Clinical Differentiation Between Acute Arterial Embolism and Acute Arterial Thrombosis of the Lower Extremities

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Background: *The primary treatments of acute arterial embolism and acute arterial thrombosis are different. The clinical differentiation of the two diseases at initial stage can provide the efficient treatment of acute limb ischemia.*
Objective: *Identification of the clinical factors significant for the differentiation between acute arterial embolism and acute arterial thrombosis in acute lower extremity ischemia.*
Material and Method: *A prospective study of the consecutive 120 patients with acute lower extremity ischemia was carried out between January 2000 and December 2004. All clinical information was compared between the proven acute arterial embolism and acute arterial thrombosis.*
Results: *Among 120 patients, 91 (75.8%) were with acute arterial embolism and 29 (24.2%) were with acute arterial thrombosis. Normal peripheral pulse on the contralateral limb was more commonly found in patients with acute arterial embolism than in patients with acute arterial thrombosis (71.4% vs. 31.0%, $p < 0.001$). Atrial fibrillation was detected more in patients with acute arterial embolism than acute arterial thrombosis (31.9% vs. 3.4%, $p = 0.004$). Mitral valve stenosis (12.1%) and previous arterial embolism (16.5%) were only detected in patients with acute arterial embolism. On the other hand, patients with acute thrombosis had the higher comorbidities such as diabetes mellitus (44.8% vs. 19.8%, $p = 0.015$), hypertension (55.2% vs. 27.5%, $p = 0.012$), and hypercholesterolemia (37.9% vs. 6.6%, $p < 0.001$). Patients with acute arterial embolism had more severe clinical manifestations such as immediately threatened ischemia (56.0% vs. 13.8%, $p < 0.001$) and higher tendency of suffering from extensive limb gangrene (18.7% vs. 6.9%, $p = 0.156$). On the contrary, patients with acute arterial thrombosis had the previous symptom of intermittent claudication (51.7% vs. 3.3%, $p < 0.001$) more than patients with acute arterial embolism.*
Conclusion: *The clinical factors significant for the differentiation between acute arterial embolism and acute arterial thrombosis were the status of peripheral pulse on the contralateral limb, the clinical risk factors of the two diseases, the previous arterial embolism, the clinical manifestation, and progression of ischemic status.*

Keywords: *Acute arterial embolism, Acute arterial thrombosis, Acute limb ischemia, Clinical differentiation, Lower extremity*

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Acute arterial occlusion of the lower extremities, of the common peripheral vascular problem with the high tendency of major limb loss and death requires emergency management[1,2]. Acute arterial embolism and acute arterial thrombosis due to the dissection of atheromatous plaque are the predominant causes of this serious condition[3-7]. Clinical manifestations of both diseases are similar whereas their specific treatments are different[8,9]. Therefore, accurate differentiation between the two diseases at the initial stage is mandatory in order to set up the primary management for this emergency problem[10]. Despite angiography of the lower

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extremities providing the definite differentiation by visualization of embolus and atheromatous plaque at the occluded arteries, this investigation may not be available in the emergency situation. The aim of the present study was to identify the significant clinical factors for the accurate differentiation between acute arterial embolism and acute arterial thrombosis of the lower extremities.

Material and Method

Between January 2000 and December 2004, the consecutive patients admitted in a vascular surgery unit with the diagnosis of acute arterial embolism and acute arterial thrombosis due to atherosclerosis of the lower extremities were included in the present study. The diagnosis of both diseases was based on the clinical manifestations of acute arterial occlusion (pain, pale, cold, impaired sensation, muscle weakness and absence of distal peripheral pulse) together with the evidences of embolism and atheromatous plaque at the occluded arteries. These evidences were as the following. Firstly, by angiography, the image of sharp cut of contrast media was demonstrated in arterial embolism whereas the image of irregular narrowing of contrast media was visualized in arterial thrombosis. Secondly, the emboli in the arterial lumens or atheromatous plaque on the arterial wall were obviously seen in the operative findings. Thirdly, the histopathology of emboli or atheromatous plaque at the occluded artery was also demonstrated in the amputated specimens. The other pathology of arterial diseases such as arteritis, arterial dissection and thrombosed aneurysm and acute synthetic graft occlusion were excluded from the present study. The demographic information, sites of arterial occlusion, contralateral peripheral pulse, clinical risk factors, comorbidities, types of clinical manifestations, and severity of ischemia were classified as clinical factors for the initial differentiation between acute arterial embolism and acute arterial thrombosis before the definitive diagnosis was confirmed by angiography, operative findings, and histopathology of the amputated specimens. Statistical analysis included the t-test was used for continuous variables. Univariate association between patients with acute arterial embolism and acute arterial thrombosis of the lower extremities was done by calculating Chi-Square test, Fisher's exact test, and the odds ratios with 95% confidence interval (CI). Multivariate analysis was also performed with logistic regression techniques. P-value < 0.05 was considered statistically significant.

Results

Of the consecutive 120 patients with clinical manifestations of acute arterial occlusion, 91 (75.8%) patients with acute arterial embolism and 29 (24.2%) patients with acute arterial thrombosis were included in the present study. Six patients with acute Pythium arteritis, three patients with aortic dissection, two patients with thrombosed aneurysm, and two patients with vascular graft occlusion were excluded from the present study. Sixty-eight images of angiography of the lower extremities, ninety-one operative findings of revascularization procedure, and thirty-eight histopathology of major amputated specimens were used to confirm the diagnosis of acute arterial embolism and acute arterial thrombosis from atherosclerosis. Table 1 summarizes data on gender and age distribution, sites of arterial occlusion, and arterial status of contralateral limb in patients with acute arterial embolism and acute arterial thrombosis. The receiver operating characteristic (ROC) curve analysis demonstration no statistical significance in the age distribution between the two diseases (area curve = 0.551, 95% CI 0.441, 0.662, p = 0.406). There was also no statistical significance in the distribution of gender and sites of arterial occlusion in both groups. However, normal peripheral pulse on the contralateral limb was more commonly examined in patients with acute arterial embolism than acute arterial thrombosis (71.4% versus 31.0%, odds ratio 5.56, 95% CI 2.06, 15.31, $p < 0.001$). Table 2 demonstrates the distribution of risk factors and comorbidities in patients with acute arterial embolism and acute arterial thrombosis. Atrial fibrillation was more commonly found in patients with acute arterial embolism than acute arterial thrombosis (31.9% versus 3.4%, odds ratio 13.1, 95% CI 1.75, 270.97, p = 0.004). Furthermore, mitral valve stenosis was detected in 12.1% of patients with acute arterial embolism whereas this problem was not detectable in patients with acute arterial thrombosis. On the contrary, patients with acute arterial thrombosis had the comorbidities such as diabetes mellitus (44.8% versus 19.8%, odds ratio 3.30, 95% CI 1.23, 8.88, p = 0.015), hypertension (55.2% versus 27.5%, odds ratio 3.25, 95% CI 1.26, 8.45, p = 0.012) and hypercholesterolemia (37.9% versus 6.6%, odds ratio 8.66, 95% CI 2.52, 30.84, $p < 0.001$) more than patients with acute arterial embolism. There was no statistical difference in smoking, the associated ischemic heart disease, disabling stroke and renal failure in patients with these two diseases. Previous embolism was found only in patients with acute arterial embolism (16.5%).

Table 1. Distribution of gender, age, sites of arterial occlusion and contralateral limb status in patients with acute arterial embolism and acute arterial thrombosis

	Embolism (91)	Thrombosis (29)	Odds ratio	95% CI	p-value
Gender					
Male	57 (62.6)	21 (72.4)	1.57	0.58-4.35	0.461
Female	34 (37.4)	8 (27.6)			
Age (years)					
Mean (SD)	61.4 (16.9)	63.5 (14.4)			0.535
Median	61	66			
Range	25-96	42-80			
Sites of arterial occlusion					
Aortic occlusion	7 (7.7)	5 (17.2)	2.50	0.62-9.90	0.159
Iliac A. occlusion	15 (16.5)	7 (24.1)	1.61	0.52-4.92	0.514
Femoral A. occlusion	50 (54.9)	11 (37.9)	2.00	0.78-5.13	0.167
Popliteal A. occlusion	19 (20.9)	6 (20.7)	1.01	0.33-3.23	0.809
Contralateral pulse					
Normal	65 (71.4)	9 (31.0)	5.56	2.06-15.31	<0.001
Abnormal	26 (28.6)	18 (62.0)	4.09	1.57-10.82	0.002
Unidentified (Major amputation)	0 (0.0)	2 (7.0)	-	-	0.057

Table 2. Risk factors and comorbidities in patients with acute arterial embolism and acute arterial thrombosis

Types	Embolism (91)	Thrombosis (29)	Odds ratio	95% CI	p-value
Atrial fibrillation	29 (31.9)	1 (3.4)	13.10	1.75-270.97	0.004
Mitral stenosis	11 (12.1)	0 (0.0)	-	-	0.064
Diabetes mellitus	18 (19.8)	13 (44.8)	3.30	1.23-8.88	0.015
Hypertension	25 (27.5)	16 (55.2)	3.25	1.26-8.45	0.012
Hypercholesterol	6 (6.6)	11 (37.9)	8.66	2.52-30.84	<0.001
Smoking	49 (53.9)	21 (72.4)	2.25	0.83-6.21	0.121
Ischemic heart disease	24 (26.4)	6 (20.7)	1.37	0.46-4.29	0.712
Stroke	8 (8.8)	3 (10.3)	1.20	0.23-5.51	0.726
Renal failure	1 (1.1)	0 (0.0)	-	-	1.000
Previous embolism	15 (16.5)	0 (0.0)	-	-	0.021

Table 3 summarizes the distribution of types of clinical manifestations and severity of limb ischemia in patients with acute arterial embolism and acute arterial thrombosis. There was no statistical difference in the duration of disease prior to hospitalization between the two diseases. Patients with arterial embolism had more severe clinical manifestations than patients with acute arterial thrombosis. Impaired sensation (86.8% versus 65.5%, odds ratio 3.46, 95% CI 1.17, 10.27, $p = 0.021$) and muscle weakness (74.7% versus 20.7%, odds ratio 11.33, 95% CI 3.76, 35.84, $p < 0.001$) were more commonly found in patients with acute arterial embolism. Subsequently, the number of patients with immediately threatened ischemia was higher in acute arterial embolism than acute arterial thrombosis (56.0% versus 13.8%, odds ratio 7.97, 95% CI 2.36, 29.57, $p < 0.001$). Furthermore, patients with acute arterial embolism had a higher tendency of suffering from extensive limb gangrene compared to patients with acute arterial thrombosis (18.7% versus 6.9%, $p = 0.156$). On the other hand, patients with acute arterial thrombosis had the symptom of intermittent claudication (51.7% versus 3.3%, odds ratio 31.43, 95% CI 7.17, 158.94, $p < 0.001$) more than patients with acute arterial embolism.

Discussion

Acute arterial embolism and acute arterial thrombosis are the common causes of acute arterial

Table 3. Clinical manifestations and severity of limb ischemia in patients with acute arterial embolism and acute arterial thrombosis

	Embolism (91)	Thrombosis (29)	Odds ratio	95% CI	p-value
Duration (days)					
Range	1-21	1-14	-	-	
Mean (SD)	4.4 (5.2)	6.2 (4.7)	-	-	0.103
Median	3	5	-	-	
Clinical manifestations					
Acute ischemic pain	87 (95.6)	28 (96.6)	1.29	0.13-31.54	1.000
Pale, cold	86 (94.5)	27 (93.1)	1.27	0.16-8.08	0.675
Impaired sensation	79 (86.8)	19 (65.5)	3.46	1.17-10.27	0.021
Muscle weakness	68 (74.7)	6 (20.7)	11.33	3.76-35.84	<0.001
Intermittent claudication	3 (3.3)	15 (51.7)	31.43	7.17-158.94	<0.001
Extensive gangrene	17 (18.7)	2 (6.9)	3.10	0.62-20.84	0.156
Severity of ischemia					
Viable	6 (6.6)	1 (3.4)	1.98	0.22-45.45	1.000
Threatened	68 (74.7)	26 (89.7)	2.93	0.74-13.43	0.149
Marginally	17 (18.7)	22 (75.9)	13.68	4.58-42.53	<0.001
Immediately	51 (56.0)	4 (13.8)	7.97	2.36-29.57	<0.001
Irreversible	17 (18.7)	2 (6.9)	3.10	0.62-20.84	0.156

occlusion of the lower extremities[7]. This clinical problem requires an urgent decision for the effective management to avoid the progressive limb ischemia and extensive gangrene. Delayed diagnosis and treatment will eventually result in major limb loss and death[11-13]. Despite the similarity of clinical manifestations, the specific treatments of the two diseases are different. Surgical embolectomy with or without intraoperative thrombolysis and catheter directed thrombolysis are the specific treatments of acute arterial embolism[14-19] whereas acute arterial thrombosis requires more complicated procedures such as arterial bypass surgery and endovascular therapy (balloon angioplasty with or without intravascular stent) after successful catheter directed thrombolysis[20-29]. The facility of equipment and instruments including the availability of vascular graft and intravascular stent are also required for the treatment of acute arterial thrombosis. Even though angiography was the most effective method to differentiate between these two diseases, this investigation is not simple and may not be available in the emergency condition. The differentiation of both diseases by using the clinical information is beneficial in this critical situation. Patients with clinical diagnosis of acute arterial embolism may also undergo the revascularization immediately in general hospital at the initial stage with the favorable result. On the other hand, patients with clinical diagnosis of acute arterial thrombosis should be referred to the medical center where the facility and an experienced vascular team are available.

It has been suggested that the significant clinical factors for the differentiation between acute arterial embolism and acute arterial thrombosis were the peripheral pulse status on the contralateral limbs, clinical risk factors of arterial embolism such as atrial fibrillation and mitral valve stenosis, and symptoms of intermittent claudication[30,31]. However, there was a paucity of the information on the accuracy of this clinical differentiation. The present study confirmed and provided the statistical information from univariate analysis of these significant clinical risk factors of the two diseases. Furthermore, in multivariate analysis, there was no confounding problem among each clinical factor. Normal peripheral pulse on the contralateral limb was more commonly found in patients with acute arterial embolism than in acute arterial thrombosis (71.4% versus 31.0%, $p < 0.001$) Table 1. Atrial fibrillation was more commonly identified in patients with acute arterial embolism than in patients with acute arterial thrombosis (31.9% versus 3.4%, $p = 0.004$). Mitral valve stenosis was only identified in patients with acute arterial embolism (12.1%) Table 2. Patients with acute arterial thrombosis had the symptom of intermittent claudication more often than patients with acute arterial embolism (51.7% versus 3.3%, $p < 0.001$) Table 3.

In addition, the clinical risk factors of atherosclerosis obliterans, the major cause of acute arterial

thrombosis were also classified as the significant clinical factors for the clinical differentiation in the present study. Diabetes mellitus (44.8% versus 19.8%, $p = 0.015$), hypertension (55.2% versus 27.5%, $p = 0.012$) and hypercholesterolemia (37.9% versus 6.6%, $p < 0.001$) were more commonly found in patients with acute arterial thrombosis than in patients with acute arterial embolism, Table 2. However, there was no statistical significance of smoking between the two groups. This result may be due to the high incidence of smoking in this population. Patients with arterial embolism have a high tendency of recurrence when the risk factors of this disease are not corrected and the dosage of anti-coagulant is not at the optimal level[32]. In the present study, previous embolism (16.5%) was found only in patients with acute arterial embolism ($p = 0.021$), Table 2. In acute arterial embolism, the artery is suddenly occluded resulting in rapidly progressive ischemia in the distal limb without adequate collateral circulation. On the other hand, ischemic process in acute arterial thrombosis is gradually progressive due to the presence of collateral circulation, previously developed during the progression of atherosclerosis[33]. Accordingly, patients with acute arterial embolism, should present with the more severe clinical manifestations than patients with acute arterial thrombosis. In the present study, patients with acute arterial embolism presented with the symptoms of impaired sensation (86.8% versus 65.5%, $p = 0.021$) and muscle weakness (74.7% versus 20.7%, $p < 0.001$) more than patients with acute arterial thrombosis resulting in the higher number of immediately threatened ischemia (56.0% versus 13.8%, $p < 0.001$) in the former group. Furthermore, there was a higher tendency of suffering from extensive limb gangrene in patients with acute arterial embolism than in patients with acute arterial thrombosis (18.7% versus 6.9%, $p = 0.156$), Table III. These results confirmed the rapid progression of ischemic status and the necessity of emergency management in patients with acute arterial embolism to avoid the rapidly progressive and irreversible ischemia[34]. On the contrary, there is a spare time reserved for the investigations and the preoperative preparation in patients with acute arterial thrombosis due to the gradually progressive ischemia. The specific treatment in acute arterial thrombosis is therefore not as urgent as acute arterial embolism.

In conclusion, the significant clinical factors for the clinical differentiation between acute arterial embolism and acute arterial thrombosis of the lower extremities were the status of peripheral pulse on the contralateral limb, clinical risk factors of embolism and atherosclerosis obliterans, previous embolism, the clinical manifestations and the progression of ischemic process. The significance of these factors may be the useful information to set up the diagnostic score to increase the accuracy for the clinical differentiation between the two diseases.

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การศึกษาข้อมูลทางคลินิกเพื่อการวินิจฉัยแยกสาเหตุของหลอดเลือดแดงของขาอุดตันอย่างเฉียบพลันระหว่างการอุดตันจากลิ่มเลือดและการอุดตันจากแผ่นไขมัน

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ภูมิหลัง: การรักษาโรคหลอดเลือดแดงของขาอุดตันจากลิ่มเลือดและจากแผ่นไขมันมีความแตกต่างกัน การวินิจฉัยทางคลินิกเพื่อแยกโรคทั้งสองประเภทได้ในระยะแรกจะเพิ่มประสิทธิภาพการรักษาผู้ป่วยที่มีภาวะขาขาดเลือดเฉียบพลัน

วัตถุประสงค์: เพื่อค้นหาข้อมูลทางคลินิกที่มีประโยชน์ต่อการวินิจฉัยแยกสาเหตุของหลอดเลือดแดงของขาอุดตันอย่างเฉียบพลันระหว่างการอุดตันจากลิ่มเลือดและการอุดตันจากแผ่นไขมัน

วัสดุและวิธีการ: การศึกษานี้ได้กระทำในผู้ป่วยโรคหลอดเลือดแดงของขาอุดตันอย่างเฉียบพลันที่มีสาเหตุจากโรคทั้งสองกลุ่มที่ได้รับการรักษาภายในโรงพยาบาลระหว่างวันที่ 1 มกราคม พ.ศ. 2543 ถึง วันที่ 31 ธันวาคม พ.ศ. 2547 จำนวน 120 ราย โดยทำการเปรียบเทียบความแตกต่าง ๆ ของลักษณะทางคลินิกและปัจจัยเสี่ยงทางคลินิกของโรคทั้งสองกลุ่ม

ผลการศึกษา: การศึกษานี้ได้พบผู้ป่วยมีหลอดเลือดแดงอุดตันจากลิ่มเลือด 91 ราย (ร้อยละ 75.8) และผู้ป่วยที่มีหลอดเลือดแดงอุดตันจากแผ่นไขมัน 29 ราย(ร้อยละ 24.2) ผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างกันทางสถิติในด้านเพศ อายุ ระยะเวลาของเกิดโรคก่อนรับการรักษา และตำแหน่งการอุดตันของหลอดเลือดแดง ในการศึกษานี้พบว่าผู้ป่วยที่มีการอุดตันของหลอดเลือดแดงจากลิ่มเลือดมีสภาพของชีพจรของขาด้านตรงข้ามอยู่ในเกณฑ์ปกติมากกว่าผู้ป่วยที่มีการอุดตันของหลอดเลือดแดงจากแผ่นไขมัน (ร้อยละ 71.4 เปรียบเทียบกับร้อยละ 31.0 ค่าระดับนัยสำคัญทางสถิตินัอยกว่า 0.001) ผู้ป่วยที่มีการอุดตันของหลอดเลือดแดงจากลิ่มเลือดมีหัวใจเต้นผิดจังหวะชนิดเอเทรียลฟิบิเลชั่นมากกว่าผู้ป่วยที่มีการอุดตันของหลอดเลือดแดงจากแผ่นไขมัน (ร้อยละ 31.9 เปรียบเทียบกับร้อยละ 3.4 ค่าระดับนัยสำคัญทางสถิติเท่ากับ 0.004) นอกจากนี้โรคลิ้นหัวใจชนิดไมตรัลตีบ (ร้อยละ 12.1) และประวัติการเกิดลิ่มเลือดอุดตันภายในหลอดเลือดแดงบริเวณอื่น (ร้อยละ 16.5) จะพบเฉพาะในผู้ป่วยที่มีการอุดตันของหลอดเลือดแดงจากลิ่มเลือดเท่านั้น ในอีกด้านหนึ่งโรคที่เป็นปัจจัยเสี่ยงต่อการก่อตัวของแผ่นไขมันจะพบในผู้ป่วยที่มีหลอดเลือดแดงอุดตันจากแผ่นไขมันมากกว่าการอุดตันจากลิ่มเลือด โรคเหล่านี้ได้แก่โรคเบาหวาน (ร้อยละ 44.8 เปรียบเทียบกับ ร้อยละ 19.8 ค่าระดับนัยสำคัญทางสถิติเท่ากับ 0.015) โรคความดันโลหิตสูง (ร้อยละ 55.2 เปรียบเทียบกับร้อยละ 27.5 ค่าระดับ นัยสำคัญทางสถิตินัอยกว่า 0.012) และโรคไขมันในเลือดสูง (ร้อยละ 37.9 เปรียบเทียบกับร้อยละ 6.6, ค่าระดับ นัยสำคัญทางสถิตินัอยกว่า 0.001) ผู้ป่วยโรคหลอดเลือดแดงอุดตันจากลิ่มเลือดมีลักษณะคลินิกของการขาดเลือดเฉียบพลันขั้นรุนแรงมากกว่า (ร้อยละ 56.0 เปรียบเทียบกับร้อยละ 13.8 ค่าระดับนัยสำคัญทางสถิตินัอยกว่า 0.001) และมีแนวโน้มของการเกิดภาวะขาเน่าตายมากกว่า (ร้อยละ 18.7 เปรียบเทียบกับร้อยละ 6.9 ค่านัยสำคัญทางสถิติเท่ากับ 0.156) ผู้ป่วยโรคหลอดเลือดแดงอุดตันจากแผ่นไขมันจะมีอาการปวดขาในขณะเดินซึ่งเป็นลักษณะของการขาดเลือดเรื้อรังมากกว่า (ร้อยละ 51.7 เปรียบเทียบกับร้อยละ 3.3 ค่าระดับนัยสำคัญทางสถิตินัอยกว่า 0.001)

สรุป: ข้อมูลทางคลินิกที่ควรเป็นประโยชน์เพื่อการวินิจฉัยแยกสาเหตุของการอุดตันหลอดเลือดแดงของขาอย่างเฉียบพลันระหว่างการอุดตันจากลิ่มเลือดและการอุดตันจากแผ่นไขมันได้แก่ สภาพชีพจรของขาด้านตรงข้าม ปัจจัยเสี่ยงทางคลินิกของการเกิดลิ่มเลือดอุดตันและการก่อตัวของแผ่นไขมัน ประวัติการเกิดลิ่มเลือดอุดตันภายในหลอดเลือดแดงบริเวณอื่น ลักษณะทางคลินิกของขาขาดเลือด และการเปลี่ยนแปลงความรุนแรงของขาขาดเลือดอย่างเฉียบพลันภายหลังการเกิดการอุดตันภายในหลอดเลือดแดง การวินิจฉัยทางคลินิกเพื่อแยกโรคทั้งสองชนิดนี้มีประโยชน์ในการวางแผนการรักษาผู้ป่วยที่มีภาวะขาขาดเลือดเฉียบพลันอย่างมีประสิทธิภาพต่อไป