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The influence of the anastomosis angle on the hemodynamics in the distal anastomosis in the infrainguinal bypass: an in-vitro study

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Short title: The influence of hemodynamics on bypass

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Abstract

Background

The geometric shape of the distal anastomosis in an infrainguinal bypass has an influence on its durability. In this article, we compared three different angles of the anastomosis with regard to the hemodynamics.

Methods

Three experimental models of the distal infrainguinal anastomosis with angles of 25°, 45°, and 60° respectively were constructed according to the similarity theory to assess flow in the anastomoses using particle image velocimetry and computational fluid dynamics.

Results

In the toe, heel, and floor of the anastomosis that correspond to the locations worst affected by intimal hyperplasia, adverse blood flow and wall shear stress were observed in the 45° and 60° models. In the 25° model, laminar blood flow was apparent more peripherally from the anastomosis.

Conclusion

Decreasing the distal anastomosis angle in a femoropopliteal bypass results in more favorable hemodynamics including the flow pattern and WSS in locations susceptible to intimal hyperplasia.

Key words: anastomosis, intimal hyperplasia, hemodynamics, angle

Introduction

Intimal hyperplasia (IH) is an excessive response to the intimal injury or altered hemodynamics. It occurs in the distal femoro-popliteal anastomosis between 2 and 24 months postoperatively due to abnormal blood flow with altered wall shear stress (WSS) (Bassiouny *et al.* 1992, Tiwari *et al.* 2003). On a microscopic level, IH is characterized by a migration of smooth muscle cells from the media and their proliferation and matrix synthesis in the intima, a process which ultimately results in stenosis (O'Brien *et al.* 2007).

WSS is a friction force between the vessel wall and the blood flow. Therefore it is parallel to the flow direction and its relation with the blood velocity, viscosity and diameter of the vessel can be expressed as:

$$WSS = \frac{blood\ velocity\ \times blood\ viscosity}{vessel\ diameter}$$

(Bassiouny *et al.* 1992, Haruguchi and Teraoka 2003, Keynton *et al.* 2001).

The influence of WSS on the endothelium plays a pivotal role in the early development of IH and early stenosis of the reconstruction. Previously, attempts have been made to optimize flow and WSS particularly by modifying the geometry of the anastomosis or the compliance of the bypass (Neville *et al.* 2011, Tiwari *et al.* 2003). In this study we hypothesized that a more acute anastomosis angle would result in more favorable flow and distribution of the WSS in the distal end-to-side anastomosis (Leon and Greisler 2003).

Material and Methods

In this experimental *in-vitro* study, we researched and constructed a model of a distal infrainguinal anastomosis (Fig. 1) based on preliminary experiments and driven by theories of interaction between the blood flow and vessel wall reported in the literature (Grus *et al.* 2007, 2009, Haruguchi and Teraoka 2003, Keynton *et al.* 2001).

The anastomosis model had the following parameters. The diameter of the target vessel and the bypass was 6 mm, which is the most common diameter of grafts used in infrainguinal reconstructions. The anastomosis angles were 60°, 45° and 25°. These values are encountered in infrainguinal bypass reconstructions and they also were used previously (Fei *et al.* 1994, Grus *et al.* 2009, Hoedt *et al.* 2015). The length of the evaluated segment was chosen according to the common location of IH that develops predominantly in the anterior wall of the target vessel 15 to 20mm distally from the toe of the anastomosis and less frequently, on the posterior wall about 12 – 13 mm from the heel of the anastomosis (Fig. 1). The flow rates of 80 ml/min, 200 ml/min, and 500 ml/min that correspond with resting, walking and running were modeled by corresponding Reynolds numbers (500, 1000, and 1400) with respect to the similarity theory that implies that the flow in the model and *in-vivo* are similar if the values of the Reynolds number are similar (Hoedt *et al.* 2015, Loth *et al.* 2008). The inflow into the bypass was modulated to simulate natural pulsatile flow as recorded by a Pulsed Wave (PW) Doppler ultrasound during routine examination in healthy human subjects. As a working fluid, water with polyamide particles 20 μm in diameter was chosen (Grus *et al.* 2007). The casing of the model was created from plexiglass by lost wax casting. To simplify the model, we decided to simulate the most common condition, where the target artery is occluded and the only inflow comes from the graft. To visualize the flow and WSS two methods were used. In particle image velocimetry (PIV) the working fluid with polyamide particles is illuminated by a red laser diode (λ=660nm). The beam is focused by a lens to create a plane. The light reflected from the particles is recorded by a high speed camera and their motion, which represents the flow, is subsequently visualized (Grus *et al.* 2007). The distribution of WSS was calculated from PIV using advanced computational fluid dynamics (CFD) software (ANSYS Fluent, ANSYS Inc., Canonsburg, PA).

Results

Visualization of the flow and flow velocity field in the 45° anastomosis is shown in Fig. 2. Comparison of images from the flow visualization by PIV revealed that turbulent flow at the toe of the anastomosis was markedly reduced in the 25° anastomosis compared to 45° and 60° (Fig. 3). At the stagnation point at the toe of the anastomosis,(which is a common location of IH) the vortical flow in the 25° model disappeared completely (Fig 3).

Visualisation of the data from PIV using CFD (Fig. 4) demonstrated that the transition from a turbulent flow to a laminar flow occurred more distally in the 45° compared to the 25° anastomosis. In the 25° anastomosis the flow passed the critical section in a laminar fashion and some whirling occurred more distally. Unlike in the 45°anastomosis, the distribution of WSS in the 25° anastomosis showed nearly physiological (10 - 70 dyne/cm^2) values (Fig. 4) (Ene-Iordache and Remuzzi 2012).

Discussion

In this work we attempted to optimize geometry of the distal infrainguinal anastomosis by modifying its angle and we evaluated the flow visualized by PIV and WSS maps obtained by CFD. The visualization of the flow in the anastomosis clearly indicated that construction of an anastomosis with an acute angle resulted in a more favorable flow in the anastomosis that is known to reduce formation of IH – remodeling of the vessel wall otherwise responsible for early failure of the reconstruction. In clinical practice, the most common locations of such changes occurs in the areas with disturbed blood flow: predominantly in the toe, less frequently in the heel, and the floor of the anastomosis (Grus *et al.* 2009).

The results of this experimental study are in accordance with previous studies that showed the relationship between IH and geometry of the anastomosis. A more acute anastomosis angle results in better hemodynamics in the anastomosis and a lower risk of IH and early graft failure (Grus *et al.* 2009). Decreasing the anastomosis angle results in the disappearance of the stagnation point at the toe of the anastomosis (Fig. 3), preservation of the laminar flow and of the physiological WSS values (10 - 70 dyne/cm^2, Fig. 4) (Ene-Iordache and Remuzzi 2012, Kamiya and Togawa 1980). Increased WSS causes direct mechanical injury to the endothelial cells including the glycocalyx while too low of a WSS results in stimulation of the endothelial cells, proliferation of the smooth muscle cells, their migration into the intima and synthesis of extracellular matrix (Jackson *et al.* 2009). The link between low WSS and IH has already been established in venous grafts (Allaire and Clowes 1997) and some studies even suggest a protective effect of normal WSS (Malek *et al.* 1999, Passerini *et al.* 2003, Wu *et al.* 2004).

The influence of the blood flow on the formation of IH is very complex and also changes in the stimulation pattern of the mechanoreceptors located on the wall and mechanical coupling of the glycocalyx with the cytoskeleton induce the production of various growth factors, cytokines, modulate the synthesis and release of vasoactive substances (NO, prostacyclin I2) and intercellular adhesion molecules (Davies 2009, Johnson *et al.* 2011, Zeng and Tarbell 2014). Macrophages that infiltrate the media can be demonstrated as early as 6 hours from the construction of the bypass (Davies 2009). Smooth muscle cells from the vessel wall that proliferate also alter their metabolic activity and begin to synthesize extracellular matrix that causes narrowing of the vessel.

The use of a supplementary cuff between the graft and the target artery is controversial, but as CFD simulations showed, it can also be optimized in terms of the length-to-height ratio of the boot (Xiong and Chong 2008). In-vivo, a supplementary cuff produces less favorable flow than a vein patch which approximates the straight anastomotic pattern (Neville *et al.* 2011). The ratio between the diameter of the target vessel and the bypass has an influence on the hemodynamics as well. The best parameters are achieved when the graft has the same or a greater diameter than the target artery (Qiao and Liu 2006). Furthermore, all these flow optimizations may be improved by connecting the graft and the target artery in a more acute angle of incidence. However, construction of an anastomosis at a more acute angle also has its implications: it requires longer arteriotomy and suture and such structure is therefore more technically difficult to embed. Finally, it is the skill and experience of the surgeon what decides the surgical technique and the ultimate outcome of the patient (Tan *et al.* 2012).

In conclusion, decreasing the distal anastomosis angle in a femoropopliteal bypass results in more favorable hemodynamics including the flow pattern and WSS in locations susceptible to IH.

This *in-vitro* study has several limitations. Firstly, although the inflow of the target artery becomes occluded in the majority of patients due to competitive flow from the bypass, minimal residual flow may reduce the negative influence of the hemodynamics at the floor of the anastomosis in a minority of them (Kute and Vorp 2001). Secondly, we used a rigid model and therefore issues related to compliance mismatch could not be studied (Tiwari *et al.* 2003). Thirdly, an *in-vivo* anastomosis is always more complex in shape and this is even more pronounced in special adjustments such as cuffs of patches (Ducasse *et al.* 2004). Lastly, unlike in our *in-vitro* model, the *in-vivo* target artery physiologically responds to flow changes induced by the conduit (Davies 2009).

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Figure legends

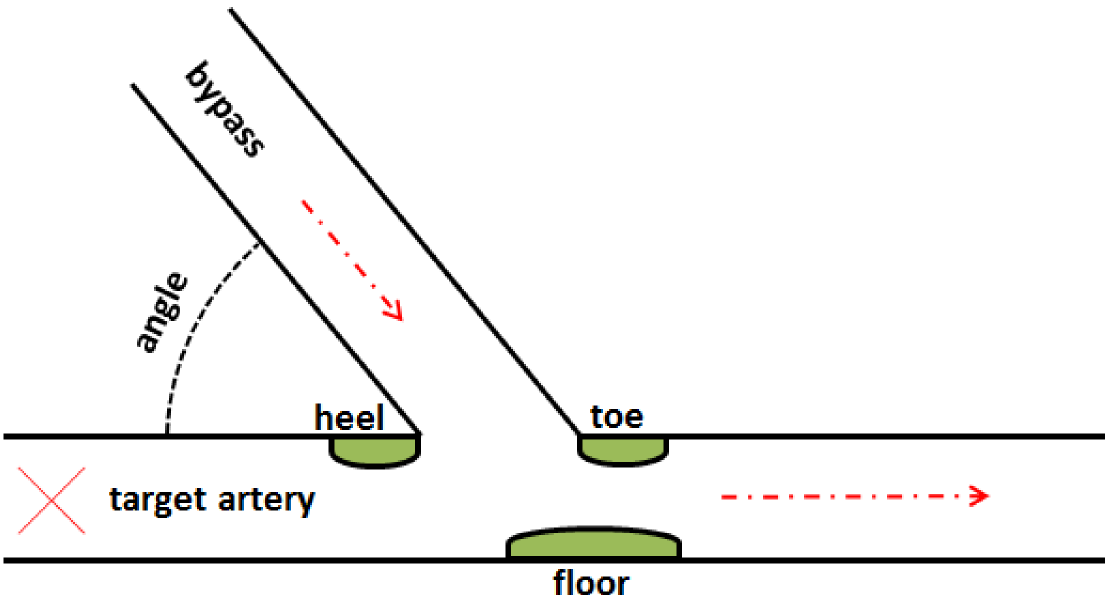

Fig. 1. Schematic drawing of the anastomosis with common locations of intimal hyperplasia at the toe, heel and floor of the anastomosis (green). To simplify the model, we decided to simulate the most common condition, where the target artery is occluded (X) and the only inflow comes from the bypass.

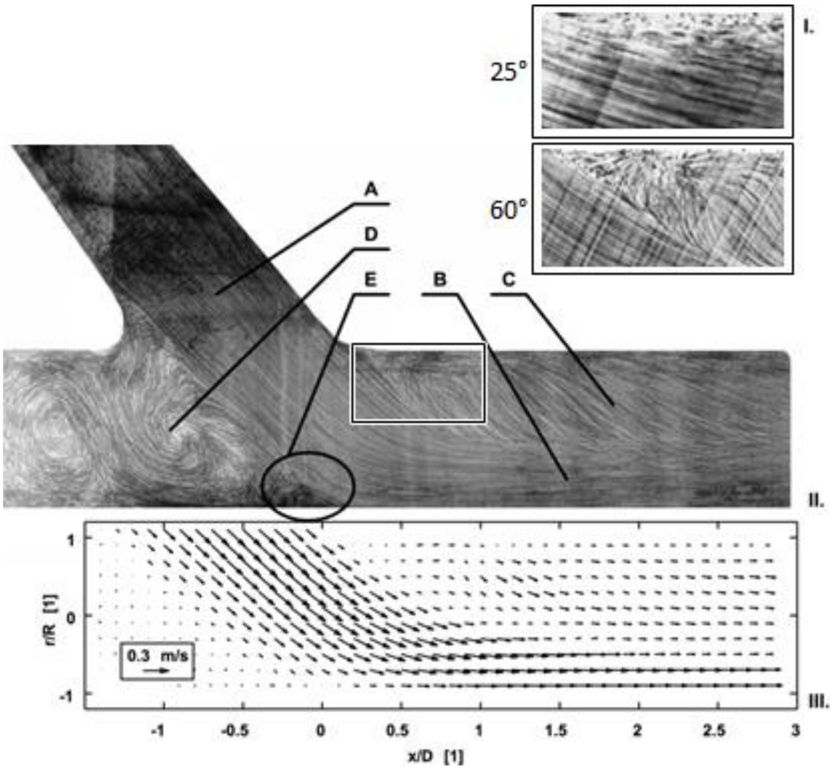

Fig. 2: Visualization of flow in the anastomosis with the bypass connected at 45° degrees angle using particle image velocimetry (middle). A: inflow to the anastomosis from the bypass; B: outflow from the anastomosis – laminar flow; C: outflow from the anastomosis – turbulent flow; D: vortex at the heel of the anastomosis; E: area with a high velocity gradient. The image below shows the flow velocity vector field. Comparison of magnified visualization of the flow in the toe of the anastomosis for 25° and 60° anastomosis shown in the right upper corner demonstrates that with the 25°design the stagnation point disappears altogether and the flow becomes laminar.

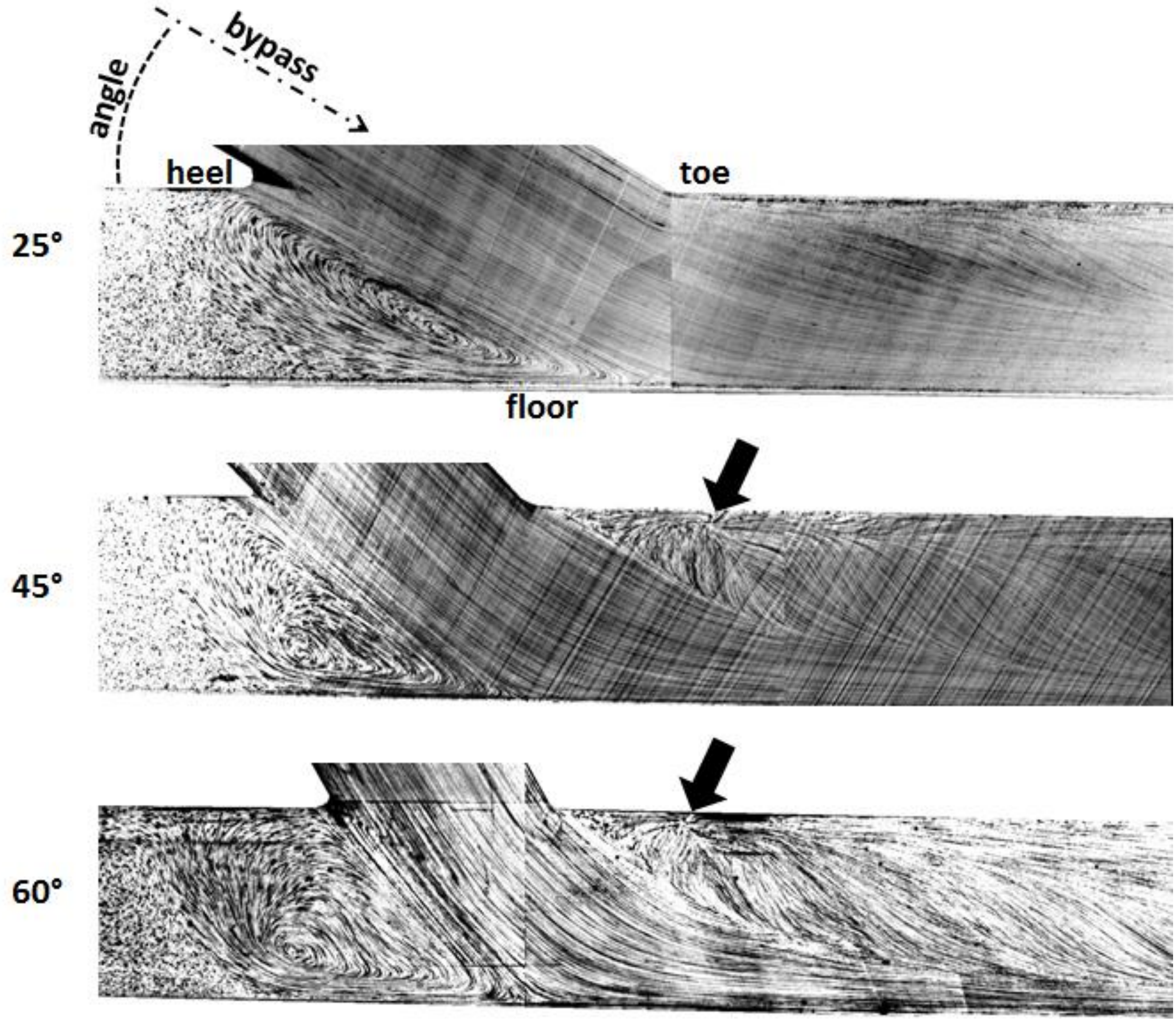

Figure 3: Comparison of flow (Re=1000) in the anastomosis with 25°, 45°, and 60° angle shows that the vortex (arrow) at the toe of the anastomosis that is present in the 60° and 45° design disappears in the 25°anastomosis, which has a more favorable flow pattern at the heel and the floor of the anastomosis as well.

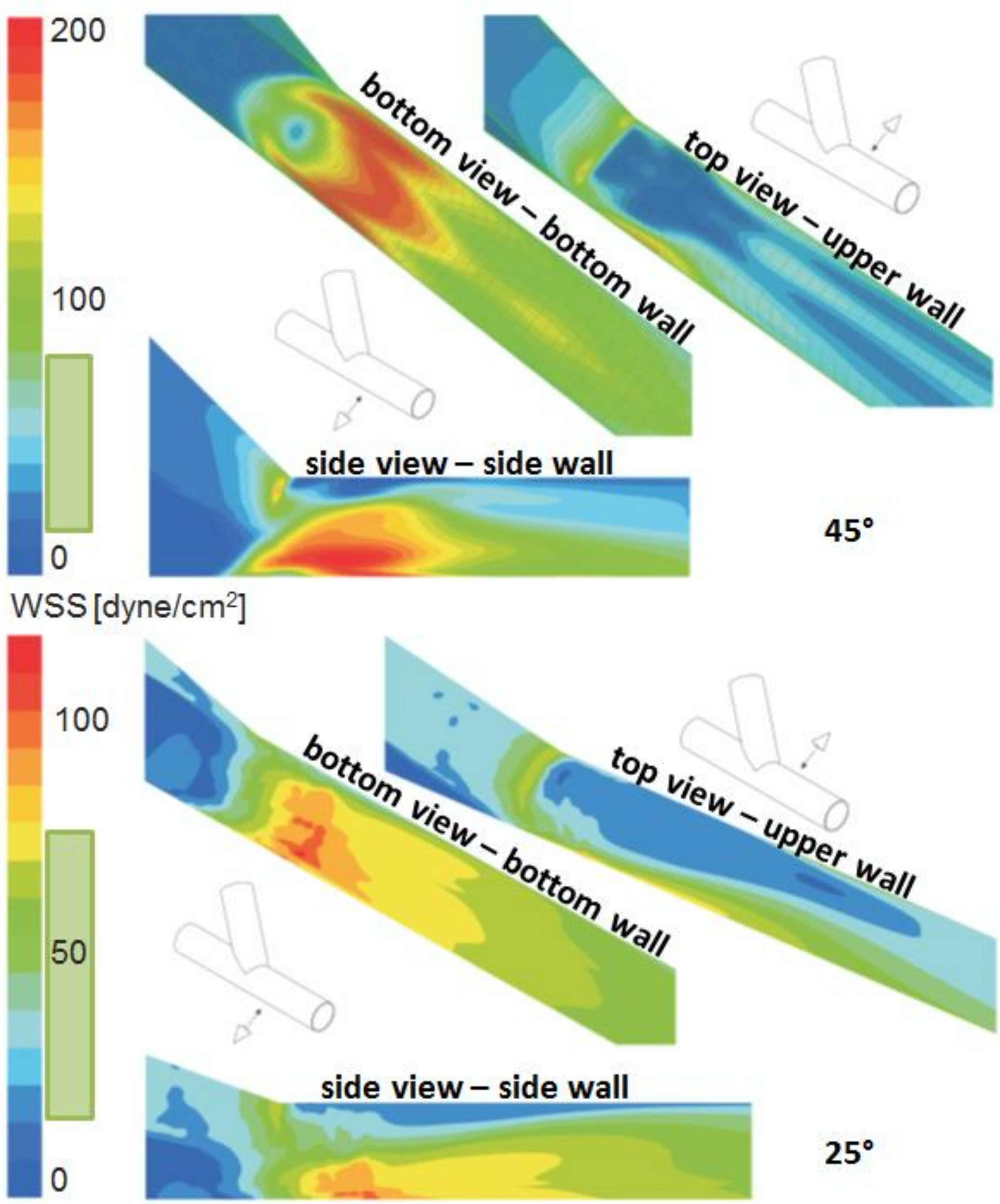

Figure 4: Distribution of WSS in the 45° (above) and 25° (below) anastomosis shows locations with too low values (dark blue) that stimulate intimal hyperplasia and with too high values (red) that cause direct mechanical injury to the endothelial cells including its epitopes. Green vertical bars delineate physiological WSS values. Note that the tow scales have a different range.