



## LJMU Research Online

Rashid, M, Rushton, CA, Kwok, CS, Kinnaird, T, Kontopantelis, E, Olier, I, Ludman, P, De Belder, MA, Nolan, J and Mamas, MA

**Impact of Access Site Practice on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention Following Thrombolysis for ST-Segment Elevation Myocardial Infarction in the United Kingdom An Insight From the British Cardiovascular Intervention Society Dataset**

<http://researchonline.ljmu.ac.uk/9346/>

### Article

**Citation** (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

**Rashid, M, Rushton, CA, Kwok, CS, Kinnaird, T, Kontopantelis, E, Olier, I, Ludman, P, De Belder, MA, Nolan, J and Mamas, MA (2017) Impact of Access Site Practice on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention Following Thrombolysis for ST-**

LJMU has developed [LJMU Research Online](http://researchonline.ljmu.ac.uk/) for users to access the research output of the University more effectively. Copyright © and Moral Rights for the papers on this site are retained by the individual authors and/or other copyright owners. Users may download and/or print one copy of any article(s) in LJMU Research Online to facilitate their private study or for non-commercial research. You may not engage in further distribution of the material or use it for any profit-making activities or any commercial gain.

The version presented here may differ from the published version or from the version of the record. Please see the repository URL above for details on accessing the published version and note that access may require a subscription.

For more information please contact [researchonline@ljmu.ac.uk](mailto:researchonline@ljmu.ac.uk)

<http://researchonline.ljmu.ac.uk/>





# Impact of Access Site Practice on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Intervention Following Thrombolysis for ST-Segment Elevation Myocardial Infarction in the United Kingdom

## An Insight From the British Cardiovascular Intervention Society Dataset

Muhammad Rashid, MBBS,<sup>a,b</sup> Claire A. Rushton, PhD,<sup>a</sup> Chun Shing Kwok, MBBS,<sup>a,b</sup> Tim Kinnaird, MBChB,<sup>a,c</sup> Evangelos Kontopantelis, PhD,<sup>d</sup> Ivan Olier, PhD,<sup>a,e</sup> Peter Ludman, MD,<sup>f</sup> Mark A. De Belder, MD,<sup>g</sup> James Nolan, MD,<sup>a,b</sup> Mamas A. Mamas, BM, BCh, MA, DPHIL<sup>a,b</sup>

### ABSTRACT

**OBJECTIVES** This study sought to examine the relationship between access site practice and clinical outcomes in patients requiring percutaneous coronary intervention (PCI) following thrombolysis for ST-segment elevation myocardial infarction (STEMI).

**BACKGROUND** Transradial access (TRA) is associated with better outcomes in patients requiring PCI for STEMI. A significant proportion of STEMI patients may receive thrombolysis before undergoing PCI in many countries across the world. There are limited data around access site practice and its associated outcomes in this cohort of patients.

**METHODS** The author used the British Cardiovascular Intervention Society dataset to investigate the outcomes of patients undergoing PCI following thrombolysis between 2007 and 2014. Patients were divided into TRA and transfemoral access groups depending on the access site used. Multiple logistic regression and propensity score matching were used to study the association of access site with in-hospital and long-term mortality, major bleeding, and access site-related complications.

**RESULTS** A total of 10,209 patients received thrombolysis and PCI during the study time. TRA was used in 48% (n = 4,959) of patients; 3.3% (n = 336) patients died in hospital, 1.6% (n = 165) of patients experienced major bleeding, 4.2% (n = 437) experienced major adverse cardiac events (MACE), and 4.6% (n = 468) experienced 30-day mortality. After multivariate adjustment, TRA was associated with significantly reduced odds of in-hospital mortality (odds ratio [OR]: 0.59; 95% confidence interval [CI]: 0.42 to 0.83; p = 0.002), major bleeding (OR: 0.45; 95% CI: 0.31 to 0.66; p < 0.001), MACE (OR: 0.72; 95% CI: 0.55 to 0.94; p = 0.01), and 30-day mortality (OR: 0.72; 95% CI: 0.55 to 0.94; p = 0.01).

**CONCLUSIONS** TRA is associated with decreased odds of bleeding complications, mortality, and MACE in patients undergoing PCI following thrombolysis and should be preferred access site choice in this cohort of patients.

(J Am Coll Cardiol Intv 2017;10:2258-65) © 2017 by the American College of Cardiology Foundation.

Primary percutaneous coronary intervention (PPCI) is currently the gold standard treatment for patients with ST-segment elevation myocardial infarction (STEMI) (1,2). However, thrombolysis is still widely used particularly in areas where PPCI services are not well established or cannot be delivered within recommended time frames. Although use of thrombolytic treatment has declined over recent years, it still remains an important reperfusion strategy for the management of patients admitted with STEMI across Europe (3), the United States (4,5), and the Far East (6). For instance, one of the largest analyses of STEMI care in China reported approximately 27% of the patients received thrombolysis as main reperfusion therapy (6) and a similar percentage (29.5%) has been reported from registry data in the United States (7). A significant proportion of these patients may require PCI either due to failure of therapy or incomplete resolution of symptoms (7). Use of potent antithrombotic and antiplatelets in addition to fibrinolytic agents is likely to increase the risk of bleeding complications in those undergoing rescue PCI (8,9). For instance, in the FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) trial (10), Thrombolysis In Myocardial Infarction major and minor bleeding rates were significantly higher (14.5% and 10.1%, respectively) in patients receiving thrombolytic agents compared with those undergoing PPCI only (6.9%;  $p < 0.001$ ). Major bleeding is one of the most serious complications of PCI and is independently associated with reduced survival and poor outcomes (11).

SEE PAGE 2266

Adoption of transradial access (TRA) has increased significantly over the past decade for acute coronary interventions across the whole spectrum of acute syndromes (12,13). This uptake is mainly driven by the evidence that TRA is associated with significant reduction in access site related bleeding complications and improved survival in patients undergoing PCI for acute coronary syndrome as well as PPCI (14-17). Importantly, there is little evidence around outcomes and the access site used in patients requiring PCI after receiving thrombolysis with majority of these data confined to patients undergoing PPCI (14,15). Previously, the impact of access site

practice in patients requiring PCI following thrombolysis was only described in either highly selected post hoc analyses of randomized trials (18,19) or in observational studies where use of TRA is significantly lower compared to transfemoral access (TFA) (20,21). These studies reported inconsistent results and were not statistically powered, with TRA patients being <15% of the total cohort. A study from the well-known CathPCI registry showed that TRA is associated with reduced major in-hospital and gastrointestinal bleeding complications, but not mortality (20), albeit only 14.2% of the cases received TRA compared with TFA. Another study encompassing individual patients level data of 1,891 patients from 7 STEMI trials evaluating PCI after thrombolysis reported no difference in major bleeding and mortality at 30-days in TRA versus TFA although TRA was only used in 17% of the patients (18). In contrast, a recent post hoc analysis of the STREAM (Strategic Reperfusion Early After Myocardial Infarction) study, Shavadia et al. (19) illustrated that TRA was associated with significant reduction in major bleeding and mortality at 30-days in patients undergoing rescue PCI after thrombolysis.

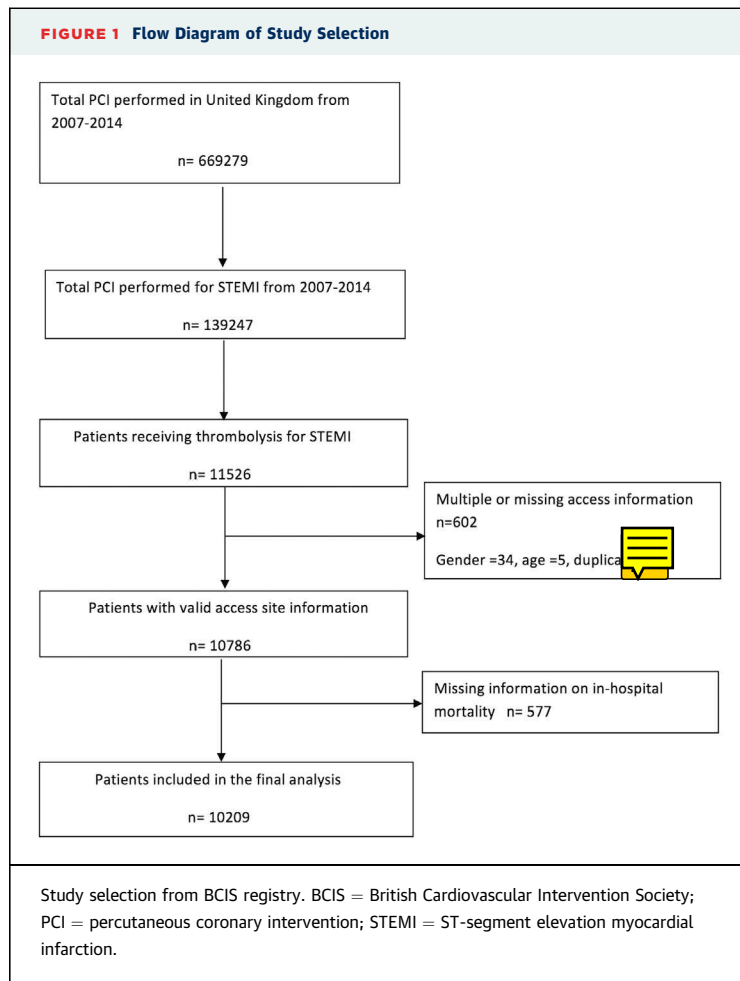
In the current study, we sought to investigate trends in procedure practice and impact of access site selection on cardiovascular outcomes in a national cohort of patients undergoing PCI after receiving thrombolysis treatment using British Cardiovascular Interventional Society (BCIS) dataset in England and Wales.

## METHODS

This study is a retrospective analysis of prospectively collected national data for all patients undergoing PCI after receiving thrombolysis for STEMI in England and Wales from January 2007 to December 2014 in the British Cardiovascular Intervention Society (BCIS) database. BCIS records information on PCI practices in the United Kingdom with data collection managed by the National Institute of Cardiovascular Outcomes Research (22-25). The BCIS database is one of the largest nationally collected datasets containing 113 clinical, procedural, and outcome variables with 80,000 new records added each year. Using the

## ABBREVIATIONS AND ACRONYMS

<b>ACS</b>	= acute coronary syndrome(s)
<b>BCIS</b>	= British Cardiovascular Intervention Society
<b>CI</b>	= confidence interval
<b>MACE</b>	= major adverse cardiac event(s)
<b>OR</b>	= odds ratio
<b>PCI</b>	= percutaneous coronary intervention
<b>PPCI</b>	= primary percutaneous coronary intervention
<b>STEMI</b>	= ST-segment elevation myocardial infarction
<b>TFA</b>	= transfemoral access
<b>tPCI</b>	= thrombolytic percutaneous coronary intervention
<b>TRA</b>	= transradial access



patient's unique National Health Service number, mortality is tracked for all patients using data from the Office of National Statistics in England and Wales. Patients from Scotland and Northern Ireland were excluded from the mortality outcome analysis because of the absence of the Office of National Statistics-linked mortality data. All the data were collected as part of a national audit and were anonymized; therefore, institutional review board approval was not required for this study.

**VARIABLES AND OUTCOMES COLLECTED.** We collected data on participants' demographic such as age and sex, cardiovascular risk factors, comorbidities, and indication for PCI. In addition, data were also collected on clinical characteristics such left ventricular ejection fraction, cardiogenic shock, use of pharmacological or mechanical inotropic support, and all aspects of the interventional treatment and adjunctive pharmacology.

**STUDY DEFINITIONS.** Thrombolytic PCI (tPCI) in the BCIS dataset is defined as acute coronary syndrome

(ACS)-facilitated PCI for STEMI (lysis+PCI), ACS rescue PCI for STEMI (failed lysis), and ACS rescue PCI for reinfarction (failed lysis). Use of either radial artery is classed as TRA and use of either femoral artery was defined as TFA, whereas multiple arterial access, brachial access, and unlisted access site were excluded from the analysis. We evaluated all-cause mortality in hospital, at 30 days, and at 1 year of follow-up. We also examined in-hospital major adverse cardiac events (MACE) (defined as a composite of in-hospital mortality, in-hospital myocardial infarction, or reinfarction and revascularization [emergency PCI or coronary artery bypass grafting]) and in-hospital major bleeding (defined as blood or platelet transfusion, intracerebral hemorrhage, retroperitoneal hemorrhage, bleed resulting in cardiac tamponade, or an arterial access site bleeding requiring surgery or intervention). Finally, we also studied the in-hospital mortality only and access site complications (defined as pseudoaneurysm or any access site hemorrhage requiring intervention or delaying discharge).

**STATISTICAL METHODS.** After initial selection of tPCI cohort as defined previously, we divided the study population into 2 groups: 1) tPCI undertaken via TRA; and 2) tPCI performed via TFA. We made further exclusions depending on missing information from age, sex, or in-hospital mortality. The characteristics of patients were compared across the 2 groups. These comparisons were performed using analysis of variance for continuous variables and Fisher exact tests for binary or categorical variables.

We used multiple imputation techniques with chained equations to impute data for all variables with missing information to account for the missing data and protect against the biases because of informative missing data mechanisms. Age, sex, access, indication for PCI, and study outcomes were registered as complete variables in the imputation models, which were used to generate 10 datasets on which we ran the analyses (imputed variables were body mass index, history of previous PCI, history of coronary artery bypass grafting, diabetes mellitus, smoking status, hypertension, hyperlipidemia, previous myocardial infarction, previous stroke, peripheral vascular disease, history of renal failure, glycoprotein IIb or IIIa use, cardiogenic shock, mechanical or pharmacological circulatory support, use of stents, mechanical ventilation, bivalirudin use, history of triple-vessel disease, and PCI to left main stem artery). Although our use of a multiple imputation framework rests on a missing at random assumption and levels of missingness are high for certain variables, it has been shown that multiple imputation frameworks are robust even when levels of

missingness are extremely high, although they can offer some protection when data are missing not at random (26).

The risk of adverse outcomes by access group was estimated with multivariable logistic regression adjusting for all patient and clinical characteristics. All potential predictors of 30-day mortality were included in the model. These were age, sex, and left ventricular function in addition to all the variables included in the multiple-imputation model.

To better control for any differences in the baseline characteristics of the 2 groups (TRA vs. TFA), we used multiple imputations with propensity score matching (mi estimate:teffects psmatch) to estimate the average treatment effect using the same covariates as in our main multiple logistic regression analysis (Online Table 1). The propensity scores of the radial and femoral procedures were graphically plotted before matching. After matching the scores are plotted for the cases (radial) and control subjects (femoral) to allow for graphical evaluation of the quality of matching (Online Figure 1). We also conducted a sensitivity analysis in the nonimputed dataset to assess the consistency of results (Online Table 2). Due to missing information the sample size drop significantly hence the confidence intervals overlap; however, over trend it remains same as in the imputed dataset. Statistical analyses were performed using Stata version 13.1 (StataCorp, College Station, Texas).

## RESULTS

**BASELINE CHARACTERISTICS.** A total of 11,526 patients received thrombolysis and PCI between 2007 to 2014 in England and Wales for STEMI. After making exclusions based on missing information on access site, age, sex, and in-hospital mortality as well as patients with multiple access sites used, 10,209 patients were included in the final analyses (Online Table 3). Full information of study inclusion and exclusion is shown in Figure 1. Among the 10,209 patients receiving thrombolysis for STEMI and tPCI, 5,250 (51%) received their procedure via TFA and 4,959 (48%) received their procedure via TRA. As shown in Table 1, patients in the TFA group were more likely to have hypertension, previous history of acute myocardial infarction, hypercholesterolemia, diabetes, history of previous coronary artery bypass grafting, and triple-vessel disease ( $p < 0.01$ ). They were also significantly more likely to have cardiogenic shock requiring pharmacological or mechanical inotropic support. The TRA group received more aggressive and potent pharmacotherapy than the TFA group did, in the form of prasugrel (2.6% vs. 0.5%),

**TABLE 1** Baseline and Procedural Characteristics of Patients Undergoing Transradial or Transfemoral Access Percutaneous Coronary Intervention Following Thrombolysis

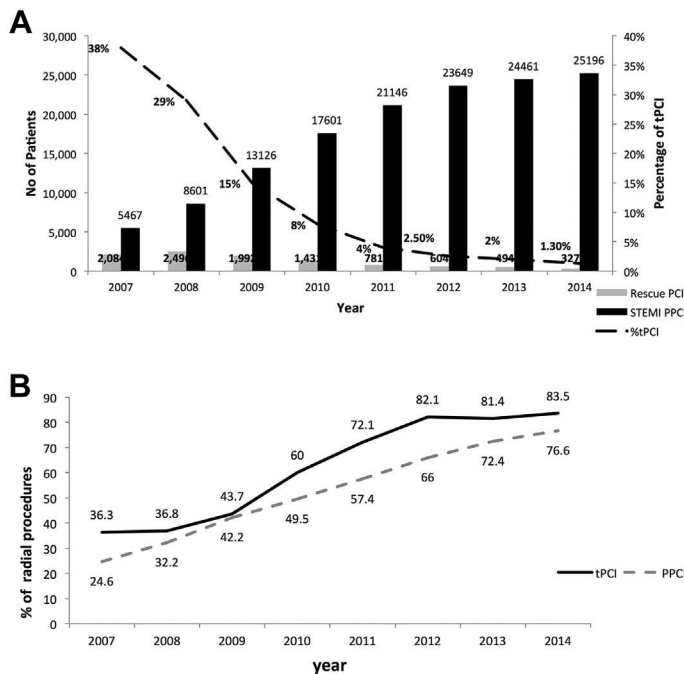
	Femoral (n = 5,250)	Radial (n = 4,959)	p Value
Age, yrs	60.9 ± 11.9	60.3 ± 11.5	0.039
Male	4,079 (78.0)	4,061 (82.0)	<0.001
BMI, kg/m <sup>2</sup>	27.6 ± 4.6	28.4 ± 4.9	<0.001
Hypercholesterolemia	1,950 (40.0)	1,933 (43.0)	<0.001
HTN	1,835 (37.8)	1,819 (40.5)	<0.008
Renal failure	35 (0.7)	22 (0.4)	0.11
Smoking	3,149 (71.3)	3,166 (69.6)	0.05
Diabetes	657 (13.3)	541 (11.2)	<0.001
Previous AMI	872 (19.5)	629 (13.5)	<0.001
Previous CVA	98 (2)	119 (2.6)	0.04
Severe LVSD	238 (13.5)	147 (6.8)	<0.001
PVD	124 (2.5)	131 (2.9)	0.28
Previous PCI	370 (7.5)	292 (6.0)	<0.001
Previous CABG	313 (8.5)	105 (3.1)	<0.001
Pharmacological inotropes	204 (4.3)	46 (0.9)	<0.001
IABP	388 (8.3)	93 (1.9)	<0.001
Cardiogenic shock	513 (10.0)	190 (3.9)	<0.001
Ventilated	259 (6.2)	93 (2.3)	<0.001
GP IIb/IIIa use	2,295 (46.0)	2,107 (43.3)	0.003
Clopidogrel	3,450 (75.0)	3,281 (77.4)	0.007
Warfarin	22 (0.48)	19 (0.45)	0.83
Bivalirudin	58 (1.3)	120 (2.8)	<0.001
Prasugrel	26 (0.5)	113 (2.6)	<0.001
Ticagrelor	35 (0.7)	122 (2.9)	<0.001
LMS PCI	106 (2.0)	59 (1.1)	<0.001
Triple vessel disease	283 (15.0)	225 (10.0)	<0.001
Stent use			
No stent	264 (5.2)	247 (5.1)	
BMS only	2,396 (47.9)	2,016 (41.7)	<0.001
DES only	2,172 (43.4)	2,400 (49.6)	<0.001
BMS and DES	169 (3.3)	169 (3.5)	
Access site complications	136 (2.5)	33 (0.6)	<0.001
In hospital death	247 (4.7)	89 (1.8)	<0.001
MACE	302 (5.7)	135 (2.7)	<0.001
Major bleeding	116 (2.2)	49 (1.0)	<0.001
30-day mortality	349 (7.5)	119 (3.7)	<0.001
1-yr mortality	458 (9.8)	181 (5.6)	<0.001

Values are mean ± SD or n (%). Major adverse cardiovascular event(s) (MACE) were defined as composite of in-hospital mortality, in-hospital myocardial infarction or reinfarction, and revascularization (emergency percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]).

AMI = acute myocardial infarction; BMI = body mass index; BMS = bare-metal stent(s); CVA = cerebrovascular accident; DES = drug-eluting stent; GP = glycoprotein; HTN = hypertension; IABP = intra-aortic balloon pump; LMS = left main stem; LVSD = left ventricular systolic dysfunction; PVD = peripheral vascular disease.

ticagrelor (2.9% vs. 0.7%), and bivalirudin (2.8% vs. 1.3%) ( $p < 0.01$ ).

**PROCEDURE TRENDS.** During the study time, the number of patients requiring PCI after thrombolysis reduced significantly from 38% in 2007 to 1.2% in 2014, shown in Figure 2A. The use of TRA in patients requiring PCI following thrombolysis versus PPCI is illustrated in Figure 2B, showing a greater uptake of TRA in patients requiring tPCI. There was a

**FIGURE 2** Temporal Trends in Thrombolytic PCI Activity and Use of Radial Access in United Kingdom

**(A)** Comparison between ST-segment elevation myocardial infarction (STEMI) primary percutaneous coronary intervention (PPCI) and thrombolytic percutaneous coronary intervention (PCI) activity in the United Kingdom from 2007 to 2014. **(B)** Use of radial access in thrombolytic PCI and PPCI for STEMI in the United Kingdom from 2007 to 2014.

particularly steep rise in the use of TRA for tPCI (almost doubling) from 43% in 2009 to 82% in 2012. [Online Figures 2A and 2B](#) demonstrate a cognate decline in number of patient undergoing PCI after the administration of thrombolysis in all parts of the United Kingdom corresponding with an overall increase in uptake of TRA at national level. However, we observed significant regional variation within the United Kingdom in use of PCI following thrombolysis. For instance, in the primary care Trusts encompassing North Wales, 53% of STEMI PCI patients had received thrombolysis in 2014. Conversely, in the mainland areas such as North West and Midlands of England the use of tPCI has declined significantly, to <10%. Similarly, there remain regional differences in access site practice despite the fact that overall UK practice has changed significantly to predominantly TRA. For examples, centers in Sheffield, Cumbria, and Lincolnshire are still performing more than 50% of their cases via the femoral route in patients undergoing PCI following thrombolysis.

#### ACCESS SITE AND OUTCOMES IN tPCI Mortality

Of the 4,959 patients in the TRA group who died in hospital, 119 (3.7%) died by 30 days and 458 (9.8%) patients in the TFA group died in 1 year, compared with 247 (4.9%) patients in the TRA group. **Table 2** presents the adjusted odds of outcomes by access site. Comparing the TRA group to the TFA group, 1-year mortality rates were similar (odds ratio [OR]: 0.82; 95% confidence interval [CI]: 0.66 to 1.02;  $p = 0.08$ ), but TRA was associated with reduced in-hospital (OR: 0.59; 95% CI: 0.42 to 0.82;  $p = 0.002$ ) and 30-day (OR: 0.72; 95% CI: 0.55 to 0.94;  $p = 0.01$ ) mortality risk.

**Access site complications, major bleeding, and MACE.** The TRA group experienced significantly less access site complications ( $n = 33$ , 0.6%), major bleeding ( $n = 49$ , 1%), and MACE ( $n = 135$ , 2.7%) than the TFA group did (access site complications:  $n = 136$ , 2.5%; major bleeding:  $n = 116$ , 2.2%; MACE:  $n = 302$ , 5.7%). After adjustment for all patient and clinical characteristics, TRA was associated with significant reduction in access site-related complications (OR: 0.30; 95% CI: 0.20 to 0.45;  $p < 0.001$ ), in-hospital MACE risk (OR: 0.72; 95% CI: 0.56 to 0.94;  $p = 0.01$ ), and major bleeding (OR: 0.45; 95% CI: 0.31 to 0.66;  $p < 0.001$ ), compared with the TFA group ([Table 2](#)).

**PROPENSITY SCORE MATCHING.** Propensity score matching to correct for baseline characteristics showed no difference in results ([Table 3](#), balance diagnostics for propensity model are presented in [Online Table 1](#)). TRA remained significantly associated with reduced risk of in-hospital mortality, access site complications, and major bleeding.

## DISCUSSION

This is one of the largest analyses demonstrating the temporal trends, regional practices, and impact of TRA on clinical outcomes in patients undergoing PCI following thrombolysis. Approximately 38% of the patients received tPCI in 2007, which was reduced to 1.3% in 2014 with a concomitant national increase in use of PPCI for STEMI patients. Although the overall use of tPCI has reduced over time, there remain important regional differences within the United Kingdom. In over a third of the regions, up to 10% of STEMI patients receiving PCI received thrombolysis whereas in other areas this was >50% with significant regional differences in access site practice. Our study shows that compared with TFA, the use of TRA is associated with reduced in-hospital and longer-term mortality, in-hospital MACE, in-hospital major

Can you please move this down as sub heading. "Mortality" is a subheading of ACCESS SITE AND OUTCOMES

**TABLE 2 Adjusted Outcomes Following Transradial Access and Transfemoral Access**

Adverse Outcome	Sample Size	Odds Ratio (95% CI)	p Value
In-hospital death	10,209	0.59 (0.42 to 0.83)	0.002
Access site complications	10,209	0.30 (0.20 to 0.45)	<0.001
Major bleeding	10,209	0.45 (0.31 to 0.66)	<0.001
MACE	10,209	0.72 (0.56 to 0.94)	0.01
30-day mortality	7,841	0.72 (0.55 to 0.94)	0.01
1-yr mortality	7,841	0.82 (0.66 to 1.02)	0.08

CI = confidence interval; other abbreviations as in Table 1.

**TABLE 3 Propensity Score Matching Analysis on 10 Imputed Datasets, Reporting Average Treatment Effects**

Radial vs. Femoral	n	Coefficient	95% CI	p Value
In hospital death	8,769	-0.01078	-0.02132 to -0.00025	0.04
Access site complications	8,769	-0.01921	-0.02675 to -0.01167	<0.001
Major bleeding	8,796	-0.01138	-0.01859 to -0.00416	<0.002
MACE	8,769	-0.01045	-0.02205 to 0.00113	0.07
30-day mortality	7,167	-0.01158	-0.02578 to 0.00262	0.11
1-yr mortality	7,167	-0.01039	-0.02734 to 0.00655	0.22

Abbreviations as in Tables 1 and 2.

bleeding, and access site complications in patients undergoing PCI post-thrombolysis.

Due to development of improved service structures and better systems of care such as regional STEMI networks (27,28), use of thrombolysis has significantly reduced over the last decade in countries including the United Kingdom, Denmark, Germany, and Austria (3). However, thrombolysis followed by PCI still remains an important reperfusion strategy in many countries across the world (6,7,29,30). The rates of PCI after thrombolysis vary between 8% (Europe) and 25% (the United States) (7,31). In our study, this proportion is lower, with only 7.3% undergoing PCI after thrombolysis over the study period. Interestingly, the temporal analysis demonstrates a significant reduction in number of patients requiring PCI after thrombolysis from 38% to 1.3% over the past decade. Data captured from the Myocardial Ischaemia National Audit Project in the United Kingdom reported that use of thrombolysis has declined to <1% in 2015 with the concomitant rise in use of PPCI to 99% (32). The decline in thrombolysis in United Kingdom over the last few years has resulted in less need of tPCI. This trend was also mirrored by significant change in access site practice with an increase in the use of radial access from 36.3% in 2007 to 83.5% in 2014.

Data from several randomized trials and observational studies have consistently demonstrated that use of TRA is associated with lower risk of major bleeding, vascular complications, and mortality (14,23,25,33,34). Adoption of TRA yields even greater benefits over TFA in patients with high baseline bleeding risk (33). In the RIFLE-STEACS (Radial Versus Femoral Investigation in ST Elevation Acute Coronary Syndrome) trial, TRA was associated with significant reduction in cardiac mortality (5.2% vs. 9.2%; p = 0.020) and bleeding complications (7.8% vs. 12.2%; p = 0.026) (15). In one the largest trials to date comparing TRA versus TFA, the MATRIX (Minimising

Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of angioX) trial reported a 28% reduction in mortality (1.6% vs. 2.2%; p = 0.045) (14) with a reduction in net adverse clinically events (9.8% vs. 11.7%; p = 0.009) mainly driven by a marked reduction in Bleeding Academic Research Consortium 3 or 5 major bleeding in the TRA group. The appended updated meta-analysis including MATRIX trial patients also showed that TRA was associated with reduced major bleeding, MACE, and all-cause mortality without any heterogeneity in the results. Patients undergoing PCI following recent thrombolysis are among the highest risk patient groups of sustaining major bleeding complications and would therefore have the greatest benefit from undergoing PCI through the transradial approach. Our data are consistent with this and not only show that odds of major bleeding are reduced by 55% associated with the use of TRA, but also translate into a reduced mortality and MACE risk in patients undergoing PCI after thrombolysis.

There is limited evidence about the impact of TRA on clinical outcomes in patients requiring PCI following thrombolysis (18-20). In a previous analysis of the CathPCI registry, TRA was associated with a significant reduction in major bleeding (OR: 0.67; 95% CI: 0.52 to 0.87; p = 0.003) but no difference between in-hospital mortality (20). However, the use of TRA was <15% in this study compared with our analysis where use of TRA was >50%. Furthermore, our analysis is over a timeframe in which TRA has become the default access site choice in patients undergoing PCI in the United Kingdom, with rates >80% in 2015 (13), whereas in the U.S. uptake is around 10% (35). Another important difference was the fact that critically ill patients such as those with hemodynamic compromise requiring intra-aortic balloon pump or mechanical support and patients needing in-hospital coronary artery bypass grafting were also included in the current analysis. Finally, this is the first study



to report impact of TRA on longer-term mortality in patients undergoing PCI in the thrombolysis setting.

Our study has several strengths: it is one of the largest to date describing national patterns of access site practice in patients requiring PCI following thrombolysis. The BCIS dataset records information about almost every single PCI procedure undertaken in United Kingdom providing real-world insight into management of patients requiring PCI following thrombolysis. We were able to include high-risk patients such as those requiring inotropic support and hemodynamic instability, who are often excluded from randomized trials. Finally, this is first study to illustrate the impact of access site practice on longer-term mortality in this cohort of patients.

**STUDY LIMITATIONS.** We acknowledge that although the mortality outcomes in the BCIS are robustly linked with the Office of National Statistics, all other complications of PCI are reliant on operator recording and may be under-reported. Our analysis focuses on outcomes associated with the access site used rather than an intention to treat (i.e., that access site that was first attempted). The BCIS dataset does not contain information on access site crossover resulting from failure for cases in which multiple access sites were used, although such cases are were 5.2% of the total number of procedures in the current analysis and were excluded from the analysis when the access site used was not clear. Many of the cases with multiple access sites are likely to represent cases in which radial was attempted and then the case was converted to femoral. In addition, these cases are likely to be more complicated, and if classified as femoral, the analyses would tend to overestimate the relative benefit of radial access (13,17). Finally, our analysis is observational in nature and prone to unmeasured confounders. Therefore, a causal relationship cannot be inferred between access site practice and clinical outcomes.

## CONCLUSIONS

In one of the largest analysis of patients receiving PCI after thrombolysis, use of TRA was associated with reduced risk of major bleeding, access site complications, in-hospital mortality, and MACE. Our analysis suggests that where PCI is required after thrombolysis, use of the radial access site may translate to more favorable clinical outcomes.

**ADDRESS FOR CORRESPONDENCE:** Dr. Muhammad Rashid, Keele Cardiovascular Research Group, Keele University, Stoke-on-Trent ST4 7QB, United Kingdom. E-mail: [doctorrashid7@gmail.com](mailto:doctorrashid7@gmail.com).

## PERSPECTIVES

**WHAT IS KNOWN?** TRA has been shown to be associated with major bleeding, access site complications, and mortality in STEMI patients. There are conflicting data regarding the clinical outcomes associated with TRA following PCI in the STEMI setting post-thrombolysis.

**WHAT IS NEW?** Using the BCIS registry, we examined 10,209 STEMI patients undergoing PCI after receiving thrombolysis and found that 48% of procedures were undertaken via TRA. After multivariate analysis, TRA was associated with significant decreased risk of major bleeding complications (OR: 0.45; 95% CI: 0.31 to 0.66;  $p < 0.001$ ), MACE (OR: 0.72; 95% CI: 0.55 to 0.94;  $p = 0.01$ ), and in-hospital (OR: 0.59; 95% CI: 0.42 to 0.83;  $p = 0.002$ ) and 30-day mortality (OR: 0.72; 95% CI: 0.55 to 0.94;  $p = 0.01$ ).

**WHAT IS NEXT?** TRA should be considered the default access site in PCI for high bleeding risk cases. Future efforts should focus around developing pathways, training and educational courses to increase uptake of TRA in such cases.

## REFERENCES

1. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2012;33:2569-619.
2. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-segment elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. *J Am Coll Cardiol* 2016;67:1235-50.
3. Kristensen SD, Laut KG, Fajadet J, et al. Reperfusion therapy for ST elevation acute myocardial infarction 2010/2011: current status in 37 ESC countries. *Eur Heart J* 2014;35:1957-70.
4. Mehta RH, Kaul P, Lopes RD, et al. Variations in practice and outcomes in patients undergoing primary percutaneous coronary intervention in the United States and Canada: insights from the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX AMI) trial. *Am Heart J* 2012;163:797-803.
5. Roe MT, Messenger JC, Weintraub WS, et al. Treatments, trends, and outcomes of acute myocardial infarction and percutaneous coronary intervention. *J Am Coll Cardiol* 2010;56:254-63.
6. Li J, Li X, Wang Q, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011.

(the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. *Lancet* 2015;385:441-51.

7. Vora AN, Holmes DN, Rokos I, et al. Fibrinolysis use among patients requiring interhospital transfer for ST-segment elevation myocardial infarction care: a report from the US National Cardiovascular Data Registry. *JAMA Intern Med* 2015;175:207-15.

8. Di Mario C, Dudek D, Piscione F, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. *Lancet* 2008;371:559-68.

9. Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet* 2006;367:569-78.

10. Ellis SG, Tendera M, de Belder MA, et al. Facilitated PCI in patients with ST-segment elevation myocardial infarction. *N Engl J Med* 2008;358:2205-17.

11. Kwok CS, Rao SV, Myint PK, et al. Major bleeding after percutaneous coronary intervention and risk of subsequent mortality: a systematic review and meta-analysis. *Open Heart* 2014;1:e000021.

12. Mamas MA, Anderson SG, Ratib K, et al. Arterial access site utilization in cardiogenic shock in the United Kingdom: is radial access feasible? *Am Heart J* 2014;167:900-8.e1.

13. Mamas MA, Nolan J, de Belder MA, et al. Changes in arterial access site and association with mortality in the United Kingdom: observations from a national percutaneous coronary intervention database. *Circulation* 2016;133:1655-67.

14. Valgimigli M, Gagnor A, Calabró P, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. *Lancet* 2015;385:2465-76.

15. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, et al. Radial versus femoral randomized investigation in ST-segment elevation acute coronary syndrome: the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study. *J Am Coll Cardiol* 2012;60:2481-9.

16. Baklanov DV, Kaltenbach LA, Marso SP, et al. The prevalence and outcomes of transradial percutaneous coronary intervention for ST-segment elevation myocardial infarction:

analysis from the National Cardiovascular Data Registry (2007 to 2011). *J Am Coll Cardiol* 2013;61:420-6.

17. Ratib K, Mamas MA, Anderson SG, et al. Access site practice and procedural outcomes in relation to clinical presentation in 439,947 patients undergoing percutaneous coronary intervention in the United Kingdom. *J Am Coll Cardiol Intv* 2015;8:20-9.

18. Graham JJ, Yan AT, Tan MK, et al. Radial versus femoral access for percutaneous coronary intervention in ST-segment elevation myocardial infarction patients treated with fibrinolysis: Results from the randomized routine early invasive clinical trials. *Cardiovasc Revasc Med* 2016;17:295-301.

19. Shavadia J, Welsh R, Gershlick A, et al. Relationship between arterial access and outcomes in ST-segment elevation myocardial infarction with a pharmacoinvasive versus primary percutaneous coronary intervention strategy: insights from the STRategic Reperfusion Early After Myocardial Infarction (STREAM) study. *J Am Heart Assoc* 2016;5:e003559.

20. Kadakia MB, Rao SV, McCoy L, et al. Transradial versus transfemoral access in patients undergoing rescue percutaneous coronary intervention after fibrinolytic therapy. *J Am Coll Cardiol Intv* 2015;8:1868-76.

21. Wang YB, Fu XH, Gu XS, et al. Thrombolysis followed by early percutaneous coronary intervention via transradial artery approach in patients with ST-segment elevation infarction. *Acta Cardiol Sin* 2014;30:284-91.

22. Ludman PF, British Cardiovascular Intervention Society. British Cardiovascular Intervention Society Registry for audit and quality assessment of percutaneous coronary interventions in the United Kingdom. *Heart* 2011;97:1293-7.

23. Mamas MA, Ratib K, Routledge H, et al. Influence of arterial access site selection on outcomes in primary percutaneous coronary intervention: are the results of randomized trials achievable in clinical practice? *J Am Coll Cardiol Intv* 2013;6:698-706.

24. Mamas MA, Anderson SG, O'Kane PD, et al. Impact of left ventricular function in relation to procedural outcomes following percutaneous coronary intervention: insights from the British Cardiovascular Intervention Society. *Eur Heart J* 2014;35:3004-12.

25. Mamas MA, Ratib K, Routledge H, et al. Influence of access site selection on PCI-related adverse events in patients with STEMI: meta-analysis of randomised controlled trials. *Heart* 2012;98:303-11.

26. Kontopantelis E, White IR, Sperrin M, Buchan I. Outcome-sensitive multiple imputation: a simulation study. *BMC Med Res Methodol* 2017;17:2.

27. Huber K, Goldstein P, Danchin N, Fox KA. Network models for large cities: the European experience. *Heart* 2010;96:164-9.

28. Labarere J, Belle L, Fourny M, et al. Regional system of care for ST-segment elevation myocardial infarction in the Northern Alps: a controlled pre- and postintervention study. *Arch Cardiovasc Dis* 2012;105:414-23.

29. Khera S, Kolte D, Gupta T, et al. Temporal trends and sex differences in revascularization and outcomes of ST-segment elevation myocardial infarction in younger adults in the United States. *J Am Coll Cardiol* 2015;66:1961-72.

30. Dharma S, Andriantoro H, Dakota I, et al. Organisation of reperfusion therapy for STEMI in a developing country. *Open Heart* 2015;2:e000240.

31. Schiele F, Hochadel M, Tubaro M, et al. Reperfusion strategy in Europe: temporal trends in performance measures for reperfusion therapy in ST-segment elevation myocardial infarction. *Eur Heart J* 2010;31:2614-24.

32. Myocardial Ischaemia National Audit Project. Annual Public Report April 2014 - March 2015. Available at: [http://www.ucl.ac.uk/nicor/audits/minap/documents/annual\\_reports/O8818-minap-2014-15-1.1](http://www.ucl.ac.uk/nicor/audits/minap/documents/annual_reports/O8818-minap-2014-15-1.1). Accessed June 22, 2017.

33. Mamas MA, Anderson SG, Carr M, et al. Baseline bleeding risk and arterial access site practice in relation to procedural outcomes after percutaneous coronary intervention. *J Am Coll Cardiol* 2014;64:1554-64.

34. Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *Lancet* 2011;377:1409-20.

35. Bradley SM, Rao SV, Curtis JP, et al. Change in hospital-level use of transradial percutaneous coronary intervention and periprocedural outcomes: insights from the national cardiovascular data registry. *Circ Cardiovasc Qual Outcomes* 2014;7:550-9.

---

**KEY WORDS** PCI, percutaneous coronary intervention, rescue PCI, TFA, thrombolysis, TRA, transfemoral access, transradial access

---

**APPENDIX** For supplemental tables and figures, please see the online version of this paper.