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Bypass Surgery Provides Better Outcomes Compared with Endovascular Therapy in the Composite Endpoint Comprising Relief from Rest Pain, Wound Healing, Limb Salvage, and Survival after Infra-inguinal Revascularisation in Patients with Chronic Limb Threatening Ischaemia

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WHAT THIS PAPER ADDS

Considering the therapeutic goals for chronic limb threatening ischaemia (CLTI), it is necessary to achieve all endpoints to ensure successful treatment. The present study aimed to determine the factors related to the composite of relief from rest pain, wound healing, major adverse limb events, and prognosis after infrainguinal revascularisation in patients with CLTI. Bypass surgery is superior to endovascular therapy with respect to the composite endpoint. Furthermore, bypass surgery may be considered as the treatment of choice, instead of endovascular therapy, for patients in the indeterminate group according to the Global Vascular Guidelines preferred revascularisation method.

Objective: The present study aimed to determine the factors related to relief from rest pain, wound healing, major adverse limb events (MALEs), and prognosis after infrainguinal revascularisation in patients with chronic limb threatening ischaemia (CLTI).

Methods: The data of patients who underwent infrainguinal revascularisation for CLTI between 2010 and 2020 was analysed retrospectively. The endpoint was the composite of relief from rest pain, wound healing, MALE, or death.

Results: A total of 234 limbs in 187 patients with CLTI were analysed. Of the 234 limbs, 149 (63.7%) underwent bypass surgery and 85 (36.3%) underwent endovascular therapy (EVT). The event free survival rates with respect to the composite endpoint at two years were 30.4% in the EVT and 48.5% in the bypass groups, respectively ($p = .005$). The event free survival rates at two years were 56.7% in bypass surgery and 29.5% in EVT in the indeterminate subgroup ($p = .051$). Multivariable analysis revealed that age (hazard ratio [HR] 1.03; 95% confidence interval [CI] 1.01 — 1.05; $p < .001$), coronary artery disease (CAD) (HR 1.45; 95% CI 1.01 — 2.07; $p = .042$), haemodialysis (HR 1.74; 95% CI 1.22 — 2.48; $p = .002$), Wound, Ischaemia and foot Infection stage (HR 1.34; 95% CI 1.07 — 1.68; $p = .012$), Global Limb Anatomical Staging System stage (HR 1.31; 95% CI 1.01 — 1.72; $p = .043$), EVT (HR 1.90; 95% CI 1.31 — 2.74; $p < .001$), Geriatric Nutritional Risk Index (HR 0.98; 95% CI 0.97 — 0.99; $p = .021$), and non-ambulatory status (HR 1.89; 95% CI 1.31 — 2.74; $p < .001$) were risk factors for the composite endpoint.

Conclusion: Bypass surgery is superior to EVT with respect to the composite endpoint including relief from rest pain, wound healing, MALE, or death. Bypass surgery may be considered as the treatment of choice, instead of EVT, in patients in the indeterminate group according to the Global Vascular Guidelines preferred revascularisation method.

Keywords: Chronic limb threatening ischaemia (CLTI), Global Vascular Guidelines (GVGs), Bypass, endovascular therapy (EVT), Composite endpoint
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INTRODUCTION

The Global Vascular Guidelines (GVGs), which were published in 2019, proposed a treatment algorithm based on the patient's risk estimate, limb staging, and anatomical pattern of the disease.[1] The GVGs stated that preferred revascularisation for infrainguinal diseases was described in

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patients with chronic limb threatening ischaemia (CLTI) who were candidates for revascularisation. Although endovascular therapy (EVT) has been reported to be a less invasive treatment modality, bypass surgery offers superior expected patency and blood flow. Therefore, bypass surgery is recommended in patients with Wound, Ischaemia and foot Infection (WIfI) stages 3 or 4 and Global Limb Anatomical Staging System (GLASS) stage III, while EVT is recommended in patients with lower WIfI and GLASS stages.

The CLTI treatment goals entail ameliorating rest pain, achieving wound healing, preventing the occurrence of major adverse limb events (MALEs), and improving prognosis. Several studies have validated the factors influencing each endpoint;[2–6] however, few published studies have assessed the composite endpoint consisting of the above mentioned parameters. Evaluating the treatment outcome by the composite endpoint is essential, considering the treatment goals in patients with CLTI. Thus, the present study aimed to determine the factors related to the amelioration of rest pain, wound healing, MALEs, and prognosis after infrainguinal revascularisation in patients with CLTI from the perspective of the preferred revascularisation method described in the GVGs.

MATERIALS AND METHODS

Study approval

The institutional review board of Kyushu University approved this study (no. 21061-00). The need for informed consent was waived owing to the retrospective study design. All information about the study protocol was disclosed to patients using patient bulletins as an alternative to informed consent.

Patients

Infra-inguinal revascularisation was performed for 232 patients and 286 limbs for the treatment of CLTI between 2010 and 2020. Patients with WIfI stage 1, a previous history of revascularisation or missing data were excluded; thus, 187 patients and 234 limbs with rest pain, ulcer, and gangrene were analysed. A retrospective analysis was performed using the data obtained from the medical, operative, and radiological records.

Follow up

The ankle brachial index (ABI) was measured at one week and one month after revascularisation, and every three months thereafter with skin perfusion pressure (SPP), duplex ultrasound, and contrast enhanced computed tomography as needed. Re-intervention entailed repeat EVT or surgical intervention for patients with incomplete wound healing or recurrent symptoms. Ischaemic rest pain was defined as ABI $<$ 0.4 or SPP $<$ 30 mmHg with significant stenosis. Re-intervention was performed using EVT in patients with $>$ 50% recurrent stenosis of the native artery or stent/stent graft as measured by duplex ultrasound imaging or digital subtraction angiography. Any re-intervention for vein grafts was performed in patients with vein graft occlusion, or stenosis with a peak systolic velocity $>$ 300 cm/s or velocity ratio $>$ 3.5.[7]

Study endpoint

The primary endpoint was the composite of relief from rest pain, wound healing, MALE, or death. The secondary endpoints included individual outcomes (evaluated separately), including unrelieved pain, absence of wound healing, MALE, and death. Major amputation or any re-intervention was designated as a MALE.[8]

Treatment selection

The endovascular approach was selected for patients with advanced age, short lesions, significant comorbidities, or non-ambulatory status. Bypass surgery was selected in patients with long lesions, major tissue loss, availability of a vein graft, and those with an acceptable operative risk. The final determination of EVT or bypass surgery as the first line of treatment strategy was based on consensual agreement between three vascular surgeons from the department.

Definitions

Foot lesions were classified according to the Society for Vascular Surgery (SVS) WIfI classification system.[9] The femoropopliteal (FP) and infrapopliteal (IP) grades ranging from 0 to 4 were used to determine the GLASS stage.[1] Inframalleolar (IM)/pedal disease was classified into P0, P1, and P2.[1] Coronary artery disease (CAD) was defined as the presence of angina pectoris, history of myocardial infarction or any coronary artery revascularisation. Congestive heart failure was defined as a history of heart failure or ejection fraction $<$ 40%. Cerebrovascular disease was defined as a history of stroke, transient ischaemic attack, or carotid artery revascularisation. The Geriatric Nutritional Risk Index (GNRI) was calculated from the height, body weight, and serum albumin level obtained from each individual on admission as follows: GNRI $=$ 14.89 $\times$ albumin (g/dL) $+$ 41.7 $\times$ body weight/ideal body weight.[10] The ambulatory status due to CLTI was assessed on admission. Non-ambulatory status was defined as the state of being wheelchair bound or bedridden. Wound healing was defined as the complete epithelialisation of an original ulcer or stump of minor amputation.

Statistical analysis

Data were analysed using JMP® 14 software (SAS Institute Inc., Cary, NC, USA). The Student's *t* test or Mann—Whitney U test was used to compare continuous variables. Comparisons of categorical variables between endovascular and bypass surgery were performed using Fisher's exact test. The Kaplan—Meier method and log rank test were used to compare the differences in the composite endpoint. Risk factors for each endpoint were analysed using uni- and

multivariable (backward elimination procedure) Cox proportional hazards models. A p value $< .050$ was considered statistically significant.

RESULTS

Patient characteristics

The patients' characteristics are shown in Table 1. The average age was 75.9 ± 9.9 years in the EVT group and 73.0 ± 10.9 years in the bypass group ($p = .047$). Thirty-one (36.5%) in the EVT group and 63 (42.3%) in the bypass group ($p = .41$) were on haemodialysis (HD). The number of limbs with WIfI stages 2, 3, and 4 was 26 (30.6%), 27 (31.8%), and 32 (37.7%), respectively, in the EVT group and 32 (21.5%), 54 (36.2%), and 63 (42.3%), respectively, in the bypass group ($p = .30$). The frequency of GLASS stages I, II, and III was 23 (27.1%), 34 (40.0%), and 28 (32.9%) respectively, in the EVT group and 7 (4.7%), 36 (24.2%), and 106 (71.1%) respectively, in the bypass group ($p < .001$). The number of EVT preferred, indeterminate, and bypass preferred according to the GVGs was 31 (36.5%), 36 (42.4%), and 18 (21.2%) in the EVT group, respectively, and 11 (7.4%), 58 (38.9%), and 80 (53.7%) in the bypass group ($p < .001$), respectively.

Details of revascularisation procedures are shown in Tables 2 and 3. Tibial vessels were the most frequent target vessel in bypass surgery 109 (73.2%) and 135 (90.6%) were with autogenous conduits. EVT had targeted FP, FP + IP, and IP vessels in 30 (35.3%), 24 (28.2%), and 31 (36.5%), respectively.

Table 1. Characteristics of 187 patients with 234 limbs treated by infrainguinal bypass surgery or endovascular therapy (EVT) for chronic limb threatening ischaemia

Characteristic	EVT (n = 85 limbs)	Bypass (n = 149 limbs)	p
Age − y	75.9 ± 9.9	73.0 ± 10.9	.047
Male sex	49 (57.7)	103 (69.1)	.088
Smoking			.14
Current	6 (7.1)	24 (16.1)	
Past	40 (47.1)	62 (41.6)	
Never	39 (45.9)	63 (42.3)	
Hypertension	65 (76.5)	116 (77.9)	.87
Diabetes mellitus	51 (60.0)	105 (70.5)	.11
Dyslipidaemia	43 (50.6)	43 (28.9)	.001
Coronary artery disease	38 (44.7)	70 (47.0)	.79
Congestive heart failure	12 (14.1)	18 (12.1)	.69
Cerebrovascular disease	28 (32.9)	38 (25.5)	.23
Haemodialysis	31 (36.5)	63 (42.3)	.41
Non-ambulatory status	29 (34.1)	46 (30.9)	.66
GNRI	95.9 ± 13.7	97.2 ± 12.2	.45
WIfI			.30
Stage 2	26 (30.6)	32 (21.5)	
Stage 3	27 (31.8)	54 (36.2)	
Stage 4	32 (37.7)	63 (42.3)	
GLASS stage			<.001
GLASS I	23 (27.1)	7 (4.7)	
GLASS II	34 (40.0)	36 (24.2)	
GLASS III	28 (32.9)	106 (71.1)	
GLASS IM			.032
P0	14 (16.5)	31 (20.8)	
P1	63 (74.1)	115 (77.2)	
P2	8 (9.4)	3 (2.0)	
Preferred revascularisation			<.001
Bypass	18 (21.2)	80 (53.7)	
Indeterminate	36 (42.4)	58 (38.9)	
EVT	31 (36.5)	11 (7.4)	

Data are presented as n (%) or mean ± standard deviation. EVT = endovascular treatment; GNRI = geriatric nutritional risk index; WIfI = Wound Ischaemia and foot Infection; GLASS = Global Limb Anatomical Staging System; IM = inframalleolar.

Table 2. Revascularisation details of 149 infrainguinal bypass operations for chronic limb threatening ischaemia

Inflow	Outflow	Bypasses (n = 149)	Vein graft	Prosthetic graft
CFA	AK popliteal	19 (12.8)	6	13
	BK popliteal	17 (11.4)	17	
	TPT	1 (0.7)	1	
	ATA/DPA	12 (8.1)	12	
	PTA	13 (8.7)	13	
	Peroneal	2 (1.3)	2	
SFA	AK popliteal	1 (0.7)	1	
	BK popliteal	2 (1.3)	1	1
	ATA	5 (3.4)	5	
	PTA	2 (1.3)	2	
AK popliteal	BK popliteal	1 (0.7)	1	
	ATA/DPA	8 (5.4)	8	
	PTA	4 (2.7)	4	
	Peroneal	2 (1.3)	2	
BK popliteal	ATA/DPA	30 (20.1)	30	
	PTA/Plantar	28 (18.8)	28	
	Peroneal	1 (0.7)	1	
PTA	Plantar	1 (0.7)	1	

Data are presented as n (%). CFA = common femoral artery; SFA = superficial femoral artery; AK = above knee; BK = below knee; TPT = tibioperoneal trunk; ATA = anterior tibial artery; DPA = dorsalis pedis artery; PTA = posterior tibial artery.

Table 3. Revascularisation details of 85 infrainguinal endovascular procedures for chronic limb threatening ischaemia

Endovascular therapy	Total	Therapy	Vessel stented
Target lesion	85		
FP		30 (35.3)	15
FP + IP		24 (28.2)	2
IP		31 (36.5)	
FP device			
Stenting	17		
Bare metal stent		12 (75.0)	
Drug eluting stent		1 (6.3)	
Covered stent		4 (25.0)	
Angioplasty	37		
Balloon angioplasty		30 (81.1)	
Drug coating balloon		7 (18.9)	
IP device	55		
Balloon angioplasty		55 (100)	

Data are presented as n (%). FP = femoropopliteal; IP = infrapopliteal.

Composite endpoints including relief from rest pain, wound healing, major adverse limb events, or death

The Kaplan–Meier curves (Fig. 1) represent event free survival with respect to the composite endpoints (43.9% at one year, 30.4% at two years, and 5.3% at five years in the EVT group; 58.2% at one year, 48.5% at two years, and 22.3% at five years in the bypass group; log rank $p < .001$). Figure 2 shows the Kaplan–Meier curves of event free survival with respect to composite endpoints in the indeterminate subgroup according to the GVGs preferred revascularisation method. The event free survival of bypass surgery appeared to be superior to EVT in the indeterminate subgroup ($p = .051$).

Table 4 shows the results of the uni- and multivariable analyses for the risk factors associated the composite endpoint. Age (hazard ratio [HR] 1.03; 95% confidence interval [CI] 1.01 – 1.05; $p < .001$), CAD (HR 1.45; 95% CI 1.01 – 2.07; $p = .042$), HD (HR 1.74; 95% CI 1.22 – 2.48; $p = .002$), WIfI stage (HR 1.34; 95% CI 1.07 – 1.68; $p = .001$), GLASS stage (HR 1.31; 95% CI 1.01 – 1.72; $p = .043$), EVT (HR 1.90; 95% CI 1.31 – 2.74; $p < .001$), GNRI (HR 0.98; 95% CI 0.97 – 0.99; $p = .021$), and non-ambulatory (HR 1.89; 95% CI 1.31 – 2.74; $p < .001$) were independent risk factors for the composite endpoint, according to the multivariable analysis.

Associations between bypass surgery or endovascular therapy and each endpoint (major adverse limb events, wound healing, overall survival)

The associations between bypass or EVT with MALE, wound healing, and survival were analysed to further assess the associations between the treatment method and the composite endpoint. Multivariable analysis revealed that the WIfI stage (HR 1.60; 95% CI 1.19 – 2.20; $p = .003$) and EVT (HR 2.58; 95% CI 1.63 – 4.09; $p < .001$) were risk factors for MALE. Multivariable analysis of wound healing showed that the WIfI stage (HR 0.64; 95% CI 0.50 – 0.83; $p < .001$) and EVT (HR 0.61; 95% CI 0.41 – 0.90; $p = .014$) were risk factors for the absence of wound healing. Independent risk factors associated with poor overall survival included advanced age (HR 1.06; 95% CI 1.04 – 1.09; $p < .001$), CAD (HR 1.68; 95% CI 1.07 – 2.62; $p = .024$), HD (HR 2.83; 95% CI 1.78–4.52; $p < .001$), GNRI (HR 0.98; 95% CI 0.96 – 0.99; $p = .019$), and non-ambulatory status (HR 2.54; 95% CI 1.61 – 4.00; $p < .001$), according to the multivariable analysis.

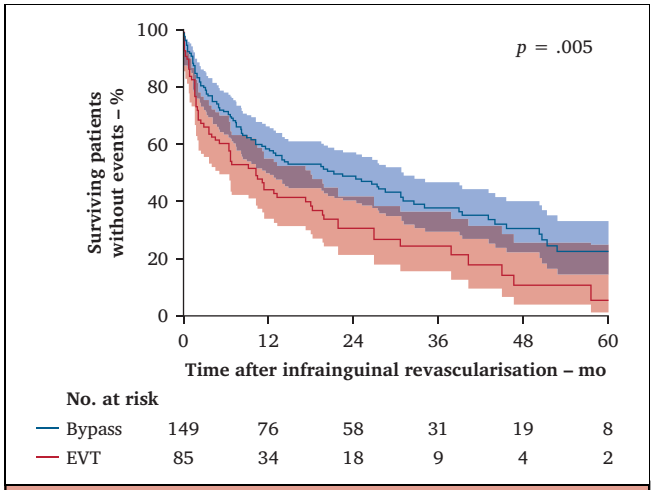

Figure 1. Cumulative Kaplan–Meier estimate of composite endpoints including relief from rest pain, wound healing, major adverse limb events, or death between infrainguinal bypass surgery and endovascular therapy (EVT) of 234 limbs in 187 patients treated for chronic limb threatening ischaemia. The event free survival was 43.9% at one year, 30.4% at two years, 24.2% at three years, 10.6% at four years, and 5.3% at five years in the EVT group and 58.2% at one year, 48.5% at two years, 37.5% at three years, 30.3% at four years, and 22.3% at five years in the bypass group ($p = .005$).

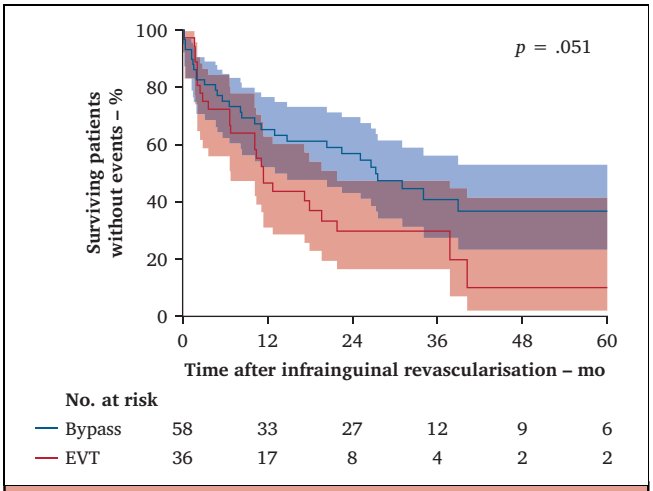

Figure 2. Cumulative Kaplan–Meier estimate of the composite endpoints including relief from rest pain, wound healing, major adverse limb events, or death between infrainguinal bypass surgery and endovascular therapy (EVT) in the indeterminate subgroup of 94 limbs treated for chronic limb threatening ischaemia according to Global Vascular Guidelines preferred revascularisation method. No significant differences were observed in the event free survival between bypass surgery and EVT ($p = .051$).

DISCUSSION

The present study has demonstrated that bypass surgery provided better outcomes compared with EVT with respect to the composite endpoint that consisted of unrelieved pain, absence of wound healing, MALE, or death. The WIfI stage and EVT were associated with poor outcomes for MALE and lack of wound healing. Meanwhile, the revascularisation procedure was not related to the prognosis. Advanced age, CAD, HD, low GNRI, and non-ambulatory status were independent risk factors for poor prognosis.

The treatment goals for patients with CLTI include not only relief from rest pain and achieving wound healing by revascularisation, but also the prevention of MALEs, and improvement in prognosis.[1] Most previous studies focused on a certain endpoint such as overall survival, limb salvage, wound healing, amputation free survival, or MALEs.[2–6] Considering the therapeutic goals for CLTI, it is necessary to achieve all endpoints to ensure successful treatment in

Table 4. Risk factors for composite endpoints including rest pain, no wound healing, MALE, or death in 234 limbs in 187 patients treated for chronic limb threatening ischaemia

Variables	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Age, per 1 year increment	1.02 (1.01−1.04)	.003	1.03 (1.01−1.05)	<.001
Hypertension	0.92 (0.65−1.32)	.67		
Diabetes mellitus	1.17 (0.83−1.65)	.37		
Dyslipidaemia	0.99 (0.71−1.37)	.94		
Coronary artery disease	1.31 (0.96−1.80)	.089	1.45 (1.01−2.07)	.042
Congestive heart failure	1.13 (0.71−1.79)	.61		
Cerebrovascular disease	1.42 (1.02−2.00)	.040		
Haemodialysis	1.44 (1.05−1.98)	.021	1.74 (1.22−2.48)	.002
WIfI, per 1 stage increment	1.31 (1.07−1.62)	.011	1.34 (1.07−1.68)	.012
GLASS, per 1 stage increment	1.10 (0.88−1.39)	.39	1.31 (1.01−1.72)	.043
GLASS IM, per 1 stage increment	1.50 (1.05−2.14)	.026		
EVT (ref. bypass)	1.59 (1.15−2.19)	.005	1.90 (1.31−2.74)	<.001
GNRI, per 1 point increment	0.98 (0.97−0.99)	.002	0.98 (0.97−0.99)	.021
Non-ambulatory status	2.14 (1.54−2.97)	<.001	1.89 (1.31−2.74)	<.001

MALE = major adverse limb event; HR = hazard ratio; CI = confidence interval; WIfI = Wound, Ischaemia, and foot Infection; GLASS = Global Limb Anatomical Staging System; IM = inframalleolar; EVT = endovascular therapy; GNRI = geriatric nutritional risk index.

these patients. For example, amputation free survival cannot determine whether wound healing is achieved in patients with CLTI. Although a MALE represents re-intervention or major limb amputation, wound healing or prognosis including peri-procedural mortality cannot be evaluated on the basis of MALEs. Therefore, the composite endpoint including relief from rest pain, wound healing, major limb amputation, re-intervention after revascularisation, and prognosis may be more appropriate for the evaluation of treatment outcomes in patients with CLTI. In fact, the primary endpoint was defined as MALE free survival and the secondary endpoints included overall survival, freedom from MALE and POD, freedom from CLTI, etc., in the Best Endovascular *vs.* BEST Surgical Therapy for Patients with Critical Limb Ischaemia (BEST CLI) trial.[11]

With regard to the composite endpoint, rest pain was included in the present study. Occasionally, it is hard to diagnose ischaemic leg pain in clinical practice because other causes such as neuropathy can cause leg pain. Therefore, including rest pain into composite endpoint can be confounding in its interpretation. However, rest pain was included into the composite endpoint in the present study to evaluate the total treatment goal including relief from rest pain, wound healing, major limb amputation, re-intervention after revascularisation, and prognosis.

In the present study, all re-interventions including angioplasty were defined as MALEs. Although EVT is a less invasive treatment, poor outcome after repeat EVT in patients with CLTI has been reported.[12] Therefore, it is appropriate to evaluate all adverse events when considering the treatment goals for patients with CLTI.

The GVGs proposed preferred revascularisation according to the grade of WIfI and GLASS stage.[1] The present study found that bypass surgery was superior to EVT with respect to the composite endpoint. Subgroup analysis also revealed that bypass surgery tended to demonstrate better outcomes in the indeterminate group, which may be attributed to a type II error. In the present study, advanced age, CAD, HD, low GNRI, and non-ambulatory status were poor prognostic factors for patients with CLTI undergoing infra-inguinal revascularisation. The Bypass *vs.* Angioplasty in Severe Ischaemia of the Leg (BASIL) trial proposed bypass surgery in patients who were likely to survive for more than two years.[13] As proposed by the BASIL trial, bypass surgery may be the preferred method of revascularisation in patients without poor prognostic factors. The evaluation of each endpoint, i.e., MALEs or wound healing, revealed that EVT was a risk factor for MALEs or failure of wound healing. These findings also support the superiority outcomes obtained with bypass surgery. Although further studies are needed to confirm these observations, the BEST CLI trial may provide answers to these questions.

The study has several limitations. First, it was a single centre, non-randomised study, and retrospective in design with a small sample size. The number of patients and limbs may be too small to evaluate the composite endpoint. Second, approximately 15% of patients were excluded due to missing data, a selection bias that may affect the treatment outcomes. Third, although the treatment strategy was determined as described in the method sections, there is the possibility of a treatment selection bias. Fourth, endovascular device evolution, which may affect treatment outcomes, was not considered because it is difficult to include this factor in analysis. Fifth, the follow up protocol and indication for re-intervention differ by studies; therefore, the findings of the present study may not be applicable to other cohorts. Finally, subjective outcomes were not evaluated. The assessment of the quality of life or patient satisfaction is also necessary to ensure comprehensive evaluation of treatment outcomes. Despite these limitations, the present study is meaningful, since it evaluated the composite endpoint, which represents the therapeutic goal in patients with CLTI. Furthermore, these results were based on real world data in Japanese patients, a high

proportion of whom were on HD. The present study adds to the knowledge base of treatment selection between bypass surgery and EVT in patients with CLTI.

Conclusions

Bypass surgery is superior to EVT with respect to the composite endpoint including relief from rest pain, wound healing, MALE, or death. Advanced age, CAD, HD, low GNRI, and non-ambulatory status, WIfI stage, and GLASS stage were independent risk factors for the composite endpoint after infrainguinal revascularisation in patients with CLTI. Bypass surgery may be considered as the treatment of choice, instead of EVT, in patients in the indeterminate group.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

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REFERENCES

1 Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg* 2019;**58**:S1–109.
2 Morisaki K, Yamaoka T, Iwasa K, Ohmine T. Influence of frailty on treatment outcomes after revascularization in patients with critical limb ischemia. *J Vasc Surg* 2017;**66**:1758–64.
3 Ramanan B, Ahmed A, Wu B, Causey MW, Gasper WJ, Vartanian SM, et al. Determinants of midterm functional outcomes, wound healing, and resources used in a hospital-based limb preservation program. *J Vasc Surg* 2017;**66**:1765–74.
4 Soga Y, Iida O, Takahaera M, Hirano K, Suzuki K, Kawasaki D, et al. Two-year life expectancy in patients with critical limb ischemia. *JACC Cardiovasc Interv* 2014;**7**:1444–9.
5 Simons JP, Schanzer A, Flahive JM, Osborne NH, Mills Sr JL, Bradbury AW, et al. Survival prediction in patients with chronic limb-threatening ischemia who undergo infrainguinal revascularization. *J Vasc Surg* 2019;**69**:137S–51S.
6 Causey MW, Ahmed A, Wu B, Gasper WJ, Reyzelman A, Vartanian SM, et al. Society for Vascular Surgery limb stage and patient risk correlate with outcomes in an amputation prevention program. *J Vasc Surg* 2016;**63**:1563–73.
7 Tinder CN, Bandyk DF. Detection of imminent vein graft occlusion: what is the optimal surveillance program? *Semin Vasc Surg* 2009;**22**:252–60.
8 Iida O, Soga Y, Hirano K, Kawasaki D, Suzuki K, Miyashita Y, et al. Long-term results of direct and indirect endovascular revascularization based on the angiosome concept in patients with critical limb ischemia presenting with isolated below-the-knee lesions. *J Vasc Surg* 2012;**55**:363–70.
9 Mills Sr JL, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy AN, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). *J Vasc Surg* 2014;**59**:220–34.
10 Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric Nutritional Risk Index: a new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr* 2005;**82**:777–83.
11 Menard MT, Farber A, Assmann SF, Choudhry NK, Conte MS, Creager MA, et al. Design and Rationale of the Best Endovascular Versus Best Surgical Therapy for Patients With Critical Limb Ischemia (BEST-CLI) Trial. *J Am Heart Assoc* 2016;**5**:e003219.
12 Kobayashi N, Hirano K, Yamawaki M, Araki M, Sakai T, Sakamoto Y, et al. Characteristics and clinical outcomes of repeat endovascular therapy after infrapopliteal balloon angioplasty in patients with critical limb ischemia. *Catheter Cardiovasc Interv* 2018;**91**:505–14.
13 Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, et al. Bypass versus angioplasty in severe ischemia of the leg (BASIL): multicenter, randomised controlled trial. *Lancet* 2005;**366**:1925–34.