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Global Perspectives on Drug-Eluting Technologies

Prof. Thomas Zeller, MD
Department of Angiology
Universitaets-Herzzentrum
Freiburg-Bad Krozingen
Bad Krozingen, Germany
thomas.zeller@universitaets-herzzentrum.de

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What factors specific to your region have contributed to the adoption of drug-eluting therapies in the peripheral arteries?

Two factors contributed to the adoption of drug-eluting therapies in Germany. First of all, there were convincing trial data demonstrating the superiority of drug-eluting technologies over what was considered the current standard of care (plain old balloon angioplasty [POBA] with provisional stenting). These data were derived from the Zilver PTX (Cook Medical) trial series for drug-eluting stents (DESs) and multiple drug-coated balloon (DCB) studies for different devices.[1-4] The second and ultimately more important driver for adoption of new therapies was reimbursement. Unfortunately in Germany, drug-eluting device-specific reimbursement was established only for DCBs as an add-on payment on top of the Operationen- und Prozedurenschlüssel code-driven diagnosis-related payment for an in-hospital interventional treatment. To establish a dedicated DES reimbursement in the future, additional DES trials in the superficial femoral artery (SFA) are mandatory for proving a beneficial class effect of DES in this particular vessel territory.

Do you expect we will see adoption of drug-eluting technologies continue to increase over time? What evolution do you anticipate to occur with reimbursement for drug-eluting technologies considering the positive outcomes in drug-eluting clinical trials?

With additional companies entering the DCB market, the percentage of DCB users will increase in Germany as long as the reimbursement system will cover the additional device costs in the future. A second aspect of DCB adoption is its efficacy below the knee (BTK). To date, we have only positive outcome data for DCB use above the knee. No independently controlled study has yet shown any efficacy of DCBs in BTK interventions. The BTK market is at least as important as the femoral market, because for long BTK lesions, no comparable treatment options regarding longer-term durability exist in this particular vessel territory. For short lesions (defined as < 10 cm), coronary DES platforms have shown excellent BTK patency data and therefore have become the first-line treatment choice in most institutions. The YUKON BTK study was able to show a significantly reduced overall amputation rate 2 years after DES treatment when compared to bare-metal stenting.[5] However, for longer lesions, POBA is still considered the gold standard with all the device-specific limitations. As such, the interventional community is eagerly waiting for the first positive randomized controlled trial proving superiority of DCBs over POBA in tibial interventions.

In terms of DES use in femoropopliteal lesions, the MAJESTIC study continues to show outstanding clinical results at 2 years with a 92.5% freedom from target lesion revascularization (TLR) rate and 91% of patients had no or minimal claudication.[6] In addition, larger comparative trials are mandatory to evaluate the performance of the Eluvia DES (Boston Scientific Corporation) in longer lesions and compared to last-generation bare-metal stents and DCBs. Should these upcoming studies confirm the initial positive experience with this particular DES, payers should be willing to cover additional device costs due to the potential long-term cost savings.

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Antonio Micari, MD, PhD
Interventional Cardiologist
Maria Cecilia Hospital,
GVM Care and Research
Cotignola, Ravenna, Italy
micariantonio@gmail.com

Disclosures: Consultant for Medtronic, Bard Peripheral Vascular, and Terumo Corporation.

What factors specific to your region have contributed to the adoption of drug-eluting therapies in the peripheral arteries?

Peripheral artery angioplasty is often a technically challenging procedure, but it is successful in most cases; however, mid- and long-term efficacy in terms of vessel patency remain a problem. In either the SFA or in tibial arteries, we know that the restenosis rate of POBA is not acceptable. TLR occurs in about 30% of SFA cases and in 45% of BTK angioplasties. This clearly depicts the existence of an unmet need to be solved by drug-eluting technologies. DCBs and DESs have shown very satisfactory results, both in randomized controlled trials and global registries, at least in TASC A and B lesions. Further studies are ongoing for TASC C and D lesions with longer follow-up. Several companies have invested in robust DCB clinical programs, and data generated by evidence-based medicine are definitely more convincing than just marketing initiatives.

When asked whether DCBs or DESs are better, my answer is that they are complementary. If new-generation DESs confirm the preliminary results, which have been striking, I believe we will use DES as the first option in some subsets of lesions (eg, one-stent lesion, calcified, ostial).

BTK interventional therapy is an area of intense interest right now. How do you believe drug-eluting technologies will advance the treatment of BTK disease in the next 3 to 5 years?

BTK disease and critical limb ischemia (CLI) are challenging and complicated clinical settings that are considered controversial battlefields. Initial results of DCBs in BTK arteries have been very confusing. After an analysis of the results from the IN.PACT DEEP trial, Medtronic recalled their In.Pact Amphirion DCB from the market. However, many investigator-driven registries in high-volume, highly experienced centers had opposite results. I believe that many factors influenced the failure, and I think that second-generation DCBs with better-designed trials will provide us with a definitive answer. I expect to see restenosis and TLR reduction with DCBs. Coronary DESs and bioresorbable vascular scaffolds have shown very good results, but they are limited to a very selective population of proximal and focal disease, which is quite unusual in CLI.

Konstantinos Katsanos, MSc, MD, PhD, EBIR
Guy's and St. Thomas Hospitals
NHS Foundation Trust
London, United Kingdom
katsanos@med.upatras.gr

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What factors specific to your region have contributed to the adoption of drug-eluting therapies in the peripheral arteries?

Vessel restenosis and recurrent limb ischemia remain the main limitations of POBA and bare-nitinol stents in the femoropopliteal and infrapopliteal arteries. Patients suffering from CLI are at risk of imminent limb loss if not urgently revascularized, whereas those suffering from intermittent claudication may alternatively benefit from programs of independent or supervised exercise therapy as a stand-alone treatment or in combination with early angioplasty in order to augment long-term walking capacity. Hence, prevention of amputations and improvement of limb functional outcomes have been the main driving forces behind adoption of DESs and DCBs in the peripheral arteries in the United Kingdom.

Physicians in the UK and many other European countries are increasingly being incentivized to avoid interventions when possible. Do you believe this is the right health care model for the future? Given the better long-term outcomes demonstrated by drug-eluting technologies, how do you believe these technologies will impact this model?

Paclitaxel-eluting stents and paclitaxel-coated balloons have been consistently shown to inhibit neointimal hyperplasia, improve long-term anatomical outcomes, and thereby reduce the need for repeat limb revascularization procedures.[1,2] In addition, infrapopliteal DESs have been shown to significantly reduce amputations and accelerate wound healing in patients with CLI.[3,4] Furthermore, a recent health economic analysis has highlighted the very favorable cost utility of drug technologies in the femoropopliteal segment. Projected incremental cost-effectiveness ratios were found to be on the order of a few thousand British pounds per quality of life-year

gained and well below the acceptability threshold of the UK National Institute for Health and Care Excellence.[5]

Given that repeat procedures and limb amputations are not only detrimental to quality of life and patient longevity but also pose a significant financial burden for the overall health care budget, peripheral drug technologies are expected to gradually change the landscape of peripheral endovascular treatments by producing more durable results, while saving costs for the UK National Health System. Traditional ineffective treatment pathways would need to be indirectly disinvested, while adoption of innovative drug technologies should be directly incentivized in order to improve patient care and improve clinical outcomes and quality of life. I believe that it is prime time for DCB and DES technologies to help transform the outdated historical standard of POBA and bailout metal stents for a more effective and efficient utilization of health care resources.

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Yann Gouëffic, MD, PhD
Professor and Chief
Department of Vascular Surgery
University Hospital of Nantes
Nantes, France
yann.goueffic@chu-nantes.fr

Disclosures: Consultant for Boston Scientific Corporation, Cook Medical, Hexacath, Medtronic, Perouse, and Spectranetics Corporation.

What factors specific to your region have contributed to the adoption of drug-eluting therapies in the peripheral arteries?

In France, the adoption of drug-eluting therapies is currently low. For example, DESs represent < 3% of the total implanted stents for peripheral disease. Different reasons could explain the reluctance to develop the use of drug-eluting therapies in France. Cardiologists have been long been exposed to the physiopathology of restenosis and understand the need to prevent or to treat restenosis. Despite French vascular surgeons' involvement in endovascular procedures for peripheral artery disease since the late 1990s, a deficit of education regarding restenosis physiopathology still exists. This could explain the low adoption of drug-eluting therapies.

Secondly, the French market is characterized by a reimbursement system where only implantable devices are reimbursed. Implantable devices, such as stents, are reimbursed separately from the diagnosis-related groups (DRGs). On the contrary, DCBs are not considered as implantable, and thus are not reimbursed, which decreases the level of DCB adoption in routine practice.

Finally, it is noteworthy that few data are available to help the physician choose the right devices to treat the right lesions. Indeed, femoropopliteal trials have shown the superiority of drug-eluting therapies over balloon angioplasty, but so far no recent study has focused on comparisons such as drug-eluting therapies versus bare-metal stents or DESs versus DCBs. Furthermore, for BTK treatment, the clinical advantages of drug-eluting therapies over POBA have yet to be demonstrated.

How do the dynamics of your local health care system and economic environment impact the use of drug-eluting technologies? How do you anticipate it changing in the next 3 to 5 years?

Last month, the French health care system announced promising changes for peripheral vascular interventionists. Until recently, Zilver PTX was the only DES that was reimbursed by the French health care system. Now, a second DES (Eluvia) is being reimbursed. Thanks to a last-generation platform (Innova, Boston Scientific Corporation) and a polymer-based sustained drug release, Eluvia offers new options for physicians who want to improve femoropopliteal endovascular treatment outcomes with regard to decreasing in-stent restenosis and reintervention in their routine practice. The EMINENT and IMPERIAL trials, currently in process, should provide additional data over the next few years.

In December 2015, the French health care system modified its policy to allow the reimbursement of innovative and nonimplantable devices. Consequently, DCBs could potentially benefit from this new policy. Discussions are now underway to determine the reimbursement price. Given the anticipated duration of this process, DCBs could be reimbursed in France in 2017.

Currently, stents are not included in the DRGs and therefore benefit from a separate reimbursement. There are rumors that this could change in the next few years and that stents could be included in the DRGs, which would certainly make stents less profitable. There is no doubt that including drug-eluting technologies in the DRGs could alter their use according their reimbursement price. This is why high-level evidence-based medicine is mandatory to establish device choice not only on economic parameters, but also in a patient's best interest. ■