# Treatment Algorithms: This Is How I Use a DCB

An expert panel discusses the current role, data, and techniques for the use of drug-coated balloons in tackling PAD.

## PARTICIPANTS


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### How do you think drug-coated balloons (DCBs) have changed the overall treatment of peripheral artery disease (PAD) in the superficial femoral artery (SFA)?

**Dr. Mustapha:** I believe DCBs have created a significant paradigm shift in treating claudicants. They allow us to treat more aggressively, especially lesions at the ostium of the SFA and those that involve the P2 and P3 segments of the popliteal artery.

**Dr. Laurich:** I think the biggest impact that DCBs have on changing the overall treatment, particularly in the SFA, is the decreased use of stenting as the primary therapy. We're going to see a shift away from stenting as first-line treatment, meaning that we'll try to minimize our stent usage. Stenting creates a more permanent change to the vessel, and shifting away from that is a good thing, because it leaves more treatment options open to the patient in the future. In vascular disease treatment, every therapy that we deliver has a lifespan, even bypass. If we can keep all options open for as long as possible, I think that greatly benefits patients.

**Dr. Garcia:** The SFA has been one of the most challenging areas to treat. We've bailed out to using stents for many years, with the understanding that stents can do reasonably well at 1 year, but don't have a great success rate out to 2 and 3 years. Additionally, there's been a movement that a lot of us have championed and is now becoming more mainstream, which is to leave nothing behind in the SFA. With DCBs, leaving nothing behind is really appealing because if you need further interventions in the future, you won't have to deal with the stent that was previously left in the vessel. Overall, I would say that they've changed our practice by affording us at least a bit of a pause in therapy, allowing us to treat various lesions without having to leave a stent behind in the SFA.

**Dr. Geraghty:** They've been a nice addition to the toolbox. Particularly for small-caliber arteries and for enthusiasts of the "no metal left behind" approach,

they're a real boon. We'd still like to see some longer-term data, particularly when we look at DCB use in claudication patients.

**Dr. Krishnan:** For the first time, we have level 1 evidence that compares a DCB to plain balloon angioplasty out to 1 year, with very good results. This gives us the confidence to treat SFA disease without leaving a prosthesis behind. Even though we previously saw that the Zilver drug-eluting stent (Cook Medical) provided great outcomes in this area, it has the downside of leaving a stent in the vessel.

### In what ways does DCB use affect both the treated vessel segment and future treatment options?

**Dr. Laurich:** Recurrence is obviously the Achilles' heel of endovascular therapy. The long-term result is really the primary focus now. The problem that we struggle with most is recurrence via the intimal hyperplasia process, and until now, we haven't had a tool that directly focused on addressing this. There is a lot of excitement surrounding DCBs because this is the first medical therapy that we can deliver endovascularly, instead of relying solely on mechanical forces to treat the vessel. Everything we do mechanically affects the biology of the vessel, but this is the first therapy directed at the biological process itself, which is exciting because this is the number one issue we struggle with. There are no "silver bullets," but I believe this will certainly be an effective tool that could ultimately provide a longer-lasting solution for our patients.

**Dr. Garcia:** I think DCB treatment has the potential to address what I call the proverbial creep of disease associated with repeated stent treatments. This refers to a situation when you have a 10- or 12-cm-long lesion, and you place a 15-cm stent that fails, so then you start adding stents, which makes a 15-cm lesion now 20 cm. If the stents continue to fail, the treatment area keeps growing, and then you ultimately need to do a bypass. If a DCB fails, you can still retreat that same lesion length rather than progress to lengthier and lengthier areas of the vessel. With the DCB, you don't have to overcompensate for failure based on restenosis due to repeated stent treatments of increasing length. If you asked those who treat this disease on a daily basis whether we'd rather see in-stent restenosis or restenosis without a stent, I think it's safe to say that we'd all much prefer to treat restenosis without a stent. The "leaving nothing behind" strategy is really picking up steam in the SFA. It may not be ready for prime time in regard to all-comers, but I think it's really shifting the practice paradigm for many patients who have SFA disease and claudication.

**Dr. Geraghty:** One notable advantage is the theoretical ease of reintervention, in the sense of not having to deal with the metal scaffolding, which gives us more options for reintervention. I think as long as DCBs can maintain a favorable patency profile that will keep them competitive with other options in the SFA, the ease of reintervention certainly makes them very attractive.

**Dr. Krishnan:** We know that once the paclitaxel is in the vessel, it significantly inhibits restenosis compared to a non-coated balloon, at least up to 1 year. What we don't know is how these results will endure long-term. However, even if the vessel does restenose, we won't have to deal with a previously implanted prosthesis, which makes it a lot easier to go back and reintervene, if needed.

### How do DCBs fit into your treatment algorithm?

**Dr. Mustapha:** It is becoming a primary choice of therapy in my algorithm, regardless of which vessel preparation I do first. As you know, at this point, it is not approved or available in the United States for below-the-knee disease. However, for the patients with multilevel critical limb ischemia (CLI), such as in the popliteal and SFA, DCBs play a major role in treating CLI patients in my practice.

**Dr. Laurich:** DCBs have become first-line therapy for claudicants and CLI patients. Using an antirestenotic therapy to reduce the likelihood of a repeat intervention decreases the risk for every patient. I strongly believe that vascular physicians should keep a life-long treatment algorithm in mind when delivering therapies. DCBs play a role in that by helping you keep as many options open for them as possible.

**Dr. Geraghty:** I've actually been using them more for CLI than claudication. The thought is that with smaller-caliber arteries and oftentimes more distal lesions in terms of the popliteal, I'm more reluctant to leave behind metal scaffolding. The caliber is not as well matched for some of the available drug-eluting stent products, so I prefer DCBs in these cases.

### Considering that the two DCBs that are approved in the United States market are different in design and drug dose, how do you decide which DCB to use in a particular case?

**Dr. Mustapha:** Both are good DCB balloons. I tend to use the LUTONIX® DCB (Bard Peripheral Vascular,

Inc.) more because their 6-mm balloon goes through a 6-F sheath, and the 6-mm In.Pact balloon (Medtronic) requires a 7-F sheath.

**Dr. Laurich:** Well, there are issues of both efficacy and safety to be discussed. As far as efficacy, both have been proven effective. I don't think the drug concentration on the balloon is necessarily the important number; one has 2 μg/mm$^2$, and the other has 3.5 μg/mm$^2$. The issue is really the amount of drug you are able to deliver to the deep intimal and medial layers of the vessel wall.

**Dr. Garcia:** One factor we consider is the range of balloon lengths available, as we definitely need longer balloons to treat the longer lesions we're seeing. Overall, I don't think there's a huge difference between the two designs, even though the drug dosing on each is a bit different.

**Dr. Geraghty:** I personally don't care so much about the drug dose, I care more about the results. You can have different drug doses, and if different balloons have different washout rates and transfer rates to the wall, the drug dose matters very little. In the end, I look at the results that the balloon generates in terms of efficacy and safety. Thus far, at year 1, both competitors had very good efficacy and safety, and at year 2, I see the LUTONIX® DCB story, but I don't have the other balloon's data to look at yet.

**Dr. Krishnan:** I choose which DCB to use based on the balloon sizing options each provides and what I need in order to best treat the lesion in front of me.

## How does lesion length and severity affect your decision on which DCB to select? When do you use a DCB, and when do you use a stent?

**Dr. Geraghty:** In the past, I favored stenting over atherectomy for complex SFA lesions. As part of that procedure, I would predilate, particularly when treating chronic total occlusions (CTOs). Once I crossed the lesion, I'd predilate a 3- or 4-mm channel, just to know that I could open the stent without difficulty and then postdilate within the stent. Now, I'm much more aggressive with my predilatation to see if I can achieve that good lumen and potentially use the DCB as a treatment option. This is how my practice has changed, particularly for short to mid-length lesions.

**Dr. Garcia:** When you have a long CTO, I think most interventionists would choose to stent based on the available data. But if you look at moderately long lesions, they all had fairly robust CTO numbers between 25% and 33% of enrolled patients in the THUNDER, LEVANT, and IN.PACT trials. I think the paradigm of, "If it's occluded, you have to put a stent in," may not actually be valid. We're all trying to decide how best to treat this disease, but I think most of us are leaning toward leaving nothing behind, even in the CTO.

**Dr. Laurich:** With CLI patients, I am more apt to stent, but I will use a DCB as first-line therapy. You often have multilevel disease to treat as well, so you want to be sure you've maximized your SFA and popliteal flow. In general, I will use DCBs in the SFA and popliteal and be a little more liberal with my stenting, and then treat their tibiopedal diseases with angioplasty or atherectomy/angioplasty.

**Dr. Mustapha:** Vessel preparation is key when it comes to complex calcified lesions. There aren't any specific data to support the superiority of one particular balloon over the other in calcified lesions. In that regard, I go back to my previous point that sizing determines balloon choice. Vessel preparation for calcified lesions has no specific tool that fixes all. So, I look at the vessel and make a decision based on what I see, as well as the location of the lesion in the vessel.

## How do you typically predilate, and why is that important?

**Dr. Garcia:** I tend to believe that predilatation is very important for two reasons. One reason is you want to see the reaction of the artery to predilatation. Although we usually undersize the predilatation balloon, if this step creates a major catastrophe (i.e., dissection or perforation), then you know to stent it and perhaps skip the DCB altogether. Alternatively, the predilatation might look great, so do your definitive therapy with the DCB.

The second reason I predilate, and the way to get the best angioplasty result, is not only to go long in your duration of therapy, but also do multiple inflations. What happens is the artery finally releases and tends to dilate rather than tear, and the smooth muscles usually relax when you do multiple inflations. In terms of inflation time, we don't inflate for long during the predilatation, and then we use a DCB for a protracted period of time (3 to 4 minutes), with the goal to have the artery resist the recoil response to dilatation.

**Dr. Mustapha:** I personally prefer to predilate using a 1:1 ratio to create the most suitable environment for the DCB to deliver the drug to a vessel wall that no

longer requires any additional dilatation. Therefore, I use the DCB as a tool of drug delivery and not a tool to dilate.

**Dr. Laurich:** Predilatation was included as part of the United States trials, and we saw that there are two important reasons to predilate. Number one is that it allows good vessel prep. The second is to understand sizing. With DCBs, you definitely want to size your balloon to the vessel 1:1 or slightly oversize; it should never be undersized. There are a number of studies that show that you need 1:1 apposition of that balloon to the vessel wall in order to provide adequate drug transfer.

It is also important to use good angioplasty technique. I think interventionists are becoming more aware that this should be done slowly, and the balloon should be inflated for an appropriate amount of time. There has been some evidence that better angioplasty results can be achieved by inflating the balloon for 3 minutes instead of only 1 minute.

So, if possible, one should try to achieve the desired profile with slightly less pressure and leave the balloon inflated a little longer to allow the vessel more time to remodel, which may ultimately lead to better results.

**Dr. Geraghty:** In the trials, we saw that even plain balloon angioplasty did significantly better than we would have historically expected. I think part of that was the good angioplasty technique using predilation and appropriate balloon sizing. For me, that's changed the way that I approach the SFA with my first dilation; I try to get to nominal size so that I can really tell if the artery is going to be a good candidate for DCB application.

## What steps do you take to ensure proper alignment between your predilatation balloon and the DCB?

**Dr. Laurich:** My method is that I always physically mark the vessel on the screen and map out the goal of treatment. I think it's important to have a standard method of marking the location of the lesion. Some will use a road map technique, which is fine, but patient shift can be a problem. I find that the screen-marking technique allows me to be more precise.

When I predilate, I prevent geographic miss by never using a predilatation balloon longer than my DCB. So, for example, if the lesion is 8 cm, I'll predilate with an 80-mm balloon, and I'll use a 100-mm DCB, just to be sure that I'm not ballooning beyond the region of where I intend to treat with the medicine.

**Dr. Garcia:** Geographic miss is critical. In the old days when you had a lesion, it was like throwing a grenade or playing horseshoes. You could get close with a stent, and it was fine in covering the lesion. If you had a 10-cm lesion and placed a 15-cm stent, you could miss it by 2 cm on either side and still cover the lesion.

When it comes to DCBs, you have to be a little better at not only visually assessing where the lesion lives, but also accurately treating it. When we predilate, we always have a ruler in view of the lesion to avoid geographic miss. For example, we'll use a 40- or 60-mm balloon to predilate in preparation for using an 80-mm DCB. You always want to go longer than the original predilatation. However, you have to be careful when you have multiple predilatations, because you want to be sure to clearly mark the front and back end of the lesion to avoid geographic miss.

**Dr. Geraghty:** We've always used the radiopaque markers on the leg. In the past, we tended to put those on the drape, but more and more, we are putting them directly on the patient because it gives you a more stable marker that you can refer to. Even a couple of millimeters of shift might throw you off and cause geographic miss. It's also important to record the predilation images so that we know exactly where our proximal and distal ends are, and then we can be sure that we have good overlap.

**Dr. Krishnan:** This is a very important technical aspect of DCB use. It is important to use glow or marker tape on the patient, and once you balloon the lesion, the reference needs to be marked on the side monitor. Once this is done, you should ensure that you cover 1 mm distal to where you predilate with the regular balloon; otherwise, you will see geographic miss and high restenosis rates.

## What are the implications of misalignment between your predilatation balloon and the DCB?

**Dr. Mustapha:** Misalignment can lead to many potential untoward side effects. The most common is the lack of drug delivery to the vessel wall. Therefore, misalignment should be avoided as much as possible.

**Dr. Laurich:** You just want to be sure you're providing treatment to the desired area. This is a basic skill that we all need to make sure we pay attention to.

**Dr. Garcia:** One of the best ways to recreate restenosis is an overstretch model in any artery, particularly

a diseased artery. If you miss by predilating an area that you don't cover with medication (i.e., drug), then that area will have the simplest response to that injury, which would be a restenosis due to recoil and hyperplasia. Moreover, the edge between where the drug was placed and the nontreated area can cause the so-called candy wrapper effect. This was very common in the early days of drug-coated stents in the coronaries. Basically, this refers to when there's an inhibition to restenosis from the medication and then 2 to 4 mm from that area, a hyperplastic response makes the edges of the segments look like a candy wrapper.

**Dr. Geraghty:** We know that in the SFA trials, when they went back and looked at study images and could identify areas of geographic miss, they could track those treatment failures. This makes sense from the biology standpoint, as we're trying to get the drug onto every area that undergoes an angioplasty injury. If that doesn't happen, you haven't achieved the desired result with your intervention. The same thing holds for drug-eluting stenting, in that you don't want to angioplasty outside the confines of the stent. With DCBs, it takes a little more attention to detail because you don't have the metal markings of the stent, but I think for any experienced operator, it just takes a minute or two of attention to the predilation images to be precise and successful.

**Dr. Krishnan:** The implications of geographic miss are simple: higher restenosis rates.

### Where do you foresee the future of DCBs going in the next few years? Bare-metal stents? Drug-eluting stents?

**Dr. Mustapha:** I see the future of DCBs to be part of our everyday practice in both claudicant and CLI patients. I don't see DCBs overtaking other therapeutic vascular interventions completely, as there is a good possibility that various combinations of DCBs with other therapies may in the future prove to be viable options. I am very optimistic about the future with DCBs, including their potential to treat more complex lesions than we are treating today.

**Dr. Laurich:** I think we can look to Europe for some sense of where our future is going with DCBs, as they've had them for a few years now, with multiple products on the market. I've had the pleasure of speaking with some of our European colleagues, and they saw that after the initial excitement for DCBs died down, and as the market matured, there was a shift back toward stent usage overall. If you look at the large trials and the real-world trials, what we find is that there's about a 20% to 25% stenting rate in all patients. So, I think there is always going to be a certain need for stents, but what I'm curious about is how far are we going to swing in that spectrum. This remains to be seen in the United States.

**Dr. Garcia:** One issue is that we'll need 200-mm balloons that have reasonably good inflation pressures in terms of volume and diameter and that deliver the drug to a longer swath of vessel to keep costs low. We also need head-to-head comparator trials between DCBs and drug-eluting stents and/or DCBs and bare-metal stents. If the dominoes fall in favor of the DCB across these types of trials, then I would only foresee that DCB use will go up. If at any time the DCB falters, and a different therapy is better suited, then that will become the default therapy. It's survival of the fittest when it comes to these head-to-head comparator trials.

Overall, I think DCBs have an exceedingly good chance of winning because the downstream failures of endoprotheses, whether it be bare metal or drug eluting, are critical. Once those failures occur, there's no taking it back—the damage is done. Those failures portend poor prognostic events over time, and if we see these failures, then DCBs will take off and become the default therapy.

**Dr. Krishnan:** The future of DCBs is bright; however, we still need longer-term data.

**Dr. Geraghty:** We're currently running the LUTONIX DCB below-the-knee trial, and we're very excited to see the results of that. CLI is an area in which we're in desperate need of better therapies. The DCB manufacturers have put a lot of effort and funding into doing this study right, and we hope to complete enrollment this year. If the results confirm that this DCB offers better results than traditional angioplasty in treating the distal popliteal and tibial disease that almost universally affects CLI patients, that would be a real step forward. ■

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