The Safety and Effectiveness of Polyethylene Glycol Sealant for Femoral Venous Access-site Closure

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Introduction:

Over 5 million central venous catheters are placed each year in the United States [1]. Such procedures are often done without direct visualization of the vessel wall, which risks vessel damage and bleeding. Vascular closure devices (VCDs) offer the potential for enhanced control of access-site hemostasis and reduced complications in comparison with manual compression. VCDs have shown to reduce time to ambulation, increase patient comfort, accelerate time to discharge, and, for patients undergoing diagnostic angiography, reduced bleeding complications compared with manual compression [2, 3].

Two principal reasons exist for using a VCD, namely to improve the safety and to enhance the efficacy of the percutaneous procedure. The MynxGripGrip™ Vascular Closure Device (AccessClosure, Inc, Santa Clara, CA) has previously demonstrated both of these features when used for arterial access-site closure [4]. In this study, major complications occurred in 0.5% of patients and the device allowed for rapid hemostasis (1.3 minutes) independent of anticoagulation use. The MynxGrip VCD received Food and Drug Administration (FDA) approval in 2007 for arterial access closure.

With increasing volume and complexity of cardiac interventional procedures requiring venous access, venous hemostasis and subsequent groin complications are a significant concern. The MynxGrip VCD appears to be an excellent choice for venous closure due to its extravascular use of a water-soluble, polyethyleneglycol matrix. In a recent large, single center study, propensity score-matched analysis, the MynxGrip device was successfully deployed in the femoral vein for immediate hemostasis. Results showed consistent safety and efficacy, similar to arterial device deployment, with low complication rates (<1%) and no major bleeding events. Importantly, no vessel injury or deep vein thrombosis were noted [5]. The ability to achieve rapid and reliable venous hemostasis following either a diagnostic or interventional procedure appears feasible, although no device has FDA approval for such an indication.

STUDY AIM

This study is aimed to assess safety of the MynxGrip™ Vascular Closure Device (VCD) [AccessClosure, Mountain View, CA] system for venous access site hemostasis following diagnostic and interventional procedures.

HYPOTHESIS

1. The MynxGrip™ Vascular Closure Device is as safe as manual compression for venous hemostasis following diagnostic or interventional procedures.

OBJECTIVES

PRIMARY

1. Evaluate the safety of the MynxGrip extravascular sealant for common femoral vein closure following both diagnostic and interventional procedures as assessed by clinical and imaging criteria.

ENDPOINTS

PRIMARY

The primary safety endpoint will include both deep venous thrombotic and bleeding/vascular injury related complications prior to discharge and at 1 week follow-up. Outcomes will be assessed via clinical evaluation and imaging with clinically indicated as follow:

- Assessment of venous thrombosis
    i. Clinical: Physical exam findings consistent with venous thrombotic/thromboembolic related complication:
    - Redness or swelling at the venous puncture site
    - Increased lower extremity edema
    - Calf pain
    - New onset or worsening shortness of breath
    - New onset of pleuritic chest pain

    ii. and if clinically indicated, imaging: venous Doppler ultrasound assessment of obstructive or non-obstructive deep vein thrombosis (DVT)
- Bleeding or vascular related complications
    i. Damage to the vessel requiring surgical repair
    ii. Access site bleeding requiring the need for transfusion
    iii. Nerve injury at access site
    iv. Generalized infection (septicemia with typical signs, symptoms and positive blood cultures shortly after the index procedure, and requiring treatment with intravenous (IV) antibiotics)Pseudo-aneurysms requiring invasive treatment
- Device/procedure failure

    Device failure is defined as either the inability to deploy the device or device deployment with inadequate hemostasis requiring conversion to immediate manual pressure, or the eventual need for alternative methods to obtain hemostasis.

.Efficacy will be assessed by time to hemostasis:

Time to hemostasis is defined as the time from advancer tube removal (i.e., device removal) to the time when hemostasis was first observed.

STUDY POPULATION

NUMBER OF SUBJECTS

A total of 208 patients undergoing either diagnostic or interventional procedures will be enrolled into this trial.

ELIGIBILITY OF SUBJECTS

GENERAL INCLUSION CRITERIA

Patients > 18 years of age scheduled for a percutaneous diagnostic or interventional procedure that have either a 5, 6, or 7F sheath placed in the common femoral vein.

EXCLUSION CRITERIA

1. Patient has a history of a bleeding disorder
2. Previous history of venous thrombosis or thromboembolism
3. Patient is pregnant or lactating
4. Patient has a known severe allergy to contrast medium
5. Patient has a known allergy to PEG
7. Patient is know to require an extended hospitalization or re-hospitalization (e.g.patient is undergoing coronary artery bypass graft (CABG) surgery) or patient is scheduled to have a CABG surgery <30 days following the procedure)
9. Multiple (>1) attempts at venous access were attempted
10. Patient has intra-procedural bleeding around the access site prior to sheath removal
11. Critically ill patients requiring intravenous vasopressors for blood pressure stabilization
12. Ipsilateral femoral artery puncture or sheath insertion
13. Glycoprotein IIb/IIIIa use
14. Any bleeding or vascular access-site complication evident pre-venous closure

STUDY DESIGN

OVERVIEW

The polyethylene glycol (PEG) sealant utilized for arteriotomy site closure in the MynxGrip system was previously demonstrated to be safe and effective in the Matrix VSG study, a prospective, randomized, 500-patient proof of concept trial at 13 US centers. Furthermore, the pivotal trial demonstrated absence of major complications requiring surgical repair, low minor complication rates without need for additional intervention or hospitalization, rapid time to hemostasis regardless of ACT levels or anti-coagulant use, and high device success rates (4).

MynxGrip is currently an FDA approved VCD for arterial use, with a venous indication currently in review by the FDA. No technique change is proposed for the venous study. Hence, this is primarily a safety study for the MynxGrip extravascular, water-soluble sealant vascular closure device for use in venous hemostasis.

The study will be conducted entirely at the MedStar Washington Hospital Center. Following either diagnostic or interventional procedures where venous access was required (via the common femoral vein with insertion of either 5, 6, or 7F sheath), femoral vein hemostasis will be achieved with either manual compression or the MynxGrip VCD system. A total of 208 patients will be prospectively enrolled in this study and will be followed for 7 days post procedure for safety purposes. To assess the primary safety outcome of venous patency and lack of occurrence of DVT, clinical assessment will be performed by the study team vascular access assessment group

and when clinically indicated a duplex ultrasound will be performed on patients prior to discharge to evaluation the presence of venous thrombosis. Patients will have final post-procedure telephone follow-up at 7 days to assess clinical findings consistent with any vascular or bleeding complications.

After enrollment, subjects will be randomized 1:1 to:

- Treatment Group A: Subjects will have venous hemostasis achieved using the MynxGrip vascular closure system in the common femoral vein.
- Treatment Group B: Subjects will have venous hemostasis achieved using manual compression over the common femoral vein.

Subjects who meet all inclusion criteria and none of the exclusion criteria, who agree to participate in this clinical study, and who sign an informed consent will be enrolled.

Statistial Analysis

Sample Size Calculation: The statistical objective was to evaluate whether the MynxGrip device was as safe as manual compression for achiving venous hemostasis. The rare occurance of venous thrombosis following catheter placement was used as the primary safety endpoint for calculation, with rates reported to be 2.4%. Using the Blackwelder method with α of 0.05, assuming event rates of 2.4% [6] in both arms, and a δ of 5% for noninferiority, the minimum required sample size for the MynxGrip group is 104 patients. A total of 208 patient will be included. Analyisis will be performed on an intention-to-treat basis.

References:

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