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Radial Versus Femoral Access for Acute Coronary Syndromes

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Abstract The feasibility and safety of transradial coronary intervention was demonstrated soon after the description of the transfemoral approach, despite which the use of the femoral artery still dominates in acute coronary syndrome intervention. The advantages of using the radial artery are virtual elimination of access site complications and an important reduction in bleeding, both of which are of utmost importance to the patient with myocardial infarction. Randomised controlled trials have now documented what seems inherent; that transradial intervention should bring with it an advantage in terms of morbidity and mortality in this cohort. The potential disadvantages in terms of speed of procedure and radiation exposure are negated by operator experience. Registries have illustrated that conversion on a large scale from the femoral to the transradial approach is safe and saves lives, most convincingly so in acute coronary syndrome intervention. This review discusses the potential benefits and risks of the alternative access sites in acute patients and explores how these are borne out in the published data.

Keywords PCI · Radial · ACS · Bleeding

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Introduction

In 1989, Lucien Campeau published the first 100 cases of selective coronary angiography undertaken using radial rather than femoral or brachial artery cannulation [1]. Just 6 years on, Ferdinand Kimeneij was ready to show that the transradial approach was an equally safe and practical one for coronary angioplasty [2]. He went on to demonstrate a virtual elimination of access site bleeding complications [3•]. Surprisingly, the enthusiasm for conversion from transfemoral to transradial percutaneous coronary intervention (PCI) more than 20 years later remains very variable across the developed world and perhaps the slowest uptake has been in the acute setting.

The undisputable benefit of transradial over transfemoral PCI is the reduction in vascular access site bleeding, such that targeting those patients at highest risk of bleeding should bring the greatest gain. Bleeding complications to some extent replace ischaemic complications in patients who are subjected to the most aggressive anti-coagulant and anti-platelet regimes, and hence, these are the vulnerable patients that stand to benefit. Reducing access site bleeding in acute coronary syndrome (ACS) patients, who receive high doses of aspirin and thienopyridines with or without thrombolytics, glycoprotein IIb/IIIa or factor Xa inhibitors, should certainly lead to the greatest benefit in rates of morbidity if not mortality.

Potential Advantages and Disadvantages of Transradial PCI in ACS

Over recent years, a strong association between major bleeding and adverse outcomes in acute coronary syndrome patients has been repeatedly demonstrated [4•]. Whether this is a causal association or a marker of a frail patient, avoidance of both bleeding and transfusion in this clinical setting is

paramount. Whilst a change to radial access cannot eliminate bleeding from all sources, access site complications are the commonest documented cause of blood loss post PCI [5].

The potential advantages of transradial access in urgent PCI are not however limited to bleeding complications. Amongst the sequelae of femoral artery access site complications is the need for vascular surgery. Surgery under general anaesthesia presents an additional significant mortality risk to the patient with a recent coronary artery event. Moreover, even fairly straightforward and successful vascular surgery here necessitates cessation of dual anti-platelet therapy (DAPT) for the peri-operative period, precisely when the ACS patient is at highest risk of acute vessel closure or stent thrombosis. The risk does not stop post-operatively as adequate anti-platelet therapy may not be re-instigated in a timely manner, with loading doses or at all, thus prolonging the risk of recurrent myocardial infarction or stent thrombosis. Whilst it is exceptionally rare for a radial artery complication to require surgical intervention, if this were to occur, then regional anaesthesia is feasible and bleeding easy to control with a tourniquet so that DAPT can continue uninterrupted.

The length of hospital stay, which also of course relates to overall cost to the patient, institution or health care service, is potentially reduced by use of the radial artery for PCI [6]. The transradial approach lends itself to day-case procedures in the elective setting but will also encourage early ambulation and thus a reduction in complications and an as early as possible discharge in the acute and even primary percutaneous coronary intervention (PPCI) cohort. In fact, the cost-savings derived from the transradial approach have been shown to be greatest amongst patients at higher risk for post-PCI bleeding that is in the ACS cohort [7].

Finally, patient preference is an important consideration for our conscious patients in the cardiac catheter laboratory. This naturally comes to the forefront of discussion more often in the elective setting, where the majority of patients who do have the opportunity to express an opinion, request the radial rather than femoral approach (for reasons of dignity, comfort, post-procedure cleanliness and early ambulation). This can probably be assumed to be the case in the urgent and emergency cohort too.

The disadvantages of the radial approach in acute PCI intervention are largely restricted to the operator and, as will be discussed, may only be of relevance to the inexperienced operator or during his or her learning curve. Obtaining vascular access initially may be a little slower and more prone to repeated attempts. Access to the coronary arteries with diagnostic and then an appropriate and supportive guide catheter may also take longer depending on the patient's anatomy. In certain patient groups such as the short stature and very elderly, this difficulty can persist even for the more experienced operator. These difficult patient groups are discussed below (in special considerations section). The extra time, though likely a matter of a few minutes, may be truly relevant to the patient in the clinical context of ST segment elevation myocardial infarction (STEMI).

The suggestion that more X-ray contrast and higher radiation doses result from a change to the radial approach is still disputed and has been tested as a secondary endpoint within some of the clinical trials of radial versus femoral PCI (discussed below). Again, this may only be relevant to the less experienced convert but must be incorporated into the decision-making process particularly when intervening urgently on young patients or those at significant risk of contrast nephropathy.

Of particular relevance in the ACS setting is the reduction in flexibility that can result from the use of the radial artery. Although most standard equipment is now 6 F compatible, various devices such as burrs for rotational atherectomy and some of the dedicated bifurcation stents or CTO equipment require a larger-bore guide. As most ACS PCI is undertaken as ad-hoc procedures, then the unexpected need for such equipment could necessitate change to a 7- or 8-F system usually from the femoral artery.

The final disadvantage of the radial approach is the risk of radial artery occlusion. With the larger calibre of the femoral vessels, this occurs very infrequently following transfemoral PCI. The incidence of radial artery occlusion post-intervention is somewhere between 1 and 10 % in most series [8], but this is almost always asymptomatic. Because of the dual blood supply to the hand, the risks of radial artery occlusion to the patient are simply that of needing a transfemoral procedure if a further PCI entails (remembering that staged procedures are not uncommon in ACS PCI) and of the loss of the radial artery as a conduit for CABG surgery or for AV-fistula formation for renal replacement therapy. Operators must be aware of and instigate measures to minimise the risk of radial artery occlusion such as awareness of sheath to artery ratio [9], use of hydrophilic sheaths [10] and strict monitoring of patent haemostasis and compression of the radial artery for the shortest period practicable post procedure [11].

For the radial enthusiast, it is easy to preach this list of potential benefits and to discount the 'minor inconveniences' of the radial approach. Before concluding however that acute coronary syndrome PCI should be undertaken preferentially via the radial artery worldwide, as in any intervention, an examination of the current evidence base is warranted.

The Data from Clinical Trials

The first randomised clinical trial of radial versus femoral access for PCI in patients with acute coronary syndromes was published in 1998 and did demonstrate significant reductions in access site bleeding, length of stay and hospital costs for patients in the radial group [12]. The study enrolled just

142 patients and reported no differences in myocardial infarction (MI) or death.

In the PREVAIL study, a larger but non-randomised comparison of the radial and femoral artery approaches, 1052 patients undergoing PCI of whom 40 % were ACS cases were studied [13]. A significantly lower occurrence of the primary endpoint: bleeding, stroke or access site complication, was observed in the radial group (1.96 vs 4.2 %, p=0.03). There also appeared to be a significant advantage in terms of the secondary endpoint: in-hospital death or MI/reinfarction, in the radial group (0.6 vs 3.1 %, p=0.005).

A meta-analysis of randomised studies comparing radial to femoral artery access highlighted the heterogeneity of the published trials, with many enrolling small numbers of patients, using different definitions of bleeding and including different proportions of stable and ACS patients [14]. Of the 23 studies selected for analysis, only one, the trial by Mann et al. [12], enrolled exclusively ACS patients, and six included STEMI patients only. In this meta-analysis, the authors reported that radial access reduced major bleeding by 73 % as compared to femoral access (0.05 vs 2.3 %, odds ratio [OR] 0.27 [95 % confidence interval (CI) 0.16, 0.45], p<0.001). Whilst not statistically significant, they also described a trend toward reductions in the composite of death, myocardial infarction or stroke (2.5 vs 3.8 %, OR 0.71 [95 % CI 0.49–1.01], p= 0.058) and fewer actual deaths (1.2 vs 1.8 % OR 0.74 [95 % CI 0.42–1.30], p=0.29) in the radial groups. The need for larger randomised studies focusing on cohorts at higher risk of bleeding (such as ACS patients) was emphasised.

The RIVAL study published in 2011, addressed this need, recruiting 7021 patients with acute coronary syndromes from 158 hospitals in 32 countries, and randomly assigning them to radial or femoral access [15]. There was no significant difference between the groups in the primary outcome of death, MI, stroke or non-CABG major bleeding at 30 days (128 (3.7 %) vs 139 (4.0 %), respectively, hazard ratio [HR] 0.92, 95 % CI 0.72–1.17; p=0.50). Surprisingly, in light of previous studies, there was no difference in non-CABG-related bleeding between the two groups, although large haematomas and pseudoaneurysms occurred significantly less frequently in the radial group.

A number of pre-specified subgroup analyses were undertaken in the RIVAL study, including centre volume, operator volume, STEMI versus NSTEMI and body mass index [15]. There was a significant interaction for the primary outcome, with benefit for radial access, in the highest tertile volume radial centres (HR 0.49, 95 % CI 0.28–0.87; p=0.015) and in patients treated for STEMI (0.60, 0.38–0.94; p=0.026). In the STEMI subgroup, a significant mortality benefit was also found for patients undergoing transradial intervention. In another paper, from the same study, authors reported that radiation dose (air kerma) was higher with radial than femoral access, but that these differences were present only in lower volume centres and operators [16].

Whilst the RIVAL study was clearly a landmark advance in the evidence base for the feasibility of radial PCI in ACS, the lack of overall superiority of radial access in ACS patients was disappointing to radial enthusiasts. This was attributed by many to the bleeding definitions used (exemplified by the lack of difference in bleeding outcomes despite more access site complications) and the inclusion of lower volume radial centres.

The recently published MATRIX study [17] was larger than RIVAL, randomly assigning 8404 patients with acute coronary syndrome, with or without ST-segment elevation, to radial or femoral access for coronary angiography and PCI. Patients with radial access had fewer net adverse clinical events (death, myocardial infarction, stroke or major non-CABG bleeding) compared with femoral access (410 (9.8 %) versus 486 (11.7 %); RR 0.83, 95 % CI 0.73–0.96; p=0.0092). The difference in outcome between radial and femoral access groups in this study was driven by BARC major bleeding unrelated to coronary artery bypass graft surgery (1.6 vs 2.3 %, RR 0.67, 95 % CI 0.49–0.92; p=0.013) and all-cause mortality (1.6 vs 2.2 %, RR 0.72, 95 % CI 0.53–0.99; p=0.045). As with the RIVAL study, there was a significant interaction by radial centre volume. The greatest benefit of radial access was found in the highest volume centres (i.e. those doing at least 80 % of their procedures via the radial artery). The MATRIX study thus provided the previously lacking unequivocal data to support radial access in ACS patients to reduce bleeding and mortality. It is possible that the higher risk cohort of patients recruited and different bleeding definitions compared to the RIVAL study allowed this difference to be demonstrated.

Both the MATRIX and RIVAL studies suggest that centres should endeavour to maximise their volumes of radial procedures, rather than reserving the procedure for patients in whom femoral access is not possible.

As well as randomised study data, analysis of national registries has confirmed the benefits of radial versus femoral access in much larger cohorts of ACS patients. In a study analysing 210,000 radial and 230,000 femoral access procedures from the British Cardiovascular Intervention Society database [18], radial access was associated with fewer major adverse cardiac events in patients with unstable syndromes (stable OR 1.08, p=0.25; NSTEACS OR 0.72, p<0.001; STEACS OR 0.70, p<0.001). The additional importance of these data is their acquisition over a time period during which the UK interventionalists swung from a vast majority of femoral to majority of radial procedures; so by definition, these data included the learning period of many operators and units. These results then go against the notion that only patients in very experienced radial centres gain benefit from this approach.

The published literature comparing radial and femoral access specifically in STEMI patients is extensive and has been recently reviewed [19] Three notable randomised trials warrant mention here. As described above, STEMI patients comprised a pre-specified subgroup analysed in RIVAL [15], where a significant benefit in favour of radial access was seen in both the composite primary outcome and for mortality. Patients with cardiogenic shock, severe peripheral vascular disease or previous coronary bypass surgery were however excluded from RIVAL.

In RIFLE-STEACS, 1001 patients from four high-volume radial centres were randomised to compare the radial and femoral approach for primary or rescue PCI [20]. This time, high-risk patients with cardiogenic shock and/or haemodynamic instability and those who had already received thrombolysis were included. Radial as compared to femoral access was associated with less cardiac mortality (5.2 vs 9.2 %), fewer Net Adverse Clinical Events (13.6 vs 21 %), less bleeding (7.8 vs 12.2 %) and fewer haemorrhagic access site complications (2.6 vs 6.8 %). The use of glycoprotein IIb/IIIa inhibitors in the majority of patients (68.6 %) likely contributed significantly to the magnitude of the benefits seen in favour of radial access. Critics again have highlighted the substantial radial experience of the centres involved thus questioning the widespread applicability of the results.

In the trial STEMI-RADIAL in four high-volume radial centres, 707 patients undergoing PPCI were randomised to radial or femoral access [21]. Rescue PCI patients were not included in this study. The primary outcome was the rate of bleeding and access site complications using HORIZONS-AMI definitions. In this study, radial access was shown to have significantly lower rates of bleeding and vascular complications compared to femoral access (1.4 vs 7.2 % $p=0.0001$). Although this study was not sufficiently powered to study mortality, there was a non-significant survival benefit in the radial group. Interestingly, door-to-balloon times were almost identical between the two access sites, showing no time penalty for a radial approach in experienced hands.

In the last 3 years, three published meta-analyses of studies in PPCI patients have demonstrated the significant reduction in mortality and bleeding that the radial approach can bring [22–24]. In the largest of these, Karrowni et al. included 12 studies and a total of 5055 patients [24]. They reported that radial approach was associated with decreased risk of mortality (2.7 vs 4.7 %; odds ratio [OR] 0.55, 95 % confidence interval [CI] 0.40 to 0.76; $p<0.001$) and decreased risk of major bleeding (1.4 vs 2.9 %; OR 0.51, 95 % CI 0.31 to 0.85; $p=0.01$). Radial access was also associated with a relative risk reduction for access site bleeding (2.1 vs 5.6 %; OR 0.35, 95 % CI 0.25 to 0.50; $p<0.001$). The disadvantage was a statistically but not clinically significant longer procedure time (mean difference 1.52 min; 95 % CI 0.33 to 2.70, p 1⁄4 0.01).

In terms of applicability to the 'real-world' setting, the findings of the UK BCIS registry have already been discussed. Of course, these observational data are subject to bias and it is likely that femoral access was used in the sicker and older patients, contributing to their higher number of adverse events. The favourable outcomes, when using the radial approach in STEMI cases [25], were subjected to and persisted after propensity score matching and multivariate logistic regression analysis for differences in measurable baseline covariates at least. Similar work in North America with the National Cardiovascular Data Registry (NCDR) database has looked at 90,979 patients presenting for primary or rescue PCI [26]. Here, radial access came with a lower risk of in-hospital mortality (OR 0.76 95 % CI 0.57 to 0.99) and lower adjusted risk of bleeding (OR 0.62 95 % CI 0.53 to 0.72) than femoral access.

Special Considerations

There are some patients in whom radial access can be more challenging even to the experienced radial operator. These are the very elderly, who often have tortuous subclavian anatomy; the very petite frail female patients whose radial arteries may be too small to safely and painlessly advance standard 6-F catheters; and those of very short stature, in whom the standard catheters designed in the main for the femoral approach do not easily engage the coronary ostia when advanced from the right arm. Unfortunately, in the first two scenarios at least, it is often these patients who would be likely to benefit from avoiding a femoral artery puncture as they are at greatest risk of an arterial complication. The more experience that can be gained in the radial approach, the more operators will at least attempt a radial procedure in these cases and be successful in some. For the short stature and elderly patient, starting with a left radial approach especially in ad-hoc ACS intervention will often avoid the difficulties of navigating the subclavian and engaging the coronary ostia.

For the small radial and also for the circumstances which are unavoidable in ad-hoc PCI where larger equipment such as rotablator burrs, two stents or bifurcation stents, a range of radial catheters is becoming available using 'sheathless' technology such that previously only 6- or 7-F compatible coronary devices can be used via guides whose external diameter is smaller than a traditional 5- or 6-F sheath [27] These can be exchanged for in the arm after a diagnostic case where needed allowing the ACS case to be completed radially whatever the findings. The last remaining femoral devices used in ACS PCI which are yet to be adapted and 'miniaturised' are the intra-aortic balloon pump and the percutaneous LVADs.

Conclusions

There is no doubt that radial access confers a benefit to the patient and the tranquillity of the operator by virtually eliminating access site bleeding and reducing enormously the risk of any clinically significant access site complication. Patients being treated invasively for acute coronary syndromes are at greatest risk of periprocedural bleeding and so hypothetically have the most to gain. Whilst the first large randomised study was unable to demonstrate a survival benefit and raised questions about the applicability to anyone other than dedicated radialists, subsequent work in a large randomised ACS trial and a number of very large registries has confirmed that radial access in urgent and emergency PCI gives the patient a better chance of survival and survival free of complications than the femoral approach. The case for STEMI PCI, with patients who are most likely to suffer an adverse event, needs no more investigation. Operators worldwide must become familiar with this approach in order to give their ACS patients the safest treatment available.

Compliance with Ethical Standards

Conflict of Interest Helen Routledge and Sanjay Sastry declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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