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Influence of Arterial Access Site Selection on Outcomes in Primary Percutaneous Coronary Intervention

Are the Results of Randomized Trials Achievable in Clinical Practice?

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Objectives This study sought to investigate the influence of access site utilization on mortality, major adverse cardiac and cardiovascular events (MACCE), bleeding, and vascular complications in a large number of patients treated by primary percutaneous coronary intervention (PPCI) in the United Kingdom over a 5-year period, through analysis of the British Cardiovascular Intervention Society database.

Background Despite advances in antithrombotic and antiplatelet therapy, bleeding complications remain an important cause of morbidity and mortality in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing PPCI. A significant proportion of such bleeding complications are related to the access site, and adoption of radial access may reduce these complications. These benefits have not previously been studied in a large unselected national population of PPCI patients.

Methods Mortality (30-day), MACCE (a composite of 30-day mortality and in-hospital myocardial re-infarction, target vessel revascularization, and cerebrovascular events), and bleeding and access site complications were studied based on transfemoral access (TFA) and transradial access (TRA) site utilization in PPCI STEMI patients. The influence of access site selection was studied in 46,128 PPCI patients; TFA was used in 28,091 patients and TRA in 18,037. Data were adjusted for potential confounders using Cox regression that accounted for the propensity to undergo radial or femoral approach.

Results TRA was independently associated with a lower 30-day mortality (hazard ratio [HR]: 0.71, 95% confidence interval [CI]: 0.52 to 0.97; $p < 0.05$), in-hospital MACCE (HR: 0.73, 95% CI: 0.57 to 0.93; $p < 0.05$), major bleeding (HR: 0.37, 95% CI: 0.18 to 0.74; $p < 0.01$), and access site complications (HR: 0.38, 95% CI: 0.19 to 0.75; $p < 0.01$).

Conclusions This analysis of a large number of PPCI procedures demonstrates that utilization of TRA is independently associated with major reductions in mortality, MACCE, major bleeding, and vascular complication rates. (J Am Coll Cardiol Intv 2013;6:698–706) © 2013 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (PPCI) represents the current gold standard reperfusion strategy in the setting of acute ST-segment elevation myocardial infarction (STEMI) (1,2). Advances in antithrombotic therapy have improved the prognosis of patients presenting with STEMI by reducing ischemic events and mortality (3), although this has been at the expense of increased procedure-related bleeding complications. Such procedure-related bleeding complications are independently associated with adverse events, including 30-day mortality, reinfarction, and stroke (4–6). Recent studies evaluating new antithrombotic therapies have focused on the reduction of bleeding events as a major therapeutic goal (7–9). Patients with STEMI undergoing percutaneous coronary intervention (PCI) are at high risk for the development of such bleeding complications. For example, data from the National Heart, Lung, and Blood Institute Dynamic Registry have documented a significant increase in bleeding and transfusions in patients presenting with STEMI compared with those with non-STEMI (10). A significant proportion of these major bleeding complications are related to the access site (11), and adoption of the transradial access (TRA) site in patients undergoing PCI has been shown to reduce access site–related bleeding complications in selected populations (12).

See page 707

The recent randomized controlled trial RIFLE-STEACS (Radial versus Femoral Randomized Investigation in ST Elevation Acute Coronary Syndrome) suggests that adoption of the transradial route may be associated with a reduction in cardiac mortality, MACCE (major adverse cardiac and cerebrovascular events), and access site–related bleeding complications in patients presenting with STEMI (13), whereas a recent meta-analysis of randomized controlled studies suggested that the TRA is associated with a 47% reduction in mortality and a 38% reduction in major adverse cardiac events in STEMI patients undergoing PCI (14). These randomized controlled trials that have studied the influence of access site on outcomes in patients undergoing STEMI PCI are relatively small in size and have excluded many high-risk patient groups such as those presenting with cardiogenic shock (15–19), elderly patients (15), and those with previous coronary artery bypass grafting (CABG) (15–18), hence, the applicability of such data to real-world practice remains unclear. Furthermore, previous data derived from randomized controlled studies in STEMI PCI patients often include a significant proportion of rescue and facilitated PCI cases (16,17,19), hence, its applicability to the PPCI setting remains uncertain. We have therefore analyzed outcomes from a large observational database of primary PCI cases performed in the United Kingdom over a 5-year period, to investigate the relationship between access site practice and outcomes in a nonselected, high-risk, real-world cohort of patients.

Methods

The British Cardiovascular Intervention Society database. The British Cardiovascular Intervention Society (BCIS) was formed in 1988 to collect PCI data relating to the nationwide practice of PCI in the United Kingdom. From 1988 to 1991, annual national PCI data were published in the *British Heart Journal* whereas annual reports from 1992 onwards are available for download from the society's website. The data are collected via the Central Cardiac Audit Database (20) under the auspices of the National Institute of Cardiovascular Outcomes Research (NICOR). The aim of the BCIS-NICOR database is to record all PCI procedures performed in any hospital in the United Kingdom (England, Scotland, Wales, and Northern Ireland). In 2009, 97% of all PCI procedures performed in National Health Service hospitals in England and Wales had been entered into the database.

The BCIS-NICOR database records clinical, procedural, and outcome information with a total of 113 variables collected and available in the form of an Excel spreadsheet (Microsoft, Redmond, Washington). Information recorded in the database includes patient demographic features, indications for PCI, procedural details, and outcome data (20). As of March 2010, there were approximately 460,000 records in the BCIS database, with approximately 80,000 new records being added each year. Mortality tracking is undertaken by the Medical Research Information Service using patients' National Health Service number that provides a unique identifier for any person registered with the National Health Service in England and Wales.

Abbreviations and Acronyms

AMI = acute myocardial infarction
BCIS = British Cardiovascular Intervention Society
CABG = coronary artery bypass grafting
CI = confidence interval
GP = glycoprotein
HR = hazard ratio
IABP = intra-aortic balloon pump
MACCE = major adverse cardiac and cerebrovascular event(s)
OR = odds ratio
PCI = percutaneous coronary intervention
PPCI = primary percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TFA = transfemoral access
TRA = transradial access

Study definitions. PPCI procedures performed in patients presenting with STEMI in the United Kingdom between January 1, 2006, and December 31, 2010, were analyzed in this study. Patients who underwent PCI through the left or right femoral artery or the left or right radial artery were included in the femoral and radial cohorts, respectively. The primary outcomes examined were 30-day mortality and

MACCE (a composite of 30-day mortality and in-hospital myocardial re-infarction, target vessel revascularization, and cerebrovascular events). Total mortality was defined as mortality up to the date of latest census (December 31, 2010). In-hospital major bleeding complications were defined as gastrointestinal bleed, intracerebral bleed, retroperitoneal hematoma, blood or platelet transfusion, or an arterial access site complication requiring surgery. An access site complication was defined as a hematoma that delayed discharge, a pseudoaneurysm, retroperitoneal hematoma, or any other vascular complication requiring surgery.

Statistical analysis. Continuous variables are presented as means ± SD. Chi-square tests were used for analysis of categorical variables, and Student *t* tests were used to analyze continuous variables. The relationship of baseline variables with 30-day mortality, MACCE, access site complications, and bleeding was assessed with stepwise logistic regression with univariable and multivariable analysis. Factors thought to be important for the endpoints were entered for the analysis, and this model included: age, sex, diabetes, hypertension, hypercholesterolemia, family history, smoking status, shock, left ventricular function, intra-aortic balloon pump (IABP) use, previous acute myocardial infarction (AMI), previous CABG, thrombectomy catheter, year of procedure, and glycoprotein (GP) IIb/IIIa use. Variables that were found to be significant on univariate analysis for the endpoints of 30-day mortality, MACCE, access site complications, and bleeding ($p < 0.05$) were then entered into the multivariate stepwise logistic regression model. Kaplan-Meier cumulative survival and MACCE curves were constructed and compared by the log-rank test. To further account for confounding variables and bias, propensity matching was performed on the study cohort. A logistic regression model was fit for access site use (radial vs. femoral) to patient demographics. Variables included in the logistic regression model to calculate the propensity score were age, sex, diabetes, hypertension, hypercholesterolemia, peripheral vascular disease, previous cerebral vascular accident, renal failure, previous AMI, previous PCI, previous CABG, cardiogenic shock, IABP, and ventilation. Propensity score matching was performed using nearest-neighbor matching with a caliper of 0.05. The Hansen and Bowers balance test p value was 0.659, showing good covariate balance. Cox proportional hazards regression models were used in the propensity-matched cohort to calculate the adjusted hazard ratio (HR).

All statistical tests were 2-tailed. A value of $p < 0.05$ was used to indicate statistical significance. Statistical analysis was performed using MedCalc version 10.4 (MedCalc Software, Mariakerke, Belgium), SPSS (version 19.0, SPSS-MAC, Chicago, Illinois), and Kaplan Meier curves were constructed with Prism 5 for Mac (GraftPad Software, La Jolla, California).

Results

Primary PCI cohort and changes in access site utilization over time. A total of 48,603 PPCI procedures were performed in patients presenting with STEMI in the United Kingdom between January 1, 2006, and December 31, 2010, of which 46,128 procedures utilized a single access route and were included in further analysis (Fig. 1). Transfemoral access (TFA) was utilized in 28,091 patients (60.9%), whereas TRA was used in 18,037 patients (39.1%). Figures 2A and 2B illustrate the trends in access site use for PPCI between the years 2006 and 2010. In 2006, only 12.5% of all PPCI cases were performed via TRA, whereas by 2010, access site practice had evolved rapidly so that TRA accounted for 49.5% of all cases.

Procedural characteristics and demographics. Table 1 details demographic features of patients undergoing PPCI through either the TRA site or the TFA site. Procedural characteristics are summarized in Table 2. Of note, TRA patients were more likely to receive GP IIb/IIIa receptor inhibitor therapy or be treated with thrombectomy devices, whereas TFA patients had more graft PCI, shock, and IABP use.

Relationship between access site and mortality outcomes. Total mortality (at date of latest census, August 2011, when mean follow up was 668.8 ± 502.4 days (mean ± SD) was 5,013 of 46,128 (10.9%), of which 3,812 of 28,091 (13.6%) occurred in those cases that were performed through the TFA site, whereas 1,201 of 18,037 (6.7%) occurred in those cases that were performed through the TRA site ($p < 0.0001$).

Thirty-day mortality was 2,331 of 46,128 (5.1%) of which 1,875 of 28,091 (6.7%) occurred in those cases performed though the TFA site, whereas 456 of 18,037 (2.5%)

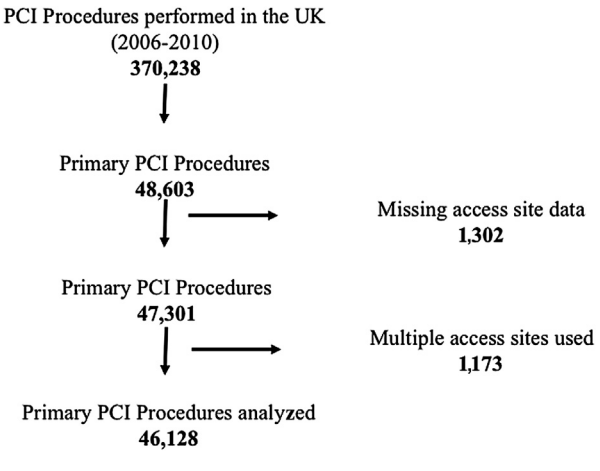

Figure 1. Study Sample Selection From the BCIS Dataset

Sample selection from the British Cardiovascular Intervention Society (BCIS) dataset illustrating patient inclusion and exclusion from analysis. PCI = percutaneous coronary intervention.

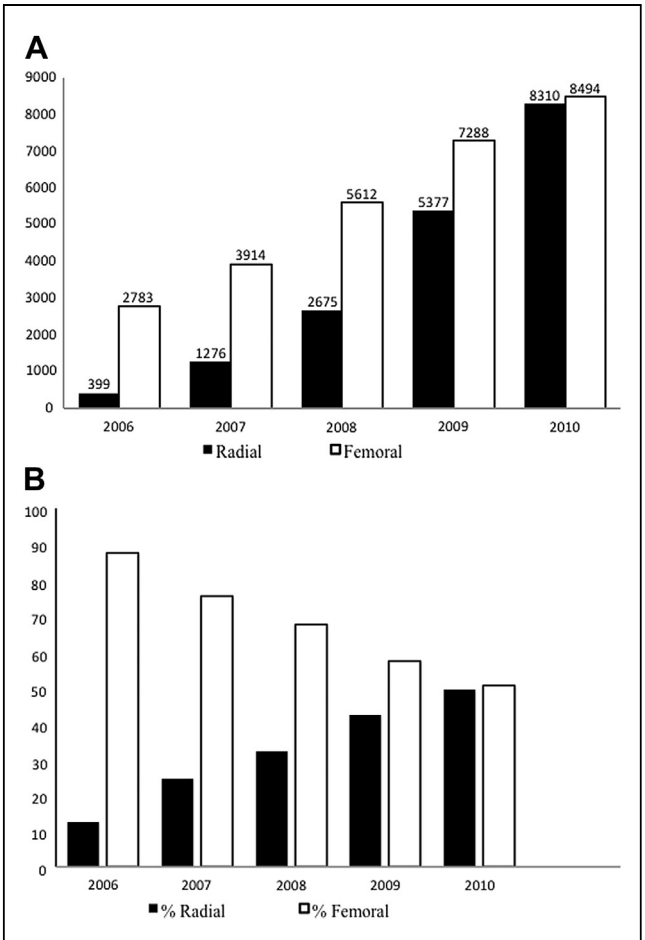

Figure 2. Utilization of the Radial and Femoral Access Sites During PPCI (January 2006 to December 2010)

(A) Number of cases of radial **(solid columns)** and femoral access **(open columns)** site utilization during primary percutaneous coronary intervention (PPCI) (2006 to 2010). **(B)** Percent of cases of radial **(solid columns)** and femoral access **(open columns)** site utilization during PPCI (2006 to 2010).

occurred in those cases performed through the TRA site ($p < 0.0001$). Figure 3 illustrates Kaplan-Meier unadjusted survival curves for both the TFA and TRA site groups, with a statistically significant decrease in mortality associated with the use of TRA (HR: 0.66, 95% confidence interval [CI]: 0.62 to 0.70; $p < 0.0001$ [unadjusted]; HR: 0.79, 95% CI: 0.74 to 0.85; $p < 0.0001$ [multivariate adjusted for baseline procedural and baseline characteristics] log rank test). Multivariate stepwise logistic regression analysis adjusted for baseline procedural and demographic characteristics demonstrated that TRA was independently associated with a reduction in 30-day mortality (HR: 0.71, 95% CI: 0.52 to 0.97; $p < 0.05$). Table 3 illustrates other independent predictors of 30-day mortality following adjustments of baseline covariates. Figure 4 illustrates 30-day mortality rates over time, from 2006 until 2010, and for the individual TRA and TFA cohorts over the same time period. Thirty-day mortality decreased from 5.75% in 2006 to 4.68% in 2010, which may in part reflect the increase in TRA utilization from 12.5% in 2006 to 49.5% in 2010.

Table 1. Baseline Clinical Demographics for Radial and Femoral Access Sites

Variable	Radial (n = 18,037)	Femoral (n = 28,091)	p Value
Age, yrs	62.6 ± 14.2	63.7 ± 13.2	<0.05
Male	13,731 (76.1%)	20,454 (72.8%)	<0.001
Diabetes	2,210 (12.3%)	4,196 (14.9%)	<0.001
Hypertension	7,232 (40.1%)	10,775 (38.4%)	<0.001
Hypercholesterolemia	7,558 (41.9%)	10,736 (38.2%)	<0.001
Previous AMI	2,023 (11.2%)	3,957 (14.1%)	<0.001
Previous CABG	195 (1.1%)	991 (3.5%)	<0.001
Family history	6,321 (35.0%)	8,854 (31.5%)	0.66
Smoking			
Current	7,517 (41.6%)	9,730 (34.6%)	<0.001
Ex-smoker	4,171 (23.1%)	6,557 (23.3%)	0.59
Never smoked	4,867 (26.9%)	7,429 (26.4%)	0.20
PVD	589 (3.3%)	893 (3.2%)	0.61

Values are means ± SD or n (%).
AMI = acute myocardial infarction; CABG = coronary bypass grafting; PVD = peripheral vascular disease.

Relationship between access site and MACCE outcomes. MACCE was 2,158 of 28,091 (7.7%) in those cases performed through the TFA site and 616 of 18,037 (3.4%) in cases performed through the TRA ($p < 0.001$). Table 4 illustrates individual components of MACCE. Multivariate stepwise logistic regression analysis adjusted for baseline procedural and demographic characteristics demonstrated that TRA was independently associated with a reduction of in-hospital MACCE (HR: 0.73, 95% CI: 0.57 to 0.93; $p < 0.05$). Table 5 illustrates independent predictors of MACCE following adjustments of baseline covariates.

Table 2. Procedural Characteristics for Radial and Femoral Access Sites

Variable	Radial (n = 18,037)	Femoral (n = 28,091)	p Value
GP IIb/IIIa	12,621 (65.7%)	18,159 (62.8%)	<0.001
Target vessel			
LAD	7,963 (44.1%)	12,568 (44.7%)	0.21
LCX	2,858 (15.8%)	4,454 (15.9%)	0.98
RCA	7,716 (42.7%)	11,676 (41.6%)	0.10
LMS	222 (1.2%)	600 (2.1%)	<0.001
Grafts	233 (1.3%)	697 (2.5%)	<0.001
Thrombectomy devices	7,370 (40.9%)	8,639 (30.6%)	<0.001
Cardiogenic shock	576 (3.2%)	2,264 (8.1%)	<0.001
IABP	384 (2.1%)	1947 (6.0%)	<0.001
DES use	7,820 (43.4%)	12,139 (43.2%)	0.75
Number of stents used	1.39 ± 0.88	1.43 ± 1.00	<0.05

Values are means ± SD or n (%).
DES = drug-eluting stent; GP = glycoprotein; IABP = intra-aortic balloon pump; LAD = left anterior descending coronary artery; LCX = left circumflex artery; RCA = right coronary artery.

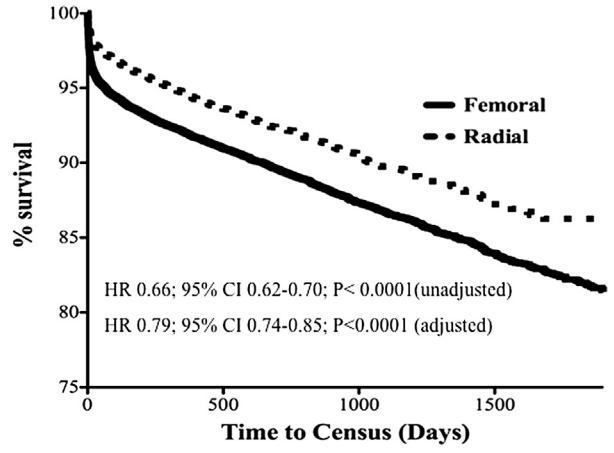

Figure 3. Kaplan-Meier Survival Curve for Mortality in Patients With STEMI Undergoing PPCI According to Access Site Utilization

Kaplan-Meier survival curve for mortality in patients with STEMI undergoing PPCI according to access site utilization. The **solid line** represents the femoral access site, and the **broken line** represents the radial access site. CI = confidence interval; HR = hazard ratio; PPCI = primary percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

Relationship between access site and access site complications and major bleeding outcomes. A total of 295 (0.64%) in-hospital major bleeding events were recorded, of which 260 occurred in those cases performed through the TFA site (0.93%) and 35 occurred in those cases performed through the TRA site (0.19%); $p < 0.0001$. Multivariate stepwise logistic regression analysis adjusted for baseline procedural and demographic characteristics demonstrated that TRA was independently associated with a reduction of in-hospital major bleeding complications (HR: 0.37, 95% CI: 0.18 to 0.74; $p < 0.01$). Finally, a total of 273 arterial access site complications (0.59%) were recorded, of which 204 occurred in those cases performed through the TFA site (0.72%) and 69 through the TRA site (0.38%); $p < 0.0001$; following multivariate stepwise logistic regression analysis adjusted for baseline procedural and demographic characteristics, TRA was independently associated with a reduction of access site complications (HR: 0.38, 95% CI: 0.19 to 0.75; $p < 0.01$).

Table 3. Multivariate Predictors of 30-Day Mortality

Variable	HR (95% CI)*	p Value
Access site (radial)	0.71 (0.52–0.97)	<0.05
Age, yrs	1.05 (1.04–1.06)	<0.0001
No GP IIb/IIIa	1.43 (1.07–1.90)	<0.05
Severe LV dysfunction	6.23 (4.67–8.30)	<0.0001
Shock	5.10 (3.62–7.18)	<0.0001
IABP use	3.07 (2.15–4.40)	<0.0001

*Adjusted for age, sex, diabetes, hypertension, hypercholesterolemia, smoking status, shock, family history, intra-aortic balloon pump use, previous AMI, previous CABG, thrombectomy catheter, left ventricular (LV) function, year of procedure, and GP IIb/IIIa use.

CI = confidence interval; HR = hazard ratio; other abbreviations as in Tables 1 and 2.

Propensity score matching and mortality and MACCE outcomes. To further account for confounding variables and bias in our study cohort, propensity score matching was performed to adjust for differences in clinical baseline variables (age, sex, diabetes, hypertension, hypercholesterolemia, peripheral vascular disease, previous cerebral vascular accident, renal failure, previous AMI, previous PCI, previous CABG, cardiogenic shock, IABP, and ventilation), producing a total of 24,710 patients (12,355 in the TFA group and 12,355 in the TRA group). Table 6 illustrates the baseline demographics were well balanced in the 2 propensity-matched cohorts. Thirty-day mortality in the propensity-matched cohort was 449 of 12,355 (3.6%) in those cases performed though the TFA site, whereas 304 of 12,355 (2.5%) occurred in those cases performed through the TRA site ($p < 0.0001$). Cox multivariate regression analysis was performed adjusting for baseline characteristics, and TRA was independently associated with a reduction in 30-day mortality (HR: 0.67, 95% CI: 0.60 to 0.79; $p < 0.0001$).

MACCE was 565 of 12,355 (4.6%) in the propensity-matched TFA cohort and 430 of 12,355 (3.5%) in the TRA cohort ($p < 0.0001$). Cox multivariate regression analysis was performed adjusting for baseline characteristics, and TRA was independently associated with a reduction in 30-day MACCE (HR: 0.80, 95% CI: 0.70 to 0.92; $p < 0.005$).

Discussion

In the current analysis of 46,128 PPCI cases recorded in the BCIS database over a 5-year period, our data suggest that TRA is independently associated with lower rates of mortality, MACCE, bleeding, and vascular complications. We also demonstrate that TRA is now extensively utilized for arterial access in the setting of primary PCI in the United Kingdom.

Significant progress in the management of STEMI has occurred in the last decade, leading to appreciable improvements in the prognosis associated with this condition (21), led in part through advances in antithrombotic therapy that reduce ischemic events and mortality (3). This has been at the expense of increased procedure-related bleeding complications, which are independently associated with adverse outcomes (22,23). A significant proportion of these major bleeding complications are related to the access site (11,19), a major determinant of which is use of the femoral artery during PCI (24). Reduction of bleeding complications during PCI is an important therapeutic strategy in improving outcomes during PCI. Treatments that reduce the risk of bleeding, but retain efficacy similar to that of standard treatment, have shown reductions in mortality in acute coronary syndromes (8,25). Similarly, adoption of TRA in patients undergoing PCI has been also been shown to reduce

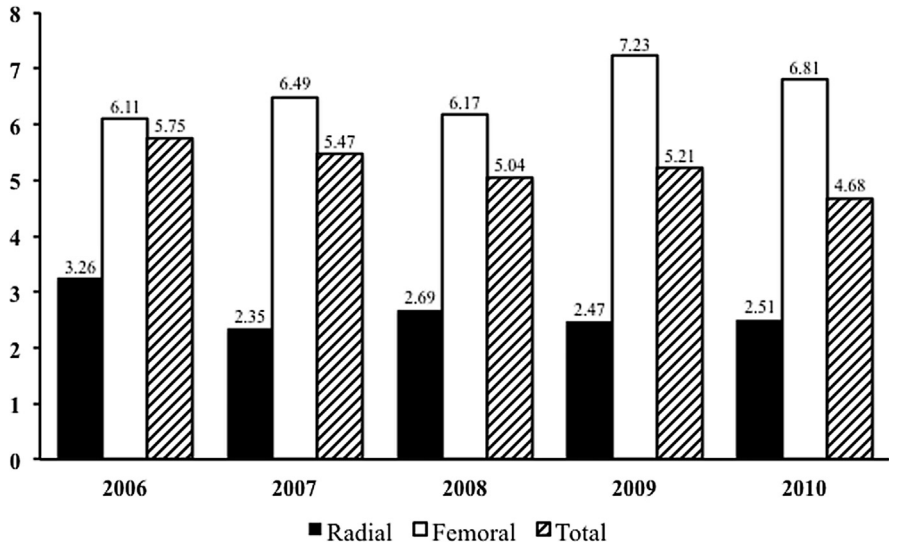

Figure 4. PPCI 30-Day Mortality (%) Between 2006 and 2010 for Radial, Femoral, and Combined Cohort

PPCI 30-day mortality (%) between 2006 and 2010 for radial **(solid columns)**, femoral **(open columns)**, and combined **(hatched columns)** cohort.

major bleeding complications (6,26) and may have an impact on mortality (27).

Our study suggests that adoption of TRA in the setting of PPCI is independently associated with a significant reduction in mortality and MACCE outcomes, with an associated 60% reduction in major bleeding complications, and a 70% reduction in major access site complications. This is in keeping with outcomes derived from previous small, observational and randomized studies reporting outcomes in PPCI related to access site selection (28–31). Analysis of the Scottish Coronary Revascularization Register of 4,534 patients undergoing primary or rescue PCI has shown that use of the TRA site was associated with reduced access site bleeding complications (adjusted odds ratio [OR]: 0.21, 95% CI: 0.08 to 0.56; $p < 0.002$), myocardial infarction (adjusted OR: 0.66, 95% CI: 0.51 to 0.87; $p < 0.003$), and 30-day mortality (adjusted OR: 0.51, 95% CI: 0.04 to 0.52; $p < 0.001$), with differences in myocardial infarction and death remaining significant up to 9 years of follow-up (31).

Table 4. MACCE

Variable	Radial (n = 18,037)	Femoral (n = 28,091)	p Value
MACCE	616 (3.4%)	2,158 (7.7%)	<0.001
Death at 30 days	456 (2.5%)	1,875 (6.7%)	<0.001
Reinfarction	60 (0.3%)	131 (0.5%)	0.10
Reintervention	87 (0.5%)	169 (0.6%)	0.09
TIA or stroke	47 (0.3%)	92 (0.3%)	0.20

Values are n (%).
MACCE = major adverse cardiac and cardiovascular events; TIA = transient ischemic attack.

Similarly, analysis of the North American National Cardiovascular Data Registry CathPCI registry that included 90,879 who underwent either primary or rescue PCI for STEMI showed that TRA was independently associated with reduction of in-hospital mortality (OR: 0.76, 95% CI: 0.57 to 0.99) and of bleeding (OR: 0.62, 95% CI: 0.53 to 0.72) (32). The recently published RIVAL (RadIal Vs femorAL access for coronary intervention) randomized multicenter trial (19) demonstrated a statistically significant 40% reduction in the primary endpoint (death, myocardial infarction, stroke, or non-coronary artery bypass graft–related major bleeding), and a 61% reduction in overall mortality in the STEMI subgroup associated with TRA. Similarly, in the HORIZONS-AMI (Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction) trial, TRA was associated with a 55% reduction in the rate of non-CABG–related major bleeding rates and a 77% reduction in death or reinfarction at 30 days (33).

Table 5. Multivariate Predictors of In-Hospital MACCE

Variable	HR (95% CI)*	p Value
Access site (radial)	0.73 (0.57–0.93)	<0.05
Age, yrs	1.04 (1.03–1.05)	<0.0001
No GP IIb/IIIa	1.40 (1.11–1.76)	<0.005
Severe LV dysfunction	4.48 (3.54–5.66)	<0.0001
Shock	4.10 (3.06–5.50)	<0.0001
IABP use	2.96 (2.18–4.04)	<0.0001

*Adjusted for age, sex, diabetes, hypertension, hypercholesterolemia, smoking status, shock, intra-aortic balloon pump use, previous AMI, previous CABG, thrombectomy catheter, LV function, year of procedure, and GP IIb/IIIa use.
Abbreviations as in Tables 1, 2, 3, and 4.

Table 6. Baseline Clinical Demographics for Radial and Femoral Access Sites in Propensity-Matched Cohort

Variable	Radial (n = 12,355)	Femoral (n = 12,355)	p Value
Age, yrs	62.9 ± 13.0	62.3 ± 15.1	0.69
Male	9,512 (77.0%)	9,490 (76.8%)	0.74
Diabetes	1,411 (11.4%)	1,461 (11.8%)	0.32
Hypertension	4,955 (40.1%)	5,063 (41.0%)	0.16
HCholesterol	5,424 (43.9%)	5,555 (45.0%)	0.09
PVD	358 (2.9%)	378 (3.1%)	0.45
Previous CVA	453 (3.7%)	466 (3.8%)	0.66
Renal failure	28 (0.2%)	36 (0.3%)	0.32
Previous MI	1,430 (11.6%)	1,429 (11.6%)	0.98
Previous PCI	923 (7.5%)	885 (7.2%)	0.35
Previous CABG	126 (1.0%)	111 (0.9%)	0.33
Cardiogenic shock	390 (3.2%)	371 (3.0%)	0.48
IABP	230 (1.9%)	241 (2.0%)	0.61
Ventilated	130 (1.1%)	140 (1.1%)	0.54

Values are n (%).

CVA = cerebral vascular accident; HCholesterol = hypercholesteremia; MI = myocardial infarction; PCI = percutaneous coronary intervention; other abbreviations as in Tables 1 and 2.

The recent randomized controlled trial RIFLE-STEACS (Radial versus Femoral Randomized Investigation in ST Elevation Acute Coronary Syndrome) study has also shown that adoption of the transradial route is associated with a reduction in cardiac mortality, MACCE, and access site–related bleeding complications in patients presenting with STEMI (13). Similarly, a recent meta-analysis of 9 randomized controlled studies involving 2,977 patients demonstrated that TRA PCI was associated with similar reductions in mortality (OR: 0.53, 95% CI: 0.33 to 0.84; p = 0.008) and MACCE (OR: 0.62, 95% CI: 0.43 to 0.90; p = 0.012) with trends towards a significant reduction in major bleeding events (OR: 0.63, 95% CI: 0.35 to 1.12; p = 0.12) (14).

The mechanism by which TRA exerts these favorable effects in PPCI may be related in part to the reduction in both major bleeding and access site complications that we have documented. Large access site bleeds can lead to hemodynamic instability and blood transfusion with an associated range of deleterious consequences. Although some access site complications will not result in substantial blood loss, they may still require intervention with consequent activation of systemic inflammation and coagulation and compromised antiplatelet regimens. This results in a disproportionate risk of cardiovascular events even though the initial insult is not hemodynamically significant. Bleeding or access site complications can also lead to withdrawal of antiplatelet agents, increasing the risk of ischemic complications. The 0.7% absolute reduction in major bleeding and 0.3% absolute reduction in access site–related complications associated with TRA utilization cannot, however, fully explain the magnitude of the mortality benefit associated with TRA in PPCI that we have observed. Our major bleeding and access site–related complication event rates that we report are significantly lower than those reported in contemporary randomized trials that include STEMI patients (13,19,25), which may reflect under-reporting of such complications in our dataset. It is therefore possible that the real magnitude of major bleeding and access site complication reduction associated with the TRA is significantly greater than captured in our BCIS dataset, which may account for the magnitude of mortality benefit observed to be associated with TRA. Furthermore, our analysis indicates that the patients treated via TRA had a greater use of thrombus aspiration and GP IIb/IIIa usage. Use of these specific strategies may also indicate that the TRA operators were more likely to change practice in line with emerging data, resulting in improved outcomes through the delivery of a more contemporary evidence-based practice.

Major practice-changing advances in the treatment of STEMI have occurred over the past few decades that have led to improvements in mortality outcomes. Thrombolysis has been shown to reduce mortality in STEMI by the order of 25% (34); when compared with thrombolysis, PPCI has been shown to reduce mortality in STEMI by the order of 40% (35). These reductions in STEMI mortality are of a similar magnitude to the reduction in mortality that we have observed to be associated with TRA in the current study (29%) and in our recent meta-analysis of randomized controlled studies (48%) (14). Although thrombolysis and PPCI strategies were widely adopted for the management of STEMI, adoption of TRA has been slow in some countries, despite the existing favorable data. This may reflect the small sample size and selective nature of previous studies. We have now confirmed the findings of these studies in a large, nonselected, real-world analysis of over 40,000 PPCI procedures. Our findings have important implications for the optimal delivery of PPCI, and support use of the TRA as the current gold standard access site.

Our analysis has several strengths. The BCIS dataset includes an almost complete collection of all PCI procedures performed in the United Kingdom. This dataset, therefore, includes all comers and reflects a national, real-world experience that includes many high-risk patients encountered in daily interventional practice who are often excluded from randomized controlled trials. Furthermore, given that this analysis reflects the U.K. experience, it includes over 40,000 PPCI procedures and so represents the largest analysis of access site–related outcomes in PPCI procedures in the literature to date.

Study limitations. Although mortality tracking within the United Kingdom is very robust, which is particularly appropriate for interventions aimed at reducing mortality such as PPCI, the cause of death is not currently available, and all other outcomes and complications are self-reported and are not formally audited by BCIS. This may account for the relatively low incidence of both major bleeding and access site complication events reported in our dataset. Therefore, the analysis is subject to reporting biases, and complications

may be underreported. Furthermore, higher-risk patients (e.g., those with cardiogenic shock) were more likely to be managed using TFA, resulting in case-selection bias (although cardiogenic shock was adjusted for in the multivariable analysis); and although propensity score matching was performed to account for confounding variable and bias, there is a possibility of unmeasured confounders and therefore residual bias. We observed a reduction in major bleeding complications although the BCIS dataset does not collect data utilizing bleeding definitions that are known to have different implications on prognosis in other studies. Although we did not have access to door-to-balloon time data and although the reduction in bleeding/vascular complications observed with adoption of the radial approach should be balanced with maintaining rapid reperfusion, previous data have suggested that door-to-balloon times are not significantly increased through adoption of TRA in the PPCI setting (36). Although these data are very compelling, caution should be exercised regarding the preferential choice of the radial artery as an access site in PPCI cases by individuals at the very start of their transradial learning curve with little or no previous transradial experience. Finally, our analysis is of observational data and so cannot be used to infer a causal relationship between access site and outcomes, because unmeasured confounders might account for some of the differences in outcomes observed despite the inclusion of multiple procedural and demographic factors in our multivariate regression analysis and propensity score matching.

Conclusions

The current analysis of data derived from the BCIS database of 46,128 PPCI procedures performed in the United Kingdom over a 5-year period demonstrates that, compared with the TFA, the TRA is independently associated with lower mortality and MACCE rates, similar in magnitude to the mortality benefits associated with the introduction of thrombolysis and primary PCI in the management of STEMI. Although our analysis of an observational database can never infer causality, the observations are consistent with previous smaller and more selective randomized trials that support the preferential use of TRA for PPCI.

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Key Words: access site ■ femoral ■ outcomes ■ PCI ■ radial ■ STEMI.