**Two-year Clinical Outcomes Post Implantation of Epic™ Self-Expanding Nitinol Stents for the Aortoiliac Occlusive Disease in Patients with Peripheral Arterial Disease**

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**Aim:** We investigated 2-year clinical outcomes after implantation of Epic™ self-expanding nitinol stents for patients with peripheral artery disease (PAD) due to the aortoiliac occlusive disease (AIOD).

**Methods:** This study was a multicenter and retrospective study. From February 2013 through October 2014, 292 lesions (chronic total occlusion, 21%; TASC II C/D, 35%) in 217 consecutive patients (74 ± 8 years; male, 81%; diabetes mellitus, 47%; dialysis, 21%; critical limb ischemia, 29%) who had undergone endovascular therapy (EVT) with Epic™ self-expanding nitinol stents for PAD with AIOD were analyzed. The primary endpoints were 2-year primary patency and target lesion revascularization (TLR)-free rate. The primary patency and freedom from TLR were determined by Kaplan–Meier analysis. Additionally, predictors for loss of patency were estimated by Cox proportional hazard model.

**Results:** The mean follow-up duration was 19.1 ± 8.5 months. Primary patency was 87.3% at 2 years. Freedom from TLR rate was 94.1% at 2 years. Multivariate analysis revealed that the presence of diabetes mellitus was associated with a loss of patency.

**Conclusion:** The Epic™ self-expanding nitinol stent was demonstrated to be safe and effective for AIOD when tested for two years in patients with PAD.

**Key words:** Peripheral artery disease, Aortoiliac occlusive disease, Endovascular therapy, Epic self-expanding nitinol stent

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**Introduction**

The endovascular therapy (EVT) has been widely used as an alternative to surgical bypass therapy for revascularization of the lower limbs in patients with symptomatic peripheral arterial disease (PAD). In particular, EVT is popular in the treatment of patients with aortoiliac occlusive disease (AIOD), and is a standard revascularization method¹-⁶.

The Epic™ stent (Boston Scientific Corp., Natick, MA, USA) is a self-expanding nitinol stent that has been available for the treatment of AIOD since February 2013 in Japan. One-year results after the implantation of an Epic™ stent is available⁷). However, there are no follow-up reports after the implantation of an Epic™ stent.

**Aim**

The aim of this study was to investigate the clinical outcomes in patients with symptomatic PAD and conduct two-year follow ups after implantation of an Epic™ stent.

**Methods**

**Subjects**

A retrospective investigation was conducted on...
The primary endpoints were the primary patency rate two years after implantation of the Epic™ stent and target lesion revascularization (TLR)-free rate. The secondary endpoints included procedure success, clinical success, major adverse cardiac events (MACE), major adverse limb events (MALE), and predictors of 2-year loss of patency after the treatment. Patency was defined as (i) the absence of a significant decrease (0.2 or more) in the ABI, (ii) a peak systolic velocity ratio of less than 2.4 in the stenting site, observed by ultrasonography of the lower limb artery, and (iii) the absence of significant (50% or more) stenosis, confirmed by angiography. TLR was defined as any surgical or percutaneous intervention for the target lesion after the index procedure. The procedure success was defined as the state in which a stent could be implanted and the residual stenosis determined by angiography was less than 30%. The clinical success was defined as an improvement in terms of at least one class on the Rutherford class scale observed after two years of treatment. The MACE was a composite of all-cause mortality, myo-

**Table 1. Baseline patient characteristics**

| Age (years) | 74 ± 8 |
| Male sex, n (%) | 177 (81) |
| Body mass index (kg/m²) | 22.0 ± 3.6 |
| Critical limb ischemia, n (%) | 62 (29) |
| Hypertension, n (%) | 189 (87) |
| Dyslipidemia, n (%) | 127 (59) |
| Diabetes mellitus, n (%) | 107 (49) |
| Chronic kidney disease | 148 (68) |
| Hemodialysis, n (%) | 46 (21) |
| Current smoker, n (%) | 60 (28) |
| Coronary artery disease, n (%) | 126 (58) |
| Medication |
| Aspirin, n (%) | 189 (87) |
| Ticlopidine, n (%) | 2 (1) |
| Clopidogrel, n (%) | 148 (68) |
| Cilostazol, n (%) | 80 (37) |
| Warfarin, n (%) | 26 (12) |
| Direct oral anticoagulant, n (%) | 12 (6) |
| Statin, n (%) | 105 (48) |

Data given as mean ± SD or n (%).

**Table 2. Baseline patient characteristics**

| TASC II classification |
|------------------------|
| A, n (%) | 106 (36) |
| B, n (%) | 84 (29) |
| C, n (%) | 61 (21) |
| D, n (%) | 41 (14) |
| Lesion location |
| Common iliac artery, n (%) | 114 (39) |
| External iliac artery, n (%) | 101 (35) |
| Common to external iliac artery, n (%) | 77 (26) |
| Chronic total occlusion, n (%) | 60 (21) |
| Ostial lesion, n (%) | 150 (51) |
| In-stent restenosis, n (%) | 7 (2) |
| Pre balloon dilation, n (%) | 103 (35) |
| Post balloon dilation, n (%) | 292 (100) |
| Reference vessel diameter (mm) | 8.7 ± 1.0 |
| Lesion length (mm) | 58 ± 34 |
| Mean stent diameter (mm) | 9.6 ± 1.1 |
| Mean stent diameter in common iliac artery lesions (mm) | 10.0 ± 1.0 |
| Mean stent diameter in external iliac artery lesions (mm) | 9.3 ± 1.2 |
| Mean stent diameter in common to external iliac artery lesions (mm) | 9.5 ± 1.0 |
| Mean stent length (mm) | 85 ± 40 |
| Number of stent (per lesion) | 1.3 ± 0.5 |

Data given as mean ± SD or n (%). TASC II, TransAtlantic Inter-Society Consensus II.

**Endovascular Therapy**

The common femoral arteries or brachial arteries were selected as access sites for procedure, and EVT was performed through the iliac artery via an ipsilateral or contralateral approach. In most cases with severely calcified lesions or chronic total occlusion lesions, predilation with plain balloon angioplasty was performed according to the angiographic finding. In most stenotic cases, direct stent strategy was conducted. In the use of Epic™ stents, a diameter that is 1 mm larger than the reference diameter was chosen. Post-dilation with a diameter that is 1 or 2 mm smaller than the stent diameter was performed in all cases.

**Follow-Up**

In most cases, the calculation of ankle brachial pressure index (ABI) and duplex ultrasound was performed 1 day after EVT. Follow-up examinations were performed 1 month later and every 3 months thereafter.

292 lesions in 217 consecutive patients who had received an Epic™ stent for symptomatic PAD with AIOD in Kansai Rosai Hospital or Kishiwada Tokushukai Hospital from February 2013 through October 2014. An AIOD in symptomatic PAD was defined as a lesion showing 75% or more stenosis, confirmed by diagnostic angiography.

**Endpoints**

The primary endpoints were the primary patency rate two years after implantation of the Epic™ stent and target lesion revascularization (TLR)-free rate. The secondary endpoints included procedure success, clinical success, major adverse cardiac events (MACE), major adverse limb events (MALE), and predictors of 2-year loss of patency after the treatment. Patency was defined as (i) the absence of a significant decrease (0.2 or more) in the ABI, (ii) a peak systolic velocity ratio of less than 2.4 in the stenting site, observed by ultrasonography of the lower limb artery, and (iii) the absence of significant (50% or more) stenosis, confirmed by angiography. TLR was defined as any surgical or percutaneous intervention for the target lesion after the index procedure. The procedure success was defined as the state in which a stent could be implanted and the residual stenosis determined by angiography was less than 30%. The clinical success was defined as an improvement in terms of at least one class on the Rutherford class scale observed after two years of treatment. The MACE was a composite of all-cause mortality, myo-
cardiac infarction, and stroke. The MALE was a composite of major amputation of the lower limb on the treatment side or repeat revascularization of the target vessel. Major amputation of the lower limb was defined as any amputation at a more central side from the ankle.

Statistical Analysis

SPSS version 24 was used for statistical analysis. The primary patency rate and the TLR-free rate were obtained using the Kaplan–Meier method and a log-rank test was used for comparison between groups. The predictors of restenosis were investigated using a multivariate analysis of the Cox proportional hazard model. The level of significance was set at \( p < 0.05 \).

Results

Patient Characteristics

The mean follow-up period was 19 ± 9 months. The mean age of patients was 74 ± 8 years, and there were 177 male subjects (82%). A total of 59 patients (27%) had critical limb ischemia, 148 (68%) had chronic kidney disease (estimated glomerular filtration rate; eGFR < 60 mL/min/1.73 m²), 46 (21%) needed maintenance dialysis, and 107 (47%) had diabetes mellitus (Table 1).

Lesion Characteristics and Therapeutic Procedures

The number of lesions classified as A, B, C, and D lesions, based on the Trans-Atlantic Inter-Society Consensus (TASC) II classification, were 107 (37%), 83 (28%), 61 (21%), and 41 (14%), respectively, with 60 (21%) of chronic total occlusion (CTO) lesions. The average reference vessel diameter and lesion length were 8.7 ± 1.0 mm and 58 ± 34 mm, respectively. The average stent diameter and stent length were 9.6 ± 1.1 mm and 85 ± 40 mm, respectively (Table 2).

Treatment Results

The rate of procedure success was 100%. The pre-procedure Rutherford classifications were Rutherford class 1, 2%; 2, 16%; 3, 54%; 4, 9%; 5, 15%; and 6, 4%. The classes at two years after the treatment were class 0, 64%; class 1, 23%; 2, 6%; 3, 1%; 4, 1%; 5, 3%; and 6, 2%. The rate of clinical success two years after treatment was 91%. The primary patency rate two years after implantation of the Epic™ stent was 87.3% (Fig. 1A). The TLR-free rate was 94.1% (Fig. 1B). The MACE and MALE results two years after the treatment were 85.8% and 89.6%, respectively (Fig. 2A and 2B). The multivariate analysis of the Cox proportional hazard model showed that diabetes mellitus (hazard ratio [HR], 3.76; 95% confidence interval [CI]: 1.60–8.83, \( P=0.002 \)) was predictor of restenosis (Tables 3). A comparison of the primary patency rates at two years on the basis of the presence or absence of diabetes mellitus showed a significantly lower primary patency rate in the group with diabetes mellitus than in the group without diabetes mellitus (80.3% versus 94.0%, log-rank \( p=0.002 \)).
Discussion

In this research, the primary patency rate two years after implantation of an Epic™ stent for AIOD in PAD was 87.3%, and the TLR-free rate was 94.1%, which were acceptable results. The presence of diabetes mellitus was significantly associated with a loss of patency.

EVT has been widely used to treat PAD in recent years and excellent results have been reported in the treatment of AIOD. A multicenter study in Japan reported that the primary patency rates after EVT for AIOD were superior, i.e., 92.5% at one year, 82.6% at three years, and 77.5% at five years. A meta-analysis by Bosch et al. showed that the initial success and long-term patency after stent implantation were superior to those after plain balloon angioplasty only, and stent-supported EVT was widely used in clinical settings. The Epic™ stent became available in Japan since 2013 as a new self-expanding nitinol stent for use in the iliac artery. The Epic™ stent comprised of three struts — the micro strut (for maintaining flexibility), the medium strut (for dispersing stress/durability), and the macro strut (for maintaining dilatation force) — of varying lengths and widths. The conative dilatation force and flexibility of this stent are achieved by its hybrid cell structure and tandem architecture design. Furthermore, we expect more precise positioning during stent implantation facilitated by the superior visibility of the stent and the stent deployment system with the ergonomic handle. Owing to this structure, the Epic™ stent could prevent vessel collapse and provide stability, radial force, and scaffolding for complex aorto-iliac (AI) lesions such as calcified or tortuous lesions. In this study, TASC C/D and calcified lesions, which have been reported as a risk factor causing the loss of patency in a previous report, are not associated with 2-year restenotic predictor. So far, the Epic™ stent is considered to be suitable for inexperienced operators because its usability is relatively good. The ORION study reported superior clinical results after implantation of the Epic™ stent; the primary patency rate one year after implantation in 125 PAD patients with an iliac artery lesion was 94.4%. Considering that the frequencies of critical limb ischemia, diabetes mellitus, chronic kidney disease, maintenance dialysis, TASC II C and D lesions, and CTO lesions were high, and that the patient characteristics were slightly inferior in this research than in the ORION study, the results in this research are outstanding. A previous study reported that primary patency rates were 86.1% for S.M.A.R.T. and 88.6% for Luminexx at 2 years after stent implantation. In this research, the primary patency rate of Epic™ stent was 87.3% at 2 years after stent implantation and it was comparable to the previous report.

Reported predictors of restenosis after EVT for iliac artery lesions include female gender, diabetes mellitus, renal dysfunction, not taking aspirin, a target vessel diameter of less than 8.0 mm, and the presence of stenotic lesions in the outflow. The current study demonstrated that diabetes mellitus (HR, 3.76; 95% CI: 1.60–8.83, \(P = 0.002\)) was a predictor for restenosis, subsequently showing that the 2-year primary patency rate in the group with diabetes mellitus was lower than that in the group without diabetes mellitus. This
result was consistent with the previous study. There is a general agreement that diabetes mellitus is a significant risk factor for the development of PAD. Furthermore, diabetes mellitus was considered as one of the significant risk factors for loss of patency after femoropopliteal intervention. As mentioned in previous studies, the presence of diabetes mellitus is also a risk factor that may cause restenosis in Al lesion. In addition, we speculated that PAD patients with diabetes mellitus have more severe arteriosclerotic disease in infrapopliteal lesion. Previous literature reported that the outflow condition was a predictor of restenosis in Al lesion. Consequently, PAD patients with diabetes mellitus presenting severe outflow situations are thought to be at a risk for restenosis after stent implantation in Al lesion. Long-term close follow-up is mandatory in patients with diabetes mellitus.

**Limitations of This Research**

This study had the following limitations. First, this research was a retrospective investigation with a small sample size. The primary patency rate and the TLR-free rate were evaluated; however, there were only a few patients with restenosis and repeat revascularization of the target lesion. The small sample size might have affected the results of the multivariate analysis. Second, the observation period was only two years, and the treatment results thereafter in the chronic phase are unknown. Third, the research was conducted in a limited number of institutions in Japan. Fourth, although previous literature reported that the outflow condition was a predictor of restenosis in Al lesion.

**Table 3. Predictors of primary patency**

| Predictor                        | Univariate analysis | Multivariate analysis |
|----------------------------------|---------------------|-----------------------|
|                                 | Hazard ratio [95%CI] | P value               | Hazard ratio [95%CI] | P value               |
| Age                              | 1.04 [0.99-1.09]     | 0.10                  | 0.71 [0.30-1.69]     | 0.44                  |
| Male sex                         | 0.62 [0.26-1.45]     | 0.27                  |                       |                       |
| Body mass index                  | 0.93 [0.84-1.04]     | 0.21                  |                       |                       |
| Critical limb ischemia           | 1.68 [0.74-3.81]     | 0.22                  |                       |                       |
| Hypertension                     | 0.78 [0.27-2.25]     | 0.65                  |                       |                       |
| Dyslipidemia                     | 1.04 [0.49-2.20]     | 0.93                  |                       |                       |
| Diabetes mellitus                | 3.52 [1.50-8.25]     | 0.004                 | 3.76 [1.60-8.83]      | 0.002                 |
| Chronic kidney disease           | 0.70 [0.34-1.47]     | 0.35                  |                       |                       |
| Hemodialysis                     | 0.84 [0.32-2.20]     | 0.72                  |                       |                       |
| Current smoker                   | 0.60 [0.24-1.47]     | 0.26                  |                       |                       |
| Coronary artery disease          | 0.85 [0.41-1.77]     | 0.67                  |                       |                       |
| Aspirin                          | 1.73 [0.41-7.25]     | 0.46                  |                       |                       |
| Ticlopidine                      | 0.05 [0.01-99.99]    | 0.75                  |                       |                       |
| Clopidogrel                      | 0.81 [0.38-1.74]     | 0.58                  |                       |                       |
| Cilostazol                       | 0.67 [0.30-1.51]     | 0.34                  |                       |                       |
| Warfarin                         | 1.23 [0.43-3.54]     | 0.70                  |                       |                       |
| Direct oral anticoagulant        | 0.73 [0.10-5.38]     | 0.76                  |                       |                       |
| Statin                           | 1.11 [0.53-2.30]     | 0.79                  |                       |                       |
| TASC II classification C/D       | 0.63 [0.27-1.46]     | 0.28                  |                       |                       |
| Common iliac artery              | 1.13 [0.51-2.47]     | 0.77                  |                       |                       |
| External iliac artery            | 0.76 [0.37-1.58]     | 0.46                  |                       |                       |
| Common to external iliac artery  | 0.79 [0.32-1.94]     | 0.61                  |                       |                       |
| Ostial lesion                    | 0.93 [0.44-1.96]     | 0.85                  |                       |                       |
| In-stent restenosis              | 2.73 [0.65-11.47]    | 0.17                  |                       |                       |
| Chronic total occlusion          | 1.96 [0.89-4.30]     | 0.10                  |                       |                       |
| Reference vessel diameter        | 0.71 [0.50-1.02]     | 0.07                  | 0.70 [0.49-1.01]      | 0.06                  |
| Lesion length                    | 1.01 [0.99-1.02]     | 0.14                  |                       |                       |
| Mean stent diameter              | 0.72 [0.51-1.01]     | 0.054                 |                       |                       |
| Mean stent length                | 1.01 [0.99-1.02]     | 0.10                  |                       |                       |
| Number of stent (per lesion)     | 1.49 [0.80-2.78]     | 0.21                  |                       |                       |

TASC II, TransAtlantic Inter-Society Consensus II.
we did not evaluate the outflow lesions such as femoro-popliteal artery disease and below the knee disease in all enrolled patients. Therefore, we could not evaluate the impact of outflow lesions on patency after AI stent implantation. Fifth, seven in-stent restenosis lesions were included in this study. Although, compared with de-novo lesion, in-stent restenosis lesion was not an independent predictor of restenosis, it may affect patency after EVT in longer follow-up. Lastly, the EVT surgeon in this research was relatively experienced, and we may not be able to generalize the successful results achieved here. Treatment results including the rate of procedure success may differ for complicated lesions, and additional large-scale investigations are necessary.

**Conclusion**

The Epic™ iliac stent showed excellent performance and a high patency rate was confirmed up to two years.

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