Incidence, determinants and outcomes of left and right radial access use in patients undergoing percutaneous coronary intervention in the United Kingdom, a national perspective using the British Cardiovascular Intervention Society (BCIS) dataset

Short Running Title: left or right radial access and clinical outcomes

Muhammad Rashid MBBS\(^1\), Claire Lawson PhD\(^1\), Jessica Potts MSc\(^1\), Evangelos Kontopantelis PhD\(^3\), Chun S Kwok MBBS\(^1,2\), Olivier F. Bertrand\(^4\), Ahmad Shoaib MBBS, MD\(^1,2\), Peter Ludman MD\(^3\), Tim Kinnaird MBBCh\(^6\), Mark de Belder MD\(^7\), James Nolan MD\(^1,2\) and Mamas Mamas BM,BCh, DPhil\(^1,2\)

1. Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute of Primary Care and Health Sciences, Keele University, UK
2. Academic Department of Cardiology, Royal Stoke Hospital, University Hospital North Midlands, Stoke-On-Tent, UK
3. Faculty of Biology, Medicine and Health, University of Manchester, Manchester
4. Quebec Heart-Lung Institute, Laval University, Quebec City, Quebec, Canada
5. Queen Elizabeth Hospital, Birmingham, UK
6. Department of Cardiology, University Hospital of Wales, Cardiff, UK
7. The James Cook University Hospital, Middlesbrough, UK

Corresponding Author:

Dr Muhammad Rashid
Keele Cardiovascular Research Group
Keele University, Stoke-on-Trent,
United Kingdom, ST4 7QB
Email: doctorrashid7@gmail.com
Phone: +441782671621
Fax: +441782674467
Abstract

Background: Left radial access (LRA) has been shown to offer procedural advantages over right radial access (RRA) in PCI although few data exist from a national perspective around its use and association with clinical outcomes.

Objectives: To determine the relationships between LRA or RRA and clinical outcomes using the British Cardiovascular Intervention Society (BCIS) database.

Methods: We investigated the relationship between use of LRA or RRA and clinical outcomes of in-hospital or 30-day mortality, Major Adverse Cardiovascular Events (MACE), in-hospital stroke and major bleeding complications in patients undergoing PCI between 2007 to 2014.

Results: Out of 342,806 cases identified, 328,495 (96%) were RRA and 14,311 (4%) were LRA. Use of LRA increased from 3.2% to 4.6% between 2007 to 2014. In patients undergoing a repeat PCI procedure, the use of RRA dropped to 72% at second procedure and was even lower in females (65%) and patients age > 75 (70%). Use of LRA (compared to RRA) was not associated with significant differences in-hospital mortality (OR 1.19 95% CI 0.90-1.57 p=0.20), 30-day mortality (OR 1.17 95%CI 0.93-1.74 p=0.16), MACE (OR 1.06 95%CI 0.86-1.32 p=0.56), major bleeding (OR 1.22 95%CI 0.87-1.77 p=0.24). In propensity match analysis, LRA was associated with a significant decrease in in-hospital stroke (average treatment effect coefficient 0.000977 95%CI -0.001654 to -0.00299, p=0.005).

Conclusion: In this large PCI database, use of LRA is limited compared to RRA but conveys no increased risk of adverse outcomes but may be associated with reduction in PCI related stroke complications.

Keywords: Right radial access, Left radial access, Successive PCI, in-hospital stroke, major bleeding, Major Adverse Cardiac Events (MACE), in hospital and 30-day mortality.
Condensed abstract:

Left radial access (LRA) has been shown to offer procedural efficacy over right radial access (RRA). In this study, we explored the national use of LRA, access site switch in patients undergoing repeat PCI after RRA and association between use of either access with clinical outcomes. Our results suggest that use of LRA remains modestly low at 4% compared to RRA (96%). Use of LRA is not associated with increased risk of in-hospital or 30-day mortality, major adverse cardiovascular events or major bleeding complications but may be associated with decreased risk of PCI related stroke complication. Despite of these advantages, femoral access is still predominantly (23.5%) used in patients requiring repeat PCI following a first RRA PCI procedure compared to LRA (4.5%).

Clinical Perspective:

WHAT IS KNOWN? Use of left radial access (LRA) has been shown to have better procedural efficacy compared to right radial access (RRA).

WHAT IS NEW? Using the BCIS registry, we investigated the temporal changes in use of LRA and its association with clinical outcomes. We found that use of LRA remains modestly low in national practice (4%) compared to RRA (96%). Approximately one third of the patients undergoing RRA PCI at the first procedure will have their access changed to femoral route at the subsequent PCI. LRA does not confer patients to increase risk of in-hospital or 30-day mortality, MACE and major bleeding complications. However, it may be associated with reduced risk of PCI related in-hospital stroke complications.

WHAT IS NEXT? LRA offers a safe alternative access site and may help to reduce PCI related stroke complications. A greater understanding for the reasons of higher access site switch from radial to femoral rather than contralateral arm is needed with educational program development to improve familiarity amongst operators for the LRA approach.

Abbreviations: PCI (percutaneous coronary intervention), TRA (Transradial access), TFA (Transfemoral access), LRA (left radial access), RRA (right radial access), BCIS (British Cardiovascular Intervention Society),
Introduction:

The radial artery is now the most common vascular access site utilised for percutaneous coronary interventions (PCI) across many European (1), Canadian and South Asian countries (2, 3) and continues to gain popularity in the US (4, 5). The main advantages of transradial access (TRA) over transfemoral access (TFA) include a lower incidence of vascular complications, significant reductions in major bleeding, a lower rate of MACE and, in some settings, death (6-8) as well as earlier ambulation, shorter hospital stay and greater patient satisfaction (9, 10). Most radial operators use the right radial access (RRA) as their initial access site due to ease of working on the right hand side of the patients and catheter lab setup (11). However, radial operators may need to switch to the left side in the event of radial artery spasm (12), radial artery occlusion (13), the presence of arteriovenous shunt in the right arm, or presence of extreme tortuosity in the right forearm or right subclavian artery (14, 15). Left radial access (LRA) also offers much more favourable vascular anatomy particularly in short stature patients or those with previous coronary artery bypass grafts resulting in lesser catheter manipulation, shorter procedure time and a theoretically smaller risk of procedure related stroke(16-19).

Data from published studies comparing the RRA versus LRA have only compared the procedural efficacy such as procedure time, contrast use, fluoroscopy time and crossover to femoral access reporting conflicting results(18,20). The TALENT study investigators randomised 1,540 patients in two hospitals to RRA or LRA for either diagnostic coronary angiography or PCI. In the diagnostic group, LRA was associated with lower fluoroscopy time and lower dose area product; however, there were no differences in either of these primary endpoints in patients undergoing PCI(21). Another study comparing RRA versus LRA for primary endpoints of radiation exposure and operator discomfort reported decreased radiation exposure to the operators in the LRA group albeit at the expense of increase operator discomfort (17). The majority of these studies were limited to single centres and small sample sizes, therefore, one cannot determine whether there are any clinically relevant differences between either access site.

As the population requiring PCI grows and ages, it is likely that LRA will become more commonplace. There are few data that describe the differences in patient and clinical
characteristics relating to the use of LRA compared to RRA, whether this practice is changing over time nationally, how multiple successive procedures influences the use of LRA or importantly whether the use of LRA is associated with different risks to patients. This study used a large national registry of all PCI procedures to answer these questions.

**Methods:**

*Study population*

We used data from the British Cardiovascular Intervention Society (BCIS) registry to define the patient cohort and study variables. The BCIS registry is a national registry that prospectively collects data around the clinical, procedural and outcome of almost all PCI undertaken in the United Kingdom and is managed by the National Institute of Cardiovascular Research Outcome (NICOR)(22-24). Mortality outcomes are robustly tracked via a linkage to the Office of National Statistics (ONS) using the unique national health system (NHS) number of all patients in England and Wales only. All data collected in the BCIS registry are a part of a national audit initiative by NICOR and were anonymised; therefore, ethical approval was not required for this study. The initial cohort selection was made by including all patients undergoing at least one PCI via either RRA or LRA in the United Kingdom however, as the out of hospital mortality data is not available for patients in Scotland, therefore they were excluded from the outcome analyses. Patients with femoral, brachial, multiple, unknown or missing access site information were excluded.

*Clinical characteristics*

We collected data on each patient’s baseline demographics, clinical and cardiovascular risk profile, indication for PCI, and all other aspects of interventional and pharmacological treatment administered. In order to explore the access site practice in patients undergoing repeat PCI, we undertook a sub-group analysis of patients with RRA procedure as their first procedure and tracked the access site at each subsequent procedure as RRA is most widely practised radial access.

*Outcomes*
The primary end points were in-hospital and 30-day mortality, in-hospital major bleeding (defined as a composite of blood or platelet transfusion, intracerebral haemorrhage, retroperitoneal haemorrhage, bleed resulting in cardiac tamponade, or an arterial access site bleeding requiring surgery or intervention), in-hospital Major Adverse Cardiovascular Events (MACE defined a composite of in-hospital mortality, in-hospital myocardial infarction or re-infarction and revascularization- emergency PCI or CABG) and In-hospital Stroke complications (defined as haemorrhagic, ischemic, embolic stroke or transient ischemic attack).

Statistical analysis

First, we compared the characteristics between patients with RRA and LRA used at the first procedure. We employed analysis of variance for continuous variables and Fisher’s exact tests for binary/categorical variables. The predictive analysis was undertaken using backward stepwise approach by including all the variables as above in the MLR and then removing the variables with significance above the defined threshold of (p>0.011).

In order to protect against the biases arising from informative missing data mechanisms, we used multiple imputation with chained equations framework to impute for all variables with missing information. The patients with missing information on mortality outcomes were excluded before the imputation, since the inclusion of these cases in the imputation model makes no difference (25). Complete variables registered in the imputation model were age, sex, access site and study outcome variables and imputed variables were indication for PCI, previous AMI, previous CABG, history of diabetes mellitus, peripheral vascular disease, previous PCI, hypercholesterolaemia, hypertension, cerebrovascular accident, renal disease, body mass index, left ventricular systolic function, smoking status, mechanical ventilation, use of intra-aortic balloon pump, pharmacological inotropic support, use of GP2b3a inhibitor, Ticagrelor, Prasugrel, bivalirudin, PCI to left main stem, multi-vessel PCI, cardiogenic shock, stent use and operator status.

The final analyses were run on the 10 datasets generated under the multiple imputation framework. The approach can deal with data missing completely at random (MCAR) or on missing at random (MAR), and not necessarily missing not at random (MNAR) scenarios, while levels of missingness are high for certain variables. However, it has been previously illustrated that multiple imputation frameworks are robust even with high levels of missingness and can offer some protection with MNAR data (26). Multivariable logistic regression (MLR)
modelling was used for risk estimation of all outcomes across both groups, adjusting for age, sex and all the other variables included in the multiple imputations. To account for any systematic differences in the baseline characteristics between the two groups, multiple imputations with propensity score matching were used to calculate the average treatment effects using the same variables as in our main MLR model. Finally, in order to minimise selection bias in LRA group, we performed a sensitivity analysis by excluding patients with previous history of CABG.

Results:

Patient characteristics and temporal changes

There were 343,725 patients undergoing PCI using radial access during the study period from which 328,495 (96%) were undertaken through the RRA and 14,311 (4%) via the LRA (Figure 1). Use of LRA access increased from 3.2% (n=527) in 2007 to 4.6% (n=3110) in 2014 (Figure 2). Temporal changes and regional variation in LRA practices are depicted in Figure 3a-3b showing a significant heterogeneity in use of LRA access amongst different primary care trust areas across Scotland, England and Wales. During the study period, the highest proportions of LRA procedures were undertaken in England with some areas performing almost 20% of their radial procedures via the LRA, whereas use of LRA access was sporadically low in Scotland (10%) and Wales (7%).

We studied the relationship between different demographic characteristics and LRA use as illustrated in Figures 4a-4d. It can be seen that LRA PCI was undertaken in Asians (27.9% n=1854) far more than in Caucasians (4.2% n=228,908) and other ethnic groups. LRA access was used relatively commonly in patients with a previous history of CABG (23.4% vs 3% with no such history). LRA access was used infrequently for patients requiring PCI for STEMI indication compared to elective PCI (1.8% vs 5.5%). We also observed a strong inverse relation between height and the use of LRA access with 6.8% of procedures undertaken via the LRA in short stature patients (height <150cm) compared to only 3.4% in taller patients (height >190cm).

Table 1 shows the demographics, cardiovascular risk profile, procedural characteristics and crude outcomes differences across the two groups. Patients in the LRA group were older and had a higher risk baseline cardiovascular profile, with an increased incidence of diabetes, hypertension, history of previous cerebrovascular event (CVA), acute myocardial infarction, coronary artery bypass grafting (CABG) and peripheral vascular disease (PVD). Patients in the
RRA access group received more aggressive pharmacotherapy with a higher rate of use of Ticagrelor, Prasugrel, Glycoprotein 2b3a inhibitors and bivalirudin. Missing data information about each variable is provided in supplementary Table 1.

Access site switch

During the study period, 35,388 patients from the radial cohort had multiple PCI procedures. RRA was used in 33,956 patients at their index PCI whereas 1,432 patients had their first PCI using LRA. In patients receiving their first PCI using RRA, subsequent successful RRA PCI was only possible in 72% of the patients. Notably, the majority of the switch from RRA was to femoral (23.5%) access instead of LRA (4.5%). However, LRA remained relatively stable between 4.5% to 6% at four or more procedures (Figure 5). We explored the patterns of access site switch during successive procedures in different subgroups and found females were less likely to undergo a subsequent procedure through the RRA approach compared to males (Figure 6a,6b) with similar trends observed in the elderly (Figure 7a, 7b).

Predictors of LRA

We studied independent predictors of LRA at any time in the stepwise multivariate analysis and found that previous CABG (OR 9.32 95%CI 7.72-11.24 P<0.001), PCI to vein graft (OR 2.10 95%CI 1.61-2.74 p<0.001), renal failure (OR 2.65 95%CI 1.63-4.30), mechanical ventilation (OR 2.61 95%CI 1.64-4.15 p<0.001), peripheral vascular disease (OR 1.81 95%CI 1.48-2.22 p<0.001), previous AMI (OR 1.29 95%CI 1.11-1.51 p<0.001), female sex (OR1.27 95%CI 1.10-1.46 p<0.001) and repeat PCI (OR 1.09 95%CI 1.05-1.35 p<0.006) were strong predictors of LRA access (Table 2).

Outcomes

Crude MACE (1.6% n=225 vs 1.3% n= 4234, p=0.004), in-hospital (0.9% n=120 vs 0.7% n=2,206, p=0.01) and 30-day mortality (1.9% n=211 vs 1.5% n=3881, p<0.001) rates were significantly higher in the LRA group but there were no differences in stroke and bleeding complications (Table 1). In our MLR analysis (Table 3), there were no differences between use of either access site and clinical outcomes, in-hospital death (OR 1.19 95% CI 0.90-1.57, p=0.20), 30-day mortality (OR 1.17 95%CI 0.93-1.74, p=0.16), MACE (OR 1.06 95%CI 0.86-1.32, p=0.56), in-hospital stroke complication (OR 0.45 95%CI 0.16-1.26, p=0.13) and major
bleeding (OR 1.22 95%CI 0.87-1.77, p=0.24). Notably, in our propensity score matching analysis (Table 4), LRA was associated with a significant decrease in in-hospital stroke risk (average treatment effect coefficient 0.000977 95%CI -0.001654 to -0.00299, p=0.005).

**Sensitivity analyses**

In our sensitivity analyses after excluding patients with previous history of CABG, we did not find any material differences in the baseline characteristics, clinical outcomes and predictors of LRA from the original analyses (supplementary tables 2-4).

**Discussion:**

To our knowledge, this is the first study describing the patterns of radial access from a national perspective over a period where access site practice has transitioned to predominantly transradial in the United Kingdom. Our results show that use of LRA has modestly increased over time in UK practice and is used more often in females, the elderly, Asian ethnicity, patients with a previous history of CABG and short stature patients. In patients undergoing repeat PCI, over one third of the patients (28%) had access site switched from RRA at each successive procedure to mainly femoral access with only a minority undergoing procedures through the contralateral arm. In our main MLR analyses, complications with LRA access were similar to those seen with RRA access with no difference in in-hospital or 30-day mortality, in-hospital MACE or major bleeding complications, although there was a significantly decreased odds of in-hospital stroke following PCI using the LRA approach in the propensity matched cohort.

In line with best available evidence from randomised trials, national bodies are recommending use of TRA instead of TFA access (27-29). RRA access is more commonly practiced by radial operators because of ergonomics of the cardiac catheter lab, previous training experience and increased operator discomfort due to the need of having to bend over to the left side of patient. On the other hand, a recent meta-analysis of 12 prospective randomised trials enrolling 6,450 patients confirmed that LRA access provides more favourable anatomy for catheter manipulation and coronary engagement translating into a small but statistically significant reduction in fluoroscopy time and contrast use(18). Despite the advantages of offering similar anatomical considerations applicable to the TFA access even early in the training(21), uptake of LRA access remains low, although there has been a marginal increase over time in the UK (3.2% to 4.6% during the period of study). We observed significant heterogeneity in LRA usage across different regions of England, Scotland and Wales. The proportions of radial procedures undertaken via the LRA varied from as low as
0.5% to 20% in England, from 2.3% to 6.9% in Wales and 0.3% to 10.2% in Scotland. We investigated independent predictors of LRA usage in the multivariate predictive analysis, and found that a history of previous CABG and PCI to a vein graft were strong predictors of LRA use. The most likely explanation for this is that LRA offers better access to grafts in patients with previous CABG compared to RRA. Similarly, factors that are associated with an increased risk of radial artery spasm and access site failure such as female gender, repeat procedure and history of peripheral vascular disease were significant predictors of LRA use.

We described the access site practice in patients undergoing repeat PCI and found that when RRA is used at the first procedure, future use of the RRA for PCI drops by 28% overall, by 35% in females and 27% in patients age >75 at a second procedure with a concomitant increase mainly in the use TFA access but with a slight increase in LRA usage. Although success rates and complication rates of repeat transradial access have been described in small case series from single centres (30-32), the utility of different radial access has not previously been reported at a national level. For example in an early series from Japan, Sakai et al described that the failure rate of repeat radial access was approximately 16% in male and 30% in women(32). More recently published data from a high volume radial centre illustrated that TRA access can be safely attempted in about 60% of cases for up to 10 procedures (30). Progressive luminal narrowing and radial artery occlusion are known to occur following transradial access and may limit the use of ipsilateral radial access for a repeat procedure(13, 33). Our study shows a higher switch rate of a RRA approach in elderly and female patients with a concomitant increase in the use of TFA and LRA access. It is possible that the higher switch from RRA to TFA was observed because the subsequent procedure was undertaken by a femoral operator instead of a radial operator. However, our analysis is from an era where more than 80% of the PCIs in the United Kingdom are undertaken via TRA, which may suggest that that this is less likely (23). The key message from our findings are that although repeat RRA access can safely be performed in the majority of cases, alternative access is used in a significant minority of patients and currently, a transfemoral approach is undertaken more commonly than the contralateral radial artery, particularly in elderly and female patients. Given the established advantages of radial access in terms of reducing major bleeding and access site complications, there may be benefits in using the LRA access site as the default in such circumstances. These observations have implications for training. Trainees should be exposed to LRA early in their training so that the potential benefits of TRA access can still be offered in the event of RRA failure.
Finally, in the clinical outcome analysis, we did not find any statistically significant differences between the use of the LRA and RRA and in-hospital or 30-day mortality, in-hospital major bleeding and MACE. We did however observe (statistically non–significant) decreased odds of in hospital stroke (OR 0.45 95%CI 0.16-1.26, p=0.13) albeit with wide confidence intervals that may reflect the low event rate, with a similar significant risk reduction in our propensity score matched cohort that was statistically significant (average treatment effect coefficient 0.000977 95%CI -0.001654 to -0.00299, p=0.005). A number of previous studies have reported on procedural outcomes of LRA versus RRA showing that LRA offers small advantage over RRA in terms of lower fluoroscopy time, radiation dose and contrast use (17, 18, 20, 21, 34). There is very little information on the association of LRA or RRA with clinical outcomes(18, 21). There is a multitude of evidence confirming the advantages of radial over femoral access in reducing major bleeding, vascular access site complications and MACE translating into mortality benefit in some clinical scenarios. With RRA access, the anatomical variations such as increase incidence of tortuosity and loops in arm and subclavian artery may require extra catheter manipulation. Additionally, during RRA access the catheter needs to be passed from the innominate artery into the ascending aorta where the right carotid comes off resulting in a theoretically increased risk of embolization of plaque into the right carotid artery resulting in embolic stroke. In contrast, LRA access offers very similar anatomy to the TFA approach as the left common carotid artery arises directly from the aortic arch. Our analysis suggests that LRA access may be associated with a lower stroke risk than the RRA and possible reasons may relate to the anatomical reasons outlined above. Given that stroke is a relatively rare event(35, 36), whilst we observe a signal, we estimate that an operator would need to undertake 1,818 PCI procedures through the LRA to avoid 1 stroke (in comparison to RRA use). Given low event rates, it is unlikely that a randomised controlled trial will ever be adequately powered to investigate this further.

Our study offers several key messages albeit with some limitations. In this study we illustrate the patterns of left and right radial access over time in a national registry. We have analysed the predictors of LRA usage and the association between use of LRA or RRA with clinical outcomes. We studied the regional variations and reported switch rates of RRA use in patients undergoing repeat PCI. One of the limitations of the BCIS dataset is that it does not collect information around procedure outcomes such as fluoroscopy time, procedure time, contrast use and operator or patient radiation dose, therefore differences between procedural outcomes could not be reported. Secondly, data around access site attempt and failure and
crossover to the contralateral radial artery is not captured which makes it difficult to ascertain if the access was used as the primary default access or because of failure to cannulate the contralateral artery for other reasons. Furthermore, the BCIS registry only started collecting operator level data from the last two years of this study period; we therefore limited analysis to patient level data. Consequently, changes in access site practice in patients undergoing repeat PCI may actually reflect differences in operator practice. Finally, our findings are observational in nature and a possibility of biases from unmeasured confounders may have contributed to the results.

**Conclusion:**

Using our national registry, we have shown that LRA access provides a safe and effective alternative access site choice compared to the RRA. There is significant variation in use of the LRA across different health care regions in the UK with higher proportions of LRA PCI being undertaken in England compared to Wales and Scotland regions. In patients undergoing repeat PCI, although TRA access was safely used in about two thirds of patients, a change to a predominantly TFA approach, particularly in females and elderly patients, was used in up to one third of patients despite established advantages of radial access in this high-risk group. Finally, we observed an important signal that LRA access may be associated with a reduced risk of stroke compared to the RRA. Future efforts need to focus around education and training to preserve radial artery patency and increase skills in the use of LRA access.

**Contributorship:**

MAM conceived the study and developed study protocol and analysis plan. MR analysed the data and drafted the paper. All authors contributed in interpretation of results and in making an important contribution to the manuscript. MR & MAM are the guarantors.

**Acknowledgement:**

None

**Disclosures:**

None
References:


