

Cost-Effectiveness Analysis of Drug-Eluting Stents and Drug-Coated Balloons

Considerations unique to a single-payor system.

BY KONSTANTINOS KATSANOS, MSc, MD, PhD, EBIR

Driven by the compelling outcomes in the coronary arteries, drug-eluting stents (DESs) were quickly adopted in the femoropopliteal arteries. However, their use did not go without some initial failures and reasonable time delay once the fundamental differences in vessel histology, biomechanical environment, and unique spatial and temporal patterns of restenosis between the two vascular beds were realized.^{1,2} Still, the superficial femoral and popliteal arteries remained challenging areas for endovascular procedures, and shortly thereafter, drug-coated balloons (DCBs) emerged in an attempt to deliver antirestenotic medication without the need for a permanent metal implant.³ In parallel, paclitaxel has become the mainstay drug for inhibition of restenosis above the knee, contrary to the sirolimus analogs that have dominated percutaneous coronary interventions.

Evidence from observational and randomized controlled trials (RCTs) has shown that both DESs and DCBs inhibit restenosis, improve patency outcomes, reduce the incidence of recurrent limb ischemia because of target vessel failure, and reduce the need for target limb revascularization (TLR).^{1,4} Consequently, DESs and DCBs may improve functional limb outcomes and prevent major amputations. On one hand, because of the metal scaffold, DESs are best suited for the treatment of complex disease to eliminate vessel recoil and maximize immediate hemodynamic gain necessary for limb salvage. On the other hand, DCBs are a more elegant option for the

treatment of less complex disease without leaving anything permanent behind. The latest meta-analyses on DES and DCB outcomes report a significant reduction of vessel restenosis and TLR by > 50% at 1 year post-procedure.⁵ Recently reported outcomes from early RCTs up to 5 years clearly show a sustained, long-term clinical benefit.^{6,7}

ANALYSIS OF DEVICE COSTS

Arguably, both DESs and DCBs command a price premium as novel medical devices, and hospital administration often challenges physicians to prove the value of DESs and DCBs. We recently performed a budget impact model and cost-effectiveness analysis in the National Healthcare System (NHS) in England of primary DES or DCB use in the femoropopliteal segment to gain some insights into the health economics of using these devices.⁸ We performed a large systematic review of the literature of single-arm or controlled studies that evaluated endovascular options for the femoropopliteal artery to inform a health economic analysis comparing primary bare-metal stent (BMS), DES, or DCB with percutaneous transluminal angioplasty (PTA) and bailout BMS as the historical treatment of reference.

Results in Single-Payor Systems

Overall, 28 clinical studies were pooled, reporting on more than 5,167 femoropopliteal artery lesions. Most patients had intermittent claudication, and critical limb

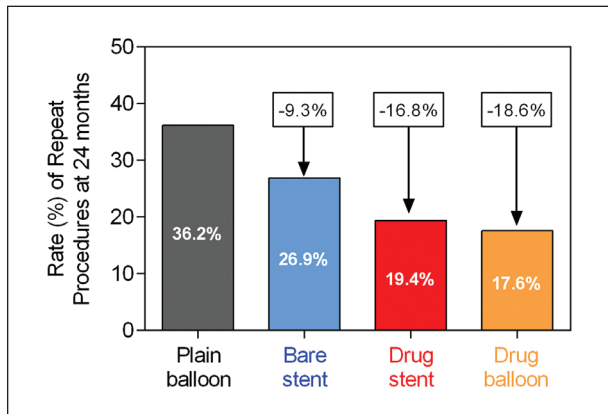


Figure 1. Average aggregate rates of repeat procedures in the femoropopliteal segment for primary BMS, DES, and DCB compared to PTA and bailout stenting as the reference treatment. Data from Katsanos K, Geisler BP, Garner AM, et al. Economic analysis of endovascular drug-eluting treatments for femoropopliteal artery disease in the UK. *BMJ Open*. 2016;6:e011245.

ischemia (CLI) represented 15% to 20% of cases.⁸ In line with previous evidence, a significant reduction in the rate of TLR up to 24 months was noted with the use of drug-eluting technologies, driving TLR rates from 36.2% in cases of PTA to 26.9% in cases of BMSs (-9.3%) and further down to 19.4% in cases of DESs (-16.8%) and 17.6% in cases of DCBs (-18.6%) (Figure 1). Based on the aggregated trial-reported data, the budget impact model allowed for one TLR after the index procedure up to 24 months. As a result, the number needed to treat to avoid one TLR in 24 months was 10.8, 6, and 5.4 in BMS, DES, and DCB, respectively, at an average incremental cost per patient of £112, £44, and £43 (economic comparison included the index procedure and any applicable reinterventions costs within 2 years).⁸

We also expanded the health economic analysis to include cost-utility factors in order to calculate the projected incremental cost-effectiveness ratio (ICER) of the drug technologies under investigation. ICER is defined as the difference in costs between two interventions (or medical devices) divided by the difference in their treatment effects. In health care, ICER is best expressed as the average incremental cost per patient associated with one quality-adjusted life-year (QALY) gained. QALYs are generic measures of the quality and quantity of life-years accrued after different health care interventions, with a value of one referring to perfect health for a whole year. Symptomatic vessel restenosis can diminish a patient's quality of life and drive the need for TLR earlier or later depending on the severity of recurrent disease and type of symptoms (eg, claudication vs CLI). Therefore, the

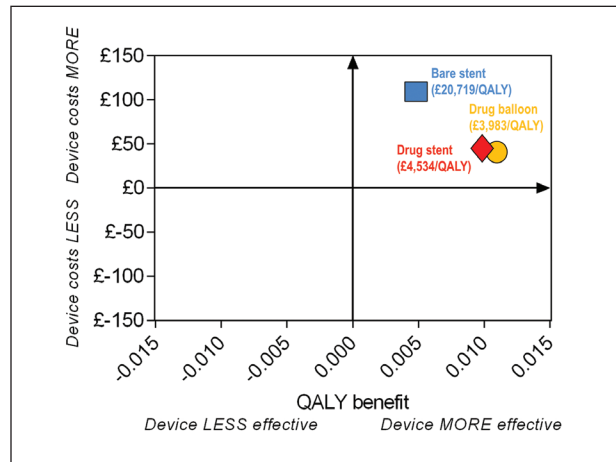


Figure 2. Cost-effectiveness plane for the femoropopliteal artery. ICER for BMSs, DESs, or DCBs are reported. The x-axis shows the QALY benefit and the y-axis shows the average per-patient price premium of each technology. Analysis up to 24 months from the perspective of the NHS in England. Data from Katsanos K, Geisler BP, Garner AM, et al. Economic analysis of endovascular drug-eluting treatments for femoropopliteal artery disease in the UK. *BMJ Open*. 2016;6:e011245.

clinical benefit of reducing clinically driven TLR was converted to the equivalent QALY gain with the use of appropriate utility factors to allow calculation of ICER for each endovascular strategy. Figure 2 shows the derived cost-effectiveness plane for BMS, DES, and DCB in de novo femoropopliteal lesions up to 2 years. The projected ICER is only £4,534 per QALY gained for DES and £3,983 per QALY for DCB.⁸ Overall, calculated ICERs are well below the accepted threshold of £20,000 per QALY for widespread adoption of the technology and centralized government funding to be justified.

Our analysis has allowed for the development of a robust decision analytic per-patient cost impact model for the NHS system in England. The results clearly question the recommended standard of PTA and bailout BMS in the femoropopliteal segment. In fact, a more in-depth sensitivity analysis showed that a modest 10% price reduction would raise both DES and DCB as dominant technologies (ie, medical devices that not only offer superior clinical outcomes, but may also save money for the NHS). Therefore, the adoption of drug-eluting technologies is an ongoing paradigm shift in the treatment of the femoropopliteal artery, and under the free market competition, price premiums will continue to decrease, allowing for an ever-expanding market share and continuous improvement of patient outcomes.

Pietzsch and colleagues published a budget impact model for the United States and German health care sys-

tems that follows a similar methodology. Comparable TLR probabilities were reported over 24 months for PTA, BMSs, DESs, and DCBs.⁹ However, because of more favorable nominal tariff systems, the primary DES or DCB strategies were found to have a lower projected budget impact over 24 months compared with BMSs and PTA. Average aggregate patient costs were \$10,214 for DCBs, \$12,904 for DESs, \$13,114 for PTA, and \$13,802 for BMSs for the United States Medicare system and €3,619 for DCBs, €3,632 for DESs, €4,026 for BMSs, and €4,290 for PTA for the German public health care system. The authors concluded that the latest drug-eluting technologies are not only associated with improved clinical outcomes, but also with some cost savings for the taxpayers up to 2 years.⁹

Limitations

There are certain fundamental limitations in the health economic analyses of DESs and DCBs. First, published models are limited by a 24-month time horizon and the allowance of a single TLR event. Incorporation of long-term data with multiple event analyses would probably lead to different but more realistic findings. On one hand, restenosis of long lesions may often require more than one repeat treatment. On the other hand, TLR may involve more than one adjunct medical device (eg, atherectomy and/or reentry devices) or even fail in the case of vessel reocclusion.

Second, there is an underrepresentation of CLI cases in the literature, since most RCTs have universally recruited claudicants. Arguably, CLI is a more challenging patient population with different priorities and endpoints—freedom from a major amputation is the primary treatment aim instead of vessel patency and freedom from TLR. A budget impact model focusing on CLI patients and outcomes would probably require a fundamentally different model and assumptions with a stronger focus on wound healing, patient hospital readmissions, and amputation-free survival, all of which are missing from the base of available evidence to date.

CONCLUSION

In addition to these drug-eluting technologies, the market has also seen the advent of other stent technologies to treat peripheral arteries. Biomimetic stents have been pursued to reduce restenosis and improve clinical results building on the superior stent architecture instead of the paclitaxel coating. Robust randomized comparative data are still missing; however, propensity-matched cohorts have shown that the Supera biomimetic stent (Abbott Vascular) may achieve comparable patency outcomes compared to DCBs

in the superficial femoral artery¹⁰ and even improve amputation-free survival under the more challenging conditions of chronic total occlusions and CLI.¹¹ Head-to-head randomized studies between different types of novel stent designs (eg, DESs, biomimetic stents) would be welcomed in an attempt to answer the question of which stent is the best and most cost-effective option. In this author's opinion, the future holds significant promise for bioresorbable DES platforms that may ultimately combine the best from both worlds (ie, a temporary vessel scaffold combined with prolonged and tunable drug elution to allow for more physiologic vessel healing and repaving).¹² ■

1. Katsanos K, Tepe G, Tsetis D, et al. Standards of practice for superficial femoral and popliteal artery angioplasty and stenting. *Cardiovasc Intervent Radiol*. 2014;37:592-603.
2. Dake MD, Ansel GM, Jaff MR, et al. Paclitaxel-eluting stents show superiority to balloon angioplasty and bare metal stents in femoropopliteal disease: twelve-month Zilver PTX randomized study results. *Circ Cardiovasc Interv*. 2011;4:495-504.
3. Tepe G, Zeller T, Albrecht T, et al. Local delivery of paclitaxel to inhibit restenosis during angioplasty of the leg. *N Engl J Med*. 2008;358:689-699.
4. Kitrou P, Karnabatidis D, Katsanos K. Drug-coated balloons are replacing the need for nitinol stents in the superficial femoral artery. *J Cardiovasc Surg (Torino)*. 2016;57:569-577.
5. Katsanos K, Spiliopoulos S, Karunanithy N, et al. Bayesian network meta-analysis of nitinol stents, covered stents, drug-eluting stents, and drug-coated balloons in the femoropopliteal artery. *J Vasc Surg*. 2014;59:1123-1133.e8.
6. Tepe G, Schnorr B, Albrecht T, et al. Angioplasty of femoral-popliteal arteries with drug-coated balloons: 5-year follow-up of the THUNDER trial. *JACC Cardiovasc Interv*. 2015;8:102-108.
7. Dake MD, Ansel GM, Jaff MR, et al. Durable clinical effectiveness with paclitaxel-eluting stents in the femoropopliteal artery: 5-year results of the Zilver PTX randomized trial. *Circulation*. 2016;133:1472-1483.
8. Katsanos K, Geisler BP, Garner AM, et al. Economic analysis of endovascular drug-eluting treatments for femoropopliteal artery disease in the UK. *BMJ Open*. 2016;6:e011245.
9. Pietzsch JB, Geisler BP, Garner AM, et al. Economic analysis of endovascular interventions for femoropopliteal arterial disease: a systematic review and budget impact model for the United States and Germany. *Catheter Cardiovasc Interv*. 2014;84:546-554.
10. Steiner S, Schmidt A, Bausback Y, et al. Midterm patency after femoropopliteal interventions: a comparison of standard and interwoven nitinol stents and drug-coated balloons in a single-center, propensity score-matched analysis. *J Endovasc Ther*. 2016;23:347-355.
11. Parakevopoulos I, Diamantopoulos A, Abisi S, et al. Katsanos SUPERA stent versus standard nitinol stents for recanalization of chronic total occlusions of the femoropopliteal artery: the SUPERFAST study. Presented at: Cardiovascular and Interventional Radiological Society of Europe (CIRSE); September 10-14 2016; Barcelona, Spain.
12. Kassimis G, Spiliopoulos S, Katsanos K, et al. Bioresorbable scaffolds in peripheral arterial disease. *Expert Rev Cardiovasc Ther*. 2014;12:443-450.

Konstantinos Katsanos, MSc, MD, PhD, EBIR

Assistant Professor, Interventional Radiology

Patras University Hospital

School of Medicine, Rion

Patras, Greece

Honorary Consultant Interventional Radiologist

Guy's and St. Thomas' Hospitals

King's Health Partners

London, United Kingdom

konstantinos.katsanos@gstt.nhs.uk

Disclosures: Travel sponsorship, honoraria, and speaker fees from Abbott Vascular, Cook Medical, Boston Scientific Corporation, and Medtronic.