developing and exuberant collateral system, which may improve their survival by reducing reperfusion injury to the musculature and improving collateral circulation. However, Dossa et al. [3] reported there was no difference in-hospital mortality between the two groups. Moreover, the in-hospital mortality in our series tended to be higher in patients with thrombotic AAOs than in those with embolic AAOs (43.8% for thrombotic occlusion vs. 14.3% for embolic occlusion; P=0.345), and patients who underwent by bypass surgery demonstrated higher mortality than patients who underwent thromboembolectomy.

According to our series, age, preoperative renal function and combined iliac arterial occlusive disease were associated with in-hospital mortality. After revascularization of an AAO, systemic metabolic consequences, such as myonephropathic syndrome can develop and affect the life and viability of limbs. Muscle cell ischemia and cell death leads to the release of myoglobin, potassium, and lactic acid [17]. Consequently, AKI can occur, and HD becomes necessary. In addition, when renal function is not maintained, the excessive potassium released by the ischemic muscle cannot be cleared, and hyperkalemia becomes an additional problem. Therefore, preoperative renal function is important for the prognosis of patients with AAOs, and as a result, postoperative AKI is also associated with in-hospital mortality, as was found in our series.

Another interesting finding in our series was that com-

bined iliac and femoropopliteal arterial occlusion was surprisingly high. In patients with AAOs, this kind of combined arterial occlusion further impairs the blood supply to lower extremities, and the resultant ischemia can be severe. Although this finding was not statistically significant, the proportion of EIA occlusions in patients with thrombotic AAOs tended to be higher than in those with embolic AAOs (76.0% vs. 43.0%; P=0.122). Furthermore, the frequency of combined femoropopliteal arterial occlusion in patients with thrombotic AAOs was significantly higher than in patients with embolic AAOs (94.0% vs. 43.0%, P=0.003). This combined peripheral arterial occlusion may be a preexisting lesion or a newly developed lesion that occurred concurrently with AAO. However, peripheral arterial occlusion is expected to be more frequent in patients with thrombotic occlusion than in patients with embolic occlusion because of preexisting atherosclerotic disease [16]. In any case, combined arterial occlusion is an additional obstacle to the blood supply to the lower limbs and intensifies ischemic damage and increases reperfusion injury. This finding may be another explanation for the differences in postoperative mortality in patients with AAOs of different etiologies.

The major limitation of this study was its retrospective design. Additionally, the small patient sample size that was monitored over a long period might have resulted in patient selection and treatment bias. Furthermore, although we included all patients with AAOs who were admitted to our department, some patients who presented to the emergency department who were in poor general condition with high comorbidities may have died without treatment because their families refused treatment. This particular limitation prevented us from assessing the exact rate of in-hospital mortality; thus, selection bias might have been present.

In conclusion, AAO is a rare disease that is associated with high mortality. In our series, 42.0% of the patients are mistakenly evaluated for a central nervous system lesion, leading to a delay in diagnosis. Thus, vascular examinations should always be performed in every patient presenting with lower limb neurologic deficits. Age, perioperative renal dysfunction, and combined iliac arterial occlusion were associated with in-hospital mortality. Treating physicians need to pay attention to risk factors and these patients should be managed more closely.

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