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Access Site Practice and Procedural Outcomes in Relation to Clinical Presentation in 439,947 Patients Undergoing Percutaneous Coronary Intervention in the United Kingdom

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ABSTRACT

OBJECTIVES This study sought to determine the relationships among access site practice, clinical presentation, and procedural outcomes in a large patient population.

BACKGROUND Transradial access (TRA) has been associated with improved patient outcomes in selected populations in randomized trials. It is unclear whether these outcomes are achievable in clinical practice.

METHODS Using the BCIS (British Cardiovascular Intervention Society) database, we investigated outcomes for percutaneous coronary intervention procedures undertaken between 2007 and 2012 according to access site practice. Patients were categorized as stable, non-ST-segment elevation acute coronary syndrome (NSTEACS) and ST-elevation acute coronary syndrome (STEACS). The impact of access site on 30-day mortality, major adverse cardiac events, bleeding, and arterial access site complications was studied.

RESULTS Data from 210,260 TRA and 229,687 transfemoral access procedures were analyzed. Following multivariate analysis, TRA was independently associated with a reduction in bleeding in all presenting syndromes (stable odds ratio [OR]: 0.24, $p < 0.001$; NSTEACS OR: 0.35, $p < 0.001$; STEACS OR: 0.47, $p < 0.001$) as well as access site complications (stable OR: 0.21, $p < 0.001$; NSTEACS OR: 0.19; STEACS OR: 0.16, $p < 0.001$). TRA was associated with reduced major adverse cardiac events only in patients with unstable syndromes (stable OR: 1.08, $p = 0.25$; NSTEACS OR: 0.72, $p < 0.001$; STEACS OR: 0.70, $p < 0.001$). TRA was associated with improved outcomes compared with a transfemoral access (TFA) with a vascular closure device in a propensity matched cohort.

CONCLUSIONS In this large study, TRA is associated with reduced percutaneous coronary intervention–related complications in all patient groups and may reduce major adverse cardiac events and mortality in ACS patients. TRA is superior to transfemoral access with closure devices. Use of TRA may lead to important patient benefits in routine practice. TRA should be considered the preferred access site for percutaneous coronary intervention. (J Am Coll Cardiol Intv 2015;8:20–9)
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Over the past decade, transradial access (TRA) has become the preferred access route for percutaneous coronary intervention (PCI) in the United Kingdom (1). This has been driven by the advantages that TRA offers over other access sites with reduced vascular access complications, earlier ambulation, improved patient comfort, and reduced procedural cost (2–4). Additionally, development of dedicated TRA equipment has shortened the learning curve (5), facilitated treatment of complex coronary lesions (6–8), and, in experienced hands, reduced the rate of cross over to transfemoral access (TFA) in all patient subgroups (9–12). Importantly, TRA is associated with a reduction in the need for blood transfusion (13) and a reduction in major bleeding (14). TRA has also been associated with reduced mortality following PCI for ST-segment elevation acute coronary syndrome (STEACS) in both observational (15) and randomized studies (12,16,17). Prevention of access site bleeding has been postulated to be an important mechanism through which use of TRA reduces mortality. This hypothesis is supported by randomized trials in which pharmacological measures that reduced bleeding also reduced mortality (18–20).

The risk of post-PCI bleeding is variable and dependent on the syndrome with which patients present. In PCI for STEACS and non-ST-segment elevation acute coronary syndromes (NSTEACS), the presence of thrombus and plaque instability means that more potent antithrombotic regimes are often required. Additionally, patients with STEACS have higher inherent risks of bleeding by virtue of their presentation (21), as well as the time-sensitive nature of primary PCI allowing for less patient pre-selection. Conversely, patients with stable syndromes can frequently be treated using less potent antithrombotics and more time is available to stratify and select patients before electing to undertake PCI. These factors may act to enhance the beneficial effects of TRA in unstable patients.

To date, TRA has largely been studied in selected populations enrolled in randomized controlled trials, small observational studies, or large registries in which transfemoral access (TFA) is the dominant access site. Although many of these studies have demonstrated favorable outcomes associated with TRA, this may have been driven by PCI procedures undertaken at a few early adopting specialist centers and may not translate to a national setting in which TRA is more widely adopted. The purpose of this study is to document patient outcomes in relation to access site practice and clinical presentation in a large population of patients undergoing PCI in an environment where TRA is frequently employed.

METHODS

THE BCIS PCI DATABASE. This study is based on analysis of data collected by British Cardiovascular Intervention Society (BCIS) under the auspices of the National Institute for Cardiovascular Outcomes Research. BCIS was formed in 1988, and since its inception, has collected data to monitor the practice of coronary intervention in the United Kingdom. The BCIS PCI database aims to record all PCI procedures performed in every hospital in the United Kingdom (22). Annual reports on PCI activity from 1992 onward are publicly available for download from the society's website. As of 2011, 97.3% of all procedures in the United Kingdom were recorded in the database. The database records patient demographic details, comorbid conditions, indication for PCI, procedural details, and outcome data. In total, 113 variables are recorded for every procedure. The full list is available to download from the BCIS website. To the end of the year 2012, over 500,000 procedures were recorded on the database with over 90,000 procedures being added each year. In England, data on mortality is linked to each procedure via the National Health Service central register using a patient's individual National Health Service number. It is a legal requirement that all deaths in the United Kingdom are registered with this body.

STUDY POPULATION AND DEFINITIONS. For the purpose of this study, we performed a retrospective analysis of all PCI procedures recorded in the BCIS database over a 6-year period from January 1, 2007, to December 31, 2012, where access site was limited to either TRA or TFA (use of either or both radial arteries was classed as TRA and use of either or both femoral arteries was classed as TFA). Patients recorded as undergoing PCI using mixed access sites (e.g., TRA and TFA) and other access sites (such as brachial artery access) were excluded. The patients were divided into 3 cohorts based on indication for PCI; stable (elective PCI in cardiac biomarker-negative patients), NSTEACS (biomarker-positive or -negative patients admitted to hospital with an unstable pattern of cardiac ischemia), and STEACS (primary, rescue, and facilitated PCI).

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

BCIS = British Cardiovascular Intervention Society

CABG = coronary artery bypass graft(s)

CI = confidence interval

MACE = major adverse cardiac event(s)

NSTEACS = non-ST-segment elevation acute coronary syndrome(s)

OR = odds ratio

PCI = percutaneous coronary intervention(s)

STEACS = ST-segment elevation acute coronary syndrome(s)

TFA = transfemoral access

TIMI = Thrombolysis In Myocardial Infarction

TRA = transradial access

VCD = vascular closure device(s)

Cardiogenic shock was defined as blood pressure <100 mm Hg, pulse >100 beats/min, with cool peripheries, or requiring inotropes or mechanical circulatory support. Peripheral vascular disease was defined as history or evidence of any of occlusive peripheral vascular or carotid disease, aortic aneurysm, previous vascular surgery, and carotid or femoral bruit. Hypercholesterolemia was defined as a total cholesterol >5.2 mmol/l or the prescription of lipid-lowering drug therapy. Circulatory support was defined as use of inotropes, intra-aortic balloon pump, or other mechanical support. A major adverse cardiac event (MACE) was defined as a composite of in-hospital mortality, myocardial infarction, or repeat intervention. Arterial access site complication was defined as any pseudoaneurysm or any access site hemorrhage requiring intervention or delaying discharge. Bleeding was defined as any gastrointestinal bleed, intracerebral bleed, retroperitoneal bleed, or transfusion of a blood product.

STATISTICAL ANALYSIS. The relationship of baseline variables with 30-day mortality, MACE, access site complications, and bleeding was assessed with binary logistic regression using univariate and multivariate analysis. Factors including terms for interaction between access site and indication for PCI were entered for the analysis and this model included the following: access site; age; sex; diabetes; hypertension; hypercholesterolemia; peripheral vascular disease; previous myocardial infarction; previous stroke; previous PCI; previous coronary artery bypass graft (CABG); smoking status; pre-procedural cardiogenic shock; use of circulatory support; the need for pre-procedural ventilation; and year of procedure. The discriminative performance of the models was assessed using the C-statistic using bootstrapping methods in Stata/MP statistical software (version 13.1, Stata Corp., College Station, Texas). We also adjusted our estimate of the C-statistic for optimism using 10-fold cross validation (23).

Propensity-matched populations based on access site were derived for each cohort of presentation (Stable, NSTEACS and STEACS), matching for the following: age; sex; diabetes; smoking status; history of hypertension; hyperlipidemia; peripheral vascular disease; previous myocardial infarction; previous PCI; previous CABG; previous stroke or transient ischemic attack; use of invasive ventilation prior to PCI; pre-procedural cardiogenic shock; and year of procedure. To obtain the propensity-matched cohorts, only procedures with complete data on access site and the matched variables, as detailed, were included. A second propensity-matched population of TFA with a vascular closure device (VCD) matched to a TRA cohort was derived from the whole cohort in order to assess the impact of VCD. Propensity matching was performed using SPSS (version 19, SPSS, IBM Corporation, Armonk, New York) and the R for SPSS plug-in MatchIt. Logistic regression was used to estimate the propensity score and matching was performed using a nearest neighbor algorithm with a caliper of 0.002 matching in a 1:1 ratio. Categorical variables are presented as frequency values and proportions. Continuous variables with a normal distribution are presented as mean ± SD. Chi-square tests were used for analysis of categorical variables, and the Student *t*-tests were used to compare continuous variables that were normally distributed, and the Mann-Whitney *U* test was used for those that were not. All statistical tests were 2-tailed. $P < 0.05$ was used to indicate statistical significance.

RESULTS

PATIENT CHARACTERISTICS AND OUTCOMES IN THE TOTAL POPULATION. In the study period, a total of 495,913 procedures were performed and recorded in the database. Access site was recorded as TRA in 222,954 cases (45%) and TFA in 246,105 (49.6%). Procedures using multiple access sites and those in which the access site used was unclear or missing were recorded in 26,854 procedures (5.4%). TRA was mainly via the right radial route at 213,323 of 222,954 (95.7%) with 8,968 of 222,954 (4%) left radial and 663 of 222,954 (0.3%) both radials. Over the period studied, there has been a year-on-year increase in TRA from 17,005 of 70,066 (24.3%) in 2007 to 58,189 of 94,486 (61.6%) in 2012. Use of TFA peaked in 2007 with a reduction in use of TFA in subsequent years (**Figure 1**). Over the study period, procedures for NSTEACS and STEACS increased from 35,311 of 70,066 (50.4%) in 2007 to 59,459 of 94,486 (62.7%) in 2012 (**Figure 2**). A total of 55,966 patients (11.3%) with missing data on indication, adverse events, or access site, as well as procedures with mixed or other access sites were excluded from the analysis leaving a study population of 439,947 procedures.

There were significant differences in the baseline characteristics of patients undergoing TRA and TFA (**Table 1**). In the TRA cohort, patients were more frequently male and had a lower mean age. They were less likely to have had previous myocardial infarction or CABG. TRA was used more frequently for acute syndromes (NSTEACS and STEACS) but less frequently with pre-procedural shock or

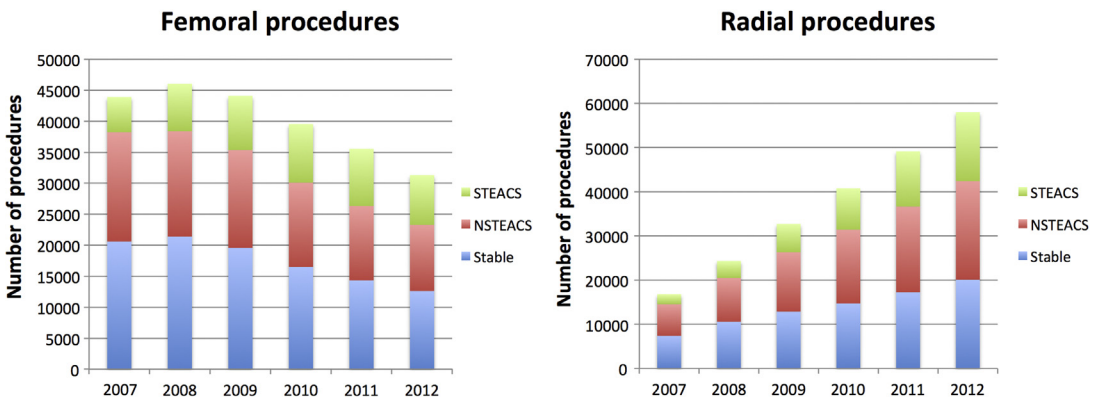

FIGURE 1 Use of Access Site for PCI Between 2007 and 2012

Numbers of procedures using femoral or radial access and indication for percutaneous coronary intervention (PCI) in the United Kingdom between 2007 and 2012. NSTEACS = non-ST-segment elevation acute coronary syndrome; STEACS = ST-segment elevation acute coronary syndrome.

pre-procedural ventilation. In the TRA group, use of glycoprotein inhibitors, bivalirudin, and thrombus aspiration devices were recorded more frequently, whereas use of circulatory support was less frequent.

MACE was recorded in 9,166 of 439,947 procedures (2.1%) across the entire cohort: 6,079 of 229,687 (2.6%) for TFA and 3,087 of 210,260 (1.5%) for TRA (TRA vs. TFA unadjusted odds ratio [OR]: 0.55, 95% confidence interval [CI]: 0.53 to 0.57, $p < 0.001$). Additionally, TRA compared with TFA was associated with reduced bleeding, access site complications, but equivalent rates of neurological complications (Table 2). Data on 30-day mortality was available for 391,159 procedures (89%) and occurred in 7,766 of 391,159 (2%) across the entire cohort. Unadjusted 30-day mortality was 5,428 of 216,804 (2.5%) for TFA and 2,338 of 174,355 (1.3%) for TRA (TRA vs. TFA unadjusted OR: 0.53, 95% CI: 0.50 to 0.56, $p < 0.001$).

STABLE COHORT. The stable cohort consisted of 178,662 procedures with MACE recorded in 1,530 (0.9%) and a 30-day mortality of 0.3% (517 of 159,410). The incidence of MACE, 30-day mortality, bleeding, and arterial access site complications were lower with TRA than with TFA (Table 3). Following multivariate analysis, TRA was not independently associated with a reduction in MACE but maintained a significant association with a reduction in bleeding and arterial access complications as well as a reduction in 30-day mortality (Figure 3). The propensity matched cohort of 85,034 procedures showed less bleeding and access site complications with TRA but no difference in 30-day mortality or MACE (Table 4).

NSTEACS COHORT. The NSTEACS cohort consisted of 167,161 procedures with MACE recorded in 2,509 of procedures (1.5%) and a 30-day mortality of 1.6% (2,368 of 147,862). Bleeding, arterial access complications, 30-day mortality, and MACE were significantly lower in the TRA group (Table 3). Following multivariate analysis, the same associations remained (Figure 3). The propensity-matched cohort of 80,386 procedures showed the same associations with significantly less bleeding, access site

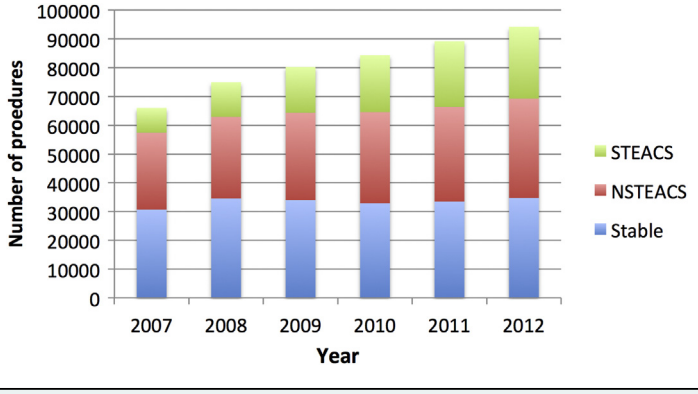

FIGURE 2 Indication for PCI Between 2007 and 2012

Annual number of procedures and indication for PCI in the United Kingdom between 2007 and 2012. Abbreviations as in Figure 1.

TABLE 1 Baseline Patient Procedural Characteristics for TFA and TRA Procedures

	TRA (n = 210,260)	TFA (n = 229,687)	p Value
Age, yrs	64.1 ± 14	65.2 ± 13.7	<0.001
Female	50,583 (24.1)	63,354 (27.6)	<0.001
Diabetes	36,761 (17.5)	42,749 (18.6)	<0.001
Hypertension	107,891 (51.3)	119,017 (51.8)	0.02
Hypercholesterolemia	114,708 (54.6)	126,291 (55)	0.65
Peripheral vascular disease	10,116 (4.8)	10,574 (4.6)	0.001
Previous stroke or TIA	8,504 (4)	8,600 (3.7)	<0.001
Smoking, ex-smoker or current	125,344 (59.6)	127,437 (55.5)	<0.001
Previous myocardial infarction	50,855 (24.2)	61,411 (26.7)	<0.001
Previous CABG	9,777 (4.6)	25,807 (11.2)	<0.001
Previous PCI	40,856 (19.4)	53,176 (23.2)	<0.001
Indication for PCI			
Stable	78,356 (37.3)	100,306 (43.7)	<0.001
NSTEACS	84,490 (40.2)	82,671 (36)	<0.001
STEACS	47,414 (22.6)	46,710 (20.3)	<0.001
Pre-procedural shock	2,049 (1)	5,710 (2.5)	<0.001
Pre-procedural ventilation	1,364 (0.6)	3,471 (1.5)	<0.001
Circulatory support	1,946 (0.9)	6,118 (2.7)	<0.001
Glycoprotein inhibitor use	44,339 (21.1)	44,559 (19.4)	<0.001
Bivalirudin use	6,985 (3.3)	4,520 (2)	<0.001
Thrombus aspiration	25,983 (12.4)	20,155 (8.8)	<0.001
Number of stents	1.47 ± 1.2	1.49 ± 1.07	0.01
Vascular closure device	-	137,895 (60)	

Values are mean ± SD or n (%).

CABG = coronary artery bypass graft; NSTEACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEACS = ST-segment elevation acute coronary syndrome; TFA = transfemoral access; TIA = transient ischemic attack; TRA = transradial access.

complications, 30-day mortality, and MACE in the TRA group (Table 4).

STEACS COHORT. The STEACS cohort consisted of 94,124 procedures with MACE occurring in 5,127 (5.4%) and a 30-day mortality of 5.8% (4,881 of 83,887). Bleeding, arterial access complications, 30-day mortality and MACE were significantly lower in the TRA group (Table 3). Following multivariate analysis, the same associations remained (Figure 3). The propensity matched cohort of 45,382 procedures also showed the same associations with significantly less bleeding, access site complications, 30-day mortality, and MACE in the TRA group (Table 4).

TABLE 2 Unadjusted Outcomes Following TFA and TFA PCI Across the Whole Study Population

	TRA (n = 210,260)	TFA (n = 229,687)	OR (95% CI)	p Value
MACE	3,087 (1.5)	6,079 (2.6)	0.55 (0.53–0.57)	<0.001
In-hospital death	1,744 (0.8)	4,275 (1.9)	0.44 (0.42–0.47)	<0.001
Reinfarction	870 (0.4)	1,150 (0.5)	0.83 (0.76–0.90)	<0.001
Reintervention	656 (0.3)	932 (0.4)	0.77 (0.70–0.85)	<0.001
Bleed	360 (0.2)	1,113 (0.5)	0.35 (0.31–0.40)	<0.001
Access site complication	209 (0.1)	1,159 (0.6)	0.19 (0.17–0.22)	<0.001
Neurological complication	250 (0.1)	298 (0.1)	0.92 (0.77–1.08)	0.33

Values are n (%).

CI = confidence interval; MACE = major adverse cardiac events; OR = odds ratio; other abbreviations as in Table 1.

INFLUENCE OF VASCULAR CLOSURE DEVICES. VCD were used in 137,895 of 229,687 TFA procedures (60%). TRA compared with TFA with a VCD was associated with a reduction in mortality, MACE, bleeding, and access site complications (Figure 4). Outcomes were further investigated in a propensity-matched cohort with 76,469 patients in each group. In this analysis, the favorable associations with TRA remained. For TRA compared with TFA with a VCD, 30-day mortality (OR: 0.78, 95% CI: 0.71 to 0.85, $p < 0.001$), MACE (OR: 0.88, 95% CI: 0.81 to 0.95, $p = 0.001$), bleeding (OR: 0.42, 95% CI: 0.35 to 0.51, $p < 0.001$), and access site complications (OR: 0.24, 95% CI: 0.19 to 0.30, $p < 0.001$) (Table 5) were all significantly lower in the TRA cohort.

DISCUSSION

In the United Kingdom, use of TRA has increased dramatically since 2007 and is currently the most commonly used access site for PCI. In this study with over 210,000 TRA procedures, 30-day mortality, MACE, bleeding, and access site complications were all less frequent than in the TFA group. After adjustment with multivariate and propensity-matched analyses, the association of TRA with reduced MACE remained significant in patients undergoing PCI for ACS. The reduction in bleeding and access site complications with TRA remained significant regardless of presenting syndrome. An association with reduced 30-day mortality was observed in all cohorts following multivariate analysis. However, after propensity matching, the association remained significant only in patients undergoing PCI for ACS. The association with reduced bleeding and TRA appears strongest in the stable cohort and less in the ACS cohorts. This is likely to be due to the low event rate of bleed in stable patients and the increasing effects of non-access site bleeding in the ACS cohorts.

The superficial nature of the radial artery and its easy compressibility allows for safe and simple hemostasis with minimal risk of access site complications (24,25). Even complete occlusion of the radial artery does not usually result in important clinical sequelae (26) as the hand receives blood via the ulnar and interosseous arteries. This is in contrast to the femoral and brachial arteries, which are end

arteries, and any interruption to blood supply is likely to result in ischemia. Since Campeau (27), first described the use of TRA for angiography and Kiemeneij et al. (28) reported on TRA for PCI, numerically small studies have suggested that TRA reduces access site complications and major bleeding (4,12,29,30), and our results are entirely compatible with this body of data. However, the RIVAL (Radial Versus Femoral Access for Coronary Intervention) study, the largest contemporaneous randomized trial of TRA versus TFA, was equivalent for its primary composite endpoint (a composite of death, myocardial infarction, stroke, or non-CABG bleeding at 30 days) and did not show any difference in major bleeding between access sites for the non-CABG-related major bleeding definition used in this study, although an exploratory analysis using the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy Trial) definition of major bleeding revealed a 57% significant reduction in major bleeding associated in the TRA arm (12). Furthermore, there was a significant reduction in major access site complications with TRA in the RIVAL study and for bleeding and access complications in the whole cohort of the SAFE PCI (Study of Access Site for Enhancement of Percutaneous Coronary Intervention) study (31). These 2 studies also highlighted a potential drawback of TRA with a higher rate of cross over from TRA to TFA, mainly due to radial artery spasm.

Mortality benefits for TRA have been demonstrated in randomized trials only in STEACS PCI populations. The 29% relative reduction for 30-day mortality in this study is comparable to that observed in a meta-analysis of randomized studies (17), as well as the RIVAL STEACS cohort and the RIFLE-STEACS (Radial Versus Femoral Randomized Investigation in ST Elevation Acute Coronary Syndrome), randomized trial (12,16). For NSTEACS, we observed a 25% relative risk reduction in 30-day mortality and in MACE for TRA procedures in a propensity-matched cohort. This contrasts the findings of previous studies of patients undergoing urgent PCI without ST-segment elevation, including subgroups of the RIVAL and EARLY-ACS trials (32,33). The reduction in bleeding and access site complications is consistent with the findings of a recent observational study of over 2.5 million patients from the NCDR (National Cardiovascular Data Registry) that showed a reduction with TRA across all groups (34). However, in that study, the use of TRA was low at 6.3% and mortality was not reported.

Attenuating access site bleeding is likely to be an important mechanism by which TRA improves outcomes. Bleeding following PCI is a strong predictor of in-hospital and long-term mortality (35–38). Additionally, large access site hematomas and the use of blood transfusions (13,39) are associated with worse outcomes. In our study, the association with TRA and reduced mortality was strongest and highly significant in the NSTEACS and STEACS cohorts. In these groups, bleeding in the context of an ACS is more likely to be associated with MACE and death (40). This was well demonstrated in the post-hoc analysis of the ACUITY trial where bleeding or blood transfusion had a similar impact on 1-year mortality as reinfarction (41). Importantly, the syndrome at presentation appears to be related to bleeding, with patients presenting with STEACS having the highest risk. In a patient-level pooled analysis of the REPLACE-2 (Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events), ACUITY, and HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) studies, 30-day TIMI (Thrombolysis In Myocardial Infarction) major bleeding was assessed (42). There was an increase in major bleeding from 0.7% in patients with stable angina to 1.6% for NSTEACS and 2.6% for STEACS. Despite the different definition of bleeding used in our study, a similar trend remains with 0.14%, 0.29%, and 0.78% for stable, NSTEACS, and STEACS, respectively. The reason for this increase risk may be due to the more frequent use of potent anticoagulants and antiplatelets in acute presentations to combat thrombus. Additionally, in acute presentations such as STEACS, oral antiplatelet agents may not be fully effective by the time PCI is carried out and parenteral

TABLE 3 Unadjusted Outcomes Following PCI for Stable, NSTEACS, and STEACS

	TRA	TFA	OR (95% CI)	p Value
Stable				
30-day mortality	175/65,011 (0.3)	342/94,399 (0.4)	0.74 (0.62–0.89)	0.001
MACE	621/78,356 (0.8)	909/100,306 (0.9)	0.87 (0.79–0.97)	0.01
Bleed	41/78,356 (0.1)	211/100,306 (0.2)	0.25 (0.18–0.35)	<0.001
Access site complication	80/72,486 (0.1)	450/92,074 (0.5)	0.23 (0.18–0.29)	<0.001
NSTEACS				
30-day mortality	786/69,780 (1.1)	1,582/78,082 (1.8)	0.55 (0.51–0.60)	<0.001
MACE	910/84,490 (1.1)	1,599/82,671 (1.9)	0.55 (0.51–0.60)	<0.001
Bleed	118/84,490 (0.1)	373/82,671 (0.5)	0.31 (0.25–0.38)	<0.001
Access site complication	94/78,098 (0.1)	466/74,844 (0.6)	0.19 (0.15–0.24)	<0.001
STEACS				
30-day mortality	1,377/39,564 (3.5)	3,504/44,323 (7.9)	0.57 (0.54–0.61)	<0.001
MACE	1,556/47,414 (3.3)	3,571/46,710 (7.6)	0.41 (0.39–0.44)	<0.001
Bleed	201/47,414 (0.4)	529/46,710 (1.1)	0.37 (0.32–0.44)	<0.001
Access site complication	35/44,013 (0.1)	243/42.358 (0.6)	0.14 (0.10–0.20)	<0.001

Values are n/n (%).
Abbreviations as in Tables 1 and 2.

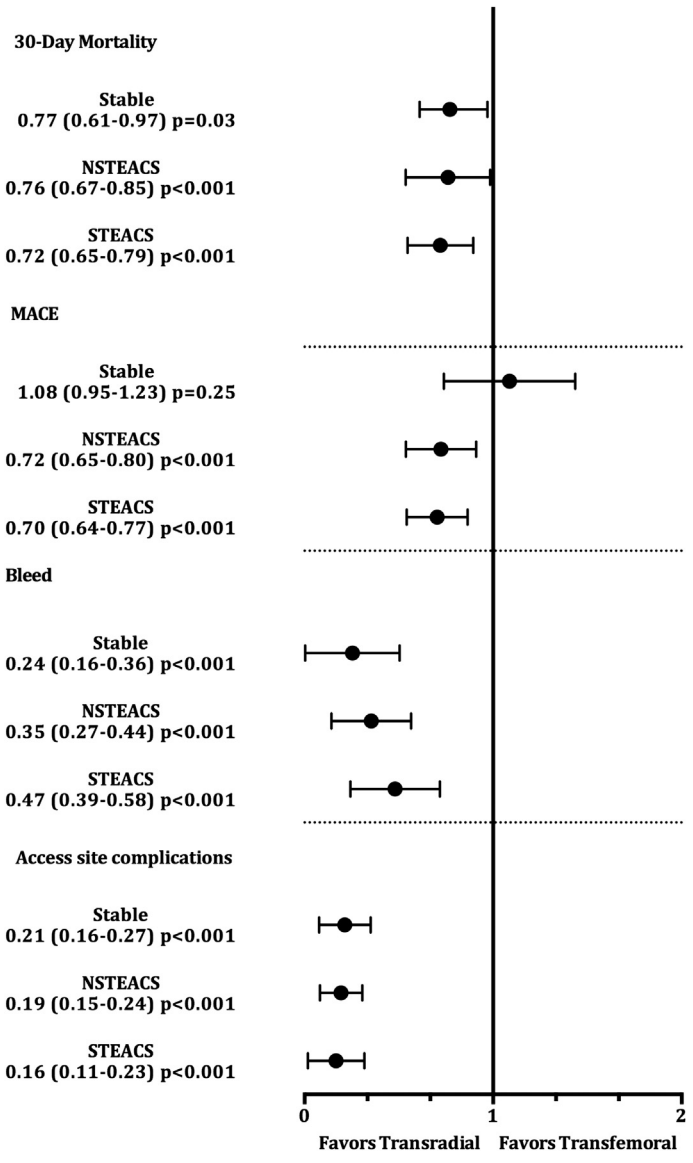

FIGURE 3 Forest Plot of OR for Outcomes Following Multivariate Logistic Regression

Outcomes following multivariate logistic regression. Interaction terms for indication for PCI and access site were included in the multivariate models and these were significant for major adverse cardiac events (MACE) ($p < 0.001$) and major bleeding ($p < 0.005$). OR = odds ratio; other abbreviations as in Figure 1.

antithrombotics may be required. Pre-screening and identification of patients with STEACS at high risk of bleeding may not be possible partly due to time pressures involved in effectively treating STEACS. Simple blood tests such as renal function, hemoglobin, and white cell count, and all predict the risk of bleeding (43). With stable and NSTEACS patients, PCI may be deferred if these adverse prognostic markers are encountered. Alternatively, when armed with this knowledge, additional measures may be taken to reduce the risk of bleeding such as using less potent antithrombotic regimes.

Over time, outcomes following TFA PCI have improved with optimization of antithrombotic regimens and the use of smaller sheath sizes resulting in a reduction of femoral access site bleeding as observed in the NCDR CathPCI registry (44). The use of VCD has had varied benefits in reducing access site complications and may introduce complications of their own (45-47). The largest meta-analysis to date of VCD did not show a significant reduction in surgery for vascular complications (47). In our study, VCD were used in 60% of TFA cases. TRA was associated with reduction in mortality, MACE, bleeding, and vascular access complications compared with TFA with a VCD, despite the more frequent use of glycoprotein inhibitors in the TRA group. This mirrors the findings of a previous study in which TRA was associated with fewer vascular complications and less patient discomfort than TFA with a VCD (48). Use of bivalirudin with TFA procedures has been shown to be associated with reduced bleeding complications in higher risk patients (18,49). Use of bivalirudin was infrequent in our study, which may have led to exaggerated rates of bleeding complications, particularly in the TFA cohort. Additionally expert TFA operators have demonstrated low risks of bleeding and vascular access site complications in contemporaneous trials with bivalirudin and VCD (50,51). Nevertheless, when optimal antithrombotic regimes are employed, further improvement may be gained by use of TRA (52,53). The RIVAL study highlighted the fact that a significant proportion of post-PCI bleeds may be non-access site-related, and minimizing any bleed remains important given its influence on morbidity and mortality. This may be increasingly important given the aging population and the increasing numbers of unstable patients being treated with PCI with their higher attendant risks of bleeding. A recent registry study of PCI in the United States, showed that 12.1% of deaths following PCI were related to bleeding (38) and therefore may be modifiable, in part, by using TRA. Despite the growing body of evidence supporting TRA, its use in some parts of the world and particularly in the United States, has remained low (44,54).This may reflect misconceptions about procedural limitations and learning curve requirements based on historical rather than contemporary data. The changes in access site practice observed in our study have shown that nationwide conversion is possible and brings with it the potential for significant patient benefits.

TABLE 4 Outcomes Following Propensity Matching in the Stable, NSTEACS, and STEACS Cohorts

	TRA	TFA	OR (95% CI)	p Value	C-Statistic
Stable					
30-day mortality	109/36,611 (0.3)	140/40,302 (0.3)	0.86 (0.67-1.1)	0.23	0.75
MACE	407/42,517 (1)	369/42,517 (0.9)	1.10 (0.96-1.27)	0.17	0.61
Bleed	24/42,517 (0.1)	92/42,517 (0.2)	0.26 (0.17-0.41)	<0.001	0.76
Access site complication	54/42,002 (0.1)	232/41,913 (0.6)	0.23 (0.17-0.31)	<0.001	0.72
NSTEACS					
30-day mortality	419/35,264 (1.2)	607/38,443 (1.6)	0.75 (0.66-0.85)	<0.001	0.80
MACE	493/40,193 (1.2)	651/40,193 (1.6)	0.75 (0.67-0.85)	<0.001	0.73
Bleed	64/40,187 (0.2)	190/40,190 (0.5)	0.34 (0.25-0.45)	<0.001	0.74
Access site complication	58/39,736 (0.1)	278/39,743 (0.7)	0.21 (0.16-0.28)	<0.001	0.75
STEACS					
30-day mortality	703/19,711 (3.6)	1,069/21,709 (4.9)	0.71 (0.65-0.79)	<0.001	0.86
MACE	811/22,691 (3.6)	1,130/22,691 (5)	0.71 (0.65-0.78)	<0.001	0.83
Bleed	116/22,673 (0.5)	232/22,677 (1)	0.50 (0.40-0.62)	<0.001	0.74
Access site complication	24/22,292 (0.1)	146/22,278 (0.7)	0.16 (0.11-0.25)	<0.001	0.77

Values are n/n (%).
Abbreviations as in Tables 1 and 2.

STUDY LIMITATIONS. This is a retrospective analysis of observational data over several years and as such its findings are limited by information bias and systematic errors. Differences in the observed estimates of treatment between the 2 groups may be accounted for by unmeasured confounders. However, the large number of patients treated with TRA across all groups and the real-world nature of the study mean that the findings remain relevant to contemporary practice. Outcomes other than 30-day mortality may be under-reported as the completion of in-hospital complications in the database is operator-initiated. Nevertheless, the degree of under-reporting is likely to be the same in both TRA and TFA cohorts. A limitation of this study relates to the definitions of arterial access site complications and major bleeding events that we have used in the BCIS dataset. These definitions are not directly comparable to commonly used definitions of these endpoints in clinical trials because some of the events that make up these clinically used definitions are not recorded in the BCIS dataset. For example in several commonly used definitions of major bleeding such as TIMI major and minor bleeding, a quantifiable decrease in hemoglobin levels (TIMI minor: 3 to 5 g/dl, TIMI major: >5 g/dl) forms part of the definition of bleeding, but such information is not recorded in the BCIS dataset. Additionally, there may be significant overlap between our 2 outcomes (bleeding and access site complications) as patients with access site complications may require blood transfusions, and therefore it would not be clear in such patients whether they have sustained 2 separate events or a single access site complication necessitating a blood transfusion. However, these endpoints still provide useful information in relation to practical outcomes and remain the best indicators available from the BCIS dataset.

Another potential limitation is the absence of recorded access site cross over in the database. Assuming a higher rate of cross over from TRA to TFA, this selection bias may lead to the accumulation of more high-risk patients in the TFA group.

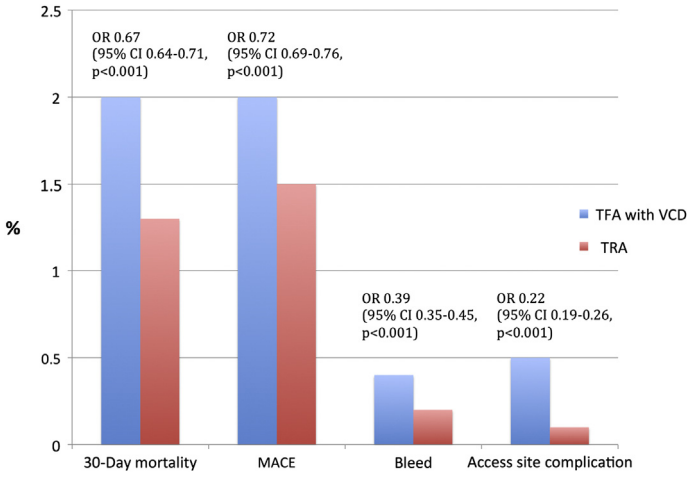

FIGURE 4 Outcomes Following TFA With VCD Compared With TRA

Unadjusted outcomes following PCI with transfemoral access (TFA) and a vascular closure device (VCD) compared with a transradial access (TRA). CI = confidence interval; other abbreviations as in Figure 3.

TABLE 5 Outcomes for the Propensity Matched Cohort, Comparing TRA to TFA With VCD

	TRA	TFA With VCD	OR (95% CI)	p Value	C-Statistic
30-day mortality	885/67,072 (1.3)	1225/72,304 (1.7)	0.78 (0.71–0.85)	<0.001	0.82
MACE	1,252/76,469 (1.6)	1,424/76,469 (1.9)	0.88 (0.81–0.95)	0.001	0.73
Bleed	165/76,469 (0.2)	389/76,469 (0.5)	0.42 (0.35–0.51)	<0.001	0.74
Access site complication	98/75,452 (0.1)	409/75,362 (0.5)	0.24 (0.19–0.30)	<0.001	0.67

Values are n/n (%).
VCD = vascular closure device; other abbreviations as in Tables 1 and 2.

Even though we have used a sophisticated statistical technique in propensity matching, it still cannot fully account for unmeasured confounders. In generating matched groups, a proportion of procedures will not be included in the analysis and this appears to affect higher risk procedures more given that the mortality is lower in the matched groups. However, as matching attempts to select similar risk patients, the results may infer that in a group that can been treated by either access, outcomes would be more favorable with TRA.

CONCLUSIONS

In this large study of national access site practice for PCI, there is a significant association with reduced 30-day mortality and MACE with TRA procedures for both NSTEACS and STEACS. TRA is associated with significant reductions in bleeding and access site complications in all cohorts. Our study indicates that the benefits of TRA seen in selected populations in randomized trials and other observational studies may translate into real patient benefits in day-to-day clinical practice. The use of VCD in conjunction with TFA is associated with less benefit than use of TRA is. Combining TRA with optimal antithrombotic therapy and other antibleeding strategies has the potential to deliver major patient benefit.

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