Patient-level Pooled Meta-analysis of Patients With Chronic Limb-threatening Ischemia and Complex Femoropopliteal Lesions Treated With the BioMimics 3D Stent

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Abstract

Objectives: Endovascular treatment of peripheral artery disease is challenging in patients with chronic limb-threatening ischemia (CLTI) and complex lesions, and optimal treatment strategies are not established. This meta-analysis was conducted to investigate the safety and performance of a helical centerline stent in these indications. **Methods:** This patient-level pooled meta-analysis includes 3 trials in which the helical centerline BioMimics 3D stent (Veryan Medical) was implanted in femoropopliteal lesions. High-risk subgroups were CLTI, chronic total occlusion (CTO), peripheral artery calcification scoring system (PACSS) 3,4, and Trans-Atlantic Inter-Society Consensus (TASC) C/D lesions. Outcomes included target lesion revascularization (TLR), survival, major amputation, and clinical improvement. **Results:** In total, 828 patients were included. Patients in the 4 high-risk subgroups had higher rates of baseline risk factors such as diabetes mellitus, kidney disease, occluded vessels, and calcification. Freedom from TLR at 24 months was 73.3% vs 84.5%, *P* = .004, for CLTI vs intermittent claudication; 80.6% vs 85.0%, *P* = .047, for CTO vs no CTO; 81.5% vs 83.8%, *P* = .717, for PACSS 3,4 vs PACSS 0-2; and 75.9% vs 84.7%, *P* = .016, for TASC C/D vs TASC A/B lesions. Freedom from 24-month major target limb amputation was 93.7%, 98.5%, 98.4%, and 97.9% for the subgroups of CLTI, CTO, PACSS 3,4, and TASC C/D, respectively. Clinical improvement at 24 months ranged between 85.0% and 97.3%. **Conclusion:** Despite some differences among high- and low-risk subgroups, the helical centerline stent performs well in all subgroups.

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Key words: femoropopliteal artery, chronic limb-threatening ischemia, complex lesions

There is a paucity of data and lack of consistent clinical evidence in patients with chronic limb-threatening ischemia (CLTI) and patients with complex lesions. These patients, particularly those with Rutherford class 5 and 6 peripheral arterial disease (PAD), are often excluded from device trials. As a result of excluding those patients with the most severe stages of PAD, the available data cannot offer meaningful results and are not generalizable to high-risk subgroups.[1-5]

Despite the limited representation of these patients in clinical trials, they are all too common in routine clinical practice. For example, CLTI represents the end stage of PAD[6] and is a global health care problem, occurring in 11% to 13% of the approximately 236 million patients with PAD worldwide, with the prevalence increasing with age.[7-9]

Complex lesions, frequently seen in patients with CLTI, are difficult to treat, and to date no optimal or consistent treatment strategy exists as there is insufficient evidence to recommend one specific device or technique over another. It is generally accepted, however, that these indications will more frequently require stenting due to residual stenosis and flow-limiting dissections in order to achieve on-table technical success.[1,10] The majority of the published literature on complex femoropopliteal lesions and CLTI has evaluated straight slotted-tube nitinol stents, which have not performed particularly well long-term in this patient population.[1,11]

The BioMimics 3D stent (Veryan Medical) has a unique helical centerline design which, in contrast to conventional straight stents that reduce arterial curvature, imparts a 3-dimensional

FIGURE 1. BioMimics 3D stent system. The stent has a 3-dimensional helical centerline that imparts a 3-dimensional helical shape onto the artery to generate swirling flow and increase wall shear stress. Image courtesy of Veryan Medical.

helical shape onto the artery, promoting laminar swirling flow to increase wall shear stress that has been shown to be protective against atherosclerosis and restenosis.[12] This has been confirmed by less intimal hyperplasia in animal studies and in the superior 24-month patency observed in the MIMICS randomized controlled trial (RCT) when compared with a straight stent.[12-14]

To add to the body of knowledge and further assess the safety and performance of the helical centerline stent in patients with CLTI and complex lesions (chronic total occlusion [CTO], bilateral calcification, and Trans-Atlantic Inter-Society Consensus [TASC] C/D lesions), a meta-analysis of 3 MIMICS trials was conducted.[13,15-17]

Materials and Methods

Study Design

This is a pooled analysis of 3 trials, the MIMICS RCT, the MIMICS-2 study, and the MIMICS-3D registry; all trials have previously been published.[15-18] Details of the study designs are provided in **Supplemental Table 1**.

Follow-ups were conducted at 30 days, 6 months, 1 and 2 years, and for MIMICS-2 and MIMICS-3D, additionally at 3 years. Herein, data through 2 years are reported.

All studies were approved by the local or national ethics committees and all patients provided written informed consent prior to any study procedure. The studies were conducted according to the Declaration of Helsinki, international standards and regulations, relevant data protection guidelines, and local and national regulations. An independent clinical events committee adjudicated all clinical endpoints. The trials were registered at ClinicalTrials.gov (NCT02163863, NCT02400905, NCT02900924).

Study Participants

The inclusion and exclusion criteria are provided in **Supplemental Table 1**.

Endpoints

The collective endpoints include survival, freedom from major amputation, freedom from clinically driven target lesion revascularization (CD-TLR), and clinical improvement (defined as a decrease of at least 1 Rutherford class).

Study Procedure

The BioMimics 3D stent system (**Figure 1**) features a helical centerline stent that imparts natural curvature to the diseased vessel. Pre-dilatation was performed according to the site's standard of care. The stents were to be implanted according to the instructions for use, and concomitant antiplatelet medication was to be given in accordance with the site's standard of care.

Statistics

Continuous data were summarized by numbers, means, and standard deviations. Categorical data were summarized by numbers and percentages. Kaplan-Meier analyses with 95% confidence interval were used for time-to-event data. The analyses were performed based on the data available.

In a post-hoc analysis, patients with CLTI and those with intermittent claudication (IC), patients with CTO lesions and those

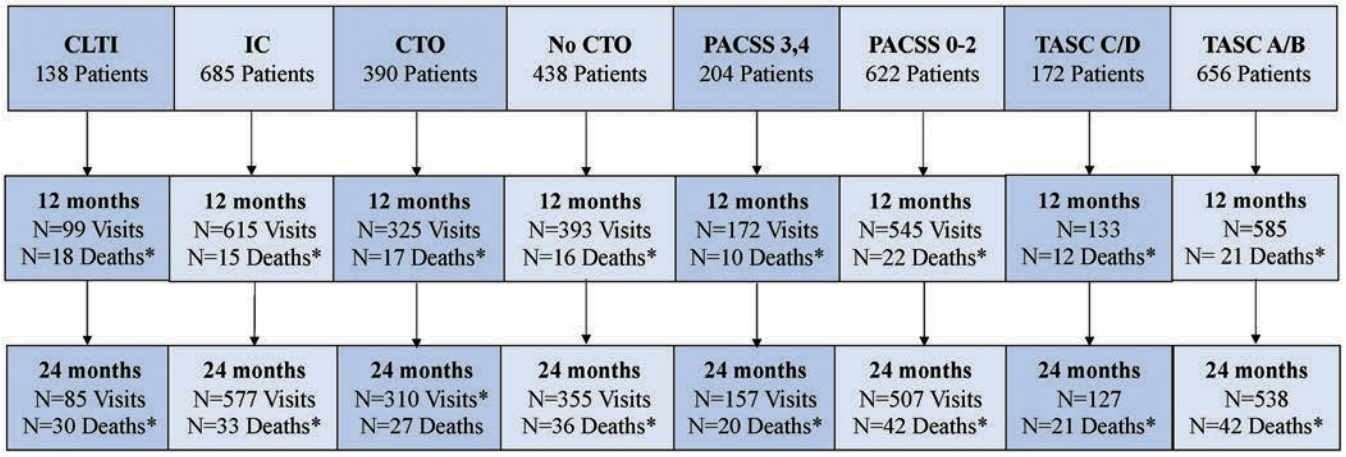


FIGURE 2. Patient flow chart. *Refers to the time window of the visit.

Abbreviations: CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; IC, intermittent claudication; PACSS, peripheral arterial calcification scoring system; TASC, Trans-Atlantic Inter-Society Consensus.

TABLE 1. BASELINE PATIENT CHARACTERISTICS

	CLTI N = 138 P	IC N = 685 P	*P* value	CTO N = 390 P	No CTO N = 438 P	*P* value	PACSS 3,4 N = 204 P	PACSS 0-2 N = 622 P	*P* value	TASC C/D N = 172 P	TASC A/B N = 656 P	*P* value
Age (years)	71.5 ± 10.6	69.0 ± 9.7	.007	68.2 ± 10.1	70.5 ± 9.5	.0008	71.4 ± 9.9	68.7 ± 9.8	.0007	69.8 ± 10.2	69.3 ± 9.8	.581
Male	84 (60.9)	458 (66.9)	.201	255 (65.4)	290 (66.2)	.826	155 (76.0)	389 (62.5)	.0005	113 (65.7)	432 (65.9)	1.000
Female	54 (39.1)	227 (33.1)	.201	135 (34.6)	148 (33.8)	.826	49 (24.0)	233 (37.5)	.0005	59 (34.3)	224 (34.1)	1.000
BMI (kg/m²)	26.3 ± 4.8	27.5 ± 4.9	.006	27.0 ± 4.8	27.5 ± 5.0	.099	27.8 ± 5.0	27.1 ± 4.8	.127	26.4 ± 4.2	27.5 ± 5.0	.047
CVA or TIA	21 (15.4)	69 (10.8)	.141	44 (11.9)	46 (11.2)	.823	21 (10.5)	69 (12.0)	.611	25 (14.5)	65 (10.7)	.177
Hypertension	118 (85.5)	599 (87.4)	.577	328 (84.1)	394 (90.0)	.013	184 (90.2)	537 (86.3)	.182	154 (89.5)	568 (86.6)	.369
Hypercholesterolemia/ dyslipidemia	87 (63.0)	494 (72.1)	.040	258 (66.2)	326 (74.4)	.010	141 (69.1)	441 (70.9)	.659	109 (63.4)	475 (72.4)	.024
Previous MI, CABG, PCI, or CAD	45 (33.1)	242 (38.0)	.328	115 (31.2)	175 (42.8)	.0008	92 (46.0)	197 (34.2)	.004	50 (29.1)	240 (39.6)	.012
Smoking	90 (65.2)	508 (74.2)	.036	285 (73.1)	317 (72.4)	.876	138 (67.6)	463 (74.4)	.070	128 (74.4)	474 (72.3)	.631
Current	57 (41.3)	263 (38.4)	.566	179 (45.9)	142 (32.4)	< .0001	64 (31.4)	256 (41.2)	.013	71 (41.3)	250 (38.1)	.482
Diabetes mellitus	67 (48.6)	255 (37.2)	.017	144 (36.9)	179 (40.9)	.254	101 (49.5)	222 (35.7)	.0005	64 (37.2)	259 (39.5)	.600
Insulin-dependent	37 (26.8)	91 (13.3)	.0002	57 (14.6)	71 (16.2)	.564	46 (22.5)	82 (13.2)	.003	33 (19.2)	95 (14.5)	.154
Renal insufficiency	16 (11.6)	30 (4.4)	.002	19 (4.9)	27 (6.2)	.450	19 (9.3)	26 (4.2)	.007	27 (15.7)	35 (5.3)	.577
Dialysis	7 (5.1)	3 (0.5)	.0003	5 (1.4)	5 (1.2)	1.000	8 (4.0)	2 (0.3)	.0005	11 (6.4)	8 (1.3)	1.000
Nonhealing wound target limb	72 (52.9)	4 (0.6)*	< 0001	47 (12.7)	29 (7.1)	.011	22 (11.0)	54 (9.4)	.493	25 (14.5)	51 (8.4)	0.020
Venous	72 (52.9)	4 (0.6)	< .0001	2 (0.5)	3 (0.7)	1.000	1 (0.5)	4 (0.7)	1.000	2 (1.2)	3 (0.5)	.306
Arterial	4 (2.9)	1 (0.2)	.004	38 (10.3)	22 (5.4)	.011	16 (8.0)	44 (7.6)	.878	21 (12.2)	39 (6.4)	.015
Other / unknown	59 (43.4)	1 (0.2)	< .0001	7 (1.9)	4 (1.0)	.366	5 (2.5)	6 (1.0)	.163	2 (1.2)	9 (1.5)	1.000
CLTI	138 (100)	0 (0.0)	NA	83 (21.3)	55 (12.6)	.001	43 (21.4)	94 (15.1)	.049	43 (25.1)	95 (14.5)	.002
Rutherford class												
4	54 (39.1)	0 (0.0)	NA	33 (8.5)	21 (4.8)	.035	16 (8.0)	37 (5.9)	.323	14 (8.2)	40 (6.1)	.384
5	73 (52.9)	0 (0.0)	NA	46 (11.8)	27 (6.2)	.005	24 (11.9)	49 (7.9)	.087	26 (15.2)	47 (7.2)	.002
6	11 (8.0)	0 (0.0)	NA	4 (1.0)	7 (1.6)	.554	3 (1.5)	8 (1.3)	.735	3 (1.8)	8 (1.2)	.706

Data are displayed as mean ± standard deviation or n (%) and are based on data available. *The patients were not classified as Rutherford class ≥ 4.
Abbreviations: CABG, coronary artery bypass graft; CAD, coronary artery disease; CLT, chronic limb-threatening ischemi;, CTO, chronic total occlusion; CVA, cerebrovascular accident; IC, intermittent claudication; MI, myocardial infarction; P, patients; PACSS, peripheral artery calcification scoring system; PCI, percutaneous coronary intervention; TASC, Trans-Atlantic Inter-Society Consensus; TIA, transient ischemic attack.

without, patients with peripheral artery calcification scording system (PACSS) 3,4 calcification and PACSS 0-2 calcification, and patients with TASC C/D and A/B lesions[19] were compared using Fisher's exact test for categorical variables, student's t-test for continuous variables, and log-rank test for Kaplan-Meier estimates. A *P* value less than .05 was considered significant. The analyses were performed using SAS version 9.4 (SAS institute).

Results

Overall, 828 patients with femoropopliteal occlusive disease were enrolled across the 3 trials (50 in the MIMICS RCT, 271 in the MIMICS-2 study, and 507 in the MIMICS-3D registry) (**Figure 2**).

Baseline Characteristics

There were distinct differences in baseline characteristics (**Tables 1** and **2**). Regarding patient characteristics, in addition to a higher rate of diabetes mellitus, renal insufficiency, and nonhealing wounds, patients with CLTI had more CTO lesions and a higher PACSS calcification grade. Regarding lesion characteristics, patients with CTO had more nonhealing wounds of the target limbs, a higher prevalence of CLTI, and longer lesions than patients without CTO lesions. Patients with PACSS 3,4 lesions had more concomitant disease, diabetes mellitus, renal insufficiency, CLTI, and longer lesions. Patients with TASC C/D lesions had more nonhealing wounds of the target limbs, more restenotic lesions, nearly 3 times longer lesion length, a higher PACSS 4 grade, and a higher prevalence of CLTI. Furthermore,

TABLE 2. BASELINE LESION CHARACTERISTICS BY SUBGROUP

	CLTI N = 142 L	IC N = 692 L	*P* value	CTO N = 397 L	No CTO N = 442 L	*P* value	PACSS 3, 4 N = 209 L	PACSS 0-2 N = 628 L	*P* value	TASC C/D N = 179 L	TASC A/B N = 660 L	*P* value
De novo lesions	128 (91.4)	606 (94.1)	.252	352 (93.6)	386 (93.5)	1.000	188 (91.7)	549 (94.3)	.186	128 (71.5)	610 (100)	< .0001
Restenotic lesions	12 (8.6)	38 (5.9)	.252	24 (6.4)	27 (6.5)	1.000	17 (8.3)	33 (5.7)	.186	51 (28.5)	0 (0.0)	< .0001
Maximum RVD (mm)	5.5 ± 0.7	5.4 ± 0.6	.712	5.4 ± 0.7	5.5 ± 0.6	.081	5.4 ± 0.7	5.5 ± 0.6	.363	5.5 ± 0.7	5.4 ± 0.6	0.403
Lesion length (mm)	120.8 ± 84.3	108.3 ± 75.3	.150	140.7 ± 91.6	83.2 ± 45.7	< .0001	129.1 ± 84.7	104.2 ± 73.0	< .0001	210 ± 100	83.3 ± 37.0	< .0001
Diameter stenosis (%)	94.6 ± 8.7	92.7 ± 9.2	.002	99.9 ± 1.6	86.9 ± 8.7	< .0001	94.0 ± 8.8	92.7 ± 9.2	.10	96.9 ± 6.7	92.0 ± 9.4	< .0001
Occlusion	86 (60.6)	306 (44.2)	.0004	395 (99.5)*	0 (0.0)	< .0001	104 (49.8)	290 (46.2)	.380	136 (76.0)	259 (39.2)	< .0001
Calcification (PACSS)												
Grade 0 (no visible calcium)	20 (14.2)	175 (25.3)	.004	89 6 (22.5)	107 (24.3)	.568	0 (0.0)	196 (31.2)	< .0001	31 (17.4)	165 (25.0)	.036
Grade 1 (unilateral, < 5 cm)	38 (27.0)	189 (27.4)	1.000	115 (29.0)	113 (25.6)	.277	3 (1.4)*	225 (35.8)	< .0001	43 (24.2)	185 (28.1)	.343
Grade 2 (unilateral, ≥ 5 cm)	39 (27.7)	168 (24.3)	.395	88 (22.2)	119 (27.0)	.127	0 (0.0)	207 (33.0)	< .0001	41 (23.0)	166 (25.2)	.625
Grade 3 (bilateral, < 5 cm)	29 (20.6)	79 (11.4)	.006	52 (13.1)	57 (12.9)	1.000	109 (52.2)	0 (0.0)	< .0001	27 (15.2)	82 (12.4)	.379
Grade 4 (bilateral, ≥ 5 cm)	15 (10.6)	80 (11.6)	.885	52 (13.1)	45 (10.2)	.196	97 (46.4)	0 (0.0)	< .0001	36 (20.2)	61 (9.3)	.0002

Data are displayed as mean ± standard deviation or n (%). The categorization was done based on the data available, hence the subgroup might not match the overall number of patients. *Patients with 2 lesions fitting into different categories were categorized to the more complex category (ie, CTO and PACSS 3,4).
Abbreviations: CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; IC, intermittent claudication; L, lesions; PACSS, peripheral artery calcification scoring system; RVD, reference vessel diameter; TASC, Trans-Atlantic Inter-Society Consensus.

there were more patients without patent infrapopliteal vessels in the CLTI, CTO, and TASC C/D groups (**Table 3**).

The use of intravascular lithotripsy (IVL) was not recorded due to the fact that enrollment was several years ago and IVL was rarely used at that time. However, the use of cutting balloon angioplasty and atherectomy is recorded in **Table 3**.

Procedural Characteristics

Pre-dilatation with percutaneous transluminal angioplasty was performed in 87.2% (for TASC C/D lesions), in 93.7% (for CTO lesions), with a drug-coated balloon (DCB) in 10.2% (for TASC A/B lesions), and in 34.1% (for TASC C/D lesions). Post-dilatation was performed in 73.2%, 88.5%, 12.2%, and 25.7%, respectively (**Table 3**). Unfortunately, it was not assessed how many stents were used as bailout in the MIMICS-3D registry. Prior DCB use would suggest that the stent was used as bailout; however, some operators intentionally pretreat the vessel with DCB.

Follow-up

Concomitant medication at baseline and follow-up is provided in **Supplemental Table 2**.

The 24-month freedom from TLR rate was significantly lower in the CLTI group compared with the IC group (73.3% vs 84.5%; *P* = .004), in the CTO group compared with the no CTO group (80.6% vs 85.0%; *P* = .047), and in the TASC C/D group compared with the TASC A/B group (75.9% vs 84.7%; *P* = .016). There was, however, no significant difference for PACSS 3,4 vs PACSS 0-2 lesions (81.5% vs 83.8%; *P* = .717).

TABLE 3. PROCEDURAL CHARACTERISTICS BY SUBGROUP

	CLTI N = 138 P N = 142 L	IC N = 685 P N = 692 L	*P* value	CTO N = 390 P N = 397 L	No CTO N = 438 P N = 442 L	*P* value	PACSS 3,4 N = 204 P N = 209 L	PACSS 0-2 N = 622 P N = 628 L	*P* value	TASC C/D N = 172 P N = 179 L	TASC A/B N = 656 P N = 660 L	*P* value
Procedure time (min)	80.2 ± 57.6	60.7 ± 38.3	< 0.001	76.8 ± 51.0	52.5 ± 29.3	< .0001	75.8 ± 50.8	60.2 ± 39.1	.0002	92.9 ± 60.8	56.4 ± 32.7	< .0001
Number of Bio-Mimics stents deployed												
1	110 (77.5)	566 (81.8)	.240	272 (68.5)	409 (92.5)	< .0001	163 (78.0)	516 (82.2)	.186	83 (46.4)	598 (90.6)	< .0001
2	25 (17.6)	106 (15.3)	.527	100 (25.2)	31 (7.0)	< .0001	36 (17.2)	95 (15.1)	.510	72 (40.2)	59 (8.9)	< .0001
3	4 (2.8)	15 (2.2)	.548	17 (4.3)	2 (0.5)	.0002	7 (3.3)	12 (1.9)	.2807	16 (8.9)	3 (0.5)	< .0001
4	3 (2.1)	5 (0.7)	.141	8 (2.0)	0 (0.0)	.0024	3 (1.4)	5 (0.8)	.4196	8 (4.5)	0 (0.0)	< .0001
Total stented length (mm)	129.0±73.1	118.4±61.3	.180	145.3±82.6	101.9±41.8	<.0001	128.9±69.4	120.4±67.4	.039	187.7±100.4	104.8±40.9	<.0001
No patent infrapopliteal vessel	12 (8.8)	10 (1.6)	<.0001	18 (4.9)	4 (1.0)	.002	6 (3.0)	16 (2.8)	.809	13 (7.6)	9 (1.5)	.0002
PTA balloon												
Pre-dilatation	128 (90.1)	638 (92.2)	.402	372 (93.7)	397 (89.8)	.046	194 (92.8)	575 (91.6)	.662	156 (87.2)	613 (92.9)	.021
Post-dilatation	117 (82.4)	552 (79.8)	.563	304 (76.6)	370 (83.7)	.012	185 (88.5)	487 (77.5)	.0004	131 (73.2)	543 (82.3)	.008
DCB												
Pre-BioMimics stent placement	29 (20.7)	93 (14.4)	.072	87 (23.1)	36 (8.7)	< .0001	34 (16.6)	89 (15.3)	.656	61 (34.1)	62 (10.2)	< .0001
Post-BioMimics stent placement	21 (15.0)	116 (18.0)	.462	79 (21.0)	58 (14.0)	.011	25 (12.2)	112 (19.2)	.024	46 (25.7)	91 (14.9)	.002
Cutting balloon	5 (3.6)	11 (1.7)	.182	10 (2.7)	6 (1.5)	.313	10 (4.9)	2 (1.0)	.036	6 (3.4)	10 (1.6)	.222
Atherectomy	7 (5.0)	32 (5.0)	1.000	23 (6.1)	16 (3.9)	.188	12 (5.9)	11 (5.5)	1.000	16 (8.9)	23 (3.8)	.0009
Post-stent diameter stenosis (%)	8.3 ± 11.2	11.3 ± 15.2	.123	9.7 ± 14.4	11.8 ± 14.9	.009	12.6 ± 15.0	11.0 ± 16.6	.040	6.8 ± 10.3	11.9 ± 15.5	< 0.0001
Technical success (lesion based)	141 (99.3)	687 (99.4)	1.000	392 (99.0)	441 (99.8)	.193	207 (99.0)	624 (99.5)	.604	176 (98.3)	657 (99.7)	.068
Acute procedural success	133 (96.4)	665 (97.1)	.593	376 (96.4)	427 (97.5)	.419	199 (97.5)	602 (96.8)	.814	165 (95.9)	541 (82.5)	.451

Data are displayed as mean ± standard deviation or n (%). The categorization was done based on the data available, hence the subgroup might not match the overall number of patients. Rutherford class and calcification grade were not available for all patients; thus, the subgroups do not add up to the total of 507 patients.

Abbreviations: CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; DCB, drug-coated balloon; PACSS, peripheral artery calcification scoring system; PTA, percutaneous transluminal angioplasty; TASC, Trans-Atlantic Inter-Society Consensus.

Freedom from 24-month major target limb amputation was significantly lower in the CLTI group vs the IC group (93.7% vs 100%; $P < .0001$) (**Table 4, Figure 3**). Of the 7 patients with major amputation in the CLTI group, 6 were in Rutherford class 5 or 6 at baseline, 4 had insulin-dependent diabetes mellitus, 3 had restenotic lesions, 2 had no patent infrapopliteal vessels (3 patent infrapopliteal vessels were only present in 1 patient), and 2 subsequently died (**Supplemental Tables 3-6**). There was no difference in major amputations across the remaining subgroups (**Table 4, Figure 3**).

X-ray assessment of the implanted stent was not mandatory in all studies but was done in 9.7% of patients at 30 days, 40.1% at 12 months, and 38.2% at 24 months. This could introduce a bias as the cases with x-ray assessment are likely to be those with a suspicion of stent fracture considering that x-rays are by default not required in registries. In the overall cohort of patients, 4 stent fractures were observed (0.5%), of which 1 stent fracture was not confirmed by the clinical events committee. The rate of stent fractures was 0.8% (n = 1) in the CLTI group, 1.1% (n = 4) in the CTO group, 0% (n = 4) in the PACSS 3,4 group, and 1.2% (n = 2) in the TASC C/D group.

Clinical improvement (improvement of at least 1 Rutherford class) at 24 months was observed in 85.0% to 97.3% (**Figure 4**) of patients, with a statistically significant difference between the CLTI and IC subgroups (97.3% vs 85.9%; $P < .0003$) but no statistically significant difference between the other subgroups.

TABLE 4. CLINICAL OUTCOMES AT 12 AND 24 MONTHS

	Survival	Ff major TLA	Ff TLR
12 months			
CLTI	85.7% [79.6;91.8]	93.7% [89.2;98.3]	80.6% [73.1;88.0]
IC	97.7% [96.6;98.9]	100% [100;100]	90.0% [87.7;92.3]
CTO	95.3% [93.1;97.5]	98.5% [97.3;99.8]	86.1% [82.5;89.8]
No CTO	96.2% [94.4;98.0]	99.5% [98.9;100]	90.9% [88.1;93.7]
PACSS 3,4	94.8% [91.6;97.9]	98.4% [96.6;100]	85.7% [80.7; 90.8]
PACSS 0-2	96.3% [94.8;97.8]	99.3% [98.6;100]	90.0% [87.5;92.4]
TASC C/D	92.6% [88.6;96.6]	97.9% [95.6;100]	82.6% [76.5;88.7]
TASC A/B	96.6% [95.2;98.0]	99.4% [98.7;100]	90.2% [87.8;92.6]
24 months			
CLTI	75.8% [68.2;83.4]	93.7% [89.2;98.3]	73.3% [64.8;81.8]
IC	94.8% [93.1;96.5]	100% [100;100]	84.5% [81.7;87.4]
***P* value**	< .0001	< .0001	.004
CTO	92.4% [89.7;95.2]	98.5% [97.3;99.8]	80.6% [76.4;84.8]
No CTO	91.2% [88.5;94.0]	99.5% [98.9;100]	85.0% [81.5;88.6]
***P* value**	.703	.176	.047
PACSS 3,4	89.3% [84.8;93.7]	98.4% [96.6;100]	81.5% [75.8;87.3]
PACSS 0-2	92.7% [90.6;94.9]	99.3% [98.6;100]	83.8% [80.7;86.8]
***P* value**	.118	.245	.717
TASC C/D	93.1% [(91.1;95.1]	97.9% [95.6;100]	75.9% [69.0;82.9]
TASC A/B	86.8% [81.6;92.1]	99.4% [98.7;100]	84.7% [81.8;87.6]
***P* value**	.007	.127	.016

Data are displayed as Kaplan-Meier estimate [95% confidence interval] and *P* values reflect log-rank *P* values.

Abbreviations: CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; Ff, freedom from; IC, intermittent claudication; PACSS, peripheral artery calcification scoring system; TASC, Trans-Atlantic Inter-Society Consensus; TLA, target limb amputation; TLR, target lesion revascularization.

Discussion

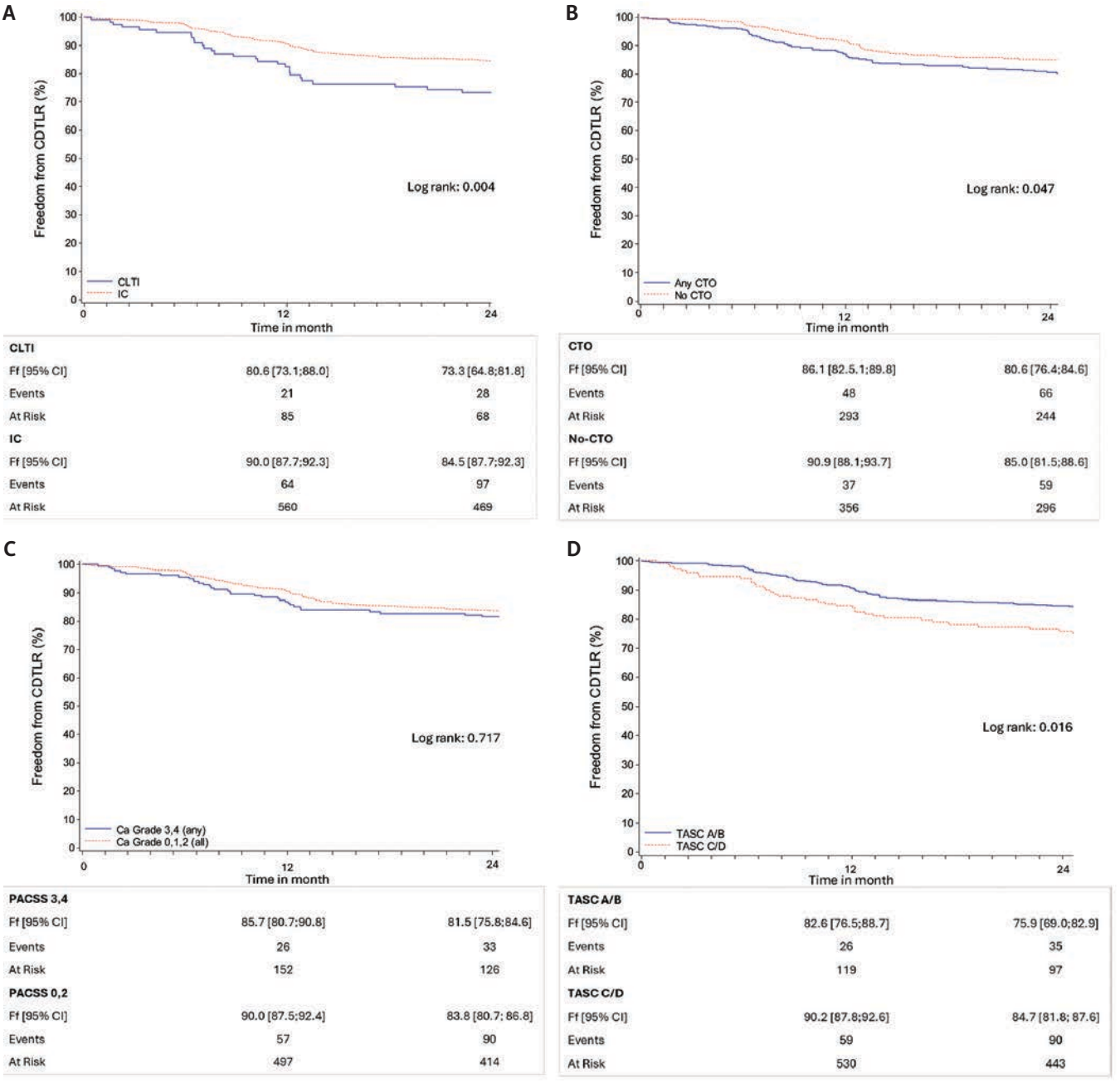
The pooled analysis demonstrated good and durable results through 2 years across all subgroups, despite those subgroups typically being associated with poorer clinical outcomes. Patients with CLTI in this study had higher rates of TLR and target limb amputation, which is to be expected considering that these patients had more diabetes, nonhealing wounds, and complex lesions with a higher rate of CTO and degree of calcification compared with patients with IC, a phenomenon well-known in the literature.[7,20] Similarly, patients with CTO and TASC C/D lesions had more TLRs but no difference in major amputations. There was no difference in outcomes between PACSS 3,4 and PACSS 0-2 lesions.

CLTI represents an advanced stage of atherosclerosis and is in itself a predictor of poor outcomes, particularly with higher Rutherford classes.[20,22-24] Systemic arterial calcification contributes to arterial stiffening, hypertension, heart failure, and pulse-pressure-related organ damage,[25] and other vascular beds are nearly always affected.[22,25] Similarly, diabetes mellitus, renal failure, CTO, calcification, and lack of patent outflow vessels are predictors for poor outcomes.[6,18,23,25-28]

Mimetic stents have a higher flexibility with a higher resistance to compression and resistance to fracture, which is particularly useful in the femoropopliteal bed with its high mechanical stresses of compression and twisting.[21] The BioMimics 3D stent is unique in this category in that the helical centerline design is intended to promote swirling flow, thereby increasing wall shear stress to ultimately reduce intimal hyperplasia.[12,18,21] In addition, it has a transition zone with reduced outward radial force at both ends of the stent to avoid flow disturbances between the stented and not-stented regions to minimize the risk of edge restenosis.[12] These features could be especially relevant in complex lesions such as CTOs, severe calcification, and long TASC C/D lesions, and in patients with CLTI.

In the current analysis, patients with CLTI had more severe calcification, a higher rate of CTO, and longer lesions; as expected, these more complex lesions were more frequently associated with CLTI compared with IC. Thus, while the lower freedom from TLR in patients with CLTI or with CTO or TASC C/D lesions is expected, the outcomes are still good, ie, the 12-month data in the CLTI group are in alignment with the Superficial Femoral Artery-Popliteal EvidencE Development (SPEED) objective performance goals (OPG) of 79% for superficial femoral artery lesions, which is based on the Society for Vascular Surgery Vascular Quality Initiative (VQI) Peripheral Vascular Intervention registry data.[29] It is surprising that there was no difference in outcomes related to lesion calcification severity. From 12 to 24 months, the TLR curves start to flatten, possibly attributable to the 3-dimensional helical centerline design of the stent with its enhanced swirling flow and wall shear stress.[12-14] Pooled 3-year data are not available as the MIMICS RCT was followed for 2 years only, but the 3-year outcomes from MIMICS-3D report a 3-year freedom from TLR of 73.8% in patients with CLTI, which was not significantly different to patients with IC, offsetting the differences in baseline characteristics.[15] Notably, Rutherford class 5 and 6 patients were excluded in the MIMICS RCT and MIMICS-2 studies, which could have introduced a bias in the pooled analysis.

Data of stent usage in complex femoropopliteal lesions in similar populations are scarce, but the outcomes of the subgroups compare well across a variety of devices to the data in the available literature (**Supplemental Table 7**). Twelve- and 24-month freedom from TLR in CTO lesions were 82.6% and



CLTI		
Ff [95% CI]	80.6 [73.1;88.0]	73.3 [64.8;81.8]
Events	21	28
At Risk	85	68
IC		
Ff [95% CI]	90.0 [87.7;92.3]	84.5 [87.7;92.3]
Events	64	97
At Risk	560	469

CTO		
Ff [95% CI]	86.1 [82.5.1;89.8]	80.6 [76.4;84.6]
Events	48	66
At Risk	293	244
No-CTO		
Ff [95% CI]	90.9 [88.1;93.7]	85.0 [81.5;88.6]
Events	37	59
At Risk	356	296

PACSS 3,4		
Ff [95% CI]	85.7 [80.7;90.8]	81.5 [75.8;84.6]
Events	26	33
At Risk	152	126
PACSS 0,2		
Ff [95% CI]	90.0 [87.5;92.4]	83.8 [80.7; 86.8]
Events	57	90
At Risk	497	414

TASC A/B		
Ff [95% CI]	82.6 [76.5;88.7]	75.9 [69.0;82.9]
Events	26	35
At Risk	119	97
TASC C/D		
Ff [95% CI]	90.2 [87.8;92.6]	84.7 [81.8; 87.6]
Events	59	90
At Risk	530	443

FIGURE 3. Freedom from CD-TLR. Kaplan-Meier curves for CD-TLR in **(A)** patients with CLTI vs IC, **(B)** patients with CTO lesions vs those without, **(C)** patients with PACSS lesions grade 3,4 vs grade 0-2, and **(D)** patients with TASC C/D lesions vs those with TASC A/B lesions.

Abbreviations: CD-TLR, clinically driven target lesion revascularization; CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; Ff, freedom from; IC, intermittent claudication; PACSS, peripheral arterial calcification scoring system; TASC, Trans-Atlantic Inter-Society Consensus.

80.6% vs 83.5% and 81.8% in a population treated with the Supera stent (Abbott Vascular),[5] however, this study excluded lesions with severe PACSS 2 and 4 calcification and calcification of 270 degrees or more in vessel circumference; 81% freedom from TLR at 12 months was described in a series of patients with CTO treated with bare metal stents (BMS), drug-eluting stents (DES), and covered stents.[30] In patients with PACSS 3,4 lesions, the 24-month freedom from TLR in this analysis was 81.5% compared with 59.8% for PACSS 3 and 62.3% for PACSS 4 patients treated with either BMS or DES.[28] For patients with TASC C/D lesions, in our meta-analysis we observed a freedom from TLR of 85.7% at 12 months compared with 64% to 85.4% for the Zilver PTX DES

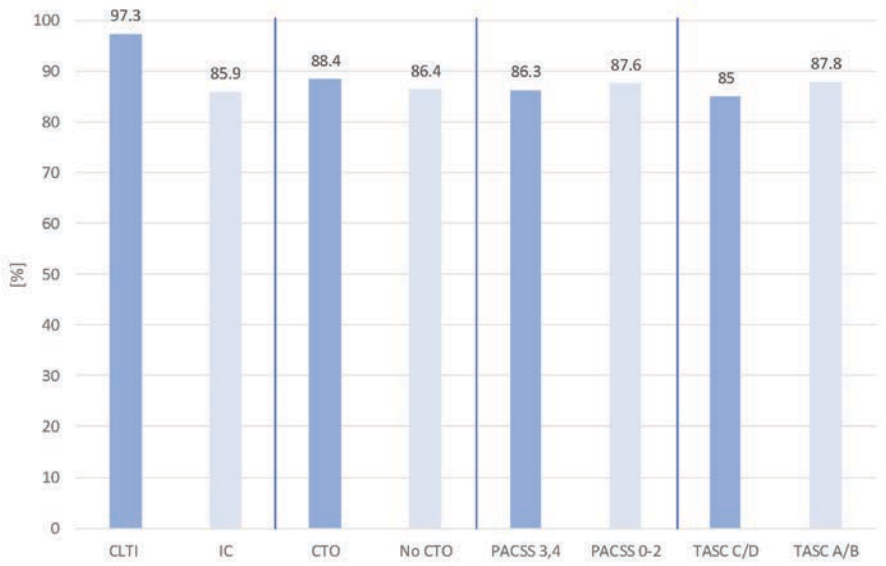


FIGURE 4. Clinical improvement is defined as improvement of at least one Rutherford class. There was a significant difference between CLTI and IC lesions (P = .0003, while there was no significant difference in the remaining subgroups.

Abbreviations: CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; IC, intermittent claudication; PACSS, peripheral arterial calcification scoring system; TASC, TransAtlantic Inter-Society Consensus.

(Cook Medical) in a subgroup analyses of the STELLA-PTX trial and the Zilver PTX single arm study,[31,32] and compared with 70.5% to 80.3% reported in trials with BMS.[33-35] At 24 months in our meta-analysis, freedom from TLR was 81.5% compared with 73% for conventional nitinol stents,[35] and 81.8% and 86.9% in 2 small series of 50 patients treated with the Supera stent.[5,36] The good outcomes in TASC C/D lesions are particularly relevant as there is an increased use of endovascular therapy in these lesions,[37] and patients with a high TASC class are more severely diseased and at increased risk when treated with surgery.[1] Furthermore, a recent study demonstrated cost-effectiveness through 3 years of percutaneous transluminal stenting with optional stenting over bypass surgery in TASC B and C lesions.[38]

Freedom from major amputation through 24 months was 93.7% in patients with CLTI vs 100% in patients with IC. It is acknowledged that there should be no anticipated major amputation at 24 months for the IC group. No patient with IC had a major amputation, so the major amputations in the other subgroups were in patients with CLTI. The higher rate in patients with CLTI is not surprising considering that, of the 138 patients with CLTI, 61% were Rutherford 5 or 6, and these patients had more comorbidities and more complex lesions with fewer patent infrapopliteal vessels.

Importantly, no major amputation occurred beyond 1 year. This rate compares favorably to published literature for femoropopliteal stents; it is well above the SPEED OPG of 90% at 12 months for stents in patients with CLTI with superficial femoral artery lesions,[29] or the VQI data of 89.2% for freedom from amputation for paclitaxel-coated devices at 12 months and 86.5% for non-paclitaxel-coated devices in patients with CLTI at 18 months.[39] For the remaining high-risk subgroups, freedom from major amputation at 24 months was close to 100%, ranging from 97.9% to 98.5%.

As stated above, the helical centerline stent has high flexibility with a high resistance to compression and stent fractures. Accordingly, only 4 stent fractures in 828 patients were reported, of which only 3 were confirmed by the clinical events committee. While calcification is a predictor for stent fractures,[26] stent fractures were absent in PACSS 3,4 lesions. Importantly, while long and TASC C/D lesions are associated with a high risk of stent fractures,[37] in this pooled analysis with a substantial number of patients with x-ray analysis, the 24-month stent fracture rate in TASC C/D lesions was only 1.2%. This is significantly lower than the 9.0% to 17.8% fracture rate at 12 months for straight, slotted-tube nitinol BMS.[32,33,37] A study of the Supera stent reported 0% stent fracture at 24 months; however, it only included 52 patients with TASC C/D lesions, and calcification above 5 cm in vessel length or 270-degree circumference was excluded.[5]

Overall, treatment with the helical centerline stent across the 3 studies led to a sustained high clinical improvement across all subgroups with a minimum improvement of at least 1 Rutherford class in 85% of TASC C/D lesions and the highest clinical improvement (97.3%) in patients with CLTI.

Limitations

This meta-analysis has several limitations. Patency was assessed with different peak systolic velocity ratio thresholds within the studies and was voluntary and not core laboratory assessed in the MIMICS-3D registry, so reporting the patency endpoint would have been inaccurate and hence was not performed. No wound staging (Wound Infection and Foot Infection) or Global-Limb Anatomic Staging System assessments were done. Further, there was significant heterogeneity in terms of adjunctive therapy with drug-coated angioplasty/DCB. Lastly, the data were not randomized and the comparison to outcomes of other studies has to be interpreted with caution considering the heterogenous baseline characteristics.

Conclusion

In a patient-level meta-analysis of 3 key trials, the BioMimics 3D helical centerline stent performed well in CLTI and in complex

lesions with CTO, severe calcification, and TASC C/D lesions with low revascularization, amputation, and stent fracture rates and a high rate of Rutherford clinical improvement. The flattened event curves beyond 1 year speak to the mid-term effectiveness of the device. While superiority over a straight stent has already been demonstrated in an earlier RCT, a separate RCT powered for performance across complex lesion subgroups may be helpful in determining additional clinical utility over conventional straight stents.

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Supplemental Tables

SUPPLEMENTAL TABLE 1. STUDY DETAILS OF MIMICS RCT, MIMICS-2, AND MIMICS-3D

	MIMICS RCT	MIMICS-2 IDE	MIMICS-3D
Design	Multicenter RCT (2:1) against a straight bare metal stent conducted in Germany	Multicenter single-arm study conducted in the United States, Europe, and Japan	Multicenter real-world registry conducted in Europe
Follow-up	2 years	3 years	3 years
Inclusion criteria	1. > 18 years 2. Informed consent 3. Willingness to attend follow-ups 4. Rutherford 1-4 5. Single target lesion at least 1 cm distal to the takeoff of the profunda femoris artery and at least 3 cm proximal to the highest point of the cortical margin of the femur 6. Target lesion RVD ≥ 3.5 mm and ≤ 7.0 mm 7. Target lesion length ≥ 4.0 cm and ≤1 0.0 cm, intended to be covered with one stent; a second stent is permitted only in case the first stent did not achieve an optimal result 8. Adequate distal runoff to the ankle in the target limb (defined as at least 1 patient calf vessel < 50% stenosed) 9. Life expectancy > 24 months	1. Age >18 and ≤ 85 years 2. Informed consent 3. Willingness to attend follow-up 4. Suitable candidate for angiography and endovascular intervention and, if required, for standard surgical repair 5. Symptomatic PAD of the lower extremities requiring intervention to relieve de novo obstruction or occlusion of the native femoropopliteal artery. 6. Rutherford class 2, 3, or 4. 7. Documented PAD 8. Single or multiple stenotic or occlusive lesions within the native femoropopliteal artery ("target lesions") that can be crossed with a guidewire and fully dilated (Note: multiple target lesions must be treated as a single lesion) 9. Single or multiple target lesions must be covered by a single stent or 2 overlapping stents; in the case of tandem lesions, the gap between lesions must be ≤ 3 cm 10. Target lesion at least 1 cm distal to the origin of the deep femoral artery and at least 3 cm above the bottom of the femur. 11. RVD between 4.0 mm and 6.0 mm by operator's visual estimate 12.Target lesion lengths ≥ 40 mm to ≤ 140 mm with ≥60% diameter stenosis by operator's visual estimate 13. Subject has a patent popliteal artery (no stenosis ≥ 50%) distal to the treated segment 14. Subject has at least 1 patent infrapopliteal vessel (< 50% stenosis) with runoff to the ankle	1. Age ≥ 18 and ≤ 85 years 2. Informed consent 3. Symptomatic PAD scheduled for treatment with the BioMimics 3D stent in accordance with the approved CE Mark indication and Instructions for Use

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SUPPLEMENTAL TABLE 1. STUDY DETAILS OF MIMICS RCT, MIMICS-2, AND MIMICS-3D

	MIMICS RCT	MIMICS-2 IDE	MIMICS-3D
Exclusion criteria	1. Pregnancy 2. Uncontrolled infectious disease 3. Condition that inhibits radiographic visualization 4. Conditions that preclude safe access with PTA devices 5. Known allergy to nitinol 6. Known hypersensitivity to contrast media that cannot be pretreated 7. Participation in another device or drug study 8. Unwillingness to comply with study procedures 9. History of bleeding diatheses or coagulopathy or will refuse blood transfer 10. Impaired renal function (< 2.5 mg/dL creatinine except under dialysis 11. Platelet count < 80.000 cells/mm³ or > 700.000 cells/mm 12. White blood cells < 3.000 cells/mm³ 13. Subject is unable to bend the knee or has a knee prosthesis 14. Previous treatment of the target lesion within 6 months or previous femoropopliteal bypass of the target vessel or previous stenting of the target lesion 15. Previous stenting of the superficial femoral artery, popliteal and tibial arteries within the target limb 16. Target lesion located within an aneurysm or associated with an aneurysm 17. Target lesion requires treatment other than standard PTA prior to stent placement (eg, cutting balloons or laser atherectomy) 18. Lesion in contralateral superficial femoral artery that requires intervention during the index procedure or within 30 days thereafter unless both limbs are included in the study 19. Multiple lesions in the target vessel that require stenting within 30 days after the study procedure 20. Target lesion length > 10 cm or the physician believes prior to stent placement that the lesion cannot be covered by 1 stent 21. Severely calcified target lesion	1. Unwillingness to comply with study procedures 2. Comorbidities that would limit life expectancy to < 36 months. 3. Iliac stent in the target limb that requires treatment 12 months prior to index procedure 4. Planned major surgical procedure within 30 days after the index procedure 5. Target vessel that has been treated with any type of surgical or endovascular procedure prior to enrollment 6. Subject has a target vessel that has been treated with bypass surgery 7. Subject has PAD classified as Rutherford clinical category 0, 1, 5, or 6. 8. Active systemic infection 9. Known coagulopathy or bleeding diatheses, thrombocytopenia with platelet count < 100,000/microliter or INR >1.8 10. Stroke diagnosis within 3 months prior to enrollment 11. History of unstable angina or myocardial infarction within 60 days prior to enrollment 12. Contraindication to antiplatelet, anticoagulant, or thrombolytic therapies 13. Known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately premedicated 14. Known allergy to titanium, nickel, or tantalum. 15. Thrombolysis within 72 hours prior to the index procedure 16. Acute or chronic renal disease (eg, serum creatinine > 2.5 mg/dL or > 220 umol/L), or peritoneal or hemodialysis 17. Subject requiring coronary intervention within 7 days prior to enrollment 18. Pregnancy or breastfeeding 19. Participation in another research study involving an investigational product 20. Subject has other medical, social, or psychological problems that preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment 21. Significant disease or obstruction (≥ 50%) of the inflow tract that has not been successfully treated at the time of the index procedure (success measured as ≤ 30% residual stenosis, without complication) 22. Lesion in the contralateral limb requiring intervention during index procedure or within next 30 days 23. No patent (≥ 50% stenosis) outflow vessel providing runoff to the ankle 24. Lack of full expansion in the predilatation balloon 25. Target lesion(s) requires percutaneous interventional treatment beyond standard balloon angioplasty alone, prior to placement of the study stent 26. Evidence of aneurysm or acute thrombus in the target vessel	1. Lesions cannot be crossed with a wire and/or balloon catheter and cannot be dilated sufficiently to allow passage of the delivery system 2. History of intolerance or adverse reaction to antiplatelet and/or anticoagulation therapies, bleeding diathesis, severe hypertension. or renal failure 3. Hypersensitivity to nickel-titanium 4. Comorbidity that would limit life expectancy to < 12 months 5. Pregnancy or breastfeeding 6. Unwillingness to comply with study procedures
Number of patients enrolled	50	271	507

Abbreviations: IDE, investigational device exemption; INR, international normalized ratio; PAD, peripheral arterial disease; PTA, percutaneous transluminal angioplasty; RCT, randomized controlled trial; RVD, reference vessel diameter.

SUPPLEMENTAL TABLE 2. CONCOMITANT MEDICATION

Preprocedure	**N = 828**
Aspirin	643 (77.7%)
Clopidogrel	237 (28.6%)
Cilostazol	16 (1.9%)
Other antiplatelet therapy	19 (2.3%)
Anticoagulant	126 (15.2%)
Any antiplatelet	261 (31.5%)
Dual antiplatelet	227 (27.4%)
30 days	**N = 823**
Aspirin	733 (89.1%)
Clopidogrel	599 (72.8%)
Cilostazol	13 (1.6%)
Other antiplatelet therapy	22 (2.7%)
Anticoagulant	97 (11.8%)
Any antiplatelet	621 (75.5%)
Dual antiplatelet	568 (68.8%)
12 months	**N = 807**
Aspirin	655 (81.2%)
Clopidogrel	255 (31.6%)
Cilostazol	9 (1.1%)
Other antiplatelet therapy	18 (2.2%)
Anticoagulant	95 (11.8%)
Any antiplatelet	275 (34.1%)
Dual antiplatelet	234 (28.8%)
24 months	
Aspirin	570 (73.7%)
Clopidogrel	195 (25.3%)
Cilostazol	6 (0.8%)
Other antiplatelet therapy	20 (2.6%)
Anticoagulant	105 (13.6%)
Any antiplatelet	218 (28.2%)
Dual antiplatelet	175 (22.4%)

Data are displayed as n (%).

SUPPLEMENTAL TABLE 3. BASELINE CHARACTERISTICS OF PATIENTS WITH CLTI ACCORDING TO THEIR AMPUTATION STATUS

	CLTI patients with major amputation N = 7 P	CLTI patients without major amputation N = 131 P
Age (years)	75.3 ± 7.4	71.3 ± 10.8
Male	5 (71.4%)	79 (60.3%)
Female	2 (28.6%)	52 (39.7%)
BMI (kg/m²)	26.9 ± 6.9	26.3 ± 4.7
CVA or TIA	0 (0.0%)	21 (16.3%)
Hypertension	6 (85.7%)	112 (85.5%)
Hypercholesterolemia/ dyslipidemia	4 (57.1%)	83 (63.4%)
Previous MI, CABG, PCI, or CAD	4 (57.1%)	41 (31.8%)
Smoking	4 (57.1%)	86 (65.6%)
Current	2 (28.6%)	55 (42.0%)
Diabetes mellitus	4 (57.1%)	63 (48.1%)
Insulin dependent	4 (57.1%)	33 (25.2%)
Renal insufficiency	1 (14.3%)	15 (11.5%)
Dialysis	1 (14.3%)	6 (4.7%)
Nonhealing wound target limb	2 (28.6%)	70 (54.3%)
Venous	0 (0.0%)	4 (3.1%)
Arterial	0 (0.0%)	59 (45.7%)
Other/unknown	2 (28.6%)	7 (5.4%)
Rutherford Class		
4	1 (14.3%)	53 (40.5%)
5	4 (57.1%)	69 (52.7%)
6	2 (28.6%)	9 (6.9%)

Data are displayed as mean ± standard deviation or n (%).

SUPPLEMENTAL TABLE 4: BASELINE LESION CHARACTERISTICS OF PATIENTS WITH CLTI ACCORDING TO THEIR AMPUTATION STATUS

	CLTI patients with major amputation N = 7 L	CLTI patients without major amputation N = 131 L
De novo L	4 (57.1%)	124 (93.2%)
Restenotic L	3 (42.9%)	9 (6.8%)
Maximum RVD (mm)	5.1 ± 0.9	5.5 ± 0.7
L length (mm)	133.6 ± 55.9	120.2 ± 85.6
Diameter stenosis (%)	95.0 ± 8.7	94.6 ± 8.7
Occlusion	5 (71.4%)	81 (60.0%)
Calcification (PACSS)		
Grade 0 (no visible calcium)	0 (0.0%)	20 (14.9%)
Grade 1 (unilateral, < 5cm)	2 (28.6%)	36 (26.9%)
Grade 2 (unilateral, ≥ 5cm)	2 (28.6%)	37 (27.6%)
Grade 3 (bilateral, < 5cm)	2 (28.6%)	27 (20.1%)
Grade 4 (bilateral, ≥ 5cm)	1 (14.3%)	14 (10.4%)

Data are displayed as mean ± standard deviation or n (%).

Abbreviations: CLTI, chronic limb-threatening ischemia; L, lesions; PACSS, peripheral artery calcification scoring system; RVD, reference vessel diameter.

SUPPLEMENTAL TABLE 6. CLINICAL OUTCOMES OF PATIENTS WITH CLTI ACCORDING TO THEIR AMPUTATION STATUS

	CLTI patients with major amputation N = 7 P	CLTI patients without major amputation N = 131 P
12-month survival	71.4% [38.0;100.0]	86.5% [80.4;92.7]
24-month survival	71.4% [38.0;100.0]	76.0% [68.3;83.8]
12-month freedom from CD-TLR	41.7% [0.0;85.1]	82.4% [75.0;89.8]
24-month freedom from CD-TLR	41.7% [0.0;85.1]	74.8% [66.2;83.4]

Data are displayed as Kaplan-Meier estimate [95% confidence interval]. Two patients in the major amputation group died and 3 had a CD-TLR.

Abbreviations: CD-TLR, clinically driven target lesion revascularization; CLTI, chronic limb-threatening ischemia; P, patients.

SUPPLEMENTAL TABLE 5: PROCEDURAL CHARACTERISTICS OF PATIENTS WITH CLTI ACCORDING TO THEIR AMPUTATION STATUS

	CLTI patients with major amputation N = 7 P N = 7 L	CLTI patients without major amputation N = 131 P N = 135 L
Procedure time (min)	108.9 ± 58.8	78.7 ± 57.3
Number of BioMimics stents deployed		
1	3 (42.9%)	107 (79.3%)
2	4 (57.1%)	21 (15.6%)
3	0 (0.0%)	4 (3.0%)
4	0 (0.0%)	3 (2.2%)
Total stented length (mm)	164.3 ± 77.4	130.3 ± 78.6
Number of patent infrapopliteal vessels		
0	2 (28.6%)	10 (7.8%)
1	1 (14.3%)	43 (33.3%)
2	3 (42.9%)	35 (27.1%)
3	1 (14.3%)	41 (31.8%)
PTA balloon		
Pre-dilatation	4 (57.1%)	124 (91.9%)
Post-dilatation	6 (85.7%)	111 (82.2%)
DCB		
Pre-BioMimics stent placement	1 (14.3%)	28 (21.1%)
Post-BioMimics stent placement	0 (0.0%)	21 (15.8%)
Technical success (lesion based)	7 (100.0%)	134 (99.3%)
Acute procedural success	6 (85.7%)	127 (96.9%)

Data are displayed as mean ± standard deviation or n (%).

Abbreviations: CLTI, chronic limb-threatening ischemia; DCB, drug-coated balloon; L, lesion; P, patient; PTA, percutaneous transluminal angioplasty.

SUPPLEMENTAL TABLE 7. SUMMARY OF DATA REPORTED IN LITERATURE

Study	Device	Number of patients	CLTI	CTO	PACSS 3,4	TASC C/D	Lesion length, mm	Ff Major TLA	Ff TLR	Clinical improvement
CLTI										
SPEED OPG[23]	Self-expanding stent	9217	100%	NR	NR	NR	NR	@12m 90%	@12m 79.5%	NR
Vascular Quality Initiative[39]	PTX vs Non-PTX	14065 14065	100%	NR	NR	NR	NR	@18m 89.2% 86.5%	NR	NR
CTO										
STELLA-SUPERA SIBERIA[5]	Supera	52	16.3%	100%	Excluded PACSS 2,4, or calcification ≥ 270°	100%	198	@24m 100%	@12m 83.5%, @24 m 81.8%	@12 m 80.2% @24 m 63.6%
XLPAD CTO[30]	BMS, DES, covered stents, 8% mimetic stents	1516	39.64	100%	NR	NR	167	@12m 97.6%	@12m 81.0%	NR
Calcification										
Retrospective, single center study[28]	Luminexx, SMART, Zilver, Misago, Zilver PTX	394	NR	NR	100%	NR	NR	NR	@24m 59.8% (grade 3) and 62.3% (grade 4)	NR
TASC C/D lesions										
STELLA-SUPERA[36]	Supera	48	29%	78%	NR	100%	234	NR	@12m 91.6% @24m 86.9%	@12m 87.2% @24m 79.7%
ZILVER PTX single-arm study[31]	Zilver DES	135	0.7%	84.4%	NR	100%	226	NR	@12m 85.4%	NR
STELLA PTX registry[32]	Zilver DES	45	51%	NR	NR	100%	252	@12m 97.3%	@12m 64%	@12m 63.3%
Prosepctive, multicenter study[33]	Primary stenting with straight stents	209	42.6%	NR	NR	100%	NR (Stented length 252)	@12 m 96.2%	@12m 70.5%	@12m 82.2%
STELLA[34]	LifeStent	58	59.7%	NR	NR	100%	220	@12m 0%	@12m 80.3%	@12m 82.6%
Single-center RCT[35]	Nitinol stents	103	53%	80%	NR	100%	264	@12m 99%, @24m 96%	@12m 75% @24m 73%	NR
STELLA-SUPERA SIBERIA[5]	Supera	52	16.3%	100%	Excluded PACSS 2,4, or calcification ≥ 270°	100%	198	@24 m 100%	@12m 83.5%, @24m 81.8%	@12m 80.2% @24m 63.6%

Abbreviations: BMS, bare metal stent; CLTI, chronic limb-threatening ischemia; CTO, chronic total occlusion; DES, drug-eluting stent; DCB, drug-coated balloon; Ff, freedom from; NR, not reported; PACSS, peripheral artery scoring system; PTX, paclitaxel; RCT, randomized controlled trial; TASC, Trans-Atlantic Inter-Society Consensus; TLA, target limb amputation; TLR, target lesion revascularization.