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TECHNICAL NOTE

Personalized Antiplatelet Therapy Following Endovascular Revascularization in Peripheral Artery Occlusive Disease: A Novel Concept

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Case: A 73 year old patient with a longstanding history of peripheral artery occlusive disease (PAOD) presented with an acute on chronic progression of symptoms, based on a long occlusion of the superficial femoral artery (SFA), which was treated by thrombosuction, percutaneous transluminal angioplasty, and SFA stenting. Post-procedural dual antiplatelet therapy was initiated and subsequently adjusted based on platelet reactivity testing.
Discussion: Increasingly complex arterial lesions are treated by an endovascular approach; however, long-term patency rates are often disappointing. In order to optimize the patency rates (dual) antiplatelet therapy is initiated. It is known that a substantial proportion of patients have high platelet reactivity despite the use of antiplatelet drugs. Several methods have been published to test the individual response to different antiplatelet drugs. There is evidence that adjusting antiplatelet therapy based on platelet reactivity testing results in a reduction of cardiovascular events and bleeding complications; however, the optimal test and the exact role of personalized antiplatelet therapy in PAOD is currently unknown.
Conclusion: Although some important hurdles should be overcome before routine implementation, the concept of post-procedural antiplatelet therapy in patients with PAOD is advocated in order to optimize the results of endovascular interventions, as apparent from the presented case.

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CASE

A 73 year old male with acute progression of chronic peripheral artery occlusive disease (PAOD) Rutherford stage 5, visited the outpatient clinic of a tertiary vascular referral center. The patient had a medical history of kidney transplantation, stage 3 chronic kidney disease (CKD), deep venous thrombosis complicated by a pulmonary embolism, and intermittent claudication for which he had undergone stenting of both common iliac arteries 10 years earlier and had been prescribed aspirin. A digital subtraction angiography (DSA) was performed, which revealed a 23 cm long occlusion of the superficial femoral (SFA) and proximal anterior tibial artery (Fig. 1A). Thrombosuction (AngioJet, Boston Scientific, Marlborough, MA, USA) and subsequent percutaneous transluminal angioplasty (PTA) of the SFA were performed (Fig. 1B). Because of multilevel residual stenoses, three self expandable stents and a balloon expandable stent were placed in the SFA over a total length of 27 cm with satisfactory results (no residual stenosis >30%). After the procedure, dual antiplatelet therapy (DAPT) was initiated: clopidogrel (loading dose 300 mg) was added to the aspirin. The next day a VerifyNow $P2Y_{12}$ assay (Accumetrics, San Diego, CA, USA) and a CYP2C19 polymorphism DNA test (Spartan RX CYP2C19, Spartan Bioscience Inc., Ottawa, Canada) were performed, which showed 0% platelet inhibition and two loss of function CYP2C19 alleles, respectively, which suggested that clopidogrel was not effective. Therefore, clopidogrel was switched to the stronger $P2Y_{12}$ inhibitor, prasugrel. A VerifyNow showed an effective platelet inhibition on prasugrel (41% inhibition, PRU 171). At the 6 month follow up the patient did not report any pain, and duplex ultrasound confirmed patency of the stents without restenosis.

Endovascular revascularization

Nowadays, minimally invasive endovascular techniques are often the first line of therapy in PAOD. The choice of the specific endovascular technique depends on various factors,

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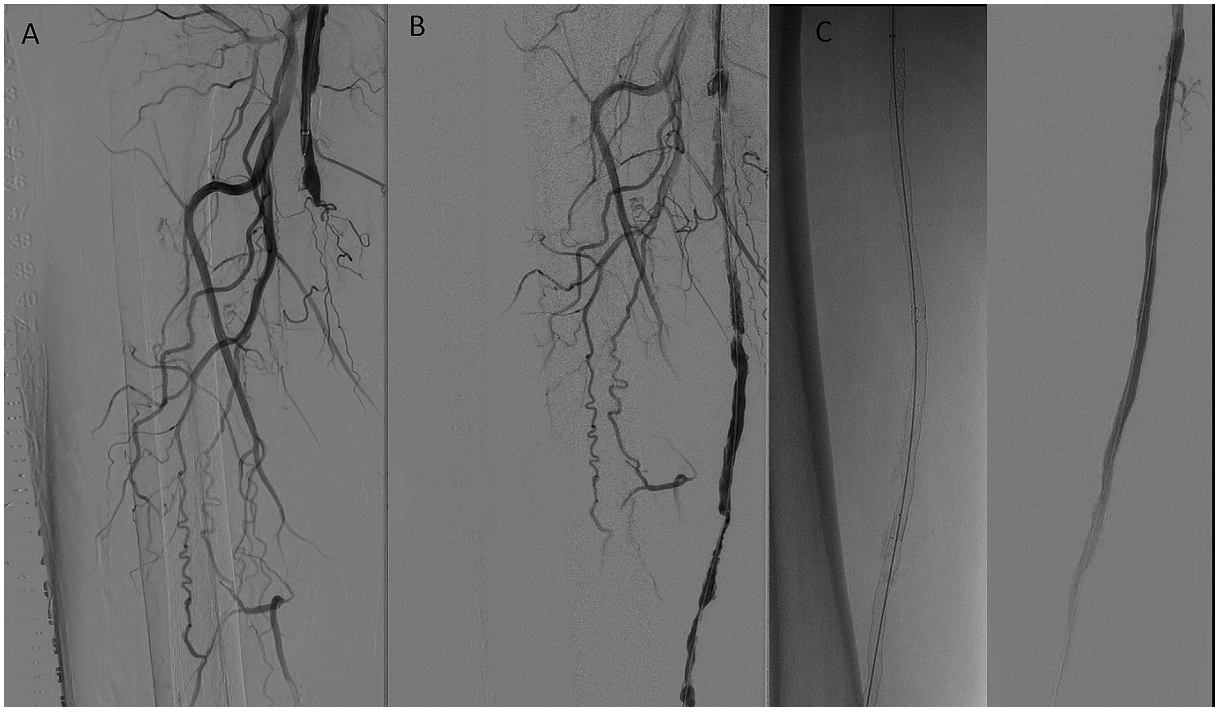

Figure 1. (A) Digital subtraction angiography (DSA), which shows a 23 cm occlusion in the superficial femoral artery. (B) DSA after two thrombosuctions with the Angiojet catheter. (C) DSA after percutaneous transluminal angioplasty and stenting.

such as the cause, length and degree of stenosis or occlusion, and the duration of the occlusion. Mechanical thrombectomy or thrombosuction is most effective in removing fresh thrombi, causes minimal peripheral embolization, and is less time consuming than medicinal thrombolysis.[1] PTA is usually the preferred choice in limited disease such as stenosis or occlusions up to 10 cm in length and stenting is advised when there is a residual stenosis of $\geq$30—50% or a flow limiting dissection.[2,3]

One year primary patency rates of balloon angioplasty in long femoral occlusions vary from 27% to 43.5%,[4] which is improved by the use of drug eluting balloons (primary patency up to 76.1%).[5] Primary patency at 1 year for stenting of long femoral occlusions varies from 64.8% to 66% and secondary patency rates vary between 70% and 83%, which depends on the characteristics of the atherosclerotic lesion and type of stent.[5—8] Because of the acute on chronic presentation in the current case, due to a total and likely recent occlusion of the SFA, mechanical thrombectomy followed by PTA and stenting due to residual multilevel stenosis was chosen.

Post-procedural antiplatelet therapy

The fast and continuous evolution of endovascular technologies allows for successful revascularization of increasingly complex atherosclerotic lesions. Lifelong antiplatelet therapy (APT) is generally recommended to promote patency after peripheral endovascular interventions of the femoropopliteal segment, although no evidence based guidelines exist.[1] Nowadays, many different types of antiplatelet regimen are used (Table 1). Studies on APT in patients with PAOD have major limitations due to small study populations and potential risk of bias.[9] This lack of high quality evidence leads to a great (inter)national variety in the administered APT, duration of treatment, and platelet reactivity test used to assess the effect of APT.[10] In cardiology trials, a relative risk reduction of secondary cardiovascular events (cardiovascular death, myocardial infarction or any revascularization) of around 30% is seen when adding clopidogrel to aspirin after percutaneous coronary intervention (PCI).[11—13] It is not known exactly whether this is the case in PAOD; however, a similar risk reduction is assumed.

Prior to PTA and stenting of femoropopliteal arteries, a loading dose of clopidogrel is often added to aspirin, and DAPT is continued for 1—3 months after PTA. The rationale for this practice is largely based on extrapolation of data derived from percutaneous coronary interventions (PCIs), and is not supported by international guidelines.[1,14]

The patient in this case received a loading dose of 300 mg of clopidogrel after the procedure followed by a maintenance dose of 75 mg once daily for 6 months. Several recent cardiology trials suggest that a loading dose of 600 mg might be more effective in preventing major adverse cardiac events, without increasing the risk of bleeding.[15] However, for PAOD patients there is no evidence that suggests superiority of a higher loading dose.

Analogous with observations in patients undergoing PCI, a natural variation in response to APT can be expected among patients undergoing peripheral revascularization. A recently published review showed that high on aspirin platelet reactivity (HAPR) occurred in 22.2% of the patients in a pooled analysis of 102 studies containing a total of