

Acute Arterial Embolism of the Lower Extremities: Impact of 24-Hour Duration on the Outcome of Management

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Objective: Determine the impact of 24-hour duration of arterial embolism on the outcomes of management.

Material and Method: A prospective study of 91 patients with acute arterial embolism of the lower extremities was carried out.

Results: Among the 91 patients, 31(34.1%) were with early acute embolism(< 24 hours) and 60 (65.9%) were with late acute embolism (> 24 hours). Extensive limb gangrene was more common in patients with late acute embolism (26.7% versus 3.2%, $p = 0.009$). Subsequently, primary major amputation was higher in those patients (20% versus 3.2%, $p = 0.05$). In early acute embolism, surgical embolectomy was only the primary treatment of revascularization (87.1%) whereas in late acute embolism, there were varying modalities of revascularization (68.3%) in addition to surgical embolectomy. The successful revascularization after the initial surgical embolectomy was significantly higher in patients with early acute embolism (92.6% versus 43.9%, $p < 0.001$). Patients with late acute embolism had a higher tendency of undergoing major amputation after revascularization (24.4% versus 7.4%, $p = 0.106$). Successful outcome was higher in patients with early acute embolism (83.9% versus 58.3%, $p = 0.014$).

Conclusion: The 24- hour duration of arterial embolism may be a crucial factor influencing the outcome in the management of this disease.

Keywords: Arterial embolism, Acute ischemia, Lower extremity, 24 hour duration of embolism, Outcome of management

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Arterial embolism is well recognized as the emergency problem of peripheral vascular disease causing sudden ischemia in the organ supplied by the occluded artery⁽¹⁾. Irreversible ischemia is inevitable whenever the revascularization has not been accomplished in a proper time⁽²⁾. Arterial embolism is more prevalent in the lower extremity^(3,4). Acute limb ischemia, the most common clinical manifestation of this disease⁽⁵⁾, substantially causes the disturbance of haemodynamic status and multiple organ functions

due to the release of the accumulated anaerobic metabolites into the systemic circulation when the ischemic process is ongoing through a long period⁽⁶⁾. Major amputation and death can be expected in the management of this disease due to several factors⁽⁷⁻¹³⁾. Duration of arterial embolism, correlating well with the degree of distal organ ischemia, is one of the important factors influencing the clinical consequence and the result of treatment^(8,14). However, there was a paucity of information on the definite length of duration of arterial embolism to determine the outcomes of management of this disease. The objective of the present study was to identify the significant difference in the outcomes of management between the patients suffering from acute embolism within 24 hours and after 24 hours prior to revascularization.

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Material and Method

Between January 2000 and December 2005, patients with clinical manifestations of acute limb ischemia (acute ischemic pain, pallor, poikilothermia, paresthesia, and paralysis) and the absence of peripheral ankle pulse were admitted to a vascular surgery unit for diagnosis and treatment. Criteria for diagnosis of acute arterial embolism included one of the following, a typical angiographic image of sharp cut off, emboli found in the lumen during the operation or histological confirmation of arterial embolism in the amputated specimen. Acute arterial thrombosis due to atherosclerosis obliterans, arteritis, aortic dissection, and vascular graft occlusion were excluded from the present study. Acute arterial embolism of the lower extremity was categorized into early acute and late acute with reference to 24 hours prior to revascularization. The severity of limb ischemia was classified into three categories: viable, threatened ischemia and irreversible ischemia⁽¹⁵⁾. Fig. 1 demonstrates the guideline of management in each group of limb ischemia. In the viable group, no immediate therapeutic intervention was required to maintain limb viability. However, revascularization procedures including surgical embolectomy, thrombolytic therapy, and arterial bypass surgery were the treatments for limb salvage in the threatened ischemia. Fig. 2 demonstrates the guideline of treatment for the threatened ischemia in acute arterial embolism. Surgical embolectomy was the primary treatment of acute embolism in this group⁽¹⁶⁾. Intraoperative thrombolysis was a supplemental adjunct in adequate run off following surgical embolectomy⁽¹⁷⁻¹⁹⁾. Arterial bypass surgery was performed whenever surgical embolectomy or intraoperative thrombolysis produced partial success with in complete distal run off demonstrated by intraoperative arteriography. Major amputations (below and above knee amputation) were indicated in the treatment of extensive irreversible limb ischemia and failure of revascularization procedures. Successful outcomes were characterized by the resolution of limb pain and restoration of limb viability without major amputation or death within six months after the treatment.

The demographic information on the duration of arterial embolism prior to revascularization, sites of arterial occlusion, risk factors, comorbidities, types of clinical manifestations, the severity of limb ischemia, types of treatment and the outcomes of management in patients with early and late acute embolism were recorded and analyzed. Statistical analysis included the *t*-test was used for continuous variables. Univariate

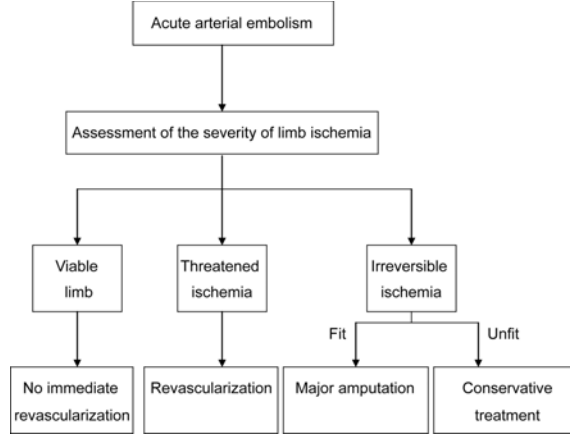


Fig. 1 Outline of the management of acute arterial embolism in the lower extremities

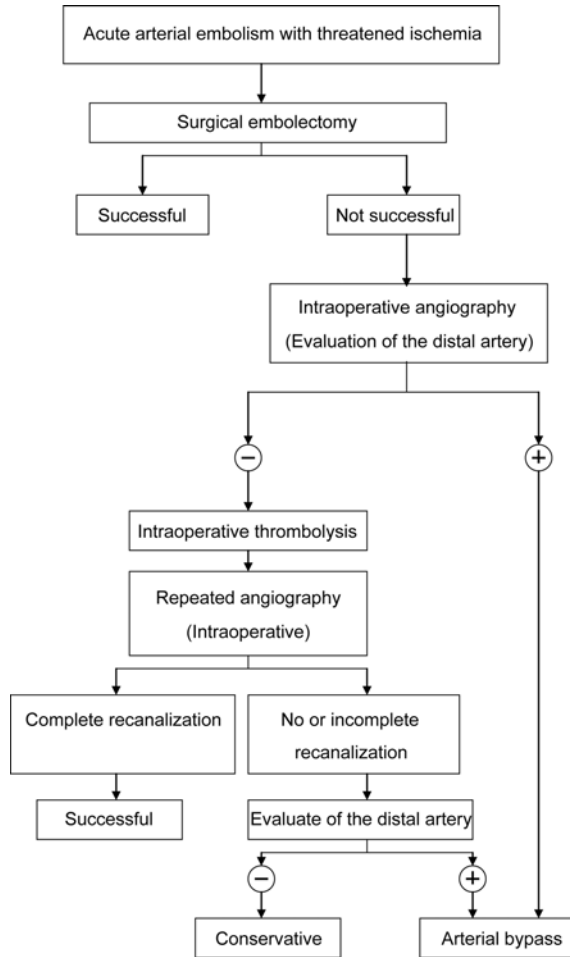


Fig. 2 Guideline of revascularization procedure in immediately threatened ischemia of acute arterial embolism in the lower extremities

association between patients with early and late acute embolism of the lower extremities was done by calculating Chi-Square test, Fisher's exact test, and the odds ratios with 95% confidence interval (CI). p-values < 0.05 were considered statistically significant.

Results

Of the consecutive 131 patients with clinical manifestations of acute arterial occlusion, 91 patients who fulfilled the criteria of acute arterial embolism were included in the present study. Twenty-nine patients with acute arterial thrombosis, six patients with Pythium

arteritis, three patients with aortic dissection, and two patients with vascular graft occlusion were excluded from the present study. Of these patients with acute arterial embolism, 31 (34.1%) patients were early acute and 60 (65.9%) patients were late acute. Table 1 summarizes data on gender and age distribution, sites of arterial occlusion, contralateral limb status, risk factors, and comorbidities of each type of arterial embolism. Males had a higher ratio than females in late acute embolism (42:18 vs. 15:16, p = 0.043). There was no difference in age distribution between these two groups. In the present study, femoral artery bifurcation

Table 1. Demographic informations, sites of arterial occlusion, contralateral limb status, risk factors and comorbidities of patients with early acute embolism and late acute embolism of the lower extremities

	Early acute (31)	Late acute (60)	Total (91)	p-value
Gender				
Male	15 (48.4)	42 (70.0)	57 (62.6)	0.043
Female	16 (51.6)	18 (30.0)	34 (37.4)	
Age				
Range	34.0-88.0	25.0-96.0	25.0-96.0	0.877
Mean ± SD	61.0 ± 17.0	61.6 ± 17.0	61.4 ± 16.9	
Median	63.0	60.0	61.0	
Sites of arterial occlusion				
Aortic occlusion	3 (9.7)	4 (6.7)	7 (7.7)	0.658
Iliac A. occlusion	3 (9.7)	12 (20.0)	15 (16.5)	0.337
Femoral A. occlusion	18 (58.0)	32 (53.3)	50 (54.9)	0.667
Popliteal A. occlusion	7 (22.6)	12 (20.0)	19 (20.9)	0.774
Contralateral limb status				
Aortic occlusion	3 (9.7)	4 (6.7)	7 (7.7)	0.686
Iliac A. occlusion	2 (6.5)	0 (0.0)	2 (2.2)	0.114
Femoral A. occlusion	3 (9.7)	7 (11.7)	10 (11.0)	1.000
Popliteal A. occlusion	2 (6.5)	5 (8.3)	7 (7.7)	1.000
Normal	21 (67.7)	44 (73.3)	65 (71.4)	0.576
Major amputation	0 (0.0)	0 (0.0)	0 (0.0)	-
Risk factors				
Atrial fibrillation	11 (35.5)	18 (30.0)	29 (31.9)	0.595
Myocardial infarction	4 (12.9)	7 (11.7)	11 (12.1)	1.000
Mitral stenosis	6 (19.4)	5 (8.3)	11 (12.1)	0.175
Proximal aneurysm	1 (3.2)	2 (3.3)	3 (3.3)	1.000
Polycythemia	1 (3.2)	1 (1.7)	2 (2.2)	1.000
Cardiac tumor	1 (3.2)	0 (0.0)	1 (1.1)	0.341
Previous thromboembolism	5 (16.1)	1 (16.7)	15 (16.5)	0.948
Unknown	11 (35.5)	34 (56.7)	45 (49.5)	0.055
Comorbidities				
Smoking	15 (48.4)	34 (56.7)	49 (53.9)	0.453
Hypertension	9 (29.0)	16 (26.7)	25 (27.5)	0.811
Diabetes mellitus	5 (16.1)	13 (21.7)	18 (19.8)	0.530
Hypercholesterol	2 (6.5)	4 (6.6)	6 (6.6)	1.000
Ischemic heart disease	8 (25.8)	16 (26.7)	24 (26.4)	0.930
Stroke	2 (6.5)	6 (10.0)	8 (8.8)	0.711
Renal failure	0 (0.0)	1 (1.7)	1 (1.1)	1.000

(54.9%) was the most common site of occlusion in acute arterial embolism followed by popliteal artery bifurcation (20.9%), iliac artery bifurcation (16.5%), and aortic bifurcation (7.7%). There was no significant difference in the distribution of the sites of arterial occlusion between the two groups. The peripheral ankle pulse of the contralateral limb was normal in 71.4% of patients with acute arterial embolism. These findings were similar in both groups of early (67.7%) and late (73.3%) acute embolism. Arterial fibrillation (31.9%), myocardial infarction (12.1%), and mitral valve stenosis (12.1%) were the common clinical risk factors in patients with acute arterial embolism. The risk factors and comorbidities in patients with early and late acute embolism were comparable. Furthermore, two patients under respiratory support were found only in late acute embolism. The distribution of clinical characteristics of early acute embolism and late acute embolism are summarized in Table 2. Mean duration of early acute embolism and late acute embolism were 10.1 and 156.4 hours respectively. Acute ischemic pain (93.4%) was the most common clinical manifestation of acute arterial embolism followed by pallor (94.5%), sensory loss (86.8%), and paralysis (74.7%). Muscle weakness was more predominant in late acute embolism (86.7% vs. 51.6%, odds ratio = 6.090, 95% CI 1.970, 19.430; $p < 0.001$). Limb infection was occasionally seen in patients with late acute embolism but no limb infection was detected in patients with early acute embolism. However, irreversible ischemia with extensive limb

gangrene was more common in patients with late acute embolism (26.7% vs. 3.2%, odds ratio = 10.91, 95% CI 1.38, 232.18; $p = 0.015$). Table 3 outlines the treatment modalities of each type of arterial embolism. In early acute embolism, surgical embolectomy was simply the primary treatment of revascularization, performed in 27 (87.1%) patients. On the contrary, in late acute embolism, there were several modalities of revascularization (68.3%) including surgical embolectomy alone in 23 (38.3%) patients, surgical embolectomy plus thrombolysis in four (6.7%) patients, surgical embolectomy plus arterial bypass surgery in nine (15.0%) patients, and surgical embolectomy plus thrombolysis together with arterial bypass surgery in five (8.3%) patients. Primary major amputation was significantly higher in late acute embolism than in early acute embolism (20% vs. 3.2%, $p = 0.05$), Table 3. Four patients with extensive limb gangrene in late acute embolism who could not undergo primary major amputation due to their unfit medical status succumbed to multiple organ failure.

Table 4 summarizes the outcomes of management in patients with acute arterial embolism. Successful outcome was higher in the management of early acute embolism compared with late acute embolism (83.9% vs. 58.3%, odds ratio = 3.71, 95% CI 1.14, 12.82; $p = 0.014$). The successful revascularization after the initial embolectomy was higher in the management of early acute embolism than that of late acute embolism (92.6% vs. 43.9%, odds ratio = 15.97, 95% CI 3.02, 112.41; $p < 0.001$). Patients with late acute embolism had a higher

Table 2. Clinical characteristics of patients with early acute embolism and late acute embolism of the lower extremities

	Early acute (31)	Late acute (60)	Total	Odds ratio	95%CI	p-value
Duration of embolism (hours)						
Range	3-22	26-504	3-504			<0.001
Mean \pm SD	10.1 \pm 6.3	156.4 \pm 126.3	106.55 \pm 123.8			
Median	7	120	72			
Clinical manifestations						
Pain	30 (96.8)	57 (95.0)	87 (95.6)	1.58	0.14-41.20	1.000
Pallor/Poikilothermia	29 (93.6)	57 (95.0)	86 (94.5)	1.31	0.14-10.44	1.000
Sensory loss	25 (80.7)	54 (90.0)	79 (86.8)	2.16	0.54-8.60	0.326
Muscle weakness	16 (51.6)	52 (86.7)	68 (74.7)	6.09	1.97-19.43	<0.001
Extensive gangrene	1 (3.2)	16 (26.7)	17 (18.7)	10.91	1.38-232.18	0.015
Limb infection	0 (0.0)	2 (3.3)	2 (2.2)	-	-	0.546
Severity of ischemia						
Viable	3 (9.7)	3 (5.0)	6 (6.6)	2.04	0.30-13.76	0.406
Threatened	27 (87.1)	41 (68.3)	68 (74.7)	3.13	0.87-12.27	0.089
Marginally	12 (38.7)	5 (8.3)	17 (18.7)	6.95	1.92-26.45	0.001
Immediately	15 (48.4)	36 (60.0)	51 (56.0)	1.60	0.61-4.20	0.290
Irreversible	1 (3.2)	16 (26.7)	17 (18.7)	10.91	1.38-232.18	0.015

tendency of undergoing major amputation after revascularization than those with early acute embolism (24.4% vs. 7.4%, $p = 0.106$). Furthermore, the total major amputation was higher in patients with late acute embolism (36.7% vs. 9.7%, odds ratio = 5.04, 95% CI 1.34, 25.26; $p = 0.013$). There was no statistical significant difference in mortality related to the management of patients with early versus late acute embolism (9.7% vs. 15.0%, $p = 0.745$). Myocardial infarction (9.7%) was the major cause of death in patients with early acute embolism whereas reperfusion injury (10.0%) was that of the late acute embolism in the present study, Table 5.

Discussions

It is well established that arterial embolism is a common cause of acute lower limb ischemia. Emboli from the proximal sources either cardiac or proximal aorta commonly occluded at the bifurcation of the arteries of the lower extremity⁽²⁰⁻²⁸⁾. The acute disruption of arterial circulation distal to the occlusion caused anoxia and loss of function in the distal organ. Toxic free radicals accumulated in the prolonged ischemic tissue were released into the systemic circulation. The latter contributed to the disturbance of cardiopulmonary and renal function⁽²⁹⁾. Long standing arterial occlusion precipitated the propagation of clot

Table 3. Types of treatment

Types	Early acute (31)	Late acute (60)	Total (91)	Odd Ratio	95%CI	p-value
Revascularization	27 (87.1)	41 (68.3)	68 (74.7)	3.13	0.87-12.27	0.089
Embolectomy alone	27 (87.1)	23 (38.3)	50 (54.9)	10.86	3.05-42.30	<0.001
Embolectomy plus thrombolysis	0 (0.0)	4 (6.7)	4 (4.4)	-	-	0.295
Embolectomy plus arterial bypass	0 (0.0)	9 (15.0)	9 (9.9)	-	-	0.025
Embolectomy plus thrombolysis arterial bypass	0 (0.0)	5 (8.3)	5 (5.5)	-	-	0.162
Major amputation (primary)	1 (3.2)	12 (20.0)	13 (14.3)	7.50	0.92-162.19	0.054
Conservative treatment	3 (9.7)	7 (11.7)	10 (11.0)	0.81	0.15-3.89	1.000

Table 4. Outcomes of treatment

Types	Early acute (31)	Late acute (60)	Odd Ratio	95%CI	p-value
Successful outcomes	26/31 (83.9)	35/60 (58.3)	3.71	1.14-12.82	0.014
Successful revascularization (after initial embolectomy)	25/27 (92.6)	18/41 (43.9)	15.97	3.02-112.41	<0.001
Major amputation (post revascularization)	2/27 (7.4)	10/41 (24.4)	4.03	0.72-29.47	0.106
Total major amputation	3/31 (9.7)	22/60 (36.7)	5.04	1.34-25.26	0.013
Total Mortality	3/31 (9.7)	9/60 (15.0)	1.65	0.36-8.42	0.745

Table 5. Causes of death

Types	Early acute (31)	Late acute (60)	Total (91)	Odd Ratio	95%CI	p-value
Myocardial infarction	3 (9.7)	2 (3.3)	5 (5.5)	3.11	0.39-28.52	0.333
Reperfusion injury	0 (0.0)	6 (10.0)	6 (6.6)	-	-	0.092
Sepsis	0 (0.0)	1 (1.7)	1 (1.1)	-	-	1.000
Total	3 (9.7)	9 (15.0)	12 (13.2)	1.65	0.36-8.42	0.745

formation in the distal artery and aggravated the distal tissue ischemia⁽³⁰⁾. Emboli and thrombi in the arterial lumen also injured the endothelium and resulted in producing the inflammatory reaction and adhesiveness to tunica intima. The longer the emboli occupied in the arterial lumen, the more difficult emboli removal and the higher incidence of rethrombosis were found. As a consequence, there was a higher failure rate in circulation reestablishment, prolonged distal tissue ischemia and major limb loss. However, there was no conclusion of the exact crucial time of duration to determine the outcome of the management of this disease⁽¹⁴⁾.

Due to the above information, acute arterial embolism in the present study was categorized into early acute and late acute by the duration of embolism before or after 24 hours prior to revascularization. Among the consecutive 91 patients, the number of patients with late acute embolism was much higher than that of early acute embolism (65.9% vs. 34.1%). This result implied that arterial embolism of the lower extremities had been underrecognized causing the delayed diagnosis and management. However, patients with stroke or requiring respiratory support, having the disturbance of consciousness and sensation of the lower extremities precluded detecting this disease at the early stage. In the present study, there were three patients with stroke and two patients under respiratory support responsible for the delayed diagnosis of acute arterial embolism. Limb ischemia beyond 24 hours had the tendency to result in extensive gangrene (26.7% vs. 3.2%, $p = 0.015$) and a higher incidence of primary major amputation (20.0% vs. 3.2%, $p = 0.05$), Table 2 and 3. Due to the toxic metabolic product accumulated in and released by the more than 24-hour ischemic tissue, alteration of the systemic haemodynamics leading to multiple organ dysfunction and major amputation was not uncommon. There was no survival in four patients with extensive gangrene who could not undergo primary major amputation due to their unfit general health status. These untoward conditions were the major factors contributing to the less successful outcome in the management of late acute embolism compared with the early acute embolism (58.3% vs. 83.9%, $p = 0.014$). The successful revascularization after the initial embolectomy was higher in the management of early acute embolism than that of late acute embolism (92.6% vs. 43.9%, $p < 0.001$), Table 5. These were the consequence of the adhesiveness between the emboli and the endothelium of the occluded arterial segment where the duration occlusion lasted more than 24 hours. Therefore, the complete removal of those

emboli could not be simply accomplished by surgical embolectomy alone. Despite the deployment of varying modalities of primary treatment, major amputation after revascularization in patients with late acute embolism superseded those with early acute embolism (24.4% vs. 7.4%, $p = 0.106$), Table 3 and 4. Furthermore, the total major amputation was higher in the management of late acute embolism compared with early acute embolism (36.7% vs. 9.7%, $p = 0.013$) (Table 4). These results demonstrated that the more than 24 hour duration of acute arterial embolism of the lower extremities had the higher tendency of major limb loss at both initial stage and after the treatment. The major causes of death were different in both groups, Table 5. Myocardial infarction, the significant comorbidity, was the major cause of death in patients with early acute embolism in the present study. However, reperfusion injury was the major cause of death in patients with late acute embolism due to the high frequency of extensive limb gangrene. This knowledge can be applicable for the selection of the modalities of revascularization and provide the information for the expected outcome of management of this disease.

In conclusion, the 24-hour duration of embolism may be the significant factor determining the outcomes of the management of acute arterial embolism in the lower extremities. The higher tendency of developing extensive limb gangrene, the higher number of major limb loss before and after revascularization and the less successful outcomes of treatments were observed in those patients with more than 24-hour duration.

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โรคหลอดเลือดของขาอุดตันเฉียบพลันจากลิ่มเลือด: ผลกระทบของการรักษาภายหลังการเกิดโรค 24 ชั่วโมง

ประมุข มุทิรากร, เฉนีเยน เรืองเศรษฐกิจ, ชุมพล ว่องวานิช, ญัฐวุฒิ เสริมสาธณสวัสดิ์, คามิน ชินศักดิ์ชัย

วัตถุประสงค์: เพื่อศึกษาผลกระทบของการรักษาโรคหลอดเลือดของขาอุดตันเฉียบพลันจากลิ่มเลือดภายหลังการเกิดโรค 24 ชั่วโมง

วัสดุและวิธีการ: การศึกษานี้ได้กระทำในผู้ป่วยโรคหลอดเลือดแดงของขาอุดตันเฉียบพลันจากลิ่มเลือด จำนวน 91 ราย โดยแบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มแรกเป็นผู้ป่วยที่ได้รับการรักษาภายใน 24 ชั่วโมง จำนวน 31 ราย และกลุ่มที่สองเป็นผู้ป่วยที่ได้รับการรักษาภายหลัง 24 ชั่วโมง จำนวน 60 ราย เพื่อทำการเปรียบเทียบ ลักษณะทางคลินิก และผลการรักษาในผู้ป่วยทั้งสองกลุ่ม

ผลการศึกษา: ผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกันในด้านอายุ ตำแหน่งของหลอดเลือดแดงของขาที่เกิดการอุดตัน ปัจจัยเสี่ยงของการเกิดลิ่มเลือด และโรคร่วมที่พบในผู้ป่วยแต่ละราย จากการศึกษา พบว่าผู้ป่วยกลุ่มที่สองมีภาวะเน่าตายของขาเกิดขึ้นในอัตราที่สูงกว่ากลุ่มแรกมาก (ร้อยละ 26.7 เปรียบเทียบกับร้อยละ 3.2 ค่าระดับนัยสำคัญทางสถิติ = 0.009) เป็นผลให้ในระยะเริ่มแรกของการรักษา ผู้ป่วยกลุ่มที่สองถูกตัดขาในอัตราที่สูงกว่ากลุ่มแรกมาก (ร้อยละ 20 เปรียบเทียบกับร้อยละ 3.2 ค่าระดับนัยสำคัญทางสถิติ = 0.05) ในผู้ป่วยกลุ่มแรกที่ยังไม่มีภาวะขาเน่าตาย การรักษาเพื่อเพิ่มเลือดได้ใช้การผ่าตัดขจัดลิ่มเลือดเพียงวิธีเดียว ซึ่งมีความสำเร็จสูงถึงร้อยละ 92.6 ส่วนในผู้ป่วยกลุ่มที่สองที่ยังไม่มีภาวะขาเน่าตาย การรักษาเพื่อเพิ่มเลือด จำเป็นต้องใช้การรักษาหลายวิธีร่วมกับการผ่าตัดขจัดลิ่มเลือด อาทิ ฉีดยาละลายลิ่มเลือด และการผ่าตัดเปลี่ยนทางเดินหลอดเลือดแดง เนื่องจากในการศึกษาครั้งนี้ การผ่าตัดขจัดลิ่มเลือดเพียงอย่างเดียว มีความสำเร็จเพียงร้อยละ 43.9 นอกจากนี้ผู้ป่วยกลุ่มที่สองมีแนวโน้มจะสูญเสียขาภายหลังการรักษาสูงกว่าผู้ป่วยกลุ่มแรก (ร้อยละ 24.4 เปรียบเทียบกับร้อยละ 7.4) โดยภาพรวมความสำเร็จของการรักษา โดยที่ผู้ป่วยไม่มีการสูญเสียขา และไม่เสียชีวิตพบในผู้ป่วยกลุ่มแรกมากกว่าผู้ป่วยกลุ่มที่สอง (ร้อยละ 83.9 เปรียบเทียบกับร้อยละ 58.3 ค่าระดับนัยสำคัญทางสถิติ = 0.014)

สรุป: ผลกระทบของการรักษาโรคหลอดเลือดแดงของขาอุดตันอย่างเฉียบพลันจากลิ่มเลือดภายหลังการเกิดโรค 24 ชั่วโมงทำให้มีประสิทธิภาพลดลงอย่างมาก โดยมีอัตราการสูญเสียขาเพิ่มขึ้นจากการเกิดภาวะขาเน่าตายมากขึ้น ก่อนเริ่มการรักษา และความสำเร็จในการเก็บรักษาขาลดลงถึงแม้จะมีการพยายามใช้การรักษาเพื่อเพิ่มเลือดหลายวิธีร่วมกันแล้วก็ตาม
