A Comparative Matched Analysis of Clinical Outcomes between Transradial versus Transfemoral Percutaneous Coronary Intervention

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ABSTRACT: **Background:** Several trials support the transradial route of percutaneous coronary intervention (PCI) since it reduces access-site vascular complications and bleeding.

Objectives: To examine the effects of transradial interventions (TRI) on clinical outcomes in a 'real-world' cohort of patients undergoing PCI.

Methods: We analyzed 4873 consecutive patients who underwent PCI at a tertiary center and identified 373 patients who underwent TRI. Patients (radial vs. femoral) were compared using a propensity score analysis to best match between groups. Outcome parameters included total mortality, myocardial infarction (MI), repeat target vessel revascularization (TVR) rates, length of hospitalization and ΔHt/Hb/creatinine values during hospitalization. These were evaluated at 6 months and 1 to 3 years after PCI.

Results: The rates of major adverse cardiovascular event (MACE) and its constituents were similar in the transradial vs. transfemoral groups at all time intervals: 6.7% vs. 5.5% at 6 months, 10.3% vs. 10% at 1 year, 15.7% vs. 15% at 2 years, 15.7% vs. 16% at 3 years, respectively ($P = 0.6$). The length of hospitalization was shorter in the TRI group (2.87 days ± 2.04 vs. 3.3 days ± 3.12, $P = 0.023$). We did not find significant differences between the groups in the mean ΔHt/Hb/creatinine values during the hospitalization course.

Conclusions: In a real-world setting of PCI, the TRI route of PCI is as safe and efficient as the femoral approach. TRI is associated with shorter duration of hospitalization.

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KEY WORDS: trans-radial intervention (TRI), transfemoral intervention (TFI), percutaneous coronary intervention (PCI), major adverse cardiovascular events (MACE)

Use of the radial route for percutaneous coronary intervention (PCI) has gradually increased. In recent years, several trials examined transradial versus transfemoral access site for coronary interventions in different clinical scenarios. Overall they showed that use of the transradial approach is associated with similar procedural efficacy to that of the transfemoral approach, but with reduced access-site bleeding and vascular complications, especially in the hands of highly trained operators and in the setting of ST-elevation myocardial infarction (STEMI) when patients are treated with more intensive anticoagulation regimens [1-5]. Since bleeding is associated with morbidity, mortality and costs [6-8], it is believed that by reducing bleeding and its complications the transradial approach reduces the net adverse cardiovascular events (NACE), an outcome that consists of MACE and bleeding. Despite the growing body of evidence in favor of the transradial approach, there are limited data on the outcomes of transradial interventions (TRI) in a 'real-world' all-comers PCI setting.

We aimed to examine the proportion of transradial interventions in our tertiary center, characterize this population, and evaluate the effects of TRI on outcomes in a real-world PCI setting. We hypothesized that with increased use of TRI, this approach will be associated with improved outcome.

PATIENTS AND METHODS

From April 2007 to July 2012, a total of 4873 consecutive patients underwent PCI at the Rabin Medical Center, Petah Tikva, Israel, and were prospectively observed and entered into a clinical database. Of those patients, we identified 373 patients who underwent PCI via the transradial route and compared them with 373 propensity score-matched patients who underwent PCI via the transfemoral route. The cohort included demographic, clinical, angiographic and procedural data. Due to the methodological nature of the study no patients were excluded. This registry was approved by the Ethics Committee of Rabin Medical Center.

All patients were treated with aspirin 200–300 mg before PCI, clopidogrel 300–600 mg, or prasugrel 60 mg either before PCI (pretreatment) or immediately after completion of the procedure. Bivalirudin (0.75 mg/kg bolus dose followed by 1.75 mg/kg/hour for the duration of PCI) or, alternatively, unfractionated heparin (70 U/kg loading) was given before PCI and adjusted to achieve an activated clotting time of 200–250 seconds during the procedure. Glycoprotein IIb/IIIa inhibitors were used during the

procedure and immediately following the PCI, at the discretion of the operator. Changes in blood hemoglobin concentration and renal function were evaluated in both groups at different time intervals after PCI.

Outcomes were evaluated using survival analysis, at 6 months, 1 year, 2 years and 3 years after PCI. All events were further adjudicated by an experienced cardiologist from our research team who was blinded to access-site selection. All operators participated in the study and all are experienced in both access approaches.

PROPENSITY SCORE CALCULATION AND MATCHING

To compensate for the non-randomized design in this observational study, a propensity score was computed using a multivariate logistic regression model with the route of intervention (transradial vs. transfemoral) considered as the independent variable, and all baseline clinical characteristics and procedural characteristics as covariates. Propensity score matching was performed using a "closest neighbor, greedy" algorithm, attempting to match to each patient in the transradial access cohort a patient from the transfemoral access cohort with the closest propensity score, with a maximal difference of less than 0.25 times the standard deviation of the scores. Each pair was used once. Unpaired patients were discarded from analysis.

POPULATION ANALYSIS OF THE STUDY

We analyzed the propensity score-matched cohort of patients to compare the outcome of patients treated with TRI to that of patients with the transfemoral intervention (TFI). Study endpoints during follow-up included: death (all-cause mortality), MI (STEMI and non-STEMI), acute coronary syndrome (ACS as a cause of hospitalization), coronary artery bypass grafting (CABG requirement), target vessel revascularization (TVR) defined as any revascularization that involved the target vessel, and major adverse cardiovascular events (MACE) that included the combination of death, non-fatal MI, TVR, CABG, and ACS.

We further analyzed the effects of the access approach on outcome (death, MI, TVR, CABG) in two patient subgroups, in patients presenting in acute and elective setting and in males and females.

STATISTICAL METHODS

Analyses were performed using IBM SPSS version 20 software (IBM, Inc.). All tests were two-tailed, and $P < 0.05$ was considered significant. Continuous variables are presented as mean ± SD, and the groups were compared using Student's *t*-test. Categorical variables are presented as frequencies (percent) and the groups were compared using chi-square test. Cumulative event rates were derived from life table analysis. Event-free survival analysis was computed from the Cox regression model with the access method, propensity score, and any unbalanced variables as covariates.

RESULTS

The analyzed cohort consisted of 373 patients who underwent TRI and their 373 propensity-matched patients who underwent TFI. The follow-up ranged from 6 months to 3 years. All the variables were well balanced by this method.

The clinical and procedural characteristics of each group are presented in Tables 1 and 2. There were no significant differences since these groups were well matched. Patients elected for TRI were relatively young (median age 63 years), tended to be males, with neither anemia nor renal failure, and only a minority had undergone bypass surgery. There were no differences in the blood hemoglobin (Hb) concentration prior to intervention versus up to 30 days after the intervention (The differences in the Hb concentration before PCI vs. up to 30 days after PCI was 0.6 ± 0.75 mg/dl in the TRI group, and 0.65 ± 0.8 mg/dl in the TFI group, $P = 0.6$) [not presented]. There were also no alterations in renal function prior to the procedure and up to 96 hours after intervention (The differences in plasma creatinine concentration before vs. 96 hours after PCI were 0.1 ± 0.5 mg/dl in the TRI group and 0.09 ± 0.3 mg/dl in the TFI group, $P = 0.7$) [not presented]. The length of hospitalization was significantly shorter with TRI (2.87 days ± 2.04 vs. 3.3 days ± 3.12, $P = 0.023$).

Over the past 5 years TRI had increased exponentially. The frequency of TRI had increased from 0.3% of all PCIs in 2007

Table 1. Clinical characteristics

	Transradial (n=373)	Transfemoral (n=373)	*P* value
Age (years)	63 ± 11.9	63 ± 12.3	NS
Male gender (%)	79.5	82	NS
Diabetes mellitus (%)	38.6	33.5	NS
Hypertension (%)	69	71	NS
Smoking history (%)	37	32.5	NS
Dementia (%)	0.55	0.55	NS
Malignancy (%)	7.2	8	NS
Congestive heart failure (%)	2.4	2.4	NS
Ejection fraction < 40% (%)	8.3	8.6	NS
Coronary artery bypass grafting (%)	5.1	6.2	NS
Chronic anticoagulation therapy (%)	4.6	4.3	NS
Hemoglobin (mg/dl)	13.7 ± 1.7	13.7 ± 1.7	NS
Minimal hemoglobin concentration (mg/dl) prior to intervention	13 ± 2	12.9 ± 2	NS
Platelet count (k/μl)	231 ± 71	235 ± 72	NS
Maximal creatinine concentration (mg/dl) prior to intervention	1.2 ± 1.2	1.3 ± 1.4	NS
Estimated glomerular filtration rate (ml/min/m²) prior to intervention	87 ± 25	86 ± 26	NS

Estimated glomerular filtration rate was calculated with the MDRD equation
NS = non-significant

Table 2. Angiographic and procedural characteristics

	Transradial (n=373)	Transfemoral (n=373)	*P* value
Proximal main vessel treated (%)	41	41.5	NS
Unprotected LM (%)	1.6	1.9	NS
Proximal LAD (%)	19	20	NS
1 vessel disease (%)	37	27.5	
2 vessel disease (%)	23.6	36.4	
3 vessel disease (%)	39.5	36.2	NS
Mean total stent length (mm)	31.8 ± 20	31.9 ± 22	NS
Mean stent diameter (mm)	3 ± 0.5	3 ± 0.5	NS
Drug eluting stent use (%)	53.4	58.7	NS
1 territory treated (%)	82	82.3	NS
2 territories treated (%)	15	15.5	
3 territories treated (%)	3.2	2.1	
Complexity score*	1.36 ± 0.6	1.39 ± 0.6	NS
STEMI (%)	12.3	11.2	NS
Non-STE-ACS (%)	60	62.7	NS
Severe state (%)	0.54	0.27	NS

LM = left main artery, LAD = left anterior descending artery, STEMI = ST-segment elevation myocardial infarction, Non-STE-ACS = non-ST segment elevation acute coronary syndrome, NS = non-significant

* Score of sites/territories, reflecting the number of discrete lesions treated per territory

to 35.2% at the end of 2011. Transition occurred between the last quartile of 2010 where TRI comprised 5.8% of all PCIs to the first quartile of 2011, where TRI comprised 10.2% of all PCIs, a rise of 177%. The next rise occurred between the first quartile of 2011 and its last quartile, a rise of 240%.

Figures 1A and B present comparisons of propensity score-adjusted cumulative incidence curves for death, MI, TVR or CABG with hazard ratio (HR) of 0.9; 95%confidence interval (CI) 0.54–1.53 (P = 0.73) for male patients, and HR of 1.2; 95%CI 0.56–2.7 (P = 0.6) for female patients. As depicted in these figures there was no advantage of one approach over the other in the different genders except for a trend for benefit for the radial approach over the femoral approach in female patients (not statistically significant). When examining the rates of death, MI, TVR or CABG in the acute and the elective setting [Figures 1 C and D], there was no significant benefit of the radial over the femoral approach. HR of 0.9 (95%CI 0.53–1.57, P = 0.7) for the acute setting, and HR of 1.2 (95%CI 0.6–2.5, P = 0.6) for the elective. Outcome parameters regarding the route of PCI are presented in Table 3. It demonstrates that outcome (MACE and its individual constituents) in the TRI group were not statistically different from that of the TFI group. We did not find any effect of the access approach on outcome of death, MI, TVR or CABG neither in the acute vs. elective setting nor in the effects of gender on outcome.

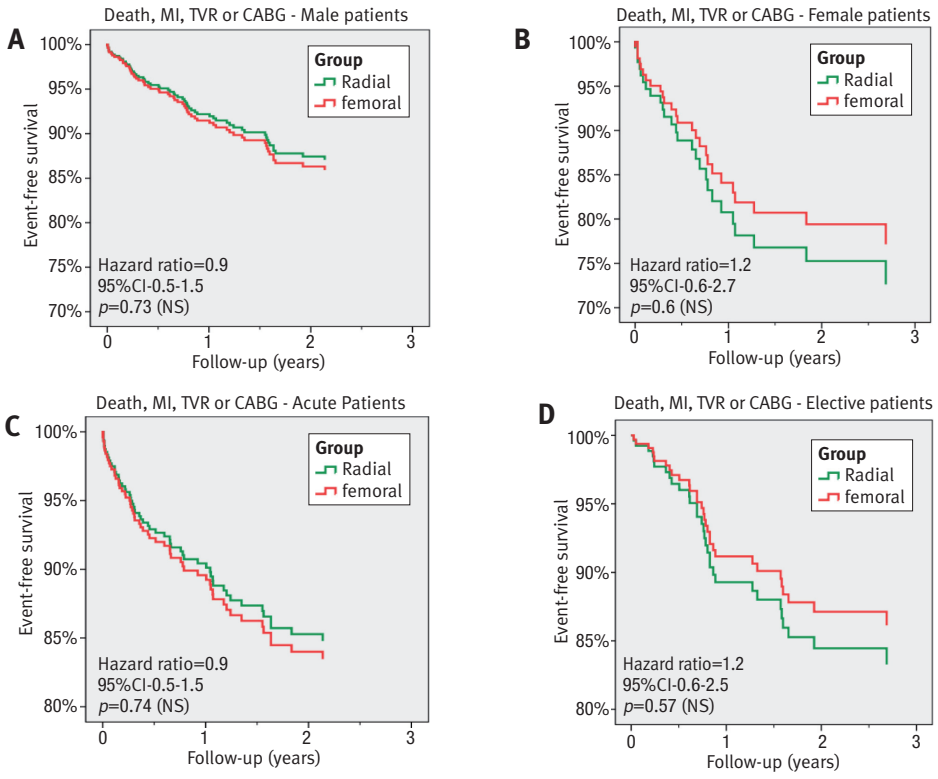

Figure 1. Cox regression analysis of Kaplan Meier event-free survival curves in: **[A]** male patients, **[B]** female patients, and in the setting of **[C]** acute and **[D]** elective presentation. *P* values denote significance of the access approach (radial and femoral) as an independent predictor of outcomes

CABG = coronary artery bypass grafting, MI = myocardial infarction, NS = non-significant, TVR = target vessel revascularization

Table 3. Propensity-matched cumulative outcome rates

	6 months	1 year	2 years	3 years
Death (*P* = NS)				
Transradial (%)	3.7 (n=373)	4.6 (n=267)	9.7 (n=162)	9.7 (n=88)
Transfemoral (%)	1.94 (n=373)	3.7 (n=343)	5.4 (n=318)	6.4 (n=224)
Myocardial Infarction (*P* = NS)				
Transradial (%)	0.6 (n=373)	1 (n=277)	1 (170)	1 (n=99)
Transfemoral (%)	1.4 (n=373)	1.4 (n=345)	1.7 (n=326)	1.7 (231)
Target vessel revascularization (*P* = NS)				
Transradial (%)	2.8 (n=373)	5 (n=269)	5.9 (n=164)	5.9 (n=94)
Transfemoral (%)	2.5 (n=373)	4.8 (n=341)	7 (n=314)	7 (n=218)
Death/ Myocardial Infarction (*P* = NS)				
Transradial (%)	4.3 (n=373)	5.6 (n=266)	10 (n=160)	10 (n=87)
Transfemoral (%)	3 (n=373)	4.8 (n=339)	6.8 (n=314)	7.8 (n=219)
Death/ Myocardial Infarction/ Target vessel revascularization (*P* = NS)				
Transradial (%)	6.7 (n=373)	9.8 (n=258)	14.5 (n=154)	14.5 (n=82)
Transfemoral (%)	5 (n=373)	8.5 (n=332)	12.8 (n=301)	13.8 (n=203)
Acute coronary syndrome (*P* = NS)				
Transradial (%)	1.2 (n=373)	1.2 (n=274)	1.9 (n=169)	1.9 (n=97)
Transfemoral (%)	1.9 (n=373)	3.4 (n=345)	4.1 (n=321)	5 (n=229)
Coronary artery bypass grafting (*P* = NS)				
Transradial (%)	0.3 (n=373)	0.75 (n=277)	1.4 (n=171)	1.4 (n=98)
Transfemoral (%)	0.8 (n=373)	1.7 (n=347)	2.4 (n=325)	2.4 (n=229)
Target vessel revascularization/ Coronary artery bypass grafting (*P* = NS)				
Transradial (%)	3 (n=373)	5.7 (n=268)	7.2 (n=163)	7.2 (n=92)
Transfemoral (%)	3.3 (n=373)	6.6 (n=338)	9.5 (n=308)	9.5 (n=210)
Any major adverse cardiovascular events (*P* = NS)				
Transradial (%)	6.7 (n=373)	10.3 (n=258)	15.7 (n=153)	15.7 (n=80)
Transfemoral (%)	5.5 (n=373)	10 (n=330)	15 (n=296)	16 (n=196)

NS = non-significant

DISCUSSION

Use of the transradial route for coronary interventions has several potential advantages over the transfemoral route: it reduces vascular access site complications and bleeding [9-12], especially in elderly [13], obese [14], patients with STEMI [3], and patients receiving glycoprotein IIb/IIIa inhibitors [15]. Use of the transradial route also potentially reduces procedural costs [16] and improves patient comfort by expediting ambulation and shortening hospital stay [17].

Our data, derived from a contemporary tertiary hospital-based registry, demonstrate the progressively increased practice of TRI, with the steepest rise occurring in the last year (a rise of 240%), accounting for 35% of all interventions. These data coincide with recent publications. We did not observe any difference in the periprocedural hemoglobin and creatinine concentration as an indirect index for bleeding and for the amount of contrast used respectively. Our risk-adjusted event-free survival analysis indicates no significant difference between TRI vs. TFI for all parameters, including the effects of gender and setting (acute vs. elective) on outcome. These results emphasize the safety of TFI in 'all comers' who undergo PCI.

These results are in agreement with the RIVAL trial, which is the largest randomized trial to compare radial and femoral access. It showed that the primary outcome of death, MI, stroke, or non-CABG-related major bleeding at 30 days were not significantly different (3.7% vs. 4%, $P = 0.5$) in more than 7000 patients. The results are discordant with the meta-analysis by Jolly et al. [10] based on 18 randomized trials, that showed a 73% reduction in the incidence of major bleeding using TRI, with only a trend for reduction of the composite death, MI, and stroke (ischemic events). It also showed a significant reduction in hospital length of stay, with a weighted mean difference of 0.4 days [10]. In the current study the length of hospitalization was also shorter in the transradial group, a difference not observed in the RIVAL study. The observed differences between the various studies probably arise from the different patient populations (acute setting vs. 'all comers'), study design (prospective randomized vs. observational, statistical adjustment methods such as propensity scoring), and other confounders. Of note, the decision regarding the route of intervention was primarily the operator's preference. Results can be explained partly by the fact that during the period of data collection the operators achieved their learning curve as transradial interventionalists.

The future holds promise for the transradial route of intervention, in terms of both patient perspective (preference for TRI due to rapid mobilization, less discomfort and improved quality of life) and cost-effectiveness. There are indications for reduced costs of procedure and significant savings associated with TRI. And this is regardless of the efficacy and safety of either route of intervention.

LIMITATIONS

Our study was derived from a registry and not based on a randomized controlled trial, and the possibility of unmeasured confounders influencing the outcome rates cannot be excluded,

nor can possible selection bias of patients. We tried to overcome this limitation by utilizing a propensity matching scheme that balanced all well-known confounders. Despite the fact that data were collected from a registry, this study is a historical prospective study, i.e., outcome data were collected only following exposure (following PCI). In addition, we report only a single center's experience; however, this is a large primary and tertiary center with homogeneity of policy, practices and standards. We did not have direct information on peri-procedural overt bleeding and vascular complications, although we did have information regarding changes in the concentration of Hb during the first post-procedural month (as an indirect indicator for bleeding).

We did not have information on the effect of the route of PCI on the length of procedures, and its effects on fluoroscopy time. Nevertheless, we did note that TRI was not associated with worse renal function (an indirect indicator for the lack of significant difference in the volume of contrast required for the procedure).

Despite all these limitations, our data are important in that they reflect the outcome of a real-world population (all patients who underwent PCI were included), and a real-world experience which is different from that selected in randomized controlled trials and thus data can be reflected on the general population.

CONCLUSIONS

When analyzed from a real-world, unselected patient population, the route of PCI did not affect clinical outcome. Different routes of access were associated with similar outcomes. TRI is associated with shorter duration of hospitalization.

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