Is there a relationship of operator and center volume with access site related outcomes? an analysis from the British Cardiovascular Intervention Society

Short title: Volume and access site related outcomes

William Hulme[1], Matthew Sperrin[1], Helen Rushton[1], Peter F. Ludman MD[2], Mark De Belder MD[3], Nick Curzen BM PhD[4], Tim Kinnaird MD[5], Chun Shing Kwok MBBS MSc BSc[6,7], Iain Buchan MD[1], James Nolan MD[6,7], Mamas A. Mamas BM BCh DPhil[1,6,7].

1. Farr Institute, Institute of Population Health, University of Manchester, Manchester, UK

2. Queen Elizabeth Hospital, Edgbaston, Birmingham, UK

3. The James Cook University Hospital, Middlesbrough, UK

4. University Hospital Southampton & Faculty of Medicine, University of Southampton, Southampton, UK

5. Department of Cardiology, University Hospital of Wales, Cardiff, UK

6. Keele Cardiovascular Research Group, Institutes of Science and Technology in Medicine and Primary Care and Health Sciences, UK

7. Royal Stoke Hospital, University Hospital North Midlands Trust, Stoke on Trent, UK

Corresponding author:

Mamas A. Mamas

Professor of Cardiology

Keele Cardiovascular Research Group,

University of Keele,

Stoke-on-Trent, United Kingdom.

Tel :+44(0) 1612768666

Fax :+44 (0) 1612763335

Email: mamasmamas1@yahoo.co.uk

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Abbreviations and Acronyms

TRA = transradial access

TFA = transfemoral access

PCI = percutaneous coronary intervention

MACE = major adverse cardiovascular events

ACS = acute coronary syndrome

NHS = National Health Service

OTV = the yearly Operator Total Volume

ORV = the yearly Operator Radial Volume

ORP = the yearly Operator Radial Proportion (ORP=ORV/OTV)

CTV = the yearly Centre Total Volume

CRV = the yearly Centre Radial Volume

CRP = the yearly Centre Radial Proportion (CRP=CRV/CTV)

STEMI = ST elevated myocardial infarction

NSTEMI = non-ST elevated myocardial infarction

What is Known:

- The transradial access site has grown to be the default access site for PCI in Europe and it is rapidly growing in adoption within the United States.
- Procedural volume for PCI at both the operator and institutional level has been linked both to improved mortality and procedural outcomes.
- Procedural volume and expertise may equally be important for outcomes associated with access site.

What the Study Adds:

- This largest study to date found significant variation in access site practice at both the individual operator and center level according to volume of procedures undertaken, with TRA used more commonly as operator/center volume increase.
- We demonstrate that the lower mortality associated with TRA adoption relates to the proportion of procedures undertaken through the radial approach, and also the total volume of procedures, with operators undertaking the greatest proportion of their procedures radially having the largest relative reduction in mortality risk. We observe that the reduced mortality associated with TRA does not relate to either total volume or radial volume at the center level once other covariates of patient clinical demographics and operator experience are adjusted for.

Abstract

Background: Transradial access (TRA) is associated with reduced access site related bleeding complications and mortality post percutaneous coronary intervention (PCI). The objective of this study is to examine the relationship between access site practice and clinical outcomes and how this may be influenced by operator and center experience/expertise.

Methods and Results: The influence of operator and center experience/expertise was studied on 30-day mortality, in-hospital MACE (a composite of in-hospital mortality and in-hospital myocardial infarction and target vessel revascularization) and in-hospital major bleeding based on access site adopted (radial vs femoral). Operator/center experience/expertise were defined by both total volume and TRA proportion. A total of 164,395 procedures between 2012 and 2013 in the NHS in England and Wales were analyzed. After case-mix adjustment, TRA was associated with an average odds reduction of 39% for 30-day mortality compared with transfemoral access (TFA) (OR = 0.61, 95% CI 0.55-0.68, p<0.001). The magnitude of this risk reduction was modified by increases in total procedural volume and radial proportion at the operator level (OR reduction of 11% per 100 extra procedures, 95% CI 3-19%; OR reduction of ~~8%~~6% per 10%-point increase in radial proportion, 95% CI ~~3-12%~~1-11%) with no significant impact of operator radial volume, center total volume, center radial volume and center radial proportion.

Conclusions: The lower mortality associated with TRA adoption relates to both the total procedural volume and the proportion of procedures undertaken radially by operator, with operators undertaking the greatest proportion of their procedures radially having the largest relative reduction in mortality risk.

Keywords: Operator volume, Center volume, Access site, Mortality

Introduction

The transradial (TRA) access site has been adopted as the preferred access site for percutaneous coronary intervention (PCI) in the United Kingdom and many countries across Europe.[1-3] TRA is associated with decreased mortality rates in specific patient groups,[4-8] at least in part through a reduction in major bleeding complications.[9] Radial access is technically more challenging than femoral and has a longer learning curve requiring higher volumes to achieve and maintain proficiency.[10,11]

Procedural volume for percutaneous coronary intervention (PCI) at both the operator and institutional level has been linked both to improved mortality and procedural outcomes.[12,13] Similarly, procedural volume and expertise may equally be important for outcomes associated with TRA utilization. Data derived from the RIVAL (RadIal Vs. femorAL) trial, that randomized 7,021 patients with acute coronary syndromes (ACS) to radial versus femoral access for PCI, suggests that procedural radial volumes may impact on PCI outcomes associated with the TRA utilization.[14,15] Whilst in the subgroup of high-volume radial centers the primary outcome was reduced by adoption of TRA, this was not observed in intermediate- or low-volume radial centers and furthermore there was no significant interaction by individual operator radial volume.[14] ~~Other studies reporting outcomes in the Veteran Affairs (VA) healthcare system have suggested that blood transfusions were significantly less frequent in high volume radial centers (defined as ≥50 TRA procedures per year) compared to procedures undertaken through the transfemoral access (TFA), although this relationship was not observed in low volume radial centers, although TRA adoption in even the highest volume centers was only 35% in the setting of national TRA rates of only 9%.~~

Whilst previous work has studied the relationship between center and operator radial volume and its relationship between access site related outcomes,[15,16] these data have some limitations. Firstly, some data are derived in the setting of randomized controlled trials, therefore in highly selected patient cohorts in whom PCIs were undertaken in experienced centers with experienced operators.[14,15] Second, data are derived from centers in North America where procedural center volumes of ≥50 TRA procedures per year (defined as high volume radial centers) would be considered low volume in countries where TRA represents the default access site (such as the UK). Whilst “center” and “operator” TRA volumes may

be considered markers of TRA expertise, this will clearly be dependent on total PCI center and operator volumes, hence high volume centers and operators who only do a small proportion of their cases through the TRA route would numerically still be considered as experienced “high volume” radial centers/operators in previous analyses. The proportion of cases undertaken through the TRA, is an important marker of radial experience and expertise since high proportion TRA operators will undertake PCI cases through the TRA in the most challenging cases but this has not been considered or adjusted for in previous analyses. Often such patients are at the highest risk of bleeding complications and derive most benefit from the TRA approach.[5]

We have therefore studied the relationship between access site practice and clinical outcomes in the United Kingdom and how this relationship may be associated with operator and center experience/expertise, as defined by both the volume and proportion of cases undertaken through the TRA. Furthermore, we also study the clinical characteristics and procedural demographics of patients in whom TRA is the access site adopted for PCI by operators/centers with differing degrees of TRA experience/practice.

Methods

The British Cardiovascular Intervention Society Database

The British Cardiovascular Intervention Society (BCIS) collects data on all PCI procedures in the UK[17-19] and data collection is coordinated by the National Institute of Cardiovascular Outcomes Research (http://www.ucl.ac.uk/nicor/) via the Central Cardiac Audit Database. In 2011, this dataset collected information on 99.4% of all PCI procedures performed in National Health Service Hospitals in England and Wales. The BCIS-NICOR database comprises 113 variables, including clinical variables, procedural parameters and patient outcomes. Mortality tracking is undertaken by theMedical Research Information Service using patients' National Health Service (NHS) numbers that provide a unique identifier for any person registered with the NHS in England andWales.

Study definitions

The data presented relate to allreported PCI procedures undertaken in patients in England and Wales between January 1, 2012 and December 31, 2013.PCI procedures performed via the left or right femoral artery or the left or right radial artery were included in the TFA and TRA cohorts, respectively. Procedures involving a switch from one access site to another, or where access site was unknown, were excluded. The outcomes examined were in-hospital major adverse cardiovascular events (MACE) (a composite of in-hospital mortality and in-hospital myocardial infarction or re-infarction and target vessel revascularization), in-hospital major bleeding (defined as gastrointestinal bleed, intra-cerebral bleed, retroperitoneal hematoma, blood or platelet transfusion, or an arterial access site complication requiring surgery) and 30-day mortality.

Statistical Methods

Descriptive

Three measures of "operator experience" were considered: the yearly Operator Total Volume (OTV), the yearly Operator Radial Volume (ORV), and the yearly Operator Radial Proportion (ORP=ORV/OTV). Analogousannualized measures of "center experience", CTV, CRV, CRP, were also considered. TRA proportion was plotted against volume for operator and for center to examine their relationships. Individual operator identity was derived from a unique General Medical Council (GMC) number derived from the BCIS dataset available

from 2012 that each medical practitioner licensed to practice medicine in the UK is allocated when first registered with the GMC. It is a statuary requirement to be registered with the GMC to practice medicine in the UK.

In order to examine the relationship between case mix and experience, cases were divided into four groups according to each of these three measures; quartiles defined the group boundaries for the OTV, ORV, CTV and CRV and boundaries for ORP and CRP were at values of 25%, 50% and 75%. Important aspects of case mix (e.g. variables such as age, shock) were then tabulated per group against access site. These tables were presented with column percentages for categorical variables, which can be interpreted as an indication of how case mix varies by access site. To test for association between demographic and clinical variables and access site choice within strata, t-tests were used for continuous variables and Chi-squared-tests for categorical variables. Logistic regression was used to determine whether access site choice differed between experience groups; Access site (TRA only or TFA only) was the binary outcome, and we report the p-value from the test of inclusion of an interaction term between the demographic/clinical variable and experience group.

Modeling

Logistic regression was used for each outcome (30-day mortality, major bleeding, and MACE). The exposures of interest were access site, operator/center experience, and the interactions between access site and experience. Models were adjusted for demographic and clinical confounders. Two strategies were employed to deal with intra-patient dependencies, with analyzes from each strategy performed in parallel; the first strategy assumed all procedures were independent so that no design modifications were necessary, while the second permitted only the first procedure for each patient during the study period to enter the analysis cohort. After removing observations where the exposure was missing, multiple imputation was implemented. Ten datasets were imputed in total and the models developed on each of these were pooled using Rubin's rules.[20] The same ten datasets were used for each outcome analysis so that each analysis was drawn from the same imputation model and to eliminate the need to reimpute for each outcome. To allow for this, each of the three outcome variables were included in the chained imputation equations but crucially, at the model development and analysis stage observations were removed if the outcome of interest was originally missing, i.e., a 'multiple imputation then deletion' strategy.[21]

Clinical and demographic confounders were chosen a priori based on availability and clinical relevance: age, gender, year of operation, indication for treatment (Stable angina, Unstable angina/NSTEMI, STEMI), presence of diabetes, renal function, coronary artery bypass graft, shock, intra-aortic balloon pump, cardiopulmonary support, inotropic support, ventilation, stent type, smoking status, high cholesterol, previous myocardial infarction, left ventricular ejection fraction (LVEF), and use of glycoprotein IIb/IIIa drugs were all adjusted for. First-order interactions were considered.

Models were considered which combined all three measures of experience (along with interactions with access site). Models adjusting for a single measure of experience were also examined, with and then without adjusting for other covariates. Non-linear effects were considered for the measures of experience via restricted cubic splines with four knots[1]

Odds ratios comparing odds of adverse outcomes for radial access with odds for femoral access site were plotted against each measure of experience, along with 95% confidence intervals, for the models considered.

A secondary analysis was performed to investigate if the experience-outcomerelationships observed in the primary analysis were still present when restricting to non-cardiogenic procedures.

Software

All data preparation and analyses were performed using R version 3.2.0.[23]The mice package[24] was used for multiple imputation.

Results

Study cohort

A total of 164,395 procedures were performed in patients in England and Wales between January 1, 2012 and December 31 2013 and the influence of operator and center total volume, radial volume and radial proportions on outcomes was studied. Figure 1 illustrates a flowchart that tracks the process by which observations are removed from the analysis cohorts and the stages at which experience measures are calculated. Experience measure and the descriptive analysis was performed in 149,165 procedures. Amongst these, operators are typically high proportion radial or high proportion femoral with few operators performing around 50% of each, with high volume centers more likely to be high-proportion radial centers (Figure 2). During the study period radial proportion increased steadily from 60.4% in January-March 2012 to 70.1% in October-December 2013 as illustrated in Figure 3. In total 145,250 procedures were used in the primary mortality analysis. Restricting the analysis cohort to patients undergoing their first procedure during the study period removed 13,055 (9%) procedures from full cohort, with results from this cohort versus the full cohort practically equivalent. We therefore only present results from the analysis of the full cohort.

Operator and center volumes and access site related outcomes

The influence of operator and center volumes on access site related outcomes were studied. Table 1 illustrates clinical and procedural demographics for the TRA and TFA groups by operator annual procedural volumes. Table 1 shows that as operator volume increased across groups, TRA increased from 54.3% in lowest OTV group (≤124 procedures) to 72.9% in the highest OTV group (>237 procedures); P<0.001. Patients in the TFA cohort were consistently older, were more likely to be female gender, have a previous history of CABG, have a previous history of MI, have diabetes, be hypertensive, and present with cardiogenic shock (all P<0.001) in all operator volume groups studied. Similar observations were recorded when center volume was studied (Table 2). Table 2 illustrates clinical and procedural demographics for the TRA and TFA groups by CTV. TRA utilization increased from 57.6% in the lowest CTV group (≤682 procedures) to 76.0% in the highest CTV group (>1633 procedures), P<0.001.

Crude 30-day mortality outcomes were significantly fewer in the TRA cohort compared to the TFA cohort across all volume groups studied both at the operator level (1.6% vs 3.9% in lowest operator volume group, 1.6% vs 4.9% in the highest operator volume group; P<0.001) and at the center volume level (1.2% vs 2.6% in the lowest center

volume group, 1.6% vs 5.1% in the highest center volume group; P<0.001). Similar observations were recorded for both in hospital MACE and major bleeding complications (Tables 1 and 2).

Operator and center radial proportions and access site related outcomes

The relationship between ORP, CRP and access site related outcomes were studied. Tables 3 and 4 illustrate clinical and procedural demographics for the TRA and TFA groups stratified by radial proportion quartiles at the operator and center level respectively.

Crude 30-day mortality rates by access site (i.e., TRA versus TFA) were similar in the low ORP cohort defined as undertaking <25% of PCI procedures through the TRA route (TRA 2.2% and TFA 2.4%; P=0.561) but were significantly less in the TRA group compared to the TFA group in the remaining ORPgroups (mortality in highest ORP, TRA 1.7% and TFA 7.2%; P<0.001). In-hospital major bleeding and MACE was significantly lower in the TRA cohort compared to TFA cohort in all ORP groups studied, with this effect larger for MACE in high proportion radial operators (P<0.001) but not for bleeding (P=0.676). When crude 30-day mortality was studied according to CRP, similar findings were observed except that the effect of TRA vs TFA was not different by proportion groups for bleeding (P<0.001) (Table 4).

Operator and centerradial volume and access site related outcomes

We subsequently studied the influence of ORV and CRV on outcomes. Supplementary Table 1 illustrates clinical and procedural demographics and clinical outcomes stratified by ORV group. Patients in the TFA cohort were consistently older, had a higher prevalence of comorbidities and were more likely to present with hemodynamic compromise in all operator radial volume groups studied. Similar observations were recorded when CRV was studied (Supplementary Table 2).

TRA was associated with lower crude 30-day mortality compared with TFA in all quartiles of operator and center radial volume studied (P<0.001).

Adjusted analyses for operator/center volumes and proportions

Multiple logistic regression modeling for each experience measure independently indicated that experience increase was significantly associated with reductions in the TRA vs TFA odds-ratio (OR) for 30-day mortality, after adjustment for confounders. Supplementary Figure1illustrates and quantifies these associations for each of the experience measures.

Multiple logistic regression modeling adjusting for other experience measures in addition to confounders showed an average odds reduction of 39%for 30-day mortality for TRA when compared with TFA (OR = 0.61, 95% CI 0.55 to 0.68, p<0.001), and indicated that only increasing OTV and ORP were significantly associated with reductions in the TRA vs TFA odds-ratio (OR) for 30-day mortality. Figure 4 illustrates and quantifies these associations for each of the experience measures. The magnitude of this risk reduction was modified by increases in OPV (OR reduction of 11% per 100 extra procedures, 95% CI 3-19%) and by increases in ORV (OR reduction of 6% per 10%-point increase in radial proportion, 95% CI 1-11%) with no significant OR changes when varying by ORV, CTV, CRV and CRP.

Sensitivity analyses for these regression models indicated that while some confounder interactions were significant additional adjustments did not materially affect the exposure parameters of interest; therefore, interactions between confounders were not included. Further, non-linear experience effects were investigated via restricted cubic splines and although some non-linearities were observed, these were often in low operator/center density spaces where model uncertainty is high, and made no practical difference to the principal observation that OTV and ORP are negatively associated with the TRA vs TFA mortality odds-ratio after adjustment for confounders and other experience measures. The exclusion of repeat admission during the study period to ensure independence between patients did not significantly alter the results of the primary analysis (compare Figure 4 with Supplementary Figure 2).

Similarly restricting the analysis to PCI procedures undertakenin the non-cardiogenic shock setting, we demonstrate similar findings to the results for the whole cohort (Supplementary Figure 3).

Discussion

Our analysis of around 150,000 PCI procedures undertaken nationally between 2012-2013 suggests that there is significant variation in access site practice at both the individual operator and center level according to volume of procedures undertaken, with TRA used more commonly as operator/center volume increase. We report that TRA choice is independently associated with reduced 30-day mortality outcomes and that the magnitude of this lower mortality risk is not independently influenced by either increases in total procedural volume radial volume, or radial proportion at the center level. Finally, our study

suggests that higher total volume of procedures and higher proportion of cases undertaken radially at the operator level– are independently associated with a larger reduced odds of mortality, with an 11% reduction in the odds for 30-day mortality (compared to TFA use) for each 100 extra procedures performed per year, and an 8% reduction in the odds for 30-day mortality (compared to TFA use) for each 10% increase in the proportion of cases undertaken through the TRA approach.

Previous studies using data derived from randomized controlled trials[14,15] and data derived from the Veterans Affairs (VA) Healthcare system[16] have suggested a relationship between access site outcomes and procedural volumes. Analysis of 24,143 procedures undertaken in 49 VA sites between 2007-2010 suggested that the decreased rate of blood transfusions associated with TRA was only observed in high radial volume centers, defined as performing >50 TRA procedures a year.[16] The RIVAL study reported that in the subgroup of high volume radial centers the primary outcome was reduced by TRA versus TFA, but not in intermediate- or low-volume radial centers and there was no significant interaction by individual operator radial volume.[15] [2]In contrast, no significant differences in the primary bleeding endpoint were observed between the TRA and TFA arm by either operator radial volume, though this study suggests some evidence of a significant interaction at the center level. Subgroup analysis of the RIVAL study by center procedural volume illustrated a significant 8% reduction in the primary endpoint for overall PCI center volume a 12% reduction for radial center volume per 50 PCIs/year for median operator at center although this relationship was not observed for mortality outcomes. In a retrospective analysis derived from 8 centers in the UK, TRA utilization independently predicted decreased 30-day, 6-month and 1-year mortality in patients undergoing PCI for NSTEMI indications although this benefit was only observed in high volume radial centers.[25] Interestingly, in the recent MATRIX RCT, that demonstrated decreases in all cause mortality, MACE and major BARC 3 or 5 bleeding rates in the TRA arm, with positive tests for trend across tertiles of the centers' percentage of TRA for PCI for both co-primary outcomes and all-cause mortality, with a particularly pronounced benefit of TRA access in centers that did 80% or more radial percutaneous coronary interventions.[26]

Our analysis represents the first analysis to systematically study the relationship between TRA volume, total volume and TRA proportions at both the individual operator and center level in a nationwide setting where TRA is now the default access route[3,27] in an unselected real world cohort of patients. We show that access site practice varies according to

volume of procedures undertaken at the operator and center level, with increased utilization of the TRA approach as operator and center volume increases. Furthermore it is interesting to note that we report that the size of the 30-day mortality risk decrease associated with TRA utilization is not independently influenced bycenter radial or total volume of procedures undertaken, but is independently influenced by operator total volume and radial proportion. Higher total volume of procedures and higher proportion of cases undertaken radially at the operator level are independently associated with a larger reduced odds of 30-day mortality.

Our analysis represents a broad spectrum of operators with varying access site practice and TRA experience. Previous analyses have been limited in that they have been undertaken in highly selected cohorts of patients in the RCT setting undergoing PCI for ACS indications where the highest risk patients such as those with hemodynamic instability where excluded and only experienced operators who undertook at least 50 TRA procedures in the previous year were included in the study.[28] Similarly other studies analyzed data from US cohorts when TRA adoption was <10% at the time-points studied and the 5 high volume sites defined as >50 TRA procedures a year averaged 120 TRA procedures a year each which would place these centers in the lowest quartile (2-341 TRA procedures per year) in the current analysis.[16]

Our observation that the largest risk reduction associated with the TRA approach is amongst operators who utilize TRA in the highest proportion of their cases, and that this is not related to either total volume or radial volume at the center level once other covariates of patient clinical demographics and operator/center experience are adjusted for is of interest. Our previous work has suggested that the greatest mortality reduction associated with TRA adoption is derived from patients at highest baseline bleeding risk, who are often the most hemodynamically unstable, have adverse clinical characteristics such as the elderly, women, or are undergoing PCI for emergent indications whilst patients at low risk of bleeding complications gain little mortality benefit from adopting a TRA approach.[5] The patients who are likely to gain most from adoption of TRA access site are also those in whom TRA is more challenging. High proportion TRA operators are likely to utilize the TRA approach in such patients who are at highest risk of bleeding complications who would derive the greatest mortality benefit from radial access site adoption, whereas low proportion TRA operators are more likely to use TRA approach in less challenging cases that would derive less/little mortality benefit from utilization of this access site. Radial volume will depend on both the total volume that an operator undertakes and the proportion of cases undertaken through the

TRA route; hence individuals may be high volume radial operators by virtue of undertaking a large volume of procedures but only undertaking a low proportion of such procedures through the TRA route. Such a 'high volume' radial operator may only undertake the least challenging cases that would derive a smaller mortality benefit of undertaking the procedure through the TRA approach. Previous literature has only considered radial/total volumes in isolation and not considered the proportion of cases undertaken through the TRA route when examining relationships between radial 'experience' and outcomes.[4,14-16,25] The more recent MATRIX RCT showed a relationship between center TRA proportion and the co-primary outcome, with highest proportion radial centers having the greatest magnitude of benefit in the co-primary outcome, although data around operator proportion was not presented in this analysis.[26]

In the highest proportion radial operator and centre analysis, we have consistently observed that the cases undertaken through the femoral approach are much sicker, higher risk patients than those undertaken in the lowest proportion operators/centers. For example, at the operator level, in the highest proportion radial operator group cardiogenic shock represented 9.2% of the femoral case mix in contrast to 2.5% in the lowest proportion radial operator group (P<0.001), with similar observations recorded at the centre level (7.5% vs 2.3%; P<0.001). In addition, similar findings were observed at both the centre and operator volume analyses. It has been previously argued that the more favorable radial outcomes reported at high proportion radial centers may relate to worse femoral outcomes in these centers at both the centre and operator level.[29] Even after removal of the sickest patients such as those with cardiogenic shock in a sensitivity analysis, our findings that lower mortality associated with TRA adoption relates to both the total procedural volume and the proportion of procedures undertaken radially by operator, with operators undertaking the greatest proportion of their procedures radially having the largest relative reduction in mortality risk remain robust. Furthermore, data from the RIVAL has shown that whilst radial PCI centre volume was independently associated with a decrease in the composite primary outcome of death, myocardial infarction, stroke, non-CABG related major bleeding at 30 days(HR 0.88 95%CI 0.80-0.97), femoral PCI centre volume was not (HR 1.03 95%CI 0.94-1.07) suggesting that mechanisms other than worse femoral outcomes in high volume radial centers, contribute to their better outcomes in cases undertaken transradially.[2]

Our study has a number of potential limitations. Whilst mortality tracking within England and Wales is robust, the cause of mortality is not available; and all other outcomes

and complications such as major bleeding events are self-reported and are not formally audited by BCIS, subjecting the data to reporting biases. Secondly, we were unable to account for crossover in access site because this data is not captured in the BCIS dataset. Finally, although we have attempted to correct for differences in baseline and procedural demographics observed between the TFA and TRA cohorts using a variety of statistical techniques the relationship between access site and favorable outcomes does not infer causality, and unmeasured confounders may contribute to the unfavorable outcomes observed in the TFA cohort.

In conclusion, in the largest analysis to date undertaken nationally to systematically study access site related outcomes and procedural volumes at both the operator and institutional level, we demonstrate that the lower mortality associated with TRA adoption relates to the proportion of procedures undertaken through the radial approach, and also the total volume of procedures, with operators undertaking the greatest proportion of their procedures radially having the largest relative reduction in mortality risk. We observe that the reduced mortality associated with TRA does not relate to either total volume or radial volume at the center level once other covariates of patient clinical demographics and operator experience are adjusted for.

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References

1. Mamas MA, Ratib K, Routledge H, Neyses L, Fraser DG, de Belder M, Ludman PF, Nolan J. Influence of arterial access site selection on outcomes in primary percutaneous coronary intervention: are the results of randomized trials achievable in clinical practice? JACC Cardiovasc Interv 2013;6:698-706.
2. Bertrand OF, Rao SV, Pancholy S, Jolly SS, Rodes-Cabau J, Larose E, Costerousse O, Hamon M, Mann T. Transradial approach for coronary angiography and interventions: results of the first international transradial practice survey. JACC Cardiovasc Interv 2010;3:1022-31.
3. Ratib K, Mamas MA, Anderson SG, Bhatia G, Routledge H, de Belder M, Ludman PF, Fraser D, Nolan J. Access site practice and procedural outcomes in relation to clinical presentation in 439,947 patients undergoing percutaneous coronary intervention in the United kingdom. JACC Cardiovasc Interv 2015;8:20-9.
4. Mamas MA, Anderson SG, Ratib K, Routledge H, Neyses L, Fraser DG, Buchan I, de Belder MA, Ludman P, Nolan J. Arterial access site utilization in cardiogenic shock in the United Kingdom: is radial access feasible? Am Heart J 2014;167:900-8 e1.
5. Mamas MA, Anderson SG, Carr M, Ratib K, Buchan I, Sirker A, Fraser DG, Hildick-Smith D, de Belder M, Ludman PF, Nolan J. 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.
6. Baklanov DV, Kaltenbach LA, Marso SP, Subherwal SS, Feldman DN, Garratt KN, Curtis JP, Messenger JC, Rao SV. 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.
7. Mehta SR, Jolly SS, Cairns J, Niemala K, Rao SV, Cheema AN, Steg PG, Cantor WJ, Dzavik V, Budaj A, Rokoss M, Valentin V, Gao P, Yusuf S. Effects of radial versus femoral artery access in patients with acute coronary syndromes with or without ST-segment elevation. J Am Coll Cardiol 2012;60:2490-9.
8. Romagnoli E, Biondi-Zoccai G, Sciahbasi A, Politi L, Rigattieri S, Pendenza G, Summaria F, Patrizi R, Borghi A, Di Russo C, Moretti C, Agostoni P, Loschiavo P, Lioy E, Sheiban I, Sangiorgi G. 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.
9. Chase AJ, Fretz EB, Warburton WP, Klinke WP, Carere RG, Pi D, Berry B, Hilton JD. 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;94:1019-25.
10. Hess CN, Peterson ED, Neely ML, Dai D, Hillegass WB, Krucoff MW, Kutcher MA, Messenger JC, Pancholy S, Piana RN, Rao SV. The learning curve for transradial percutaneous coronary intervention among operators in the United States: a study from the National Cardiovascular Data Registry. Circulation 2014;129:2277-86.
11. Ball WT, Sharieff W, Jolly SS, Hong T, Kutryk MJ, Graham JJ, Fam NP, Chisholm RJ, Cheema AN. Characterization of operator learning curve for transradial coronary interventions. Circ Cardiovasc Interv 2011;4:336-41.
12. Badheka AO, Patel NJ, Grover P, Singh V, Patel N, Arora S, Chothani A, Mehta K, Deshmukh A, Savani GT, Patel A, Panaich SS, Shah N, Rathod A, Brown M, Mohamad T, Makkar RR, Schreiber T, Grines CL, Rihal CS, Cohen MG. Impact of

annual operator and institutional volume on percutaneous coronary intervention outcomes: a 5-year United States experience (2005-2009). Circulation 2014;130:1392-406.
13. Strom JB, Wimmer NJ, Wasfy JH, Kennedy K, Yeh RW. Association between operator procedure volume and patient outcomes in percutaneous coronary intervention: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2014;7:560-6.
14. Jolly SS, Yusuf S, Cairns J, Niemela K, Xavier D, Widimsky P, Budaj A, Niemela M, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Gao P, Afzal R, Joyner CD, Chrolavicius S, Mehta SR. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicenter trial. Lancet 2011;377:1409-20.
15. Jolly SS, Cairns J, Yusuf S, Niemela K, Steg PG, Worthley M, Ferrari E, Cantor WJ, Fung A, Valettas N, Rokoss M, Olivecrona GK, Widimsky P, Cheema AN, Gao P, Mehta SR. Procedural volume and outcomes with radial or femoral access for coronary angiography and intervention. J Am Coll Cardiol 2014;63:954-63.
16. Gutierrez A, Tsai TT, Stanislawski MA, Vidovich M, Bryson CL, Bhatt DL, Grunwald GK, Rumsfeld J, Rao SV. Adoption of transradial percutaneous coronary intervention and outcomes according to center radial volume in the Veterans Affairs Healthcare system: insights from the Veterans Affairs clinical assessment, reporting, and tracking (CART) program. Circ Cardiovasc Interv 2013;6:336-46.
17. 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.
18. Mamas MA, Anderson SG, O'Kane PD, Keavney B, Nolan J, Oldroyd KG, Perera D, Redwood S, Zaman A, Ludman PF, de Belder MA. 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.
19. Kwok CS, Anderson SG, McAllister KS, Sperrin M, O'Kane PD, Keavney B, Nolan J, Myint PK, Zaman A, Buchan I, Ludman PF, de Belder MA, Mamas MA. Impact of age on the prognostic value of left ventricular function in relation to procedural outcomes following percutaneous coronary intervention: Insights from the British cardiovascular intervention society. Catheter Carddiovasc Interv 2015;86:944-51.
20. Little RJ, Rubin DBR. Statistical analysis with missing data. 2nd Edition. Wiley. 2002.
21. von Hippel PT. Regression with missing Ys: an improved strategy for analyzing multiply imputed data. Sociol Methodol 2015;37:83-117.
22. Durrleman S, Simon R. Flexible regression models with cubic splines. Stat Med 1989;8:551-61.
23. R Core Team. R: A language and environment for statistical computing. 2015. R Foundation for Statistical Computing, Vienna, Austria.
24. van Burren S, Groothuis-Oudshoorn K. MICE: Multivariable Imputation by Chained Equations in R. J Stat Softw 2011;45:1-67.
25. Iqbal MB, Arujuna A, Ilsley C, Archbold A, Crake T, Firoozi S, Kalra S, Knight C, Lim P, Malik IS, Mathur A, Meier P, Rakhit RD, Redwood S, Whitbread M, Bromage D, Rathod K, Wragg A, MacCarthy P, Dalby M. Radial versus femoral access is associated with reduced complications and mortality in patients with non-ST-segment-elevation myocardial infarction: an observational cohort study of 10,095 patients. Circ Cardiovasc Interv 2014;7:456-64.

26. Valgimigli M, Gagnor A, Calabro P, Frigoli ELeonardi S, Zaro T, Rubartelli P, Briguori C, Ando G, Repetto A, Limbruno U, Cortese B, Sganzerla P, Lupi A, Galli M, Colangelo S, Ierna S, Ausiello A, Presbitero P, Sardella G, Varbella F, Esposito G, Santarelli A, Tresoldi S, Nazzaro M, Zingarelli A, de Cesare N, Rigattieri S, Tosi P, Palmieri C, Brugaletta S, Rao SV, Heg D, Rothenbuhler M, Vranckx P, Juni P. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicenter trial. Lancet 2015;385;2465-2476.
27. Anderson SG, Ratib K, Myint PK, Keavney B, Kwok CS, Zaman A, Ludman PF, de Belder MA, Nolan J, Mamas MA. Impact of age on access site-related outcomes in 469,983 percutaneous coronary intervention procedures: Insights from the British Cardiovascular Intervention Society. Catheter Cardiovasc Interv 2015. doi:10.1002/ccd.25896.
28. Jolly SS, Niemela K, Xavier D, Widimsky P, Budaj A, Valentin V, Lewis BS, Avezum A, Steg PG, Rao SV, Cairns J, Chrolavicius S, Yusuf S, Mehta SR. Design and rationale of the radial versus femoral access for coronary intervention (RIVAL) trial: a randomized comparison of radial versus femoral access for coronary angiography or intervention in patients with acute coronary syndromes. Am Heart J 2011;161:254-260 e1-4.
29. Le May MR, Singh K, Wells GA. Efficacy of Radial Versus Femoral Access in the Acute Coronary Syndrome: Is it the Operator or the Operation That Matters? JACC Cardiovasc Interv. 2015;8:1405-9.

Table 1: Clinical and procedural demographics stratified by access site and Operator Total Volumes.

Volume of TFA only or TRA only procedures performed by operator (OTV)		**1. Lowest volume N=37,391 (1-123 procedures)**			**2. lower-mid volume N=37,242 (124-173 procedures)**			**3. upper-mid volume N=37,389 (174-237 procedures)**			**4. Highest volume N=37,143 (238-658 procedures)**			**P-value for same effect size over groups**
		TRA	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		
All procedures, N		20,336	17,055		23,673	13,569		26,293	11,096		27,074	10,069		
		Mean (SD)	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	
Age		64.0 (12.1)	65.4 (12.1)	<0.001	64.0 (11.9)	66.0 (12.2)	<0.001	64.5 (11.9)	66.4 (12.1)	<0.001	64.9 (12.0)	67.2 (12.3)	<0.001	<0.001
		N (%)	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	
Sex	-Male	15,560 (76.5)	12,261 (71.9)	<0.001	18,116 (76.5)	9,573 (70.6)	<0.001	19,911 (75.7)	7,786 (70.2)	<0.001	20,377 (75.3)	7,055 (70.1)	<0.001	0.252
	-Female	4,776 (23.5)	4,794 (28.1)		5,557 (23.5)	3,996 (29.4)		6,382 (24.3)	3,310 (29.8)		6,697 (24.7)	3,014 (29.9)		
Indication	-Stable angina	6,484 (31.9)	5,986 (35.1)	<0.001	7,436 (31.4)	5,104 (37.6)	<0.001	8,481 (32.3)	4,536 (40.9)	<0.001	9,269 (34.2)	4,268 (42.4)	<0.001	<0.001
	-UA/NSTEMI	7,950 (39.1)	6,012 (35.3)		9,007 (38.0)	4,863 (35.8)		10,128 (38.5)	3,876 (34.9)		10,700 (39.5)	3,336 (33.1)		
	-STEMI	5,902 (29.0)	5,057 (29.7)		7,230 (30.5)	3,602 (26.5)		7,684 (29.2)	2,684 (24.2)		7,105 (26.2)	2,465 (24.5)		
Shock		290 (1.4)	792 (4.7)	<0.001	374 (1.6)	651 (4.8)	<0.001	338 (1.3)	556 (5.0)	<0.001	311 (1.2)	515 (5.2)	<0.001	<0.001
MI		4,249 (22.1)	4,057 (26.7)	<0.001	4,996 (22.6)	3,689 (30.7)	<0.001	6,019 (24.0)	3,559 (33.8)	<0.001	6,583 (25.4)	3,474 (36.1)	<0.001	<0.001
CABG		887 (5.3)	1,952 (13.8)	<0.001	978 (5.8)	1,559 (15.7)	<0.001	1,080 (5.6)	1,529 (17.6)	<0.001	1,334 (5.8)	1,538 (21.3)	<0.001	<0.001
Diabetes		3,925 (19.9)	3,560 (22.3)	<0.001	4,396 (19.1)	2,889 (22.8)	<0.001	4,816 (19.1)	2,488 (24.1)	<0.001	5,036 (20.0)	2,304 (24.7)	<0.001	<0.001
Hypercholesterolemia		9,873 (50.5)	8,120 (49.8)	0.246	12,515 (54.5)	7,169 (55.4)	0.112	14,701 (58.2)	6,403 (60.7)	<0.001	14,230 (56.2)	5,579 (59.9)	<0.001	<0.001
Hypertension		10,138 (51.8)	8,833 (54.2)	<0.001	12,286 (53.5)	7,393 (57.1)	<0.001	13,663 (54.1)	6,374 (60.4)	<0.001	14,464 (57.1)	6,010 (64.6)	<0.001	<0.001
Renal	-Normal	19,113 (98.0)	15,483 (96.2)	<0.001	22,219 (98.4)	12,272 (95.7)	<0.001	24,788 (98.5)	10,246 (95.9)	<0.001	25,537 (98.4)	8,955 (95.2)	<0.001	<0.001
	-High creatinine	258 (1.3)	374 (2.3)		243 (1.1)	324 (2.5)		291 (1.2)	253 (2.4)		301 (1.2)	235 (2.5)		
	-Dialysis	123 (0.6)	243 (1.5)		122 (0.5)	223 (1.7)		96 (0.4)	183 (1.7)		112 (0.4)	212 (2.3)		
Smoking		11,388 (60.9)	9,065 (61.2)	0.692	13,746 (63.5)	7,114 (60.6)	<0.001	15,764 (64.7)	6,131 (61.6)	<0.001	16,394 (65.2)	5,453 (60.4)	<0.001	<0.001
Glycoprotein IIb/IIIa		4,373	3,398	0.014	4,701	2,151	<0.001	4,743	1,622	<0.001	4,209	1,281	<0.001	<0.001

inhibitors		(22.2)	(21.1)		(20.8)	(17.4)		(18.8)	(15.3)		(15.7)	(13.0)		
Intra-aortic balloon pump		141	440	<0.001	150	426	<0.001	163	376	<0.001	183	325	<0.001	0.027
		(0.7)	(2.7)		(0.7)	(3.4)		(0.6)	(3.6)		(0.7)	(3.3)		
Cardiopulmonary support		15	41	<0.001	8	41	<0.001	22	23	0.003	19	18	0.005	0.018
		(0.1)	(0.3)		(<0.1)	(0.3)		(0.1)	(0.2)		(0.1)	(0.2)		
Inotropes		127	267	<0.001	116	218	<0.001	111	161	<0.001	144	163	<0.001	0.175
		(0.6)	(1.6)		(0.5)	(1.8)		(0.4)	(1.5)		(0.5)	(1.6)		
Ventilated		187	578	<0.001	210	448	<0.001	238	373	<0.001	256	344	<0.001	0.975
		(1.0)	(3.8)		(1.0)	(4.0)		(1.0)	(3.7)		(1.0)	(3.8)		
Stents	-BMS only	2,770	2,119	<0.001	3,118	1,571	<0.001	3,315	1,267	<0.001	2,422	963	<0.001	<0.001
		(14.2)	(13.1)		(13.9)	(12.5)		(12.9)	(11.7)		(9.1)	(10.0)		
	-DES only	15,042	12,439		17,043	9,547		19,751	8,141		20,758	7,336		
		(77.2)	(77.2)		(76.0)	(76.0)		(77.0)	(75.2)		(77.8)	(75.9)		
	-BMS and DES	429	289		565	323		604	233		552	170		
		(2.2)	(1.8)		(2.5)	(2.6)		(2.4)	(2.2)		(2.1)	(1.8)		
LVEF	-Good (>50%)	6,425	4,982	<0.001	7,999	4,042	<0.001	9,938	3,884	<0.001	10,599	4,340	<0.001	<0.001
		(71.1)	(68.6)		(72.9)	(65.9)		(73.3)	(68.2)		(71.1)	(69.9)		
	-Fair (30-50%)	2,113	1,731		2,409	1,630		2,958	1,342		3,446	1,373		
		(23.4)	(23.8)		(22.0)	(26.6)		(21.8)	(23.6)		(23.1)	(22.1)		
	-Poor (<30%)	494	545		558	465		664	469		854	492		
		(5.5)	(7.5)		(5.1)	(7.6)		(4.9)	(8.2)		(5.7)	(7.9)		
30-day mortality		317	641	<0.001	389	569	<0.001	411	447	<0.001	418	483	<0.001	0.025
		(1.6)	(3.9)		(1.7)	(4.3)		(1.6)	(4.1)		(1.6)	(4.9)		
Bleeding		65	223	<0.001	92	168	<0.001	93	192	<0.001	84	136	<0.001	0.110
		(0.3)	(1.3)		(0.4)	(1.3)		(0.4)	(1.8)		(0.3)	(1.4)		
MACE		284	524	<0.001	347	477	<0.001	367	368	<0.001	334	430	<0.001	<0.001
		(1.4)	(3.1)		(1.5)	(3.6)		(1.4)	(3.4)		(1.2)	(4.3)		

Table 2: Clinical and procedural demographics stratified by access site and Centre Total Volume.

Volume of TFA only or TRA only procedures performed yearly by center (CTV)		**1. Lowest volume N=37,425 (71-682 procedures)**			**2. lower-mid volume N=37,474 (717-1296 procedures)**			**3. upper-mid volume N=37,306 (1301-1603 procedures)**			**4. Highest volume N=36,960 (1633-2944 procedures)**			**P-value for same effect size over groups**
		TRA	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		
All procedures, N		21,581	15,844		23,066	14,408		24,645	12,661		28,084	8,876		
		Mean (SD)	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	
Age		65.1 (11.8)	66.5 (11.8)	<0.001	64.3 (12.1)	66.2 (12.3)	<0.001	63.9 (12.0)	65.5 (12.4)	<0.001	64.2 (12.0)	66.2 (12.4)	<0.001	0.020
		N (%)	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	
Sex	-Male	16,357 (75.8)	11,278 (71.2)	<0.001	17,572 (76.2)	10,298 (71.5)	<0.001	18,809 (76.3)	8,943 (70.6)	<0.001	21,226 (75.6)	6,156 (69.4)	<0.001	0.091
	-Female	5,224 (24.2)	4,566 (28.8)		5,494 (23.8)	4,110 (28.5)		5,836 (23.7)	3,718 (29.4)		6,858 (24.4)	2,720 (30.6)		
Indication	-Stable angina	8,191 (38.0)	6,691 (42.2)	<0.001	6,456 (28.0)	5,178 (35.9)	<0.001	7,619 (30.9)	4,467 (35.3)	<0.001	9,404 (33.5)	3,558 (40.1)	<0.001	<0.001
	-UA/NSTEMI	10,565 (49.0)	6,782 (42.8)		8,560 (37.1)	4,803 (33.3)		8,398 (34.1)	3,669 (29.0)		10,262 (36.5)	2,833 (31.9)		
	-STEMI	2,825 (13.1)	2,371 (15.0)		8,050 (34.9)	4,427 (30.7)		8,628 (35.0)	4,525 (35.7)		8,418 (30.0)	2,485 (28.0)		
Shock		240 (1.1)	442 (2.8)	<0.001	446 (2.0)	886 (6.2)	<0.001	354 (1.4)	677 (5.4)	<0.001	273 (1.0)	509 (5.7)	<0.001	<0.001
Myocardial infarction		5,571 (26.8)	4,249 (31.1)	<0.001	4,701 (22.5)	3,907 (29.5)	<0.001	5,250 (22.6)	3,707 (31.1)	<0.001	6,325 (23.0)	2,916 (34.2)	<0.001	<0.001
Coronary artery bypass graft		1,018 (5.3)	1,947 (14.7)	<0.001	757 (4.6)	1,684 (14.8)	<0.001	1,040 (8.2)	1,357 (19.8)	<0.001	1,464 (5.4)	1,590 (18.6)	<0.001	<0.001
Diabetes		4,337 (20.6)	3,247 (22.3)	<0.001	4,202 (18.7)	3,231 (23.5)	<0.001	4,438 (18.4)	2,690 (21.8)	<0.001	5,196 (20.3)	2,073 (27.0)	<0.001	<0.001
Hypercholesterolemia		11,787 (56.5)	8,343 (54.7)	<0.001	12,088 (54.5)	7,603 (55.4)	0.086	14,859 (61.3)	7,508 (61.3)	0.994	12,585 (48.8)	3,817 (48.5)	0.652	0.004
Hypertension		11,613 (55.6)	8,508 (55.8)	0.780	12,254 (55.2)	8,411 (61.3)	<0.001	13,046 (53.8)	7,106 (58.0)	<0.001	13,638 (52.9)	4,585 (58.2)	<0.001	<0.001
Renal	-Normal	20,395 (98.0)	14,375 (95.9)	<0.001	21,396 (98.1)	13,015 (95.5)	<0.001	23,629 (98.5)	11,587 (96.0)	<0.001	26,237 (98.6)	7,979 (96.0)	<0.001	<0.001
	-High creatinine	296 (1.4)	430 (2.9)		304 (1.4)	326 (2.4)		235 (1.0)	258 (2.1)		258 (1.0)	172 (2.1)		
	-Dialysis	111 (0.5)	183 (1.2)		112 (0.5)	292 (2.1)		125 (0.5)	228 (1.9)		105 (0.4)	158 (1.9)		
Smoking		12,475 (62.6)	8,527 (62.2)	0.482	13,694 (66.2)	7,941 (63.4)	<0.001	15,254 (64.9)	6,700 (57.7)	<0.001	15,869 (61.7)	4,595 (59.5)	<0.001	<0.001
Glycoprotein IIb/IIIa		3,445	2,423	0.904	5,214	2,496	<0.001	4,758	2,056	<0.001	4,609	1,477	0.400	<0.001

inhibitors		(16.0)	(16.1)		(23.5)	(18.0)		(20.5)	(18.1)		(16.7)	(17.1)		
Intra-aortic balloon pump		95	273	<0.001	234	514	<0.001	187	493	<0.001	121	287	<0.001	<0.001
		(0.4)	(1.8)		(1.0)	(3.6)		(0.8)	(4.5)		(0.4)	(3.3)		
Cardiopulmonary support		20	47	<0.001	20	44	<0.001	7	15	<0.001	17	17	<0.001	0.926
		(0.1)	(0.3)		(0.1)	(0.3)		(0.0)	(0.1)		(0.1)	(0.2)		
Inotropes		94	190	<0.001	190	289	<0.001	113	153	<0.001	101	177	<0.001	<0.001
		(0.4)	(1.2)		(0.8)	(2.0)		(0.5)	(1.4)		(0.4)	(2.0)		
Ventilated		222	340	<0.001	228	570	<0.001	160	406	<0.001	281	427	<0.001	<0.001
		(1.1)	(2.4)		(1.1)	(4.2)		(0.8)	(4.4)		(1.0)	(5.0)		
Stents	-BMS only	2,859	1,682	<0.001	3,148	1,683	<0.001	2,964	1,568	<0.001	2,654	987	<0.001	<0.001
		(13.6)	(11.3)		(14.6)	(12.7)		(12.4)	(12.8)		(9.6)	(11.3)		
	-DES only	15,907	11,697		16,502	10,080		18,352	9,111		21,833	6,575		
		(75.8)	(78.3)		(76.4)	(75.9)		(76.9)	(74.5)		(78.6)	(75.4)		
	-BMS and DES	748	331		401	255		546	276		455	153		
		(3.6)	(2.2)		(1.9)	(1.9)		(2.3)	(2.3)		(1.6)	(1.8)		
LVEF	-Good (>50%)	9,198	6,590	<0.001	7,176	3,262	<0.001	8,606	4,423	<0.001	9,981	2,973	<0.001	<0.001
		(76.1)	(72.1)		(67.8)	(62.7)		(72.4)	(69.3)		(71.8)	(65.0)		
	-Fair (30-50%)	2,335	2,062		2,701	1,403		2,708	1,502		3,182	1,109		
		(19.3)	(22.6)		(25.5)	(27.0)		(22.8)	(23.5)		(22.9)	(24.2)		
	-Poor (<30%)	549	487		709	534		574	458		738	492		
		(4.5)	(5.3)		(6.7)	(10.3)		(4.8)	(7.2)		(5.3)	(10.8)		
30-day mortality		259	399	<0.001	449	657	<0.001	392	639	<0.001	435	445	<0.001	<0.001
		(1.2)	(2.6)		(2.0)	(4.7)		(1.6)	(5.3)		(1.6)	(5.1)		
Bleeding		78	186	<0.001	93	267	<0.001	104	172	<0.001	59	94	<0.001	0.048
		(0.4)	(1.2)		(0.4)	(1.9)		(0.4)	(1.4)		(0.2)	(1.1)		
MACE		235	318	<0.001	366	552	<0.001	372	584	<0.001	359	345	<0.001	<0.001
		(1.1)	(2.0)		(1.6)	(3.9)		(1.6)	(4.9)		(1.3)	(3.9)		

Table 3: Clinical and procedural demographics stratified by access site and Operator Radial Volume.

Proportion of procedures performed via TRA yearly, by operator (ORP)		**1. Lowest proportion N=25,754 (0-25% TRA procedures)**			**2. lower-mid proportion N=8,956 (25-50% TRA procedures)**			**3. upper-mid proportion N=34,491 (50-75% TRA procedures)**			**4. Highest proportion N=79,964 (75-100% TRA procedures)**			**P-value for same effect size over groups**
		TRA	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		
All procedures, N		2,008	23,746		3,415	5,541		22,843	11,648		69,110	10,854		
		Mean (SD)	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	
Age		64.6 (12.1)	65.6 (12.0)	<0.001	63.5 (11.8)	65.4 (12.4)	<0.001	64.3 (12.1)	66.7 (12.2)	<0.001	64.4 (11.9)	67.1 (12.3)	<0.001	<0.001
		N (%)	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	
Sex	-Male	1,583 (78.8)	17,594 (74.1)	<0.001	2,757 (80.7)	4,011 (72.4)	<0.001	17,564 (76.9)	7,936 (68.1)	<0.001	52,060 (75.3)	7,134 (65.7)	<0.001	0.012
	-Female	425 (21.2)	6,152 (25.9)		658 (19.3)	1,530 (27.6)		5,279 (23.1)	3,712 (31.9)		17,050 (24.7)	3,720 (34.3)		
Indication	-Stable angina	859 (42.8)	9,270 (39.0)	<0.001	1,350 (39.5)	2,184 (39.4)	<0.001	7,662 (33.5)	4,433 (38.1)	<0.001	21,799 (31.5)	4,007 (36.9)	<0.001	<0.001
	-UA/NSTEMI	837 (41.7)	8,314 (35.0)		1,210 (35.4)	1,655 (29.9)		8,714 (38.1)	4,179 (35.9)		27,024 (39.1)	3,939 (36.3)		
	-STEMI	312 (15.5)	6,162 (25.9)		855 (25.0)	1,702 (30.7)		6,467 (28.3)	3,036 (26.1)		20,287 (29.4)	2,908 (26.8)		
Shock		21 (1.1)	585 (2.5)	<0.001	38 (1.1)	244 (4.4)	<0.001	233 (1.0)	692 (6.0)	<0.001	1,021 (1.5)	993 (9.2)	<0.001	<0.001
Myocardial infarction		544 (28.0)	5,427 (25.3)	0.008	759 (23.1)	1,536 (29.2)	<0.001	4,983 (23.6)	3,806 (36.1)	<0.001	15,561 (23.6)	4,010 (39.9)	<0.001	<0.001
Coronary artery bypass graft		117 (7.5)	1,997 (11.1)	<0.001	127 (5.0)	654 (15.4)	<0.001	986 (5.3)	1,937 (20.4)	<0.001	3,049 (5.7)	1,990 (24.1)	<0.001	<0.001
Diabetes		467 (24.2)	4,445 (20.4)	<0.001	746 (23.1)	1,300 (24.9)	0.06	4,546 (20.8)	2,906 (26.2)	<0.001	12,414 (18.8)	2,590 (25.5)	<0.001	<0.001
Hypercholesterolemia		1,192 (61.2)	11,888 (52.6)	<0.001	1,894 (58.5)	2,965 (56.3)	0.055	11,621 (53.5)	6,387 (58.0)	<0.001	36,612 (55.3)	6,031 (59.1)	<0.001	<0.001
Hypertension		1,199 (61.6)	12,448 (55.1)	<0.001	1,941 (59.9)	3,144 (59.7)	0.876	11,992 (55.2)	6,814 (61.8)	<0.001	35,419 (53.5)	6,204 (60.8)	<0.001	<0.001
Renal	-Normal	1,883 (97.5)	21,612 (96.9)	0.298	3,208 (97.6)	5,090 (95.7)	<0.001	21,680 (98.0)	10,564 (94.5)	<0.001	64,886 (98.5)	9,690 (94.9)	<0.001	<0.001
	-High creatinine	29 (1.5)	449 (2.0)		44 (1.3)	121 (2.3)		297 (1.3)	340 (3.0)		723 (1.1)	276 (2.7)		
	-Dialysis	20 (1.0)	233 (1.0)		36 (1.1)	109 (2.0)		143 (0.6)	271 (2.4)		254 (0.4)	248 (2.4)		
Smoking		1,193 (65.8)	12,645 (61.2)	<0.001	1,930 (62.4)	2,907 (58.9)	0.002	13,009 (62.7)	6,166 (59.9)	<0.001	41,160 (64.1)	6,045 (62.6)	0.003	0.067
Glycoprotein IIb/IIIa		187	3,407	<0.001	478	1,085	<0.001	4,484	2,107	0.002	12,877	1,853	<0.001	<0.001

inhibitors		(9.6)	(15.5)		(14.6)	(20.4)		(20.4)	(19.0)		(19.1)	(17.7)		
Intra-aortic balloon pump		6	425	<0.001	18	144	<0.001	159	403	<0.001	454	595	<0.001	<0.001
		(0.3)	(1.9)		(0.6)	(2.8)		(0.7)	(3.6)		(0.7)	(5.7)		
Cardiopulmonary support		2	39	0.663	1	13	0.036	6	23	<0.001	55	48	<0.001	0.469
		(0.1)	(0.2)		(<0.1)	(0.2)		(<0.1)	(0.2)		(0.1)	(0.5)		
Inotropes		10	195	0.134	4	61	<0.001	89	197	<0.001	395	356	<0.001	0.002
		(0.5)	(0.9)		(0.1)	(1.2)		(0.4)	(1.8)		(0.6)	(3.4)		
Ventilated		15	398	<0.001	14	143	<0.001	176	564	<0.001	686	638	<0.001	0.013
		(0.8)	(1.9)		(0.5)	(2.9)		(0.9)	(5.5)		(1.1)	(6.6)		
Stents	-BMS only	238	2,392	0.176	458	728	0.023	2,638	1,415	<0.001	8,291	1,385	<0.001	<0.001
		(12.3)	(10.7)		(13.7)	(13.4)		(12.0)	(12.7)		(12.4)	(13.4)		
	-DES only	1,524	17,880		2,592	4,118		17,269	8,129		51,209	7,336		
		(79.0)	(80.3)		(77.8)	(76.1)		(78.4)	(73.1)		(76.5)	(70.8)		
	-BMS and DES	30	390		57	115		401	270		1,662	240		
		(1.6)	(1.8)		(1.7)	(2.1)		(1.8)	(2.4)		(2.5)	(2.3)		
LVEF	-Good (>50%)	683	8,179	0.074	1,213	1,800	<0.001	7,542	3,598	<0.001	25,523	3,671	<0.001	<0.001
		(76.7)	(75.1)		(78.9)	(71.5)		(71.8)	(62.8)		(71.8)	(59.7)		
	-Fair (30-50%)	159	2,235		261	565		2,343	1,539		8,163	1,737		
		(17.8)	(20.5)		(17.0)	(22.4)		(22.3)	(26.9)		(23.0)	(28.2)		
	-Poor (<30%)	49	484		63	152		612	591		1,846	744		
		(5.5)	(4.4)		(4.1)	(6.0)		(5.8)	(10.3)		(5.2)	(12.1)		
30-day mortality		42	550	0.561	44	191	<0.001	322	635	<0.001	1,127	764	<0.001	<0.001
		(2.2)	(2.4)		(1.4)	(3.6)		(1.5)	(5.6)		(1.7)	(7.2)		
Bleeding		6	291	<0.001	6	48	<0.001	85	186	<0.001	237	194	<0.001	0.676
		(0.3)	(1.3)		(0.2)	(0.9)		(0.4)	(1.6)		(0.4)	(1.8)		
MACE		30	516	0.052	38	195	<0.001	314	508	<0.001	950	580	<0.001	<0.001
		(1.5)	(2.2)		(1.1)	(3.6)		(1.4)	(4.4)		(1.4)	(5.4)		

Table 4: Clinical and procedural demographics stratified by access site and Centre Radial Proportion.

Proportion of procedures performed via TRA yearly, by center (CRP)		**1. Lowest proportion N=12,846 (0-25% TRA procedures)**			**2. lower-mid proportion N=19,478 (25-50% TRA procedures)**			**3. upper-mid proportion N=53,039 (50-75% TRA procedures)**			**4. Highest proportion N=63,802 (75-100% TRA procedures)**			**P-value for same effect size over groups**
		TRA	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		**TRA**	**TFA**		
All procedures, N		1,864	10,982		7,119	12,359		35,289	17,750		53,104	10,698		
		Mean (SD)	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	**Mean (SD)**	**Mean (SD)**	**p-value**	
Age		65.8 (11.6)	66.6 (12.0)	0.004	64.4 (12.1)	65.7 (12.2)	<0.001	64.2 (12.0)	65.9 (12.3)	<0.001	64.4 (11.9)	66.6 (12.2)	<0.001	<0.001
		N (%)	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**	
Sex	-Male	1,485 (79.7)	8,046 (73.3)	<0.001	5,504 (77.3)	9,021 (73.0)	<0.001	27,155 (77.0)	12,442 (70.1)	<0.001	39,820 (75.0)	7,166 (67.0)	<0.001	0.002
	-Female	379 (20.3)	2,936 (26.7)		1,615 (22.7)	3,338 (27.0)		8,134 (23.0)	5,308 (29.9)		13,284 (25.0)	3,532 (33.0)		
Indication	-Stable angina	878 (47.1)	4,802 (43.7)	0.024	2,475 (34.8)	4,436 (35.9)	<0.001	11,825 (33.5)	6,718 (37.8)	<0.001	16,492 (31.1)	3,938 (36.8)	<0.001	<0.001
	-UA/NSTEMI	685 (36.7)	4,260 (38.8)		2,770 (38.9)	4,238 (34.3)		12,930 (36.6)	5,654 (31.9)		21,400 (40.3)	3,935 (36.8)		
	- STEMI	301 (16.1)	1,920 (17.5)		1,874 (26.3)	3,685 (29.8)		10,534 (29.9)	5,378 (30.3)		15,212 (28.6)	2,825 (26.4)		
Shock		22 (1.2)	244 (2.3)	0.004	106 (1.5)	490 (4.0)	<0.001	456 (1.3)	977 (5.5)	<0.001	729 (1.4)	803 (7.5)	<0.001	<0.001
Myocardial infarction		518 (28.8)	2,646 (28.8)	0.998	1,602 (23.9)	3,200 (27.0)	<0.001	7,650 (23.8)	5,152 (32.0)	<0.001	12,077 (23.4)	3,781 (37.0)	<0.001	<0.001
Coronary artery bypass graft		87 (5.9)	1,130 (12.9)	<0.001	342 (6.8)	1,188 (14.5)	<0.001	1,561 (5.7)	2,500 (17.3)	<0.001	2,289 (5.5)	1,760 (20.5)	<0.001	<0.001
Diabetes		466 (25.7)	2,313 (23.1)	0.019	1,392 (20.1)	2,535 (21.2)	0.062	6,703 (20.9)	3,901 (24.5)	<0.001	9,612 (18.4)	2,492 (23.9)	<0.001	<0.001
Hypercholesterolemia		1,163 (63.0)	6,159 (57.4)	<0.001	3,990 (58.0)	6,493 (55.2)	<0.001	17,895 (54.3)	8,782 (53.7)	0.176	28,271 (54.9)	5,837 (57.0)	<0.001	<0.001
Hypertension		1,224 (66.3)	6,471 (60.3)	<0.001	3,999 (58.2)	6,708 (57.0)	0.126	17,881 (54.3)	9,333 (57.1)	<0.001	27,447 (53.3)	6,098 (59.6)	<0.001	<0.001
Renal	-Normal	1,728 (96.5)	9,973 (96.6)	0.834	6,702 (97.5)	11,247 (95.6)	<0.001	32,579 (98.2)	15,992 (95.7)	<0.001	50,648 (98.6)	9,744 (95.5)	<0.001	<0.001
	-High creatinine	44 (2.5)	231 (2.2)		122 (1.8)	324 (2.8)		398 (1.2)	367 (2.2)		529 (1.0)	264 (2.6)		
	-Dialysis	19 (1.1)	115 (1.1)		47 (0.7)	192 (1.6)		191 (0.6)	359 (2.1)		196 (0.4)	195 (1.9)		
Smoking		1,113 (67.0)	6,059 (65.0)	0.132	3,915 (59.9)	6,074 (54.5)	<0.001	19,815 (63.2)	9,478 (62.3)	0.061	32,449 (64.5)	6,152 (62.3)	<0.001	<0.001
Glycoprotein IIb/IIIa		149	1,063	0.004	1,121	2,041	0.066	7,074	3,549	0.209	9,682	1,799	0.002	<0.001

inhibitors		(8.1)	(10.3)		(16.3)	(17.4)		(21.2)	(21.6)		(18.5)	(17.2)		
Intra-aortic balloon pump		4	190	<0.001	70	328	<0.001	247	564	<0.001	316	485	<0.001	<0.001
		(0.2)	(1.8)		(1.1)	(2.9)		(0.7)	(3.4)		(0.6)	(4.6)		
Circulatory support		1	22	0.274	1	26	<0.001	19	25	0.002	43	50	<0.001	0.092
		(0.1)	(0.2)		(<0.1)	(0.2)		(0.1)	(0.2)		(0.1)	(0.5)		
Inotropes		3	82	0.006	33	183	<0.001	114	237	<0.001	348	307	<0.001	0.497
		(0.2)	(0.8)		(0.5)	(1.6)		(0.3)	(1.4)		(0.7)	(2.9)		
Ventilated		14	221	<0.001	63	315	<0.001	274	671	<0.001	540	536	<0.001	<0.001
		(0.8)	(2.2)		(1.1)	(3.1)		(0.9)	(4.4)		(1.1)	(5.4)		
Stents	-BMS only	211	1,141	0.006	796	1,385	0.21	4,296	2,162	<0.001	6,322	1,232	<0.001	<0.001
		(11.8)	(11.3)		(11.8)	(11.7)		(12.6)	(12.8)		(12.2)	(11.9)		
	-DES only	1,438	7,998		5,306	9,261		26,387	12,702		39,463	7,502		
		(80.4)	(79.2)		(78.6)	(78.4)		(77.7)	(75.3)		(76.3)	(72.2)		
	-BMS and DES	38	162		177	268		613	332		1,322	253		
		(2.1)	(1.6)		(2.6)	(2.3)		(1.8)	(2.0)		(2.6)	(2.4)		
LVEF	-Good (>50%)	590	3,938	0.937	2,273	3,861	<0.001	13,159	5,767	<0.001	18,939	3,682	<0.001	<0.001
		(76.1)	(75.5)		(81.2)	(75.8)		(73.5)	(65.5)		(70.2)	(59.6)		
	-Fair (30-50%)	147	1,016		401	998		3,855	2,290		6,523	1,772		
		(19.0)	(19.5)		(14.3)	(19.6)		(21.5)	(26.0)		(24.2)	(28.7)		
	-Poor (<30%)	38	259		125	235		888	754		1,519	723		
		(4.9)	(5.0)		(4.5)	(4.6)		(5.0)	(8.6)		(5.6)	(11.7)		
30-day mortality		33	229	0.484	112	449	<0.001	541	818	<0.001	849	644	<0.001	<0.001
		(1.9)	(2.2)		(1.6)	(3.8)		(1.6)	(4.7)		(1.6)	(6.1)		
Bleeding		18	182	0.034	29	135	<0.001	101	198	<0.001	186	204	<0.001	<0.001
		(1.0)	(1.7)		(0.4)	(1.1)		(0.3)	(1.1)		(0.4)	(1.9)		
MACE		29	229	0.158	105	403	<0.001	471	637	<0.001	727	530	<0.001	<0.001
		(1.6)	(2.1)		(1.5)	(3.4)		(1.4)	(3.7)		(1.4)	(5.0)		

Figure 1: Flow chart of cohort selection, data processing and analysis.

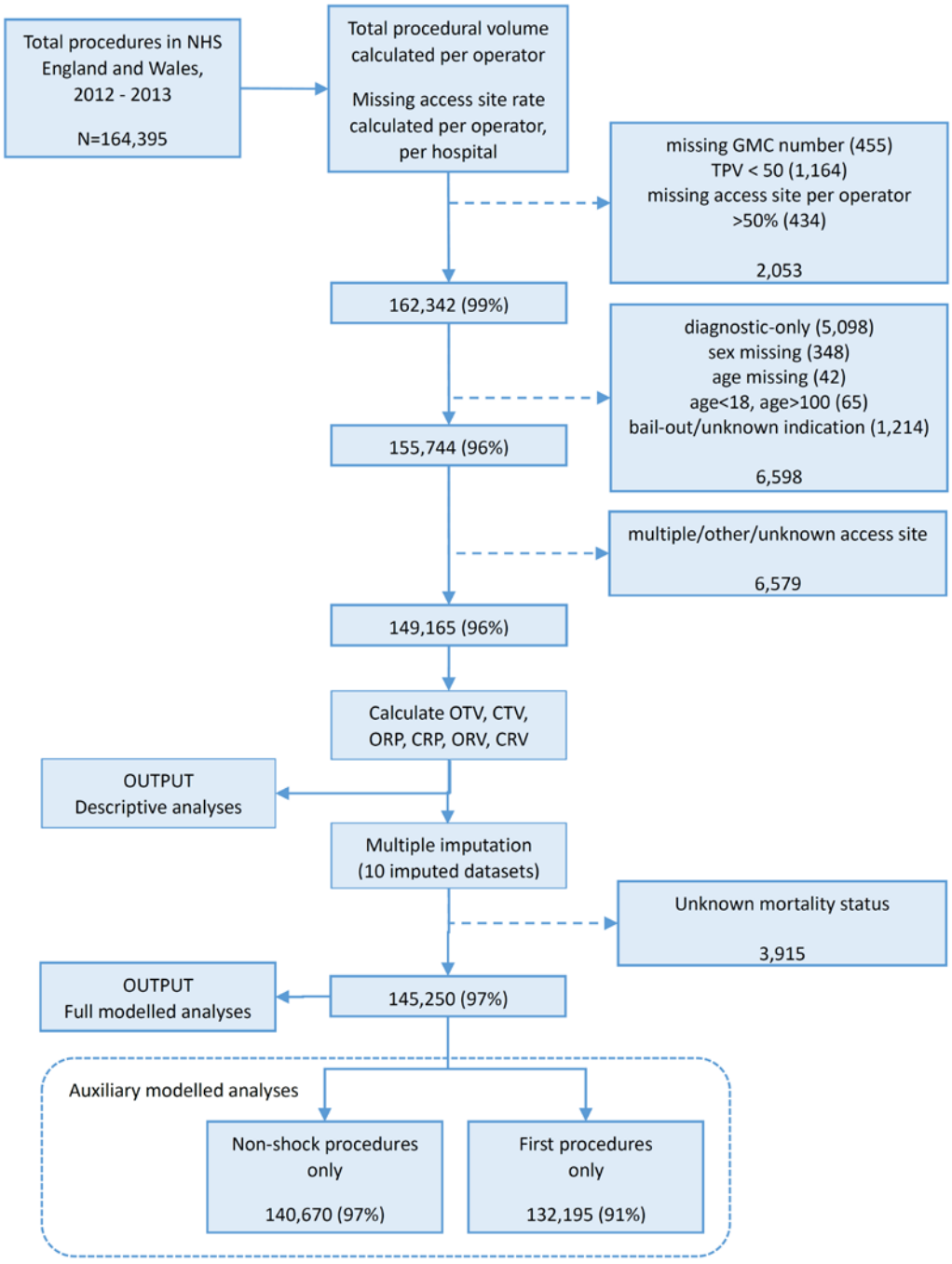

Figure 2: Yearly Radial Proportion against Total Volume, by operator (ORP vs OTV) and by centre (CRP vs CTV).

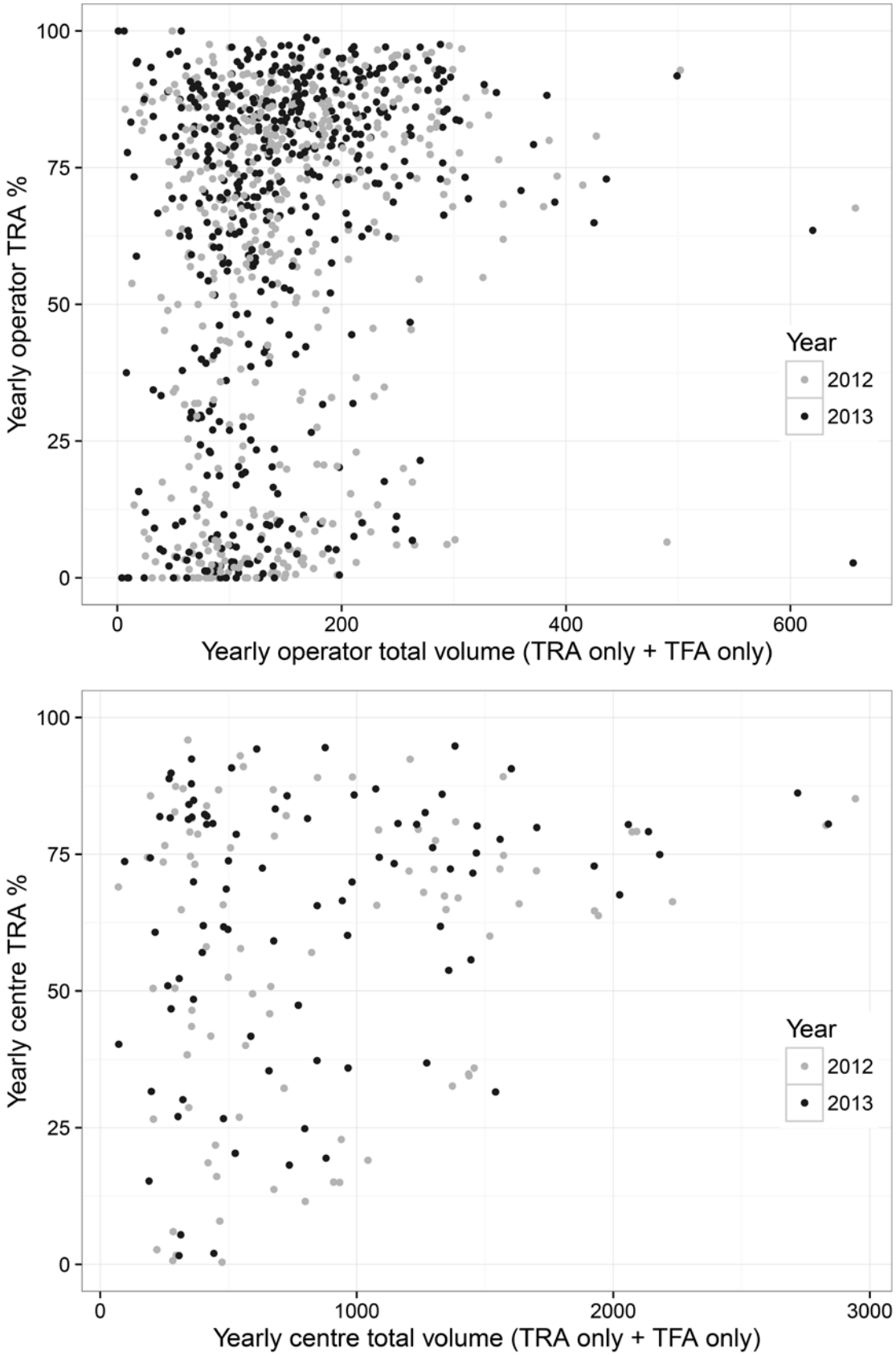

Figure 3: Procedures according to access site by year quarter

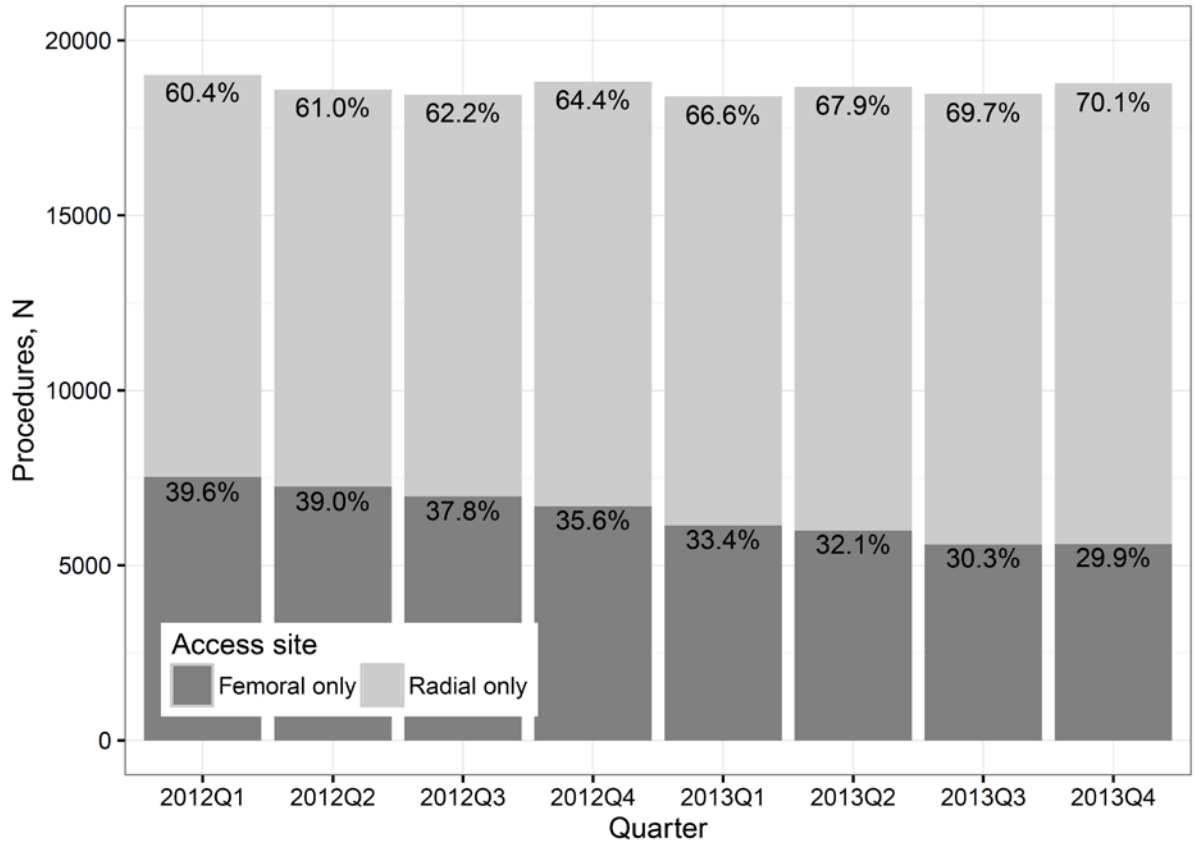
20000
15000
10000
5000
0
Procedures, N
60.4%
61.0%
62.2%
64.4%
66.6%
67.9%
69.7%
70.1%
39.6%
39.0%
37.8%
35.6%
33.4%
32.1%
30.3%
29.9%
Access site
Femoral only
Radial only
2012Q1
2012Q2
2012Q3
2012Q4
2013Q1
2013Q2
2013Q3
2013Q4
Quarter

Figure 4: Relationship between access site and 30-day mortality against different experience variables, after adjustment for clinical confounders and other experience variables.