Chronic Arterial Embolism of the Lower Extremities: An Unusual Etiology of Critical Limb Ischemia

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Background: *Chronic arterial embolism of the lower extremities, the unusual cause of critical limb ischemia (CLI), is not well recognized in the medical practice.*
Objective: *To study the clinical problem of chronic arterial embolism in the aspects of the clinical characteristics and treatment outcomes.*
Material and Method: *Between January 2000 and December 2004, 411 consecutive patients with chronic limb ischemia, including 16 (3.8%) patients with chronic arterial embolism were included in the present study. The diagnosis of chronic arterial embolism was confirmed by angiography, operative finding, and histopathology of amputated specimen. The clinical characteristics and management outcomes were recorded and analyzed.*
Results: *Of the 16 patients with chronic arterial embolism, the mean duration of clinical manifestation was 2.4 months (range, 1-6). Femoral artery was the most common site of arterial occlusion (63.1%). Atrial fibrillation was the most common clinical risk factor (25.0%). Of the 14 patients (87.5%) suffering from CLI, nine patients (56.25%) underwent the various types of revascularization. In five patients (31.25%), the authors could not perform revascularization due to the fibrotic arteries. Successful limb salvage and disappearance of rest pain with complete healing of ulcer in patients with CLI were only 50%. One patient (6.25%) expired after major amputation.*
Conclusion: *Chronic arterial embolism of the lower extremities is the unusual cause of CLI with a high rate of major amputation. Early detection and appropriate management of arterial embolism at the initial stage may reduce this serious vascular problem.*

Keywords: *Chronic arterial embolism, Critical limb ischemia Major amputation, Lower extremities*

J Med Assoc Thai 2011; 94 (12): 1457-64
Full text. e-Journal: *http://www.jmat.mat.or.th*

Arterial embolism is the most common cause of acute arterial occlusion in the lower extremities[1]. The majority of patients with acute arterial embolism have the rapid progression of acute limb ischemia with the high tendency of major limb loss[2,3]. Reperfusion injury can be expected when the prolonged limb ischemia is not urgently corrected[4]. The favorable outcomes of acute arterial embolism treatment usually occur in the patients with the onset of symptom of less than 24 hours[5,6]. However, in an unusual circumstance, limb viability can be maintained by the collateral circulation[7] at the initial stage of arterial occlusion. In such patients, the ischemic process may not be completely resolved enough for normal activities leading to various symptoms of chronic limb ischemia according to Fontaine's staging classification[1,8].

Chronic arterial embolism is defined as chronic limb ischemia of the patient complaints related to the previous history of the abrupt onset of claudication or rest pain of the affected lower extremity[9]. In addition, this clinical manifestation is defined as critical limb ischemia (CLI) when the suffering arose from chronic ischemic ulcer, gangrene, or rest pain[1], which is consistent with Fontaine's stage III and IV. In the meantime, chronic arterial embolism is not well recognized in the medical practice and has not been mentioned in the literature review. Furthermore, the clinical characteristics, the guideline management, and the treatment outcomes of nonacute arterial embolism remain controversial[9-11].

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Table 1. Gender-age distributions, clinical risk factors, duration of embolism, staging of severity and types of clinical manifestations of patients with chronic arterial embolism

No.	Sex	Age	Risk factors	Duration (months)	Fontaine's stages	IC	Rest pain	Ulcer	Gangrene	Limb infection
1	M	58	MI	1	IV	+	+	+	+ (digital)	-
2	M	42	-	2	IV	+	+	+	-	-
3	M	56	Previous embolism	4	IV	+	+	+	+ (foot)	+
4	M	72	AF	6	III	+	+	-	-	-
5	M	50	-	2	IV	+	+	-	+ (foot)	-
6	M	63	AF	2	IV	+	+	+	+ (foot)	-
7	M	48	Proximal aneurysm Previous embolism	3	IV	+	+	+	-	-
8	M	44	-	2	IV	+	+	+	+ (digital)	+
9	M	58	Previous embolism	2	I	-	-	+	-	+
10	M	40	-	2	III	+	+	-	-	-
11	M	35	-	2	III	+	+	-	-	-
12	M	35	-	1	II	+	-	-	-	-
13	M	22	-	2	III	+	+	-	-	-
14	F	70	AF	2	IV	+	+	+	+ (digital)	+
15	F	74	AF	2	IV	+	+	+	-	-
16	M	35	-	4	IV	+	+	-	+ (digital)	-

IC = intermittent claudication; MI = myocardial infarction; AF = atrial fibrillation

The objective of the present study was to analyze retrospectively the clinical characteristics and the management outcomes in the patients admitted to surgery with the diagnosis of chronic arterial embolism in observational descriptive study.

Material and Method

Between January 2000 and December 2004, 411 consecutive patients with chronic limb ischemia, including 16 patients with chronic arterial embolism were selected in the present study (Table 1). The Siriraj ethical committee for research in humans approved the present study. The criteria of chronic arterial embolism included the clinical basis as previous definition with at least one of the following diagnostic criteria: the sharp-cut image in the occluded artery without the associated atherosclerotic disease in adjacent segment of arteries demonstrated by angiography[12] (Fig. 1), the evidence of embolus in the arterial lumen during the operation, and the histopathology of

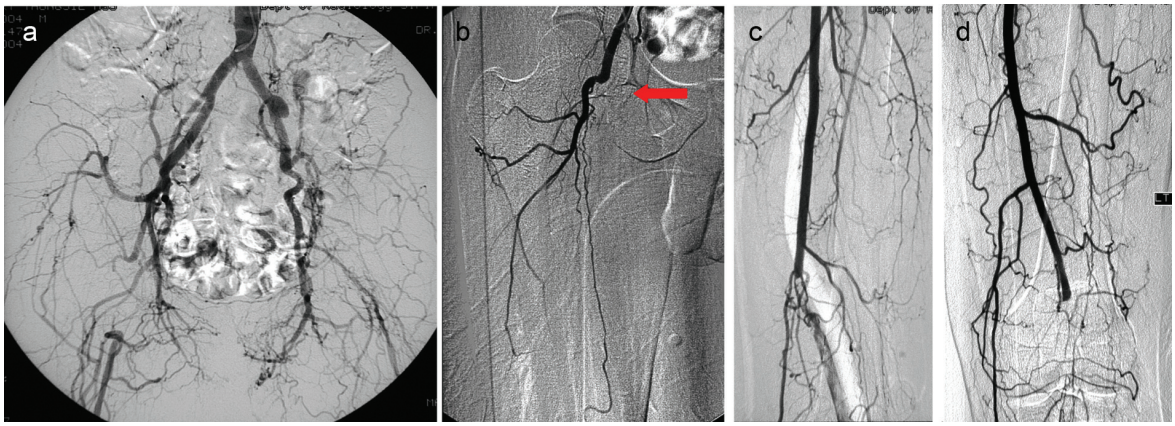

Fig. 1 Evidence of arterial embolism by angiography at different levels: (a) bilateral external iliac arteries, (b) proximal superficial femoral artery, (c) distal superficial femoral artery and (d) popliteal artery

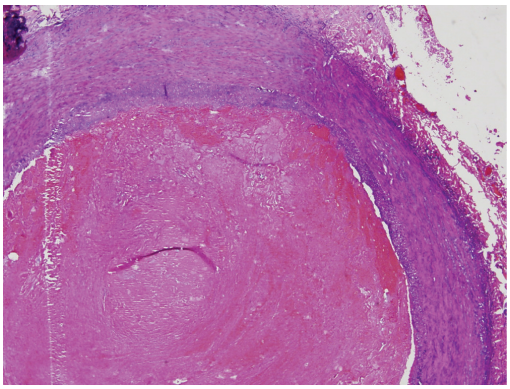

Fig. 2a In the right distal superficial femoral artery, recent thrombus was demonstrated in the lumen without evidence of atherosclerosis or arteritis in the intimal and intramural layers

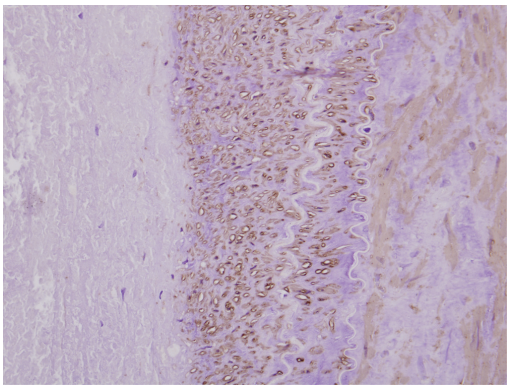

Fig. 2b In the same artery, the intimal layer contained the proliferation of myointimal cells with positive immunohistochemical staining for 1A4, a smooth muscle actin marker. (No evidence of bacterial or fungus infection is seen by gram and GMS stains)

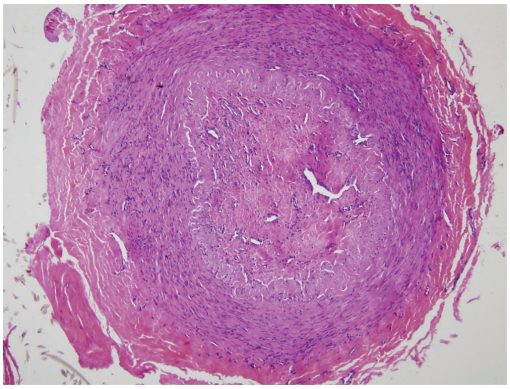

Fig. 2c In the right posterior tibial artery at ankle level, the lumen was completely obliterated by fibrous tissue

arterial embolism from the amputated specimen (Fig. 2). The patients with CLI underwent the attempt of revascularization.

The guideline of the revascularization procedures in the chronic arterial embolism with CLI is shown in Fig. 3. Preoperative angiography was performed to identify the patency of distal artery run off. Arterial bypass surgery was selected to be the primary treatment of limb salvage whenever the patent distal artery run off could be demonstrated. In the patients with no distal artery run off, the artery was explored at the occlusion site to identify the pathology of occluded segment whether it was fibrotic artery or embolus in the lumen. Revascularization was not performed in fibrotic artery and poor distal artery run off. When the embolus remained in the lumen of the occluded artery, the removal of embolus was attempted by a Fogarty embolectomy catheter. Furthermore, intraoperative angiography was performed to identify the patency of the distal artery. Intraoperative thrombolysis was also performed to remove the residual embolus, when the patency of

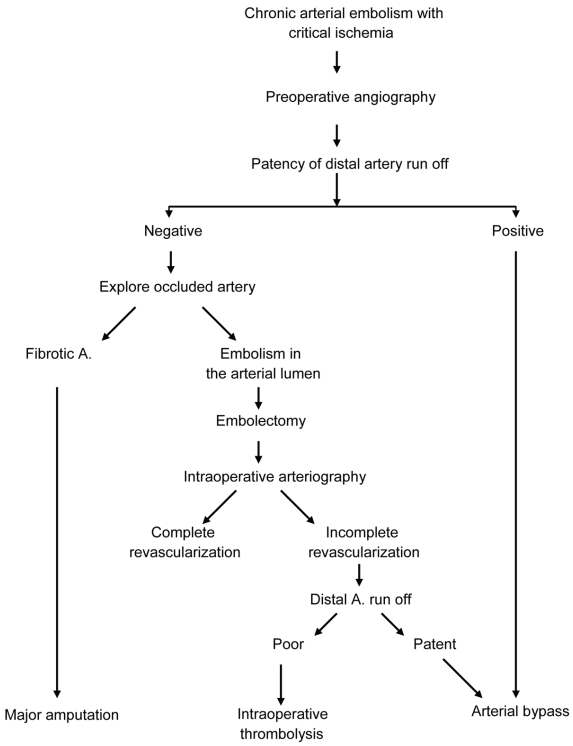

Fig. 3 The outline of revascularization procedures in the critical ischemia of patients with chronic arterial embolism

the distal artery could not be demonstrated by angiography. On the other hand, arterial bypass surgery was considered in the demonstrable patency of the distal artery. Major amputation was indicated in the patients with ischemic process or severe infection that extended beyond the forefoot level.

The primary endpoint was the limb salvage rate. The secondary endpoints included the freedom from rest pain with complete healing of ischemic ulcer within six months and mortality rate after the treatments.

Statistical analysis

SPSS Window 16.0 statistical software was used for analyzing the patient record. The continuous data are presented as mean $\pm$ standard deviation and percentages for discrete variables.

Results

Four hundred eleven consecutive patients with chronic limb ischemia, including 16 (3.8%) patients with the complete criteria of chronic arterial embolism were analyzed. Table 1 summarizes demographic data and clinical manifestations of the patients in the present study. Among these patients, there were 14 male with mean age of 50.1 $\pm$ 15.2 years (range, 22-74). The most common risk factor was atrial fibrillation (25%). All but two patients had CLI. The duration of symptoms ranged between one and six months (mean 2.4 $\pm$ 1.3 months). All of the patients with CLI had rest pain.

The pathology of arterial characteristics, the types of operation and the survival status of the patients are listed in Table 2. Of the 19 sites of chronic arterial embolism, femoral artery was the most common site of arterial occlusion (62.5%). Twelve patients (75%) had the normal peripheral pulse on the contralateral limb. Two patients (12.5%) with viable limb presented with intermittent claudication. One of them underwent minor amputation due to foot infection and the other did not require any intervention to maintain limb viability. Fig. 4 depicts the operative procedures and treatment outcomes of patients with CLI. Two of these patients with patent distal artery underwent arterial bypass surgery. Unfortunately, only one patient had successful limb salvage while the other underwent

Table 2. Gender-age distributions, sites of arterial occlusion, contralateral status of arterial occlusion, severity of limb ischaemia, types of revascularization, types of amputation and survival status of patients with chronic arterial embolism

No.	Sex	Age	Sites of A. occlusion	Contralateral A. occlusion	Severity	Vascular procedures	Minor amputation	Major amputation	Survival status
1	M	58	Iliac	Nil	Critical	A. Exploration	-	+	Survive
2	M	42	Femoral (bilateral)	Femoral	Critical	Embolectomy	+	-	Survive
3	M	56	Aorta	Aorta	Critical	A. Exploration	-	+	Dead
4	M	72	Femoral	Nil	Critical	Bypass	-	-	Survive
5	M	50	Femoral	Nil	Critical	A. Exploration	-	+	Survive
6	M	63	Femoral	Nil	Critical	A. Exploration	-	+	Survive
7	M	48	Popliteal	Nil	Critical	Embolectomy Bypass	-	-	Survive
8	M	44	Femoral	Nil	Critical	Embolectomy	+	-	Survive
9	M	58	Popliteal	Nil	Viable	-	+	-	Survive
10	M	40	Popliteal	Nil	Critical	Embolectomy	-	-	Survive
11	M	35	Femoral	Nil	Critical	A. Exploration	-	+	Survive
12	M	35	Femoral	Nil	Viable	-	-	-	Survive
13	M	22	Femoral	Nil	Critical	Embolectomy Bypass	-	+	Survive
14	F	70	Iliac (bilateral)	Iliac	Critical	Bypass	-	+	Survive
15	F	74	Femoral	Nil	Critical	Embolectomy Thrombolysis	-	-	Survive
16	M	35	Femoral (bilateral)	Femoral	Critical	Embolectomy Thrombolysis	-	-	Survive

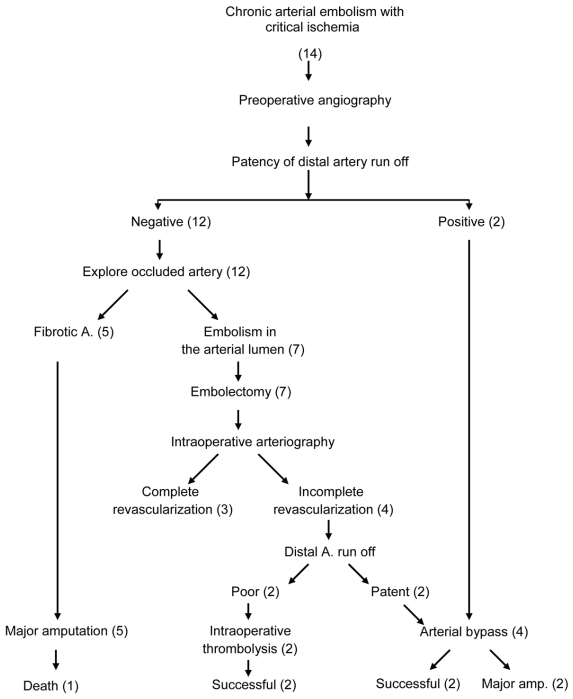

Fig. 4 The results of revascularization procedures in the critical ischemia of patients with chronic arterial embolism

below knee amputation due to the infective process extending beyond the forefoot level. For patients with no patency of the distal artery, fibrotic artery was found in five patients. Major amputation was inevitable in them due to no possibility of revascularization. In patients with emboli, three patients had complete revascularization. In the remaining four patients with incomplete revascularization, two patients with no patency of distal artery underwent the additional intraoperative thrombolysis with successful revascularization. The other two patients with patent distal artery underwent arterial bypass surgery. Only one patient had successful revascularization while the other underwent major amputation due to the failure of arterial bypass surgery from the high resistance in distal artery.

Successful limb salvage rate in patients with CLI was only 50% (7/14). The successful outcomes with complete healing of ischemic ulcer and disappearance of rest pain within 6 months after this procedure were 50% (7/14). One patient (6.25%) expired after major amputation due to sepsis from the infection of non-healed major amputation stump and pneumonia.

Discussion

While the patients with acute arterial embolism had more than 90% of the highly successful revascularization rate when surgical embolectomy was performed within 24 hours[5,6], the authors proposed that chronic arterial embolism with CLI had less successful revascularization rate (only 50%). For the patients with successful operation, however, all of them had the complete healing of ulcer and disappearance of rest pain.

Embolus, occluded in the lumen of the lower extremity artery, is a common cause of acute limb ischemia[2,13]. The occlusion site is commonly located at the bifurcation of the artery causing sudden reduction of blood supply without compensated collateral circulation. The severity of ischemia was rapidly and progressively worse to the level of irreversible status whenever the circulation in the distal tissue is not immediately reestablished[14]. However, the progression of ischemia is not rapidly worse in the unusual two following conditions.

Firstly, the site of embolic occlusion, not exactly at the arterial bifurcation (Fig. 1) may provide some degree of collateral circulation through the branches of non-occluded proximal artery into the distal ischemic tissue.

Secondly, the breaking of embolus into smaller pieces together with their migration into the distal artery may be another additional factor contributing to the increase of collateral blood flow to the distal limb.

Patients with arterial embolism under these circumstances may not suffer from acute extensive limb gangrene and reperfusion injury at the initial stage. The progression of ischemia in the distal limb depends on the adequacy of the collateral circulation at surrounding area of the occlusion site and the patency of the distal artery. Patients with inadequate collateral circulation for the normal activities may present with chronic limb ischemia defined as chronic arterial embolism. The degree of collateral circulation can be improved by walking exercise and medications for patients with intermittent claudication. On the contrary, this collateral circulation can be markedly diminished by the recurrent embolic process and the propagation of blood clot in the distal artery. The ischemia of the distal limb in these situations will eventually progress to CLI. The retained clot in the lumen distal to the occlusion site stimulates the inflammatory reaction on the tunica intima of the adjacent arterial wall at the initial stage[15-17] (Fig. 2a & 2b). Then, it formulates the organized thrombus together with fibrous tissue at

the terminal stage (Fig. 2c). These pathological finding can be found in the whole segment of the distal artery whenever the clot is propagated continuously into the most distal artery.

This clinical problem of chronic arterial embolism is not intensively clarified in the literatures[2,7,9,11]. The incidence of this problem may be minimal in developed countries due to the early detection and effective treatment. However, in the countries where vascular disease is not well recognized by general physicians, patients with chronic arterial embolism can be found due to the delayed management. The risk factors of chronic arterial embolism are similar to acute arterial embolism. Seven patients, under the age of 45 had no demonstrable clinical risk factor. However, the hypercoagulability state not intensively assessed in the present study may be the significant risk factors in these young patients[18].

Despite the similarity of their clinical manifestations, the duration of clinical manifestations of chronic arterial embolism was much shorter than that of atherosclerosis obliterans[19] (Table 1). The preoperative differentiation between the two diseases was beneficial by providing the awareness of the postoperative outcome and the correction of risk factors[19-22]. As for chronic arterial embolism with CLI, the high major amputation rate was due to the extensive fibrosis involving the arterial wall and lumen precluding the successful revascularization. The result of revascularization of chronic arterial embolism was unpredictable due to the variations of pathophysiologic change in the distal artery affecting the patency and the degree of collateral circulation (Fig. 4). The high resistance in the fibrotic distal artery detected during the procedure is one of the essential causes of unsuccessful revascularization resulting in major amputation despite the patent distal artery. Catheter directed thrombolysis was not introduced as the primary treatment in the present study because of the prolonged duration of arterial embolism[23-25]. Due to all of the above information, the extensive fibrosis in the lumen and the wall of the distal artery as the result of prolonged arterial embolism prohibited the possibility of revascularization. This problem was considered as the major factor influencing the limb salvageability in patients suffering from this disease. However, the present study was limited with a small sample size, descriptive study, and the mid-term follow-up. Further research should be undertaken to randomly compare with the other surgical options in a large sample size and evaluate their results in the long term.

In conclusion, the authors proposed the so-called chronic arterial embolism of the lower extremities as the unusual type of CLI with the high rate of major amputation. The clinical risk factors were similar to acute arterial occlusion, especially cardiovascular comorbidity. Avoiding the adverse outcomes by the early detection of arterial embolism together with the effective treatment at the initial stage may be the most important strategy to reduce adverse outcomes in this serious vascular problem.

Acknowledgment

The authors wish to thank Associate Professor P. Vessakosol (PhD) for a final edit of the manuscript. The authors also wish to thank Miss S. Tunpornpituk for the analysis of the statistics and her assistance in preparing the manuscript.

Potential conflicts of interest

None.

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โรคหลอดเลือดแดงของขาอุดตันจากลิ่มเลือดที่มีอาการขาดเลือดอย่างเรื้อรัง

เฉนียน เรืองเศรษฐกิจ, คามิน ชินศักดิ์ชัย, ชุมพล วงวานิช, ณัฐวุฒิ เสริมสาธนสวัสดิ์, ประมุข มุทิรางกูร

ภูมิหลัง: *โรคหลอดเลือดแดงของขาอุดตันจากลิ่มเลือดที่มีอาการขาดเลือดเรื้อรัง เป็นโรคที่ทำให้เกิดการสูญเสียขาได้ง่าย แต่ในปัจจุบันยังไม่มีข้อมูลเกี่ยวกับโรคเป็นที่แพร่หลายในเวชปฏิบัติทั่วไป*

วัตถุประสงค์: *เพื่อศึกษาปัญหาที่สำคัญทางคลินิกของโรคนี้ ในด้านลักษณะทางคลินิกและผลการรักษา*

วัสดุและวิธีการ: *ในระหว่างเดือนมกราคม พ.ศ. 2543 ถึง เดือนธันวาคม พ.ศ. 2547 ได้ทำการศึกษาในผู้ป่วยที่มีอาการของขาขาดเลือดเรื้อรังจำนวน 411 ราย มีจำนวน 16 ราย (ร้อยละ 3.8) ที่ได้รับการวินิจฉัยโรคหลอดเลือดแดงของขาอุดตันจากลิ่มเลือดที่มีอาการขาดเลือดอย่างเรื้อรัง การอุดตันของหลอดเลือดแดงของขาจากลิ่มเลือดได้รับการวินิจฉัยยืนยันโดยภาพถ่ายหลอดเลือดแดงภายหลังการฉีดสารทึบรังสี, การตรวจพบลิ่มเลือดในขณะผ่าตัดและผลการตรวจทางพยาธิวิทยาจากขาส่วนที่หลอดเลือดแดงอุดตันลักษณะทางคลินิก และผลการรักษาได้รับการบันทึกและวิเคราะห์ทางสถิติ*

ผลการศึกษา: *พบผู้ป่วย 16 ราย ระยะเวลาเฉลี่ยที่ผู้ป่วยมีอาการทางคลินิกก่อนเข้ารับการรักษาประมาณ 2.44 เดือน ในผู้ป่วยกลุ่มนี้ ปัจจัยเสี่ยงทางคลินิกที่พบบ่อยที่สุดของผู้ป่วยในการรักษาโรคนี้ได้แก่ การเต้นของหัวใจผิดจังหวะชนิดเอเทรียล ฟิบิเลชั่น (ร้อยละ 25.0) ผู้ป่วย 3 ราย (ร้อยละ 18.75) มีประวัติการอุดตันของหลอดเลือดแดงจากลิ่มเลือดในบริเวณอื่นมาก่อน ตำแหน่งของหลอดเลือดแดงที่มีการอุดตันจากลิ่มเลือดบ่อยที่สุดได้แก่ หลอดเลือดแดงเฟมอรัล (ร้อยละ 63.1) ผู้ป่วย 14 ราย (ร้อยละ 87.5) มีการขาดเลือดของขาอยู่ในขั้นวิกฤต ผู้ป่วยจำนวน 9 ราย (ร้อยละ 56.25) ได้รับการรักษาโดยวิธีการเพิ่มเลือดโดยวิธีการต่าง ๆ อีก 5 ราย (ร้อยละ 31.25) ไม่สามารถผ่าตัดได้เนื่องจากหลอดเลือดแดงมีพังผืด การรักษาประสบความสำเร็จเพียงร้อยละ 50 ของผู้ป่วยที่มีขาขาดเลือดขั้นวิกฤต การตัดขาในผู้ป่วยกลุ่มนี้สูงถึงร้อยละ 43.75 มีผู้ป่วย 1 ราย (ร้อยละ 6.25) เสียชีวิตภายหลังการตัดขา*

สรุป: *โรคหลอดเลือดแดงของขาอุดตันจากลิ่มเลือดและมีการอาการขาดเลือดเรื้อรังเป็นโรคที่พบได้ไม่บ่อย แต่มีแนวโน้มจากถูกตัดขาสูง การวินิจฉัยการอุดตันของหลอดเลือดแดงของขาจากลิ่มเลือดในระยะแรก พร้อมทั้งได้รับการรักษาที่เหมาะสมทันทีน่าจะมีประโยชน์ในการช่วยให้รอดพ้นจากการตัดขาในผู้ป่วยเหล่านี้*