# Arterial access site utilization in cardiogenic shock in the United Kingdom: Is radial access feasible?

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**Background** Cardiogenic shock (CS) remains the leading cause of mortality in patients hospitalized with acute myocardial infarction (AMI). The transradial access site (TRA) has become increasingly adopted as a default access site for percutaneous coronary intervention (PCI); however, even in experienced centers that favor the radial artery as the primary access site during PCI, patients presenting in CS are often treated via the transfemoral access site (TFA); and commentators have suggested that CS remains the final frontier that has given even experienced radial operators pause. We studied the use of TRA in patients presenting in CS in a nonselected high-risk cohort from the British Cardiovascular Intervention database over a 7-year period (2006-2012).

**Methods** Mortality (30-day) and major adverse cardiac and cerebrovascular events (a composite of in-hospital mortality, in-hospital myocardial reinfarction, target vessel revascularization, and cerebrovascular events) were studied based on TFA and TRA utilization in CS patients. The influence of access site selection was studied in 7,231 CS patients; TFA was used in 5,354 and TRA in 1,877 patients.

**Results** Transradial access site was independently associated with a lower 30-day mortality (hazard ratio [HR] 0.56, 95% CI 0.46-0.69, $P = 0 < .001$), in-hospital major adverse cardiac and cerebrovascular events (HR 0.64, 95% CI 0.53-0.76, $P < .0001$) and major bleeding (HR 0.37, 95% CI 0.18-0.73, $P = .004$).

**Conclusions** Although the majority of PCI cases performed in patients with cardiogenic shock in the United Kingdom are performed through the TFA, the radial artery represents an alternative viable access site in this high-risk cohort of patients in experienced centers. (Am Heart J 2014;167:900-908.e1.)

Despite advances in medical therapy, percutaneous coronary intervention (PCI), and mechanical support during the past 2 decades, cardiogenic shock remains the leading cause of mortality in patients hospitalized with AMI.[1] Although the incidence of cardiogenic shock has decreased over the past 3 decades (from around 7% to 3%),[1,2] mortality rates remain significant, with in-hospital mortality rates of between 30% and 60% reported.[1-3] Major bleeding complications commonly occur in as many as 1 in 10 patients with cardiogenic shock.[4] These major bleeding complications accounted for 14% of 30-day "noncardiac" mortality in a secondary analysis of the SHOCK trial.[5]

The transradial access site (TRA) has become increasingly adopted as a default access site for PCI across many centers, having been shown to reduce major bleeding, access site–related complications, and mortality. However, even in experienced centers that favor the radial artery as the primary access site during PCI, patients presenting in cardiogenic shock are often treated via the transfemoral access site (TFA); and commentators have suggested that cardiogenic shock remains the final frontier that has given even experienced radial operators pause.[6]

Most studies that have compared access site–specific outcomes in patients undergoing PCI have excluded cardiogenic shock as an indication for the radial approach.[7] More recently, small retrospective case series of patients with cardiogenic shock undergoing PCI in experienced high-volume radial centers reported that TRA was associated with a independent reductions in mortality [8,9] in patients presenting with cardiogenic shock.

However, it remains unclear whether it is feasible to undertake PCI in patients with cardiogenic shock through

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the TRA outside of a few such specialist transradial centers and whether the observed outcomes associated with the TRA are reproducible nationally. We have studied access site utilization in patients presenting in cardiogenic shock undergoing PCI in a nonselected high-risk national cohort from the British Cardiovascular Intervention Society (BCIS) database to study changes in access site utilization over time, the feasibility of TRA access site utilization in this high-risk cohort of patients, and its associated outcomes.

## Methods

### The BCIS database

The BCIS was formed in 1988 to collect PCI data relating to the nationwide practice of PCI in the United Kingdom. Data are collected via an electronic database under the auspices of the National Institute of Cardiovascular Outcomes Research,[10] and annual reports are available for download from the society's Web site (http://www.bcis.org.uk) from 1992 onwards. As of December 2012, there are approximately 569,600 records in the BCIS database. Mortality tracking is undertaken by the National Health Service (NHS) Central Register using the patients' NHS number that provides a unique identifier for any person registered with the NHS in England and Wales.

### Study definitions

Percutaneous coronary intervention procedures performed in patients with cardiogenic shock in the United Kingdom between January 2006 and December 2012 were analyzed in this study. *Cardiogenic shock* is defined in the BCIS dataset as a blood pressure <100 mm Hg with pulse >100 beats/min combined with signs of peripheral hypoperfusion (cold, clammy, pallor, etc), or a requirement for inotropes or intraaortic balloon pump (IABP) to support the circulation and maintain a blood pressure. 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, whereas patients where the access site was unknown were excluded. The primary outcome examined was 30-day mortality. Major adverse cardiac and cerebrovascular events (MACCE) were a composite of in-hospital mortality and in-hospital myocardial reinfarction, target vessel revascularization, and cerebrovascular events. *Cerebrovascular events* were defined as a clinically detected ischemic stroke, hemorrhagic stroke, or transient ischemic attack that occurred during or after PCI and before hospital discharge. *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.

### Statistical analysis

All statistical analyses were performed with the statistical package Stata/MP version 13.1 (Stata Corp, College Station, TX).

Data are expressed as arithmetic mean ± SD (or 95% CIs) and number (percentage) for continuous and categorical variables, respectively. To compare proportions for nonparametric data, we used the $\chi^2$ test or analysis of variance. Tests for linear trend used $\chi^2$ models. A value of $P < .05$ was used to indicate statistical significance.

We used the Stata module *teffects ipw* to estimate treatment effects via inverse-probability weighting. Inverse-probability weighting uses the reciprocal of the probability of being in the observed treatment group from fitted models of treatment status. Treatment independent covariates such as patient demographic factors and procedural and interaction terms were included in all models. To ensure the validity of the standard errors, a bootstrap procedure was applied to the whole process.

To further account for confounding variables and bias, propensity score methods with nearest neighbor matching were performed on the naive study cohort. A propensity score was estimated for each episode of radial or femoral access using a logistic regression model to fit access site use to patient demographics. Variables included in the model were age, sex, diabetes, hypertension, hypercholesterolemia, peripheral vascular disease, previous stroke (cerebrovascular accident [CVA]), renal failure, previous AMI, previous PCI, previous coronary artery bypass graft (CABG), IABP, and ventilation. Interaction terms for demographic and procedural risk factors were also included in the model. Mahalanobis distance matching with the propensity score as the distance matrix was then undertaken. Standardized differences between groups were estimated to assess the balance achieved by matching. A baseline characteristic was considered to be well balanced if the standardized difference was <10%.

The relationship of baseline variables and 30-day mortality and MACCE was assessed by Cox proportional hazard models in the naive and propensity score methods cohorts. We constructed bootstrapped multivariate Cox regression models using factors thought to be important for the end points and included age, sex, diabetes, hypertension, hypercholesterolemia, smoking status, clinical syndrome, previous history of AMI, renal function, family history, left ventricular function, IABP use, ventilation status, access site, glycoprotein (Gp) IIb/IIIa inhibitor use, and center volume (quartile of radial access site use) as covariates. For all models, we tested for interaction by adding terms for access site and relevant demographic or periprocedural risk factors. Tests for statistical significance used the Wald test of the interaction terms. If the interaction terms were not significant, they were excluded from the final models. We evaluated the predictive power of the Cox regression models by

computing the Harrell C concordance and the Somers rank correlation. In general, a Harrell C value of 0.5 and a Somers D value of 0 indicate no predictive ability of the model.

Kaplan-Meier cumulative survival curves were constructed and compared by the log-rank test. Multivariate logistic regression models were constructed to estimate predictors for the utilization of the TFA vs TRA. The Hosmer and Lemeshow goodness-of-fit test for logistic regression models was used to assess the validity of the models. Model discrimination was quantified by the C statistic. We adjusted our estimate of the C statistic for optimism using 10-fold cross-validation with random resampling to generate average predicted probabilities. Bootstrapping techniques were used to validate the model, that is, to adjust the estimated model performance for overoptimism or overfitting.

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## Results

A total of 483,381 eligible PCI procedures were performed in patients in the United Kingdom between January 1, 2006, and December 31, 2012, of which 8,222 were performed in patients categorized as presenting with cardiogenic shock (1.7%). The access site or clinical indication was unknown or was unclear in 991 (12.0%) patients; and hence, these were excluded from further analysis, leaving 7,231 eligible procedures. The most common clinical syndrome in patients presenting with cardiogenic shock was primary PCI for ST-elevation myocardial infarction (4,898/7,231; 67.74%). The mean age of the patients was 67.2 (66.9-67.5) years (mean [95% CIs]), and 5,055 (70.1%) were male.

Transfemoral access site was used in 5,354 procedures (74.0%), whereas TRA was used in 1,877 procedures (26.0 %). Figure 1 illustrates the trends in access site use for cardiogenic shock between 2006 and 2012. Transradial access site utilization increased from 9.5% of all cardiogenic shock cases in 2006 to 34.2% of all cases in 2012 ($P$ value for trend <.0001). A relationship between utilization of the TRA approach in cases with cardiogenic shock and total TRA center experience based on percentage of cases undertaken through TRA approach was observed (Table I). Whereas only 2,937/7,923 (37.1%) of cases with cardiogenic shock were undertaken in centers with >50% TRA utilization, 1,172/1,877 (62.4%) of all cardiogenic shock cases treated through the TRA were performed in these centers.

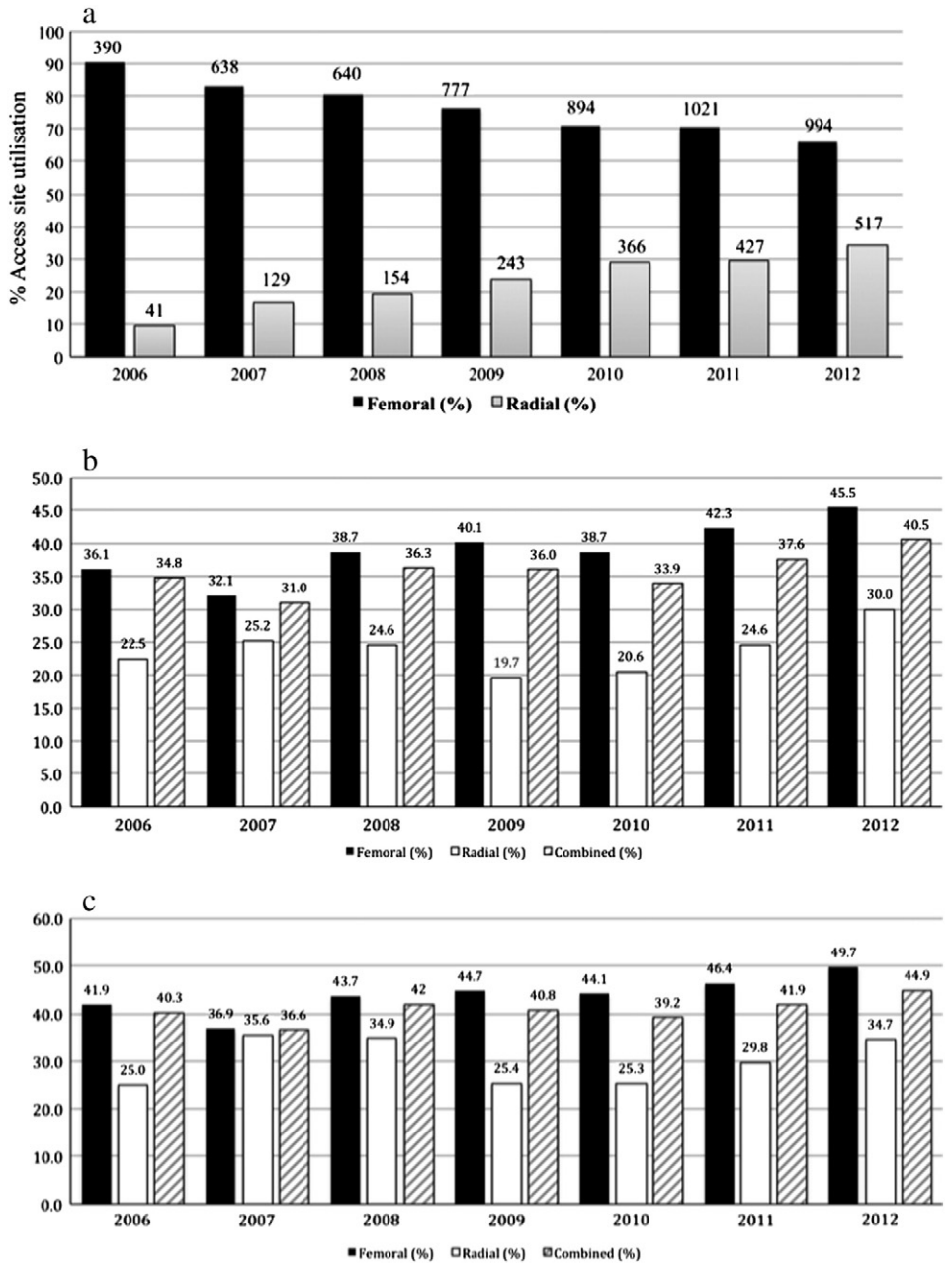
Table II details the clinical demographic features, and Table III details the procedural characteristics of patients with cardiogenic shock undergoing PCI via the TRA site or the TFA site. The clinical features were similar in both groups, although patients treated with the TFA were more likely to be diabetic, be female, receive an IABP and inotropic support, or be ventilated. In general, patients treated with a TFA approach were sicker. Multivariate predictors from logistic regression models for the utilization of the TFA site in patients presenting with cardiogenic shock are presented in Table IV.

Thirty-day mortality in the total cohort was 2,296/6,323 (36.3%), of which 1,934 (39.8%) occurred in those cases performed though the TFA site, whereas 362 (24.7%) occurred in those cases performed through the TRA site ($\chi^2$=110.2, $P$ < .001). There were no trends in 30-day mortality rates by year in the TRA group ($P$ for trend = .06) for patients with cardiogenic shock; however, rates have increased in TFA-treated group over time ($P$ for trend < .0001; Figure 1, *B*). Figure 2 illustrates unadjusted Kaplan-Meier survival curves for both the TFA and TRA site groups, with a statistically significant lower all-cause mortality associated with the use of TRA (hazard ratio [HR] 0.54, 95% CI 0.50-0.60, $P$ < .0001).

Bootstrapped multivariate Cox proportional hazard models adjusted for baseline procedural and demographic characteristics demonstrated that utilization of the TRA was independently associated with a lower 30-day mortality (HR 0.56, 95% CI 0.46-0.69, $P$ = 0 < .001). When the impact of access site on 30-day mortality was studied in relation to TRA center experience (based on percentage of cases undertaken through the TRA approach), there was no prognostic benefit associated with TRA if undertaken in a center with the lowest percentage of TRA cases (0%-25% TRA cases) (HR 0.68, 95% CI 0.45-1.03, $P$ = .06). In contrast, in centers where the proportion of radial cases was 26% to 50% (HR 0.64, 95% CI 0.48-0.87, $P$ = .004), 51% to 75% (HR 0.66, 95% CI 0.48-0.90, $P$ = .008), and >75% (HR 0.50, 95% CI 0.35-0.73, $P$ < .0001), utilization of the TRA was independently associated with a lower 30-day mortality. Other multivariate predictors of 30-day mortality outcomes are presented in Table V.

Bootstrapped inverse probability weights were used to estimate the causal effect of treatment (access site) on mortality (Table VI). There was an estimated 8% lower risk of 30-day mortality (odds ratio [OR] 0.92, 95% CI 0.88-0.97, $P$ = .001) for TRA vs TFA. To further reduce the potential for confounding variables and bias in our study cohort, propensity score matching was performed using nearest neighbor matching to create 2 propensity score–matched patient cohorts. A propensity score–matched cohort of 2,804 patients was created—1,402 in the TFA group and 1,402 in TRA group (online Appendix Supplementary Table)—with baseline demographics well balanced in the 2 propensity-matched cohorts. Thirty-day mortality was 267/1,173 (22.8%) in the TRA cohort and 306/1,296 (29.9%) in the TFA cohort ($P$ < .001). Multivariate Cox regression analysis adjusted for baseline procedural and demographic characteristics demonstrated that TRA was independently associated with a lower 30-day mortality

**Figure 1**




**A**, Utilization (number of cases) of the radial and femoral access site during PCI in patients presenting with cardiogenic shock (January 2006-December 2012). **B**, Thirty-day mortality (%) between 2006 and 2012 for radial, **femoral, and **combined cohort in patients with cardiogenic shock. Test for trend across ordered categorical groups: *$P < .05$, **$P < .0001$. **C**, In-hospital MACCE (%) outcomes between 2006 and 2012 for radial, **femoral, and **combined cohort in patients with cardiogenic shock. Test for trend across ordered categorical groups: *$P < .05$, **$P < .0001$.

(HR 0.64, 95% CI 0.54-0.74, $P < .001$) in the propensity score–matched cohort.

Major adverse cardiac and cerebrovascular events occurred in 2,180/4,889 (44.9%) in those cases performed through the TFA site and in 458/1,501 (30.5%) in cases performed through the TRA ($P < .001$). Changes in MACCE over time and according to access site are presented in Figure 1, *C*. Multivariate Cox proportional hazard models adjusted for baseline procedural and demographic characteristics demonstrated that TRA was independently

**Table I.** Relationship between access site utilization and TRA center experience based on percentage of cases undertaken through TRA approach

| | ≥75% | 51%-75% | 26%-50% | 0%-25% | Total |
|---|---|---|---|---|---|
| Femoral (n) | 629 | 1136 | 2139 | 1450 | 5354 |
| (%) | 52.7 | 65.2 | 78.9 | 91.7 | 74.0 |
| Radial (n) | 565 | 607 | 573 | 132 | 1877 |
| (%) | 47.3 | 34.8 | 21.1 | 8.3 | 26.0 |
| Total | 1194 | 1743 | 2712 | 1582 | 7231 |
| | 100 | 100 | 100 | 100 | 100 |

**Table II.** Baseline clinical demographics presented as mean ± SD or number (percentage) for radial and femoral access site

| Variable | Radial (n = 1877) | Femoral (n = 5354) | P |
|---|---|---|---|
| Clinical presentation | | | |
| Primary PCI | 1246 (66.4) | 3652 (68.2) | |
| Rescue PCI | 142 (7.6) | 453 (8.5) | 6.33, P = .042 |
| NSTEMI/UA | 489 (26.1) | 1249 (23.3) | |
| Age (y) | 67.3 (66.8-67.5) | 67.2 (66.7-67.8) | 0.74 |
| Gender (male) | 1389 (74.2) | 3666 (68.7) | 20.1, P < .0001 |
| Diabetes | 302 (17.1) | 1036 (21.3) | 14.15, P = .002 |
| Hypertension | 777 (43.6) | 2379 (46.6) | 4.72, P = .030 |
| Hypercholesterolemia | 744 (41.7) | 2316 (41.8) | P = .957 |
| Previous AMI | 365 (21.2) | 1141 (24.8) | 9.16, P = .001 |
| Previous PCI | 176 (9.69) | 689 (13.6) | 18.17, P < .0001 |
| Previous CABG | 36 (2.0) | 295 (5.8) | 42.19, P < .0001 |
| Renal failure | 94 (5.5) | 429 (9.2) | 22.6, P < .0001 |
| Smoking | | | |
| Current | 484 (30.3) | 1270(31.0) | |
| Ex-smoker | 577 (36.2) | 1381 (33.7) | P = .21 |
| Non-smokers | 535 (33.5) | 1444 (35.3) | |

*NSTEMI*, Non–ST-elevation myocardial infarction.

**Table III.** Procedural characteristics presented as mean ± SD or number (percentage) for radial and femoral access site

| Variable | Radial (n = 1877) | Femoral (n = 5354) | P |
|---|---|---|---|
| IABP | 523 (29.0) | 1923 (37.8) | 44.52, P < .001 |
| Inotrope use | 205 (10.9) | 948 (17.7) | 47.73, P < .001 |
| Ventilated | 315 (18.6) | 1639 (34.0) | 141.12, P < .001 |
| Gp IIb/IIIa | 1014 (55.6) | 2940 (57.7) | 2.46, P = .116 |
| Lysis | 206 (11.0) | 579 (10.8) | P = .85 |
| Target vessel | | | |
| LAD | 1012 (54.1) | 2744 (52.0) | P = .27 |
| LCx | 254 (13.6) | 756 (14.3) | P = .77 |
| RCA | 513 (27.4) | 1408 (26.7) | P = .76 |
| LMS | 74 (4.0) | 258 (4.9) | P = .74 |
| Grafts | 17 (0.9) | 108 (2.1) | P = .28 |
| DES use | 912 (48.6) | 2443 (45.6) | 4.89, P = .027 |
| Mean no. of stents used | 1.90 (1.84-1.96) | 1.83 (1.79-1.88) | P = .18 |

*LAD*, Left anterior descending; *LCx*, Left circumflex; *RCA*, right coronary artery; *LMS*, left main stem; *DES*, drug eluting stent; *IABP*, intra-aortic balloon pump.

**Table IV.** Predictors for utilization of the TFA from multivariate logistic regression

| | OR | 95% CI | | P>z |
|---|---|---|---|---|
| Clinical syndrome | | | | |
| NSTEMI/UA | 1.00 | | | |
| PPCI | 1.31 | 1.10 | 1.56 | .002 |
| Rescue PCI | 1.36 | 1.00 | 1.84 | .047 |
| Age (per year) | 1.00 | 0.99 | 1.00 | .571 |
| Gender (female) | 1.40 | 1.19 | 1.64 | <.0001 |
| Smoking | | | | |
| Never | | | | |
| Ex | 0.86 | 0.72 | 1.03 | .107 |
| Current | 0.86 | 0.71 | 1.03 | .1 |
| Ventilated (yes) | 2.51 | 2.08 | 3.04 | <.0001 |
| Inotrope use (yes) | 1.59 | 1.27 | 1.98 | <.0001 |
| IABP use (yes) | 1.88 | 1.60 | 2.22 | <.0001 |
| GPI (yes) | 1.10 | 0.95 | 1.27 | .19 |
| Renal disease (yes) | 1.49 | 1.09 | 2.04 | .013 |
| Previous PCI (yes) | 1.65 | 1.28 | 2.13 | <.0001 |
| Previous CABG (yes) | 3.39 | 1.93 | 5.93 | <.0001 |
| Previous MI (yes) | 0.99 | 0.81 | 1.21 | .934 |
| Diabetes (yes) | 1.09 | 0.90 | 1.32 | .369 |

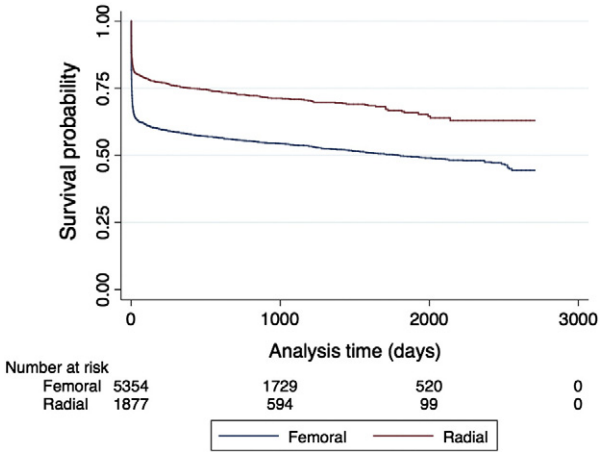
Bootstrapped logistic regression with Hosmer-Lemeshow: $\chi^2$ = 5.39, P = .7153, C statistic = 0.67.
*GPI*, Glycoprotein IIb/IIIa inhibitor; *PPCI*, primary *PCI; NSTEMI/UA*, non ST-elevation myocardial infarction/Unstable angina.

associated with a lower in-hospital MACCE (HR 0.64, 95% CI 0.53-0.76, P < .0001). Other multivariate predictors of in-hospital MACCE are presented in Table VII. When the impact of access site on in-hospital MACCE was studied in relation to TRA center experience (based on percentage of cases undertaken through TRA approach), there was no prognostic benefit associated with TRA if undertaken in a center with the lowest percentage of TRA cases (0%-25% TRA cases) (HR 0.68, 95% CI 0.44-1.11, P = .13). In contrast, in centers where the proportion of radial cases was 25% to 50% (HR 0.77, 95% CI 0.62-0.95, P = .02), 50% to 75% (HR 0.65, 95% CI 0.50-0.85, P < .0001), and >75% (HR 0.51, 95% CI 0.36-0.72, P < .0001), utilization of the TRA was independently associated with lower in-hospital MACCE.

In a model with similar characteristics, inverse probability weights were used to estimate the causal effect of treatment (access site) on MACCE. There was an estimated 6% lower risk of MACCE (OR 0.94, 95% CI 0.89-0.98, P = .002) for TRA vs TFA.

Major bleeding complications occurred in 192/6,494 (3.0%) cases, of which 167/4,798 (3.5%) occurred in those cases performed through TFA, whereas 25/1,696 (1.5%) occurred in those cases performed through TRA (P < .0001) (Table VIII). Multivariate Cox regression analyses adjusted

**Figure 2**




Kaplan-Meier survival curve comparing outcomes of PCI performed in patients with cardiogenic shock according to access site.

**Table V.** Multivariate predictors for 30-day mortality using Cox proportional hazard models

| | HR | 95% CI | | P |
|---|---|---|---|---|
| Access site (TRA vs TFA) | 0.56 | 0.46 | 0.69 | <.001 |
| Gender (female vs male) | 0.93 | 0.77 | 1.12 | .425 |
| Age (per year) | 1.03 | 1.02 | 1.04 | <.001 |
| Smoking | | | | |
| Never | 1.00 | | | |
| Ex | 1.16 | 0.95 | 1.41 | .148 |
| Current | 1.19 | 0.94 | 1.50 | .146 |
| Hypertension | 1.16 | 0.96 | 1.40 | .131 |
| Hypercholesterolemia | 1.09 | 0.90 | 1.31 | .395 |
| Peripheral vascular disease | 1.17 | 0.92 | 1.49 | .21 |
| Previous CVA | 1.19 | 0.91 | 1.56 | .193 |
| Family history | 1.20 | 1.00 | 1.43 | .046 |
| Previous MI | 0.85 | 0.69 | 1.05 | .123 |
| Previous CABG | 1.04 | 0.71 | 1.53 | .832 |
| Previous PCI | 0.99 | 0.76 | 1.30 | .95 |
| Renal disease | 1.39 | 1.09 | 1.77 | .008 |
| GPI use | 0.72 | 0.61 | 0.86 | <.001 |
| Clinical syndrome | | | | |
| NSTEMI/UA | 1.00 | | | |
| PPCI | 1.41 | 1.16 | 1.72 | .001 |
| Rescue PCI | 1.34 | 0.95 | 1.88 | .091 |
| Left ventricular function | | | | |
| Good | 1.00 | | | |
| Fair | 1.32 | 1.00 | 1.75 | .048 |
| Poor | 2.54 | 1.94 | 3.31 | <.001 |
| IABP use (yes) | 1.16 | 0.96 | 1.40 | .133 |
| Inotrope use (yes) | 1.69 | 1.35 | 2.12 | <.001 |
| No. of vessels (per unit) | 1.06 | 0.99 | 1.14 | .081 |

Harrell C concordance = 0.72 and Somers D = 0.44.

for baseline procedural and demographic characteristics demonstrated that TRA was independently associated with a lower rate of major bleeding complications (HR 0.37, 95% CI 0.18-0.73, $P = .004$).

**Table VI.** Inverse probability weighting–derived bootstrapped treatment effects estimates for 30-day mortality using by access site (TFA vs TRA)

| | Rate ratio | 95% CI | | P |
|---|---|---|---|---|
| ATE for radial vs femoral | 0.92 | 0.88 | 0.97 | .001 |
| Gender (female vs male) | 0.68 | 0.52 | 0.90 | .007 |
| Age (per year) | 1.01 | 1.00 | 1.02 | .01 |
| Smoking | | | | |
| Never | 1.00 | | | |
| Ex | 1.24 | 0.93 | 1.65 | .135 |
| Current | 1.22 | 0.90 | 1.65 | .204 |
| Hypertension | 0.77 | 0.60 | 0.99 | .039 |
| Hypercholesterolemia | 0.98 | 0.75 | 1.28 | .903 |
| Peripheral vascular disease | 0.70 | 0.45 | 1.09 | .114 |
| Previous CVA | 1.15 | 0.80 | 1.66 | .447 |
| Family history | 1.45 | 1.15 | 1.84 | .002 |
| Previous MI | 0.84 | 0.61 | 1.15 | .269 |
| Previous CABG | 0.29 | 0.12 | 0.69 | .005 |
| Previous PCI | 0.72 | 0.49 | 1.06 | .094 |
| Renal disease | 0.64 | 0.39 | 1.05 | .076 |
| GPI use | 0.77 | 0.63 | 0.96 | .018 |
| Clinical syndrome | | | | |
| NSTEMI/UA | 1.00 | | | |
| PPCI | 0.83 | 0.63 | 1.09 | .177 |
| Rescue PCI | 0.67 | 0.41 | 1.10 | .114 |
| Left ventricular function | | | | |
| Good | 1.00 | | | |
| Fair | 0.82 | 0.64 | 1.04 | .105 |
| Poor | 0.87 | 0.65 | 1.16 | .345 |
| IABP use (yes) | 0.65 | 0.51 | 0.83 | .001 |
| Ionotrope use (yes) | 0.67 | 0.50 | 0.91 | .01 |
| Number of vessels (per unit) | 1.02 | 0.92 | 1.13 | .697 |

*ATE,* Average treatment effect.

## Discussion

In the largest analyses of its kind investigating outcomes in a contemporary cohort of patients with cardiogenic shock undergoing PCI in the United Kingdom, we observe that although the majority of PCI cases performed in patients with cardiogenic shock in the United Kingdom are performed through the TFA, TRA can be used in many shocked patients and that TRA access site utilization in cardiogenic shock has grown progressively from 2006, reflecting the increased adoption of the TRA within United Kingdom interventional practice over this time period.[11] Our analysis also shows an association between an operator deciding to use a TRA access site and lower 30-day mortality, in-hospital MACCE, and major bleeding complications, although these favorable outcomes associated with TRA choice in patients with cardiogenic shock are not observed in centers with very low rates of TRA experience (<25%). Finally, our observations suggest that the femoral artery remains the preferred access site in cases with significant hemodynamic compromise with independent predictors of TFA utilization including the presence of severe left ventricular dysfunction, female gender, inotropic drug use, IABP use, and ventilation.

Although 2 recent small single-center studies have studied outcomes associated with access site utilization in

**Table VII.** Multivariate predictors for MACCE using Cox regression analyses

| | HR | 95% CI | | P>z |
|---|---|---|---|---|
| Access site (radial vs femoral) | 0.64 | 0.53 | 0.76 | <.0001 |
| Gender (female vs male) | 0.99 | 0.84 | 1.17 | .908 |
| Age (per year) | 1.03 | 1.02 | 1.04 | <.0001 |
| Smoking | | | | |
| Never | 1.00 | | | |
| Ex | 1.03 | 0.86 | 1.24 | .717 |
| Current | 1.15 | 0.94 | 1.40 | .183 |
| Hypertension | 1.08 | 0.92 | 1.28 | .351 |
| Hypercholesterolemia | 0.98 | 0.83 | 1.15 | .783 |
| Peripheral vascular disease | 1.34 | 1.08 | 1.68 | .009 |
| Previous CVA | 1.27 | 1.00 | 1.61 | .053 |
| Family history | 1.06 | 0.91 | 1.25 | .452 |
| Previous MI | 0.88 | 0.73 | 1.07 | .209 |
| Previous CABG | 1.06 | 0.75 | 1.49 | .747 |
| Previous PCI | 1.08 | 0.85 | 1.38 | .538 |
| Renal disease | 1.46 | 1.17 | 1.82 | .001 |
| GPI use | 0.75 | 0.64 | 0.87 | <.0001 |
| Clinical syndrome | | | | |
| NSTEMI/UA | 1.00 | | | |
| PPCI | 1.53 | 1.29 | 1.82 | <.0001 |
| Rescue PCI | 1.11 | 0.81 | 1.51 | .526 |
| Left ventricular function | | | | |
| Good | 1.00 | | | |
| Fair | 1.52 | 1.19 | 1.94 | .001 |
| Poor | 2.59 | 2.04 | 3.28 | <.0001 |
| IABP use (yes) | 1.21 | 1.02 | 1.43 | .031 |
| Inotrope use (yes) | 1.55 | 1.25 | 1.91 | <.0001 |
| Number of vessels (per unit) | 1.06 | 1.00 | 1.13 | .053 |

Harrell C concordance = 0.71 and Somers D =0.42.

**Table VIII.** Bleeding rates according to access site utilization

| Variable | Radial (n = 1877) | Femoral (n = 5354) | P |
|---|---|---|---|
| CVA bleed | 2 (0.1) | 17 (0.3) | $P = .12$ |
| Blood transfusion | 10 (0.6) | 117 (2.3) | 21.90, $P < .0001$ |
| Platelet transfusion | 1 (0.06) | 19 (0.37) | 4.56, $P = .03$ |
| Retroperitoneal bleed | 1 (0.06) | 6 (0.12) | 21.90, $P < .0001$ |
| Other hemorrhage | 11 (0.6) | 8 (0.4) | $P = .08$ |
| Total bleed | 25 (1.5) | 167 (3.5) | 17.58, $P < .001$ |

patients presenting with cardiogenic shock,[8,9] to the best of our knowledge, this is the first time that TRA access site use utilization and its associated outcomes have been studied from a national perspective.

The relationship that we have observed between mortality/MACCE outcomes and access site utilization does not infer causality. Our data suggest that TFA is used in more clinically unstable patients, which may in part contribute to the increased rates of mortality associated with TFA. Although we have attempted to adjust for such factors through the use of both multivariate analysis as well as propensity score matching and inverse probability weighting analysis, unmeasured confounders may contribute to residual case selection bias that cannot be completely controlled for.

An important contributory mechanism that may account for the observed association between TRA and 30-day mortality is a lower rate of major bleeding complications associated with the use of TRA. We show that utilization of the TRA is independently associated with a 63% lower risk of major bleeding complications in this high-risk cohort. Similar, reductions in major bleeding complications have been reported in a cardiogenic shock cohort through a reduction in access site–related bleeding complications associated with TRA utilization.[9]

Major bleeding complications are an important cause of mortality in patients with cardiogenic shock, with in-hospital major bleeding rates reported to be as high as 37% in patients with cardiogenic shock in a contemporary cohort of patients undergoing primary PCI.[12] Similarly, in an analysis of 302,152 PCI procedures from the National Cardiovascular Data Registry, the presence of cardiogenic shock was associated with a 4-fold increase in major bleedings rates.[13] This increase in major bleeding risk is related to several factors. Use of IABP in contemporary PCI is one of the strongest predictors of major bleeding complications. In the Global Registry of Acute Coronary Events, the incidence of major bleeding was 18% in those patients treated with IABP compared to 3.5% in the remaining cohort, whilst in the BCIS-1 study, use of the IABP bleeding complications occurred in 19.2% of patients in the elective PCI setting.[14] Abnormalities in platelet physiology[15] and coagulation/fibrinolysis pathways[16] following the development of cardiogenic shock may also contribute to the increase in bleeding complications.

Major bleeding complications are a powerful predictor of mortality,[17] with a significant proportion of major bleeding complications occurring through the access site[18]; and utilization of TRA in PCI procedures is associated with both a reduction in access site–related major bleeding complications and mortality outcomes.[19] In patients presenting with AMI and cardiogenic shock treated with an IABP, utilization of bifemoral access has been reported to almost double major bleeding complications compared to a single femoral puncture.[20] Utilization of TRA to limit the number of groin punctures needed in cardiogenic shock patients may be an important mechanism to explain some of the beneficial effects we have observed.

Previous commentators have suggested that cardiogenic shock remains the final frontier that has given even experienced radial operators pause[6]; and even in the very highest volume radial centers in the United Kingdom where TRA rates exceed 75%, the TRA was used in less than half of procedures. A significant learning curve exists in undertaking PCI procedures through the TRA, and patients with cardiogenic shock represent the most complex and hemodynamically unstable patients with significant technical challenges. Operators at the start of their learning curve should consider the TFA as the default access site

until their familiarity and experience with TRA increase. Indeed, in centers with the lowest rates of TRA adoption (<25%), the favorable outcomes associated with the TRA (compared to TFA) in mortality or MACCE were not observed. This would be in keeping with findings from the RIVAL study[7] in which TRA was only associated with a significant reduction in the primary composite end point in the highest tertile volume radial centers. In such low-volume radial centers (<25% TRA), it is not clear why 8% of cardiogenic shock cases were still performed through the TRA approach. It may have been related to the presence of significant peripheral vascular disease preventing adoption of the TFA in these cases or that the patient was more stable at the start of the procedure, with hemodynamic compromise and shock developing during the procedure.

Our analysis has several strengths. The BCIS data set includes an almost complete collection of all PCI procedures performed in the United Kingdom, reflecting a national real-world experience that includes many high-risk patients who are often excluded from randomized controlled trials. This analysis includes >7,000 patients and so represents the largest analysis of access site–related outcomes in PCI procedures performed in patients with cardiogenic shock in the literature to date.

However, as with any analysis of this kind, a number of limitations exist. The diagnosis of cardiogenic shock is self-reported by individual operators with no external validation, although our reported 30-day mortality rates of 36.3% for our cohort are in line with those reported in other contemporary cohorts,[1,5,21] with similar 30-day mortality rates as in the IABP-II SHOCK trial (40%),[22] suggesting that cardiogenic shock is not over- or underreported in our study population. Similarly, our reported rate of cardiogenic shock in patients undergoing PCI of 1.7% is similar to rates reported in other large national data sets such as the National Cardiovascular Data Registry dataset (2.1%).[23]

Secondly, although mortality tracking within the United Kingdom is very robust, the cause of mortality is not currently available; and all other outcomes and complications are self-reported and are not formally audited by BCIS, which may mean that our analysis may be subject to reporting biases.

Finally, although we have attempted to correct for differences in baseline covariates between the TFA and TRA groups using multivariate analysis, propensity score matching, and inverse-probability weighting, unmeasured confounders may be present that contribute to the unfavorable outcomes observed in the TFA cohort.

In conclusion, the current analysis of data derived from the BCIS database of >7,000 PCI procedures performed in the United Kingdom in patients with cardiogenic shock shows that although the majority of PCI cases performed in patients with cardiogenic shock in the United Kingdom are performed through the TFA, the radial artery represents an alternative viable access site in this high-risk cohort of patients in experienced centers.

## Disclosures

Conflict of interest: none declared.

## References

1. Goldberg RJ, Spencer FA, Gore JM, et al. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. Circulation 2009;119(9):1211-9.
2. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. N Engl J Med 1999;341(9):625-34.
3. Lim HS, Farouque O, Andrianopoulos N, et al. Survival of elderly patients undergoing percutaneous coronary intervention for acute myocardial infarction complicated by cardiogenic shock. JACC Cardiovasc Interv 2009;2(2):146-52.
4. Valente S, Lazzeri C, Crudeli E, et al. Intraaortic balloon pump: incidence and predictors of complications in the Florence registry. Clin Cardiol 2012;35(4):200-4.
5. Jeger RV, Assmann SF, Yehudai L, et al. Causes of death and re-hospitalization in cardiogenic shock. Acute Card Care 2007;9(1):25-33.
6. Levy MS, Moussa ID. Transradial PCI in cardiogenic shock, the final frontier? Catheter Cardiovasc Interv 2011;78(6):886-7.
7. Jolly SS, Yusuf S, Cairns J, et al. RIVAL trial group. 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(9775):1409-20.
8. Rodriguez-Leor O, Fernandez-Nofrerias E, Carrillo X, et al. Transradial percutaneous coronary intervention in cardiogenic shock: a single-center experience. Am Heart J 2013;165(3):280-5.
9. Bernat I, Abdelaal E, Plourde G, et al. Early and late outcomes after primary percutaneous coronary intervention by radial or femoral approach in patients presenting in acute ST-elevation myocardial infarction and cardiogenic shock. Am Heart J 2013;165(3):338-43.
10. 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(16):1293-7.
11. 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? JACC Int 2013;6(7):698-706.
12. Fuchs S, Kornowski R, Teplitsky I, et al. Major bleeding complicating contemporary primary percutaneous coronary interventions-incidence, predictors, and prognostic implications. Cardiovasc Revasc Med 2009;10(2):88-93.
13. Mehta SK, Frutkin AD, Lindsey JB, et al. Bleeding in patients undergoing percutaneous coronary intervention: the development of a clinical risk algorithm from the National Cardiovascular Data Registry. Circ Cardiovasc Interv 2009;2(3):222-9.
14. Perera D, Stables R, Thomas M, et al. Elective intra-aortic balloon counterpulsation during high-risk percutaneous coronary intervention: a randomized controlled trial. JAMA 2010;304(8):867-74.
15. Yip HK, Chang LT, Sun CK, et al. Platelet activity is a biomarker of cardiac necrosis and predictive of untoward clinical outcomes in patients with acute myocardial infarction undergoing primary coronary stenting. Circ J 2006;70(1):31-6.

16. Kirsch M, Vermes E, Boval B, et al. Blood activation during long-term mechanical circulatory support. Pathol Biol (Paris) 2005;53(2): 97-104.
17. 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 http://dx.doi.org/10.1136/openhrt-2013-000021.
18. Verheugt FW, Steinhubl SR, Hamon M, et al. Incidence, prognostic impact, and influence of antithrombotic therapy on access and nonaccess site bleeding in percutaneous coronary intervention. JACC Cardiovasc Interv 2011;4(2):191-7.
19. Chase AJ, Fretz EB, Warburton WP, et al. Association of the arterial access site at angioplasty with transfusion and mortality: the M.O.R.T.A.L study (Mortality benefit Of Reduced Transfusion after percutaneous coronary intervention via the Arm or Leg). Heart 2008;94(8): 1019-25.
20. Abdel-Wahab M, Saad M, Kynast J, et al. Comparison of hospital mortality with intra-aortic balloon counterpulsation insertion before versus after primary percutaneous coronary intervention for cardiogenic shock complicating acute myocardial infarction. Am J Cardiol 2010;105(7):967-71.
21. Katz JN, Stebbins AL, Alexander JH, et al. Predictors of 30-day mortality in patients with refractory cardiogenic shock following acute myocardial infarction despite a patent infarct artery. Am Heart J 2009;158(4):680-7.
22. Thiele H, Zeymer U, Neumann FJ, et al. Intraaortic balloon support for myocardial infarction with cardiogenic shock. N Engl J Med 2012; 367(14):1287-96.
23. Brennan JM, Curtis JP, Dai D, et al. Enhanced mortality risk prediction with a focus on high-risk percutaneous coronary intervention: results from 1,208,137 procedures in the NCDR (National Cardiovascular Data Registry). JACC Cardiovasc Interv 2013;6(8):790-9.

# Appendix

**Supplementary Table.** Baseline clinical demographics for radial and femoral access site in propensity-matched cardiogenic shock cohort

| Variable | Radial (n = 1402) | Femoral (n = 1402) | *P* |
|---|---|---|---|
| Age (y) | 66.2 (65.5-66.9) | 66.8 (66.1-67.4) | .22 |
| Gender (male, %) | 1042 (74.3) | 1037 (74.0) | .83 |
| Diabetes (%) | 261 (18.6) | 237 (16.9) | .24 |
| Hypertension (%) | 633 (45.2) | 598 (42.7) | .18 |
| Hypercholesterolemia | 617 (44.0) | 600 (42.8) | .52 |
| PVD (%) | 117 (8.4) | 115 (8.2) | .89 |
| Renal failure (%) | 76 (5.4) | 66 (4.7) | .39 |
| Previous MI (%) | 311 (22.2) | 281 (20.0) | .17 |
| Previous PCI (%) | 142 (10.2) | 211 (15.1) | .001 |
| Previous CABG (%) | 30 (2.1) | 32 (2.2) | .80 |
| IABP (%) | 356 (25.4) | 346 (24.7) | .66 |
| Ventilated (%) | 216 (15.4) | 239 (17.1) | .24 |

Data are means (95% CI) or percent (%). Differences between proportions used $\chi^2$ tests.