Vascular Closure Device Update

What's on the market, and what's in the pipeline.

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The description of the Seldinger technique in 1953 created a novel problem—physicians were creating holes in the common femoral artery that now needed to be closed. The first, and still gold standard, method for addressing this problem was the use of manual compression. As the holes got bigger and constraints on physicians' time became greater, novel solutions to this problem began to emerge.

The vascular closure device (VCD) market has grown exponentially since its inception in the early 1990s. Global estimates for the market in 2013 approach $1 billion; this growth reflects several factors. The use of manual compression may be of limited utility in obese patients or patients on anticoagulation, and the complexity of procedures performed with a percutaneous endovascular approach has grown, often with an associated increase in sheath size. In such situations, the ability for manual compression to achieve hemostasis may be decreased. As the economic landscape of health care becomes more competitive, VCDs are becoming increasingly valuable because their use can free up medical personnel for other responsibilities. Early ambulation and improved comfort also boost patient satisfaction—an increasingly monitored metric.

This article is an update of a previous review of VCDs,[1] beginning with a review of the recent literature and trends in VCD development. The Society of Interventional Radiology quality improvement guidelines for the use of VCDs will be referenced.[2] Later, concepts of VCDs will be revisited, and the most popular VCDs will be discussed. A more thorough list, with brief description, is presented in Table 1.

RECENT LITERATURE

The past year has seen the release of two pivotal randomized controlled trials that will have a major impact on the use of VCDs in clinical practice. The results of the ISAR-CLOSURE trial were published in the November 2014 issue of the *Journal of the American Medical Association*.[3] This was a large, multicenter trial that enrolled more than 4,500 patients across Germany to manual pressure or closure using the FemoSeal (St. Jude Medical, Inc.) or the Exoseal VCD (Cordis Corporation). Patients were randomized 1:1:1; the primary endpoint was the incidence of vascular access site complications (composite of hematoma > 5 cm, pseudoaneurysm, arteriovenous fistula, access site–related major bleeding, acute ipsilateral leg ischemia, need for vascular surgical or interventional treatment, or local infection at 30 days). The study found that access site–related vascular complications were observed in 6.9% of VCD patients versus 7.9% of manual compression patients, confirming the noninferiority of VCDs compared to manual compression. Time to hemostasis and closure device failure were significantly lower in the FemoSeal group compared to the Exoseal group.

The PEVAR trial (Endologix, Inc.) was designed and conducted to assess the safety and effectiveness of percutaneous endovascular aortic aneurysm repair with use of a 21-F stent graft system and either a 6- or 10-F suture-mediated closure system.[4] Similar to the ISAR-CLOSURE trial, the study was constructed using a noninferiority trial design to compare percutaneous access with open surgical femoral exposure. One hundred fifty-one patients were randomized 2:1 to percutaneous access or open femoral exposure. The 6-F Perclose ProGlide device (Abbott Vascular) was used in 50 patients, and the 10-F Prostar XL device (Abbott Vascular) was used in 51 patients. The primary trial endpoint was defined as technical success without vascular complications at 30 days. The results of the study were striking. Compared with open surgical femoral exposure, the use of a VCD was associated with shorter

procedure time, shorter time to hemostasis, and trends in decreased blood loss and groin pain. The test of noninferiority of VCDs to femoral exposure was confirmed, with this finding sustained to 6 months. There were no conversions to open femoral repair.

This year also saw the release of quality improvement guidelines for the use of VCDs from the Society of Interventional Radiology.[2] Overall, the committee found that the existing evidence, weighted heavily toward the cardiology literature, demonstrates high success rates of VCDs, regardless of device mechanism. The committee warned, however, that the relevance of existing cardiology data to interventional radiology procedures is of limited value because different procedures and larger sheaths may confer greater risk to interventional radiology patients.

VCD MECHANISMS OF ACTION

When discussing VCDs, it is helpful to conceptualize them in a systematic way based on their mechanisms of action. For the purposes of this discussion, VCDs will be divided into three main categories. *Active approximators* physically close the arteriotomy with the use of a suture or a nitinol clip. *Passive approximators* deploy a plug, sealant, or gel at the arteriotomy site without actively closing the arteriotomy. Finally, external hemostatic devices are placed on top of the skin and are designed to achieve hemostasis by providing mechanical pressure at the arteriotomy site or by accelerating the clotting cascade.

ACTIVE APPROXIMATORS

Active approximators are designed to replicate surgical closure of an arteriotomy. By physically closing the arteriotomy, these devices theoretically do not require the use of any manual compression. With these VCDs, the use of anticoagulation is not a concern, and a procoagulant plug is not needed. As a result, groin scarring and discomfort related to inflammation are not a concern with this device class.

Suture-Based Devices

Suture-based VCDs were some of the initial devices designed. They percutaneously deploy a suture on either side of the arteriotomy site, mimicking open surgical closure. The sutures are then pulled together, closing the arteriotomy site, and resulting in mechanical hemostasis.

The Perclose device (Figure 1) is the prototypical suture-based VCD. This device was initially approved in 1997, but it has been revised several times over the years. Recent improvements include a pretied knot, a change to a monofilament suture, and a new mechanism to cut the suture. ProStar XL is indicated for 8.5- to 10-F closure. Perclose ProGlide can accommodate 5- to 21-F arteriotomies, making it a popular device in this category due to its versatility in closing small and large arteriotomy sites.

There are several advantages to this class of VCD. The arteriotomy is physically closed, so there are no reaccess restrictions, and anticoagulation is theoretically irrelevant. The main limitations of these devices are the learning curve and luminal distortion secondary to suture closure. When multiple devices are used to "preclose," even large arteriotomies can be safely closed, as shown in the recent PEVAR trial results.[4]

Clip-Based Devices

The StarClose SE (Abbott Vascular) deploys a 4-mm nitinol clip over the arteriotomy and requires a sheath exchange, but leaves nothing intravascularly. The metallic clip remains in place indefinitely, potentially limiting the evaluation of immediately adjacent structures on magnetic resonance imaging.

PASSIVE APPROXIMATORS

Passive approximators deploy a plug, sealant, or gel at the arteriotomy site without actively closing the arteriotomy. With this class of VCD, the plug is deployed on top of the arteriotomy, although the arteriotomy is not physically closed. Hemostasis is achieved because the plug expands when deployed in the subcutaneous tissues, and collagen in the plug accelerates the clotting cascade. If the plug is not collagen based, hemostasis is achieved through expansion of the plug on top of the arteriotomy, not through clot acceleration.

Collagen Plugs

Angio-Seal (St. Jude Medical, Inc.) is the most widely used VCD. The device uses an intravascular anchor to secure an extravascular collagen plug on top of the arteriotomy site. All components, including the intravascular anchor, are fully absorbed within 60 to 90 days. Use of an intravascular footplate to secure the plug atop the arteriotomy is unique, representing both a strength and limitation of the device. The footplate secures the plug, encouraging hemostasis without the need for compression. However, the footplate is an intraluminal device, making distal embolization a possibility. This concern is particularly relevant if re-entry within 90 days is necessary.

The VASCADE vascular closure system (Cardiva Medical, Inc.) is a fully integrated, extravascular, bioabsorbable femoral access closure system. The system

offers dual mechanism of action, mechanical and physiological, and combines Cardiva's collapsible disc technology and a thrombogenic resorbable collagen patch in an integrated design. VASCADE demonstrated rapid hemostasis and low complication rates in a multicenter, prospective, randomized trial of 420 patients (the RESPECT IDE trial). In this trial, there were no major complications, and the incidence of minor complications was 1.1%, demonstrating a statistically significant reduction as compared to manual compression.

The FemoSeal VCD (not yet approved by the US Food and Drug Administration) is similar to the AngioSeal device, as there is an intravascular anchor plate that is approximated to the femoral arteriotomy. The main difference is that instead of an extravascular collagen plug being anchored to the intravascular footplate, there is an extravascular locking disk that is apposed to the vessel wall, which is secured in place to the intravascular footplate by an absorbable filament.

Sealant- or Gel-Based Devices

New to the sealant- or gel-based platform is the X-Seal VCD (Essential Medical, Inc.), which recently received CE Mark approval. The same company is developing a platform that will be suitable for closure of an 18-F arteriotomy. First-in-man studies have been successful, with the device producing rapid hemostasis of a large-bore arteriotomy with good clinical and angiographic results in a small number of patients.

The Mynx (Cardinal Health) family of devices functions by delivering a polyethylene glycol sealant to the extravascular space over the arteriotomy site. The sealant does not enhance coagulation, but conforms to the arteriotomy site, sealing the vessel. The devices contain a new Grip sealant that is designed to increase the sealant volume by up to 300% when the device is deployed. The sealant also advertises increased adherence of the plug to the arteriotomy. One benefit of the MynxGrip device is that it does not require a sheath exchange, and it also recently received approval to close femoral veins. The MynxAce device was recently added to the product line and features an easy-to-use delivery system.

The Exoseal VCD (Figure 2) uses a similar mechanism by deploying a polyglycolic acid plug over the arteriotomy. The deployment system is different from the Mynx device in that visual indicators guide deployment. As a result, tactile feedback is not needed, which may potentially shorten the operator learning curve.

The FastSeal (Vascular Closure Systems) is a bioabsorbable plug that is advanced through the 6- or 7-F procedural sheath, at which time, the plug expands intravascularly. The sheath is then withdrawn, and the plug locks into place at the arteriotomy site, producing hemostasis. The intravascular component absorbs in 2 to 3 weeks, and the extraluminal component absorbs in approximately 2 months. Per the company's website, the device has completed first-in-man studies but has not yet received CE Mark or US Food and Drug Administration approval. There is a version of this device suitable for 18-F arteriotomy closure that is in development as well.

Compression-Assist Devices

Compression-assist devices are a type of passive approximator that do not use a retained suture, clip, or plug. The Axera 2 access system (Arstasis) creates a low-angle arteriotomy to achieve hemostasis. Femoral artery access is achieved using a 19-gauge needle in a conventional manner. Using the Axera 2 device, this access is converted to a shallow 10° to 15° access through which the procedure will be performed. After the procedure is complete, the sheath is removed, and manual pressure is held. The shallower angle hastens hemostasis due to increased arterial wall overlap and tract compression by the radial pressure of pulsatile blood.

The Catalyst II and Catalyst III devices (Cardiva Medical, Inc.) have an intravascular nitinol disk at the

TABLE 1. FDA-APPROVED VASCULAR CLOSURE DEVICES

Device Category	Device Name	Manufacturer	Puncture Size (F)	Comments
Active Approximators				
Clip or staple	StarClose SE	Abbott Vascular	5, 6	Second generation. Extravascular nitinol clip approximates arteriotomy site.
Suture	Perclose A-T	Abbott Vascular	5–8	Percutaneous deployment of a braided polyester suture with a pre-tied knot around the arterial puncture site.
	Perclose ProGlide	Abbott Vascular	5–21	Percutaneous deployment of a monofilament polypropylene suture with automatic knot formation. Two devices and a preclose technique are required for sheath sizes > 8 F.
	Prostar XL	Abbott Vascular	8.5–10	Percutaneous braided polyester suture delivered, designed for use after procedures requiring larger procedural sheaths.
Passive Approximators				
Collagen based	Angio-Seal	St. Jude Medical	5/6, 7/8	Device deploys an absorbable collagen plug to close the arteriotomy site, secured in place by intraluminal anchor and absorbable suture. New delivery mechanism allows for one-handed and decreased variability.
	Vascade Vascular Closure System (VCS)	Cardiva Medical, Inc.	5–7	Bioabsorbable femoral access closure system leaves no permanant components behind. Combines collapsible disc technology and a thrombogenic resorbable collagen patch in an integrated design.

end of an 18-gauge nitinol wire. After the procedure, the disk is introduced into the artery, and gentle traction is then applied to the wire to appose the disk to the arteriotomy. The device is left in place for 30 minutes and then removed in its entirety. The family of devices can be delivered through 5- to 7-F procedural sheathes. Catalyst II is coated with kaolin and chitosan, used to promote coagulation by activating the clotting cascade and causing platelet aggregation. Catalyst III is coated with an additional drug, protamine sulfate, acting locally to neutralize heparin and further aid the body's natural healing process.

EXTERNAL HEMOSTATIC DEVICES

Broadly, this category includes patches or pads that promote coagulation by concentrating clotting factors and devices that manually exert pressure on the arteriotomy. These devices can also be used in concert with other VCDs, should the operator desire.

Due to the increased use of transradial access at several centers, external manual hemostatic devices are increasingly being used in many settings. Transradial access has several advantages over transfemoral access. The cost of a radial hemostatic device is significantly less than that of most VCDs used after transfemoral

TABLE 1. FDA-APPROVED VASCULAR CLOSURE DEVICES (CONTINUED)

Device Category	Device Name	Manufacturer	Puncture Size (F)	Comments
Sealant or gel based	Mynx Ace	Cardinal Health	5–7	Grip Technology sealant actively adheres to the artery for secure mechanical closure; Grip technology is completely extravascular and dissolves within 30 days. New delivery system uses 1, 2, 3–button approach for consistent deployment.
	MynxGrip	Cardinal Health	5–7	Grip Technology at the distal end of the original Mynx Sealant adheres to and seals the arteriotomy while expanding to fill the tissue tract; the Grip Technology Sealant is completely extravascular and dissolves within 30 days. Indicated for femoral arteries and veins.
	Exoseal	Cordis Corporation	5–7	Device deploys polyglycolic acid plug through existing sheath into the extravascular space.
	FISH CombiClose	Morris Innovative, Inc.	5–8	Device uses an extracellular matrix closure patch premounted onto the access sheath through which intervention is performed.
	FISH ControlClose	Morris Innovative, Inc.	6, 7	Device uses an extracellular matrix closure patch premounted onto the access sheath through which intervention is performed.

access. Although VCDs decrease time to ambulation compared to manual pressure for transfemoral interventions, there are no ambulation restrictions after radial access. Transradial access may be particularly attractive in coagulopathic patients in whom a retroperitoneal or groin hematoma could lead to significant morbidity and mortality. A small hematoma in the wrist is blatantly obvious, whereas significant bleeding may occur before a retroperitoneal or groin hematoma becomes obvious.

Radial access is not appropriate for all patients. If a sheath size > 6 F is needed, radial access is likely not appropriate. In tall patients or those in whom lower extremity intervention is needed, catheter length can become an issue. In a small minority of patients, radial access is not appropriate because the perfusion to their hands completely depends on the radial artery. In these patients, a radial artery occlusion, however unlikely, could have a devastating consequence.

Finally, there are several external hemostatic devices suitable for achieving hemostasis after radial puncture (TR Band, Terumo Interventional Systems; Safeguard Radial, Merit Medical, to name a few).

THE FUTURE

New developments continue to advance the utilization of VCDs. Current trends are focused on developing devices that can safely and efficiently close large-caliber femoral arteriotomies. As transcatheter aortic valve repair and percutaneous endovascular aneurysm

TABLE 1. FDA-APPROVED VASCULAR CLOSURE DEVICES (CONTINUED)

Device Category	Device Name	Manufacturer	Puncture Size (F)	Comments
Compression Assist				
	Cardiva Catalyst II	Cardiva Medical, Inc.	5–7	Intravascular disk left in place under tension to create hemostasis. After hemostasis is achieved, the disk is removed.
	Cardiva Catalyst III	Cardiva Medical, Inc.	5–7	Intravascular disk left in place under tension to create hemostasis. Device has protamine coating to locally neutralize heparin. After hemostasis is achieved, the device is removed.
	Axera 2 Access Device	Arstasis, Inc.	5, 6	Access to femoral artery is achieved with a micropuncture kit. Axera 2 access device is then used to create an access tract with a longer and shallower trajectory. Brief compression is held for a few minutes.

For listings of available hemostatic patches and assisted compression devices, see the Endovascular Today 2015 Buyer's Guide.

repair become commonplace, there will be tremendous incentive to develop and prove the utility of a simple but effective VCD. There remains no perfect device. While balancing the goals of early ambulation and patient comfort against anatomic and procedural details, as well as coagulation status, one thing is clear: in order for the endovascular physician to safely and effectively achieve hemostasis in a range of patients and clinical situations, comfort and knowledge of a variety of VCDs is of paramount importance. ■

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