Atherosclerosis 233 (2014) 76–82

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

Wall shear stress in the stented superficial femoral artery in peripheral arterial disease

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ARTICLE INFO

Article history:
Received 9 July 2013
Received in revised form
14 November 2013
Accepted 13 December 2013
Available online 4 January 2014

Keywords:
Wall shear stress
Superficial femoral artery
Peripheral arterial disease
Stent
Endovascular treatment
Blood viscosity

ABSTRACT

Objective: Local changes in wall shear stress (WSS) contribute to vascular wall thickening and subsequent stenosis. Restenosis after stenting is a major concern, especially in the superficial femoral artery (SFA) of patients with peripheral arterial disease (PAD). Local alterations in WSS after stenting might contribute to restenosis/reocclusion. To test the hypothesis that WSS is impaired along the stented SFA segment, we studied the profile of WSS along the femoro-popliteal axis after stent placement in a cross-sectional design.
Methods: Eighty-seven patients with PAD (89 limbs) were included one day after stenting of the SFA. Flow velocities (peak and mean) and vessel diameter were measured by duplex ultrasound in five predefined segments along the femoro-popliteal axis, at rest and after exercise (30 toe raises); WSS (peak and mean) was calculated from flow velocities, vessel diameter and whole blood viscosity.
Results: WSS progressively declined along the stented segment at rest (peak WSS, $p < 0.0001$; mean WSS, $p < 0.05$); after exercise, WSS increased in all segments (all $p < 0.001$), but, again, progressively declined along the stent (peak WSS, $p < 0.0001$; mean WSS, $p < 0.05$). The internal vessel diameter remained unchanged after exercise in the stented and in the non-stented parts of the femoro-popliteal axis (all $p > 0.05$).
Conclusion: In PAD patients with SFA stenting WSS is impaired along the femoro-popliteal axis. The consequences of this finding in terms of local effects on the vessel wall that might favor restenosis/reocclusion needs further investigation.

1. Introduction

Wall shear stress (WSS) is the frictional force that flowing blood exerts on the vascular endothelium [1]. Endothelial cells sense variations of WSS and subsequently adapt vascular lumen dimensions via biomechanical transduction mechanisms [2]. Segmental disturbances of WSS potentially provoke endothelial dysfunction and subsequent vessel wall thickening [2–6]. In particular, non-laminar, disturbed flow associated with low WSS increases the regional expression of vascular adhesion molecules and enhances transmigration of inflammatory cells into the arterial vessel wall, which promotes the atherosclerotic process [4,7]. Previously, we have demonstrated that WSS in the common carotid artery is decreased both in patients with symptomatic peripheral arterial disease (PAD) and in patients with abdominal aortic aneurysm [8]. As common clinical manifestation of atherosclerosis PAD preferably affects the Hunter's canal of the superficial femoral artery (SFA). In healthy adults, we found that WSS does not vary along the SFA at rest [9]; during exercise, however, the increase of WSS was observed to be less pronounced within the Hunter's canal, which might contribute to the susceptibility of this particular arterial segment to the emergence of atherosclerotic lesions.

For revascularization of obstructive SFA disease endovascular stenting has become a common practice in recent years. Although much effort has been made to improve stent-design and -material, patients still face unsatisfactorily high restenosis rates following SFA stenting, though [10,11]. Stent insertion unavoidably causes vascular injury, which consequently promotes neointimal hyperplasia [12]. Apart from promoting neointimal hyperplasia and vascular remodeling, stent implantation might alter the profile of

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http://dx.doi.org/10.1016/j.atherosclerosis.2013.12.035

WSS along the respective vessels, especially along the stented segment. Previous data on vascular hemodynamics in the coronary circulation suggest an impact of stenting on local shear forces, which has further been linked to intimal thickening [13,14]. Whether and to what extent long-segment stenting—as it is increasingly performed in the peripheral circulation—might affect WSS in the lower limbs has not been investigated before.

Thus, the primary aim of the present study was to assess WSS (peak and mean) along the SFA one day after stenting to test the hypothesis that stent placement affects the profile of WSS along the femoro-popliteal axis. Further, we were interested to study the WSS after stent placement in relation to clinical and laboratory characteristics.

2. Patients and methods

2.1. Inclusion criteria

From May 2006 until October 2007 consecutive PAD patients undergoing long-segment stenting of the SFA were eligible for the study. The inclusion criterion was successful stenting of the SFA, defined as the absence of >30% residual stenosis demonstrated by duplex-sonography of the femoro-popliteal segment the day after the interventional procedure. Any hemodynamically relevant obstruction of the ipsilateral iliac arteries had to be revascularized within the same endovascular procedure or in a separate procedure before SFA stenting. Regarding the infrapopliteal arteries at least a one-vessel run-off was mandatory.

Exclusion criteria were a residual stenosis >30% of the target lesion as well as a flow limiting dissection or the presence of an untreated >50% stenosis of the ipsilateral femoro-popliteal axis, further, unability to perform 30 toe raises due to concomitant cardiac or pulmonary disease, uncontrolled blood pressure, heart rate >100 bpm or restrictions of the musculoskeletal system.

The study was performed according to the recommendations of the Declaration of Helsinki and the protocol was approved by the institutional ethics committee. Written informed consent was obtained in all patients before inclusion.

2.2. Clinical surveillance

Before the revascularization procedure all patients routinely underwent a complete clinical examination and routine laboratory tests. Patients were classified according to Rutherford categories for PAD. Demographic data including patients' age, sex, body mass index (BMI), smoking habits and each patient's medication were systematically recorded. Systolic and diastolic blood pressures were measured in a supine position on both arms using the average of both measurements for further analyses. In all patients ankle-brachial-index (ABI) measurements were obtained before and one day after the revascularization. Before revascularization duplex scans of the iliac, femoro-popliteal and the proximal infrapopliteal arteries were performed to identify the target lesion as well as any in- or outflow obstruction. In cases of inconclusive duplex results, magnetic resonance angiography or computed tomography angiography was additionally performed.

Prior to the revascularization, medical therapy was optimized in all patients according to current recommendations [15,16]. At least one antiplatelet medication, usually aspirin (100 mg daily), was started at the institutional outpatient clinic before admission to the hospital for the endovascular procedure. In patients who were not on clopidogrel (75 mg daily) at least two days prior to stent implantation, a loading dose of 300 mg was given ahead of the intervention. Following stenting a dual antiplatelet therapy was installed for three months followed by an indefinite single antiplatelet medication. One day after stenting all patients underwent duplex scans of the puncture site and the entire femoro-popliteal axis of the treated limb.

2.3. Stenting procedure

Access to the target vessel was achieved percutaneously by an antegrade 4F sheath or via a retrograde approach using a 6F "crossover" sheath. After insertion of the sheath an intravenous bolus of 3000–5000 units of heparin was administered. The femoro-popliteal axis and its run-off vessels were examined by digital subtraction angiography. After precise documentation of the target lesion within the femoro-popliteal axis dilation was performed by gradual balloon inflation. If no satisfying result could be achieved by plain balloon angioplasty of the SFA, one or more serially connected, self-expanding, bare-metal nitinol stents were implanted. In case of an ipsilateral iliac artery stenosis an iliac angioplasty was performed prior to or immediately after stenting of the SFA. The final result was documented by digital subtraction angiography, and the patency status of infrapopliteal run-off vessels was documented in all patients. All endovascular procedures were performed by the same two experienced interventionists (M.E.G., A.W.E., acknowledgment section).

2.4. Duplex ultrasound

Duplex ultrasound was performed prior to revascularization and one day after the procedure in a quiet room with a constant room temperature (22–24°) after an acclimatization period of 15 min in a supine position. All duplex scans were performed by the same trained operator (O.S.) using Acuson machines [Acuson XP 128 or Acuson Sequoia 512 (both Siemens, Erlangen, Germany)] and a 7.5 MHz linear transducer probe. A stenosis was graded using the peak systolic velocity ratio (PVR), which was defined as the ratio of the peak systolic velocity (PSV) in the stenosis divided by the PSV in the preceding normal segment. A PVR ≥2.4 was defined as a stenosis >50 percent [17].

Routinely, the iliac arteries, the femoro-popliteal axis and the proximal infrapopliteal arteries were scanned to exclude any residual stenosis of the target vessel or a hemodynamically relevant stenosis of the in- and outflow vessels.

For calculation of pWSS and mWSS PSV, the mean velocity and the internal diameter were recorded in 5 different segments of the femoro-popliteal axis: in the native proximal SFA (distance from the femoral bifurcation ± SD; 8.1 ± 6.2 cm), at the proximal stent edge (13.1 ± 7.8 cm), in the middle of the stent (17.0 ± 7.0 cm), at the distal stent edge (21.0 ± 6.8 cm) and in the P1 segment of the popliteal artery (37.1 ± 2.3 cm). In each segment the PSV and the mean velocity were determined using the smallest possible sample volume placed in the center of the vessel and by keeping the angle between the ultrasound beam and the longitudinal vessel axis between 45 and 59°. The internal diameter, defined as the distance between the near wall intima-lumen-interface to the far wall lumen-intima-interface, was measured from frozen, longitudinally enlarged images of the respective vessel segment showing the lumen-intima-interface most clearly. Aiming at synchronized determination of vessel diameter and PSV, frozen enlarged images were acquired from the "live mode" during spectral Doppler. Then the "cine mode" allows the determination of the vessel diameter in a PSV-triggered fashion. In each arterial segment the vessel diameter was measured twice in two orthogonal planes, and the mean of these two measurements was calculated.

To determine the intra-observer (O.S.) variability of duplex ultrasound examinations of the lower limbs we performed 10 repetitive measurements of the SFA on 3 consecutive days. The