PANEL DISCUSSION

Trends and Needs in Deep Vein Thrombosis and Central Venous Occlusion Care

Experts discuss their approaches to deep venous occlusion, preventing redo procedures, dealing with challenges, and current and future needs.

With Kush R. Desai, MD, FSIR; Rick de Graaf, MD, PhD; Misaki Kiguchi, MD, MBA, FACS; and Jorinde van Laanen, MD

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When you approach a deep venous occlusion case, how do you plan ahead to reduce the likelihood of a redo procedure? What has past experience taught you about how to predict these outcomes?

Dr. Desai: Let me reframe the question: What are the possible failure mechanisms after treatment of a thrombotic (acute or chronic postthrombotic) venous obstruction? Broadly, they separate into technical (procedural) errors and management issues, with the latter including patient factors. I will focus on a few of the dominant concerns. Starting with technical issues, whether acute or chronic, inflow must be respected. If there is insufficient inflow, reocclusion is likely. In chronic obstruction (and indeed some acute), there is significant postthrombotic involvement of the common femoral vein (CFV); therefore, I have found that close attention to the quality of profunda inflow is vital. Without a good-quality profunda, I have found that there is a high risk of rethrombosis. To assess the profunda, selective venography and intravascular ultrasound (IVUS) are often both necessary, and unfortunately, as of now, judgment is largely subjective and experiential. Assuming that the profunda is sufficient, stent placement in the CFV is needed and usually leads to durable patency. The second common technical issue where failure occurs is incomplete disease coverage, whether at the inflow or outflow end. Bridging disease from the profunda (in the event of a diseased CFV) to healthy outflow is the key to success, and IVUS can be very helpful here. The only difference in acute cases is that if there is thrombus in the inflow, particularly pro-

funda or CFV, it needs to be removed to ensure that the iliofemoral outflow tract remains patent.

Management after the procedure, including ensuring patient compliance, is often overlooked but is as important as the procedure itself. Before I do the procedure, I assess the patient's ability to take anticoagulation, including comorbidities and financial concerns. Some questions I ask: Can they afford the medicine, and if not, how can I arrange for them to be able to successfully obtain medication? Are there barriers to them taking the medication? These can vary, including medical (ie, fall risk, recent surgery, metastatic disease) and psychiatric comorbidities. If I have concerns about whether the patient can take anticoagulation, this must be addressed before intervention. If there is a clear contraindication to anticoagulation, I see little value in treating other than in the very rare potential limb loss situation (ie, phlegmasia). After the procedure, I impart to the patient that compliance with anticoagulation is critical to success.

Dr. de Graaf: A redo is most likely the result of suboptimal inflow. If my MR venography shows scar tissue at the level of the femoral confluence, I take a contralateral crossover approach. After IVUS evaluation, I select the optimal landing spot for the stent without being constrained by access side. An inadvertent deep position will thus be prevented as well. One thing we have learned is that severe involvement of both the femoral and deep femoral veins is not supportive of stent patency. Neither an endovascular nor a hybrid strategy has a good outcome and should be avoided in these patients.

Dr. van Laanen: In the workup, we try to get as much information as possible about inflow and outflow. Inflow is especially important. We evaluate by duplex ultrasound and MR venography. In case there are severe postthrombotic changes in both the femoropopliteal and deep femoral veins, there is a high risk of occlusion due to impaired flow. In the past, we tried to solve this issue with endophlebectomy and arteriovenous (AV) fistula. In this hybrid surgery there is a high risk of complications, mostly (deep) infection and lymphorrhea. Nowadays, we tend to stay conservative in cases of severe involvement of both femoral veins. Also, the patient's general condition is important for outcome. Is the patient mobile, able to use anticoagulants, willing to take medication, and compliant to therapy? If not, risk of reocclusion is high. We give pneumatic compression both during the procedure as well as the first day after the procedure. Heparin is also used during the procedure, with low-molecular-weight heparin directly after and direct oral anticoagulants (DOACs) starting on day 1.

Dr. Kiguchi: The key to success of a deep venous occlusion case lies in having adequate inflow and outflow. If a patient does not have good inflow at the end of the case, the likelihood of needing a redo procedure is high, and thus, I consider adjuvant therapies to increase the inflow (ie, extending the stents down to the profunda vein, endovenectomy, AV fistula).

Past experience in treating redo procedures has readily shown me that there is often a reason that can be identified on a previous venogram that predicts need for reintervention, and thus, identifying them with a critical eye at the original case has led me to mitigate the need for redo procedures, and if not fixable at the time of the procedure, have a high index of suspicion of what needs to be done if symptoms recur.

What do you consider a "threatened" venous stenting case? Is your threshold stenosis on imaging or presence of symptoms? Do you intervene in the asymptomatic patient with prior venous stenting who has stenosis on surveillance imaging? How do you decide when to intervene and when to wait?

Dr. van Laanen: Good question, and I think that is a subject for further research. Both stenosis on imaging and symptoms play a role. For asymptomatic restenosis < 50%, we do follow-up and no intervention. For asymptomatic stenosis > 50% in the first weeks after stenting, we do a reintervention. In the long term, asymptomatic stenosis > 50% requires close monitoring (repeat duplex at 4 weeks) and, in case of further progression, reintervention. Symptomatic stenosis > 50% also requires reintervention.

Dr. Desai: This builds a bit off the answer to the previous question. "Threatened" stents are those where some element is not optimized, either technical or medical; experience and attention to detail, along with making the patient an active participant in their care, are the critical components to mitigating stent occlusion.

The discussion on stent "stenosis" is nuanced. Early in my career, I was concerned when I would see stent buildup; I took this as a sign of impending occlusion. With time and experience, I have observed that is not necessarily the case; attention to patient symptoms is important here. If symptoms initially improved and have returned and are not attributable to another cause (ie, superficial venous disease or phlebolymphedema), then the stenosis needs to be addressed. However, if the symptom burden remains improved, then I think close surveillance is sufficient. Why have I changed my position? It's the observation that the stent—which is by definition noncompliant—is a fixed diameter. If the size of the inflow vessel is smaller than the stent, the laminar flow column through the stent is smaller than the expanded diameter of the stent. We can expect the edges in the stent to develop scar from turbulent flow/eddy currents in these cases without change in symptoms. I certainly don't have data to support this observation, but I have seen this consistently throughout my career.

Dr. Kiguchi: I typically order surveillance imaging quarterly; however, intervention based on imaging depends on the individual patient. If a patient had severe symptoms, recurrent symptoms such as venous ulcers, and the degree of initial intervention was complex, my threshold to reintervene based on positive imaging is low. Because there is no evidenced-based criteria of degree of stenosis predicting stent occlusion, I tend to be more aggressive in patients with moderate to severe asymptomatic stenosis on imaging, as intervention of stenosis is likely much less complex than total occlusion. If the patient has mild stenosis and is asymptomatic, I continue surveillance and monitor symptoms to guide when to intervene.

Dr. de Graaf: Those cases with increasing lumen reduction should be closely followed and treated when it exceeds 50%, regardless of symptoms. When this threshold is identified on duplex ultrasound, venography with IVUS is performed with angioplasty and restenting in the same session. The first follow-up is performed at 2 weeks. When no stenosis is seen, the next follow-up is scheduled at 6 months, usually 2 weeks after termination of oral anticoagulation. Depending on the result, the patient is either released from follow-up or put back on oral anticoagulation with strict follow-up with a 2-week interval.

Do you extend medical management if incidental and asymptomatic?

Dr. van Laanen: Yes, normally we stop anticoagulants after 6 months if there is no indication other than venous stent. In case of restenosis—also < 50% and asymptomatic—we continue anticoagulants.

Dr. Kiguchi: In my practice, I tend to keep stented patients on low-dose anticoagulation and antiplatelet as long as the patient can tolerate it, and thus, extending medical management does not necessarily apply to these patients. However, if this were not the case, medical management is not my first line to treat asymptomatic positive surveillance imaging. The only exception would be if the patient had acute deep vein thrombosis (DVT), despite being asymptomatic, and in this case, I'd treat according to the CHEST guidelines.

Dr. Desai: I largely base medical management on the cause of the event; was it provoked or unprovoked? The latter usually requires indefinite anticoagulation, and I seek the help of my hematology colleagues in these cases. If provoked but a recurrent event, similar to unprovoked, indefinite anticoagulation is often necessary. There is a bit of nuance in the treatment of patients with extensive postthrombotic obstruction. In these cases, there is far more "art," meaning that if a patient only had one thrombotic event but an extensive occlusion, I may be inclined to implement low-intensity DOAC therapy after 1 year of patency. More research is needed in this area, much like antiplatelet and statin therapy in venous obstructive disease.

When you consider the current endovascular armamentarium, what is most lacking? What capabilities would be a game-changer in your practice?

Dr. Kiguchi: Dedicated inferior vena cava (IVC) stents are coming down the pipeline and will help in patients with IVC disease. Drug-coated venous stents, in addition, may also increase stent patency and decrease the need for redo interventions and maintenance anticoagulation/antiplatelet. Crossing devices across chronic venous obstruction will also be helpful in treating deep venous disease.

Dr. de Graaf: Endovascular lumen gain techniques below the femoral confluence, with additional focus on valve incompetence. Obviously, the straightforward recanalizations of the iliac veins have very good mid- to long-term patency. For patients with extensive iliofemoral obstructions, the inflow into the stents is compromised and, with that, patency suffers. To facilitate optimal patency in those patients, inflow has to improve. To achieve this, debulking techniques are the preferred option. Without functional valves though, this technique will be counterproductive. Therefore, (endovascular) valve implantation is an essential additive.

Dr. van Laanen: What would be very interesting is a sharp recanalization device with feedback on the tissue it's in. This would be useful for difficult recanalizations in which we could use sharp devices with lower risk of complications.

Dr. Desai: Purpose-built venous stents have really propelled the treatment of venous obstruction; we now have devices for the treatment of even more complex venous obstruction (ie, iliocaval disease) in clinical trial. However, the data thus far suggest that occlusion rates in postthrombotic disease remain high. Paired with the fact that venous patients skew younger than arterial disease patients, this trend is alarming. Thus, we need advancements that specifically address these concerns.

Acutely thrombosed stents are generally straightforward, provided that you identify the reason for thrombosis. Newer mechanical thrombectomy devices are quite efficient at removing thrombus, many of which work well in acutely thrombosed stents. For existing chronically occluded stents, we are currently left with the problem of crossing (a frequently grueling task) and then simply ballooning and/or placing another stent. We also know that once occlusion has occurred, it is more likely to occur again. Thus, we need devices to aid in crossing these occlusions quickly and safely (hopefully, some promising devices are on the way) and then debulking the dense, fibrotic material within stents

(type 1 and 3 collagen, predominantly) such that when patency is restored and the cause of occlusion is addressed, a "stent in a stent" is not needed. Finally, it would be ideal to build in antithrombotic properties into stents. We know that "life happens"—patients forget medications or become acutely ill for example. In these cases, a margin of safety "built in" to the stent may limit the need for reintervention in such cases.

What devices are we currently in need of with respect to acute and chronic in-stent restenosis?

Dr. Desai: I will add one element: We need validated, objective metrics that demonstrate when restenosis is the cause of the patient's symptoms. This is a difficult task, given that symptoms can be multifactorial, including superficial and lymphatic causes.

Dr. van Laanen: Interesting question. In restenosis, I think mostly the flow is the major problem, so it is not necessarily a device/stent problem. Further research into whether restenosis is mostly thrombus or also some hyperplasia in the long term is interesting and might direct us further to optimizing medical therapy. Antithrombogenic stent material can be interesting in this respect. Stents with maximum radial force and limited material can also be very interesting to further reduce foreign body. More optimal devices for sharp recanalization in total occlusion can be helpful; however, often the flow is the major problem, and after recanalization, the rate of reocclusion remains high.

Dr. de Graaf: Obviously, everyone is begging for debulking devices. However, without treating the cause of the in-stent restenosis (ie, improving venous inflow), stent recanalization will be an endless endeavor. With proper anticoagulation and sufficient inflow, it is extremely unlikely that venous stents reocclude, at least in my experience.

Dr. Kiguchi: Although some markets have this already, a stent debulking device will be useful in attaining luminal gain for reinterventions.

Do we need a new randomized controlled trial (RCT) for deep venous occlusion? What are the data that would help better inform practice?

Dr. de Graaf: RCTs for chronic deep venous obstructions are not only going to be very unpopular with the patients, due to the unlimited variables in these patients, but also it will be vastly impossible to obtain reliable results. I am more in favor of a global registry of selected centers with independent core lab evaluation of clinical, procedural, and imaging data.

Dr. Kiguchi: With the advent of new, large-bore thrombectomy devices, we need RCTs to compare proximal endovascular deep venous treatment in the acute system versus anticoagulation alone to prevent progression of venous symptoms and quality of life. The answers to when to intervene and which patients most benefit would likely be answered. Although ideal, conducting these randomized trials to establish strong evidence-based guidelines will be difficult given the already available technologies on the market and patient variability.

Patients with severe symptoms from chronic occlusions should be treated with endovascular deep venous intervention to improve quality of life; an RCT comparing patients with chronic occlusions versus anticoagulation alone is unlikely to change practice, as most would agree to treat based on symptoms.

Dr. Desai: RCTs are difficult to conduct and enroll but represent the best mechanism to obtain bias-limited evidence that can move the field forward. Take ATTRACT, for example. With a reasonably high degree of certainty, we now know that acute iliofemoral DVT patients are the ones most likely to benefit from intervention in terms of postthrombotic syndrome severity reduction. It is now on us in the endovascular community to demonstrate value with newer devices utilizing rigorous trial design. For postthrombotic occlusions, we need to support the currently enrolling C-TRACT trial. This represents the best opportunity to evaluate the role of endovascular therapy in chronic iliofemoral obstructive disease and, like ATTRACT, will result in a clearer understanding on the management of postthrombotic deep vein obstruction.

Dr. van Laanen: I think we do. The main questions are still in optimizing patient selection, trying to prevent postthrombotic syndrome (so, optimizing DVT treatment), patient-reported outcome measures, and determining the value of long-term follow-up and anticoagulants. Collaboration between all centers is very important here because it is very difficult to do RCTs on generally accepted treatment.

Thank you for your work here, these are very important and interesting topics! ■

Disclosures
Dr. Desai: Speaker's bureau for/consultant to Cook Medical, Boston Scientific, Becton Dickinson/CR Bard, Medtronic, Penumbra, Tactile Medical, and Philips; consultant to W.L. Gore, Shockwave Medical, Asahi Intecc, Veryan, and Cordis.
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