Vascular closure devices (VCDs) introduce a novel means for improving patient comfort and accelerating ambulation after invasive cardiovascular procedures performed via femoral arterial access. Vascular closure devices have provided simple, rapid, and reliable hemostasis in a variety of clinical settings. Despite more than a decade of development, however, VCD utilization has neither been routine in the U.S. nor around the world. Their limited adoption reflects concerns of higher costs for cardiac procedures and a lack of data confirming a significant reduction in vascular complications compared with manual compression. Recent data, however, suggest that VCD are improving, complication rates associated with their use may be decreasing, and their utilization may improve the process of care after femoral artery access. Challenges in the second decade of VCD experience will include performing definitive randomized trials, evaluating outcomes in higher-risk patients, and developing more ideal closure devices. (J Am Coll Cardiol 2007;50:1617–26) © 2007 by the American College of Cardiology Foundation

Vascular closure devices (VCDs) were first developed in the mid-1990s, largely propelled by concerns of high rates of access site bleeding associated with percutaneous coronary intervention (PCI) procedures. Despite the goals of improving patient outcomes, patient comfort, and catheterization laboratory efficiency (1,2), VCD adoption has not paralleled the rapid pace of other interventional cardiology technologies (e.g., drug-eluting stents) (3). In an American College of Cardiology-National Cardiovascular Data Registry (ACC-NCDR) analysis of 166,680 diagnostic catheterization or PCI procedures performed in 2001, only one-third of patients received a VCD (4). Despite the considerable knowledge that has been gained in the past 10 years regarding the strengths, weaknesses, and potential applications of VCD, concerns about costs of VCD use and lack of superiority over manual compression have dampened enthusiasm for their routine use. While VCD use is not routine, the volume of VCD utilization in 2006 suggests that this technology is an important part of invasive cardiovascular procedures in many institutions: over 2 million VCD were sold in 2006 (1.6 million in the U.S. and 0.5 million in Europe) with a market growth of 11% in the U.S. and 8% in Europe (5). In this review, we will examine the evidence base concerning VCD use and comment on the challenges facing more widespread adoption of VCD use in the next decade.

VCDs: The First Decade

A brief history. Vascular closure devices are in their second decade of development for diagnostic and interventional cardiovascular procedures. The technologies approved from 1995 to 1998 focused on active closure methods including suture alone (2), extravascular collagen alone (6), and suture-collagen combinations (1) (Fig. 1). Since their introduction, the original devices (Perclose, Abbott Vascular, Redwood City, California; Angio-Seal, St. Jude Medical, St. Paul, Minnesota) have undergone multiple iterations while maintaining their core concept (7). Recently, a conceptually different type of active-closure VCD involving surgical staple/clip technology has also become available (StarClose, Abbott Vascular, Redwood City, California; EVS-Angiolink, Medtronic Co., Minneapolis, Minnesota) (8–10) (Fig. 2, Table 1). “Passive closure” technologies have been developed in parallel with the active closure devices. Passive closure approaches have focused on enhanced manual compression utilizing external patches with prothrombotic coatings (Syvek Patch, Marine Polymer Technologies, Danvers, Massachusetts) (11,12), wire-stimulated track thrombosis (Boomerang Wire, Cardiva Medical, Mountainview, California) (13), or assisted compression with me-
mechanical clamps; the passive closure devices do not afford immediate (<5 min) hemostasis (14,15) (Fig. 2). This review will focus on the immediate, active hemostasis closure devices given their greater utilization over the past decade.

The adoption of VCD has occurred because of a clear technological feat: VCD reliably shortens the time to hemostasis (elapsed time between sheath removal and first observed hemostasis) compared with manual compression and thus allows earlier patient ambulation (1,8,10,16,17) (Table 2). Alternative strategies for achieving early ambulation are the use of smaller sheaths for diagnostic catheterization as well as the use of the radial artery approach. The advantage of femoral vascular closure is that it can be performed immediately at the end of the procedure regardless of anticoagulation status; procedural success is expected in >95% of patients, and time to hemostasis is generally less than 5 min with Angio-Seal, Perclose, and staple/clip-mediated VCD (1,2,10,18). This compares favorably with hemostasis times of 15 to 30 min with standard 6-F manual compression. In addition, sheath removal via manual compression generally requires the operator to wait for the activated clotting time to reach a level of 180s (19), while VCD allows immediate removal of the femoral sheath regardless of anticoagulation status. While length of stay for PCI patients will not necessarily be reduced by early ambulation (unless same-day PCI is adopted), it can be reduced for diagnostic patients (2,16,20). And, for many patients, VCD can allow improved patient satisfaction and comfort related to the avoidance of prolonged sheath insertion and manual compression (19). Given this technological feat, it may be somewhat surprising that VCD have not become the standard of care for invasive cardiac procedures (21).

**Issues Challenging VCD Adoption: Complications and Cost**

What is the current rate of vascular complications associated with VCD? Vascular closure device pivotal studies have generally included 250 to 600 randomized patients. Given their limited sample sizes, such studies can reliably identify those complications that occur in 3% to 5% of the highly selected subjects enrolled in the trials (1,2,8,10,22). Vascular closure device trials have not been expanded to higher-risk patient cohorts; thus, there is a lengthy list of precautions and warnings on the instructions for use for each device (Table 1). For example, in the randomized trial leading to Food and Drug Administration (FDA) approval of the StarClose nitinol clip system for diagnostic cardiac catheterization, the list of angiographic and clinical exclusions included obesity, small femoral artery diameters, bleeding diatheses, femoral arterial disease, and nonfemoral sheath insertion (20).

There are concerns that the VCD may cause increased rates of rare complications, primarily based upon anecdotal case reports. Infections, femoral artery compromise, arterial laceration, uncontrolled bleeding, pseudoaneurysm, atrio-ventricular fistula, as well as device embolism and limb ischemia have all been reported after VCD utilization (4,23). These reports span all VCD types including Perclose (24,25), Angio-Seal (26), and StarClose (27). One study suggests that the severity of individual complications may be worse after VCD use compared with manual compression for PCI patients as VCDs are deployed at the point of maximal anticoagulation while manual compression is de-
Table 1 Indications, Contraindications, and Cautions for 3 VCDs

<table>
<thead>
<tr>
<th></th>
<th>Anglo-Seal®</th>
<th>Perclose†</th>
<th>StarClose†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Closure indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnostic cath</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PCI</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5-F sheath</td>
<td>NM</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6-F sheath</td>
<td>+</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>7-F sheath</td>
<td>+</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>8-F sheath</td>
<td>+</td>
<td>+</td>
<td>No</td>
</tr>
<tr>
<td>Ipsilateral access &lt;90 days</td>
<td>1 cm higher</td>
<td>No restriction‡</td>
<td>Not indicated</td>
</tr>
<tr>
<td>MRI safe</td>
<td>NM</td>
<td>NM</td>
<td>+</td>
</tr>
<tr>
<td><strong>Contraindication</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

**Warnings:** “Do not use if…”

- SFA or Profunda insertion: +
- Bilirubution insertion: +
- Above inguinal ligament: +
- Posterior wall puncture: NM
- Multiple punctures: NM

**Precautions: “Safety and effectiveness of the VCD has not been established if…”**

- Patient on warfarin: +
- Inflammatory disease: +
- Morbid obesity: NM
- Thrombolysis: +
- Access via vascular graft: +
- Significant PVD:
- Uncontrolled HTN: +
- Bleeding diathesis:
- Ipsilateral venous sheath: NM
- Femoral artery calcium: NM
- Small femoral artery size:
- Iliofemoral stenosis >50%: NM
- Use of GP IIb/IIIa inhibitor: NM

*Instructions for Use: Anglo-Seal VIF; St. Jude Medical February 2004 (www.sjm.com); †Instructions for Use Perclose A+T (August 2006) and StarClose (February 2007); Abbott Vascular (www.abbottvascular.com/ifu); ‡no restriction is only for reaccess after prior arteriotomy repaired with Perclose.

layed (27). Thus, the severity of bleeding complications (when they occur) would be expected to be greater with VCD than manual compression.

Reports of adverse events after VCD use prompted the FDA to initiate the largest study of 166,680 patients via the ACC-NCDR database “to assess the relative risk of complications after the use of the 2 main types of hemostasis device” (4). However, concerns that VCD outcomes are worse in comparison with manual compression are not supported by review of published meta-analyses, multicenter registries, and longitudinal registries (Table 3). These studies evaluated a larger number of patients than were studied in the pivotal trials, but are limited by variable study end points. Some studies use a composite end point (4,7,16,22,28–34), some studies use a single end point, (16,35,36), and some studies define “vascular complications” differently (37). Nevertheless, there are several conclusions that may be drawn from these larger studies of vascular complications:

- Among patients undergoing diagnostic cardiac catheterization, there is a 0.5% to 1.7% rate of vascular complications (4,7,16,31,34,38); this risk is not consistently increased or decreased by VCD usage across all studies; the largest study, from the ACC-NCDR, suggested a significant decrease in complications with VCD usage compared with manual compression (4); it is possible this reduction in complications is directly related to the VCD or alternatively reflects a reluctance by the operator to use a VCD in patients who are already having a complication at the completion of the diagnostic procedure or in circumstances where both VCD use and manual compression have been associated with increased complications (e.g., high or low femoral insertion sites).

- Among patients undergoing PCI, there is a 0.8% to 5.5% rate of heterogeneously defined vascular complications; with the exception of Vasoseal, there are no data to clearly suggest an increased risk of vascular complications with VCD use (4,29,33); some studies suggest that VCDs decrease complications compared with manual compression (17,33,34,36), some studies suggest potentially increased risk with VCD (22,28,30), and some suggest complication rates are similar (7,29,31,35); the ACC-NCDR study suggests a nonsignificant reduction in complications with VCD as compared with manual compression for patients undergoing PCI (4).

Given the equipoise with respect to vascular complications suggested by overview of these many VCD studies, it is not surprising that manual compression has remained the most common method for achieving hemostasis after invasive cardiac procedures both in the U.S. and worldwide (4,8) (Fig. 2). An example of this practice pattern can be seen in the TARGET (Comparison of 2 Platelet Glycoprotein IIb/IIIa Inhibitors, Tirofiban and Abciximab, for the Prevention of Ischemic Events With Percutaneous Coronary Revascularization) trial comparing abciximab to tirofiban. Of 4,809 patients undergoing PCI, 4,736 had femoral access. Use of VCD was left to the discretion of investigators—only 20% (n = 985) were treated with a VCD (35). While the interventional cardiology community has been noted for its aggressive adoption of new technologies beyond FDA labeling and randomized clinical trial conclusions (3), VCD utilization demonstrates the critical perspective that hospitals and interventional cardiologists do bring to adoption of new technology.

Factors Affecting Vascular Complication Rates: Patient Selection, Newer Anticoagulation, and Antiplatelet Strategies and Device Improvements

Accurate estimation of the relative benefits of VCD versus manual compression should also reflect what appears to be a change in the incidence of vascular complications in the
current era. In studies from the 1990s, vascular and bleeding complications after PCI were frequently in the 3% to 6% range (17,28,30,39,40). Recently, rates of major vascular complications after PCI are estimated at closer to 2% (4,40,41) (Fig. 3). This observation is supported by data from the PCI Registry of the Northern New England Cardiovascular Study Group. Using a standard definition of major vascular complications (arterial injury and/or arterial-injury-related bleeding), there has been a 42% relative decrease in complications from 2002 to 2006 ($p<0.001$) (D.J. Malenka and W.D. Piper, personal communication, January 2007) (40). Changes in the characteristics of patients undergoing PCI do not appear to account for this reduction in complications, since the major known risk factors for vascular complications have remained constant during this period—advanced age (39,40), vascular disease

### Table 2

<table>
<thead>
<tr>
<th>CLIP Study Diagnostic Arm—ITT</th>
<th>StarClose ($n = 136$)</th>
<th>Standard Compression ($n = 72$)</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure success (%)</td>
<td>100 (136/136)</td>
<td>100 (72/72)</td>
<td>NA</td>
</tr>
<tr>
<td>Mean time to hemostasis (min)</td>
<td>1.5 ($\pm$ 4.5)</td>
<td>15.5 ($\pm$ 11.4)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Mean time to ambulation (min)</td>
<td>162 ($\pm$ 104.6)</td>
<td>269.3 ($\pm$ 134.8)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Major complications (% patient-based)</td>
<td>0 (0/136)</td>
<td>0 (0/72)</td>
<td>—</td>
</tr>
<tr>
<td>Minor complications (% patient-based)</td>
<td>2.2 (3/136)</td>
<td>1.4% (1/72)</td>
<td>1.000</td>
</tr>
<tr>
<td>Mean time to dischargeability (h)</td>
<td>3.5 ($\pm$ 2.1)</td>
<td>5.2 ($\pm$ 2.1)</td>
<td>$&lt;0.001$</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>$n$</th>
<th>Device Comparison</th>
<th>End Point</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cura et al. (28)</td>
<td>Registry</td>
<td>2,918</td>
<td>VCD vs. MC</td>
<td>Vascular complication*</td>
<td>Angio-Seal 2.9% Perclose 3.2% MC 3.1% $p = NS$</td>
</tr>
<tr>
<td>Dangas et al. (30)</td>
<td>Registry</td>
<td>5,093</td>
<td>VCD vs. MC</td>
<td>Surgical repair</td>
<td>VCD 2.5% MC 1.5% $p = 0.03$</td>
</tr>
<tr>
<td>Resnic et al. (17)</td>
<td>Registry</td>
<td>3,027</td>
<td>VCD vs. MC</td>
<td>Vascular complication</td>
<td>MC 5.5% VCD 3.0% $p = 0.02$</td>
</tr>
<tr>
<td>Dangas et al. (22)†</td>
<td>Pooled randomized trials</td>
<td>2,095</td>
<td>VCD vs. MC</td>
<td>Device complications</td>
<td>VCD 8.5% MC 5.9% $p = 0.02$</td>
</tr>
<tr>
<td>Tavris et al. (4)†</td>
<td>ACC-NCDR</td>
<td>166,680</td>
<td>VCD vs. MC</td>
<td>Vascular complication</td>
<td>1.05% to 1.48% VCD 1.7% for MC $p &lt; 0.001$</td>
</tr>
<tr>
<td>Exaire et al. (35)</td>
<td>TARGET trial substudy</td>
<td>4,736</td>
<td>VCD vs. MC</td>
<td>Transfusions</td>
<td>VCD 1.0% MC 0.8% $p = NS$</td>
</tr>
<tr>
<td>Koreny et al. (16)†</td>
<td>Meta-analysis</td>
<td>4,000</td>
<td>VCD vs. MC</td>
<td>Hematoma</td>
<td>RR 1.14 for VCD (0.86–1.51)</td>
</tr>
<tr>
<td>Vaitkus et al. (33)†</td>
<td>Meta-analysis</td>
<td>5,045</td>
<td>VCD vs. MC</td>
<td>Vascular complication</td>
<td>RR 0.89 for VCD (0.86–0.91) Increased risk for Vasoseal</td>
</tr>
<tr>
<td>Nikolovsky et al. (29)</td>
<td>Meta-analysis</td>
<td>37,066</td>
<td>VCD vs. MC</td>
<td>Vascular complication</td>
<td>$p = 0.06$ for Angio-Seal benefit compared with MC Increased risk for Vasoseal</td>
</tr>
<tr>
<td>Applegate et al. (7)</td>
<td>Registry</td>
<td>4,699</td>
<td>Angio-Seal vs. MC</td>
<td>Vascular complication</td>
<td>Angio-Seal 1.5% MC 1.7% $p = NS$</td>
</tr>
<tr>
<td>Arora et al. (34)†</td>
<td>Registry</td>
<td>12,937</td>
<td>VCD vs. MC</td>
<td>Vascular complication</td>
<td>42% to 58% reduction in vascular complications with VCD vs. MC</td>
</tr>
</tbody>
</table>

*Vascular complication may be defined differently for each study; †data include both diagnostic and interventional cardiac procedures.

ACC-NCDR = American College of Cardiology-National Cardiovascular Data Registry; MC = manual compression; RR = relative risk; other abbreviations as in Table 1.
female gender (4,40), emergent procedures (4,40), and low body surface area (7,40). The reasons for the decrease in vascular complications possibly reflects the influence of several factors: better patient selection for VCD, improved femoral access techniques, changing PCI pharmacology, improved VCD, and improved operator experience with VCD use (32).

Patient selection. Routine femoral angiography at the end of the catheterization procedure is a significant advance (42–44). Such angiography allows identification of the major risk factor for retroperitoneal hemorrhage--sheath insertion above the inferior epigastric artery (44–46). In addition, femoral angiography identifies the estimated 13% of patients with nonfemoral artery sheath insertion for which VCD utilization is of unclear efficacy (Fig. 4) (20,43).

Identification of significant femoral arterial disease may allow selective use of manual compression in situations where implantation of an intravascular device may be associated with an increased risk of complications (Table 1) (7,47). Furthermore, femoral angiography may be especially important in the setting of multiple procedures at the same femoral access site; there is limited data regarding the safety of repeat access, and further study regarding the pathological and potential anatomical effects of repeat access with different devices is warranted (48–50).

Newer anticoagulation and antiplatelet strategies. Lower doses of unfractionated heparin have almost certainly contributed to the reduction in vascular complications (51). Bivalirudin also reduces the risk of bleeding complications after PCI compared with heparin + glycoprotein IIb/IIIa inhibitors (41). Thus, changes in PCI-related pharmacology could be expected to decrease bleeding and vascular complication rates up to 40%. Whether or not PCI pharmacologic changes may have preferentially benefited VCD or manual compression requires further clarification via prospective trials or subgroup analysis of recent trials (52).

Device improvements. The first VCD (Vasoseal) was a collagen device and the only VCD significantly associated with increased risk of vascular complications compared with manual compression in 2 meta-analyses (29,33). The dominant types of VCD in current practice are the suture-mediated device (Perclose), the collagen-anchor-suture-mediated device (Angio-Seal), and clip-mediated VCD (StarClose). The learning curve for each device may be steep, and thus complication rates may have been higher in the mid-to-late 1990s related to slow improvement in operator proficiency (29,30,32). In addition, each of these devices has undergone modification and simplification over time. For example, 1 longitudinal registry observed that the use of the third generation of Angio-Seal VCD was
associated with a 37% lower risk of vascular complications compared with the first Angio-Seal VCD (7).

**Cost concerns.** One important consideration in determining the optimal role of VCDs is their cost. Although most VCDs currently cost on the order of $150 to $200, given the large volume of both diagnostic angiograms and PCI procedures at many U.S. hospitals (5), even such a modest incremental cost has the potential to substantially impact catheterization laboratory and hospital budgets. Whether their utilization is cost effective depends on a variety of factors including the frequency of vascular complications, the impact of VCD use on the complication rate, and the potential for VCD to substantially alter post-procedure management patterns.

To date, several studies have examined the cost-effectiveness of vascular closure devices. The first such analysis was performed by Bos et al. (53). They used a decision analytic model to examine the potential cost-effectiveness of a collagen plug versus manual compression for achieving hemostasis at arterial puncture sites. Although they concluded (based on fairly limited evidence at the time) that a collagen plug (either Vasoseal or Angio-Seal) could reduce complications by ∼50%, they estimated that use of a VCD would increase post-procedure costs by ∼$135/patient with an overall cost-effectiveness ratio of $9,000 per vascular complication avoided. They concluded that this represented a relatively inefficient use of medical resources compared with other treatments. Whether this analysis is applicable to a contemporary U.S. catheterization laboratory population is debatable, however. In particular, it is unclear whether the vascular complication rates in their study (which were derived from a very small number of early studies) are comparable to those observed in current practice.

More recently, Resnic et al. (54) used a decision analytic approach to evaluate the potential cost savings associated with routine use of a collagen-suture plug (Angio-Seal) compared with manual compression. Data on specific complication rates for the 2 strategies were derived from pooled analysis of published randomized clinical trials while costs associated with various complications were derived from a matched case-control study conducted at a single U.S. academic medical center. They concluded that compared with manual compression (using the Femostop device, Radi Medical, Uppsala, Sweden), routine use of the Angio-Seal reduced both complications and cost. Most of the cost savings they projected were driven by reductions in vascular complications such as rebleeding, which they estimated to have an attributable cost of ∼$5,000 per event. It is important to note that the conclusions of this study were somewhat sensitive to the cost of the compression strategy. In particular, VCD use was no longer cost saving if the manual compression strategy cost <$66/patient (as might be anticipated with manual compression alone). Thus, it is unclear whether their conclusions can be generalized to all U.S. hospitals. Moreover, these findings probably do not apply to patients undergoing diagnostic catheterization alone where the expected risk of vascular complications is substantially lower than with PCI (4).

The strongest economic argument in favor of VCDs may be their potential to convert an inpatient PCI procedure into an outpatient procedure (55,56). This possibility was explored in a small randomized clinical trial by Rickli et al. (57). They randomized 191 patients undergoing elective PCI at a single Swiss hospital to either a routine manual compression strategy or use of a suture-based closure device (Perclose). Patients assigned to manual compression underwent sheath removal 4 h after PCI and were kept at bed rest overnight. In contrast, patients assigned to suture-mediated closure underwent immediate sheath removal and were ambulated after 4 h of bed rest. Although there were no significant differences between the 2 strategies in terms of major or minor vascular complications, use of suture-mediated closure was associated with a 12-h reduction in the post-PCI bed rest requirement (6.8 vs. 18.4 h) with associated benefits in terms of groin pain, back pain, and urinary problems. Their cost minimization analysis suggested that despite the cost of the closure device (225€), this was more than offset by reductions in hospital length of stay and physician time) with net savings of ∼70€/patient. Although similar savings might be achievable in a U.S. setting as well, given the current U.S. reimbursement system (which may reimburse substantially more for an inpatient PCI procedure than a similar procedure performed on an outpatient basis), many hospitals may actually lose substantial revenue by adopting such a strategy.

What can we conclude from the available studies? First and foremost, there is no single answer to the question whether VCDs are cost effective. The answer depends on a large number of factors, most of which are particular to the local healthcare environment. For example, if a hospital routinely utilizes adjuncts to manual compression (such as the Femostop device or additional staff), it appears that by reducing vascular complications a VCD device might be cost neutral or cost saving for the vast majority of patients. However, if the relevant comparator is true manual compression without additional staff, the cost offset is probably not sufficient to fully offset device costs at the present time. In this case, a more restrictive patient selection might be justified by which VCD use was reserved for those patients at greatest risk for bleeding (38,40) or for patients where a prolonged period of bed rest would lead to unacceptable discomfort or risk of complications. Finally, the major economic value of VCDs appears to be their potential to convert PCI from an inpatient to an outpatient procedure, at least for select individuals judged to be at low risk for coronary ischemic complications (55). Whether this strategy becomes accepted and viable within the U.S. health care system will depend more on changes to the reimbursement system and the associated financial incentives than on the potential cost-effectiveness of the overall strategy, however.
VCDs: The Next 10 Years

Definitive clinical trials. To date, there have been no large-scale randomized clinical trials comparing outcomes with VCD use with those with manual compression. Nor have there been large-scale trials pitting devices head-to-head to determine the possible superiority of 1 device over another. There are several factors that account for these deficiencies in our current evidence base. First, from the standpoint of revenue, the VCD market represents a relatively small component of the total interventional cardiology market (5). As such, the incentive for device companies to sponsor expensive large-scale clinical trials is reduced. Second, sheaths are pulled only after the effects of anticoagulants have worn off for manual compression but are removed immediately after PCI when a VCD is used. Thus, any clinical trial comparing manual compression to VCD would represent a comparison of 2 alternative closure strategies as well as a direct comparison of closure efficacy. Additionally, there have been no consistent standards for defining vascular complications, particularly hematoma formation (37). More recently, a consistent definition has been adopted as part of the FDA approval process and that definition would need to be the basis of any future randomized trials (10). These prior limitations have led to the circumstances of a less-than-optimal evidence base to guide VCD use. If the results of a large randomized clinical trial establishing vascular outcomes with VCD compared with manual compression indicated that rates of vascular complications were lower with VCD, however, such a study would provide a strong impetus for VCD use in routine clinical practice.

Challenges for expanded VCD utilization. Vascular closure devices decrease the time to ambulation, the time to discharge, and decrease complications for patients undergoing diagnostic angiographic procedures (4): How can similar benefits be shown for a broader group of patients? Two groups believed to be at high risk for VCD use have been routinely excluded from the pivotal studies leading to VCD approval: patients undergoing PCI for acute myocardial infarction (58) and patients who have documented femoral arterial disease or other peripheral vascular disease (8,20,40,47). Prior studies of PCI patients with clinically important peripheral vascular disease have suggested an enhanced relative risk of vascular complications of 40% to 89% with absolute rates of complications from 2.6% to 8.9% (7,40,59–62) (Fig. 4). There are only limited data regarding use of VCDs in patients with vascular disease involving the femoral artery (59,60). Whether use of an extravascular VCD could result in an overall reduction in PCI-related vascular complications for high-risk populations such as those with femoral arterial disease is an intriguing concept that requires further study (49,60,62,63) (Fig. 5).

We believe that several studies should be performed before expanding VCD use for both diagnostic and PCI patients. Several of these potential studies are enumerated in the following text:

- A randomized trial of VCD versus manual compression among patients at high risk of vascular complications; if major vascular complication rates with manual compression were expected in >5% of an enriched control population (i.e., those with femoral disease [62] and/or PCI for acute myocardial infarction [58,64]), a device that incurred a <2% rate of major vascular complication could be studied and shown to be superior to manual compression (p < 0.05) in a 1,000-patient randomized trial.
- Surveillance registries to identify high-risk patient subsets and low-frequency adverse events; utilization of post-marketing surveillance registries of >10,000 patients may be advantageous given the relatively low rate of current vascular complications; this concept is directly

Figure 5 Intravascular Versus Extravascular Closure Devices

New staple- and clip-mediated (StarClose or Angiolink) vascular closure devices have a potential advantage of being “extravascular” with no anchor (Angio-Seal) or suture (Perclose). This may be especially significant in situations where minor femoral artery lumen compromise would be clinically consequential (i.e., mild-moderate femoral arterial disease).
analogous to the challenges with analyzing other low-frequency events in high-frequency procedures (i.e., drug-eluting stent thrombosis) (65); one advantage of VCD studies is that major vascular complications occur early and thus the design of these studies (as opposed to drug-eluting stent thrombosis) might require only 30-day patient follow-up; utilizing data from only 2001, the ACC-NCDR provided the largest registry data so far on VCD (4); expanding this study to the period 2003 to 2006 could provide even more convincing data on VCD impact on complications for diagnostic and PCI patients especially among subgroups for which there are current cautions (Table 1).

- Studies to enhance detection of complication risk; use of a surrogate marker for clinically important vascular complications could provide a marker for device and manual compression complications (15); for example, a smaller randomized trial might utilize routine 30-day femoral arterial duplex ultrasound (15,66) to determine whether issues of nonclinical vascular compromise warrant caution with staple, collagen, suture, or manual closure methods.

It is clear from the first decade of experience with VCD use that outcomes in an individual patient reflect characteristics of the patient, the operator, and the device. While a considerable number of studies have identified “high-risk” patient characteristics (40,44), there are fewer studies that have evaluated the role of the operator in contributing to vascular complications. One criticism of the trials used to obtain FDA approval for a VCD is that the results reflect initial operator experience with the device, and in some cases the initial experience with closure devices in general (32). Thus, the rates of device failure and device-associated vascular complications in early studies may represent outcomes from the steep portion of the “learning curve” of VCD experience. Studies have documented a “learning curve” phenomenon associated with VCD use (26,62). Importantly, in the study by Warren et al. (26), there was a >3-fold increase in device failure for the first 50 patients treated with Angio-Seal compared with subsequent deployments (14% early learning curve failure rate vs. 3.5% later experience of nondeployments, p = 0.009) (26). In the study by Balzer et al. (62), the learning curve for technical success with suture-based closure was even steeper and longer (>350 patients).

While not definitive, these data strongly suggest that operator and programmatic expertise occurs only after substantial VCD experience has accrued. If VCD utilization is to achieve its maximum potential to improve clinical outcomes, it will thus be imperative to provide the educational and practice opportunities to achieve a high level of expertise. This education must address more than a particular VCD device: excellent access technique as a part of a successful VCD procedure cannot be overemphasized. It is difficult to determine what percentage of VCD failures are a result of suboptimal access technique, but expanding the use of VCDs will most likely occur in the setting of enhanced access skills.

**Toward a more ideal VCD.** Although the Angio-Seal and Perclose devices, the 2 VCDs with the longest period of commercial availability, have both undergone significant evolution and improvement (7), closure failures with these devices still occur. Moreover, the newest commercially available closure device, StarClose, has not eliminated this problem. In the CLIP (CLOSure In Percutaneous Procedures) study, there was an 11% failure rate in the PCI arm of the study (10). Closure failure may occur for a number of reasons independent of the VCD used. Clinical and treatment factors, such as use of glycoprotein Ilb/Ilia inhibitors and advanced age (40), will likely always challenge arterial access management. Procedural factors such as multiple attempts to gain access, back wall sticks, and access sites outside of the common femoral artery likely contribute to closure failure (10). The challenge for successful VCD use in these situations is substantial.

The patient factors influencing closure success notwithstanding, the “ideal” closure device remains to be developed. What would this device look like? 1) A single device capable of providing successful closure for all patient and access site anatomical variations; 2) an atraumatic device without a foreign body or vascular alteration of the femoral artery; and 3) a simple-to-use device with >95% procedural success and low cost. Access site closure with heat, delivered via ultrasound guidance, may be the closest approximation to the ideal VCD to date—an active closure with no potential compromise of the femoral artery (67). Unfortunately, the Therus device (Therus Corporation, Seattle, Washington) has had limitations that have delayed its introduction into clinical practice. Further innovation will be required to achieve the “ideal VCD” in the next decade.

**Conclusions**

Over the past decade, our information base has improved; so have the devices, pharmacology, and techniques associated with VCD. Based upon these more recent data, should all patients get a VCD? No—those with severe femoral arterial disease and sheath insertion above the inferior epigastric artery may have a higher risk with VCD than manual compression (45). Should most patients undergoing femoral arterial access get a VCD? For diagnostic cases, the answer may be “yes” based upon both decreased complication rates and improved time to ambulation (1,4,8,16,54). As outlined in the preceding text, however, there are numerous subgroups of diagnostic patients for whom insufficient data are available to make a clear recommendation. For PCI patients, contemporary data support a neutral effect on complications (10).
The second decade of VCD launches with a history that is characterized by cautious adoption of this particular technology and frightening case reports of adverse experiences (4,32). Fortunately, the studies of the past 5 years seem to suggest that selected VCD technology not only improves time to hemostasis, but also reduces complications at least in patients undergoing diagnostic cardiac catheterization (4,33,54). Expanded use of VCD technology seems likely over the next decade as cost-effectiveness is demonstrated with respect to reduction in complications; the driver for this expanded use will be definitive trials in enriched populations, adoption of same-day PCI, mega-registries with information on high-risk subgroups, and improving integration and percutaneous coronary intervention using thrombin hemostasis techniques to reduce femoral vascular complications after coronary intervention. Am J Cardiol 1999;81:970–6.


