

Early Treadmill ECG Stress Testing After Percutaneous Coronary Intervention Following Hemostasis with the Angioseal™ Vascular Closure Device: A Prospective Single-Center Cohort Study

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Abstract

Objective: Particularly with the transfemoral access, potential complications at the puncture site with early exercise are a major concern. The purpose of this study was to compare femoral artery access site complications after percutaneous coronary interventions (PCI) in 1) patients following a standard care procedure and 2) performing treadmill electrocardiographic (ECG) stress testing within 24 h after application of the Angioseal™ vascular closure device.

Methods: This is a prospective, randomised, single-center cohort study conducted in a high-volume tertiary interventional heart centre in Duisburg, Germany. 221 patients were included and 200 entered analysis. Patients were randomly assigned to treadmill testing within 24 h after transfemoral seven French (F) PCI or discharged with the recommendation of limited exercise for two weeks. Clinical examination and Duplex ultrasound (DUS) of the inguinal region was obtained within 24 h after PCI in both groups and repeated immediately after the treadmill test in the exercise group. Two-weeks clinical follow-up was obtained in both groups.

Results: Early treadmill testing could be performed without any major limitations or acute complications in all assigned patients. DUS showed no new pseudoaneurysm (PSA) or arteriovenous fistula (AVF) after treadmill testing. At follow-up, there were 1) no differences regarding pain or physical limitations between the two groups and 2) four patients (4%) in the exercise group and seven patients (7%) in the standard care group developed major hematoma (>6 cm)/minor bleeding, which were clinically uneventful.

Conclusions: Treadmill ECG stress testing within 24 h of PCI with the femoral access site closed by the Angioseal device was not associated with a higher complication rate compared to standard care.

Keywords: Closure device; Percutaneous coronary intervention; Treadmill ECG stress testing; Complications

Abbreviations: ACT: Activated Clotting Time; AVF: Arteriovenous Fistula; CAD: Coronary Artery Disease; CFA: Common Femoral Artery; ECG: Electrocardiogram; F: French; PAD: Peripheral Artery Disease; PCI: Percutaneous Coronary Interventions; PSA: Pseudoaneurysm; SFA: Superficial Femoral Artery; VCD: Vascular Closure Device.

Introduction

Interventional procedures require intravenous anticoagulation. The length of time to hemostasis is a major problem in the care of these patients. For this reason, vascular closure devices (VCDs) were developed and first introduced in the mid 1990s [1,2]. VCDs provide advantages over manual compression (such as shorter time to hemostasis, more rapid patient ambulation, and the potential for cost effectiveness) and seem to be safe [3,4]. Several studies tried to substantiate current recommendations on the timing and extent of mobilization [5-7]. Limited data are available for stress testing after percutaneous interventions and application of VCDs. Thus, most

physicians empirically discourage strenuous exercise or carrying heavy weights for several weeks. As a consequence, early exercise tests are not performed even when the clinical situation might recommend them. On the other hand, early detection and treatment of myocardial ischemia may be expected to reduce adverse cardiac events during follow-up [8]. Furthermore, early stress testing may reassure patients of their exercise capabilities despite recent arterial puncture.

The present study was designed to compare the vascular access site complications after PCI with femoral artery access in 1) patients following a standard care procedure and 2) performing treadmill ECG stress testing within 24 h after application of the Angioseal™ VCD.

Methods

Design

This study was an investigator-initiated, prospective, randomised, single-center cohort study conducted in a high-volume tertiary interventional heart centre in Duisburg, Germany.

Study patients

Between April 2008 and June 2009, 221 patients with coronary artery disease (CAD) who were undergoing planned PCI at the Duisburg Heart Center participated in this study. Subjects were randomly placed in either the treadmill testing group (exercise group) or the limited exercise group (standard care group) in a 1:1 ratio. Exclusion criteria for the study consisted in the presence of post-interventional bleeding, excessive subcutaneous blood oozing (requiring pressure bandage shortly after closure), or hematoma (diameter >6 cm).

Study protocol

At baseline, after informed consent was obtained, patients were placed at random in either the exercise group or control group. Clinical characteristics (sex, age, weight, height, hypertension (treated), peripheral arterial disease (PAD), Diabetes mellitus) were documented. Experienced senior investigators performed each PCI. Patients were pretreated with aspirin 100 mg/die and clopidogrel 75 mg/die and received bolus administration of weight-based heparin i.a. with additional fractions according to activated clotting time (ACT) measurements in long lasting procedures. Arterial access was established by retrograde puncture-preferably of the common femoral artery (CFA). All patients were implanted with a stent (76% bare metal stents and 24% drug eluting stents) and the nominal size of the introducer sheath was 7 French. At the end of the procedure, the operator immediately closed the puncture site using the collagen-based VCD Angioseal™ (St. Jude Medical). Bed rest was advised for three hours. Bleeding complications were treated with adjunctive manual compression and/or prolonged application of a pressure bandage. Inspection and auscultation of the puncture site took place three hours after closure of the puncture site, before discharge, and at any time after discharge as needed. All patients were drawn blood for clinical chemistry, blood count and hemoglobin at 6 h and 12 h post-PCI as well as post-treadmill testing. Duplex ultrasound (DUS) of the inguinal region 6 cm proximal to 6 cm distal to the puncture site was obtained within 24 h after PCI in both groups and repeated immediately after the treadmill test in the exercise group. A qualitative examination was performed to assess vascular problems such as pseudoaneurysm (PSA), arteriovenous fistula (AVF), hematoma, arterial/venous thrombosis or stenosis using two-dimensional gray-scale, color, and focused Doppler images.

In the exercise group, treadmill stress testing was performed within 12 to 24 h after PCI, employing maximum possible workload.

Endpoints

Evidence of PSA, AVF and arterial stenosis of the access site after stress testing in the DUS examination. Arterial/venous thrombosis, major hematoma (>6 cm) and bleeding from the puncture site in the first two weeks after discharge.

Follow-up

At discharge all patients were advised to avoid carrying heavy weights for 1-2 weeks. Standard care patients were also recommended to limit physical exercise during that period. Subjects were asked to report physical limitations, pain or complications and to grade them on a scale of 1 to 10 (maximum) and return the questionnaire after two weeks. They were advised to revisit the hospital if there were any suspicious local complications.

Statistical analysis

Numerical data are presented as mean ± SD, median (interquartile range), or as a percentage where appropriate. For statistical comparison, Student's t-test for paired values was used.

Results

Clinical and treatment characteristics

A total of 221 patients were enrolled and 21 subjects (17 in standard care group and 6 in exercise group) were excluded from further study since DUS was not performed as required by the protocol. All patients were pretreated with aspirin 100 mg/die and clopidogrel 75 mg/die and received bolus administration of weight-based heparin i.a. with additional fractions according to ACT measurements in long lasting procedures.

Baseline characteristics of the 200 study patients were well balanced between the two groups (Table 1). Hypertension was adequately controlled and the proportion of patients with peripheral arterial obstructive disease (12% in the control vs. 11% in the exercise group) or diabetes mellitus (26% in the control vs. 24% in the exercise group) reflected a typical CAD population.

| | Treadmill testing | Standard care | p-value |
|------------------------------------|-------------------|---------------|---------|
| Demographics | | | |
| Total, n | 100 | 100 | - |
| Female | 10 | 11 | 0.5 |
| Age, (years) mean (± SD) | 65.4 (± 8.6) | 67.8 (± 7.3) | 0.28 |
| Clinical presentation | | | |
| BMI, kg/m ² mean (± SD) | 27.5 (± 2.7) | 27.1 (± 3.6) | 0.43 |
| Medical history | | | |
| Coronary heart disease, n | 100 | 100 | - |
| Hypertension, n | 97 | 93 | 0.5 |
| Diabetes mellitus, n | 24 | 26 | 0.5 |
| PAD, n | 11 | 12 | 0.5 |

Table 1: Base line characteristics of patients included in study.

Initial clinical visit and DUS examination

The device success rate in this small study was 100% (221/221). Minor hematoma was found in 42 of 200 patients, 22 (22%) in the standard care group and 20 (20%) in the exercise group minor hematoma (<6 cm in diameter) was found at the three hour visit. As stated above in the Methods section these patients were included in the study. Insufficient hemostasis with prolonged bleeding was seen in one patient in the standard care group. DUS examination showed patency of the access site artery in all patients except one with pre-existing peripheral artery disease. This patient showed post-procedural stenosis of the right AFS that had to be treated by stenting. There were no episodes of arterial or venous thrombosis, groin infection, necessity of blood transfusion or vascular surgery. In the standard care group, DUS

revealed PSA and AVF in one patient each (2%). All vascular injuries were located in the proximal superficial femoral artery (SFA). In the exercise group, one PSA (1%) and no AVF were found before exercise.

Clinical visit and DUS examination post exercise

Treadmill testing could be performed without any major limitation or acute complication within 24 h of PCI. An examination of the groin area immediately after treadmill testing showed no systolic bruits or other complications. Pre-existing hematoma and bruises remained unchanged. Post-exercise DUS examination revealed no change in the size of pre-existent PSA in one patient. All other DUS examinations reproduced the primary findings.

Follow-up

During follow-up, four patients (4%) in the exercise group and seven patients (5%) in the standard care group developed major hematoma (>6 cm) and 2 patients (2%) had minor bleeding, which were clinically uneventful (Table 2). No additional complications were seen, and none of the patients revisited the clinic because of any suspicion of local complications. There was no infection or need for transfusion and surgical intervention. Patients in both groups rated the pain resulting from the femoral artery access and the resulting limitation of physical activity as “none” to “moderate”.

| | Treadmill testing | Standard care | p-value |
|---------------------------------------|-------------------|---------------|---------|
| Total, n | 4 | 7 | 0.5 |
| Hematoma (<6 cm) /minor bleeding, n | 0 | 2 | 0.5 |
| Hematoma >6 cm, n | 4 | 5 | 0.5 |
| Bleeding necessitating transfusion, n | 0 | 0 | - |
| Surgical intervention, n | 0 | 0 | - |
| Pseudoaneurysm, n | 0 | 0 | - |

Table 2: The individual components of complications.

Discussion

Key findings

The objective of this study was to compare the vascular access site complications after PCI with femoral artery access in 1) patients following a standard care procedure and 2) performing treadmill ECG stress testing within 24 h after application of the Angioseal VCD.

There were no relevant differences vascular access site complications in the two groups and post-exercise DUS examinations reproduced the primary findings of the pre-exercise DUS examinations. During follow-up, except for more bleeding in the control group, overall access site complications also did not differ significantly between the two groups. Patients in both groups rated the pain caused by the femoral artery access and the resulting limitation of physical activity the same.

Comparison with other studies and interpretation of results

While the risks and benefits of routine early stress tests are still a matter of debate [8,9] and currently are recommended only for selected groups of patients by the guidelines [10], it might be desirable to perform exercise testing in selected cases with the need for immediate assessment of the functional coronary status and working capacity.

The present study is the first to investigate on treadmill ECG stress testing 24 h after percutaneous interventions and application of a VCD. Indeed, in literature, the shortest recovery period chosen to perform treadmill ECG stress testing after interventional procedures and closure of the transfemoral access site was 30 days [11,12]. The recovery interval is supposedly determined by the time needed to physically reabsorb the VCD (30 days for Angio-Seal™) [13], driven by concerns on possible vascular complications.

Recently, three studies investigated the immediate deambulation after diagnostic coronary angiography only (RISE-Study) [7] and after diagnostic and PCI procedures with femoral access (Angio-Seal™ femoral closure device allows immediate ambulation [5] and MOBS [6]). In the RISE-Study there were no deaths or major vascular complications, and the rate of minor vascular complications not requiring surgery (like hematoma >6 cm, PSA or AVF and late access site bleeding) was 1.9%. Unfortunately in the study by Hvelplund et al. no distinction between diagnostic and interventional procedures (round about 30% of total patients included) with regard to complications was made. They observed similar overall complications in the standard-care cohort compared to those in the early deambulation cohort (9.6% vs.11.3%), mainly consisting of small hematomas/minor bleedings/oozing (6.1% vs.7.3%) and pseudoaneurysm that occurred in 1 (0.34%) vs. 3 (0.37%). The MOBS II-Study was conducted in patients undergoing 6 F PCI and no DUS was performed after closure with the Angioseal™ device. The primary endpoint was major bleeding from the puncture site. In this study overall bleeding complication rates did not differ significantly between the two groups (immediate mobilization group 26.6% vs. standard care group 28.0%). The majority of bleeding complications were due to oozing (immediate mobilization group 22.8% vs. standard care group 20.5%) and during follow-up of 30 days they observed only one PSA and in four patients groin pain.

Our data are in line with the MOBS II data in as much the presence of minor hematoma did not differ between the two groups (exercise group 20% vs. control group 22%) at the initial visit after the interventional procedure. In the initial DUS examination of the femoral access site, we observed similar rates of pseudoaneurysm and arterio-venous fistula (3%) and a tendency towards more arterial stenosis (0.5%) compared with data published in a meta-analysis on percutaneous coronary intervention procedures and closure by VCDs [14]. In contrast to this meta-analysis and in line with Hvelplund and Larsen et al. we noticed no groin infection and had no need for blood transfusion and vascular surgery. With regard to follow-up data in our study there is a tendency to more major hematoma formation/oozing in both groups, although we observed no PSA formation as Larsen et al. did. This might have been due to the fact that patients had the opportunity to self-report complications by sending in the questionnaire and not only complications requiring hospitalization as in MOBS were recorded. Another possibility is the use of warfarin in these patients, but also the MOBS II study included patients with a warfarin medication. Furthermore after evaluation of a follow-up questionnaire on patient discomfort two weeks after discharge, we

found that irrespective of the initial approach patients reported only minor pain or limitations in their physical activity at follow-up two weeks after discharge.

Although baseline characteristics of all patients enrolled were well balanced between the two groups a high percentage of our patients present arterial hypertension. This might be due to regional and racial factors. Duisburg is a highly populated, industrialized, stressful environment and is characterized by a high percentage of individuals of Eurasian origin. Furthermore this might be due to a particular high penetration of hypertensive therapy in this CAD population. One would expect more vascular complications in such a high risk population and therefore the overrepresentation of hypertensive individuals does not pose a limitation to the interpretability of the data. Furthermore there is data that the use of VCDs in hypertensive individuals lowers the vascular complication rate [15].

Thus, our findings display no acute complications after treadmill ECG stress testing and only minor adverse effects during follow-up in this limited sample size. The obtained data suggest that it is not necessary to discourage ECG stress testing for several weeks after closure with the Angio-Seal™ VCD in selected cases.

Limitations

First, this study is underpowered for the purpose of showing the safety of the VCD with regard to strenuous exercise like a treadmill ECG stress testing. Second, this was a single-center study. Third, duration of follow-up was only 14 days and as a result we might have missed some late complications. Fourth, most patients were male and this may have biased the results, because women have a more than twofold risk of bleeding and/or vascular complications compared with men [16].

Furthermore results cannot be extended to patients where a glycoprotein IIb/IIIa receptor blocker or bivalirudin were administered.

Conclusions

Sustained exercise such as treadmill exercise testing within 24 h of PCI and closure of the femoral access site with the Angio-Seal VCD is not associated with a higher complication rate at the vascular access site compared to standard care with limited exercise. Although a future larger study is needed to demonstrate the safety of this procedure, this study shows for the first time that the early use of stress ECG after Angio-Seal™ deployment is feasible whenever there is the clinical need for it.

Consent to Participate

Our study involved human participants and human data. The investigation was approved by the local hospital management. The ethics committee at the Ärztekammer Nordrhein/Germany declared that no ethics approval and consent was necessary (Ref./Nr. 19-2013).

Consent for Publication

Not applicable.

Availability of Data and Materials

The dataset(s) supporting the conclusions of this article is (are) included within the article.

Competing Interests

The authors declare that they have no financial or non-financial competing interests regarding the research conducted.

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Author's Contribution

Marco Albanese was responsible for the conception, design, and interpretation of the data. M. Albanese also drafted the manuscript. Gregor Stappert and Konstantin Chondros collected, analyzed and interpreted the data. Wolfgang Schoels examined and revised the manuscript for intellectual content and gave final approval of the manuscript submitted.

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