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Upper Limb Ischemia: Clinical Experiences of Acute and Chronic Upper Limb Ischemia in a Single Center

Miju Bae, M.D., Sung Woon Chung, M.D., Chung Won Lee, M.D., Jinseok Choi, M.D., Seunghwan Song, M.D., Sang-pil Kim, M.D.

Background: Upper limb ischemia is less common than lower limb ischemia, and relatively few cases have been reported. This paper reviews the epidemiology, etiology, and clinical characteristics of upper limb ischemia and analyzes the factors affecting functional sequelae after treatment. **Methods:** The records of 35 patients with acute and chronic upper limb ischemia who underwent treatment from January 2007 to December 2012 were retrospectively reviewed. **Results:** The median age was 55.03 years, and the number of male patients was 24 (68.6%). The most common etiology was embolism of cardiac origin, followed by thrombosis with secondary trauma, and the brachial artery was the most common location for a lesion causing obstruction. Computed tomography angiography was the first-line diagnostic tool in our center. Twenty-eight operations were performed, and conservative therapy was implemented in seven cases. Five deaths (14.3%) occurred during follow-up. Twenty patients (57.1%) complained of functional sequelae after treatment. Functional sequelae were found to be more likely in patients with a longer duration of symptoms (odds ratio, 1.251; p=0.046) and higher lactate dehydrogenase (LDH) levels (odds ratio, 1.001; p=0.031). **Conclusion:** An increased duration of symptoms and higher initial serum LDH levels were associated with prompt and proper treatment and can also be predicted by initial serum LDH levels.

Key words: 1. Upper extremity

2. Ischemia

3. Complication

4. L-lactate dehydrogenase

INTRODUCTION

Upper limb ischemia is less common than lower limb ischemia, and relatively few cases have been reported. However, delays in diagnosis and treatment are likely to result in severe functional impairment and disability, even in the absence of overt tissue loss [1,2]. In a clinical context, the shoulder and elbow are much more tolerant of ischemia

due to their well-developed collateral circulation, and it is therefore more common to observe ischemic symptoms below the elbow [3]. This study presents a review of the epidemiology, etiology, and clinical characteristics of upper limb ischemia, as well as an analysis of the factors affecting functional sequelae after treatment.

Department of Thoracic and Cardiovascular Surgery, Pusan National University Hospital

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Corresponding author: Sung Woon Chung, Department of Thoracic and Cardiovascular Surgery, Pusan National University Hospital, 179 Gudeok-ro, Seo-gu, Busan 602-739, Korea

(Tel) 82-51-240-7263 (Fax) 82-51-243-9389 (E-mail) chungsungwoon@hanmail.net

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Table 1. Demographic characteristics of the patients

Characteristic	Number (%)	
Gender		
Male	24 (68.6)	
Female	11 (31.4)	
Heart disease	18 (51.4)	
Atrial fibrillation	9 (25.7)	
Valvular disease	3 (8.6)	
Ischemic disease	2 (5.7)	
Congestive heart failure	2 (5.7)	
Bradycardia	1 (2.9)	
Dilated cardiomyopathy	1 (2.9)	
Hypertension	15 (42.9)	
Stroke	6 (17.1)	
Multiple trauma	5 (14.3)	
Diabetes mellitus	3 (8.6)	
Rheumatic arthritis	2 (5.7)	
Systemic scleroderma	2 (5.7)	

Table 2. Diagnostic tools

Diagnostic tools	Number (%)
CT angiography	22 (62.9)
Conventional angiography	10 (28.6)
Only history taking and physical examination	2 (5.7)
Duplex ultrasound	1 (2.9)

METHODS

A total of 35 patients who underwent treatment for acute and chronic upper limb ischemia in a single center between January 2007 and December 2013 were reviewed. Cases involving arterial insufficiency after the creation of arteriovenous fistulae for hemodialysis were excluded. The baseline characteristics, comorbidities, etiologies, diagnostic tools, locations of the lesion, treatments, complications, and sequelae after treatment were reviewed. Additionally, the factors that were expected to affect to functional sequelae after treatment were analyzed using binary logistic regression. The results were expressed as means with 95% confidence intervals where appropriate, and p-values <0.05 were considered to imply statistical significance. Statistical analysis was performed using IBM SPSS ver. 20.0 (IBM Co., Armonk, NY, USA).

Table 3. Etiology

Etiology	Number (%)
Acute	19
Embolus from heart origin	11 (31.4)
Trauma	7 (20.0)
Embolus from aortic arch	1 (2.9)
Chronic	16
Raynaud's disease	4 (11.4)
Burger's disease	3 (8.6)
Atherosclerosis	2 (5.7)
Thoracic outlet syndrome	2 (5.7)
Unknown	5 (14.3)
Total	35

Table 4. Locations of lesions

Locations	Number (%)
Innominate artery	1 (2.9)
Subclavian artery	4 (11.4)
Axillary artery	3 (8.6)
Brachial artery	17 (48.6)
Radial artery	2 (5.7)
Ulnar artery	4 (11.4)
Palmar arterial arch	4 (11.4)

RESULTS

The median age of the patients was 55.03 years, and the median follow-up duration was 706.23 days (23.54 months). Fifteen patients (42.9%) were current smokers and four (11.4%) were ex-smokers. Table 1 summarizes the demographic characteristics of the patients in this study.

The initial diagnosis of upper limb ischemia was mostly made on the basis of computed tomography (CT) angiography (62.9%). Conventional angiography and duplex ultrasound were also used as diagnostic tools. Two cases were diagnosed solely on the basis of a medical history and physical examination (Table 2). The most common etiology was embolism of cardiac origin (31.4%), followed by thrombosis with secondary trauma (20.0%) (Table 3), and the brachial artery (48.6%) was the most common location of lesions causing obstruction (Table 4).

A total of 28 operations were performed, while seven patients underwent conservative therapy (Table 5). The oper-

Table 5. Treatments

Treatment	Number (%)
Embolectomy or thrombectomy	16 (45.7)
Bypass with great saphenous vein	5 (14.3)
Percutaneous catheter direct thrombolysis	4 (11.4)
Primary repair	2 (5.7)
Sympathicotomy	1 (2.9)
Conservative therapy	7 (20.0)

Table 6. Complications after treatment

Complications	Number (%)	
Re-obstruction	2 (5.7)	
Wound infection	2 (5.7)	
Acute renal failure	2 (5.7)	
Minor amputation	2 (5.7)	
Bleeding	1 (2.9)	

ations included embolectomy and thrombectomy using a Fogarty balloon catheter (n=16, 45.7%), bypass surgery using the great saphenous vein (n=5, 14.3%), percutaneous catheter-directed thrombolysis (n=4, 11.4%), and primary repair (n=2, 5.7%). Patients with Raynaud's phenomenon or Burger's disease were either treated with medication only (n=7, 20%) or with sympathectomy (n=1, 2.9%).

In the case of embolism with atrial fibrillation, emergency embolectomy was performed first, followed by echocardiography to re-evaluate the status of the heart. Isolated atrial fibrillation was treated with anticoagulation drugs. If a patient had a history of other heart diseases, the treatment strategy was determined in consultation with the cardiology department. Imaging of the brain, lower extremities, or mesenteries was not performed if a patient did not complain of symptoms in other areas.

Treatment-related complications are described in Table 6. Additionally, five deaths (14.3%) occurred during the course of follow-up. One of those deaths (2.9%) occurred within 30 days of the operation, and was due to postoperative rhabdomyolysis with acute renal failure. The other deaths were due to acute small intestinal infarction (1), acute myocardial infarction (1), and unknown causes (2).

Two cases of reobstruction were noted. One case occurred seven months after surgery, and the other occurred four years

Table 7. Result of binary logistic regression for functional sequelae

Variable	p-value	Odds ratio
Gender	0.348	0.278
Age	0.531	1.026
Symptom duration	0.046	1.251
Hypertension	0.959	0.939
Diabetes	0.698	1.964
Smoking	0.725	1.372
Atrial fibrillation	0.582	0.380
Coronary arterial occlusive disease	0.999	1.885
Stroke	0.343	4.230
Hemoglonbin	0.742	1.202
Pletelet	0.992	0.943
White blood cell	0.841	0.875
Aspartate aminotransferase	0.771	0.982
Alanine aminotransferase	0.802	1.002
Lactate dehydrogenase	0.031	1.001
Albumin	0.089	0.724
Phosphate	0.425	1.259
C-reactive protein	0.074	1.424
Creatine kinase	0.885	1.576
Myoglobin	0.647	1.059

after surgery. In each of these patients, reobstruction occurred in the same location as the previous lesion, and percutaneous catheter-directed thrombolysis was performed.

Functional sequelae were observed in 20 patients (57.1%), with different patterns of symptoms in each patient. The sequelae after treatment included decreased motor function (25.7%), decreased sensory function (14.3%), persistent pain (5.7%), and tingling sensations in the fingers or on the palm (40%).

Factors thought to possibly affect the emergence of sequelae were analyzed (Table 7). Functional sequelae were found to be significantly more common in patients with a longer duration of symptoms (p=0.046) and higher initial serum lactate dehydrogenase (LDH) levels (p=0.031). The mean initial serum LDH level of the patients who experienced functional sequele was 454.71 IU/L, which was significantly higher than the normal upper reference limit of 225 IU/L.

DISCUSSION

Upper limb arterial ischemia is responsible for <5% of all cases of limb ischemia [4]. The epidemiology of upper limb

arterial disease is difficult to assess, due to its low incidence and vast number of etiologies [5]. The anatomical location and etiology are the two major criteria for categorizing upper limb arterial disease. The anatomical location is subdivided into the small or large arteries, and the etiology is subdivided into either occlusive disease or vasospasm [5].

The diseases that lead to the most severe cases of upper limb arterial ischemia are autoimmune or connective tissue diseases such as scleroderma, rheumatoid arthritis, systemic lupus, and others. Although Burger's disease (thromboangiitis obliterans) most commonly affects the lower limbs, approximately 50% of patients also have upper limb involvement with subsequent digital ischemia [6].

The most common large-vessel arteriopathy in the upper limb is atherosclerosis [7], and the most common occlusive site is the origin of the left subclavian artery. Embolism is the most common cause of acute upper limb ischemia [8]. Most emboli originate from the heart, caused by atrial fibrillation, recent myocardial infarction, and valvular heart disease [9]. Embolic occlusion from atrial fibrillation or other sources is classically seen in the brachial artery before the bifurcation of the radial and ulnar arteries [5].

In this study, the most common cause of upper limb ischemia was found to be embolism, and the distal brachial artery was observed to be the most frequent site of obstructions (Tables 3, 4). In this study, 19 patients (54.3%) had acute limb ischemia. The mean age of patients with acute upper limb ischemia was 60.42 years, and female patients comprised 42.10% of the study population.

Spinelli et al. [10] reported that duplex ultrasound was the most widely used diagnostic tool. In contrast, Licht et al. [3] reported that 88% of operations were performed based only on the patient's medical history and a physical examination. In our center, when upper limb ischemia was suspected from a patient's medical history and a physical examination, CT angiography was used as the initial diagnostic tool in 62.9% of cases. CT was useful in locating the lesion, discovering multiple lesions, and assessing the correlation of the lesion with the surrounding structure. Between 9% and 30% of patients with upper limb arterial occlusive disease seen by vascular surgeons are managed nonoperatively due to significant comorbidities or minimal symptomatology [11].

However, the treatment of choice for acute upper limb ischemia is surgical correction via embolectomy using a Fogarty balloon catheter. Incision of the antecubital fossa still remains the best treatment for removing brachial emboli [9].

Revascularization with upper limb bypass is used less commonly than other treatments, comprising approximately 4% of all vascular operations [12]. Although this procedure is infrequently performed, the results of upper extremity bypass are excellent, and are even superior to those reported for the corresponding treatment of lower extremity ischemia [5]. Brunkwall et al. [13] reported a postoperative two-year recanalization rate of 60%–90%. Moreover, Spinelli et al. [10] reported a primary patency rate of 82.6% and a secondary patency rate of 91.3% over a 34-month follow-up period [9]. In our study, 23 patients (65.7%) underwent surgical correction, of whom five (14.3%) underwent bypass surgery using the reversed great saphenous vein.

Recently, the use of endovascular treatment to treat various vascular diseases has grown exponentially. Kim et al. [14] performed percutaneous aspiration thromboembolectomy and thrombolysis in 11 patients suffering from acute upper limb ischemia, of whom nine experienced successful recanalization. In this study, four patients who suffered from acute brachial artery embolism underwent percutaneous aspiration thromboembolectomy and thrombolysis, and one of those patients died due to rhabdomyolysis with acute renal failure. In endovascular treatment, the embolus or distal embolism is dissolved after percutaneous aspiration thromboembolectomy employing various techniques. An advantage of this technique is the absence of an operative wound. Moreover, the recovery time is fairly short. However, a disadvantage is that thrombolysis requires more time for revascularization and involves a longer ischemic time, and hemorrhagic complications are more frequent. Thus, endovascular treatment is unsuitable for the reperfusion of acute cases of critical upper limb ischemia, and should be limited to stage I and IIa acute limb ischemic lesions or the cautious treatment of chronic ischemia.

In this study, some cases of upper limb ischemia were associated with Raynaud's phenomenon, which involves episodic vasospasm when the patient is exposed to cold or psychosocial stress. It usually resolves naturally, but can persevere and become a problem. If the vasospasm continues, con-

servative management is implemented using medications such as calcium channel blockers and phosphodiesterase inhibitors. Surgical intervention is performed if the patient is unresponsive to conservative management. In this study, four patients suffered from Raynaud's phenomenon; two patients had systemic scleroderma as the underlying disease, and the other two had rheumatic arthritis as the underlying disease. Two patients underwent the amputation of a digit due to the progression of finger necrosis. All four patients were prescribed calcium channel blockers and antiplatelet agents. Those who were unresponsive to medication were selectively treated with video-assisted thoracoscopic surgery sympathectomy. Cervical sympathectomy is no longer considered an appropriate treatment for Raynaud's phenomenon because the very short duration of its effectiveness. However, the long-term results of periarterial sympathectomy are more reliable than those of cervical sympathectomy [15].

Most patients were admitted to the emergency department with the acute onset of symptoms resulting from embolism and thrombosis. In such cases, the duration of symptoms is usually short. However, patients with Raynaud's syndrome, Burger's disease, or thoracic outlet syndrome-related upper limb ischemia visited through the outpatient clinic, and had a longer duration of symptoms. The duration of symptoms in cases of upper limb ischemia may vary from two hours to a year, depending on the etiology and severity of the illness. Many debates have addressed whether the time gap between the onset of symptoms and treatment predicts long-term arm function. Abbott et al. [16] reported that patients treated within 12 hours exhibited a lower mortality rate and a higher rate of limb salvage. Elliott et al. [17] also found that the results of treatment showed a linear relationship to the time gap between symptom onset and treatment. Bang and Nalachandran [18] also found that the prognosis differed significantly when >12 hours elapsed between the onset of symptoms and treatment. However, it has been suggested that the time gap does not influence the prognosis [3]. In this study, the time gap between the onset of symptoms and consequent treatment was related to postoperative sequelae. A longer duration of symptoms was associated with a higher likelihood of sequelae (odds ratio, 1.251; p=0.046).

In this study, serum LDH levels were also found to have a

significant influence on the occurrence of functional sequelae (odds ratio, 1.001; p=0.031). Higher levels of serum LDH were associated with a higher chance of functional sequelae. LDH has been used as a marker for liver disease, heart attack, anemia, muscle trauma, bone fracture, cancer, and infections such as meningitis, encephalitis, and HIV; when tissue is damaged by injury and disease, LDH is released into the bloodstream. An initial increase in LDH reflects tissue damage resulting from upper limb ischemia, and initial tissue damage is related to postoperative functional sequelae. Levels of creatine kinase or the myoglobin enzymes with muscle specificity could theoretically lead to an accurate assessment of the prognosis, but were found to show no statistically significant associations in this study. Nonetheless, the use of serum LDH levels as a basic liver function test was able to predict the development of functional sequelae to a statistically significant extent.

In conclusion, a longer duration of symptoms and higher initial serum LDH levels were associated with a greater likelihood of functional sequelae. The prognosis of upper limb ischemia is associated with prompt and proper treatment and can also be predicted by initial serum LDH levels.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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