



Zilver PTX Post-Market Surveillance Study of Paclitaxel-Eluting Stents for Treating Femoropopliteal Artery Disease in Japan

12-Month Results

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ABSTRACT

OBJECTIVES This multicenter, prospective, post-market surveillance study in Japan evaluates the paclitaxel-coated Zilver PTX stent in real-world patients with complex lesions.

BACKGROUND The Zilver PTX stent is the first drug-eluting stent (DES) approved for the superficial femoral artery. Previously, results from a large randomized study and a complementary, large single-arm study supported the safety and effectiveness of the DES.

METHODS There were no exclusion criteria, and consecutive patients with symptomatic peripheral artery disease (PAD) treated with the DES were enrolled in the study. Clinically driven target lesion revascularization (TLR) was defined as reintervention performed for $\geq 50\%$ diameter stenosis after recurrent clinical symptoms of PAD. Clinical benefit was defined as freedom from persistent or worsening symptoms of ischemia. Patency was evaluated by duplex ultrasound where physicians considered this standard of care.

RESULTS In this study, 907 patients were enrolled at 95 institutions in Japan. There were numerous comorbidities including high incidences of diabetes (58.8%), chronic kidney disease (43.8%), and critical limb ischemia (21.5%). Lesions were also complex, with an average length of 14.7 cm, 41.6% total occlusions, and 18.6% in-stent restenosis. In total, 1,861 DES were placed in 1,075 lesions. Twelve-month follow-up was obtained for $>95\%$ of eligible patients. Freedom from TLR was 91.0%, and clinical benefit was 87.7% through 12 months. The 12-month primary patency rate was 86.4%.

CONCLUSIONS Despite more challenging lesions, results from the current study are similar to outcomes from the previous Zilver PTX studies, confirming the benefit of the Zilver PTX DES in a real-world patient population. (Zilver PTX Post-Market Study in Japan; [NCT02254837](https://clinicaltrials.gov/ct2/show/study/NCT02254837)) (J Am Coll Cardiol Intv 2016;9:271-7) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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**ABBREVIATIONS
AND ACRONYMS**

ABI = ankle brachial index
BMS = bare-metal stent(s)
CLI = critical limb ischemia
DCB = drug-coated balloon(s)
DES = drug-eluting stent(s)
ISR = in-stent restenosis
PAD = peripheral artery disease
PTA = percutaneous transluminal angioplasty
SFA = superficial femoral artery
TLR = target lesion revascularization

Endovascular treatment of symptomatic peripheral artery disease (PAD) is the preferred revascularization strategy when feasible. Percutaneous transluminal angioplasty (PTA) has historically been the most common endovascular treatment option; however, restenosis rates following PTA are high, resulting in frequent revascularization procedures. In an effort to reduce restenosis rates, a number of other endovascular treatment options have been developed, including atherectomy, bare-metal stents (BMS), drug-coated balloons (DCB), and drug-eluting stents (DES). Among these, a paclitaxel-coated DES has successfully reduced restenosis and reintervention rates for patients suffering from superficial femoral artery (SFA) disease (1,2).

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A large randomized study in the United States, Germany, and Japan demonstrated the safety and effectiveness of the paclitaxel-coated DES for treating SFA disease in patients with moderate lesions (mean lesion length 6.5 cm) (1,2). A complementary single-arm study in Europe, Korea, and Canada, further supported the performance of the DES in a broader patient population with more complex lesions (mean lesion length 10.0 cm) (3). The current study evaluates the safety and effectiveness of the paclitaxel-coated DES in a large, real-world patient population with long, complex lesions in Japan.

METHODS

This multicenter, prospective, post-market surveillance study planned to enroll the first 900 consecutive patients with symptomatic PAD involving the above-the-knee femoropopliteal arteries who were treated with the Zilver PTX Drug-Eluting Peripheral Stent (Cook Medical, Bloomington, Indiana) in Japan. This DES is a self-expanding nitinol stent with a polymer-free paclitaxel coating (3 $\mu\text{g}/\text{mm}^2$ dose density). This post-market surveillance study was required and regulated by the Japanese Ministry of Health, Labour, and Welfare, and was therefore required to be conducted in accordance with Japanese Good Postmarket Surveillance Practice Regulations, which dictate that informed consent processes be determined by each institution's ethical committee policy to specify whether informed consent was necessary or outcome data could be abstracted while protecting patient's rights without requiring individual patient consent.

BASILELINE ASSESSMENT, INTERVENTIONS, AND MEDICATIONS. Rutherford classification and ankle brachial index (ABI) were assessed pre-procedure. The device instructions for use recommends that stents be oversized by 1 to 2 mm with respect to the reference vessel, and placed at least 1 cm below the SFA origin and above the medial femoral epicondyle. Treatment of lesions in both legs was permitted. Pre- and post-dilation and treatment of inflow and outflow disease were at the physician's discretion.

The same antiplatelet regimen used in previous studies was recommended for all patients: clopidogrel or ticlopidine starting at least 24 h before the procedure, or a procedural loading dose; continued clopidogrel or ticlopidine therapy for at least 60 days post-procedure; and aspirin indefinitely.

FOLLOW-UP ASSESSMENT. ABI and Rutherford classification were assessed before discharge and at the 12-month clinical visit. Clinically driven target lesion revascularization (TLR) was defined as reintervention performed for $\geq 50\%$ diameter stenosis within ± 5 mm of the target lesion after recurrent clinical symptoms of PAD. Thrombosis was site-reported as total occlusion of suspected thrombotic origin. Stent integrity was assessed by radiography at 12 months, with site-reported fractures reviewed by a radiographic core laboratory for classification of fracture type. Clinical benefit was defined as freedom from persistent or worsening symptoms of ischemia (i.e., claudication, rest pain, ulcer, or tissue loss) after the initial study treatment. Patency was evaluated by duplex ultrasonography at 12 months where physicians considered this standard of care, with loss of patency corresponding to a peak systolic velocity ratio ≥ 2.4 . Deaths were adjudicated by an independent clinical events committee.

STATISTICAL ANALYSIS. The sample size of 900 was selected to provide 95% confidence for determination of events at rates as low as 1% to 2%. The data were analyzed using SAS 9.3 (SAS Institute, Cary, North Carolina). Continuous variables were summarized with means and SD, with p values calculated using the standard *t* test. Dichotomous and polytomous variables were reported as counts and percentages, with p values calculated using the Fisher exact test. As appropriate, the number of observations represented the number of patients, the number of treated lesions, or the number of treated limbs. Kaplan-Meier analyses were performed to assess freedom from TLR, freedom from thrombosis, clinical benefit, and patency over time.

RESULTS

Between May 2012 and February 2013, 907 patients were enrolled at 95 institutions in Japan. In total, 1,075 lesions were treated with 1,861 DES in these patients. A mean of 1.7 stents per lesion, and a mean of 2.1 stents per patient, were implanted. The stents used were 6 to 8 mm in diameter and 40 to 120 mm in length. Demographics, comorbidities, and baseline lesion characteristics reported by the investigative sites are shown in **Table 1**. There was a 58.8% incidence of diabetes, a 43.8% incidence of chronic kidney disease, and a 21.5% incidence of critical limb ischemia (CLI) in these patients. The lesions were complex with an average lesion length of 14.7 ± 9.7 cm (range 0.5 to 40 cm), 41.6% total occlusions, and 18.6% in-stent restenosis (ISR).

SAFETY. Twelve-month follow-up was obtained for 787 patients, representing >95% of those eligible. The DES was safe in Japanese patients. All-cause

mortality was 5.1% through 12 months. There were no device- or procedure-related deaths. No paclitaxel-related adverse events were reported. Seven patients in the study had an amputation for a 12-month rate of 0.8%. At the time of enrollment, 6 of the 7 patients had CLI with tissue loss (Rutherford class 5). The 12-month Kaplan-Meier estimate of freedom from TLR was 91.0% (**Figure 1**). The 12-month Kaplan-Meier estimate of freedom from thrombosis was 97.0%, with 6 cases reported within 30 days, 12 cases between 30 days and 6 months, and 13 cases between 6 and 12 months of the study procedure.

STENT INTEGRITY. At 12 months, 1,118 of 1,135 DES (98.5%) were free from fracture, yielding a 12-month fracture rate of 1.5% (17 of 1,135). The core laboratory classified the fractures as 5 Type I, 2 Type II, 1 Type III, and 9 Type IV (4).

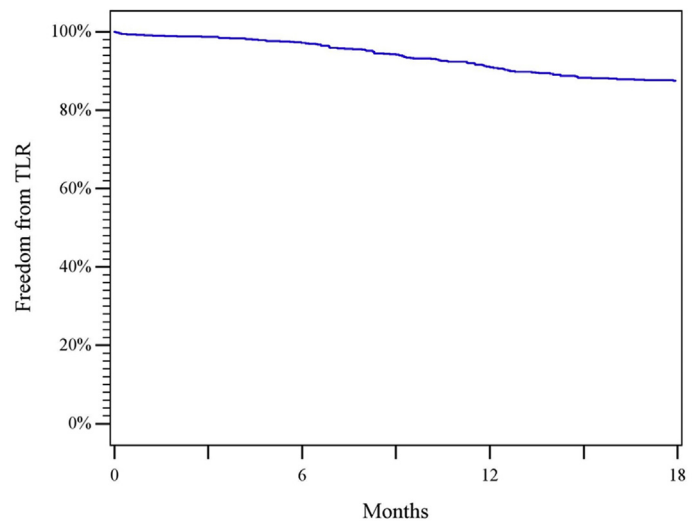
CLINICAL OUTCOMES. Clinical assessment at 12 months revealed significant improvement in Rutherford classification ($p < 0.01$) (**Table 2**). Clinical improvement of at least 1 Rutherford class was

TABLE 1 Demographics and Lesion Characteristics

Patient characteristics	
Patients, N	907
Mean age, yrs	73.5 ± 8.5 (907)
Men	70.3 (638)
Diabetes	58.8 (533)
Hypertension	85.3 (774)
Hypercholesterolemia	60.9 (552)
Chronic kidney disease	43.8 (397)
eGFR <60 ml/min/1.73 m ² and/or dialysis	35.5 (322)
Pulmonary disease	8.0 (73)
Lesion characteristics	
Lesions	1,075
Lesion length, cm	14.7 ± 9.7 (1,074)
Lesions >15 cm	42.0 (451)
Lesions >20 cm	29.7 (319)
Lesion location*	
Proximal SFA	61.1 (657)
Distal SFA	64.5 (693)
Popliteal	9.4 (101)
Total occlusion	41.6 (447)
In-stent restenosis	18.6 (200)
Percent diameter stenosis	91.9 ± 10.7 (1,075)
Reference vessel diameter, mm	5.7 ± 0.9 (1,075)
Critical limb ischemia (Rutherford classes 4-6)†	21.5 (218)
Number of patent runoff vessels‡	
0	6.6 (71)
1	31.8 (340)
2	32.4 (347)
≥3	29.2 (312)

Values are mean ± SD (n) or % (n). *Of the 1,075 lesions in this study, 376 lesions span more than 1 segment. †Rutherford classification data not available for 60 lesions. ‡Data not available for 5 lesions.
 eGFR = estimated glomerular filtration rate; SFA = superficial femoral artery.

FIGURE 1 12-Month Freedom From TLR



Kaplan-Meier Estimates for Freedom from TLR, Values Represent Patients				
Months Post-procedure	Freedom from TLR ± Standard Error	Cumulative Failed	Cumulative Censored	Number Remaining
0	100.0% ± 0.0%	0	0	907
6	97.2% ± 0.6%	25	43	839
12	91.0% ± 1.0%	77	81	749

The Kaplan-Meier curve shows 91.0% freedom from TLR through 12 months for patients treated with the DES. The life table is included. DES = drug-eluting stent(s); TLR = target lesion revascularization.

TABLE 2 Clinical Outcomes

	Pre-Procedure	Post-Procedure*	12 Months*
ABI	0.63 ± 0.18 (974)	0.90 ± 0.16 (691)	0.86 ± 0.17 (824)
Rutherford class†			
0	0.9 (9)	48.6 (352)	54.2 (427)
1	7.3 (74)	25.3 (183)	23.9 (188)
2	26.9 (273)	11.0 (80)	10.9 (86)
3	43.4 (441)	5.7 (41)	5.3 (42)
4	10.3 (105)	1.2 (9)	2.8 (22)
5	9.8 (99)	6.8 (49)	2.4 (19)
6	1.4 (14)	1.4 (10)	0.5 (4)

Values are mean ± SD (n) or % (n). *Statistically significant compared to pre-procedure, $p < 0.01$. †Pre-procedure Rutherford class was obtained for 1,015 lesions, post-procedure Rutherford class was obtained for 725 lesions, and 12-month Rutherford class was obtained for 788 lesions.
ABI = ankle brachial index.

achieved in 638 of 757 patients (84.3%), ~80% of patients were classified as Rutherford class 0 or 1 at 12 months, and the median Rutherford classification improved from class 3 to class 0 (Table 2). Similarly, the mean ABI also significantly improved at 12 months from 0.63 to 0.86. Post-treatment clinical benefit, defined as freedom from persistent or

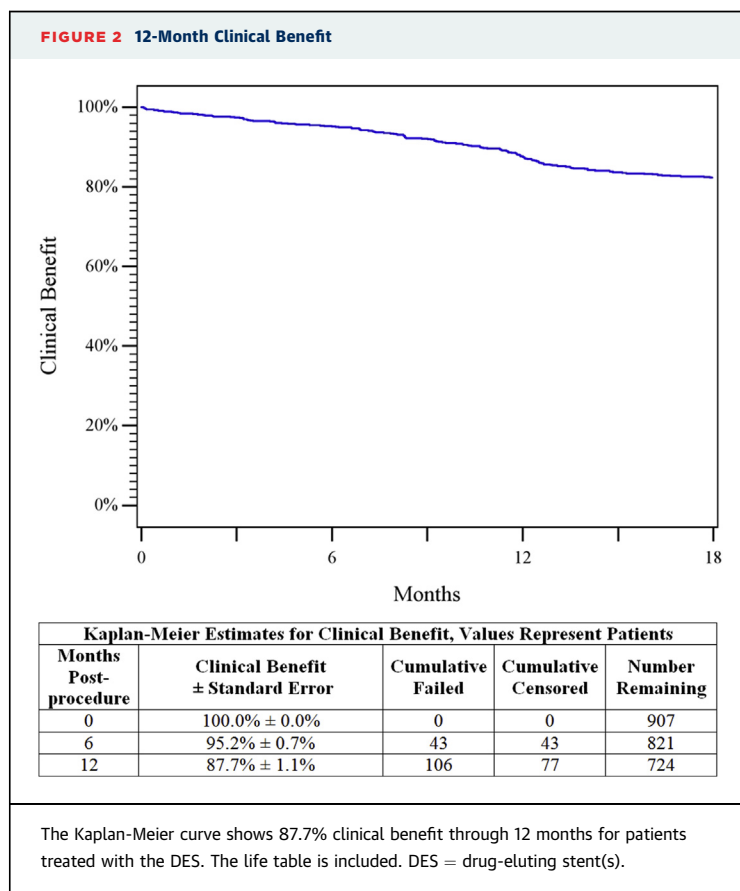
worsening symptoms of ischemia (i.e., claudication, rest pain, ulcer, or tissue loss), was 87.7% at 12 months (Figure 2).

PATENCY. Duplex ultrasound was performed for approximately 65% of patients. The DES was effective in treating SFA lesions in Japanese patients. Based on Kaplan-Meier estimates, the 12-month primary patency rate was 86.4% (Figure 3). To evaluate whether the ultrasound subset was representative of the entire patient population, the demographics, comorbidities, lesion characteristics, 12-month freedom from TLR rates, and 12-month freedom from thrombosis rates for patients who underwent ultrasound were compared with those for patients who did not undergo ultrasound, and no significant differences were found.

DISCUSSION

The 1-year results of the present study demonstrate the safety and effectiveness of the paclitaxel-coated DES for the treatment of femoropopliteal PAD in a large, real-world Japanese patient population with numerous risk factors including high incidences of diabetes, chronic kidney disease, and CLI. The lesions were also complex, including approximately 40% of lesions >15 cm and 30% >20 cm in length, and a high rate of total occlusions and ISR. The low frequencies of stent fracture and thrombotic occlusion after DES placement reported in the present study are comparable to the published rates for nitinol BMS and to previous reports with the DES (1,2,5-10). The freedom from TLR, clinical benefit, and patency results from the present study are similar to previous clinical studies that evaluated the DES in patients with femoropopliteal PAD. The previous studies included the Zilver PTX Randomized Clinical Trial, which demonstrated the benefit of the DES compared with PTA or provisional BMS through 2 years (1,2). The results with the DES in the Japanese subgroup from the randomized trial also showed no major differences in safety and effectiveness compared with the non-Japanese patient group (10). Additionally, a complementary single-arm study supported the performance of the DES in a broader patient population than the randomized trial (3). The results from the present study are similar to the previously published results and confirm the benefit of the DES despite the inclusion of patients with increased risk factors and more complex lesions.

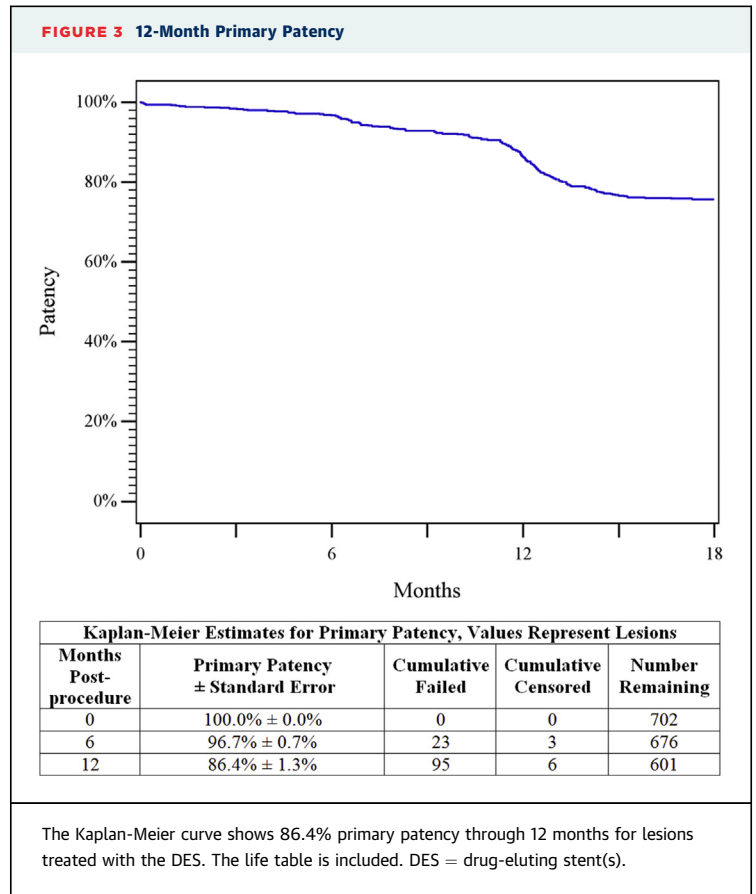
Results with this DES were also recently reported from the ZEPHYR (Zilver PTX for the Femoral Artery



and Proximal Popliteal Artery-Prospective Multi-center Registry) study, which was designed to examine the possible predictors of restenosis after DES implantation (11). The ZEPHYR study involved an even more challenging Japanese patient population that included a larger percentage of diabetic patients (69% vs. 59%) and critical limb ischemia patients (32% vs. 22%), as well as a somewhat longer average lesion length (17 cm vs. 15 cm), compared with the current study. Furthermore, there are important differences in the definitions, methodologies, and reporting practices for the ZEPHYR study compared with the current study and also compared with many previous peripheral endovascular device studies, which reinforce the difficulties in comparing results across studies.

Other than the Zilver PTX randomized study (1,2), there are currently no results available from randomized controlled studies directly comparing this DES to other endovascular therapies, and caution must be taken when comparing outcomes between different studies. Although not a randomized comparison, results from the current study of the DES, such as the 12-month patency rate, compare favorably to the limited available results with BMS in populations including complex lesions, which report patency rates ranging from 49% to 65% (9,12-14). Differences such as patient demographics and lesion characteristics can make comparisons between studies difficult, and in this regard, randomized studies usually provide more meaningful comparisons. The previously published randomized study showed significant benefit with the DES over BMS (1,2). Despite the inclusion of more complex lesions, the results with the DES in the current study are also consistent with the DES results in the randomized study.

Similarly, results from the current DES study, such as the 12-month patency rate of 86.4%, compare favorably to results for DCB, which range from 73.5% to 89.5% (15-18). However, lesions in the DES study were more challenging than those in the DCB studies. For instance, the lesions in the DES study were approximately twice as long, with approximately twice as many total occlusions, and included ISR. Successful pre-dilation was also typically required before DCB treatment. Because of such differences, comparisons between these studies should be interpreted with caution. Previously published results also show that the benefit of the DES is sustained over time (2); whereas, the long-term outcomes with the DCB are limited to a small number of patients (19). The 12-month patency rate from the current study also compares favorably to the patency



rates, ranging from 51.1% to 78.0%, reported for atherectomy (20,21).

STUDY LIMITATIONS. Stent thrombosis in the SFA can be difficult to distinguish from total occlusion caused by restenosis because there is no standardized classification for SFA stent thrombosis unlike the ARC classification for coronary stent thrombosis (22). Additionally, risk factors beyond the stented lesion, for example, untreated residual inflow or outflow stenosis or poor runoff, may contribute to the potential for thrombosis within the infrainguinal arteries. Due to these risk factors and the possible inclusion of total occlusions that are of restenotic rather than thrombotic origin, the site-reported rate may overestimate the DES thrombosis rate in this study. At longer times since the study procedure, the likelihood that the occlusions were of restenotic rather than thrombotic origin increases. Accordingly, the cases reported within 30 days of the study procedure may be considered probable thromboses, those cases reported between 30 days and 6 months may be considered possible thromboses, and those

cases reported between 6 and 12 months may be considered probable restenoses. Despite this possibility for overestimation, the thrombosis rate through 12 months in this study was low and comparable to the published rates for nitinol BMS as well as previous reports with the DES, and demonstrates no increased risk of stent thrombosis due to the paclitaxel drug coating on the DES (1,2,5-10).

In this study, duplex ultrasonography was performed by the investigative sites where physicians considered this standard of care. As a result, patency through 12 months was evaluated for a subset of approximately 65% (702/1,075) of lesions. Additional analyses indicated that the demographics, comorbidities, lesion characteristics, 12-month freedom from TLR rates, and 12-month freedom from thrombosis rates for the ultrasound subset were not significantly different from those for patients who did not undergo ultrasound. Therefore, the ultrasound subset adequately represents the overall study population, supporting the validity of the patency results.

Although this was a post-market, single-arm study without an internal control group, the study enrolled a large number of patients with symptomatic SFA disease representing a real-world patient population. The outcomes with the DES also remained similar to those from the previously published randomized study and similar to those from the complementary single-arm study (1-3).

CONCLUSIONS

Despite more challenging lesions, the results from this real-world, post-market study are similar to

outcomes from the previous Zilver PTX studies, confirming the benefit of the Zilver PTX DES.

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PERSPECTIVES

WHAT IS KNOWN? Experience with the Zilver PTX drug-eluting stent in previous studies has shown long-term benefits, including a randomized controlled trial that demonstrated superiority to standard care (balloon angioplasty with provisional bare-metal stent placement) and to bare-metal stents.

WHAT IS NEW? This large, all-comer, post-market study confirms the benefits with this drug-eluting stent and extends the results to more complex patients, lesions, and risk factors.

WHAT IS NEXT? Further understanding of the results with drug-eluting stents compared with other new therapies, such as drug-coated balloons and resorbable stents, especially in long-term outcomes, would provide valuable insights.

REFERENCES

- Dake MD, Ansel GM, Jaff MR, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv* 2011;4:495-504.
- Dake MD, Ansel GM, Jaff MR, et al. Sustained safety and effectiveness of paclitaxel-eluting stents for femoropopliteal lesions: 2-year follow-up from the Zilver PTX randomized and single-arm clinical studies. *J Am Coll Cardiol* 2013;61:2417-27.
- Dake MD, Scheinert D, Tepe G, et al. Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. *J Endovasc Ther* 2011;18:613-23.
- Jaff M, Dake M, Popma J, Ansel G, Yoder T. Standardized evaluation and reporting of stent fractures in clinical trials of noncoronary devices. *Catheter Cardiovasc Interv* 2007;70:460-2.
- Schillinger M, Sabeti S, Loewe C, et al. Balloon angioplasty versus implantation of nitinol stents in the superficial femoral artery. *N Engl J Med* 2006;354:1879-88.
- Cheng SW, Ting AC, Wong J. Endovascular stenting of superficial femoral artery stenosis and occlusions: results and risk factor analysis. *Cardiovasc Surg* 2001;9:133-40.
- Duda SH, Bosiers M, Lammer J, et al. Sirolimus-eluting versus bare nitinol stent for obstructive superficial femoral artery disease: the SIROCCO II trial. *J Vasc Interv Radiol* 2005;16:331-8.
- Cejna M, Thurnher S, Illiasch H, et al. PTA versus Palmaz stent placement in femoropopliteal artery obstructions: a multicenter prospective randomized study. *J Vasc Interv Radiol* 2001;12:23-31.
- Bosiers M, Deloose K, Callaert J, et al. Results of the Protege EverFlex 200-mm-long nitinol stent (ev3) in TASC C and D femoropopliteal lesions. *J Vasc Surg* 2011;54:1042-50.
- Ohki T, Yokoi H, Kichikawa K, et al. Two-year analysis of the Japanese cohort from the Zilver PTX randomized controlled trial supports the validity of multinational clinical trials. *J Endovasc Ther* 2014;21:644-53.
- Iida O, Takahara M, Soga Y, et al. 1-year results of the ZEPHYR registry (Zilver PTX for the femoral artery and proximal popliteal artery): predictors of restenosis. *J Am Coll Cardiol Intv* 2015;8:1105-12.
- Armstrong EJ, Saeed H, Alvandi B, et al. Nitinol self-expanding stents vs. balloon angioplasty for

very long femoropopliteal lesions. *J Endovasc Ther* 2014;21:34-43.

13. Lammer J, Zeller T, Hausegger KA, et al. Heparin-bonded covered stents versus bare-metal stents for complex femoropopliteal artery lesions: the randomized VIASTAR trial (Viabahn endoprosthesis with PROPATEN bioactive surface [VIA] versus bare nitinol stent in the treatment of long lesions in superficial femoral artery occlusive disease). *J Am Coll Cardiol* 2013;62:1320-7.

14. Geraghty PJ, Mewissen MW, Jaff MR, Ansel GM. Three-year results of the VIBRANT trial of VIABAHN endoprosthesis versus bare nitinol stent implantation for complex superficial femoral artery occlusive disease. *J Vasc Surg* 2013;58:386-95.

15. Tepe G, Laird J, Schneider P, et al. Drug-coated balloon versus standard percutaneous transluminal angioplasty for the treatment of superficial femoral and popliteal peripheral artery disease: 12-month results from the

IN.PACT SFA randomized trial. *Circulation* 2015;131:495-502.

16. Schroeder H, Meyer DR, Lux B, Ruecker F, Martorana M, Duda S. Two-year results of a low-dose drug-coated balloon for revascularization of the femoropopliteal artery: outcomes from the ILLUMENATE first-in-human study. *Catheter Cardiovasc Interv* 2015;86:278-86.

17. Micari A, Cioppa A, Vadala G, et al. 2-year results of paclitaxel-eluting balloons for femoropopliteal artery disease: evidence from a multicenter registry. *J Am Coll Cardiol Intv* 2013;6:282-9.

18. Rosenfield K, Jaff MR, White CJ, et al. Trial of a paclitaxel-coated balloon for femoropopliteal artery disease. *N Engl J Med* 2015;373:145-53.

19. Tepe G, Schnorr B, Albrecht T, et al. Angioplasty of femoral-popliteal arteries with drug-coated balloons: 5-year follow-up of the THUNDER trial. *J Am Coll Cardiol Intv* 2015;8:102-8.

20. Marmagkiolis K, Hakeem A, Choksi N, et al. 12-month primary patency rates of contemporary endovascular device therapy for femoro-popliteal occlusive disease in 6,024 patients: beyond balloon angioplasty. *Catheter Cardiovasc Interv* 2014;84:555-64.

21. McKinsey JF, Zeller T, Rocha-Singh KJ, Jaff MR, Garcia LA. Lower extremity revascularization using directional atherectomy: 12-month prospective results of the DEFINITIVE LE study. *J Am Coll Cardiol Intv* 2014;7:923-33.

22. Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;115:2344-51.

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