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ENDOVASCULAR THERAPY FOR BUERGER'S DISEASE    581
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Recently, Aragón-Sánchez et al.[14] reported a successful endovascular approach to occlusive posterior tibial and plantar arteries in a Buerger's disease patient threatened with amputation. Graziani et al.[15] had good outcomes with endovascular therapy for tibial artery occlusion due to Buerger's disease in 20 cases, with clinical improvement in 84% and 100% limb salvage over a mean 23-month follow-up. Given that occlusive lesions in Buerger's disease can be pathologically characterized by a preserved internal medial layer, concentric vasoconstriction, and absence of calcification,[4,7] these recent experiences and our case highlight the potential utility of subintimal angioplasty in the endovascular treatment of patients with Buerger's disease.

## REFERENCES

1. von Winiwarter F. Ueber eine eigenthumliche Form von Endarteriitis und Endophlebitis mit Gangran des Fusses. Arch Klin Chir. 1879;23: 202–226.
2. Buerger L. Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med Sci. 1908; 136:567–580.
3. Castronuovo JJ, Adera HM, Smiell JM, et al. Skin perfusion pressure measurement is valuable in the diagnosis of critical limb ischemia. J Vasc Surg. 1997;26:629–637.
4. Olin JW. Thromboangiitis obliterans (Buerger's disease). N Engl J Med. 2000;343:864–869.
5. Mills JL. Buerger's disease in the 21st century: diagnosis, clinical features, and therapy. Semin Vasc Surg. 2003;16:179–189.
6. Lazarides MK, Georgiadis GS, Papas TT, et al. Diagnostic criteria and treatment of Buerger's disease: a review. Int J Low Extrem Wounds. 2006;5:89–95.
7. Puéchal X, Fiessinger JN. Thromboangiitis obliterans or Buerger's disease: challenges for the rheumatologist. Rheumatology. 2007;46: 192–199.
8. Kawarada O, Yokoi Y, Morioka N, et al. Chronic total occlusions in the superficial femoral artery: a novel strategy using a 1.5 mm J-tip hydrophilic guidewire with an over-the-wire balloon catheter under ultrasound guidance. Catheter Cardiovasc Interv. 2005;65:187–192.
9. Kawarada O, Yokoi Y, Sekii H, et al. Retrograde crossing through the pedal arch for totally occluded tibial artery. J Interv Cardiol. 2008; 21:342–346.
10. Kawarada O, Yokoi Y, Higashimori A, et al. Stent-assisted below-the-ankle angioplasty for limb salvage. J Endovasc Ther. 2011;18:32–42.
11. Zhu YQ, Zhao JG, Liu F, et al. Subintimal angioplasty for below-the-ankle arterial occlusions in diabetic patients with chronic critical limb ischemia. J Endovasc Ther. 2009;16:604–612.
12. Kawarada O, Yokoi Y. Native chronic total occlusion recanalization after lower limb bypass graft occlusion: a series of nine cases. Catheter Cardiovasc Interv. 2010;76:214–219.
13. Kawarada O, Fujihara M, Higashimori A, et al. Predictors of adverse clinical outcomes after successful infrapopliteal intervention. Catheter Cardiovasc Interv. 2012;80:861–871.
14. Aragón-Sánchez J, Rabellino M, Pulido-Duque J, et al. Endovascular treatment is a hope for patient with Buerger's disease and foot ulcer: case report. Int J Low Extrem Wounds. 2012;11: 165–168.
15. Graziani L, Morelli L, Parini F, et al. Clinical outcome after extended endovascular recanalization in Buerger's disease in 20 consecutive cases. Ann Vasc Surg. 2012;26:387–395.

# PERIPHERAL VASCULAR DISEASE

## *Original Studies*

# Duplex Criteria for In-Stent Restenosis in the Superficial Femoral Artery

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**Objectives:** To elucidate the optimal cutoff and accuracy of duplex ultrasonography (DUS) parameters for in-stent restenosis (ISR) after nitinol stenting in the superficial femoral artery (SFA). **Background:** Few data are available regarding the performance of DUS for binary ISR based on quantitative vessel analysis (QVA) in the era of SFA nitinol stenting. **Methods:** This retrospective study included 74 in-stent stenoses of SFA who underwent DUS before follow-up angiography. DUS parameters, such as peak systolic velocity (PSV) and the peak systolic velocity ratio (PSVR), were compared with percent diameter stenosis (%DS) from a QVA basis. **Results:** There was a statistically significant correlation ($P < 0.001$) between "%DS and PSV" and "%DS and PSVR," and the correlation with %DS proved to be stronger in PSVR ($R = 0.720$) than in PSV ($R = 0.672$). The best performing parameter for ISR (50% or greater stenosis) was revealed PSVR, as the areas under the receiver operator characteristics curves using PSVR and PSV were 0.908 and 0.832, respectively. A PSVR cut off value of 2.85 yielded the best predictive value with sensitivity of 88%, specificity of 84%, and accuracy of 86%. The positive predictive value was 85% and the negative predictive value was 88%. **Conclusions:** A PSVR of 2.85 is the optimal threshold for ISR after nitinol stenting in the SFA. Further large prospective studies are required for the validation and establishment of uniform criteria for DUS parameters. © 2012 Wiley Periodicals, Inc.

Key words: peak systolic velocity ratio; quantitative vessel analysis; nitinol stent

## INTRODUCTION

The marriage of balloon angioplasty with a nitinol stent has gained popularity in the field of superficial femoral artery (SFA) intervention during the last dec-ade. However, a standard methodology for assessing in-stent restenosis (ISR) has yet to be established in the SFA [1]. During the last two decades, quantitative vessel analysis (QVA) based on an angiographic basis

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Conflict of interest: Nothing to report.

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has been established as the gold standard methodology for coronary intervention analysis [2–6]. Recently, a statement regarding lower limb intervention outcomes advocated the need for QVA for objective evaluation [7].

Meanwhile, given its noninvasive nature, lack of need for contrast agents, and repeatability, duplex ultrasonography (DUS) has been widely used in the identification of restenosis after lower limb intervention. However, it remains unclear as to how DUS parameters such as peak systolic velocity (PSV) and peak systolic velocity ratio (PSVR) are plausible to predict ISR in the era of SFA nitinol stenting. Even in the assessment of SFA intervention outcomes, QVA should be the gold standard method to which DUS could be compared. Thus, the aim of this study was to elucidate the optimal cut off values and accuracy of duplex parameters for ISR on QVA basis after nitinol stenting in the SFA.

## METHODS

### Study Population

A total of 74 in-stent SFA stenoses that were detected by follow-up angiography between June 2008 and December 2010 were included in this retrospective study. Follow-up angiography was performed 8.9 ± 6.7 months (1–36) after original SFA intervention with nitinol stent. The DUS examination was performed ≤14 days before follow-up angiography. The reasons for follow-up angiography were as follows: clinically driven in 65% (48 limbs) and as a part of coronary or other peripheral angiography in 35% (26 limbs). All implanted nitinol stents involved the Smart (Cordis Corporation, Miami, FL). Patients showing stent reocclusion, including subtotal occlusion, were excluded from this study.

### Duplex Ultrasonography

DUS using a commercially available machine (Aplio SSA-770A; Toshiba, Tokyo, Japan) was performed by vascular technicians with extensive experience who were blinded to other patient data. All patients were examined in a supine position using a duplex scanner with an 8-MHz transducer. The stented artery was visualized using combined B-mode and color-Doppler ultrasound. Once the stented segment was identified, the Doppler signal was acquired at an angle of 60° or as small as possible. Doppler spectral analysis determined the highest PSV in the stented segment. In addition, PSV was determined in the adjacent most proximal area of the normal segment. PSVR was calcu-lated by dividing the highest PSV by PSV proximal to the lesion.

## Quantitative Vessel Analysis

Angiograms were obtained using the anteroposterior and/or oblique view. To determine lesion severity, QVA using an automated edge detection algorithm, QCA-CMS (MEDIS: Medical Imaging Systems, Leiden, The Netherlands) was performed in a blinded fashion (Fig. 1). A catheter tip placed at the common femoral artery was not available as a calibration method because the movement of the catheterization table was required for angiographic evaluation for the entirety of SFA lesions. It was, therefore, impossible to calculate diameters of reference vessel, lumen, and lesion length, and only percent diameter stenosis (%DS) was calculated following the formula: in-stent minimum lumen diameter divided by reference vessel diameter due to the assumed vessel. If the entire SFA was stented, then the control segment, which was evaluated against in-stent stenosis, was within a widely patent segment of the more proximal and/or distal stent. Fifty percent diameter stenosis was considered significant based on theoretical and experimental studies [8]. Indeed, angiographically detected lesions of 50% or greater diameter stenosis have been historically considered a dichotomous event, "binary restenosis," in the field of cardiovascular intervention [9]. Thus, in this study, ISR was defined as diameter stenosis >50% within the stent.

## Statistical Analysis

Continuous variables are presented as the mean ± standard deviation. Data were analyzed using a commercially available statistical package (SPSS version 18.0; SPSS). Regression analysis was performed to investigate the correlation among continuous variables such as %DS, PSV, and PSVR. Receiver operator characteristic (ROC) curve analysis was performed to calculate the sensitivity, specificity, predictive values, and accuracy of DUS parameters and to determine the optimal threshold for the detection of ISR. Statistical significance was defined as $P < 0.05$.

## RESULTS

Patient characteristics are shown in Table I. Limb and lesion characteristics are shown in Table II. The stented segments evaluated were located in the SFA as follows: proximal segment in 34% (25), midsegment in 39% (29) and distal segment in 27% (20). Lesion assessment in overlapped stents was included in 8%
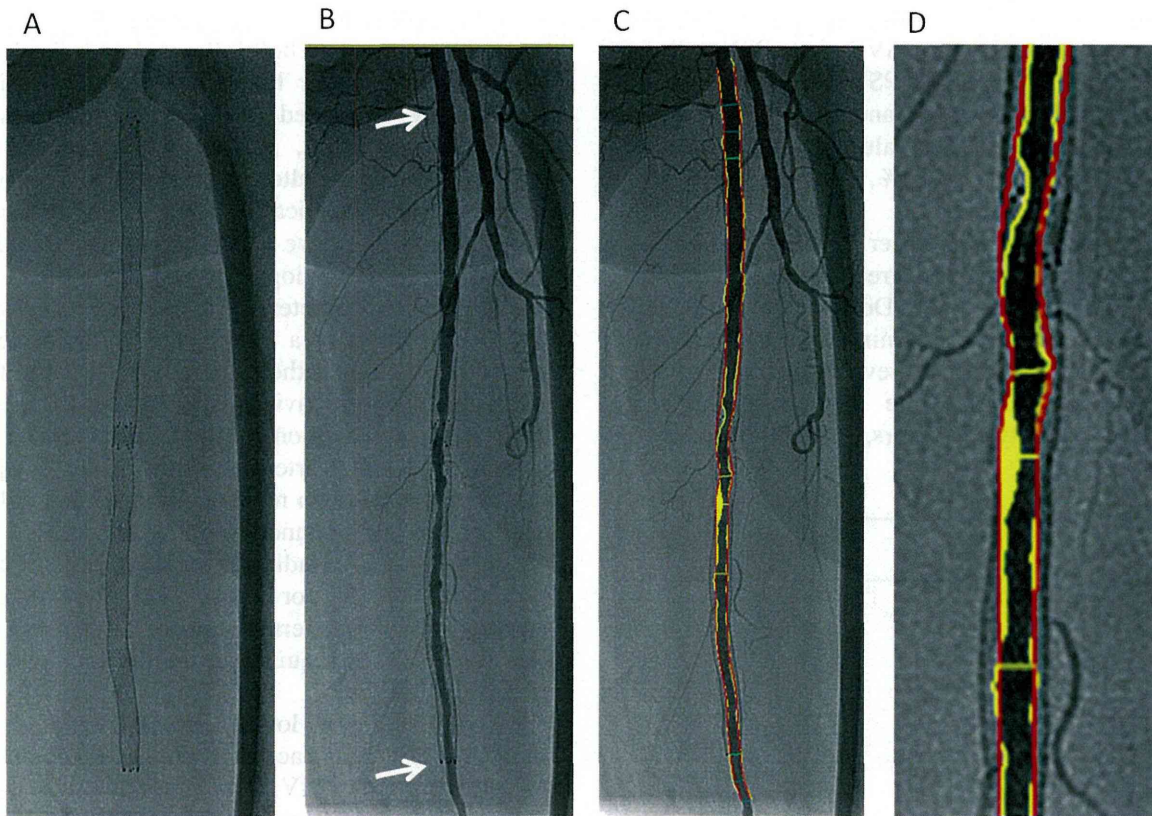
Fig. 1.  Quantitative SFA analysis. A: Nitinol stents implanted in the left SFA. B: Angiography showing intimal hyperplasia in the stented SFA. Note the proximal and distal edges of the nitinol stent (arrows). C: Automatically applied tracings show lumen contour (yellow lines) and assumed vessel (red lines). D: Magnified view of minimum lumen diameter within the stent. SFA: superficial femoral artery.

### TABLE I. Patient Characteristics

| | |
|---|---|
| Number of patients | 55 |
| Age (years) | 71 ± 7 (57–86) |
| Male (n) | 33 |
| Hypertension | 43 (79%) |
| Dyslipidemia | 28 (51%) |
| Diabetes mellitus | 36 (65%) |
| Smoking | 40 (73%) |

### TABLE II. Limb and Lesion Characteristics

| | |
|---|---|
| Right/left | 38/36 |
| Ankle-brachial index | 0.81 ± 0.17 (0.35–1.13) |
| Total stent length (cm) | 17 ± 7 (6–30) |
| Number of stents implanted | 1.9 ± 0.8 (1–3) |
| Stent diameter (mm) | 7.0 ± 0.3 (6–8) |
| Percent diameter stenosis (%) | 53 ± 18 (14–84) |
| Peak systolic velocity (cm/sec) | 246 ± 130 (27–610) |
| Peak systolic velocity ratio | 4.1 ± 2.8 (1.1–12.7) |

(6). Mean %DS was 53 ± 18% (range: 14–84). In DUS parameters, mean PSV was 246 ± 130 cm/sec (range: 27–610) and PSVR was 4.11 ± 2.75 (range: 1.1–12.7). In addition, %DS of ≥50% was observed in 57% (42).

There was a statistically significant ($P < 0.001$) linear correlation between "%DS and PSV" and "%DS and PSVR," and the correlation with %DS proved to be stronger in PSVR ($R = 0.720$) than in PSV ($R = 0.672$). Polynomial correlations can be found in the Supporting Information (Supplementary Appendix). ROC curves, illustrating the accuracy of detecting in-stent stenosis of 50% or greater, are shown in Fig. 2. The two curves are virtually identical. The area under

the ROC curve (AUC) using PSVR was 0.908 (95%CI 0.841–0.975, $P < 0.001$), while AUC using PSV was 0.832 (95%CI 0.737–0.926, $P < 0.001$). A PSVR cutoff value of 2.85 provided the best predictive value with a sensitivity of 88%, a specificity of 84% and an accuracy of 86%. The positive predictive value (PPV) was 85% and the negative predictive value (NPV) was 88%.

## DISCUSSION

To the best of our knowledge, this study is the first to scrutinize the performance of DUS parameters for the detection of ISR on a QVA basis in the stented

SFA. Our main findings were that (1) in-stent %DS was better correlated with PSVR than PSV; (2) ROC curves analysis showed that PSVR was more accurate in detecting ISR than PSV; and (3) a PSVR of 2.85 provided the best predictive value of ISR with sensitivity of 88%, specificity of 84%, PPV of 85%, NPV of 88%, and accuracy of 86%.

Over two decades ago, Jager et al. [10] proposed a system for classifying the degree of arterial stenosis in the lower limbs based on the Doppler waveform shape, the degree of spectral broadening, and the increase in PSV within the stenosis. However, spectral broadening was too subjective and the waveform shape was affected by a variety of factors, including cardiac out-

put and rhythm, resistance of the vascular bed, integrity of the intima, and both proximal and distal disease [11–13]. On the other hand, PSVR was found to be more closely correlated with the degree of stenosis than PSV [14]. Thus, increasing attention has been paid to PSVR as an alternative index to angiographic narrowing from a clinical standpoint. Enthusiastic vascular specialists have addressed the relationship between DUS and angiography, suggesting that, on angiography, 50% diameter reduction by "visual estimation" is equivalent to a PSVR of 2.0–3.0 in the lower limb artery, including the femoral artery, while there is some possibility of having different cut off points of PSVR in iliac, common femoral, superficial femoral, popliteal, and crural arteries (Table III) [14–18]; however, there has been no reliable evidence and validation regarding the performance of DUS for "ISR." Nevertheless, recent SFA studies have arbitrarily employed a "PSVR of 2.0–2.5" for binary ISR after nitinol SFA stenting. Thus, the determination of an optimal cut off value for PSVR is required in the era of nitinol stenting for SFA disease.

Previous studies of lower limb arteries have shown that PSVR is a more accurate predictive parameter of 50% stenosis than PSV. The present study exploited QVA to assess the stented SFA lesion more objectively as QVA has been emerging even in the field of peripheral vascular intervention [21], and could corroborate similar results in the stented SFA.

According to a recently published study [19], in which the majority involved were de novo lesions (de novo lesion in 97%, restenosis in 3%), a PSVR of 2.4 indicated 50% stenosis with sensitivity of 81%, specificity of 93%, PPV of 84%, and NPV of 91%. Most recently, Baril et al. [20] reported for the first time the performance of PSV and PSVR for only the stented segment of the SFA, demonstrating that PSVR is more
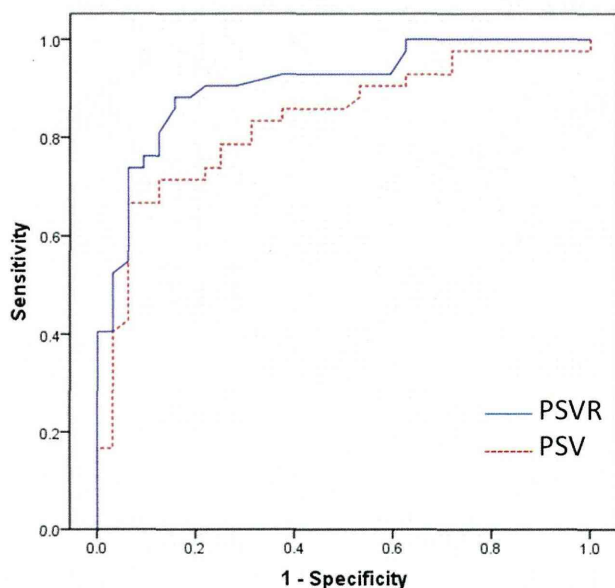


Fig. 2. Receiver operator characteristic curves for in-stent restenosis. PSV: peak systolic velocity. PSVR: peak systolic velocity ratio.

TABLE III. Comparison of the Performance of PSVR for 50% Stenosis in Native and Stented Femoral Artery

| Author (year) | Artery analyzed | Native/ stented | Denovo/ restenosis | Application of QVA | PSVR criteria for 50% stenosis | Sens. (%) | Spec. (%) | PPV (%) | NPV (%) | Accura. (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| Polak et al. (1990) | Femoropopliteal | Native | Denovo | No | 2 | 88 | 95 | NR | NR | 93 |
| Legemate et al. (1991) | Femoropopliteal | Native | Denovo | No | 2.5 | 65 | 97 | 69 | 96 | 94 |
| Ranke et al. (1992) | Iliac to femoral | Native | Denovo | No | 2.4 | 87 | 94 | 94 | 88 | NR |
| Leng et al. (1993) | Femoropopliteal | Native | Denovo | No | 3 | 70 | 96 | 95 | 74 | NR |
| Aly et al. (1998) | Femoral | Native | Denovo | No | 2 | 100 | 99 | 95 | 100 | NR |
| Aly et al. (1998) | Femoropopliteal | Native | Denovo | No | 2 | 95 | 99 | 94 | 99 | NR |
| Schlager et al. (2007) | Femoropopliteal | Native (97%) and stented (3%) | Denovo and restenosis | No | 2.4 | 81 | 93 | 84 | 91 | NR |
| Baril et al. (2009) | Femoropopliteal | Stented | Restenosis | No | 1.5 | 93 | 89 | 96 | 81 | NR |
| Present study | Superficial femoral | Stented | Restenosis | Yes | 2.85 | 88 | 84 | 85 | 88 | 86 |

Sens: sensitivity, Spec: specificity, PPV: positive predictive value, NPV: negative predictive value, Accura: accuracy, and NR: not reported.

accurate than PSV, and a PSVR of 1.5 yielded sensitivity of 93%, specificity of 89%, PPV of 96%, and NPV of 81% to predict ISR. Also in the present study, PSVR yielded a better correlation with %DS than PSV. These findings suggest that PSVR can provide better
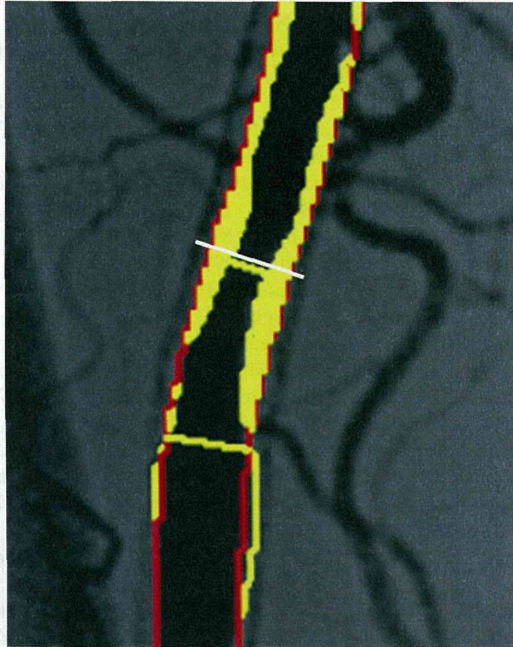


Fig. 3. Representative sample of difference in %DS between two analysis methods. Quantitative vessel analysis showed that %DS was 48%; however, when stent diameter was the reference diameter (white line), %DS was 65%. %DS: percent diameter stenosis.

performance to correlate with angiographic narrowing than PSV in stented as well as native SFA lesion assessment. More importantly, ROC analysis in this study reported a PSVR of 2.85 as the best cut off criteria with sensitivity of 88%, specificity of 84%, PPV of 85%, and NPV of 88% (Table III). The application of QVA for %DS in the present study clearly resulted in a higher PSVR (2.85) than that (1.5) in a previous study utilizing stent diameter as the reference diameter [20]. Indeed, in the present study, the degree of stenosis could be objectively calculated based on an assumed vessel automatically drawn in the QVA system. However, if stent diameter could be the reference diameter following the formula [(stent diameter − narrowest in-stent lumen)/stent diameter × 100] used in the previous study [20], %DS could be higher, as shown in Fig. 3 and, consequently, the optimal PSVR for ISR be lower.

Furthermore, the optimal cut off value of PSVR 2.85 in the present study also appears to be higher than in previous nonstented studies. Various reasons can be speculated for this difference in optimal PSVR between stented and nonstented SFA. Implantation of a stent in the SFA clearly alters arterial biomechanical properties and the resultant stent–arterial complex could decrease SFA compliance, therefore causing elevated PSV, even in stenting with a normal lumen. In addition, because plaque is not removed with stenting, residual plaque outside the stent may contribute to decreased compliance and elevated blood flow velocity (Fig. 4). Given these findings, the traditional PSVR criteria of 2.0–2.5
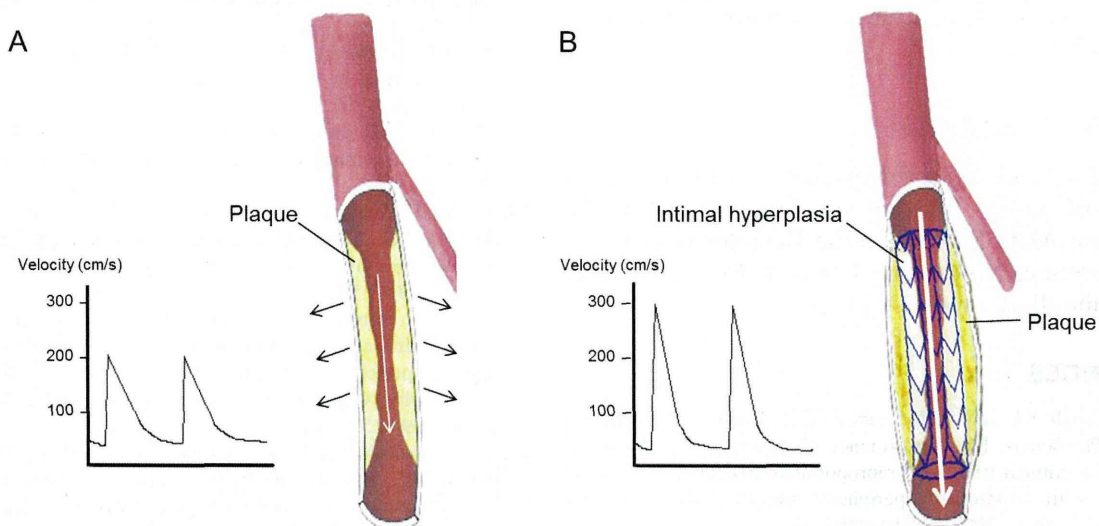


Fig. 4. Illustration showing the effect of differences in vessel compliance on flow velocity between unstented and stented SFA. A: Unstented SFA, B: stented SFA. Stented SFA has less compliance than an unstented SFA. Peak systolic velocity and the peak systolic velocity ratio increased more in a stented SFA than in an unstented SFA despite the same degree of stenosis. SFA: superficial femoral artery.

could overestimate the binary ISR rate compared to angiographic evaluation from a QVA basis. As an essential requirement for standardized assessment after contemporary SFA intervention, we emphasize the need to define optimal criteria for ISR in the era of nitinol stenting for SFA disease.

## LIMITATIONS

Several limitations need to be considered. First, the design was retrospective in nature. Second, the currently available QVA system dedicated to coronary intervention does not allow the measurement of diameters of reference vessel, lumen and lesion length in the SFA intervention, as mentioned above. Third, although the present study involved only the Smart stent, a variety of nitinol stents with distinct stent properties and platforms might potentially yield a heterogenous cutoff for PSVR. Fourth, in-stent subtotal reocclusion does not necessarily represent high-velocity flow within the stent. Fifth, a stented calcified vessel does not permit clear visualization by DUS; thus, accessibility may differ for adequate Doppler sampling. Finally, little is known about PSVR variability among operators, machines, and institutions.

## CONCLUSIONS

The present study indicated that a PSVR of 2.85 could be highly predictive of ISR from a QVA basis after nitinol stenting. With agreement of the clinical utility of DUS in the surveillance of nitinol SFA stenting, further large prospective studies are required for the validation and establishment of uniform criteria for DUS parameters.

## ACKNOWLEDGEMENTS

## REFERENCES

1. Rocha-Singh KJ, Jaff MR, Crabtree TR, Bloch DA, Ansel G; VIVA Physicians, Inc. Performance goals and endpoint assessments for clinical trials of femoropopliteal bare nitinol stents in patients with symptomatic peripheral arterial disease. Catheter Cardiovasc Interv 2007;69:910–919.
2. Serruys P, De Jaegere P, Bertrand M, Kober G, Marquis JF, Piessens J, Uebis R, Valeix B, Wiegand V. Morphologic change in coronary artery stenosis with the Medtronic Wiktor stent: Ini-

tial results from the core laboratory for quantitative angiography. Cathet Cardiovasc Diagn 1991;24:237–245.
3. Haase J, Escaned J, van Swijndregt EM, Ozaki Y, Gronenschild E, Slager CJ, Serruys PW. Experimental validation of geometric and densitometric coronary measurements on the new generation Cardiovascular Angiography Analysis System (CAAS II). Cathet Cardiovasc Diagn 1993;30:104–114.
4. Di Mario C, Di Francesco L, Moussa I, Blengino S, Martini G, Reiber JH, Colombo A. New approach to quantitative angiographic assessment after stent implantation. Cathet Cardiovasc Diagn 1997;40:343–347.
5. Serruys PW, Kay IP, Disco C, Deshpande NV, de Feyter PJ. Periprocedural quantitative coronary angiography after Palmaz-Schatz stent implantation predicts the restenosis rate at six months: Results of a meta-analysis of the BElgian NEtherlands Stent study (BENESTENT) I, BENESTENT II Pilot, BENESTENT II and MUSIC trials. Multicenter ultrasound stent in coronaries. J Am Coll Cardiol 1999;34:1067–1074.
6. Popma JJ, Leon MB, Moses JW, Holmes DR Jr, Cox N, Fitzpatrick M, Douglas J, Lambert C, Mooney M, Yakubov S, Kuntz RE; SIRIUS Investigators. Quantitative assessment of angiographic restenosis after sirolimus-eluting stent implantation in native coronary arteries. Circulation 2004;110:3773–3780.
7. Diehm N, Baumgartner I, Jaff M, Do DD, Minar E, Schmidli J, Diehm C, Biamino G, Vermassen F, Scheinert D, van Sambeek MR, Schillinger M. A call for uniform reporting standards in studies assessing endovascular treatment for chronic ischaemia of lower limb arteries. Eur Heart J 2007;28:798–805.
8. Berguer R, Hwang NH. Critical arterial stenosis: A theoretical and experimental solution. Ann Surg 1974;180:39–50.
9. Roubin GS, King SB III, Douglas JS Jr. Restenosis after percutaneous transluminal coronary angioplasty: The Emory University Hospital experience. Am J Cardiol 1987;60:39B–43B.
10. Jager KA, Phillips DJ, Martin RL, Hanson C, Roederer GO, Langlois YE, Ricketts HJ, Strandness DE Jr. Noninvasive mapping of lower limb arterial lesions. Ultrasound Med Biol 1985;11:515–521.
11. Legemate DA, Teeuwen C, Hoeneveld H, Ackerstaff RG, Eikelboom BC. The potential of duplex scanning to replace aorto-iliac and femoro-popliteal angiography. Eur J Vasc Surg 1989; 3:49–54.
12. Leng GC, Fowkes FG, Allan PL, Ruckley CV. Doppler colour flow imaging in peripheral arterial disease. Br J Hosp Med 1991;45:200–207.
13. Zierler RE. Duplex and color-flow imaging of the lower extremity arterial circulation. Semin Ultrasound CT MR 1990;11: 168–179.
14. Leng GC, Whyman MR, Donnan PT, Ruckley CV, Gillespie I, Fowkes FG, Allan PL. Accuracy and reproducibility of duplex ultrasonography in grading femoropopliteal stenoses. J Vasc Surg 1993;17:510–517.
15. Polak JF, Karmel MI, Mannick JA, O'Leary DH, Donaldson MC, Whittemore AD. Determination of the extent of lower-extremity peripheral arterial disease with color-assisted duplex sonography: Comparison with angiography. AJR Am J Roentgenol 1990;155:1085–1089.
16. Legemate DA, Teeuwen C, Hoeneveld H, Ackerstaff RG, Eikelboom BC. Spectral analysis criteria in duplex scanning of aortoiliac and femoropopliteal arterial disease. Ultrasound Med Biol 1991;17:769–776.
17. Ranke C, Creutzig A, Alexander K. Duplex scanning of the peripheral arteries: Correlation of the peak velocity ratio with angiographic diameter reduction. Ultrasound Med Biol 1992;18:433–440.

18. Aly S, Sommerville K, Adiseshiah M, Raphael M, Coleridge Smith PD, Bishop CC. Comparison of duplex imaging and arteriography in the evaluation of lower limb arteries. Br J Surg 1998;85:1099–1102.

19. Schlager O, Francesconi M, Haumer M, Dick P, Sabeti S, Amighi J, Mlekusch W, Koppensteiner R, Minar E, Schillinger M. Duplex sonography versus angiography for assessment of femoropopliteal arterial disease in a "real-world" setting. J Endovasc Ther 2007;14:452–459.

20. Baril DT, Rhee RY, Kim J, Makaroun MS, Chaer RA, Marone LK. Duplex criteria for determination of in-stent stenosis after angioplasty and stenting of the superficial femoral artery. J Vasc Surg 2009;49:133–139.

21. Kawarada O, Yokoi Y, Takemoto K, Morioka N, Nakata S, Shiotani S. The performance of renal duplex ultrasonography for the detection of hemodynamically significant renal artery stenosis. Catheter Cardiovasc Interv 2006;68:311–318.

# CLINICAL RESEARCH

# Impact of changing PSVR thresholds on the patency rates of SFA recanalisation with self-expanding nitinol stents

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## Abstract

**Aims:** The primary patency of superficial femoral artery (SFA) stents is evaluated by measuring PSVR. However, each trial uses a different definition of PSVR. We investigated the impact of changing PSVR thresholds on the patency rates of SFA recanalisation with self-expanding nitinol stents.

**Methods and results:** A single-centre retrospective study was conducted. Between 2003 and 2006, 76 consecutive patients (83 limbs) were treated using nitinol self-expanding stents for SFA disease. Primary patency was defined as categories 1 (PSVR <2.0), 2 (PSVR <2.4) and 3 (PSVR <2.85). The mean follow-up time was 51±27 months. For one, five, and seven years, Kaplan-Meier estimates for primary patency rates were 62.6%, 36.8%, and 27.6%, respectively, in category 1; 75.2%, 46.5%, and 37.1%, respectively, in 2; and 75.2%, 46.1%, and 46.1%, respectively, in 3. The primary patency between categories 1 and 3 (p=0.038) was significantly different. No difference was observed between categories 2 and 3 (p=0.786), and a trend for differences was observed between categories 1 and 2 (p=0.069).

**Conclusions:** PSVR definition may influence the reported long-term patency rate of a SFA stent. We should consider the definition of restenosis in each trial.

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## Introduction

Trials to evaluate the use of newer nitinol self-expanding stents in superficial femoral artery (SFA) disease are underway. In all trials, primary patency was examined using duplex ultrasound (DUS). However, the definition of primary patency was different in each trial. For example, in the Zilver PTX clinical trial, the definition of primary patency was a duplex peak systolic velocity ratio (PSVR) of <2[1] and, in the DURABILITY I trial, the definition was a PSVR of <2.5[2]. At present, many trials are being conducted, and DUS is employed for follow-up analyses. However, a different definition of primary patency is used in each trial. We aimed in this study to evaluate the impact of changing PSVR thresholds on the patency rates of SFA recanalisation with self-expanding nitinol stents.

## Patient population and methods

### STUDY POPULATION

A single-centre retrospective study was conducted. Between 2003 and 2006, 76 consecutive patients (83 limbs) were treated using nitinol self-expanding stents (SMART; Cordis Corporation, Miami Lakes, FL, USA) for symptomatic SFA disease (Rutherford categories 2-5) that affected their quality of life in spite of exercise and optimised medications[3]. The patients gave consent to a follow-up DUS examination at Kishiwada Tokushukai Hospital. We excluded patients who underwent stenting for restenosis and those who presented with acute limb ischaemia. The study protocol was designed in accordance with the Declaration of Helsinki, and it was approved by the ethics committee of our hospital. Written informed consent was obtained from every patient.

### PROCEDURE AND MEDICATION

Endovascular therapy (EVT) was performed percutaneously, mostly using a crossover technique with a 6 Fr sheath. Prior to the intervention, 5,000 units of unfractionated heparin were administered to maintain the activated clotting time at more than 250 seconds. A 0.014 inch or 0.035 inch guidewire was advanced and the lesion crossed. An optimally sized balloon was employed and dilated. The stent size was selected to be 1-2 mm larger than the diameter of the reference vessel. Aspirin (100 mg/day) and clopidogrel (75 mg) or ticlopidine (200 mg/day) were administered two days prior to the procedure and were continued for at least one month.

### FOLLOW-UP AND OUTCOMES

Patients received DUS within 30 days of the intervention and at six-month intervals thereafter. Lesion patency was evaluated by DUS examination.

High-resolution duplex scanning was performed on an ultrasound machine (Aplio; Toshiba Corporation, Tokyo, Japan) with a 7.5 MHz linear transducer by six investigators with at least two years of experience in peripheral vascular duplex scanning. PSVR was calculated by dividing velocity measured at the point of maximum stenosis by velocity in the closest adjacent normal vessel segment. The angle of incidence of the Doppler beam to the flow was maintained at less than 60 degrees.

Primary patency was defined by three categories. Category 1 was defined as PSVR of <2.00, category 2 was defined as PSVR of <2.40 and category 3 was defined as PSVR of <2.85[1,4,5]. The complete absence of a detected signal was graded as a complete occlusion. Primary patency was defined as no restenosis or repeat revascularisation in the treated vessel.

### STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS (SPSS Inc., Chicago, IL, USA). Data are reported as mean±SD. Time-dependent outcomes were analysed using the Kaplan-Meier method and compared using the log-rank test. A p-value <0.05 was considered statistically significant.

## Results

### BASELINE CLINICAL AND LESION CHARACTERISTICS

Between 2003 and 2006, 76 consecutive patients (83 limbs) were enrolled in this study. Patient characteristics are shown in **Table 1**. The mean age of the patients was 72±8 years; 69% of patients were male; 52% of patients had diabetes mellitus, and 17% of patients were on dialysis. Lesion characteristics are presented in **Table 2**. A total of 26.5% of lesions belonged to Rutherford categories 4 and 5. The average lesion length was 126±71 mm, and Trans-Atlantic Inter-Society Consensus (TASC) II A, B, C, and D were 22.9%, 31.3%, 22.9% and 22.9%, respectively.

**Table 1. Patient characteristics (n=76).**

| | |
|---|---|
| Male (%) | 69 |
| Age (yrs) | 72±8 |
| Hypertension (%) | 88 |
| Diabetes mellitus (%) | 52 |
| Hyperlipidaemia (%) | 69 |
| Smoking (%) | 69 |
| Dialysis (%) | 17 |
| Coronary artery disease (%) | 68 |
| Renal artery stenosis (%) | 9 |

**Table 2. Lesion characteristics (n=83).**

| Rutherford category | | |
|---|---|---|
| 1 | | 0 (0.0%) |
| 2 | | 3 (3.61%) |
| 3 | | 58 (70.0%) |
| 4 | | 8 (9.64%) |
| 5 | | 14 (16.9%) |
| 6 | | 0 (0.0%) |
| Lesion length | | 126±71 mm |
| TASC II | A | 19 (22.9%) |
| | B | 26 (31.3%) |
| | C | 19 (22.9%) |
| | D | 19 (22.9%) |