Comparison of radial access versus femoral access with the use of a vascular closure device for the prevention of vascular complications and mortality after percutaneous coronary intervention

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Abstract

Background: Radial access (RA) and vascular closure devices (VCD) have been shown to be superior to transfemoral access (TFA) with regard to the prevention of vascular complications after percutaneous coronary intervention (PCI).

Objective: The present study evaluates whether RA is associated with less vascular complications and a lower mortality than VCD.

Methods: A total of 6999 consecutive PCI patients were studied through a single centre prospective registry from January 2011 to August 2015. RA was applied in 1385 patients (20%), VCDs with Angioseal were implanted in 2145 patients (30%) and manual compression of transfemoral access was performed in 3468 patients (50%).

Results: RA and VCD patients had comparable baseline risk profiles. The overall vascular complication rate was 2.0% (n=137) and was composed of false aneurysms (n=85), clinically relevant hematomas, (n=27), arteriovenous fistulas (n=12), arterial occlusions (n=11) and local infections (n=2). Vascular complications occurred in 0.6% of RA patients, 1.8% of VCD patients, and 2.6% of TFA patients ($p<0.01$). In-hospital mortality was 0.8% in RA patients, 0.8% in VCD patients and 3.8% in TFA patients ($p<0.01$). In a multivariate logistic regression model, RA, compared to VCD, was found to be independently associated with a lower rate of vascular complications (OR 0.34, 95% CI 0.16-0.75), but not with lower mortality rates (OR 1.20, 95% CI 0.51-2,85).

Conclusions: In this large all-comers PCI population, the radial approach, compared to the femoral approach with VCD use (Angioseal), was independently associated with a reduction of vascular complications, but not with lower mortality rates.

Keywords

Percutaneous coronary intervention – Radial access– Vascular closure device – Vascular complications

Introduction

Arterial access-related vascular complications are among the most common adverse events after transfemoral percutaneous coronary intervention (PCI) and are associated with severe in-hospital morbidities, sometimes causing life-threatening bleeding[1, 2]. In the past few decades, prevention of vascular access site complication was achieved by more optimal peri-procedural antithrombotic treatment, by the use of vascular closure devices or by choosing the radial approach[3-7]. Radial access (RA) has been proposed in recent guidelines as the preferred access site in acute coronary syndrome (ACS) patients based upon two recent large-scale randomized trials[8-10]. In both trials, a greater than 65% reduction in vascular complications was observed compared to transfemoral access (TFA). In addition, Valgimigli et al. showed an approximate 30% mortality reduction for the RA group in their study[10]. In these studies, only a minority of the patients (approximately 25%) with TFA received a vascular closure device (VCD). Therefore, RA was mainly compared to conventional mechanical compression after transfemoral PCI. VCDs have emerged as an alternative to conventional mechanical compression [3]. These devices reduce the time to hemostasis, facilitate patient mobilization, and improve patient satisfaction[11]. Furthermore, the more recent devices have demonstrated a risk reduction of vascular complications by more than 50% [12-16]. Hence, the efficacy gap between standard TFA and RA could be strongly diminished if vascular closure devices are applied. Until now, no studies have compared the effect of RA versus transfemoral access with vascular closure devices. This information is important to establish the best vascular access policy for the global PCI population.

Therefore, this observational study was designed to assess the effectiveness of RA and currently available VCDs compared to TFA for the prevention of vascular access complications and in-hospital mortality in an all-comers PCI population.

Methods

Study population

Between January 2011 and August 2015, 7160 consecutive patients underwent PCI in the University Hospital of Antwerp and were included in a standardized database for further evaluation. Patients with peri-procedural placement of an IABP (n=109), with brachial access (n=12) or with missing access data (n=40) were excluded from analyses. The final study population consisted of 6999 patients, of which 1903 (27%) underwent urgent PCI in the setting of an ACS. RA was applied in 1385 patients (20%), VCDs were implanted in 2145 patients (30%) and TFA was performed in 3468 patients (50%) based upon clinical and angiographic characteristics of the patients and at the discretion of the operator. The radial-to-femoral crossover rate was 5.5%, whereas the femoral-to-radial crossover rate was 3.0%.
Based upon previous work, female patients older than 75 years were defined as having a high risk for vascular complications and represented 11% of the total study population.[15] RA was applied in 15% (113/762) of the high vascular risk patients.
A prospective catheterization laboratory database, based on the European CARDS Registry definitions, was used to record the clinical and procedural elements for each case.[17] Informed consent was obtained from all patients or from their legal representatives. The study was approved by our institutional review board.

Catheterization procedure

The PCI was performed by standard techniques using 6 Fr sheaths for the femoral procedures and 5 or 6 Fr sheaths for radial procedures. All of the PCIs were performed by ten experienced operators, each with an annual PCI volume ranging between 100 and 300 procedures. The antithrombotic regimens included aspirin, clopidogrel/ticagrelor and unfractionated heparin, which were adjusted to achieve and maintain an activated clotting time of 250 to 300 seconds (200 to 250 seconds if glycoprotein IIb/IIIa inhibitors were used). Adjunct glycoprotein IIb/IIIa receptor inhibitors were used at the discretion of the operators.
The antithrombotic regimen was chosen regardless of the vascular access route used. When VCDs were used (Angioseal, St Jude, Minneapolis, MN, USA), femoral angiograms were

obtained before their placement to identify any anatomical restrictions, such as punctures at arterial bifurcation sites, the presence of severe calcification or the presence of severe peripheral artery disease. The final decision for insertion of a VCD was based on anatomical and clinical criteria at the discretion of the operator. Patients assigned to VCDs underwent immediate sheath control and were ambulated after 4 h of bed rest. In the case of radial access, sheath removal was performed immediately after the procedure and a compression device was placed on the wrist until hemostasis was achieved.

Patients assigned to manual compression underwent sheath removal 4 h after PCI and were kept on bed rest overnight.

After the procedure and before discharge evaluation of the access site was routinely performed and recorded for each patient.

Clinical endpoints

The primary endpoint was the occurrence of a vascular access-related complications after PCI. The vascular complications were reviewed as follows: false aneurysms (confirmed by ultrasonography), arteriovenous fistulas (confirmed by ultrasonography), arterial occlusions (confirmed by ultrasonography), arterial infections and severe access-site bleeding (hematoma) confirmed by a Bleeding Academic Research Consortium [BARC] score>1. The latter category included patients with important blood loss who required prolonged hospitalization and medical/surgical interventions.[18]

An independent clinical event committee reviewed all of the reported vascular complications and a BARC score were assigned retrospectively to each site related bleeding complication.

The secondary endpoint was in-hospital death from all causes with subdivision between cardiovascular and non-cardiovascular death.

Statistical analysis

Continuous variables are presented as the mean value (±SD) and categorical variables as a proportion (%). Baseline characteristics of the patients were compared using chi-square analysis or Fisher's exact test for categorical variables and One-Way ANOVA analysis for continuous variables. Given the observational nature of the data, inverse propensity score weighting was used to balance the three groups (McCaffrey et al).[19] Fourteen different baseline risk factors were included in this weighting estimation model: age, gender, diabetes mellitus, hypercholesterolemia, the use of GP IIb/IIIa receptor inhibitors, current history of smoking, hypertension, number of diseased coronary arteries, modalities of PCI (urgent versus elective), number of stents implanted, renal failure (defined as creatinine>2.0 mg/dl), cardiogenic shock and cardiac arrest (with need for resuscitation). Total body weight and history of vascular disease were not included in the model due to insufficient data. The absolute standardized mean difference (ASMD) was used for the assessment of imbalance between the study groups. ASMD values below 0.20 are considered to indicate good balance. After reweighting the data, a logistic regression model was set up to identify independent predictors of vascular complications and in-hospital mortality. The same variables from the propensity score model were used with the exclusion of cardiogenic shock and cardiac arrest because of low incidence. All statistical tests were two-sided, and a p-value<0.05 was considered statistically significant. All of the statistical analyses were performed using IBM® SPSS® Statistics version 22 (for Macintosh).

Results

Study population

The baseline characteristics of the three cohorts are presented in Table 1. The TFA patients were older, more hemodynamically unstable and treated more frequently with Glycoprotein IIb/IIIa antagonists than the patients with VCD (Angioseal) or RA. In addition, urgent PCI was more often performed by TFA.

After propensity weighted analysis, the three study groups had a comparable baseline risk profiles (see table 1). Figure 1 depicts the evolution of access site and closure strategy over time. The proportion of RA procedures showed a linear increase at the expense of TFA. The use of VCD (Angioseal) as a closure strategy after femoral access remained unchanged.

Clinical endpoints

Table 2 lists the vascular complications and in- hospital mortality per study cohort.

The overall vascular complication rate during the study period was 2.0 % (n=137) and was composed of false aneurysms (1.2%), clinically relevant hematomas (0.4%, n=27), arteriovenous fistulas (0.2%, n=12), arterial occlusions (0.2%, n=11), and local infections (0.03%, n=2). Only five of all hematoma patients needed further intervention (BARC 3). Vascular complications occurred in 0.6% of RA patients, 1.8% of VCD(Angioseal) patients and 2.6% of TFA patients ($p<0.0001$). Over time the annual vascular complication rate decreased from 2.6% in 2011 to 1.2% in 2015 (p for trend <0.007)(see figure 2). For RA the vascular complication rate was 4.2% (3/72) in 2011 but decreased below 1% in subsequent years. Figure 3 displays the vascular complications rate stratified according to the vascular risk profile and the vascular access approach. The benefit of RA is the highest for high-vascular-risk patients (absolute difference of 2.7%), whereas for low-vascular-risk patients, the absolute benefit is 1.4%.

The in-hospital mortality occurred in 159 patients (2.3%) with mortality rates of 0.8% in RA patients, 0.8% in VCD (Angioseal) patients and 3.8% in TFA patients (p<0,0001). Mortality difference among the subgroups was mainly driven by differences in cardiovascular mortality. Mortality rate was 2.3% in patients without vascular complications (155/6880) and 3.4% in patients with vascular complications (4/119) (p=0.6).

Determinants of vascular complications

The predictors of vascular complications are shown in table 3. The most important risk predictors of vascular complications were the route of vascular access and female gender (see table 4). RA, compared to VCD (Angioseal), was found to be independently associated with a lower rate of vascular complications (OR 0,34, 95% CI 0.16-0.75). Furthermore, when compared to TFA, RA (OR 0,22, 95% CI 0,11-0,46) and VCD (OR 0,65, 95% CI 0,42-1,00) were independently associated with decreased vascular complications.

In-hospital mortality

The predictive values for in-hospital mortality are presented in table 4. The following determinants were statistically significant (p<0,05): increasing age (OR 1,07, 95% CI 1,04-1,10), diabetes (OR 2,46, 95% CI 1,40-4,35), hypercholesterolemia (OR 0,39, 95% CI 0,24-0,62) and urgent PCI (OR 6,31, 95% CI 3,86-9,75). TFA, compared to VCD (Angioseal) and RA, was a significant predictor of in-hospital mortality, with odds ratios of 0,44 (95% CI 0,24-0,79) and 0,52 (95% CI 0,26-1,04), respectively. Comparison of VCD and RA was not independently associated with lower mortality rates.

Discussion

The present study is the first head-to-head study comparing radial access to femoral access with a vascular closure device to prevent vascular complications. We demonstrated that the superiority of RA persisted with a 65% additional risk reduction of vascular complications on top of the reduction obtained with VCD (Angioseal), but without a significant effect on in-hospital mortality reduction.

Radial access has been shown to make access site hemostasis more predictable. Many registries and randomized clinical trials consistently showed that RA is associated with a more than 60% risk reduction of vascular complications compared to femoral access. [6, 9, 10] In most of the reported studies, VCD were applied, but in less than 25% of the cases.

The clinical benefit of VCDs, in patients undergoing coronary angiography or PCI, has been debated extensively over the last decades, but more recent registries and randomized trials using contemporary devices clearly have demonstrated a more than 50% reduction in vascular complications[15, 16, 20]. The present study confirms these findings and, in addition, highlights an important remaining gap between RA and VCD, particularly for high-vascular-risk patients. Despite the safety advantage of RA, our study demonstrates that RA is used less frequently in high-risk subgroups (older patients, women, patients with urgent PCI), which paradoxically could benefit them the most. This apparent risk-treatment paradox has also been observed in other trials targeting PCI bleeding complications[21]. Potential reasons for slow adoption of radial PCI include concerns about the learning curve required for radial access procedures, potentially lower procedural success rates with the necessity for crossover to the femoral approach, and concerns over longer fluoroscopy and procedure times (particularly in the case of primary PCI). Operator expertise with the radial approach is clearly important to cope with these concerns. We observed, in our study, a gradual increase in the use of RA with a concomitant decrease in overall vascular complication rate.

Whether avoiding access site bleeding and vascular complications by the use of routine transradial intervention improves outcomes in largely unselected patients remains unclear.

The study of Valgimigli demonstrated a mortality benefit of RA versus TFA in ACS patients undergoing invasive management.[10] However, this could not be confirmed in the ST Elevation Myocardial Infarction treated by RADIAL or femoral approach (STEMI-RADIAL) trial, which showed a significant reduction in bleeding and access site complications with RA, but no effect on mortality.[22] In our study, the in-hospital mortality was decreased by more than 50% for both the VCD group as well as the RA group, compared to TFA, whereas no additional mortality benefit could be demonstrated for RA versus VCD.

The mechanistic explanation for the lower mortality observed in RA/VCD patients remains speculative but the following arguments have been proposed[2]: (1) more severe cardiovascular disease in patients allocated to femoral approach without VCD, (2) hemodynamic compromise or myocardial injury caused by vascular complication-related hemorrhage, (3) putative adverse effects of red blood cell transfusion on survival, and (4) the need for abrupt cessation of antithrombotic therapy. In addition, a faster mobilization, even unrelated to vascular complications, may lead to lower morbidity and possibly lower mortality.

In the present study the superiority of RA versus VCD (Angioseal) for the prevention of vascular complications did not translate into a mortality benefit. This is most likely explained by the fact that the difference in vascular complications were mainly driven by less false aneurysms , which have been shown not to trigger mortality.[2, 23]

The practical implication of our study findings is that although RA remains the preferred strategy in an all comers PCI population, VCD is a valid alternative, particularly in patients where a radial approach is not feasible (e.g., refractory radial spasm, subclavian tortuosity) or less suitable (cf. complex PCI procedures), as it reduces vascular complications as well as seemingly improves the patient prognosis.

The results of this study should be considered in the context of the following limitations. Because the present study was conducted at a single center with high volume operators, the results cannot be automatically translated to other centers. However, a single-center study design may attenuate the confounding factor of differences in expertise, which are more prevalent in multi-center studies. Secondly, The initial learning experience with radial access could introduce a bias in the global comparison between RA and VCD with angioseal.

However, as the learning period was only one year in our practice with only a limited number of vascular complications in that period (n=3), this effect will be marginal.

Furthermore, it should be noted that due to the non-randomized study design, a selection bias could have influenced the outcomes in the different study populations. We tried to minimize this effect by using multivariate analysis after accounting for the propensity to use one of the vascular access approaches. In addition, some factors such as P2Y12 inhibitors, frailty index, PCI complexity were not systematically captured by this registry. In any case, only a randomized clinical trial will be able to overcome this limitation and will allow the accurate assessment of the beneficial effect of RA as compared to femoral access with VCD

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Conclusion

In this large all-comers PCI population, the radial approach, compared to the femoral approach with VCDs (Angioseal), was independently associated with a reduction of vascular complications, but not with lower mortality rates.

Conflict of interest statement: no conflicts

LEGEND

Figure 1

Graph showing the evolution of vascular access approach from 2011 until 2015.

RA: Radial access; TFA: transfemoral access; VCD: vascular closure device (Angioseal)

Figure 2

Graph showing the evolution of vascular complications from 2011 until 2015

Figure 3

Bar graph showing vascular complication rate for low and high vascular risk patients according to vascular access approach.

RA: Radial access; TFA: transfemoral access; VCD: vascular closure device (Angioseal)

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