IVYSPRING INTERNATIONAL PUBLISHER

International Journal of Medical Sciences

2016; 13(4): 255-259. doi: 10.7150/ijms.14476

Research Paper

Clinical and Subclinical Femoral Vascular Complications after Deployment of two Different Vascular Closure Devices or Manual Compression in the Setting of Coronary Intervention

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Received: 2015.11.19; Accepted: 2016.02.04; Published: 2016.02.20

Abstract

Background: In the past two decades vascular closure devices (VCD) have been increasingly utilized as an alternative to manual compression after percutaneous femoral artery access. However, there is a lack of data confirming a significant reduction of vascular complication in a routine interventional setting. Systematic assessment of puncture sites with ultrasound was hardly performed.

Methods: 620 consecutive patients undergoing elective or urgent percutaneous coronary intervention were randomly allocated to either Angioseal (AS; n = 210), or Starclose (SC; n = 196) or manual compression (MC; n = 214). As an adjunct to clinical evaluation vascular ultrasonography was used to assess the safety of each hemostatic method in terms of major and minor vascular complications. The efficacy of VCDs was assessed by achievement of puncture site hemostasis.

Results: No major complications needing transfusion or vascular surgery were observed. Furthermore, the overall incidence of clinical and subclinical minor complications was similar among the three groups. There was no differences in the occurrence of pseudoaneurysmata (AS = 10; SC = 6; MC = 10), arteriovenous fistula (AS = 1; SC = 4; MC = 2) and large hematoma (AS = 11; SC = 10; MC = 14). The choice of access site treatment had no impact in the duration of hospital stay (AS = 6.7; SC = 7.4; MS = 6.4 days).

Conclusions: In the setting of routine coronary intervention AS and SC provide a similar efficacy and safety as manual compression. Subclinical vascular injuries are rare and not related to VCD use.

Key words: vascular closure device, angioseal, starclose, randomized comparison

Introduction

Due to the rapidly broadening spectrum of interventional percutaneous procedures the transfemoral access route is expected to remain a cornerstone of catheter-based diagnosis and treatment and valid alternative to the transradial access [1,2]. However, complications of the vascular access site are an unresolved issue and the leading cause of morbidity associated with transfemoral catheterization [3,4].

Within the last two decades vascular closure devices (VCD) have substantially altered post-procedure

management patterns. They provide improved patient comfort and decreased time to ambulation (5). However, their impact on vascular complications is, at best, no different than manual compression and in some cases, possibly even worse [5-7]. The degree of uncertainty in VCD use is further aggravated by the fact, that our knowledge is based on few randomized studies and that these studies were mostly conducted in the setting of diagnostic procedures [5]. Although demanded, an objective outcome evaluation based on vascular ultrasonography has hardly been incorporated into study design [2].

Considering these issues we consecutively enrolled and randomized patients for a head to head comparison of two commonly used VCDs and manual compression after angioplasty.

Materials and methods

In this prospective study 620 patients undergoing elective or urgent percutaneous coronary intervention at our institution were evaluated. Allocation to one of the three approaches was made by a computer-generated sequence using random block sizes of six patients. The randomization list was managed and stored by the nursing stuff. The interventional cardiologist was not informed about the assigned approach until the end of the procedure.

The following exclusion criteria were applied: age < 18 years, women who were pregnant or breastfeeding, presence of hematoma before sheath removal, strong calcium evidence at angioscopic evaluation at the end of the procedure, history of ipsilateral claudication or vascular surgery, puncture at or distal of the femoral artery bifurcation, requirement of an intra-aortic balloon pump or percutaneous cardiopulmonary bypass device, change of the interventional cardiologist during the procedure, Coumadin derivative therapy, non-compliance with study-protocol and known allergy to bovine collagen.

Demographic and clinical information, procedural technique, and femoral complications were recorded prospectively. All patients gave their written informed consent for interventional cardiac catheterization and for participation in the randomized study. All procedures performed in human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study protocol was approved by the ethical committee of the Ruhr-University of Bochum (registration number: 3328-08).

Study protocol

Patients routinely received weight-adjusted heparin (100 U/kg). For patients with adjunctive GPIIb/IIIa platelet inhibition, an activated clotting time (ACT) of 200 to 250 seconds was targeted. For patients who received heparin alone the target ACT was ≥ 300 seconds. ACT was measured at least once during the procedure. Patients who underwent coronary stenting were treated with aspirin and clopidogrel. A femoral artery angiogram was obtained before deployment of any femoral closure devices to avoid placement in or distal of the femoral bifurcation. Both femoral closure devices were applied immediately after intervention, without reversing anticoagulation. All operators were well trained to use these devices in advance of the study period. Patients allocated to manual compression had their sheaths removed after 2 hours (ACT = 300-400s) or 4 hours (ACT ≥ 400s) after intervention. The femoral artery was compressed by hand for ≥15 minutes or until hemostasis was achieved. After receiving an elastic pressure bandage for 12 hours the patients were allowed to walk. All patients with femoral closure devices received a soft bandage for 6 hours immediately after device application if primary hemostasis was achieved. Patients were allowed to walk after 6 hours of bed rest.

Access site complications were assessed at least twice during hospital stay. The first groin check was performed by clinical examination before patients were allowed to walk. The second groin check was performed on the first post procedural day combining clinical and duplex ultrasonographic evaluation of the groin.

The primary end point of the study was the in hospital occurrence of major and minor vascular complications (safety aspect of closure devices). Both terms were used according to the definitions applied in the U.S. multicentre trial [8]. Complications were classified as major when vascular surgery or transfusion was needed.

All other complications which were treated conservatively were considered as minor complications (bleeding from puncture site, pseudoaneurysmata, arteriovenous fistula, deep vein thrombosis, infections, lymphedema, and hematomas). Secondary end point was the efficacy of both vascular closure devices. Failure in achieving hemostasis was analysed and defined as the need to use mechanical compressive methods either manual pressure or application of the Femostop device (RADI Medical Systems, Uppsala, Sweden) to obtain hemostasis.

Ultrasonographic follow-up included gray-scale and color Doppler and was performed by an experienced angiologist using a 5-12 MHz linear probe. The evaluation of the puncture site comprised qualitative information to determine the presence of vascular

injury: the presence of hematoma, arterial or venous thrombosis, arteriovenous fistula, pseudoaneurysm or vascular stenosis.

Results

666 eligible patients were primarily randomised into the three treatment arms. 46 patients missed sonographic follow up and were retrospectively excluded. The final analysis of the three arm study therefore considered n = 210 patients treated with Angioseal (AS), n = 196 patients treated with Starclose (SC) and n = 214 patients in whom manual compression was applied (MC).

Baseline characteristics and demographics are presented in Table 1. Overall, patients were characterized by an unfavourable atherosclerotic risk profile. About 80 percent had arterial hypertension and about one third suffered from diabetes. The common patient had undergone two catheterization procedures via ipsilateral groin access before. About 15% of all patients represent emergency catheterization in acute myocardial infarction. GIIbIIIa receptor antagonists were applied in 8 to 10 percent of all cases.

In the overall study population no major complications requiring transfusion or vascular surgery were observed (Table 2). However, minor complications, predominantly small hematomas, were observed in about two third of all cases. All pseudoaneursmata and arteriovenous fistula disappeared either spontaneously or after renewing the pressure bandage or ultrasound guided compression. Failure of device application occurred in 2 patients with AS-VCD and 4 patients with SC-VCD. Primary hemostasis after device application was not achieved in 4 cases with AS-VCD and 11 cases with SC-VCD (p = 0.06).

Interestingly, follow up examination revealed only few cases that were not suspected by clinical examination and auscultation. There was one inapparent small pseudoaneurysm (AS) und two arteriovenous fistula (SC and MC) detected by vascular ultrasound.

There were no differences in the duration of hospital stay between the study groups. All baseline characteristics were similarly distributed between the groups.

Discussion

The results of our study demonstrated that the risk of VCD failure is rare in contemporary practice of percutaneous coronary intervention. Efficiency and safety of both different hemostatic devices, Angioseal and Starclose, are comparable to manual compression. Based on clinical and ultrasound follow up examination our study provided objective information on the rate of apparent and inapparent complications associated with these VCDs. Our data suggest that both devices can be safely used in a routine clinical setting covering "all coming patients" as those with acute coronary syndromes, GIIBIIIa use, renal failure and frequent previous femoral artery puncture.

Table 1. Baseline and demographic characteristics

	AS n = 210	SC n = 196	MC n = 214	p-Wert
Gender (male)	153 (73%)	137 (70%)	154 (72%)	ns
Age (years)	66.0 ± 11.2	66.6 ± 10.8	64.6 ± 11.4	ns
Body mass index (kg/m²)	28.8 ± 4.2	27.7 ± 3.7	28.2 ± 4.2	ns
Previous ipsilateral puncture (n)	2.2 ± 1.5	2.1 ± 1.2	2.1 ± 1.4	ns
Diabetes	71 (34%)	66 (34%)	74 (35%)	ns
Hypertension	173 (82%)	154 (79%)	164 (77%)	ns
Venous puncture	21 (10%)	18 (9%)	17 (8%)	ns
Groin (left)	12 (6%)	10 (5%)	16 (7%)	ns
PVD	31 (15%)	42 (22%)	48 (23%)	ns
ACT (s)	440.6 ± 207.7	445.1 ± 199.5	435.1 ± 189.6	ns
Additional heparin (IU)*	2750 ± 1077	3154 ± 1317	2438 ± 800	ns
LDL (mg/dl)	113.3 ± 41.6	117.7 ± 37.8	117.9 ± 41.7	ns
NSTEMI/STEMI	28 (13%)	33 (17%)	36 (17%)	ns
GIIbIIIa-Inhibitors	16 (8%)	17 (9%)	22 (10%)	ns
GFR (ml/min)	84.1 ± 24.3	85.6 ± 29.8	85.1 ± 29.3	ns
CKD stage I	82 (39%)	83 (42%)	86 (40%)	ns
CKD stage II	97 (46%)	79 (40%)	91 (43%)	ns
CKD stage III	29 (14%)	32 (16%	33 (16%)	ns
CKD stage IV	2 (1%)	0	0	ns
CKD stage V	0	2 (1%)	3 (1%)	ns

CKD = chronic kidney disease (Kidney Disease Outcomes Quality Initiative classification); SBP = systolic blood pressure; DBP = diastolic blood pressure; MI = myocardial infarction; IU = international units; PVD = peripheral vascular disease; ACT = activated clotting time; RF = renal failure; * target ACT not achieved

Table 2. Procedural characteristics

	AS n = 210	SC n = 196	MC n = 214	p-value
Successful application	208 (99%)	192 (98%)	-	ns
Successful primary hemostasis	206 (98%)	185 (94%)	-	ns (0.06)
Major complications				
Surgical intervention	0	0	0	ns
Blood transfusion	0	0	0	ns
total	0	0	0	ns
Minor complications				
Deep vein thrombosis	1	0	0	ns
Infection	0	0	0	ns
Pseudoaneurysm	10 (5%)	6 (3%)	10 (5%)	ns
Arteriovenous fistula	1 (0%)	4 (2%)	2 (1%)	ns
Retroperitoneal bleeding	0	0	0	ns
Hematoma (≤ 3 cm)	89 (42%)	76 (39%)	83 (39%)	ns
Hematoma (3 – 6 cm)	25 (12%)	23 (12%)	36 (17%)	ns
Hematoma (≥ 6 cm)	11 (5%)	10 (5%)	14 (7%)	ns
Lymphedema	0	0	1	ns
total	137 (65%)	119 (61%)	145 (68%)	ns
Hospital stay (d)	6.7 ± 6.4	7.4 ± 8.4	6.4 ± 5.7	ns

Comparison to prior studies

A head to head comparison of both VCDs has previously been performed in a diagnostic setting randomizing 144 patients to the Angioseal and 134 to the Starclose device. Hemostatic efficiency, complication rate and patients satisfaction were similar in both groups. However, at 1 week follow up less bruising was demonstrated in the Starclose group [9]. For diagnostic procedures Nikolsky et al. reported in a large meta-analysis that closure devices including AS and CS had a similar risk of access-site related complications as manual compression [10]. This conclusion was supported by the ISAR-CLOSURE randomized trial which compared an intravascular and extravascular VCD strategy to manual compression in 4524 patients undergoing diagnostic coronary angiography. Both VCD strategies were found to reduce time to hemostasis and to be non-inferior to manual compression in terms of vascular complications [11].

Both VCD based strategies and manual compression were further compared in two studies enrolling a mix of diagnostic and PCI procedures. One prospective, non-randomized trial comprising 426 patients reported that all three methods were comparable in terms of efficacy and safety [12]. Very thin patients were found to be more likely to have failed hemostasis after initially successful Starclose application. In these cases moderate bleeding was observed which required additional manual compression. However, it did not translate into an increased major complication rate. The less successful hemostasis in the SC group was attributed to the learning curve associated with SC deployment. To minimize the influence of operator experience Deuling et al. formed two specialized physician teams based on experience and preference for a particular device. 450 patients were randomly selected to receive catheterization and hemostasis by one of both dedicated teams. Despite this regimen, SC patients showed more oozing after device placement than AS patients suggesting that minimal postdeployment bleeding is a device-related problem. All patients with oozing at the puncture site required extra nursing care and received a pressure bandage. Furthermore, SC was more often not used or successfully deployed [13].

A systematic ultrasound based analysis of VSD related complications has hardly been conducted in the past. A sub-study of the CLIP trial evaluated the safety and efficacy of the Starclose VCD in 71 subjects at day 30 after hemostasis. Ultrasound examination was performed by an independent vascular ultrasound laboratory and demonstrated no evidence of iatrogenic vascular injury compared to manual compression [14]. A non-comparative ultrasound analysis of the Angioseal VCD in diagnostic and interventional procedures demonstrated a 2% incidence of high grade stenosis or vessel occlusion. However, these cases were related to inadvertent puncture of the superficial femoral artery [15]. In comparative studies with implementation of a femoral angiogram prior to Angioseal deployment no increased incidence of vascular complications in comparison to manual compression was noted [16]. However, ultrasonographic follow up was clinically driven and therefore no information on the rate of inapparent vascular injuries was obtained. One long term study demonstrated no ultrasound derived flow abnormalities and no increased incidence of peripheral vascular disease in 27 Angioseal patients at 10-year follow up [17]. Therefore, collagen plug induced tissue inflammation observed in animal models may not translate into long term negative effects on vascular morphology and function [18].

Our study extends these previous studies by providing a detailed evaluation of both VCDs in patients who received PCI. In comparison to diagnostic angiography percutaneous coronary intervention is associated with increased access-site bleeding complications and these complications are associated with increased morbidity and mortality [19,20]. Consistent with the above mentioned data our study demonstrated a marginal trend towards a lower primary hemostatic success rate in the SC group. 11 out of 196 patients required manual compression immediately after SC application due to insufficient hemostasis or insufficient deployment. In comparison to Angioseal the Starclose device has a more rigid application mechanism and requires a larger incision of the in-

tegument. These device-specific details may explain why primary hemostasis is more difficult to achieve and why continued oozing which occurs with an incidence of 25-38% is considered to be a typical SC-related problem [12]. However, as demonstrated, the problem of continued oozing can be easily circumvented by routine application of a soft pressure bandage for several hours. It is important to emphasize that these device specific application details had no impact on overall or specific vascular complication rates. Compared to manual compression both vascular closure devices proved to be save in a routine setting of unselected PCI patients. These insights were derived from clinical assessment as well as systematic ultrasound follow up.

We therefore conclude that in the setting of routine percutaneous coronary intervention AS and SC provides a similar efficacy and safety as manual compression. Subclinical injuries that may be detected by vascular ultrasound occur rarely and are not related to the method used for achieving hemostasis.

Competing Interests

The authors have declared that no competing interest exists.

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