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Thrombotic Lesions are Associated with Poor Outcomes after Endovascular Treatment in Patients with Non-Acute Aortoiliac Total Occlusions

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Aim: The post-endovascular treatment outcomes of thrombotic lesions remain unclear. This study aimed to investigate the effects of thrombotic lesions on post-endovascular treatment outcomes in patients with non-acute aortoiliac total occlusions.

Methods: This subanalysis of a multicenter prospective observational registry study included patients from 64 institutions in Japan between April 2014 and April 2016. A total of 346 patients (394 limbs; median age, 72 years), including 186 men, underwent endovascular treatment for non-acute aortoiliac total occlusions and were included. The patients were classified as having thrombotic or non-thrombotic lesions. The primary (1-year primary patency rate) and secondary (1-year overall survival rate) endpoints were evaluated.

Results: Thrombotic lesions were identified in 18.5% (64/346) of the patients. The 1-year primary patency (85.9% versus 95.4%, log-rank $p<.001$) and overall survival (90.6% versus 97.9%, log-rank $p=.003$) rates were significantly lower in the thrombotic group than in the non-thrombotic group. Thrombotic lesions had significant effects on the post-endovascular treatment outcomes, with adjusted hazard ratios of 3.91 (95% confidence interval, 1.64–9.34, $p=.002$) for primary patency and 4.93 (95% confidence interval, 1.59–15.3, $p=.006$) for all-cause mortality.

Conclusions: Thrombotic lesions were associated with 1-year restenosis and all-cause mortality after endovascular treatment for non-acute aortoiliac total occlusions. Endovascular treatment strategies should be carefully planned for patients with thrombotic lesions.

Key words: Thrombotic lesion, Endovascular treatment, Peripheral artery diseases, Aortoiliac vessels, Outcome analysis

Clinical Trial Registration: This trial was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000013849; date, 1 May 2014).

Introduction

Endovascular treatment (EVT) is the mainstay of treatment for patients with aortoiliac (AI) artery disease, and favorable post-EVT outcomes were reported[1-2]. Among patients undergoing EVT for AI lesions, 24% have chronic total occlusions (CTOs)[1]. Generally, CTOs are hard lesions containing rigid

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fibrous tissue, calcified tissue, and organized thrombi, increasing the difficulty of passing guidewires and other devices through the lesion[3-5]. There may also be soft total occlusions composed of loose fibrous tissue, pultaceous debris, and abundant unorganized thrombi[4, 5] that are easily penetrated by wires. In clinical EVT settings, such soft lesions are customarily termed "thrombotic" lesions[6] and are associated with a higher risk of distal embolization than non-thrombotic lesions[6, 7]. Although there are no clear definitions of thrombotic lesions, operators typically assess whether a lesion is thrombotic based on intraoperative findings to estimate the risk of distal embolization, which is a serious complication during AI-EVT[8-12]. For example, when the target lesion is soft and can be easily and quickly penetrated using a guidewire[13], or mobile and radiolucent substances are observed angiographically[7], operators classify the lesion as being thrombotic. The lesion characteristics may affect the clinical outcome after EVT. However, the differences in post-EVT outcomes for thrombotic and non-thrombotic lesions have not been fully explored.

Aim

This study aimed to investigate the effects of thrombotic lesions on post-EVT outcomes in patients with non-acute AI total occlusions.

Methods

This study was a subanalysis of the "Observational prospective Multicenter registry study on Outcomes of peripheral arTErial disease patieNts treated by AngioplaSty tHerapy in aortoIliac artery" (OMOTENASHI) registry[14, 15]. The registry involved a multicenter prospective observational study of EVT for AI disease that enrolled patients from 64 institutions in Japan between April 2014 and April 2016. This trial was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000013849). All procedures involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the ethical committee at each participating hospital. All patients provided written informed consent prior to participating.

Study Population

The study participants were patients with symptomatic PAD (Rutherford Clinical Category, 2–4) who were undergoing EVT for AI total occlusions; the PAD diagnoses were confirmed in accordance with the current guidelines[16]. Patients were excluded if they were diagnosed with acute limb ischemia or acute thrombosis within one week of enrollment, had undergone EVT or vascular surgery within 30 days prior to treatment, had untreated coagulation or significant bleeding disorders, or were unable to receive anticoagulation or antiplatelet treatment.

Thrombotic Versus Non-Thrombotic Lesions

The patients were classified into thrombotic or non-thrombotic lesion groups, based on intraoperative findings during the EVT procedure, by at least two or more attending surgeons. Generally, lesions that were considered thrombotic lesions had higher probabilities of causing distal embolization; lesions that were considered to have lower risks of distal embolization were classified as non-thrombotic lesions. Specifically, the key indicators of thrombotic lesions were set as follows[7, 10, 17]: (1) the occlusion was soft and fragile during wire manipulation, or wire penetration through the occlusion was simple and rapid under the standard methods of each operator[10], (2) mobile radiolucent substances were angiographically detected during EVT[7], (3) mobile substances were observed using intravascular ultrasound (IVUS), and (4) large amounts of low echoic material were observed, using IVUS, in vessels with markedly positive remodeling[17]. Although these indications included a subjective component, all attending surgeons used the same classification criteria.

EVT Procedure

EVT was conducted with the patient under local anesthesia using either a 6-Fr sheath or a sheathless guiding catheter. The contralateral or ipsilateral femoral approaches were mainly used. The selection of stent type, length, and diameter; use of IVUS; and antiplatelet regimens were determined by the surgeon. Stent grafting was not used because of the restriction of the Japanese health insurance system. A filter

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embolic protection device or balloon-tipped occlusion catheter was used as the distal protection device.

Follow-Up and Endpoints

All patients were asked to return for a post-EVT check-up at 1, 6, and 12 months. At each visit, patient symptoms and ankle brachial index (ABI) values were evaluated; duplex ultrasonography (DUS) was routinely conducted to evaluate patency. If exacerbation was noted, the patient underwent follow-up angiography.

The primary endpoint was 1-year primary patency. Restenosis was assessed using follow-up angiography, computed tomography, or DUS, with a tolerance of ±2 months. The secondary endpoint was the overall survival rate.

Definitions

Initial technical success was defined as <30% residual stenosis. Procedure-related complications included death, stroke, acute myocardial infarction, retroperitoneal bleeding, access site complications, distal embolization, worsening renal function, surgical repair, perforation, aortic dissection, stent thrombosis, systemic embolism, or any other occurrence necessitating a prolonged hospital stay. Primary patency was defined as the absence of treated vessel restenosis requiring repeat revascularization. Restenosis was defined as ≥ 50% stenosis on computed tomography or angiography scans, DUS-determined peak systolic velocity ratio of ≥ 2.5, an ABI decrease ≥ 0.2, a DUS-determined monophasic flow pattern in the groin, or target vessel revascularization. Major adverse cardiovascular events (MACEs) were defined as death, myocardial infarction, and stroke. Clinically driven target lesion revascularization (CDTLR) was defined as re-intervention at the target lesion due to symptoms or an ABI decrease of >0.2, compared with the post-procedural ABI.

Statistical Analysis

Continuous variables are presented as medians and interquartile ranges (quartiles 1–3), and categorical variables as counts and percentages. Differences in continuous and categorical variables between the groups were compared using the Wilcoxon rank sum and chi-square tests, respectively. The incidence of each endpoint was estimated using the Kaplan-Meier method; the difference between the groups was evaluated using the log-rank test. Additionally, the impact of thrombotic lesions on endpoints, as compared with that of non-thrombotic lesions, was evaluated using univariable and multivariable Cox regression models. Because the factors affecting each endpoint were expected to be different, the analysis was performed using two separate models for each parameter. The following variables were included as possible confounders: age, sex, body mass index >25, diabetes, chronic kidney disease (≥ stage 3), both common and external iliac artery lesions, and incidence of procedural complications. Among variables with *p*-values ≤ .1 in the univariate analysis, clinically important variables with lower p-values were treated as confounders, considering the number of endpoints and multicollinearity. Statistical analyses were performed using the R software package (version 3.3.2; R Development Core Team, Vienna, Austria). The significance level for two-sided statistical hypothesis testing was set at .05.

Results

Among the 893 registered patients (1128 limbs) scheduled to undergo EVT for AI disease, 394 limbs from 346 patients (286 [82.7%] men; median age, 72 [range, 66–78] years) with total occlusion lesions were evaluated **(Fig. 1)**. Thrombotic lesions were identified in 18.5% (64/346) of the total patients or in 17.3% (68/394) of the total limbs. The median body mass index and frequency of patient dialysis were significantly lower in the thrombotic group than in the non-thrombotic group, but there were no significant between-group differences in other risk factors, comorbidities, medical histories, or medications **(Table 1)**.

The ABI values were similar in both groups, whereas extended lesions, including both external and common iliac artery disease, were more frequent in the thrombotic group than in the non-thrombotic group. The frequency of outflow femoro-popliteal lesions was comparable in both groups. Severe calcifications were observed less frequently in the thrombotic group than in the non-thrombotic group. Regarding the procedural information, distal protection devices were more frequently used in the thrombotic group than in the non-thrombotic group. The mean stent diameters were comparable in both groups, whereas the total stent length was significantly longer in the thrombotic group **(Table 2)**.

There were no differences in the post-EVT medications between the groups **(Table 3)**. Although the initial technical success rates were comparable in both groups, the frequencies of procedure-related complications and prolonged hospitalizations due to complications were significantly higher in the thrombotic group than in the non-thrombotic group **(Table 4)**.

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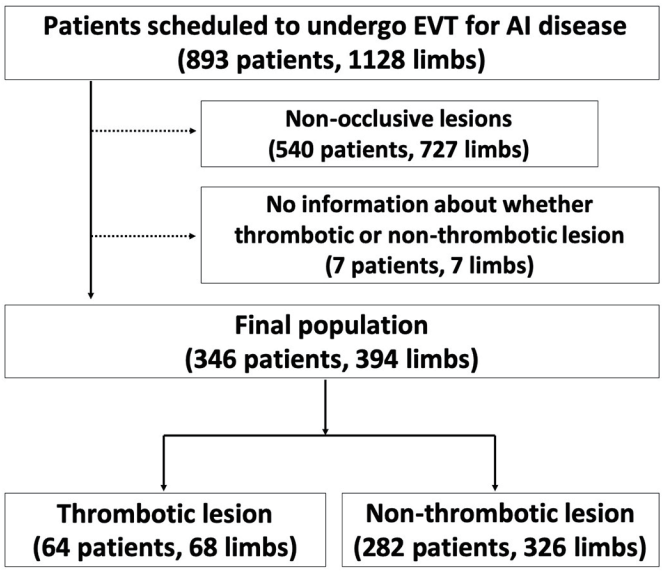

Fig. 1. Patient selection flowchart
EVT, endovascular treatment; AI, aortoiliac

The estimated 1-year primary patency (85.9% versus 95.4%, log-rank $p<.001$) **(Fig. 2)** and overall survival (90.6% versus 97.9%, log-rank $p=.003$) **(Fig. 3)** rates were significantly lower in the thrombotic group than in the non-thrombotic group. Among all-cause deaths, cardiovascular deaths were significantly more common in the thrombotic group than in the non-thrombotic group, whereas the non-cardiovascular death rates were comparable **(Table 4)**. There were no significant differences in the CDTLR or MACE rates **(Table 4)**.

Thrombotic lesions demonstrated statistically significant impacts on post-EVT outcomes with adjusted hazard ratios (HRs) of 3.91 (95% confidence interval [CI] 1.64–9.34; $p=.002$) for primary patency (**Table 5**, model 1) and 4.93 (95% CI, 1.59–15.3, $p=.006$) for all-cause mortality (**Table 6**, model 1).

Discussion

We demonstrated that the 1-year primary patency was significantly lower in patients with thrombotic lesions than in those with non-thrombotic lesions, and thrombotic lesion was independently associated with 1-year restenosis after AI-EVT. Moreover, the all-cause mortality and cardiovascular death rates were higher in the thrombotic group than in the non-thrombotic group, and thrombotic lesion was an independent predictor of 1-year mortality. Because previous studies have not shown an association between thrombotic lesions and poor outcomes, our study may provide physicians with new insights into these lesions.

Post-EVT Restenosis in Thrombotic Lesions

A previous study showed that the 1-year primary patency rate of EVT for AI-CTOs was 92.5%, and female sex, diabetes, renal failure, absence of aspirin therapy, reference vessel diameter <8.0 mm, and outflow lesions were independent predictors of primary patency[1]. However, the frequency of thrombotic lesion has not been reported, and the potential relationship between thrombotic lesion and post-EVT outcome was not evaluated. Therefore, this study investigated the clinical impact of thrombotic lesion in patients who underwent AI-EVT. Our results indicated that the presence of thrombotic lesion was associated with poor post-EVT outcome.

Generally, the technical aspects of EVT for thrombotic lesions are not considered to be a problem because of the ease of wire penetration or device delivery. However, given our results, we speculated that there were several pitfalls in the EVT procedure for thrombotic lesions, which may have contributed to the high restenosis rate. First, the high incidence of plaque protrusions after stent implantation may affect restenosis in the thrombotic lesion. Patients with plaque protrusions demonstrate larger thrombus formations and lower baseline calcium levels than those without plaque protrusions[18], indicating that thrombotic lesions carry a higher risk of plaque protrusion than non-thrombotic lesions. Moreover,

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Table 1. Baseline characteristics of participants*

Parameter	Thrombotic ($n=64$)	Non-thrombotic ($n=282$)	p-value
Median age, years (IQR)	72 (66–76)	72 (66–79)	.34
Males, *n* (%)	56 (87.5)	230 (81.6)	.26
BMI, median (IQR)	21.1 (19.9–23.4)	22.6 (20.3–24.8)	.01
BMI >25, *n* (%)	5 (7.8)	65 (23.0)	.006
Risk factors, *n* (%)			
Hypertension	55 (85.9)	261 (92.6)	.09
Dyslipidemia	51 (79.7)	229 (81.2)	.78
Diabetes	27 (42.2)	118 (41.8)	.96
Current smoking	30 (46.9)	107 (37.9)	.19
Obesity	5 (7.8)	65 (23.0)	.006
Atrial fibrillation	1 (1.6)	4 (1.4)	1.00
Coronary artery disease, *n* (%)	11 (21.1)	63 (25.9)	.47
Heart failure, *n* (%)	5 (7.8)	24 (8.5)	.86
Chronic kidney disease (≥ stage 3)	24 (37.5)	131 (46.5)	.19
Dialysis, *n* (%)	0 (0)	21 (7.4)	.02
Previous myocardial infarction, *n* (%)	9 (14.1)	31 (11.0)	.49
Previous cerebral infarction, *n* (%)	12 (18.8)	35 (12.4)	.18
Prior PCI, *n* (%)	11 (17.2)	70 (24.8)	.19
Prior CABG, *n* (%)	4 (6.2)	16 (5.7)	.77
Prior limb surgery, *n* (%)	2 (3.1)	12 (4.3)	1.00
Prior aortoiliac treatment, *n* (%)	7 (10.9)	34 (12.1)	.80
Medications, *n* (%)			
Aspirin	41 (64.1)	200 (70.9)	.28
Clopidogrel	43 (67.2)	202 (71.6)	.48
Cilostazol	17 (26.6)	72 (25.5)	.86
Warfarin	2 (3.1)	22 (7.8)	.28
Direct oral anticoagulants	2 (3.1)	8 (2.8)	1.00
Oral antidiabetic agent	13 (20.3)	71 (25.2)	.41
Insulin	5 (7.8)	22 (7.8)	1.00
Statin	32 (50.0)	144 (51.1)	.88
Vital signs			
Systolic blood pressure, mmHg (IQR)	134 (117–152)	137 (126–152)	.14
Diastolic blood pressure, mmHg (IQR)	73 (64–85)	76 (68–85)	.22
Pulse rate, per minute (IQR)	77 (68–85)	73 (65–83)	.08
Rutherford classification, *n* (%)			
2	13 (20.3)	108 (38.3)	.006
3	44 (68.8)	146 (51.8)	.01
4	7 (10.9)	28 (9.9)	.81

*Continuous variables are shown as medians (25–75th percentile) and categorical variables as counts and percentages.
IQR, interquartile range (25–75th percentile); BMI, body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

coronary optical coherence tomography analyses have shown that post-stent, irregular tissue protrusions are associated with subsequent neo-atherosclerosis after stent implantation[19]. Thus, stenting in patients with thrombotic lesions can lead to frequent plaque protrusions and high restenosis rates. Second, the avoidance of high-pressure or large-sized balloon dilation before and after stenting can be another cause of restenosis. IVUS analyses, after stent implantation, in the iliac artery lesions showed that the post-procedural minimum stent area might predict long-term stent patency[20]. In our study, the frequency of direct stenting was high, and the frequency of post-stenting balloon dilation was low in the thrombotic

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Table 2. Lesion characteristics and procedural information (per limb)*

Parameter	Thrombotic (n = 68)	Non-thrombotic (n = 326)	p-value
Lesion characteristics			
Ankle-brachial index, median (IQR)	0.6 (0.4–0.6)	0.6 (0.5–0.7)	.74
CIA lesion, n (%)	50 (73.5)	252 (77.5)	.48
EIA lesion, n (%)	57 (83.8)	186 (57.2)	<.001
Both CIA and EIA lesions, n (%)	40 (58.8)	118 (36.3)	<.001
Outflow FP lesion	23 (33.8)	93 (28.5)	.38
Outflow BK lesion	17 (25.0)	60 (18.4)	.21
Calcification, n (%)			
None	14 (20.9)	40 (12.5)	.07
Mild	37 (55.2)	141 (43.9)	.09
Moderate	10 (14.9)	79 (24.6)	.09
Severe	6 (9.0)	61 (19.0)	.048
Procedural information			
Use of intravascular ultrasonography, n (%)	54 (79.4)	254 (77.9)	.79
Use of a distal protection device, n (%)	16 (23.5)	3 (0.9)	<.001
Direct stenting, n (%)	15 (22.1)	51 (15.6)	.20
Post-dilatation, n (%)	46 (86.8)	256 (93.1)	.16
Balloon dilatation alone, n (%)	3 (4.4)	5 (1.5)	.14
Type of stent, n (%)			
Self-expandable	61 (89.7)	289 (88.7)	.80
Balloon-expandable	1 (1.5)	16 (4.9)	.33
Combined	3 (4.4)	16 (4.7)	1.00
Mean stent diameter, mm (IQR)	8.9 (8–10)	9.0 (8–10)	.65
Total stent length, mm (IQR)	120 (80–160)	100 (60–140)	.01
Procedure time			
<1 hour	18 (28.1)	84 (29.8)	.79
1–2 hours	25 (39.1)	122 (43.3)	.54
2–3 hours	15 (23.4)	49 (17.4)	.26
>3 hours	4 (6.2)	15 (5.3)	.76

*Continuous variables are shown as medians (25–75th percentile) and categorical variables as counts and percentages.
IQR, interquartile range (25–75th percentile); CIA, common iliac artery; EIA, external iliac artery; FP, femoro-popliteal; BK, below the knee.

Table 3. Post-endovascular treatment medications*

Parameter	Thrombotic	Non-thrombotic	p-value
Post-EVT medications (per patient), n (%)			
Aspirin	45/64 (70.3)	210/282 (74.5)	.50
Clopidogrel	48/64 (75.0)	213/282 (75.5)	.93
Cilostazol	17/64 (26.6)	66/282 (23.4)	.59
Warfarin	4/64 (6.2)	18/282 (6.4)	1.00
Direct oral anticoagulants	4/64 (6.2)	6/282 (2.1)	.09
Statin	34/64 (53.1)	150/282 (53.2)	.99

*Categorical variables are shown as counts and percentages.
EVT, endovascular treatment

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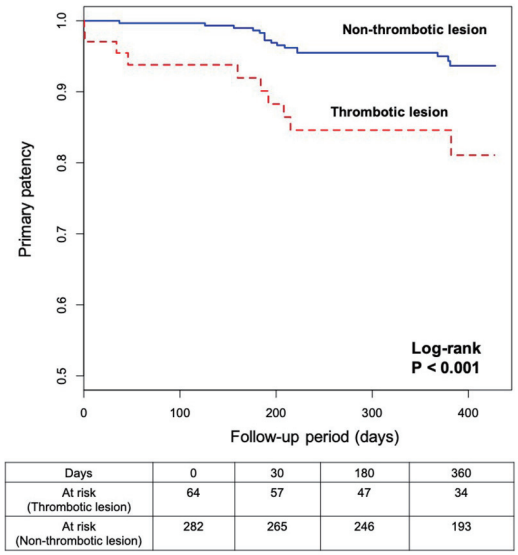
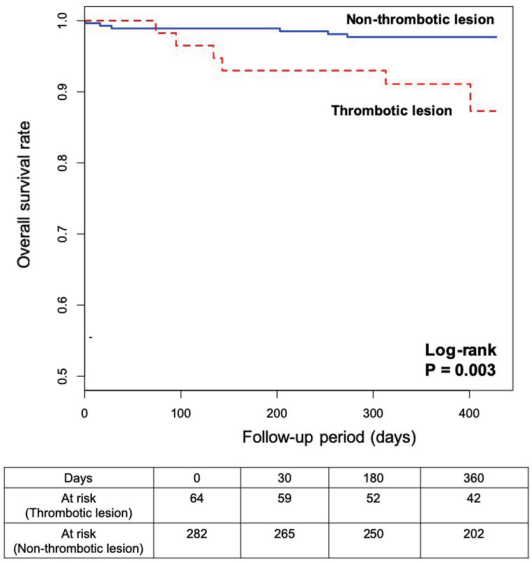


Days	0	30	180	360
At risk (Thrombotic lesion)	64	57	47	34
At risk (Non-thrombotic lesion)	282	265	246	193

Fig. 2. Kaplan-Meier curves for primary patency in patients undergoing endovascular treatment of thrombotic and non-thrombotic total occlusion lesions



Days	0	30	180	360
At risk (Thrombotic lesion)	64	59	52	42
At risk (Non-thrombotic lesion)	282	265	250	202

Fig. 3. Kaplan-Meier curves for overall survival in patients undergoing endovascular treatment of thrombotic and non-thrombotic total occlusion lesions

Table 4. Post-endovascular treatment clinical outcomes*

Parameter	Thrombotic	Non-thrombotic	*p*-value
Initial clinical outcomes			
Initial technical success (per limb), *n* (%)	67/68 (98.5)	323/326 (99.1)	.53
Procedure-related complications (per patient), *n* (%)	9/64 (14.1)	11/282 (3.9)	.005
Prolonged hospitalization due to complications (per patient), *n* (%)	6/64 (9.4)	3/282 (1.1)	.002
One-year clinical outcomes			
Primary patency (per limb), *n* (%)	58/68 (85.3)	310/326 (95.1)	.006
CDTLR (per limb), *n* (%)	2/68 (2.9)	6/326 (1.8)	.63
MACE (per patient), *n* (%)	5/64 (7.8)	9/282 (3.2)	.15
All cause death (per patient), *n* (%)	6/64 (9.4)	6/282 (2.1)	.01
Cardiovascular death (per patient), *n* (%)	4/64 (6.2)	1/282 (0.4)	.005
Non-cardiovascular death (per patient), *n* (%)	2/64 (3.1)	5/282 (1.8)	.62

*Categorical variables are shown as counts and percentages.
CDTLR, clinically driven target lesion revascularization; MACE, major adverse cardiovascular event

Table 5. Impact of thrombotic lesions on 1-year primary patency*

Endpoint	Univariable		Multivariable (model 1)		Multivariable (model 2)		Multivariable (model 3)	
	HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value
Age (per year)	0.998 (0.95 to 1.04)	.93			0.98 (0.93 to 1.03)	.42		
Sex (Male)	2.25 (0.53 to 9.59)	.27					2.58 (0.60 to 11.1)	.20
Diabetes	1.97 (0.87 to 4.43)	.10	2.15 (0.95 to 4.86)	.06				
CKD (≥ stage 3)	3.27 (1.35 to 7.89)	.01	4.06 (1.64 to 10.0)	.002	4.25 (1.70 to 10.6)	.002	4.20 (1.71 to 10.3)	.002
Both CIA and EIA lesions	1.01 (0.45 to 2.27)	.99						
Procedural complication	5.86 (2.18 to 15.7)	<.001	4.38 (1.54 to 12.4)	.005	4.38 (1.56 to 12.2)	.005	4.29 (1.53 to 12.0)	.006
Thrombotic lesions	3.71 (1.65 to 8.36)	.002	3.91 (1.64 to 9.34)	.002	3.79 (1.62 to 8.87)	.002	3.64 (1.55 to 8.57)	.003

*In the multivariable model, the adjusted HR for thrombotic lesions, compared with non-thrombotic lesions, was calculated by adjusting for age, sex, diabetes, chronic kidney disease (≥ stage 3), and the incidence of procedural complications.
CKD, chronic kidney disease; HR, hazard ratio; CI, confidence interval; CIA, common iliac artery; EIA, external iliac artery

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Table 6. Impact of thrombotic lesions on 1-year all-cause mortality*

Endpoint	Univariable		Multivariable (model 1)		Multivariable (model 2)		Multivariable (model 3)	
	HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value
Age (per year)	1.09 (1.01 to 1.17)	.02	0.10 (1.02 to 1.18)	.02				
Sex (Male)	2.21 (0.29 to 17.2)	.45			2.14 (0.28 to 16.6)	.47		
BMI >25	0.36 (0.05 to 2.78)	.33						
Diabetes	0.45 (0.12 to 1.67)	.23					0.45 (0.12 to 1.65)	.23
Thrombotic lesions	4.66 (1.50 to 14.5)	.008	4.93 (1.59 to 15.3)	.006	4.62 (1.49 to 14.3)	.008	4.68 (1.51 to 14.5)	.007

*In the multivariable model, the adjusted HR for thrombotic lesions, compared with that for non-thrombotic lesions, was calculated by adjusting for age, sex, and diabetes.
HR, hazard ratio; BMI, body mass index; CI, confidence interval

group. This may reflect that the attending physicians avoided aggressive pre- and post-balloon dilation to minimize the risk of distal embolisms, which possibly resulted in smaller lumen or stent areas.

Although further investigation is required to reveal the exact mechanism of restenosis in thrombotic lesions, the optimal EVT procedure may contribute to lower restenosis rates. Therefore, EVT strategies should be carefully developed in patients with thrombotic occlusions.

High Mortality Following EVT of Thrombotic Lesions

Certain systemic diseases, such as antiphospholipid syndrome and myeloproliferative neoplasms, have high thromboembolism risks, and cause chronic lower limb artery occlusions as well as acute thrombotic occlusions[21-23]. Such systemic diseases may be an underlying cause of thrombotic occlusions in AI disease; therefore, they might be associated with high mortality in patients with thrombotic lesions. Additionally, vascular vulnerability might be another cause of high mortality in the thrombotic group. Plaque ruptures are commonly observed in patients with PAD, especially in the iliac and femoral arteries[24], and are associated with vascular vulnerability and subsequent cardiovascular events[25]. Furthermore, patients with plaque ruptures tend to have more frequent angiographic findings indicative of thrombus formation[25], suggesting a link between plaque ruptures and thrombotic lesions. Hence, patients with thrombotic occlusions might have high mortality rates because of plaque instability in multiple vascular beds.

Although the frequency of patients with AI thrombotic lesions having specific systemic diseases or plaque ruptures is unclear, the potential risk of thromboembolism or vascular vulnerability might have been underestimated. Early identification of those underlying conditions might result in better clinical outcomes in patients with thrombotic lesions.

Clinical Implications

Total occlusion lesions exhibit various histological differences; however, because of the difficulty associated with obtaining histological information, little has been elucidated about the effects of such differences on post-EVT clinical outcomes. Our study has the following clinical implications: (1) lesion characteristics (thrombotic or non-thrombotic) should be recognized as factors that affect post-EVT prognoses; (2) in patients with thrombotic lesions, EVT procedures, including balloon/stent sizing and plaque protrusion management, should be carefully performed to lower restenosis rates; (3) in patients with thrombotic lesions, the possible underlying condition associated with higher risk of thromboembolisms should be screened.

Limitations

This study had some limitations. First, the classification of lesions as thrombotic or non-thrombotic was based on the attending physician's judgement. Because wire performance can be affected by the wire type, sheath size, microcatheter use, and physician's experience, determining whether a lesion is thrombotic or non-thrombotic was subjective. However, we believe that the validity of lesion characterization was somewhat warranted because IVUS was used in nearly 80% of cases. Considering that there are no established criteria to define the thrombotic lesion, this categorization seemed rather simple and practical in daily practice. Second, there was no histopathological evidence for the thrombotic lesions. We assumed that thrombotic occlusions contained mainly unorganized thrombi, but pathological data were not available to support this hypothesis. Third, owing to the lack of detailed

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information on the cause of death and procedure-related complications, adequately assessing the reason for the high mortality and restenosis rate in patients with thrombotic lesions was difficult. Fourth, because there was a lack of detailed procedural information, including balloon size, inflation pressure, and minimum stent area on IVUS, a more in-depth analysis of the association between EVT procedures and outcomes was difficult. Fifth, because of the low number of endpoints, potential clinical confounding factors, such as age, gender, and diabetes, were not included in the multivariate analysis. Therefore, we created several multivariate models to test the validity of this analysis. A larger study population and longer follow-up period may be necessary to confirm the impact of thrombotic lesions on 1-year primary patency and all-cause mortality.

Conclusions

Thrombotic lesion was associated with 1-year restenosis and all-cause mortality after EVT for non-acute AI total occlusions. Poor clinical outcomes in patients with thrombotic lesions may be related to differences in lesion responses to EVT procedures and to the presence of underlying conditions that can increase the thrombosis risk.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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