

Transradial versus transfemoral access for female patients who underwent primary PCI in STEMI: Two years follow-up data from acute STEMI interventional registry

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Abstract

Background: Female patients possess a higher risk for poorer outcome in ST segment elevation myocardial infarction (STEMI). There is possibility that transradial access (TRA) for primary percutaneous coronary intervention (PPCI) could provide better outcome than transfemoral access (TFA) in female patients with STEMI.

Methods: During access transition period from 2008 to 2010, 418 female patients (out of 1808 patients) underwent PPCI for acute STEMI. The registry recruited all-comers patients with acute STEMI. Major bleeding and vascular access site complications, death rates, and overall MACE rates (composite of death, stroke, re MI and TVR) after 2 years follow-up were compared between TRA and TFA.

Results: TRA for PPCI was performed in 261 patients and 157 underwent TFA PPCI. The 30-days and 1 year mortality rates were lower in TRA compared to TFA (6.9 vs. 14.6%, $p = 0.009$, and 8.8 vs. 15.3%, $p.0.032$, respectively). After 2 years follow-up, the overall MACE rates were similar (26.4% vs. 31.2%, $p.0.17$). The major bleeding and particularly major vascular access site complications were more favorable for TRA than TFA (4.4 vs. 14%, $p < 0.001$, and 2.7 vs. 10.8 %, $p.0.001$, respectively).

Conclusion: Transradial access for primary PCI in female patients provides less bleeding and lower incidence of vascular access site complications, and better early clinical outcome in acute STEMI.

Key words transradial approach; female gender; STEMI

Background

Ischemic heart disease causing acute coronary syndrome, particularly acute myocardial infarction, is the leading cause of death in many countries.¹⁻² It has been projected that it still be the main cause of mortality and disability over the year of 2020.³ In patients presenting with acute ST elevation myocardial infarction (STEMI), primary percutaneous coronary intervention (PPCI) is recommended reperfusion therapy when it can be performed in a timely fashion by experienced operators in a PCI-capable center.⁴ Various ways have been introduced to get better outcome for patients who underwent PPCI, such as optimal antiplatelet therapies and improvement procedural related aspects. Access site is an important procedural aspect related to the successful of a PCI procedure, including PPCI. Transfemoral access (TFA), which was previously used as the main access for PCI, has been associated with substantially higher risks of bleeding and transfusions than transradial access (TRA) as shown in a recent meta-analysis.⁵ Recent randomized trial, as well as data registry from our center, revealed that TRA has less bleeding events, lower vascular access site complication and better clinical outcome compared with transfemoral access (TFA) in STEMI patients undergoing PPCI in acute STEMI.⁶⁻⁸

Female gender has been known to possess poorer outcome in STEMI.⁹ Previous studies have also reported worse in-hospital and long-term mortality of women undergoing elective PCI by TFA.¹⁰⁻¹¹ On the other hand, radial approach may decrease access site-related bleeding in women undergoing elective PCI.¹¹

Anatomically, radial artery is more superficial, and close proximity to the radial bone, which makes haemostasis easier than TFA.¹² Whether these benefits of TRA would result in better clinical outcomes for female patients who underwent PPCI in the setting of acute STEMI remains to be defined.

In the present study, we sought to compare the outcome of female patients who underwent PPCI in acute STEMI with TRA and the default TFA.

Methods

Study population

With the growing evidences on the favorability of TRA in PCI, our center has completely transformed from default TFA to TRA in 2011. During the transitional period of default TFA to TRA within the year of 2007 to 2010, there were 1808 patients underwent PPCI in acute STEMI included in the registry. The registry recorded all

comers with acute STEMI, irrespective of clinical presentation. All procedures were done by 7 interventional cardiologists who have experienced in performing PCI both by TFA or TRA. All of these operators have performed at least 100 elective PCI's by TRA before commenced to do PPCI by TRA. Decision to do the PCI by TFA or TFA was left to the discretion of the operator. The results of cohort in overall 1808 patients in the registry have been published recently.⁸

We selected all female patients recruited in the registry for the present study. The data of each case was immediately entered to the registry by the operator after the procedure. The data of registry was open to the health administration and public health insurance administration

Interventional Procedures

The detail of PPCI procedure has been described elsewhere.⁸ Briefly, a modified Seldinger technique was performed to obtain TFA. After local infiltration with 3-5ml 2% lidocaine, the femoral artery was punctured with a 17G needle and 0.035 inch guide-wire, followed by 10 cm 6Fr introducer sheath placement. On TRA, radial artery was accessed after local infiltration with 1 – 1.5 ml 2% lidocaine, using counter puncture technique with a 20G plastic iv cannula and 0.025 inch mini guide-wire of 45 cm, and followed by 6Fr hydrophilic introducer sheath placement. The spasmolytic cocktail of 5 mg verapamil was administered through the sheath.

To perform PPCI, standard guiding catheters (such as: Judkins, EBU, Amplatz, etc), mostly 6Fr and sometimes 5Fr, for both TRA and TFA were used. The guide-wires for PCI, mostly Balance Middle Weight (Abbott Vascular, USA) and some hydrophilic wires, were used as indicated by the operator's judgment. The stents choice was left to the operator's consideration. Flow of infarct-related artery was evaluated before and after the PPCI procedure using the TIMI (Thrombolysis in Myocardial Infarction) score. Manual thrombus aspiration was performed in the cases with high thrombus burden. PCI only on the infarct related artery was done with the main goal to reach the TIMI-3 flow.¹³

Standard medications in acute STEMI were given to all patients. These include aspirin (300 mg followed by 100 mg/day indefinitely), clopidogrel (loading dose 600 mg followed by 75 mg/day for at least 1 year), as well as intravenous bolus of unfractionated heparin (100 IU/kg). When required, abciximab was given intracoronary or intravenous bolus of 0,25 mg/kg followed by 0,125µg/kg/min infusion for 12 hours. After completion of PCI, weight adjusted dosage protocol of heparin infusion was continued for 24 hours or 12 hours protocol of abciximab. No fibrinolytic agent was used during PPCI.

Sheath removal for TFA was done after 3-4 hours from the sheath insertion, and haemostasis was achieved by manual compression of 15-20 minutes followed by prolonged weight compression placement. Patient must remain in bed thereafter, with restricted mobility, in the following six hours (9-10 hours in total from the sheath insertion). On TRA, the arterial sheath was removed

immediately after the procedure. Haemostasis was achieved by a simple bandage compression or TR band (Terumo, Japan). 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. The TR band was gradually deflated each hour after procedure, and removed after four hours. Patients had no mobility restriction after the procedure.

Study end-points

The primary end-points for this study purposes were cardiovascular death and the major cardiovascular events (MACE) within 30 days, 1 year, and 2 years. The MACE was composite of death, stroke, re-MI, and target vessels revascularization. The secondary end-points consist of: major vascular access complications, major bleedings, and non-CABG bleeding in 30 days. Comparison of baseline and procedural characteristics between TRA and TRA were also evaluated. The baseline characteristics include variables of demography and clinical presentations. Meanwhile procedural-related characteristics during PPCI consist of variables: culprit lesions, diseased vessels, IABP use, time-frame related, and contrast use.

Cardiovascular death includes cardiovascular related death, includes: death in 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.

Major vascular access complications was defined as any access site related hemorrhage requiring red blood cell transfusion, delayed hospital discharge or requiring a surgical vascular repair.¹⁴

Major bleeding was defines as overt clinical bleeding (or documented intracranial or retroperitoneal hemorrhage) associated with a drop in hemoglobin of 5 g/dL, or in hematocrit of 15%.¹⁵

Term of Non-CABG bleeding refers to a major bleeding, which not related to any CABG procedures.¹⁶ Time from onset to intervention was defined as time from onset of acute STEMI symptoms to the start of PPCI. Meanwhile, procedural time was defined as time from puncture arterial access until the time of guide-catheter pulled out from the sheath at the end of PPCI.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation for normally distributed data and median with the range (maximum-minimum) for data that not fitting with normal distribution. Comparison of continuous data between TRA and TFA was performed with Student t-test or Mann-Whitney U test when appropriate. Categorical variables were presented in numbers and percentage, and comparison between the groups was done by Chi-square test or Fischer exact test. Clinical outcome of PPCI between TFA and TRA group was analyzed by univariate log-regression and reported as odds ratio (OR) with the corresponding 95% confidence intervals (CI), calculated for the endpoints. Survival

curves were constructed using Kaplan-Meier techniques, and comparisons were made by Mantel-Cox log rank test. The significances were considered for $p < 0.05$.

Results

During transitional period of default TFA to TRA for PCI within the year of 2007 to 2010, there were 1808 patients with acute STEMI underwent PPCI. Among them 418 women who were included in the present study. Their median age was 62 years old (range of 30-86 years). The PPCI was done 261 (62.4%) with TRA, and 157 with TFA (37.6 %). Major cardiovascular risk-factors were similar between the groups of TRA and TFA. History of major comorbidities such as previous: PCI, CABG, and renal insufficiency were not significantly different between the two groups. Clinical presentations in the time of PPCI includes: anterior MI, cardiogenic shocks, and time of MI onset to intervention were also similar between the groups of TRA and TFA. Those baseline characteristic comparing TRA and TFA is listed in the Table 1.

Table1. Baseline Characteristics

Variables	TRA (N=261)	TFA (N=157)	P
Risk factors & Comorbidities			
Age, years	62.4 ± 10.5	60.3 ± 9.6	0.05
Diabetes	89 (34.1%)	56 (35.7%)	0.41
Hypertension	181 (69.3%)	108 (68.8%)	0.49
Dyslipidemia	99 (37.9%)	63 (40.1%)	0.36
Smoker	89 (34.1%)	50 (31.8%)	0.35
Family history	40 (15.3%)	22 (14.0%)	0.41
Previous PCI	14 (5.4%)	12 (7.6%)	0.23
Previous CABG	0 (0.0%)	1 (0.6%)	0.37
Previous CHF	4 (1.5%)	5 (3.2%)	0.21
Renal insufficiency	3 (1.1%)	2 (1.3%)	0.62
Clinical Presentations:			
Anterior MI	130 (49.8%)	72 (45.9%)	0.25
Cardiogenic Shock	8 (3.1%)	7 (4.5%)	0.31
Onset to Intervention, min	230 (40-960)	254 (30-870)	0.24

During PPCI procedure, the most frequent culprit lesion finding was in the left anterior descending (LAD) coronary artery both in the group of TRA (49.8%), and in TFA (45.9%). The culprit lesion in the bifurcation part of coronary arteries was more frequent in the TRA group (18.8%) than in the TFA (8.9%). Angiographic results during PPCI showing associated coronary disease such as diseases in the LM trunk and the multivessel involvement were not different between TRA and TFA. Most of patients were with pre-interventional TIMI flow 0-1 in the culprit lesion that was not significantly different in TRA (74.7%) and TFA (79.0%). The overall PPCI procedures resulted in similar goal, in term of percentage of culprit vessels reaching TIMI 3 flow, between TRA and

TFA (91.2% vs. 91.7%). The time-frame related during PPCI includes: door to balloon time, procedural time, and fluoroscopic time were not different between the groups of TRA and TFA. The PPCI by TRA consumes significantly least amount of contrast than in the TFA ($p < 0.001$). The overall PPCI procedural-related characteristics in TRA and TFA are presented in the Table 2.

Table 2. Procedural-related characteristics

Variables	TRA (N=261)	TFA (N=157)	P
Culprit lesions			
LAD	130 (49.8%)	72 (45.9%)	0.24
LCx	32 (12.3%)	15 (9.6%)	0.24
RCA	95 (36.4%)	70 (44.6%)	0.06
Bifurcation	49 (18.8%)	14 (8.9%)	< 0.01
Diseased vessels			
With LM disease	7 (2.7%)	5 (3.2%)	0.49
Multivessel	149 (57.1%)	80 (51.0%)	0.13
IABP use	1 (0.4 %)	2 (1.3%)	0.32
Reperfusion parameter			
Baseline flow TIMI 0-1	195 (74.7%)	124 (79.0%)	0.19
Post procedural TIMI 3	238 (91.2%)	144 (91.7%)	0.50
Time-frame related			
Door to balloon time, min	40 (12-610)	40 (12-187)	0.15
Procedural time, min	22 (7-50)	22 (7-45)	0.96
Fluoroscopic time, min	7 (4-37)	8 (4-41)	0.07
Contrast used, ml	100 (45-300)	136 (46-350)	< 0.001

Primary and Secondary end-points

At 30 days after PPCI, the death incidence of female patients with acute STEMI was significantly lower in TRA group than TFA (6.8 vs. 14.6%, $p=0.012$). At 1 year and 2 years follow up, the cumulative incidence of death in TRA still lower in TRA than TFA (8.8 vs. 15.3%, $p=0.045$, and 9.2 vs. 16.6%, $p=0.027$, respectively). When these death incidences combined with stroke, re-MI, and target vessels revascularization into MACE, we found significantly lower MACE at 30 days and 1 year in TRA group compared to TFA (9.2 vs. 15.9%, $p=0.041$; and 16.1 vs. 22.9%, $p=0.042$). The MACE at 2 years follow up, although showing lower percentage number in TRA group, but not significantly different than TFA (26.4 vs. 31.2%, $p=0.179$). The Odd ratio's (95% CI) for all events are less than 1 suggesting favorable result of TRA than TFA.

Major vascular access bleeding complications during PPCI was lower in TRA than TFA (2.7 vs. 10.8%, $p=0.001$). The non-access related bleeding, in 30 days showed lower trend in TRA compared to TFA (3.4 vs. 5.7%, $p=0.227$), and overall Major bleeding was again significantly lower in TRA group (4.4 vs. 14.0 %, $p=0.001$). The Odd ratio's (95% CI) for all events are less than 1 suggesting favorable result of TRA than TFA which clearly indicated favorability of TRA than TFA. The overall primary and secondary end-points are shown in Table 3.

Table 3. Primary and secondary end-points

Study End-points	TRA (N=251)	TFA (N=157)	OR (95 % CI)	P
Primary end-points :				
30 days Death	18 (6.9%)	23 (14.6%)	0.43 (0.22-0.85)	0.012
1 year Death	23 (8.8%)	24 (15.3%)	0.53 (0.29-0.98)	0.045
2 years Death	24 (9.2%)	26 (16.6%)	0.51 (0.28-0.92)	0.027
30 days MACE	24 (9.2%)	25 (15.9%)	0.54 (0.29-0.97)	0.041
1 year MACE	42 (16.8%)	38 (24.2%)	0.60 (0.37-0.98)	0.042
2 years MACE	69 (26.4%)	49 (31.2%)	0.82 (0.51-1.22)	0.336
Secondary end-points :				
Major Vascular Access Bleeding	7 (2.7%)	17 (10.8%)	0.21 (0.10-0.64)	0.001
Major Non-Access Bleeding	9 (3.4%)	9 (5.7%)	0.59 (0.23-1.51)	0.270
Major Bleeding Overall	12 (4.4%)	22 (14.0%)	0.27 (0.13-0.58)	0.001

Survival analysis

Kaplan-Meier estimates of MACE at 30 days in women who underwent PPCI in the present study revealed a significantly higher cumulative survival in TRA compared to TFA ($p=0.009$). The survival curves at 1 year and 2 years, although juxtaposed still observed, but were not significantly different between TRA and TFA ($p=0.06$ and $p=0.209$, respectively). The survival curves at 30 days, 1 year, and 2 years are shown in Figure 1.

Discussion

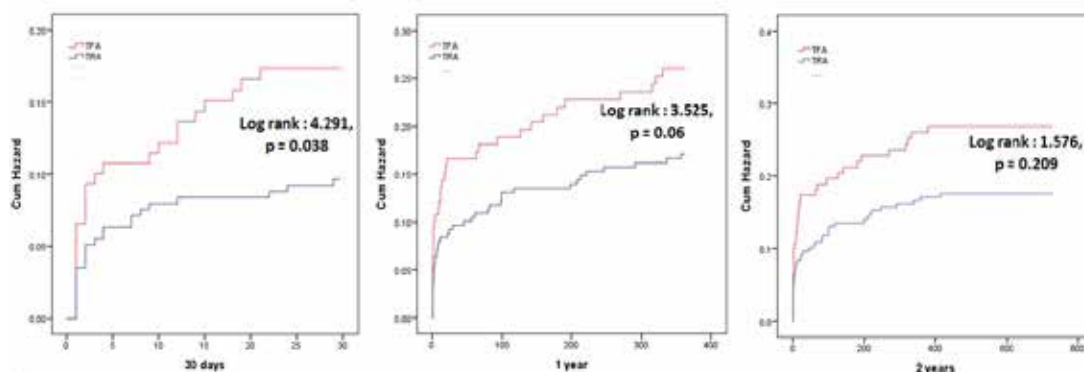
The present study revealed real world findings regarding early- and 2 years clinical outcome of female patients who underwent PPCI in acute STEMI by TRA compared to TFA. We found lower cumulative mortalities in 30 days, 1 year, and 2 years in TRA than TFA. The overall MACE at 30 days and 1 year were lower in TRA, but not significantly different in 2 years, compared to TFA. We also revealed lower 30 days major vascular access complications, major bleeding, and non CABG bleeding in female patients who underwent PPCI by TRA compared to TFA. The Kaplan-Meier curves of MACE rate up to 2 years follow-up indicated that TRA may improve early survival, particularly at 30 days after PPCI in women, but this benefit of events free survival rate was not lasting after 1 year and beyond over TFA.

Female gender has been associated with worse outcome in acute coronary syndrome, particularly in acute STEMI. Previous studies in patients with STEMI treated by primary angioplasty in the era of default TFA showed that women were associated with higher mortality rate

in comparison with men, mainly because of their high-risk profile and angiographic features.¹⁷ Among those risks, women reportedly have smaller vessels profile than men. Other report also revealed women have greater left ventricular filling pressures compared with men, independent of age, hypertension, and infarct size in acute STEMI.¹⁸ Indeed, female gender with acute STEMI who undergoing PPCI can be considered as a high risk group. Certainly, a better management, both medications and procedural related, will always be required to improve outcomes in this demographic entity.

In patients undergoing both diagnostic catheterization and PCI by TFA, previous reports have demonstrated that female gender is a powerful predictor of bleeding and vascular complication¹⁹⁻²⁰ In the setting of elective PCI, women have been known with higher risk of bleeding than men. Study in a large number gender difference in PCI concluded that despite the improvement in procedural safety, female gender continues to be associated with a 2-fold risk of bleeding and vascular complications compared with men.²¹ Over the last decade, several procedural-related improvements have been introduced, still, female gender remained associated with a higher risk of local bleeding and hematomas.²² Taken together, female gender possess a worse outcome in acute STEMI and also poorer outcome in PCI by default TFA related to vascular complications compared to men.

Bleeding and vascular complications events would affect clinical outcome after PCI, including death and overall MACE.^{19,20,23} In present study of women who underwent PPCI by TRA, we found lower bleedings and vascular complications than TFA. This may explain better early outcome and MACE rate of TRA over TFA in those pa-

**Figure 1.** Kaplan-Meier MACE curves at 30 days, 1 year, and 2 years, comparing TRA and TFA

tients as shown in the results. Thus, TRA for PPCI in female with acute STEMI provides benefits of improving clinical outcome, particularly early outcome, by reducing risk of bleeding and vascular complications if the procedure performed by TFA. These findings suggest applying default TRA for women undergoing PPCI when it is required.

Favorability of TRA over TFA in PCI has been reported in previous studies.^{5,24-25} Most of available evidences reported less risk of bleeding and vascular access complications. Some other studies also have reported lower death rate and MI by TRA compared to TFA.^{5,24} Reduction of bleedings and vascular access complications would reduce these adverse events. However recent large cohort study of more than 2 million PCI procedures in US reported that TRA for PCI is underused in patients at high risk of bleeding, such as: older patient, women, and patient presenting with ACS.²⁴ The study suggested wider adoption of TRA for PCI, particularly in high risk patients, may present opportunity to potentially improve overall PCI safety. Our study represented very high risk group, which is female and in acute STEMI. Favorable results in safety and efficacy of this study advocate for using default TRA over TFA in PPCI for this very high risk group.

Less contrast use is other advantage of applying TRA over TFA in PPCI, as seen in the result. This aspect may also beneficial to reduce the risk of contrast-induced nephropathy. In the patient's side, the TRA for PCI certainly more convenient for them, better mobilization and they may discharge earlier after procedural. Nevertheless, applying TRA as default access for PCI requires sufficient learning curve for both operator as well as the entire paramedic in a cath lab. As experience of our center, the transitional period of default TFA to TRA for PCI, including for PPCI, lasted around 3 years from 2007 to 2010. As for today, as high as 99 % procedures of coronary interventions, both elective and in acute coronary syndrome cases, and even carotid angioplasty are done through radial access in our center.^{8,26-27} We found TRA is a safe, less bleeding and lower vascular access complications, and provides better clinical outcome after PCI, including in high risk groups such as female patients and those with acute STEMI.

Study limitation

The data of present study was taken from a registry, not a randomized study. However, this study represents a real world result, since we included all-comers female patients with STEMI who underwent PPCI during certain period. Baseline characteristics of risk factors, co-morbidities, as well as clinical presentation were not significantly different between TRA and TFA groups as seen in Table 1.

Conclusions

Transradial access for female patients who underwent primary PCI in acute STEMI provides better early outcome than transfemoral access, and reveals less major vascular access complications and major bleedings.

These study suggest favorability of transradial as the default interventional access, including for PPCI, in female patients over the transfemoral access.

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