Suture-Mediated Closure of the Femoral Access Site After Cardiac Catheterization: Results of the Suture To Ambulate aNd Discharge (STAND I and STAND II) Trials

Donald S. Baim, MD, William D. Knopf, MD, Tomoaki Hinohara, MD*, Donald E. Schwarten, MD, Richard A. Schatz, MD, Cass A. Pinkerton, MD, Donald E. Cutlip, MD, Michelle Fitzpatrick, RN, Kalon K.L. Ho, MD, MS, and Richard E. Kuntz, MD, MS

Despite advances in other aspects of cardiac catheterization, manual or mechanical compression followed by 4 to 8 hours of bed rest remains the mainstay of postprocedural femoral access site management. Suture-mediated closure may prove to be an effective alternative, offering earlier sheath removal and ambulation, and potentially a reduction in hemorrhagic complications. The Suture To Ambulate aNd Discharge trial (STAND I) evaluated the 6Fr Techstar device in 200 patients undergoing diagnostic procedures, with successful hemostasis achieved in 99% of patients (94% with suture closure only) in a median of 13 minutes, and 1% major complications. STAND II randomized 515 patients undergoing diagnostic or interventional procedures to use of the 8Fr or 10Fr Prostar-Plus device versus traditional compression. Successful suture-mediated hemostasis was achieved in 97.6% of patients (91.2% by the device alone) compared with 98.9% of patients with compression (p = NS). Major complication rates were 2.4% and 1.1%, and met the Blackwelder’s test for equivalency (p < 0.05). Median time to hemostasis (19 vs 243 minutes, p < 0.01) and time to ambulation (3.9 vs 14.8 hours, p < 0.01) were significantly shorter for suture-mediated closure. Suture-mediated closure of the arterial puncture site thus affords reliable immediate hemostasis and shortens the time to ambulation without significantly increasing the risk of local complications.

The standard technique for access site management of the femoral arterial puncture site remains manual or mechanical compression followed by 4 to 8 hours of bed rest. Although this achieves hemostasis in most cases, compression and prolonged bed rest often produce significant patient discomfort and delay hospital discharge. Moreover, inadequate initial hemostasis or recurrent bleeding cause significant local complications (hematoma or false aneurysm) in up to 10% of patients, leading to transfusion or vascular surgical repair in 1% to 2%.¹⁻⁵ A number of new methods to achieve hemostasis have been introduced recently. These methods include the Vasoseal (Datascope Corp., Montvale, New Jersey)⁶⁻⁸ and Angioseal (Sherwood Medical, Bothell, Washington)⁹⁻¹¹ and the still-investigational Duett devices (Vascular Solutions, Minneapolis, Minnesota)¹², all of which use collagen to facilitate local hemostasis. In contrast, the Prostar and Techstar (Perclose, Redwood City, California) use suture-mediated closure of the arterial puncture site.¹³,¹⁴ All of these devices share common goals—providing immediate hemostasis (regardless of the patient’s anticoagulation status), allowing earlier ambulation and discharge, and reducing (or at least not increasing) the incidence of local complications. The Suture To Ambulate aNd Discharge (STAND I and II) trials evaluated the safety and efficacy of suture-mediated closure after cardiac catheterization or interventional procedures.

METHODS

Device description and procedure: The suture-mediated closure devices Techstar and Prostar-Plus precisely deploy sutures (6.0 Tevdek II) into the wall of the femoral artery surrounding the sheath insertion site. At the conclusion of the catheterization procedure, the standard vascular introducing sheath is replaced with the Perclose device. When the needle exit ports of the device lie just within the arterial lumen (as indicated by pulsatile exit of blood through “marker” lumens located adjacent to the needle exit point), the needles are deployed (Figure 1) so that they exit the
device within the arterial lumen, pass through the vessel wall, and are collected by a barrel located on the shaft of the device just outside of the artery. The delivery sheath and guidewire are then removed as tension is maintained on the knot to achieve hemostasis.

Because suture-mediated closure does not rely on blood clotting to provide hemostasis, the procedure can be performed in the catheterization laboratory under sterile conditions immediately after a catheterization procedure, regardless of the coagulation status. The choice of device is dictated by the size of the procedural sheath. The 6Fr Techstar contains 2 needles that are attached to the opposite end of one suture; the 8Fr and 10Fr Prostar-Plus contain 2 such systems (i.e., 2 pairs of needles attached to 2 separate sutures) placed at right angles. Ambulation is possible within 2 hours of closure, although recent practice has allowed ambulation at 1 hour after closure.

**Study design:** The STAND I trial was a multicenter registry of patients undergoing diagnostic catheterization procedures using 5Fr or 6Fr sheaths in which control of the puncture site was obtained using the 6Fr Techstar device. In all, 200 patients were enrolled at 7 participating sites between April and August 1997. The Stand II trial was a multicenter randomized trial to evaluate the 8Fr or 10Fr Prostar-Plus device compared with conventional compression therapy. At the end of the catheterization procedure, each patient was randomized to undergo either suture-mediated closure or conventional compression therapy. A total of 515 patients who underwent diagnostic or interventional procedures using 6Fr or larger sheaths were enrolled in the study at 8 sites between April and December 1996, stratified by whether continuous postprocedure anticoagulation was planned. Both studies excluded patients with significant peripheral artery disease, other than single-wall puncture of the common femoral artery, perivascular scarring, or thrombolytic therapy.

**Study procedures:** For those assigned to suture-mediated closure, the procedure was performed immediately at the end of the catheterization using the technique described above. If suture-mediated closure could not be performed, or if ongoing bleeding was present at the puncture site after suture-mediated closure, manual or mechanical compression was allowed but the time of any such compression was included in the study end points (as defined below). Postprocedure management called for an initial 1- to 2-hour period of bed rest.

For those randomized to conventional compression therapy, the arterial sheath was removed when the activated clotting time was $>180$ seconds. Hemostasis was obtained with either manual or mechanical compression using a C-clamp or pneumatic device per each institution’s routine practice. Patients were ambulated according to the hospital standards of care or per-physician discretion.

Patients were examined serially up to the point of hospital discharge and then at 30 days (range 3 to 6 weeks) for signs of femoral puncture site complication. The first 40% of the patients enrolled in each study underwent an ultrasound evaluation of the access site within 3 days after the procedure. All patients gave written informed consent for inclusion in this study under a protocol approved by each institution’s institutional review board.

**Study end points and definitions:** The primary safety end point was the incidence of major complications at the femoral access site within 30 days of the procedure. Major complications were defined as (1) surgical vascular repair or ultrasound-guided compression (for pseudoaneurysm, arterial-venous fistula, or laceration), (2) femoral nerve injury (sensory or motor), (3) blood transfusion related to a groin complication, and...
The secondary effectiveness end points were time to ambulation, time to hemostasis, and time to hospital discharge. Time to hemostasis was measured as the elapsed time between the time of completion of the catheterization procedure and when hemostasis was achieved with no additional manual or mechanical compression. Time to ambulation required the patient to walk at least 10 feet, and time to discharge was taken to the patient leaving the hospital.

**Sample size justification:** In the STAND I trial, study size was determined based on the primary safety end point—the expected incidence of major complications at 30 days. A 5% rate was selected as the upper bound beyond which the complication rate observed from the Techstar 6 sample would be significantly higher than the objective performance criteria of ≤1%. To reject the null hypothesis with an α error of 5% and power of 80%, a sample size of 122 patients would be required; the actual sample size for this registry was set at 200 patients.

The STAND II trial was designed as an equivalency trial for the primary combined safety end point of the incidence of major complications. The major complication rate for the conventional treatment arm was estimated to be 8%, and equivalency between the 2 arms was considered to fall within a Δ of 6%. To obtain an α error of 5% and statistical power of 80%, a sample size of 506 (250 patients/arm) was calculated.

**Data management and statistical analysis:** Case report forms were filled out at each center and processed by the Cardiovascular Data Analysis Center, Harvard Medical School and Boston’s Beth Israel Hospital. Continuous variables were expressed either as mean ± SD or median with quartile based on the distribution of variables. Differences in proportions were examined using a 2-tailed Fisher’s exact test. Because some end point variables of interest were not normally distributed, the differences between the 2 randomized groups were evaluated using the nonparametric Wilcoxon method. All analyses were performed using the SAS for Windows (version 6.12, SAS Institute, Cary, North Carolina).

A 2-sided p value of 0.05 was required for statistical significance.

**RESULTS**

Patient characteristics for both trials are summarized in Table I, efficacy end points in Tables II (diagnostic procedures) and III (interventional procedures).
STAND I trial: Two hundred patients were enrolled at 7 participating sites between April and August 1997. With 5Fr, 6Fr, or 6.5Fr sheaths used in 99% of cases, complete hemostasis without a major complication was achieved in 99% of patients in a median of 13 minutes (in 94% of patients with the device alone and in 5% after additional conventional compression). Major complications occurred in 2 patients (1%), 1 patient underwent surgical repair for a pseudoaneurysm, and 1 patient developed local site infection requiring outpatient intravenous antibiotics. Minor complications occurred in 3 patients (1.5%); 1 patient developed a hematoma >6 cm, and 2 patients developed small pseudoaneurysms not requiring further therapy. There were no instances of rebleeding after initial ambulation. Postprocedure ultrasound study of groins was obtained in the first 73 patients per protocol: two patients had small pseudoaneurysms as described above, and no patient had intra-arterial thrombus or luminal narrowing at the closure site.

STAND II trial: Between April 1996 and December 1996, 515 patients were enrolled at 8 centers; 251 patients were randomized to suture-mediated closure and 264 patients to conventional compression therapy. With ≥8Fr arterial sheaths used in 57%, complete hemostasis without major complications was achieved in 97.6% in the suture-mediated closure group and 98.9% in the conventional compression group (p = NS). In the suture-mediated group, complete hemostasis was achieved in a median of 19 minutes (in 91.2% by device alone, and in 6.8% of patients with adjunctive compression) (Table III and Figure 2). Major complications occurred in 2.4% in the suture-mediated group and 1.1% in the conventional compression group (p = NS). These complications included surgical repair of the femoral artery (1.2% vs 0.4%), transfusion (1.2% vs 0.4%), infection requiring intravenous antibiotics (0.8% vs 0.4%), and ultrasound-guided compression for pseudoaneurysm (0.8% vs 1.1%). By Blackwelder’s test, the closure device was noninferior (i.e., equivalent or better) with a p < 0.05 for these major complication rates. There was no statistical difference in the incidence of minor complications between the 2 groups (3.6% and 1.1%, respectively), which included hematoma (2.4% vs 1.1%) and superficial infection (1.6% vs 0%).

DISCUSSION
When the percutaneous Seldinger (needle and guidewire) approach to left heart catheterization from the femoral artery was introduced in 1959, hemostasis at the end of the procedure was obtained by application of manual pressure over the puncture site for 10 to 15 minutes after catheter removal, followed by overnight bed rest. It is remarkable 40 years later that we are still relying on manual compression and bed rest for control of the arterial puncture site, as outpatient procedures have become standard for diagnostic catheterization, and larger sheath sizes and more aggressive anticoagulant and antiplatelet therapies have increased the risk of bleeding complications at the fem-

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oral puncture site. In fact, femoral puncture sites problems, most notably false aneurysms and hematomas occur in 5% to 10% of patients and lead to transfusion or vascular surgical repair in roughly 1.5% of patients, making them the single greatest cause of morbidity after percutaneous femoral catheterization procedures.

Among alternative methods to control the arterial puncture site, the Perclose device is unique in using no collagen (relying instead on direct suture-mediated closure of the arterial puncture site via a sheath-like device). It is estimated that as many as 30% of current femoral catheterization procedures make use of a closure device, but achieving broader use will require that these devices demonstrate (1) prompt hemostasis, (2) early ambulation and discharge, (3) decreased (or at least not increased) incidence of major access site complications, (4) quick and easy use, and (5) cost-effectiveness by allowing earlier discharge or improved patient comfort.

Like other interventional devices, suture-mediated closure has undergone an evolutionary process of continued refinement. The original “proof-of-concept” Prostar device was approved in 9Fr and 11Fr formats in April 1997, but was supplanted in late 1997 by the 8Fr and 10Fr Prostar-Plus (double suture) and Techstar 6 (single suture) devices that offer easier delivery into the vessel. These devices have recently been evaluated against manual compression in a European study of 401 patients undergoing diagnostic catheterization and 189 patients undergoing interventional procedures, with shortening of time to hemostasis and ambulation as well as favorable complication profiles. The STAND I and STAND II trials reported here, however, are the pivotal trials upon which US approvals of the Prostar-Plus and Techstar devices were based.

The STAND trials show a high success rate of initial hemostasis with device alone (94% with the Techstar, and 91.2% with the Prostar-Plus), which is increased further (to final success of 99% and 97.6%, respectively) by brief mechanical compression. These data are comparable to the European results, and all represent a significant improvement relative to the 86.7% device success seen with the original, bulkier Prostar device. Device success may be improved by further device refinements, such as the newer Closer device (Perclose) that makes correct placement easier and has yielded a preliminary primary device success of 99% (E. Grube, personal communication).

As in the European trial, suture-mediated closure profoundly shortened the times to hemostasis and ambulation, particularly in purely diagnostic studies. In the mostly interventional experience in STAND II, the Prostar-Plus compared with conventional compression had significantly shorter median times to hemostasis (19 vs 243 minutes), and ambulation (3.9 vs 14.8 hours). These findings would support their use to decrease patient discomfort related to compression and prolonged bed rest, and also to shorten patient stay.

Shortening the times to hemostasis and ambulation would not, however, represent a net benefit if failure to place the device or obtain stable hemostasis led to an increase in complications. Neither trial reported here shows a significant increase in major complications, but ideally this technology would allow an even lower rate of complication. In the recent European study, there was a trend toward such reduction in major complications for diagnostic procedures (0.5% vs 2.5%), with no difference in complications for interventional procedures (3.2% vs 3.2%). To the extent that most hemorrhagic complications result from difficulty in correct placement of the device (rather than a failure of the suture-mediated mechanism), and most local infections (unusual after manual compression) are related to the need to enlarge the original 8Fr sheath tract to accommodate the 21Fr barrel that is used by the current device to collect the needles after they have passed through the arterial wall, ongoing modifications such as the Closer device may have even lower complication rates.

**Study limitations:** These trials have several limitations that relate to the lack of standardization of manual compression practices, and the imprecision of demonstrating “equivalence” with a manageable trial size. Also, the STAND studies do not establish the cost-effectiveness of suture-mediated closure through a potential for true outpatient intervention (i.e., no overnight stay) when this becomes a reality. Comparison with other closure devices and use of alternative access (site such as the radial artery) are required to demonstrate this.

Suture-mediated closure is a new method to achieve hemostasis at the femoral artery access site and earlier ambulation. Operator training and patient selection, as well as continued improvement in the device, will likely expand its use in the management of patients following diagnostic and interventional catheterization procedures.


