Changing from the femoral artery to the radial artery as the preferred access site for primary percutaneous coronary intervention: a real world single center registry data of 1808 consecutive acute ST-elevation myocardial infarction patients

Sasko Kedev[1], MD, Oliver Kalpak[1], MD, Surya Dharma[1,2], MD, Slobodan Antov[1], MD, Jorgo Kostov[1], MD, Hristo Pejkov[1], MD, Igor Spiroski[1], MD

[1] Department of Cardiology, Faculty of Medicine, University Clinic of Cardiology, University of St. Cyril & Methodius, Vodnjanska, Skopje, Macedonia
[2] Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Indonesia, National Cardiovascular Center Harapan Kita, Jakarta, Indonesia

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Abstract

Objective

To compare the short and long-term outcomes of trans-radial (TRA) versus trans-femoral approach (TFA) for primary percutaneous coronary intervention (PPCI) during a complete institutional transition from TFA to TRA as the site of access.

Background

PPCI is the preferred treatment for STEMI patients. Whether the TRA is associated with improved outcomes of the treated patients, as compared to the TFA, remains to be assessed.

Methods

Consecutive STEMI patients (n=1808) who underwent PPCI using TRA (n=1162) and TFA (n=646) from October 2007 to December 2010 were enrolled. By 2007, TRA was used in 25% of PPCI and in 2010 this number was 95%. Primary end-points were cardiovascular death and major adverse cardiac events (MACE) defined as a composite of death, stroke, re-infarction and target vessel revascularization at 30 days and one year.

Results

At 30 days, TRA compared to TFA was associated with less cardiovascular mortality (5.2% vs. 10.5%, OR=0.46; 95% CI=0.32-0.66, p<0.001), less MACE (7.3% vs. 12.5%, OR=0.55; 95% CI=0.39-0.76, p<0.001), less access site complications (0.9% vs. 8.2%; OR=0.11; 95% CI=0.05-0.20, p<0.0001), and less major bleeding (1.1% vs. 4.3%; OR=0.24; 95% CI=0.12-0.46, p<0.001).

At one year, the cardiovascular mortality and MACE were also in favor for TRA compared to TFA group (6.9% vs. 11.5%; OR=0.57; 95% CI=0.41-0.79, p<0.001, and 11.6% vs. 20.1%; OR=0.52; 95% CI=0.40-0.68, p<0.001, respectively).

Conclusion

Complete transition from femoral access to radial access is safe and effective for STEMI patients undergoing PPCI, with favorable effects on short-term and long-term outcomes.

Keywords: trans-radial approach, trans-femoral approach, STEMI, primary PCI.

Introduction

Primary percutaneous coronary intervention (PPCI) is the strategy of choice to re-open the occluded coronary artery, thereby improving the outcome of patients with ST-elevation myocardial infarction (STEMI) [1-3]. Access site selection is an important procedural issue in PPCI. Trans-femoral approach (TFA) has been associated with higher rate of access site bleeding and vascular complications in comparison with trans-radial approach (TRA), particularly so if combined with the aggressive use of antithrombotic and antiplatelet treatment [4,5]. Vascular access site complications have been shown to be associated with worse outcomes [6,7].

Whether there is a possibility to further improve the outcome with radial access instead of femoral access in all-comers STEMI patients remains to be assessed.

Recent randomized trials found that in acute STEMI patients undergoing PPCI, TRA is associated with less bleeding events, lower vascular access site complications, and better clinical outcomes compared with TFA [8,9].

The radial artery offers an advantage that is readily accessible due to its superficial anatomy, regardless of the patient's body mass index, and its close proximity to the radial bone, which makes hemostasis easier [10].

The change of access site strategy, from femoral access to radial access, can overcome most of the problems related to the femoral access [11]. Since 2005, TRA was gradually adopted in our center. TRA became the main access choice in 2009 and has replaced femoral access in most of the elective and emergency PCI procedures.

The objective of this study was to compare the outcomes of a large scale cohort of STEMI patients undergoing PPCI during a period in which both TFA and TRA were used as access sites. All procedures were performed by the same seven high-volume operators experienced in TFA before adopting routine TRA. Thus, although the present study is a retrospective analysis and not a randomized trial, the comparison of TFA and TRA will underestimate the benefits of the TRA approach due to the limited experience of the operators with the relatively new TRA approach.

Patients and Methods

Study population

Between October 2007 and December 2010, a total of 1808 consecutive patients with acute STEMI admitted within the first 12 hours after onset of symptoms who underwent PPCI were enrolled. There were 1162 TRA and 646 TFA patients. During 39 months, all STEMI patients treated at our center were recruited and the procedural and clinical data were recorded in an ongoing registry.

The radial artery access as an alternative to femoral artery access for PPCI was adopted in our center during the period of 2007 to 2010. The TRA was performed in 25% of all PPCI procedures in 2007. In 2010, TRA was used in 95% of all PPCI procedures. Our PPCI registry is representative of our national interventional practice and contains data from 80% of the PPCI procedures performed in the Republic of Macedonia, which has a population of two million residents.

Procedural data was entered into a dedicated database by the interventional cardiologists immediately after completion of the procedure. This database was open for evaluation and audit by the health administration and public health insurance administration.

Transition from femoral access to radial access

All operators went through the TRA learning curve with more than 100 elective PCI procedures per year before using TRA for PPCI. At the beginning of the study (in 2007), TFA was the access chosen in 75% of the cases. In mid-term of the study (transitional period), all operators has changed the access to TRA, and at the end of 2010 TRA was the access site in 95% of the PPCI procedures .

Vascular access

Femoral artery access was obtained with a modified Seldinger technique. After local anesthesia with 3-5 mL 2% lidocaine, the femoral artery was cannulated with a 17G needle and a 0.035 inch guide-wire, followed by a 10 cm 6F introducer sheath placement.

The radial artery was accessed after local anesthesia with 1-1.5 mL of 2% lidocaine, using the counter puncture technique (Seldinger technique) with a 20G plastic iv cannula and a 0.025 inch mini guide-wire of 45 cm, followed by a 6F hydrophilic introducer sheath (Terumo, Fujinomiya, Japan) placement. A spasmolytic agent (5 mg verapamil) was given intra-arterially through the radial sheath.

Interventional procedures

Standard guide-catheters were used to perform PPCI (standard shapes like Judkins, Amplatz, EBU, etc) mostly 6F and occasionally 5F, for both radial and femoral artery access. Standard guide-wires for PPCI, mostly Balance Middle Weight (Abbott Vascular, Santa Clara, CA, USA), and other wires were used according to the case specificity, without preference related to access strategy.

PPCI only on the infarct-related artery was recommended. Infarct-related artery flow was determined before and after the PPCI procedure using the TIMI (Thrombolysis in Myocardial Infarction) score [12]. Stent choice between drug-eluting stent and bare metal stent was left to the operator's discretion. Manual thrombus aspiration was performed in cases with evident high thrombus burden. Data were analyzed by intention-to-treat principle.

Anticoagulation and antiplatelet treatments

Before PPCI, patients were treated with intravenous bolus of unfractionated heparin (100 IU/kg), acetylsalicylic acid (300 mg followed by 100 mg/day indefinitely) and clopidogrel (loading dose of 600 mg followed by 75 mg/day for at least 1 year). When required, abciximab was given by intracoronary or intravenous administration of 0.25 mg/kg (bolus) followed by 0.125 μg/kg/min infusion for 12 hours using a weight-adjusted protocol. After completion of PCI, the weight-adjusted dosage protocol of heparin infusion was continued for 24 hours, and the abciximab infusion was continued for 12 hours. Only in 4.1% of the patients abciximab was used. No fibrinolytic agent was used.

Hemostasis management

For femoral group: Femoral artery sheath was removed at 3-4 hours after insertion, and hemostasis was achieved by manual compression of 15-20 minutes followed by prolonged weight compression placement. Patients must remain in bed thereafter, with restricted mobility, in the following six hours (9-10 hours from sheath insertion). Vascular closure devices were not used.

For radial group: Radial artery sheath was removed immediately after the procedure, and hemostasis was achieved by a simple bandage compression or a TR band (Terumo, Fujinomiya, Japan). Patients had no mobility restriction after the procedure. The simple bandage compression was applied with 4-6 small elastic bands compressing the radial artery at the puncture site. The TR band was applied by inflating 13-15 mL of air at the puncture site. After each hour, TR band was gradually deflated and totally removed after four hours. Patients had no mobility restriction after the procedure.

Study end-points

The primary clinical end-points were cardiovascular death rate and major adverse cardiac events (MACE) at 30 days and 12 months follow-up. Secondary end-points were major vascular access site complications and major bleeding at 30 days. Other baseline, clinical and procedural characteristics such as demographic data, risk factors, first medical contact-to-balloon time, procedural time, procedural success, and fluoroscopy time were recorded and compared between groups. Primary and secondary end-points were judged by an independent clinical event committee of which the members were blinded to the access site for PPCI.

Definitions

Cardiovascular death was defined as: death from acute MI, sudden cardiac death, death due to heart failure, death due to stroke, death due to cardiovascular procedures, death due to cardiovascular hemorrhage, and death due to other cardiovascular causes within 30 days and one year follow-up. MACE was defined as a composite of death, stroke, re-infarction, and target vessel revascularization at 30 days and one year follow up.

Major vascular access site complication was defined as any access site-related hemorrhage requiring red blood cell transfusion, delayed hospital discharge or the need for a surgical vascular repair [13].

TIMI major bleeding was defined as overt clinical bleeding (or documented intracranial or retroperitoneal hemorrhage) associated with a drop in hemoglobin of >5 g/dL (0.5 g/L) or a drop in hematocrit of ≥15% [14].

Door-to-balloon time was defined as the time from admission to the emergency department until the first balloon inflation at the culprit lesion [15].

Procedural success was determined by angiographic success, defined as the achievement of a vessel diameter >80% of normal in the presence of grade 3 TIMI flow [16]. Procedural time was calculated as the time needed from the local anesthesia injection until guide-catheter removal. Fluoroscopy time was also recorded.

Statistical analysis

Data was expressed as mean ± standard deviation for normally distributed numeric variables. If not fitting a normal distribution, data was expressed as median (range). Categorical variables were compared with chi-square test or Fisher's exact test. Student's *t*-test or Mann-Whitney *U*-test was used to compare differences between two groups (continuous data) with normal distribution and not-normal distribution, respectively. Treatment effects between trans-femoral and trans-radial group were analyzed by univariate log-regression and reported as odds ratio (OR) with the corresponding 95% confidence intervals (CI), calculated for the end-points. Time-to-event survival curves are displayed according to the Kaplan-Meier method and compared by Mantel-Cox log rank analysis. All reported p values are two-sided and p values of <0.05 were considered to identify statistically significant differences. All statistical analysis was performed using SPSS 18 (SPSS Inc. Chicago, IL, USA).

Results

During 39 months (between October 2007 and December 2010), 1808 consecutive STEMI patients were treated with PPCI in our center, 1162 patients were treated with TRA (64.3%) and 646 patients with TFA (35.7%). The mean age of the patients was similar in both groups and most of them (75%) were male. Smoking was more common in the TRA patients (55%) than in the TFA group (48%) (p=0.003). The time from symptoms to first medical contact and door-to-balloon time did not differ between the two groups. Patients with cardiogenic shock on initial presentation were similar in both groups. Baseline characteristics are shown in Table 1.

Table 1. Demographic and baseline clinical characteristics in both groups of patients.

Variables	TRA group (N=1162)	TFA group (N=646)	P Value
Demographic characteristics			
Age, years	57.9 ± 10.8	58.3 ± 10.5	0.507
Male	901 (77%)	489 (76%)	0.373
Risk factors			
Hypertension	710 (61%)	389 (60%)	0.647
Diabetes mellitus	236 (20%)	128 (20%)	0.798
Dyslipidemia	425 (37%)	200 (31%)	0.016
Smoker	642 (55%)	310 (48%)	0.003
Family history of CAD	180 (15%)	78 (12%)	0.047
Prior PCI	85 (7%)	62 (10%)	0.089
Clinical presentation			
Anterior MI	579 (49%)	315 (49%)	0.850
Cardiogenic shock	20 (2%)	13 (2%)	0.901
Time frame characteristics			
Time from symptoms to FMC,minute	167 (22-1000)	164 (15-950)	0.368
Door-to-balloon time, minute	50 (8-255)	49 (10-280)	0.684
Procedural time, minute	21.4 ± 7.5	22.8 ± 5.9	0.415
Fluoroscopy time, minute	9.2 ± 6.2	9.8 ± 6.4	0.298

Continous data are presented as mean ± standard deviation or median (range) and categorical data are expressed as numbers (percentage). TRA= trans-radial approach, TFA= trans-femoral approach, CAD= coronary artery disease, PCI= percutaneous coronary intervention, MI= myocardial infarction, FMC= first medical contact.

In both groups, left anterior descending artery was the most frequent infarct-related artery. Although baseline TIMI flow grade 0-1 was lower in the TRA group (74%) than in the TFA group (79%) (p= 0.01), the final TIMI 3 flow was similar in both groups (95% and 94%, respectively). Procedural success was obtained in 95% and 96% in the TRA and TFA group, respectively. Procedural characteristics are shown in Table 2.

Table 2. Characteristics related to intervention procedures.

Variables	TRA group (N=1162)	TFA group (N=646)	P Value
Sheath size			
5F	93 (8%)	0	<0.001
6F	1069 (92%)	646 (100%)	0.002
Culprit lesion			
LAD	570 (49%)	312 (48%)	0.419
LCX	161 (14%)	79 (12%)	0.228
RCA	426 (37%)	255 (39%)	0.084
Diseased vessel			
Multi vessel disease	628 (54%)	340 (53%)	0.187
PCI strategies			
Multivessel PCI	8 (0.7%)	6 (0.9%)	0.911
Reperfusion parameter			
Baseline TIMI flow 0 or 1	856 (74%)	511 (79%)	0.014
Final TIMI flow 3	1104 (95%)	607 (94%)	0.381
Procedural success	1108 (95%)	622 (96%)	0.741

F= French, LAD= left anterior descending artery, LCX= left circumflex artery, RCA= right coronary artery, PCI= percutaneous coronary intervention, TIMI= thrombolysis in myocardial infarction.

During the course of the study, a major shift occurred in access site preference as we changed the strategy from femoral to radial access. The transition from TFA to TRA as the preferred access site for PPCI between October 2007 and December 2010 is illustrated in Figure 1.

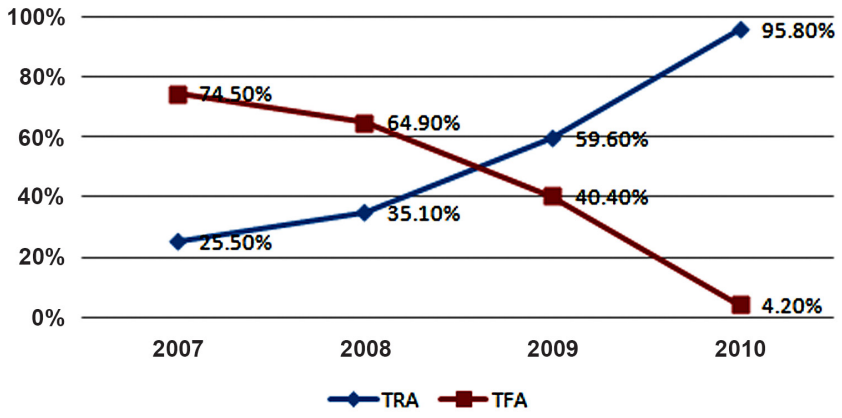

Figure 1. Time courses of the use of TRA and TFA from October 2007 to December 2010.
TRA= trans-radial approach, TFA= trans-femoral approach.

Primary and secondary end-points

Compared to TFA, the TRA was associated with lower cardiovascular mortality at 30-day and one year (5.2% vs. 10.5%, OR=0.46; 95% CI=0.32-0.66, p<0.001 and 6.9% vs. 11.5%; OR=0.57; 95% CI=0.41-0.79, p=0.001, respectively). The MACE rate at 30-day and one-year were significantly lower in TRA group compared to TFA group (7.3% vs. 12.5%; OR=0.55; 95% CI=0.39-0.76, p<0.001 and 11.6% vs. 20.1%; OR=0.52; 95% CI=0.40-0.68, p<0.001, respectively).

Major vascular access site complications were less frequent in TRA patients than in TFA patients (0.9% vs. 8.2%; OR=0.11; 95% CI=0.05-0.20, p<0.0001). At 30-day follow-up, major bleeding rate occurred less frequently in the TRA group than in the TFA group (1.1% vs. 4.3%; OR=0.24; 95% CI=0.12-0.46, p<0.001). Study end-points are displayed in Table 3.

Table 3. Study end-points in the two groups.

	TRA group (N=1162)	TFA group (N=646)	OR (95% CI)	P Value
Primary end-point				
MACE at 30 days	85 (7.3%)	81 (12.5%)	0.55 (0.39-0.76)	<0.001
MACE at 1 year	135 (12%)	130 (20%)	0.52 (0.40-0.68)	<0.001
Death at 30 days	60 (5.2%)	68 (10.5%)	0.46 (0.32-0.66)	<0.001
Death at 1 year	80 (7%)	74 (11%)	0.57 (0.41-0.79)	0.001
Secondary end-point				
Major vascular access site complication	11 (0.9%)	53 (8.2%)	0.11 (0.05-0.20)	<0.001
Non CABG major bleeding	13 (1.1%)	29 (4.3%)	0.24 (0.12-0.46)	<0.001

MACE= major adverse cardiovascular event, CABG= coronary artery bypass graft, OR= odds ratio, CI= confidence interval.

Event-free survival

The Kaplan-Meier survival curves are shown in Figures 2 and 3. After 30-day and one-year follow-up, the TRA patients had an improved cumulative survival compared to TFA patients (p<0.001 and p=0.001, respectively, by log-rank test). Furthermore, the benefit of TRA was observed in nearly all subgroups of patients (Figure 4).

At one-year follow-up, the overall cardiovascular mortality rate was 10%. The cardiovascular mortality rate was significantly lower in the TRA group than in the TFA group (6.9% vs. 11.5%, p<0.001).

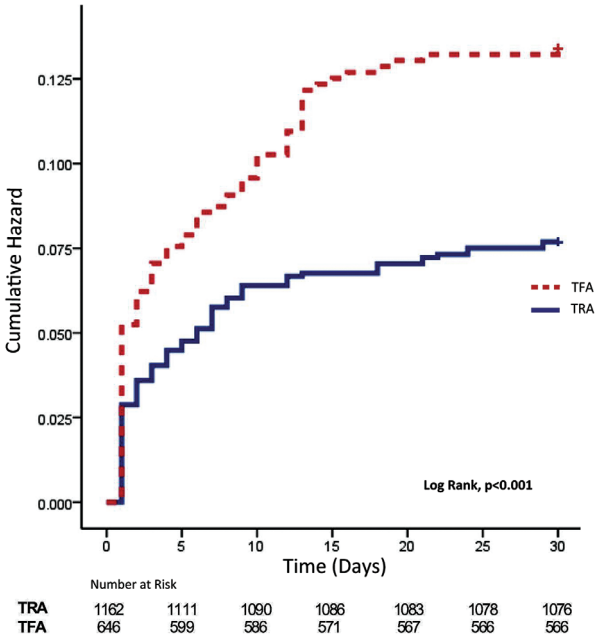

Figure 2. Kaplan-Meier survival curves in the first 30 days.
TRA= trans-radial approach, TFA= trans-femoral approach.

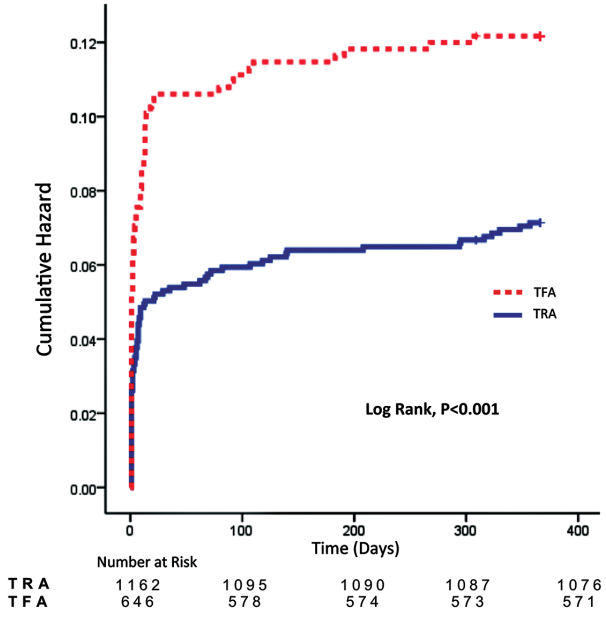

Figure 3. Kaplan-Meier survival curves at one-year follow up.
TRA= trans-radial approach, TFA= trans-femoral approach.

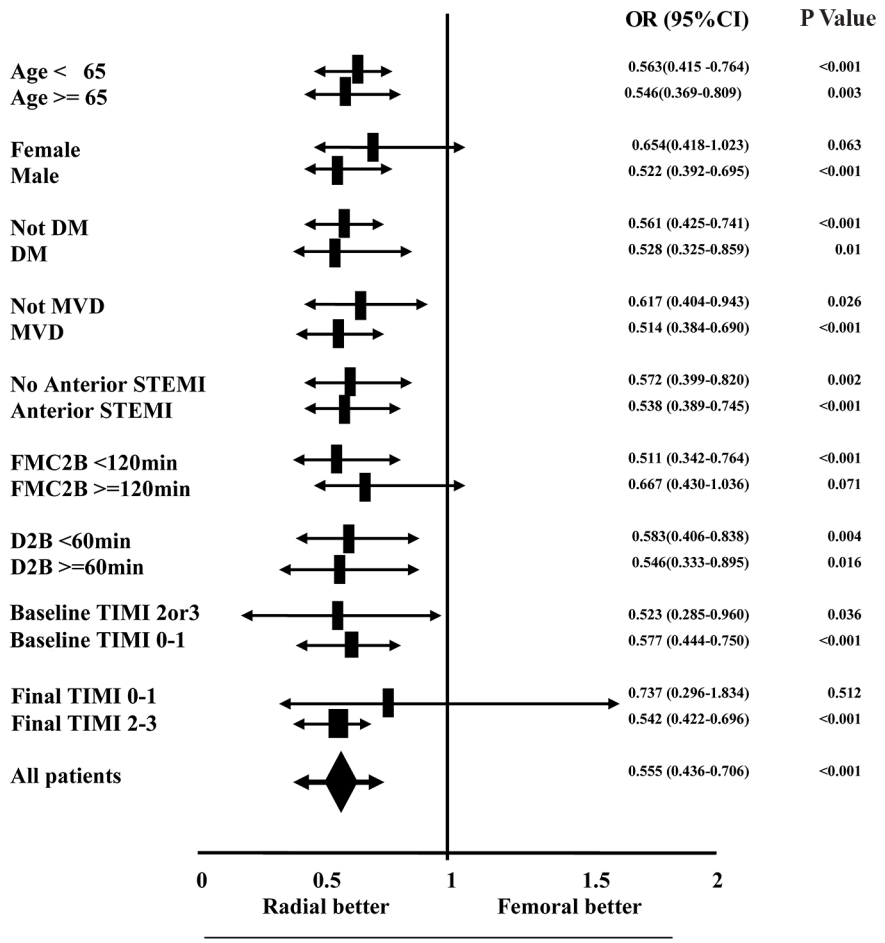

Figure 4. Sub-group analysis of all patients based on access site and its relation to clinical outcome.

OR= odds ratio, DM= diabetes mellitus, MVD= multivessel disease, STEMI= ST-elevation myocardial infarction, FMC2B= first medical contact-to-balloon time, D2B= door-to-balloon time, TIMI= Thrombolysis In Myocardial Infarction.

Discussion

The present study is the first large scale single center report analysing the impact of a transition of the access site from femoral to radial artery on (1) cardiovascular mortality, (2) bleeding events, and (3) one-year clinical outcomes in consecutive STEMI patients undergoing PPCI.

Access site is associated with bleeding events, while bleeding itself has been associated with an increased risk of death and ischemic events [17]. From the present study, the advantage of TRA compared to TFA was observed by a lower MACE rate after 30-day ($p<0.001$) and at

one-year clinical follow-up (p<0.001). Specifically, radial access was associated with lower rates of 30-day and one-year cardiovascular mortality than femoral access (5.2% vs. 10.2%, p<0.001 and 6.9% vs. 11.5%, p<0.001, respectively). The lower 30-day cardiovascular death associated with TRA was also seen in the RIFLE-STEACS study (5.2% vs. 9.2%, p=0.02) [9], as well as in the STEMI subgroup of RIVAL (1.3% vs. 3.2%, p=0.006) [21].

Although the underlying mechanisms of increased mortality of patients suffering from major bleeding remain unclear, a higher ischemic burden has been proposed to be a final common pathway. Local bleeding and femoral site hematoma formation is also thought to lead to systemic activation of pro-thrombotic pathways and activation of the clotting cascade. Cessation of antithrombotic therapies when the patient suffers from blood loss and consequences of blood transfusion in general could further increase the risk of stent thrombosis and subsequent myocardial ischemia and re-infarction [18].

Consistent with the result from the RIVAL study [19], our study shows that TRA is associated with a lower major vascular access site complication rate than TFA. Interestingly, the dramatic reduction of access site complications by TRA was associated with fewer MACE at 30 days compared to the TFA group. The reductions of major bleeding and major access site complications observed in the TRA group most probably affected the short-term and long-term mortality, and were associated with improved clinical outcome.

Since prolonged bed rest itself appears to be a predictor of worse prognosis in coronary artery disease [20], the possibility of a more rapid mobilization as a result of the decrease in access-site complications might have also influenced the outcome difference. Alternatively, it is not unlikely that subclinical bleeding in a less mobile and less active patient after femoral artery instrumentation with resultant hematoma might lead to platelet activation, precipitating intravascular thrombosis. The controversial question is whether relatively minor episodes of bleeding are actually responsible for mortality during follow-up. The reductions in cardiac mortality and bleeding found in the radial arm of the RIFLE-STEACS trial [9] and in the STEMI subgroup of RIVAL trial [21] support the link between mortality and clinically relevant access site bleeding. Further study is required in order to answer this question with confidence.

The advantage of the TRA in PPCI of patients with acute myocardial infarction was also observed in several randomized trials with follow-up periods ranging from 30 days to 2 years. These studies showed a favorable clinical outcome and lower access site complications for TRA compared to TFA [8,9,22,23].

Several studies have argued that the use of vascular closure devices (VCD) for TFA may lower the access site complications [24,25]. Several VCDs have been introduced and tested in clinical trials, but so far none of them have convincingly shown the ability to reduce major vascular complications compared with manual compression. Furthermore, a meta-analysis reported that the use of VCD increases the rate of vascular complications [26]. Recently, in a multicenter registry of 112,340 patients, Trimarchi and colleagues reported that the use of VCDs was associated with an increased risk for the development of retroperitoneal hematoma [27]. The American Heart Association has placed the VCDs when used with the purpose to reduce vascular complications in class III [28]. In our study, we did not use any VCD in any patient.

The HORIZONS-AMI study [5] showed an improved event-free survival in patients undergoing PPCI by the TRA compared with TFA, and confirmed the advantage of the TRA in terms of less hemorrhagic complications.

The present study showed that TRA did not affect the time interval measures, such as door-to-balloon time, procedural time and fluoroscopy time, a result that was shown in another study as well [22]. However, we noticed that the time the TRA procedure takes relates to the operator's experience. Based on our experience, the TRA requires a specific set of skills, and is associated with a significant learning curve. Published data suggest that 100-200 cases are necessary to become proficient in TRA and radial expertise begins to plateau at around 1,000 procedures [10]. Furthermore, the use of a dedicated radial kit (hydrophilic sheath, wire and cannula needle) is the key element in radial artery cannulation, and after dealing with the learning curve catheter manipulation is easier in TRA than in TFA, even for experienced trans-femoral operators.

Other advantages of TRA that have been reported include earlier patient mobilization, reduced procedural and hospital costs [29], and equal operator radiation exposure compared to TFA [30]. Finally, in the present study the advantages of TRA compared to TFA were observed in many subgroups of patients.

The results of this study are consistent with the recent 2012 ESC guidelines on STEMI [31], which state that TRA is preferred over TFA for PPCI, if performed by an experienced operator (Class IIa, Level B).

Limitation

The present study has several limitations. Firstly, this study was not a randomized comparison between TRA and TFA, but compares the outcomes of TRA and TFA in a period in which TRA is increasingly replacing TFA as the access site for PPCI. Secondly, the use of radial access has changed over the course of the study and the learning curve might have resulted in an underestimation of TRA's beneficial effects.

Conclusion

Complete transition from femoral access to radial access is safe and effective in the setting of PPCI in STEMI patients, and has favorable effects on short-term and long-term outcomes. Experienced PPCI centers could further improve their performance by adopting TRA in PPCI interventions in STEMI patients. However, these results should be confirmed in a prospective randomized trial comparing radial and femoral approaches for PPCI in patients with STEMI.

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