Clinical Study of the WoundCare360 SiteSeal Adjunctive Compression Device Following Interventional Endovascular Procedures – NCT03234894

Study Protocol:

Document Date: October12, 2015

PROTOCOL

SiteSeal™ Adjunctive Compression Device

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1. **STUDY TITLE:** Clinical Study of the Wound Care 360° SiteSeal™ Adjunctive Compression Device Following Interventional Endovascular Procedures

2. **PRINCIPAL INVESTIGATOR:**
Matthew B. Earnest, MD
University of Kansas Medical Center
3901 Rainbow Blvd., Mail Stop 1039
Kansas City, KS. 66160

3. **SPONSOR:**
Wound Care 360° Inc.
10900 S. Clay Blair Blvd
Suite 800
Olathe KS 66061

4. **CLINICAL FACILITY:** Cardiac Intervention Lab
University of Kansas Medical Center

5. **STUDYMONITOR** Thomas Reidy

6. **PROTOCOL DATE**
October 12, 2015

7. **PROTOCOL NUMBER**
15-012

8. **Version**
1.2

9. **Purpose**

This Clinical Study is a pivotal study to evaluate the safety of the SiteSeal™ Adjunctive Compression Device across a broad array of patients undergoing interventional endovascular procedures.

10. **Synopsis**

The study design is a single arm with 90 patients. The primary endpoints measure the risk for common femoral nerve damage and common femoral artery laceration from the blind placement of a Z-stitch in the soft tissue above the femoral bundle.

The sample size is 90 patients. The project objective is to demonstrate the safety of the device.

11. TRIAL PHASE

Pivotal Clinical Trial

12. NAME OF DEVICE

SiteSeal™

13. INTENDED USE

SiteSeal™ is intended for use in the compression of the femoral artery after cannulation. The device is intended for professional use only.

14. Background Information

Summary of Original Study Protocol in Pre-Submission

Achieving hemostasis after vascular procedures performed from the femoral artery approach is a vital component in the ultimate success of the procedure. Vascular complications are rare, but impart a significant amount of morbidity and mortality to the patient when they occur. The current “Gold Standard” is manual compression, which involves external pressure applied to the femoral artery cranial to the access site, with visual confirmation of hemostasis. Most current protocols demand 15-30 minutes of firm pressure be applied during this portion of the procedure to achieve hemostasis, followed by up to 6hours lying flat on a hard surface before ambulation. This can be very uncomfortable to the patient, and is difficult to maintain for the individual tasked with holding pressure. There is significant variability between patients with relation to body habitus and overall size. There is also variability in the skill and experience of the technician holding pressure.

About half of the procedures are closed using a variety of vascular closure devices (VCD). VCDs leave something behind in the patient, but are quick to deploy, reducing the time to achieve hemostasis. There is considerable skill required to place VCDs successfully. As a result, different types of VCD appeal to different physicians. The skilled doctor uses the VCD that the physician determines is best for his/her patient.
The SiteSeal™ device is not a VCD; it is an adjunctive compression device.

The SiteSeal™ device is placed in the catheterization laboratory, using three separate steps to improve hemostasis and remove closure process variability while leaving nothing behind. A Z-stitch is used to secure adjacent non-involved tissue and involute it over the arteriotomy site, while BioSeal powder is used to seal the wound tract itself. Compression is applied and maintained via the Adjunctive Compression Device that is sutured in place after being aligned with the sheath itself, ensuring proper positioning, and eliminating variability in pressure. The operating physician deploys the device in a minimal amount of time.

Time to hemostasis (TTH) varies with manual compression based on many variables. TTH with VCDs is really the time to deploy the device since hemostasis is achieved as soon as deployment is complete. TTH is the time to form an immature clot; TTA is the time to form a mature clot. TTA is also economically relevant as a bed is freed up only after ambulation and not after hemostasis. This trial compares an adjunctive hemostasis device to a VCD. The relevant effectiveness measure is TTA.

We postulate that the Wound Care 360° SiteSeal™ Adjunctive Compression Device is not inferior to Perclose VCD for safety during placement, time to hemostasis, time to ambulation, deployment safety, time to discharge, patient comfort and vascular complications associated with catheterization procedures performed via femoral artery access. The results of the trial are to quantify the safety and efficacy of the device and not to draw comparisons with other closure strategies. The primary outcome is to assess the risk for common femoral nerve damage and common femoral artery laceration.

The proposed Indication For Use is:

"The SiteSeal™ System is indicated for use in the compression of the femoral artery or vein after vessel cannulation."

15. OBJECTIVE

Primary: The primary endpoints assess the risk for common femoral nerve damage and common femoral artery laceration from the blind placement of a Z-stitch in the soft tissue above the femoral bundle.

Secondary: The secondary endpoints are to measure patient discomfort (per 24-hour phone interview), and the 30-day incidence of major and 30-day incidence of minor complications (per patient follow-up visit).

Patient Discomfort:

a. Patient discomfort @ discharge from the catheterization lab:
b. Patient discomfort @ 24 hours after the procedure:

30day Major Complications:

a. Vascular repair or the need for vascular repair (via surgery, ultrasound guided compression, transcatheter embolization, or stent graft)
b. Access site related bleeding requiring transfusion
c. Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram
d. Surgery or the need for surgery for access site related nerve injury
e. Permanent (lasting >30 days) access site related nerve injury
f. Access site related infection requiring intravenous antibiotics and/or extended

hospitalization

30Day Minor Complications:

a. Non treated pseudoaneurysm documented by ultrasound
b. Non treated arteriovenous (AV) fistula documented by ultrasound
c. Pseudoaneurysm treated with ultrasound guided thrombin injection or ultrasound guided fibrin adhesive injection
d. Access site hematoma greater than or equal to 6 cm
e. Access site related bleeding requiring greater than 30minutes to achieve hemostasis
f. Late (following hospital discharge) access site related bleeding
g. Ipsilateral lower extremity arterial emboli
h. Transient loss of ipsilateral lower extremity pulse
i. Ipsilateral deep vein thrombosis
j. Access site related vessel laceration
k. Transient access site related nerve injury
l. Access site wound dehiscence
m. Localized access site infection treated with intramuscular or oral antibiotics

16. PATIENT POPULATION

This study will be performed on "all comers" requiring interventional femoral artery procedures who meet the inclusion and exclusion criteria.

Inclusion Criteria

1. Patients between the ages19 to 90
2. Patient or his/her legally authorized representative, has given written informed consent for participation prior to the procedure
3. Procedure is an interventional procedure
4. Patient is willing to undergo all study procedures and adhere to data collection and follow-up requirements
5. Patient is a candidate for elective, non-emergent cardiac or peripheral vascular catheterization from the femoral artery approach
6. Patient is willing to have a pre/post procedure ultrasound.

Exclusion Criteria

1. Patients are <19 years old
2. Patients are >90years old
3. Patient has received Glycoprotein (GP) IIb/IIIa inhibitors
4. Patient or patient's representative is unable to provide written informed consent.

5. Patient is unable or unwilling to adhere to data collection and follow-up requirements
6. Procedure is emergency Percutaneous Coronary Intervention (PCI)
7. Patient is on dialysis
8. Patient has a known diagnosis of fibromyalgia
9. Patients with acute coronary syndrome (i.e., unstable angina or myocardial infarction) ≤ 48 hours before this catheterization procedure.
10. Patients with systolic blood pressure < 90 mm Hg at the end of the catheterization procedure
11. Patients who are immunocompromised
12. Patients with preexisting systemic infection or local infections at the access site
13. Patients who are known or suspected to be pregnant, or are lactating
14. Patients who have undergone prior or recent use of an intra-aortic balloon pump through the arterial access site above the inguinal ligament
15. Patients who have undergone prior vascular closure device use in the ipsilateral common femoral artery ≤ 30days before this catheterization procedure
16. Patients who have undergone prior use of manual or mechanical compression for closure in the ipsilateral common femoral artery ≤30 days before the catheterization procedure
17. Patients requiring a repuncture at a site previously punctured within 48 hours of the catheterization procedure
18. Patients who have undergone an antegrade puncture
19. Patients with puncture sites believed to be in the profunda femoris artery, superficial femoral artery, or at the bifurcation of these arteries
20. Patients with puncture tract angle >55°
21. Patients who are suspected to have experienced a femoral artery back wall puncture or who underwent > 1femoral artery puncture during the catheterization procedure
22. Patient with significant anemia (hemoglobin < 10 g/dL, Hct < 30%)
23. Patients with a known bleeding disorder, including thrombocytopenia (platelet count < 100,000 cells/μL), thrombasthenia, hemophilia, or von Willebrand's disease
24. Patients with systolic blood pressure >180 mm Hg or diastolic blood pressure >110 mm Hg at the end of this catheterization procedure, unless systolic and/or diastolic pressure was lowered by pharmacological agents prior to the end of the catheterization procedure

25. Patients with a baseline International Normalized Ratio (INR) >1.5 (e.g., on warfarin therapy)
26. Patients whose Activated Clotting Time (ACT) >300seconds at the end of the catheterization procedure
27. Patients who have undergone administration of low molecular weight heparin (LMWH) within 8hours of this catheterization procedure
28. Patients in whom continued heparin or other anticoagulant/antiplatelet therapy is planned for this patient (with the exception of glycoprotein IIb/IIIa inhibitor therapy) during the first few hours following the catheterization procedure
29. Patients having a complication or complications at the femoral artery access site during the catheterization procedure including bleeding, hematoma, intraluminal thrombus, pseudoaneurysm, or arteriovenous fistula
30. Patients with an ipsilateral or bilateral lower extremity amputation(s)
31. Patient known to require extended hospitalization (e.g., patient is undergoing cardiac surgery)
32. Patients who have a planned endovascular procedure within the next 30days after the catheterization procedure
33. Patients who are currently participating in another investigational study that has not concluded the follow-up period
34. Patients who have already participated in the Investigational Device Exemption (IDE) study
35. Patients who cannot adhere to or complete the study for any reason including but not limited to geographical residence or life-threatening disease

17. NUMBER OF INVESTIGATIONAL SITES

The trial will be performed at two sites with multiple practitioners.

Consideration was given to using a single vs. multiple sites as well as multiple practitioners. Practically, we found a learning curve in our pilot study in which proficiency (measured as deployment time < 3minutes in simple diagnostic procedures) stabilized after about n= 2-3 per practitioner. Given n= 90 for the study with all cases consisting of more complex interventional procedures, if the total number of practitioners were 6 (e.g. 2 hospitals*3 practitioners/hospital), for example, then each physician would do 15 cases, or about 5 times the number it takes to become proficient. We decided that two sites with multiple practitioners would satisfy the requirement to minimize bias without introducing excessive start-up variation.

18. METHODS / STUDY DESIGN

Institutional Review Board (IRB) approval will first be obtained. A subject's participation is a one-time event (plus follow-up) that occurs after obtaining informed consent. The subjects will not incur any costs associated with the study procedures.

At the catheter lab site, subjects will be screened through a standard of care history. After determining that the patient qualifies for enrollment into the study, an investigator or delegated study personnel will obtain an informed consent. After the patient's informed consent is obtained, study personnel will interview the subject and document subject data, including their age, gender, race, and patient history into their file. The subject source data is then recorded on a sponsor-provided Case Report Form (CRF).

Each subject will undergo the doctor-determined interventional procedure before closing with SiteSeal™.

The first 50 patients will receive a pre-device deployment ultrasound of the access site on the day of catheterization and a post-procedure ultrasound (after device removal and no later than the 30day follow-up) to detect silent complications, including vascular injury requiring repair, pseudoaneurysms requiring thrombin or fibrin adhesive injections, or bleeding requiring transfusions.

All patients will return for a follow-up visit at 30 days (±1week) post-procedure. A physician investigator (i.e. principal investigator, sub-investigators, physician assistants and/or nurse practitioners associated with the investigators) will examine the femoral artery access site. Any access site-related complications will be reported to the PI.

19. ANALYSIS OF RESULTS

For each patient, a separate set of Case Report Forms (CRFs) will be completed and comprise the following information:

- Inclusion/exclusion criteria
- Demographics: Age in years, Sex, Race, Height, Weight, BMI.
- Procedure-Related Data
- Medication history
- Previous diagnostic and/or interventional endovascular procedures
- Catheterization procedure data

Primary Endpoints

- Risk for common femoral nerve puncture and common femoral artery laceration (or needle penetration) from blind placement of the Z-stitch.
    - Nerve puncture risk is defined as "the incidence of an involuntary leg muscle contraction and an auditory response at the time of placing the device".

- Common femoral artery laceration (or needle penetration) is defined as "a common femoral artery laceration (or needle penetration) with resultant bleeding or hematoma > 6 cm diameter".

Secondary Endpoints

- Patient Discomfort @ discharge from the catheterization lab and @ 24 hours' post procedure (per phone interview)
  a. 1-10 scale with 10 being intense pain
- Assessment of complications (major and minor) 30days after leaving the catheterization lab (per visit to physician investigator).

Major complications:

b. Vascular repair or the need for vascular repair (via surgery, ultrasound-guided compression, trans-catheter embolization, or stent-graft)
c. Access site-related bleeding requiring transfusion
d. Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram
e. Surgery or the need for surgery for access site-related nerve injury
f. Permanent (lasting > 30 days) access site-related nerve injury
g. Access site-related infection requiring intravenous antibiotics and/or extended hospitalization

Minor Complications

a. Non-treated pseudoaneurysm documented by ultrasound
b. Non-treated arteriovenous (AV) fistula documented by ultrasound
c. Pseudoaneurysm treated with ultrasound-guided thrombin injection or ultrasound-guided fibrin adhesive injection
d. Access site hematoma greater than 6cm
e. Access site-related bleeding requiring greater than 30minutes to achieve hemostasis
f. Late (following hospital discharge) access site-related bleeding
g. Ipsilateral lower extremity arterial emboli
h. Transient loss of ipsilateral/contralteral lower extremity pulse
i. Ipsilateral deep vein thrombosis
j. Access site-related vessel laceration
k. Transient access site-related nerve injury
l. Access site wound dehiscence
m. Localized access site infection treated with intramuscular or oral antibiotics

20. SAFETY/RISKS

The study device comprises no risks that are in addition to manual compression with the exception of placing a blind suture around the arteriotomy site.

The blind suture carries a risk of damaging the common femoral nerve (CFN) or lacerating (or needle penetration of) the common femoral artery (CFA).

Several steps are taken to mitigate this risk.

1. The J195 suture uses a CP needle and needle holder with maximum possible depth of 12 mm (proximity control).

2. The nerve is posterior (beneath) and lateral to the common femoral artery. A portion of the psoas major muscle separates the common femoral nerve from the common femoral artery and thus is deeper than 12mm and too far lateral.

3. Revised IFU instructions teach lifting the obturator/sheath vertically to stretch soft tissue away from the femoral vessel and then place the needle through the elevated soft tissue on patients where the doctor assesses that the common femoral artery is too close to the skin surface.

4. The obturator remains in place inside the sheath for resistance control during the second needle penetration. The needle can penetrate the vessel wall (pinprick).

    a. SiteSeal™ pressure upstream and downstream of the access site allows natural clotting to seal a vessel puncture by the needle. The attending doctor determines when to remove the device and ambulate the patient. The device remains deployed until the doctor determines that a mature clot has formed.

5. The Z-stitch penetration can potentially penetrate the vessel wall. Blood will flow between the 1.5Fr suture and suture track (path of least resistance) and be immediately obvious to the doctor.

6. The mitigation is to remove the suture and needle and then use manual pressure to seal the breach.

7. A new contraindication statement says: "Avoid use of SiteSeal™ Adjunctive Compression Device if the arterial access is at or above the inguinal ligament."

    The CFA rises towards the skin surface after the inguinal ligament and then falls. The access site should be 2-3cm downstream of the inguinal ligament so that the CFA is falling where the Z-stitch is placed.

21. DATA SAFETY AND MONITORING COMMITTEE

The Data Safety and Monitoring Committee (DSMC) members are:
Robert Nesbit, M.D. – Surgeon
Craig Walker, M.D. – Cardiologist
Frank Bunch, M.D. – Cardiologist

Their CVs are in the CV Section of the IDE.

The committee will meet before the trial begins and at least twice during the trial. The pre-trial objective is to predict (to the extent possible) adverse events or outcomes before the trial begins. During the trial, the Committee will review adverse events, if any. The Committee will recommend study termination if safety concerns warrant such action. The DSMC will concurrently serve as an independent Clinical Events Committee (CEC).

22. MONITORING PROTOCOL

II. Monitors
    a. Thomas Reidy
        i. CEO
        ii. (816) 260-8476
        iii. treidy@woundcare360.com

    CEO/President: In-Vitro Medical Diagnostics career with more than thirty-five years of progressive professional experience in management, that included the reorganizing and streamlining of all departments in both the Medical Laboratory and Medical Device space with FDA, PMA, and CLIA oversight that resulted in bringing new products to market and the establishment of international distributors that resulted in 45% of total sales.

    Mr. Reidy was responsible for the overall management of all aspects of Primus Diagnostics, a medical diagnostic company.

    Thomas Reidy co-developed the protocol, the investigational device, the written informed consent form and all documents provided to subjects, applicable regulators and to the Principal Investigators.

    b. Rex Teeslink, MD (706) 373-5771 rexteeslink@bellsouth.net
    Dr. Teeslink's Curriculum Vitae is in the IDE CV Section.

III. Purpose
    a. To verify that the rights and wellbeing of human subjects are protected.
    b. The reported trial data are accurate, complete and verifiable from source documents.
    c. The conduct of the trial is in compliance with the currently approved protocol, with GCP and with the applicable regulatory requirements.

IV. Extent and Nature of Monitoring
    a. The Monitor is the main line of communication from the Sponsor to the PI

V. Monitoring site visit (biweekly)
VI. Monitoring report
    a. The monitor will submit a written report to file after each trial-site visit or trial communication with the PI.
    b. Reports will include the date, site, name of the investigator or other individual contacted.
    c. Reports will include a summary of what was reviewed and the findings/facts, deviations and deficiencies, conclusions, actions taken and/or actions recommended to secure compliance.
    d. In the event of a non-compliant investigator, the deficiency will be pointed out, documented and corrective action initiated.
    e. In the event of repeated non-compliance, the investigator will be dropped from the trial
    f. Data from an incomplete CRF will not be used in the statistical analysis.

Sponsor: Woundcare 360 LLC
Project: Clinical Study of SiteSeal following Diagnostic and Interventional Cardiovascular Procedures
Date of Site visit: _____

Monitor Name _____

Patient Number	Investigator	Followed Protocol	Prior Informed Concent obtained	Patient meets inclusion requirements	Patient Eligible	Source Documents accurate	Source documents complete	Protocol data on CRF is accurate	Adverse Events reported correctly	Follow-up visit/data collected	Patient dropped out?	Investigator informed if CRF entry error?	CRF changes initaled?	Is the Investigator maintaining essential documents?	Were deviations communicated	Did the Investigator take appropriate Actions?	Did the investigator communicate detected deviations?	Comments

Monitor Signature **DATE**

23. TRAINING

Dr. Rex Teeslink, co-inventor of the device will train the investigators on the use of the SiteSeal™ device, trial protocol and record keeping in both classroom and lab environments. Each investigator will have 2roll-in placements before beginning the trial. The results of the roll-in patients will be collected, but not tabulated as part of the trial.

24. DISPERSION, STORAGE & RETURN OF DEVICE

Upon site receipt of device, an inventory must be performed and a device receipt form filled out and signed by the person accepting the shipment. The date the device was received, the number of devices received, the lot number of the device and the person who received device must be documented on a Site/Dispersion/Return Log. Any damaged device will be documented and the sponsor notified immediately.

25. STUDY OVERSIGHT

This study is evaluating an investigational device. The decision to stop the study will be made by the CEO, Chief Medical Officer for Woundcare360 LLC and the VP Quality and Regulatory Affairs.

26. STATISTICAL PLAN

Objective

The purpose of this study is to establish the safety of the SiteSeal™ Adjunctive Compression Device.

Study Design

The study design is a single arm with 90 enrolled patients, open-label, single center clinical trial.

Handling Missing Data

No imputation will be done for missing data.

Handling Dropouts

The numbers of patients who enter and complete the trial will be tabulated, and details concerning reasons for withdrawals will be listed.

Statistical Methods

Primary Safety Analyses

For the risk of each of the two primary safety endpoints, namely common femoral nerve puncture and common femoral artery laceration, percent of patients exhibiting the risk and its one-sided 95% upper confidence limit will be shown. We expect very low risk for the above two endpoints. In case that we observe no cases for each of the above endpoints, with 90 patients for the device group, we can claim that we are 95% confident that the risk is less than 3.3%.

Secondary Safety Analyses

For the risk of each of the major complications and minor complications, percent of patients exhibiting the risk and its two-sided 95% upper confidence interval will be shown. For the score of patient discomfort, the mean score and its 95% two-sided confidence interval will be reported.

Baseline Patient Characteristic Data

For each of quantitative baseline data such as age, height, BMI, and blood pressures, etc., the mean score and its 95% two-sided confidence interval will be reported.

For each of qualitative baseline data such as procedure type, presence or absence of peripheral vascular disease, and size of the introducer sheath, etc., its frequency distribution will be shown.

Populations for Analysis

All patients in this study are expected to receive the test device, and they will be categorized as intent-to-treat (ITT) patient population. All analyses will be conducted based on this ITT population.

The calculations will be performed using SAS® software for Windows[1], Version 9.4, Copyright (c) 2002-2012 by SAS Institute Inc., Cary, NC, USA.

References

1. SAS OnlineDoc Version Nine for the Web, SAS Institute Inc., Cary, NC, USA. http://support.sas.com/documentation/onlinedoc/sas9doc.html

27. DATA MANAGEMENT

The data will be owned and maintained by Woundcare360 LLC. Woundcare360 LLC will analyze the data. This analysis may be provided to the FDA. A description of this clinical trial will be available on http://ClinicalTrials.gov as required by US Law. This website will not include information that can identify subjects. Subjects can search this website at any time. The data may be used for presentations and submitted to journals. All subject matter will remain confidential, and at no time will any subject names or other identifying data be used.

28. IRB REVIEW

The IRB for MOVI is:

Quorum Review IRB
1501 Fourth Ave. Suite 800
Seattle WA 98101

The IRB Chairman is Stephen Rosenfeld MD.

The protocol, informed consent document and relevant supporting information must be submitted to the IRB for review and must be approved before the study is initiated. In addition, any subject recruitment materials must be approved by the IRB prior to being used. This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements. The study must be conducted in accordance with the regulations of the United States Food and Drug Administration (FDA) as described in 21CFR 50 and 56 and 812, applicable laws and the IRB requirements.

The sponsor must submit any change to the protocol to the IRB for review and approval before implementation. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately provided the FDA and the reviewing IRB are notified within 5 working days.

It is the responsibility of the investigator to provide each subject with full and adequate verbal and written information using the IRB approved informed consent document, including the objective and procedures of the study and the possible risks involved before inclusion in the study. Informed consent must be obtained prior to performing any study-related procedures, including screening and changes in medications, including any washout of medications. A copy of the informed consent must be given to the study subject.

29. CONFIDENTIALITY

As described above all data will be analyzed by Woundcare360 LLC. The data may also be used for presentations and submitted to journals. If any results are published, the subject's identity will remain confidential and at no time will any patient names or other

identifying data be used. A monitor, auditor, IRB and/or other regulatory authorities will have access to study-related medical records, as this information is necessary for our study. All study related records identifying the subject will be kept confidential and, to the extent permitted by applicable laws and/or regulations will not be made publically available.

QA Review and Approval _____ Date _____

CEO/President Review and Approval _____ Date _____

References:

1. Seldinger SI. Catheter replacement of the needle in percutaneous arteriography; a new technique. *Acta radiologica*. 1953;39:368-376
2. Patel MR, Jneid H, Derdeyn CP, Klein LW, Levine GN, Lookstein RA, White CJ, Yeghiazarians Y, Rosenfield K, American Heart Association D, Interventional Cardiac Catheterization Committee of the Council on Clinical Cardiology CoCR, Intervention CoPVDCoCS, Anesthesia, Stroke C. Arteriotomy closure devices for cardiovascular procedures: A scientific statement from the american heart association. *Circulation*. 2010;122:1882-1893
3. Feldman DN, Swaminathan RV, Kaltenbach LA, Baklanov DV, Kim LK, Wong SC, Minutello RM, Messenger JC, Moussa I, Garratt KN, Piana RN, Hillegass WB, Cohen MG, Gilchrist IC, Rao SV. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: An updated report from the national cardiovascular data registry (2007-2012). *Circulation*. 2013;127:2295-2306
4. Doyle BJ, Rihal CS, Gastineau DA, Holmes DR, Jr. Bleeding, blood transfusion, and increased mortality after percutaneous coronary intervention: Implications for contemporary practice. *Journal of the American College of Cardiology*. 2009;53:2019-2027
5. Mamas MA, Ratib K, Routledge H, Neyses L, Fraser DG, de Belder M, Ludman PF, Nolan J, British Cardiovascular Intervention S, the National Institute for Cardiovascular Outcomes R. Influence of arterial access site selection on outcomes in primary percutaneous coronary intervention: Are the results of randomized trials achievable in clinical practice? *JACC. Cardiovascular interventions*. 2013;6:698-706
6. Duffin DC, Muhlestein JB, Allisson SB, Horne BD, Fowles RE, Sorensen SG, Revenaugh JR, Bair TL, Lappe DL. Femoral arterial puncture management after percutaneous coronary procedures: A comparison of clinical outcomes and patient satisfaction between manual compression and two different vascular closure devices. *The Journal of invasive cardiology*. 2001;13:354-362
7. Martin JL, Pratsos A, Magargee E, Mayhew K, Pensyl C, Nunn M, Day F, Shapiro T. A randomized trial comparing compression, perclose proglide and angio-seal vip for arterial closure following percutaneous coronary intervention: The cap trial. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2008;71:1-5
8. Kussmaul WG, 3rd, Buchbinder M, Whitlow PL, Aker UT, Heuser RR, King SB, Kent KM, Leon MB, Kolansky DM, Sandza JG, Jr. Rapid arterial hemostasis and decreased access site complications after cardiac catheterization and angioplasty: Results of a randomized trial of a novel hemostatic device. *Journal of the American College of Cardiology*. 1995;25:1685-1692
9. Slaughter PM, Chetty R, Flintoft VF, Lewis S, Sykora K, Beattie DM, Schwartz L. A single center randomized trial assessing use of a vascular hemostasis device vs. Conventional manual compression following ptca: What are the potential

resource savings? *Catheterization and cardiovascular diagnosis*. 1995;34:210-214
10. Ward SR, Casale P, Raymond R, Kussmaul WG, 3rd, Simpfendorfer C. Efficacy and safety of a hemostatic puncture closure device with early ambulation after coronary angiography. Angio-seal investigators. *The American journal of cardiology*. 1998;81:569-572
11. Gerckens U, Cattelaens N, Lampe EG, Grube E. Management of arterial puncture site after catheterization procedures: Evaluating a suture-mediated closure device. *The American journal of cardiology*. 1999;83:1658-1663
12. Chevalier B, Lancelin B, Koning R, Henry M, Gommeaux A, Pilliere R, Elbaz M, Lefevre T, Boughalem K, Marco J, Dupouy P, Investigators HT. Effect of a closure device on complication rates in high-local-risk patients: Results of a randomized multicenter trial. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2003;58:285-291
13. Nasu K, Tsuchikane E, Sumitsuji S, Investigators P. Clinical effectiveness of the prostar xl suture-mediated percutaneous vascular closure device following pci: Results of the perclose accelerated ambulation and discharge (paradise) trial. *The Journal of invasive cardiology*. 2003;15:251-256
14. Nikolsky E, Mehran R, Halkin A, Aymong ED, Mintz GS, Lasic Z, Negoita M, Fahy M, Krieger S, Moussa I, Moses JW, Stone GW, Leon MB, Pocock SJ, Dangas G. Vascular complications associated with arteriotomy closure devices in patients undergoing percutaneous coronary procedures: A meta-analysis. *Journal of the American College of Cardiology*. 2004;44:1200-1209
15. Applegate RJ, Sacrinty MT, Kutcher MA, Baki TT, Gandhi SK, Santos RM, Little WC. Propensity score analysis of vascular complications after diagnostic cardiac catheterization and percutaneous coronary intervention 1998-2003. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2006;67:556-562
16. Arora N, Matheny ME, Sepke C, Resnic FS. A propensity analysis of the risk of vascular complications after cardiac catheterization procedures with the use of vascular closure devices. *American heart journal*. 2007;153:606-611
17. Cura FA, Kapadia SR, L'Allier PL, Schneider JP, Kreindel MS, Silver MJ, Yadav JS, Simpfendorfer CC, Raymond RR, Tuzcu EM, Franco I, Whitlow PL, Topol EJ, Ellis SG. Safety of femoral closure devices after percutaneous coronary interventions in the era of glycoprotein iib/iiia platelet blockade. *The American journal of cardiology*. 2000;86:780-782, A789
18. Dangas G, Mehran R, Kokolis S, Feldman D, Satler LF, Pichard AD, Kent KM, Lansky AJ, Stone GW, Leon MB. Vascular complications after percutaneous coronary interventions following hemostasis with manual compression versus arteriotomy closure devices. *Journal of the American College of Cardiology*. 2001;38:638-641
19. Kahn ZM, Kumar M, Hollander G, Frankel R. Safety and efficacy of the perclose suture-mediated closure device after diagnostic and interventional catheterizations in a large consecutive population. *Catheterization and*

cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions. 2002;55:8-13

20. Brown DB. Current status of suture-mediated closure: What is the cost of comfort? *Journal of vascular and interventional radiology : JVIR*. 2003;14:677-681
21. Wagner SC, Gonsalves CF, Eschelman DJ, Sullivan KL, Bonn J. Complications of a percutaneous suture-mediated closure device versus manual compression for arteriotomy closure: A case-controlled study. *Journal of vascular and interventional radiology : JVIR*. 2003;14:735-741
22. Koreny M, Riedmuller E, Nikfardjam M, Siostrzonek P, Mullner M. Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: Systematic review and meta-analysis. *JAMA : the journal of the American Medical Association*. 2004;291:350-357
23. Sohail MR, Khan AH, Holmes DR, Jr., Wilson WR, Steckelberg JM, Baddour LM. Infectious complications of percutaneous vascular closure devices. *Mayo Clinic proceedings. Mayo Clinic*. 2005;80:1011-1015
24. Bos JJ, Hunink MG, Mali WP. Use of a collagen hemostatic closure device to achieve hemostasis after arterial puncture: A cost-effectiveness analysis. *Journal of vascular and interventional radiology : JVIR*. 1996;7:479-486
25. Resnic FS, Arora N, Matheny M, Reynolds MR. A cost-minimization analysis of the angio-seal vascular closure device following percutaneous coronary intervention. *The American journal of cardiology*. 2007;99:766-770
26. Turi ZG. It's time to seal every artery but... Comparing apples and oranges in the vascular sealing literature. *Catheterization and cardiovascular interventions : official journal of the Society for Cardiac Angiography & Interventions*. 2001;53:443-444