PANEL DISCUSSION

The Coronary DCB Landscape

Considering the role of DCBs in coronary intervention, including current and future opportunities, the cost-benefit relationship, hurdles to widespread application, and differences between use in the United States and Europe.

With Eric A. Secemsky, MD, MSc; Jennifer A. Tremmel, MD, MS; and Sacharias von Koch, MD

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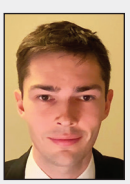

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In which patients and lesions do you find drug-coated balloons (DCBs) most advantageous? In what scenarios would you not use a DCB?

Dr. von Koch: DCBs are most advantageous for in-stent restenosis (ISR) with multiple stent layers, especially when lesion preparation results are optimal. DCBs may also be useful to simplify the procedure and to avoid long or multiple stents. A DCB is also a good option for patients at high bleeding risk or those awaiting major surgery where minimizing dual antiplatelet therapy is of importance. However, DCBs should be used selectively in noncomplex lesions where a good angiographic result can be achieved with a drug-eluting stent (DES).

Dr. Secemsky: Overall, I think there are incredibly diverse opportunities for DCBs in coronary intervention, with very few trade-offs. First and most relevant is treating ISR, which tends to be a chronic, recurrent issue for patients once it occurs. As we typically restrict percutaneous coronary intervention (PCI) to two layers of stent, it is important that we are thoughtful with our approach once ISR occurs. DCBs have the promise to treat and delay a second layer of stent, providing greater long-term options for patients. In addition, DCBs provide one of few treatment options when ISR occurs in two or more layers of stent. Previously, we were stuck primarily with plain old balloon angioplasty (POBA) alone and/or brachytherapy with two-layer ISR, which is not practical for patients. DCBs have dramatically changed our local treatment options.

The next horizon for DCBs is de novo small-vessel/branch/bifurcation disease. Small branches and long

lesions, in particular for vessels < 2.5 mm, are perfect DCB targets as there are few good options for these disease patterns. Early data suggest better outcomes with DCBs over POBA alone, and ongoing and upcoming United States trials will be focused on these lesion subsets. Side branches are also another great target for DCBs, particularly if they can help avoid the need for complicated bifurcation stenting. Having a treatment option like DCBs in vessels with few/no options is a remarkable milestone for our patients and can change how we perform PCI.

Finally, the future promise of DCBs is in de novo large-vessel disease. There are anecdotal data that in certain lesion subsets, DCBs can replace the need for a scaffold and can provide patients with a nonstented treatment option. This is particularly important for patients with early-onset disease or those with significant disease that may require bypass grafting in the future. Maintaining the vessel without a permanent implant leaves a wide array of treatment options available.

Despite all this, there will remain a need for metallic scaffolds. Disease patterns, including resistant lesions with recoil and flow-limiting dissections will require scaffolding to ensure patency. Large proximal vessels may have competitive long-term patency with stenting as the risks of ISR are low, and the role of DCBs in this location may only be for recurrent disease. Algorithms are being developed now to help navigate the optimal use of DCBs in specific lesion subsets, and as more data are generated, these approaches will be refined for contemporary PCI practice.

Dr. Tremmel: The only indication for DCB in the United States currently is ISR. We learned from the AGENT investigational device exemption trial that there is a significant reduction in target lesion failure (composite of target lesion revascularization, target vessel myocardial infarction, or cardiac death) in patients receiving DCB versus those receiving uncoated balloon for ISR.[1] This absolute risk reduction is notably greater for patients with multilayer ISR compared with those with single-layer ISR.

Personally, in the case of multilayer ISR, I will do all I can to not put another layer of stent because we know that outcomes worsen with each layer placed. If it is single-layer ISR, I tend to favor DCB if I have a really "clean" lesion preparation with no significant neointima/neoatherosclerosis, such as in a situation where the primary mode of stent failure was underexpansion. However, if there is a lot of residual neointima/neoatherosclerosis even after optimal lesion preparation, I will place a second layer of stent given data showing less repeat revascularization with DESs versus DCB.[2]

How do you see the applications for DCBs evolving? In which lesion subsets will DCBs have the most impact, and why?

Dr. Tremmel: DCBs certainly have several applications beyond ISR. Some of the most obvious are small vessels and branch vessels in bifurcation lesions (which are often small vessels). With smaller vessels, we worry about higher rates of restenosis, and certainly if ISR occurs, we will be hard pressed to put in a second layer of stent and further reduce the lumen size. On the other hand, DCBs offer the possibility of not placing any metal, maintaining vasomotion, and getting some late lumen enlargement. The data for DCB versus DES for de novo small-vessel disease has been mixed but overall encouraging.[3] Still, I would like to see trials focused on truly small vessels (< 2.5 mm), where the desire to place a stent is really low. I have used DCB in these small vessels and branch vessels of bifurcations where I have had no intention of placing a stent and feel that DCB is preferable to an uncoated balloon alone; however, we do need more data to support such practices.

Dr. von Koch: I believe the use of DCBs will evolve, particularly with hybrid PCI strategies where DCBs and DESs are used together. This approach is good for long lesions, where you stent the proximal segments and use a DCB for the distal part. The hybrid approach may also be a good option for bifurcation lesions, where a DCB is used in the side branch together with provisional stenting in the main branch to avoid a complex two-stent technique. This hybrid PCI approach can, in many cases, simplify the procedure while still achieving a good outcome.

What are the key technical differences in using a DCB versus POBA?

Dr. Secemsky: The beauty with DCBs is there are no real technical differences—they exist as the same balloon platforms we use for everyday PCI, and there is no real learning curve. I think the main evolution in practice we will observe is how to best transfer the antiproliferative agent to the vessel wall in calcified disease and ISR. We have theorized during peripheral intervention with DCBs that plaque modification is necessary to improve drug uptake. There are early animal data to support this; however, it has been challenging to demonstrate this in large-scale trials. Nonetheless, I think we will all move toward very aggressive vessel preparation, whether with specialty balloons (eg, cutting balloon), lithotripsy, or atherectomy, prior to application of a DCB.

Dr. von Koch: Before using a DCB, you need to ensure a good lesion preparation, typically with a noncompliant or semicompliant balloon to predilate the

vessel. Additional plaque modification may be useful, such as cutting balloons, intravascular lithotripsy, or rotablation. Unlike POBA, the goal with DCBs is not only to open the vessel but also to deliver the drug. A minimum inflation time of 30 seconds is recommended to ensure proper drug transfer into the vessel wall. Another key difference between POBA and DCBs is that DCBs are more sensitive to how the device is handled. For example, drug transfer can be affected by factors such as vessel manipulation prior to the DCB inflation.

Dr. Tremmel: I always remind people that we shouldn't think of a DCB as a balloon but as a drug-delivery device. The DCB is not for dilating. All of the dilating and other lesion preparation must be done prior to using the DCB, and you need a lesion that looks good enough on intravascular imaging that you would be satisfied with leaving it as is. Only then do you use your DCB and deliver the drug.

Because there is drug on the DCB, it needs to be handled a bit differently than an uncoated balloon. Specifically, it's preferable not to touch it, and you certainly do not want to wipe it or get it wet too long. You want your lesion fully prepped when you open the balloon package so that you can quickly and easily deploy it. Also, you need some time for the drug to transfer, so you leave the DCB dilated longer than you might for POBA. For example, with the Agent balloon (Boston Scientific Corporation), the data support at least 1 minute. Finally, some are reluctant to do intravascular ultrasound or even obtain a final angiogram after DCB for fear of "washing away the drug." However, because the drug transfers into the tissue, such fear is unfounded.

In Europe, there are DCBs with sirolimus as well as some with paclitaxel. What do you see as the relative benefits and limitations of each in this setting? Do you view them as complementary, interchangeable, or competitive?

Dr. Tremmel: Both paclitaxel and the limus DCBs have gone through several iterations in terms of the drug formulation and dosing, as well as the transfer technology. I suspect that we will ultimately arrive at near equivalency, but we are still in early days. We saw a similar evolution with drug-eluting stents. Head-to-head trials will promote certain DCBs over others, as will market forces, until we arrive at a few "winners."

Dr. von Koch: Paclitaxel-coated balloons are still the most frequently used DCB in Europe. This is mainly due to their high lipophilicity and rapid drug uptake. Sirolimus-coated balloons have recently emerged, but the data are still limited. At this point, I see them as potentially interchangeable. Whether they are complementary or one is superior remains to be determined. Ongoing studies will help clarify this, but as of today, paclitaxel remains the standard as most data available on DCBs come from studies using paclitaxel-coated balloons.

Dr. Secemsky: I think this is an important question that we are still figuring out. Paclitaxel has been the agent of choice for peripheral and coronary DCBs. This is in part due to the ease of transferring this drug into the vessel wall as it is lipophilic. Overall, outcomes have been very positive, with the Agent DCB being the only approved coronary DCB in the United States and several other paclitaxel-based coronary DCBs on the shelf outside the United States. However, "limus" agents have been the cornerstone of contemporary PCI, as all approved DESs in the United States are coated with a limus formula. Limus agents have potential benefits over paclitaxel, including anti-inflammatory properties. However, this agent has traditionally been very challenging to transfer to the vessel wall due to its hydrophilicity. With newer technology now able to package limus into deliverable vehicles, we are seeing promise that these devices can make a meaningful impact on PCI outcomes. Nonetheless, the pivotal randomized trials for limus DCBs remain ongoing and will be key to understanding the role of these devices in clinical practice.

How do you weigh the cost-benefit relationship of DCBs? Have you encountered any issues with respect to cost?

Dr. von Koch: In Sweden, I haven't encountered any major cost-related issues. Several options are available, and as more have entered the market, prices may have come down. However, DESs are generally cheaper, and they offer a flexibility in PCI techniques that can sometimes justify the costs.

Dr. Tremmel: This is a real issue. Currently in the United States, the only available DCB (Agent) is reimbursed through the outpatient transitional pass-through (TPT) payment, but reimbursement in the inpatient setting will not begin until October 2025 (through the new technology add-on payment [NTAP] program). Moreover, my impression is that physician reimbursement mirrors that given for POBA rather than for stenting, which is unfortunate because it fails to recognize that this device is not just a balloon and that physicians need to do as much, if not more, work for its effective use compared with DES.

Prior to the TPT payment, our group limited DCB use to on label only. Initially, we also saw several referrals for DCB because not all hospitals were purchasing them. The cost

issues are lessening but have not been resolved, and the difference between the cost in the United States compared with Europe, for example, is frustrating to many. At least in the United States, it will still be a couple of years before we see where the Centers for Medicare & Medicaid Services sets reimbursement. Likewise, cost is likely to change, hopefully lessen, as the technology matures and there are different DCBs available for physicians and hospitals to choose from.

Dr. Secemsky: Just like any breakthrough device in the United States, we currently only have restricted reimbursement on coronary DCBs. This has definitely limited our ability to use these devices as we would like in clinical practice. Nonetheless, the pathway to full reimbursement is ongoing and will certainly support greater use of coronary DCBs. The current reimbursement via the TPT payment and more recently, the new technology add-on payment, is helpful for our Medicare patient, but I think we will see an exponentially greater use of these devices once full reimbursement is achieved.

Outside of data, what have been the biggest hurdles to more widespread use of DCBs in coronary intervention?

Dr. Secemsky: I think the main hurdles to date are costs/reimbursement and clinical strategy. As mentioned, the reimbursement pathway is progressing. But now we need to figure out how to best use DCBs in our coronary practice. We have learned a lot from interventional cardiologists outside the United States who have had these devices available for some time. Now, United States operators need to get comfortable about best practices, appropriate lesion subsets, and optimizing vessel preparation for deployment.

Dr. von Koch: I don't think there have been any major hurdles with the implementation of DCBs. As of today, DCBs are widely used in many countries and continue to grow in popularity. At the same time, several new DCB devices have been developed. That being said, their use depends on good lesion preparation, and not all operators feel comfortable with this technique.

Dr. Tremmel: Cost is a factor. Also, stents work and remain our primary mode of coronary intervention. DCBs are currently most desirable where stents are suboptimal; they will ultimately need to rise to the level of stents in terms of safety and efficacy to actually supplant them. Otherwise, they will remain an adjunct, albeit important, tool. Moreso, at least in the United States, DCB are still new to us. We know that people vary in terms of the rate at which they adopt new technologies and techniques, and given that we are less than 8 months from the TPT payment and have not yet started receiving inpatient reimbursement, I'd say we're likely still in the early adopter phase. I would expect to see a much bigger uptick with the early majority in 2026.

Numerous publications have evaluated the use of DCBs to treat de novo coronary lesions. What data are needed to further understand and support this use?

Dr. Tremmel: Beyond small vessels and bifurcation lesions, there have also been investigations into using DCBs in acute coronary syndromes, long lesions, bypass grafts, high-bleeding-risk patients, and even left main. Pretty much anywhere you can put a stent, we want to know if we can use a DCB instead. While we would like large randomized controlled trials for all lesion subsets, it's unlikely to occur. We will have to rely on smaller trials and observational registry data, as well as real-life experience. Other countries have been using DCB for over a decade and we in the United States have a lot to learn from them. Overall, this is an exciting time, having a truly new and important treatment for the coronary arteries. It will be fun to see how it matures.

Dr. von Koch: There is a need for long-term data and larger randomized trials comparing DCBs with DESs for de novo lesions. There are some ongoing trials that will help clarify this and hopefully give guidance on where DCBs are the most effective.

Dr. Secemsky: I think the randomized trials will be key. The cornerstone of coronary intervention has been our dedication to large-scale, well-powered, randomized trials. Fortunately, we have several in progress and several upcoming that will really shape how DCBs are employed in clinical practice. ■

1. Yeh RW, Shlofmitz R, Moses J, et al. Paclitaxel-coated balloon vs uncoated balloon for coronary in-stent restenosis: the AGENT IDE randomized clinical trial. JAMA. 2024 Mar 26;331(12):1015–1024. doi: 10.1001/jama.2024.1361
2. von Koch S, Zhou M, Rosén HC, et al. Drug-coated balloons versus drug-eluting stents or plain old balloon angioplasty: a long-term in-stent restenosis study. J Am Heart Assoc. 2024 Dec 3;13(23):e036839. doi: 10.1161/JAHA.124.036839
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Disclosures
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