Overview of Vascular Closure

The *Endovascular Today* annual review.

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As a minor rite of spring, for the third year in a row, we are reviewing the state of vascular closure. Closure device utilization has continued to grow. The rising tide lifting this growth is the increasing expansion of diagnostic and interventional procedures, with the total estimated to be approximately 10 million cardiac and peripheral arteriograms worldwide this year. Remarkably, the use of vascular devices (VCDs) is also rising as a percentage of these cases, with a significant component of the growth fueled by increasing use of topical patches. "Remarkably" is appropriate, given the less-than-sterling evidence base supporting the use of vascular closure devices overall, and the meager information on patches in particular. The continuing enthusiasm of a segment of the invasive community is a tribute to the perceived effectiveness of closure facilitated by these devices, and the ongoing need for approaches superior to external compression.

Despite persistent concerns about overall device safety and hospital costs, the vascular closure device market is now a half billion dollar industry. Fueled by this growth, a number of small and large companies have entered or are entering the vascular closure device arena. There has been a particularly odd feature of vascular closure—the largest device companies selling coronary and peripheral stents, some with products in almost every niche of invasive medicine, have not offered closure devices until now (except for Abbott Vascular Devices [Redwood City, CA], which has a growing portfolio of both). With the purchase of AngioLink by Medtronic (Santa Rosa, CA) and an investment by Boston Scientific Corporation (Natick, MA) in Therus (Seattle, WA), as well as a number of other not as yet public initiatives, this is likely to change in the coming year.

CATEGORIZING DEVICES

In addition to the table we have provided in the past, I believe it is time to subcategorize these devices by location of application, category of action, properties that facilitate hemostasis, and whether they leave behind a foreign body (Figure 1). Thus, I would suggest using deep (D) versus surface (S) to separate the devices that are placed in the tissue track or artery versus those that are applied on the skin; active (A) versus passive (0) to separate those that actively approximate the edges of the arteriotomy versus those that do not; clot (C) inducing versus those that have no active agent such as collagen (0); and temporary (T) or permanent (P) for those that leave behind a foreign body that resorbs

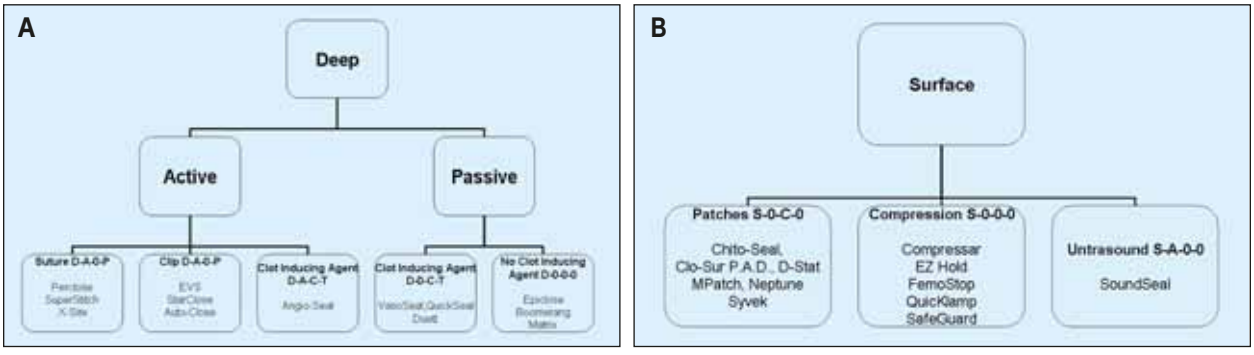

Figure 1. Classification of closure devices by deep (D) versus surface (S), active (A) versus passive (0), clot-inducing agent (C) versus none (0), and presence of foreign body beyond 24 hours (T) or permanently (P) versus no foreign body (0). Because of resorption properties, the Duett could be classified as D-0-C-0 and the Matrix as D-0-0-T. See the Closure Device Chart on pages 48-49 for details regarding manufacturer, device type, puncture size, wire compatibility, FDA approval, and CE Mark.

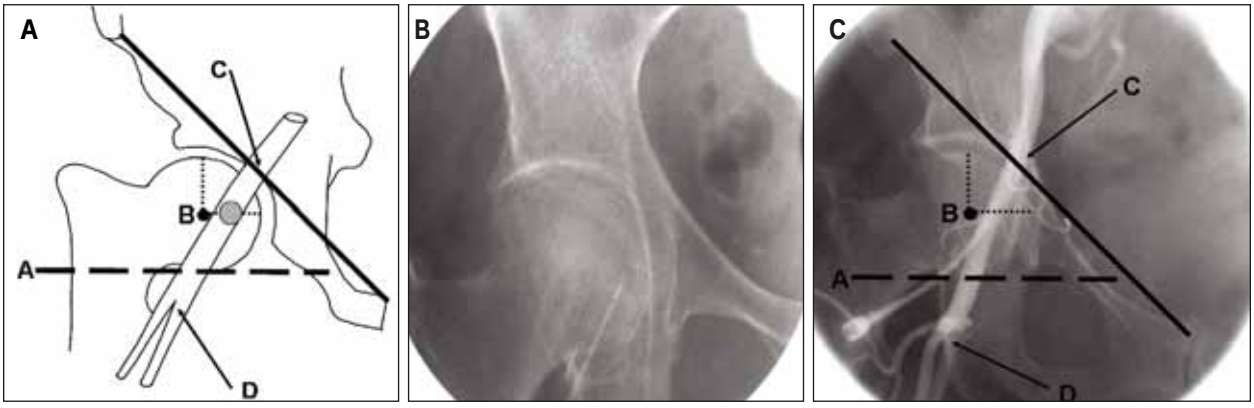

Figure 2. A suggested approach to vascular puncture. A diagram of the anatomy of the femoral head is seen in panel A. Line A represents the bottom of the femoral head, B is the center of the femoral head, and line C represents the approximate location of the inguinal ligament based on bony landmarks. The dotted lines identify the upper inner quadrant of the femoral head, with a filled circle over what we believe is the ideal puncture site. Only approximately 1.5% of femoral bifurcations occur above this spot. All except D, the femoral artery, can be visualized with plain fluoroscopy. In panel B, the needle has been placed subcutaneously to a point just over the femoral artery, which can usually be felt pulsating through the needle. Fluoroscopy in the anterior posterior view confirmed its location roughly over the filled circle seen in panel A. Panel C shows the angiographic landmarks with the sheath in place. The actual location of the puncture (best seen in the contralateral view) was at the site of the filled circle in the first panel.

either within 60 days or that stays permanently in/on the artery or tissue track. I equate those that leave no foreign body (0) with those that resorb very early (Duett, Vascular Solutions, Minneapolis, MN). Thus, one could categorize Perclose (Abbott Vascular Devices) as a D-A-0-P (deep-active-no clotting agent-permanent foreign body), AngioSeal (St. Jude Medical, St. Paul, MN) as D-A-C-T, VasoSeal (Datascope, Montvale, NJ) as D-0-C-T, and the Duett as D-0-C-0, whereas the patches are S-0-C-0. Although the coding may be impractical for the average practitioner, the categories will help differentiate the expanding list of devices.

EVOLVING TECHNOLOGIES

A number of new devices have appeared on the horizon, some in early development, some available for use in Europe, and only a few released in the US. Gels and plugs include AccessClosure's Matrix (Mountain View, CA), a polyethylene glycol gel that has a delivery system with some similarities to the Duett, but with a number of innovations. The solution itself is said to be nonthrombogenic on intravascular injection, the latter being a concern for users of the Duett's thrombin-collagen mixture. The expansion of existing technology includes several suture devices—Proglide (Abbott Vascular Devices), SuperStitch (Sutura, Fountain Valley, CA), and X-Site (Datascope). Several vascular clips have appeared, including the EVS system developed by AngioLink (recently acquired by Medtronic) and the StarClose already released in Europe by Abbott. These devices are designed to provide active closure of the arteriotomy without leaving a foreign body inside the vessel; they do, however, leave a metal clip imbedded in the arterial wall. Two devices continue in development that leave behind no foreign body and use no active thrombosing agent. The Boomerang ClosureWire (Cardiva Medical Inc., Mountain View, CA) tamponades the arteriotomy site with a disc placed inside the artery at the fenestration, and is held in place until hemostasis occurs, after which it is withdrawn (manual compression is then applied to allow the fenestration left by the smaller profile of the device to seal). Epiclose (CardioDex Ltd., Tirat-Hacarmel, Israel) uses a balloon to tamponade the vessel at the arteriotomy external to the artery. Not enough data are available as yet to determine if these devices are effective, particularly in the setting of percutaneous interventions.

In my opinion, Therus' SoundSeal is the most novel of the technologies. Of all the devices on the horizon, SoundSeal has the potential to revolutionize vascular sealing; however, one can envision multiple problems that may or may not be resolvable. As understood from the limited information available on this technology, an ultrasound probe is placed on the skin over the puncture site with the sheath in place. Once the arteriotomy, including the site of sheath entry, is properly visualized by ultrasound imaging, the sheath is withdrawn while pressure is held and ultrasound energy is applied to denature collagen in the vessel wall. The melted collagen provides a plug to seal the vessel. The entire procedure is noninvasive and no foreign body is left in place. The device attempts to address a number of limitations of exist-

ing technology. One can envision a single station in the holding area of a busy catheterization laboratory: the device could be used in patients after they leave the cath lab, saving precious laboratory time and, if medicolegal limitations were addressed, the device could potentially be deployed by a technician. There are also a number of technology-related issues that need to be resolved. First, the artificial intelligence for the algorithm (assuming the device is automated) may not be able to adapt to the many heterogeneous types of tissue anatomy to identify the proper scenario for firing the ultrasound beam. Collagen is melted by the heat of the ultrasound; presumably, one could envision potential collateral damage, such as to accessory nerve branches immediately adjacent to the arteriotomy. Although I have categorized the device as active because it heats collagen in the arterial wall, it is uncertain if the melted collagen would work any better than the passive devices in fully anticoagulated patients with, for example, a high pulse pressure.

THE EVIDENCE BASE

We have discussed in these pages during the past 2 years some of the reasons why closure device use remains ad hoc. Most areas of invasive cardiology have been explored exhaustively in terms of randomized clinical trials. Vascular closure devices are a striking exception. From initial animal testing to early and late phase clinical trials, the vascular closure device arena does not parallel much other device-related research. Animal models of vascular closure suffer in multiple ways. First, the animals used in device studies, pigs, sheep, and dogs, differ in femoral artery anatomy substantially from humans, particularly the middle-aged, obese, hypertensive, diabetic smokers that are the subject of many of the invasive procedures we perform. This is true even in the absence of frank atherosclerosis of the common femoral artery, although our data showed a 25% incidence in patients undergoing routine coronary angiography.[1] The differences in animals include very tough skin with little subcutaneous tissue, differences in the typical fibrous band seen over the femoral bundle, and lack of the typical tissue track and anatomic distortions brought about by obesity or prior invasive procedures. Vascular closure device success is also more likely in animals because of spasm of the femoral artery (particularly in pigs) and the typically low blood pressure and low pulse pressure of animals under anesthesia, all of which decrease bleeding at the puncture site and set an artificially low threshold for VCD success.

Human clinical trials have mostly lacked the basic requirements that we place on studies in other arenas. Blinding of patient and physician has been considered impossible or impractical. Randomization has necessary imbalances; for example, when manual compression is compared to a closure device, physician learning curves have frequently been included and anticoagulation between groups cannot be matched. Thus, typically very experienced technicians or nurses applied manual compression on patients with activated clotting times (ACTs) of 150 seconds, whereas physicians still learning the nuances of the device being tested deployed them in patients with ACTs of 250 seconds or greater. In an amazingly high percentage of these studies, the investigators did not bother to obtain an angiogram of the femoral artery prior to device deployment, despite the requirements expressly stated in the instructions for use, and despite the fact that skipping this step exposes the patient to needless additional risk. When closure devices are compared, physicians enrolling patients frequently have considerably more experience with one device than another. Most of the studies have relied on historical controls, have not used randomization, and have not used intention to treat or blinding. Enrollment bias has been a pervasive feature: in a number of studies comparing manual compression with closure devices, the patients with anatomic or physiologic contraindications to closure device use were enrolled in the manual compression arm, biasing the study in favor of vascular closure technology. Moreover, the endpoints used in these studies have been muddled at best. Time to hemostasis and ambulation are soft endpoints with arbitrary time frames and enormous potential for investigator bias. One could argue that in the case of topical patches, the limitation on blinding should not exist: these companies

TABLE 1. PREVENTIVE MEASURES THAT WOULD PREVENT MANY COMPLICATIONS

- Fluoroscope for access—we recommend using a hemostat to identify the level of the femoral head before injecting local anesthetic, and then fluoroscoping the needle after it has been introduced subcutaneously and the operator can feel the pulsation of the artery through the needle, but has not yet entered the vessel (Figure 2)
- Use smallest appropriate sheath
- Use weight-adjusted heparin
- Stop and compress if a vessel, artery, or vein has been entered, and a sheath has not been placed successfully.
- Re-prep both the skin and the field prior to use of a closure device, wear fresh gloves, and make sure that the work environment and devices are sterile
- Compress for an adequate period of time
- Perform femoral angiogram, whether or not a closure device is used
- Develop well thought-out plan for closure—femoral access and closure is a procedure!
- Supervise closure

should be urged to compare patches with and without active agent in the product, a readily performable exercise. It is odd that these studies, except for one small pilot of which I am aware, have not been performed.

To attempt to address the limitations of the individual clinical trials of VCDs, a second meta-analysis was published last year. Although hampered by the overall poor quality and heterogeneity of the studies, Nikolsky et al[2] analyzed 30 studies of vascular closure device complications enrolling 37,000 patients. While there was slight superiority of manual compression over vascular closure devices overall, this was not seen when only the randomized studies were included, and only VasoSeal, when used during coronary intervention (but not Angio-Seal or Perclose) actually showed inferiority. A word about VasoSeal—there are theoretical reasons for unanchored devices, whether plugs or other types, to have limitations in the fully anticoagulated patient on aggressive antiplatelet therapy. But the meta-analysis suffers from a reference data problem: the most recent study included, published in 2001, actually used VasoSeal only through the summer of 1998. Most of the VasoSeal data were from the early- to mid-1990s, an era when larger sheaths, more aggressive anticoagulation, and lack of familiarity with vascular closure devices was part of a larger learning curve for all operators. The influence of the changing platforms in cardiac intervention during the 1990s can be seen in the three early abciximab studies: the rate of major bleeding complications decreased from 10% in EPIC (published in 1994) to approximately 2% by the time of the EPISTENT trial published 4 years later.

Another suggestive article examined the American College of Cardiology–National Cardiovascular Data Registry.[3] The data set included 167,000 patients, of whom approximately 54,000 received closure devices. Overall, vascular complications were lower when vascular closure devices were used, although the protective effect appeared significant only for diagnostic, not interventional, procedures. Again, this data set suffers enormously from selection bias and missing data that could have altered the analysis substantially. In sum, the evidence base has not expanded substantially in the past year, and the need for a properly conducted, randomized, controlled trial has never been greater.

REDUCING COMPLICATIONS

The persistence of vascular complications has remained vexing to practitioners. Why do we still have approximately 20,000 vascular complications for each million diagnostic catheterizations and 40,000 vascular complications for a similar number of interventions? The list is long, but it is explained in part by attitude. For most invasive cardiologists and radiologists, access and closure is considered a pedestrian part of the procedure. Closure (especially manual compression) and, frequently, access are left to the most junior member of the team, despite the associated complication rate. A list of measures that would prevent many of these complications is provided in Table 1.

Given that vascular access remains the most important determinant (in my opinion) of ultimate success and complication rates of either manual compression or closure devices, it makes sense to anticipate complications and attempt to limit them. Death, in particular from retroperitoneal bleeding, remains an important concern for every clinician and laboratory. Repeatedly over the years, I have seen delay in recognizing transient postprocedure hypotension as retroperitoneal bleeding. Awareness of a high stick by routinely performing femoral angiography can go a long way toward anticipating which patients are most likely to have this problem (although not all retroperitoneal bleeds are due to puncture of the external iliac).

In a previous annual report in the April 2003 issue of *Endovascular Today*, I highlighted the four "Cs" of vascular closure devices: closure effectiveness, complexity of device delivery, complication rates, and cost. Closure effectiveness is now demonstrably in the 95% range for the most effective devices, especially when experienced hands follow the basic principles of optimizing access and closure. It makes sense for most clinicians to stick to one or, at most, two closure devices, to give their patient the benefits of their learning curve. Complexity of device delivery has largely improved, although it remains higher than desirable for some of the current products. Complication rates remain worrisome, not just for closure devices but for access and closure in general whether with manual compression or VCDs. Cost has trended downward, a result I believe, of competition and the advantages of expanding volume. Comfort and convenience (two more "Cs") remain important driving forces for the use of these devices, and represent the true success story for vascular closure in 2005. ■

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