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Research Article

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Clinical and regulatory review of Duplex-guided Percutaneous Transluminal Angioplasty in Iliac Arterial Occlusive Disease

M. Radwan A.G. Krasznai, T.A. Sigterman, R.J. Welten, R. Heijboer, C.J.J.M. Sikkink, L.H.J.M. van de Akker, L.H. Bouwman

What this paper adds

Chronic renal insufficiency (CRI) is a growing mondial problem with a prevalence as high as 16%. Exposure to nephrotoxic agents can lead to contrast-induced nephropathy (CIN) in 50% of CRI patients undergoing percutaneous transluminal angioplasty (PTA). PTA can be performed without nephrotoxic contrast, utilizing Dopplerultrasound (Duplex) guidance. In our study we evaluate the safety and efficacy of duplex-guided percutaneous transluminal angioplasty in 31 patients. Duplex-guided PTA has previously been described in femoral and popliteal lesions. As the iliac anatomy is somewhat more challenging, only one case report has been written with regards to stenotic iliac pathology. We consider this new method to be of general interest to any vascular surgeon and interventional radiologist.

Abstract

Background: Chronic renal insufficiency (CRI) is a growing global problem. PTA can be performed without nephrotoxic contrast, utilizing Doppler-ultrasound (Duplex) guidance.

Clinical and regulatory review are applied to review safety and efficacy of **HP PTA Balloon Catheter** which is intended for percutaneous transluminal angioplasty (PTA) in the peripheral vasculature, including iliac, femoral, popliteal, tibial, peroneal, subclavian and for the treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistulae.

Duplex-guided infra-inguinal interventions and access-related interventions have been reported. Duplex-guided iliac interventions have not been performed to any extent because of the anatomic location. In our study we evaluated the safety and efficacy of Duplex-guided percutaneous transluminal angioplasty (DuPTA) in iliac arteries.

Methods: From June 2012 until February 2013, 31 patients (35 iliac lesions), underwent DuPTA. Indications ranged from Rutherford 3 to 5. Preoperative evaluation included Ankle Brachial Index (ABI), Duplex and MRA.

Procedural success was defined as crossing the lesion with a guidewire and dilating or stenting the lesion. Clinical success was defined as 50% reduction in peak systolic velocity (PSV) or clinical improvement. PSV was evaluated after PTA, then at 2 weeks. Clinical results were assessed 2 weeks after the procedure.

Additional literature and regulatory review has been applied to support clinical safety and performance of HP PTA Balloon Catheter manufactured by **Zhejiang Zylox Medical Device Co., Ltd**.

Results: Procedural success was achieved in 94% of patients (33/35), all of whom also had clinical success. Postprocedural PSV reduction showed an average improvement of 63% (431 cm/s to 153 cm/s). Mean preoperative ABI was 0.72 and improved to 0.88 postoperatively.

Conclusions: PTA using Duplex-guidance in significant iliac stenosis is a safe method with major advantages in patients at high risk for developing contrast-induced nephropathy. Full clinical review has been done according to New Medical Device Regulation MDR (2017/745/EC), MDD 93/42/EEC and BS EN ISO 14155:2020. Clinical data was sufficient to address clinical performance, safety and benefits of the device and compliance with relevant applicable regulatory requirements.

Keywords: CRI, PTA, DuPTA, Duplex and MRA, HP PTA Balloon Catheter

Introduction

Doppler-ultrasound (Duplex) is one of the major diagnostic tools in vascular surgery. Using Duplex, reliable measurements of stenosis can be provided. Some studies show good results treating patients endovascular with infra-inguinal stenotic lesions utilizing Duplex-guidance.1-8 Infra-inguinal stenotic lesions can easily be visualized because of the anatomical location. In 2010, Kawarada 9 reported two cases of Duplex-guidance percutaneous transluminal angioplasty (PTA) in the iliac arteries. As no nephrotoxic contrast is used, Duplex-guided PTA (DuPTA) is especially favourable in patients with chronic renal insufficiency at high risk for developing contrast-induced nephropathy (CIN).Chronic renal insufficiency (CRI) is a global health problem, involving 10-16% of the general adult population.

CRI patients have an increased risk for developing CIN after exposure to nephrotoxic agents. The incidence of CIN is highly dependent on the clinical characteristics of the patient population, with an incidence of 50% or more in high risk patients.11

Prevention of CIN can ultimately be accomplished by restricting the use of nephrotoxic contrast agents. The useof contrast is abolished in Duplex-guided PTA. Additional advantages are that patients and medical staff are not exposed to radiation.

This feasibility study evaluates the safety and efficacy of DuPTA in the iliac arteries.

Methods

From June 1, 2012 until February 1, 2013, 31 patients (25 men [71%]) were treated for 35 significant iliac lesions in a large teaching hospital in the south of the Netherlands, the Atrium Medical Centre Parkstad. Inclusion criteria were chronic renal insufficiency (eGFR <60 ml/min/1.73 m2) or allergy for contrast media. Exclusion criteria were difficulties in visualizing lesions with Duplex. All patients meeting the criteria with an indication for iliac PTA in the period of this study were screened for a possible DuPTA. Three-hundred conventional iliac PTAs are performed annually (2012) in our centre. The reported experience represents approximately 10% of all iliac PTAs performed. All patients meeting inclusion criteria were briefed extensively and given the choice of conventional PTA or DuPTA. Patients were seen in the outpatient clinic and presented with symptoms of peripheral artery disease (PAD) with Rutherford classification from 3 (*N* 27, 87%), 4 (*N* 3, 10%), and 5 (*N* 1, 3%). TASCII A (*N* 22), B (*N* 11), and C (*N* 2) lesions were treated.

Preoperatively all patients underwent Ankle Brachial Index (ABI), Duplex arterial mapping and magnetic resonance imaging (MRI) of the arterial vessels. A Duplex was performed to determine whether these lesions would be feasible for Duplex-guided endovascular treatment. All patients were evaluated in a multi-disciplinary setting (vascular surgeons, interventional radiologist, and vascular technicians).

Significant stenosis was defined as more than 70% diameter reduction or more on MRA and a PSV ratio reduction of 2 or more as shown by Duplex.

Technique

All procedures were performed in the operating room (OR) under spinal anaesthesia or short general anaesthesia (based on request of the patient or the use of anticoagulation therapy). Patients were examined by Duplex in the OR, prior to performing anaesthesia confirming preoperative Duplex findings. All procedures were performed using latest generation Colour Duplex sonography (Aloka Prosound Alfa7, Aloka Co., Ltd., Tokyo, Japan) with a linear 3.5 MHz probe for iliac PTA. Duplex examination was performed by experienced vascular technologist. The vascular surgeon and vascular technologist took place at opposite sides of the patient.

The linear probe was inserted in a sterile plastic cover with covering gel. The common femoral artery (CFA) was punctured by the surgeon in a retrograde fashion under ultrasound control (5 MHz linear probe). In all cases an uncalcified segment of the artery was punctured without complications. An 11 cm, 6 Fr Brite Tip introducer sheath (Cordis, Cordis Congregation, FL, USA) was inserted under Duplex control (guiding the sheath into the external iliac artery). Heparin 2500 U was administered intravenously to all patients. A Terumo Standard 180 cm, 0.035 guidewire (Terumo, Terumo Europe N.V., Leuven, Belgium) was introduced in all cases and followed by ultrasound passing through the artery and the stenosis. After localizing the stenosis, the length of the stenotic segment and diameter of the artery were measured using B-mode. PSV ratio was measured using colour mode (Fig. 1A and B). Balloon diameters (Admiral Extreme PTA balloon, Medtronic; Medtronic Luc., Minneapolis, MN, USA. Mustang PTA balloon, Boston Scientific, Boston Scientific international S.A., France), stent sizes and length (Scuba stent, Medtronic; Omnilink Elite stent, Abbott Vascular, Abbot Vascular international BVBA, Diegen, Belgium; Silver PTX drug eluting stent, Cook Medical, Cook Medical Inc., Bloomington, IN, USA) were chosen based on the Duplex measurement of the stenotic segment. All PTA balloons were inflated (Encore inflation device, Boston, MA, USA) and stents were deployed under Duplex visualization (Fig. 2). After deflating and withdrawing the balloon, leaving the guidewire in position, the PSV ratio was measured. Procedural success was achieved if in B mode no stenosis was visible and the PSV ratio was reduced below 50% of the original PSV. Duplex examination of the infrapopliteal arterial segment was performed in all cases searching for distal embolization. Following removal of the endovascular material, manual pressure was performed and a compression bandage was placed on the puncture site.

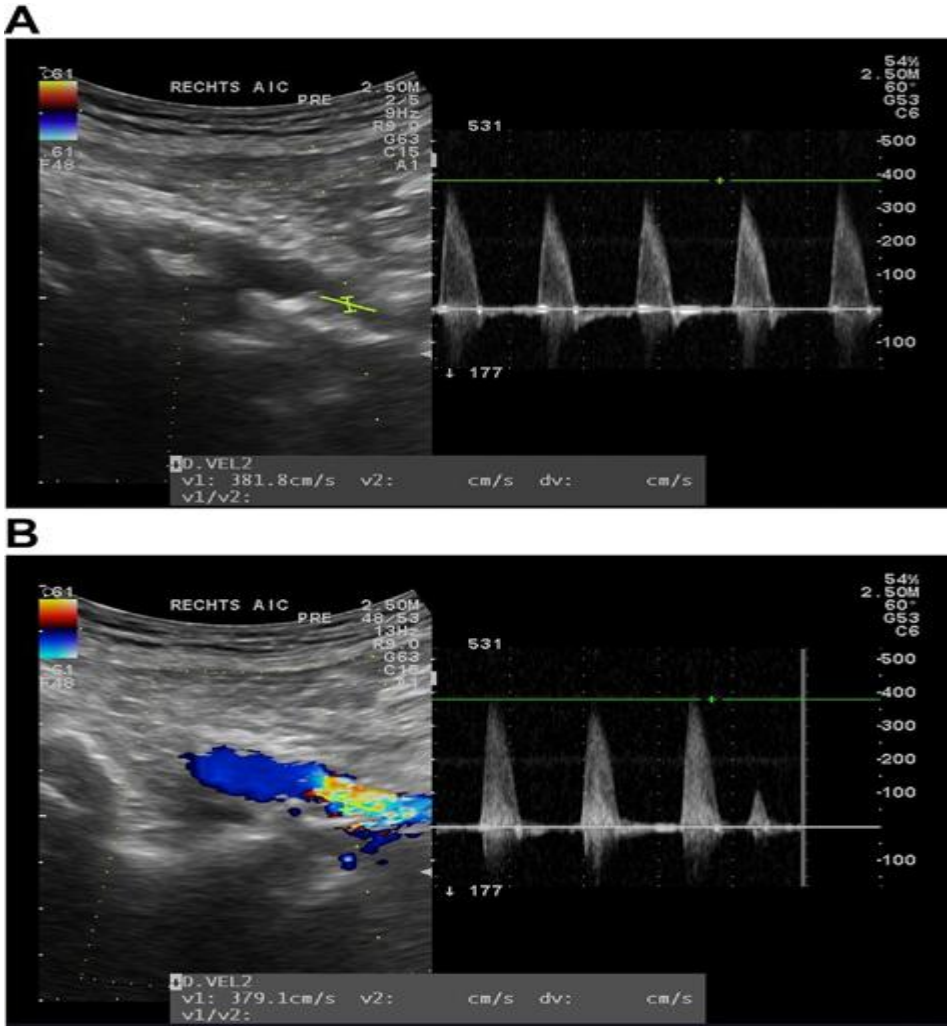

Figure 1. (A) Stenosis common iliac artery as depicted by ultrasound in B-mode; (B) stenosis common iliac artery as depicted by ultrasound in colour mode.

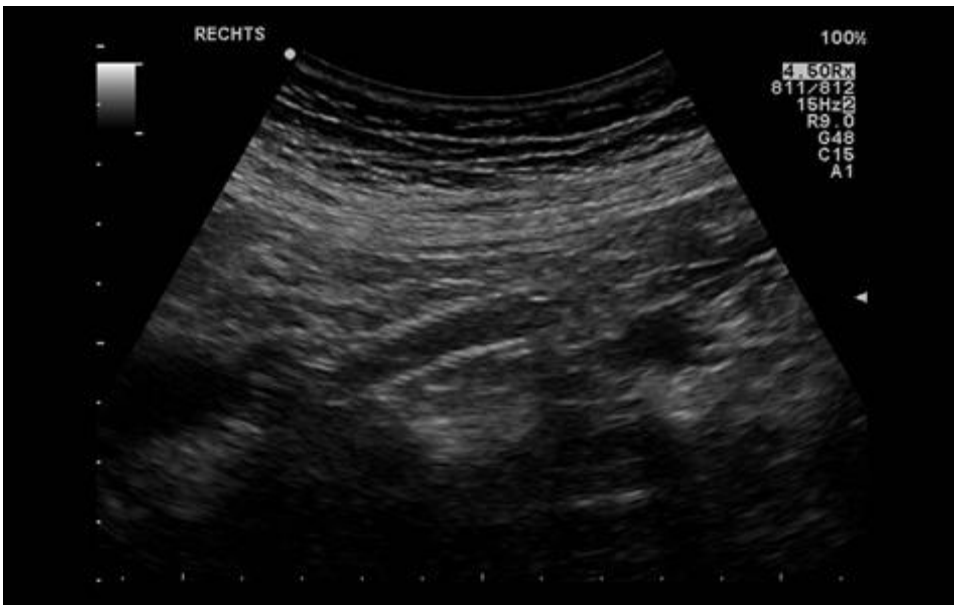

Figure 2. Stent in the common iliac artery as depicted by ultrasound in B-mode.

All procedural steps of DuPTA are shown in a compilation video (Video 1). Supplementary video related to this article can be found online at http://dx.doi.org/10.1016/j.ejvs.2013.08.011.

The following is the Supplementary video related to this article: Video 1Compilation of the entire DuPTA procedure.

Follow-up and evaluation

Patients were seen at the outpatient clinic 2 weeks after the procedure. Patients underwent control arterial duplex, PSV measurement, and ABIs. Procedural success was defined as crossing the lesion with a guidewire and dilating or stenting the lesion. Clinical success was defined as 50% reduction in PSV or subjectively without complaints 2 weeks post procedure.

This study was performed in accordance with local rules of the medical ethics committee.

Results

Average age of the patients ranged from 44 to 84 years (mean 60 years). Body mass index (BMI) of the patients ranged from 15.4 to 35.3 kg/m2 (mean 25.3). Stenotic lesions varied from 50% to 100% (mean 77.7%). Ten patients with known contrast allergy were treated, all other patients had impaired renal function (eGFR <60 ml/min/1.73 m2).

External iliac artery (EIA) was treated in 11 patients, all other lesions were located in the common iliac artery (CIA)stenosis (*N* 20). A total of 14 stents were placed (45%).

Concomitant risk factors included hypertension (55%), diabetes mellitus (19%), congestive heart failure (16%), smoking (72%), hypercholesterolemy (55%), and familiar vascular disease (48%). (Confounding factors are shown in Table 1.) All patients received statin and antiplatelet therapy.

Table 1. Patient characteristics and risk factors.

Characteristics	*N* (%) patients	
Male	25	(71)
Renal insufficiency	21	(68)
Contrast allergy	10	(32)
Age (years)	60 (44e84)[a]	
BMI	25.3	(15.4e35.3)[a]
Risk factors		
Diabetes mellitus	6	(19)
Smoking	23	(72)
Familiar vascular disease	15	(48)
Hypercholesterolemy	17	(55)
Heart failure	5	(16)
Hypertension	17	(55)

[a] Continuous variables are represented as mean with range.

A total of 33 (94%) lesions were successfully treated. Procedural success of TASCII-A-B lesions was 100%. In the TASCII-B group, one occlusion was successfully recanalized. Two TASCII-C lesions were treated. Both lesions could not be recanalized.

The first patient with a TASCII-C lesion was subsequently treated successfully with conventional angiography with contrast. The second patient was treated surgically because of a known severe allergy for contrast. Treatment consisted of a femoro-femoral crossover bypass with an 8 mm Braun (Braun Melsungen, Berlin Germany) silver-coated prosthesis. Postoperative follow-up was uneventful.

Mean PSV prior to treatment was 440 mm/s, mean PSV post procedure was 160 mm/s. An average reduction of 63% (Fig. 3). Mean PSV 2 weeks following DuPTA was 179 mm/s, showing a reduction of 60%. Mean preoperative ABI was 0.72 and improved to 0.88 postoperatively.

Procedure time included a minimum of 10 minutes of pressure. Mean procedure duration was 54 minutes, ranging from 26 to 124 minutes. A total of 15 (43%,15/35) stents were placed.

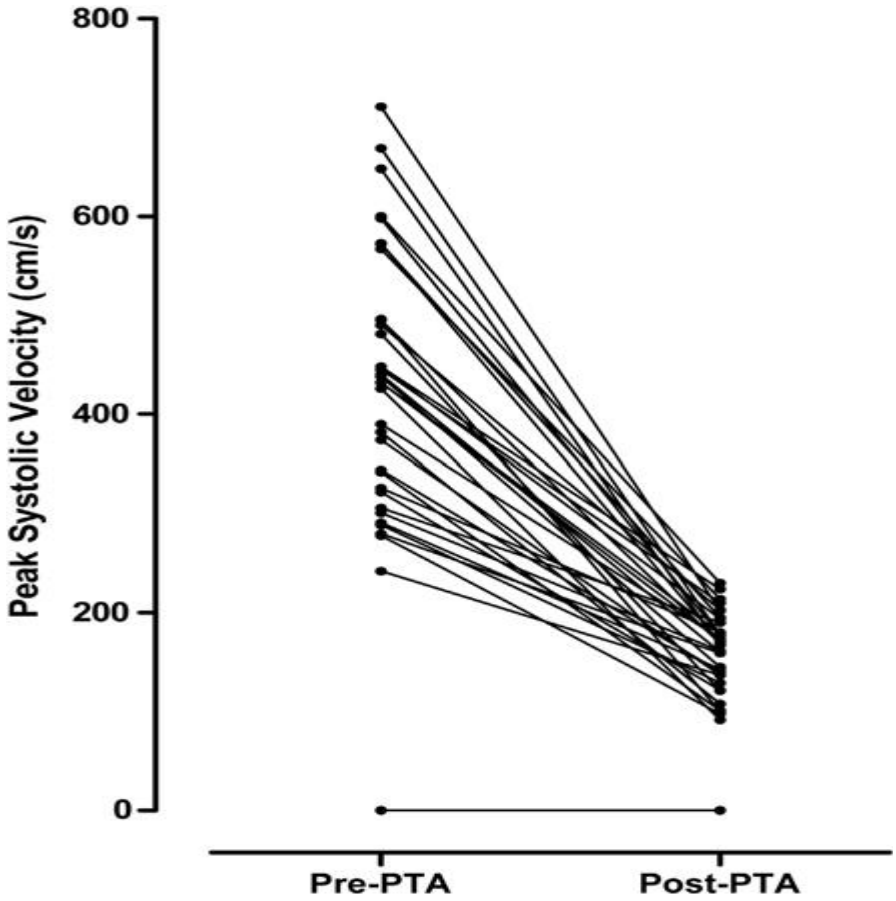

Figure 3. Peak systolic velocity (PSV) pre- and post-DuPTA.

Intraoperative and early complications

During one procedure (right CIA), a stent was dislocated from the mounted balloon during retraction. The lesion was successfully crossed with a 9 mm stent. However when positioning the stent, the balloon mounted stent had to be retracted, which was not inflated at that point. The stent dislodged from its balloon during retraction. This was most probably caused by the high-grade stenosis (90%). This unfortunate mishap is a well acknowledged complication, also seen in conventional PTA.The stent was positioned proximal from the lesion in the proximal common iliac artery, leaving no haemodynamic flow limitation.

Discussion

Advancing Doppler-ultrasound technology, with high resolution colour Duplex has provided a safe and reliable method for diagnosing peripheral artery disease. Currently all reports describing Duplex-guided angioplasty involve infrainguinal arterial stenosis and show good results.1-8 These studies show the feasibility of DuPTA in the femoro-popliteal segment. To the best of our knowledge there is one report of two patients that describes PTA of iliac arteries using duplex guidance. 9

As a consequence of the anatomical location, treatment of significant stenosis in iliac arteries using DuPTA is more challenging in comparison with infra-inguinal limb lesions. Other challenges include bowel gas and the patient's habitus. The goal of this feasibility study was to evaluate the safety and efficacy of DuPTA in the iliac arteries.

In DuPTA all procedural handlings are performed under direct ultrasound guidance, puncture of the CFA is performed avoiding atherosclerotic lesions. Conventional PTA techniques are used during this novel method.

A major technical advantage of ultrasound is that diameters and length of the stenotic lesion can be measured. One must appreciate that conventional digital substraction angiography (DSA) provides images of the intraluminal diameter of a stenotic lesion. True vessel diameter can be measured by ultrasonography, as opposed to DSA. Subsequently, more detailed attention can be given to sizing of balloons and stents. Duplex renders direct and real time reliable measurements of the stenotic lesions. After balloon dilation it is therefore possible to directly measure the improvement in PSVs, giving trustworthy information concerning elastic recoil. Duplex can also be used to provide reliable information of the haemodynamic significance of dissections. Angiography is not able to provide reliable measurements to determine whether a dissection is haemodynamically significant. Doppler ultrasound can predict an unsuccessful procedure in 14% of cases despite earlier satisfactory initial completion angiography.12 Completion angiography is only accurate in 76%, signalling the need for further dilatation to optimize the luminal diameter.8 Studies reveal that angiography fails to identify haemodynamically abnormal segments in nearly 30% of patients who had multilevel disease compared with Duplex.13 Our anticipated problem of the visualization of the iliac arteries in obese patients appeared unjust. Patients with a BMI as high as 35.3 were able to be treated. The use of spinal anaesthesia relaxes the abdominal muscles, leading to optimal visualization of the iliac arteries. Bowel gas is the most common cause of failing Duplex imaging in the iliac arteries.8 A possible solution may be dietary advice in order to reduce bowel gas formation. In our study, all patients were starved overnight, potentially contributing to the effect of optimal visualization and reaching 100% visibility in this study. Visualizations pre-operatively and on the day of the intervention were performed in order to assure 100% visibility.

In one patient we encountered dislodgement of the stent. Visibility in this patient was not an issue. The authors believe that the root of the problem was over advancement of the undeployed stent. Dislodgement occurred during retraction. This technical problem can be avoided by crossing the lesion with a sheet, then positioning the stent precisely where the lesion is.The sheath is retracted without moving the positioned stent and subsequently the stent is deployed.

In visualization of TASCII-C lesions it is possible to clearly visualize the subintimal positioned guidewire. We declined from performing difficult and strenuous subintimal crossing of TASCII-C lesions at this point. One TASCII-B occlusion was crossed with success.

The authors are convinced that in the future TASCII-C lesions can be tackled. However, currently we are still in the learning curve of this novel method.

In patients with an allergy for intravenous contrast agents, DuPTA is a feasible and safe alternative when requiring angioplasty. Mild allergic reactions are seen often, appearing in 5e8% of the patients receiving intravenous contrast. In 1% of patients moderate reactions occur, such as nausea and vomiting. Serious anaphylactic reactions present in 0.1%, with one fatal reaction in every 75,000 patients.14

This study was set up as a feasibility study. To maximize patient safety we decided to perform all procedures under the most controlled conditions, that is in the operation theatre under general or spinal anaesthesia. An additional advantage is that maximum muscle relaxation would improve visibility of the iliac vessels. However, all patients

met exclusion criteria, Duplex visibility. We conclude that this advantage of muscle relaxation is of slight benefit for visibility of the iliac arteries. Currently we are exploring the possibility of performing Duplex-guided PTA under local anaesthesia in a randomized control trial comparing conventional PTA with DuPTA.

Clinical and regulatory Review:

Assessment is applied to review all relevant favorable clinical literature to support performance, safety, benefits and efficacy of HP PTA Balloon Catheter:

#	Document source	Literature title	Data quality	Conclusion and data contribution
1.	European Journal of Vascular and Endovascular Surgery	Duplex-guided Percutaneous Transluminal Angioplasty in Iliac Arterial Occlusive Disease A.G. Krasznai et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
2.	Annals of surgical Treatment and research	Balloon-assisted maturation for arteriovenous fistula maturation failure: an early period experience Park, Sun Cheol et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
3.	Journal of geriatric cardiology: JGC	Prolonged high-pressure balloon angioplasty of femoropoplite al lesions: Impact on stent implantation rate and mid-term outcome Rigatelli, Gianluca et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
4.	Clinical Medicine Insights. Cardiology	Transpopliteal Balloon-Assisted Excimer– Laser Atherectomy for the Treatment of Chronic Femoropoplite al Occlusions: Feasibility and Initial Results Lüdtke, Christopher W et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
5.	American Journal of Roentgenol ogy	Endovascular diagnosis and management of chronic cerebrospinal Venous insufficiency: retrospective analysis of 30- day morbidity and mortality in 95 consecutive	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
6.	Journal of Vascular Surgery	The Use of Inflated Balloons to Improve Fenestration Alignment During the Deployment of Fenestrated Grafts Scherrer et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
7.	Cardiovasc ular and intervention al radiology	Combined Endoscopic-Radiological Rendezvous for Distal Tail Postoperative Pancreatic Fistula (POPF) Lucatelli, Pierleone et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects

#	Document source	Literature title	Data quality	Conclusion and data contribution
8.	J Innov Card Rhythm Manage	Balloon dilatation atrial septostomy permitting difficult transseptal catheterization Perzanowski,	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
9.	MEDtube Science	Early detected vascular complication following femoral artery puncture for endovascular SFA revascularisation. Case report Białek, awel Et al	Same use, Appropriate patient group High quality data collation	Appropriate study design, statistical analysis, Clinically significant treatment effects
Data provided sufficient clinical evidence of clinical safety, benefits and performance of HP PTA Balloon Catheter				

Conclusion

Duplex-guided balloon angioplasty and stenting is a safe and effective technique treating patients with significant iliac artery stenosis. Although we appreciate that DuPTA will not replace conventional PTA, this new method may be superior in selected patients. Currently a prospective study in our clinic has been started comparing DuPTA with conventional PTA.

Full clinical review has been done according to New Medical Device Regulation MDR (2017/745/EC), MDD 93/42/EEC and BS EN ISO 14155:2020. Clinical data was sufficient to address clinical performance, safety and benefits of the device and compliance with relevant applicable regulatory requirements.

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