

Percutaneous coronary intervention (PCI) is the commonest form of revascularization in patients with coronary heart disease. The benefit of early invasive treatment with PCI in patients presenting with acute coronary syndromes are well accepted. Traditionally, PCI has been performed via the femoral access with significant risks for the development of access site-related bleeding complications. Increased international adoption of the transradial access site for PCI procedures has been shown to reduce such major access site-related bleeding complications and mortality, especially in the high-risk patient groups. We provide a brief overview of the historical perspective on transradial approach and the evidence supporting its use. We then discuss the current data supporting transradial access in high-risk populations and factors that have limited its adoption.

Keywords: high risk • outcome • percutaneous coronary intervention • transradial

Percutaneous coronary intervention (PCI) is the commonest form of revascularization in patients with coronary heart disease and the prognostic benefits of an early invasive revascularization strategy with PCI in patients presenting with acute coronary syndrome (ACS) are well established [1,2]. Advances in antiplatelet and antithrombotic therapies have improved the prognosis of patients undergoing PCI through a reduction of ischemic events albeit at the expense of increased procedure related bleeding complications [3,4]. These procedure-related bleeding complications are not benign. They are associated with adverse clinical outcomes [5,6]. A recent meta-analysis of 42 studies involving over half a million patients illustrated that major bleeding complications following PCI were independently associated with a threefold increase in major bleeding complication and major adverse cardiovascular events (MACE) [6] and that the provision of blood transfusions may increase this risk further, independent of the index bleeding event [7]. Significant proportions (30-70%) of the bleeding complications that occur are related to vascular access site [8–10]. There is growing evidence that the transradial approach reduces mortality, major bleeding events and access site complications [11,12]. In this review, we discuss the historical perspective on transradial approach and the evidence supporting its use. We then discuss transradial access in high-risk populations.

Historical perspective of transradial access

PCI is an endovascular procedure that can be performed via the femoral, brachial or radial arteries. Transradial access appeared early in the development of cardiac catheterization techniques. Radner described radial artery cut-down technique in 1948 [13]. The adoption of using this novel technique was limited mainly due to lacking of contemporary equipment. This resulted in a shift to larger arterial access for catheter-based procedures. In 1989, Campeau successfully undertook transradial angiography in Canada [14]. Three years later, Kiemeneij and Larrman performed the first coronary angioplasty via radial access [15]. Despite the observed Chee W Khoo*.¹, Eric W Holroyd¹, Rob Butler^{1,2}, James Nolan^{1,2} & Mamas A Mamas^{1,2} ¹Department of Cardiology, Royal Stoke Hospital, University Hospitals of North Midlands NHS Trust, Stoke-on-Trent, UK ²Keele Cardiovascular Research Group, Institutes of Science & Technology in Medicine & Primary Care, Keele University, UK *Author for correspondence: chee.khoo@nhs.net

Interventional

Cardiology



improvement in patient comfort, transradial access was mostly ignored and neglected by majority of interventional cardiologist and generally considered only as a niche technique or an alternative in comparison to traditionally femoral access [16].

Over the years, with more experience in transradial access and studies that demonstrated safety and superiority of transradial procedures with respect to vascular access site complications, speed of recovery, patient preference as well as cost-effectiveness [17-23], transradial access has gained ground over femoral access, with transradial access representing the default access site for all indications of PCI in many countries including the UK in which the radial access site is adopted in over 70% of procedures [24]. Other countries such as the USA have also seen a significant growth in the adoption of the radial access site for PCI although this has lagged behind the growth observed in European, Asian and Canadian centers with rates of 10-15% reported [25]. Traditionally, transradial approach has been associated with longer learning curve and higher rates of procedural failure [26,27]. Whilst some of the longer learning curve may have been historical in nature, particularly at the time when transradial access was in its infancy with the absence of radial specific equipment, contemporary literature suggests crossover rates of around 5-10% [28]. Even in experienced centers procedural failure and cross over rates have been reported at 3%, with independent predictors of failure including cardiogenic shock, previous coronary artery bypass graft (CABG) and female gender. A recent contemporary study from the National Cardiovascular Data Registry over a 3-year period demonstrated that as caseload increases, the transradial approach is chosen as the default access site for more complex procedures and that the learning curve may be as low as 30-50 cases [29]. A further limitation of the radial artery is that complex procedures requiring 7 French or larger catheters may often not be able to be completed through the radial approach, since the radial artery is smaller than 7-French diameter in a proportion of patients, particularly women [30]. Even with sheathless guide catheters [31], that obviate the need for a sheath, a proportion of cases requiring 7-French catheters cannot be undertaken through the radial approach particularly in the elderly or in females with small diameter radial arteries.

Impact of major bleeding after PCI

Bleeding complications after modern PCI practice are highly variable and are related to the vascular access site in up to half of all major bleeding events. Thirty-day major bleeding rates between 1 and 9% in ST-elevation myocardial infarction (STEMI) [32-35], 1-5% in non-ST-elevation myocardial infarction (NSTEMI) [32-33,36-37] and about 1% in elective cases [32,38] have been reported, although incident rates will depend on the definition of major bleeding used [6]. Major bleeding events post-PCI are not benign complications, but are associated with adverse outcomes such as an increased risk of mortality and MACE [39,40]. For example, Doyle et al. analyzed 17,901 unselected patients who presented to Mayo clinic and underwent PCI between 1994 and 2005. The group reported that major bleeding complications were associated with an increase in 30-day mortality risk even after adjustment for baseline covariates (HR: 9.96; 95% CI: 6.94-14.3; p < 0.0001) [41]. Similar findings have been reported in ACUITY study (OR: 7.55; 95% CI: 4.68-12.18; p < 0.0001) [42] and by Kinnaird et al. (OR: 3.5; 95% CI: 1.9–6.7; p < 0.0001) [43]. Major bleeding accounts for a significant proportion of mortalities post PCI, for example in the National Cardiovascular Data Registry's CathPCI registry, major bleeding complications contribute up to 12.1% of all in-hospital mortality after PCI [44].

A recent meta-analysis of 42 studies which involved 533,333 patients demonstrated that major bleeding complications are associated with sixfold increased risk of death when confounding comorbidities not adjusted for [6]. Major bleeding was still independently associated with a threefold increased in mortality and MACE outcome after adjusted for baseline comorbidities. Patients who are older, female gender, have renal failure, history of heart failure, presented with acute coronary syndromes or are hemodynamically compromised are more likely to sustain major bleeding complication post PCI [38,45].

Access & nonaccess site bleeding

Bleeding complications can occur from the access site or nonaccess site sources such as intracranial, gastrointestinal tract or retroperitoneal space. Nearly all significant access site related bleeding complications occur as a result of undertaking PCI through the femoral access site, with such femoral arterial bleeds independently predicting 1-year mortality [9.43,46].

Both access and nonaccess site related bleeding complications are associated with adverse outcomes. Verheugt *et al.* demonstrated that access site bleeds were independently associated with 1-year mortality with an adjusted HR of 1.82 (95% CI: 1.17–2.83) and nonaccess site bleeds with an adjusted HR of 3.94 (95% CI: 3.07–5.15) [9]. Another study also demonstrated that the prognostic impact of nonaccess site bleeds (adjusted HR: 2.66; 95% CI: 1.21–5.8) was greater than that of access site bleeds (adjusted HR: 0.74; 95% CI: 0.16–3.4) [47]. A recent meta-analysis of 25 studies that involved more than 2 million patients that underwent PCI demonstrated that both access site (RR: 1.71; 95% CI: 1.37–2.13) and nonaccess site (RR: 4.06; 95% CI: 3.21–5.14) related bleeding complications were independently associated with increased risk of mortality although nonaccess site related bleeds had a greater prognostic impact [10]. The greater impact on mortality related to nonaccess site bleeding is likely to be multi-factorial in origin and may reflect the greater severity of bleeds derived from nonaccess site sources.

Whilst several studies have shown that access site related bleeding complications are associated with an increased risk of adverse outcomes, recent studies have shown that reductions in such access site related bleeding complications through use of alternate access sites such as the radial artery may reduce mortality risk. The MORTAL study demonstrated a reduction in 30-day and 1-year mortality when using transradial instead of femoral access in all comers to PCI [48]. Transradial access was also associated with half the transfusion rate which itself was an independent predictor of 1-year mortality. In the RIVAL (Radial vs Femoral Access for Coronary Intervention) study, there was a significant reduction of mortality, myocardial infarction, stroke and non-CABG related bleeding for radial access in highest tertile volume radial centers (HR: 0.49; 95% CI: 0.28-0.87; p = 0.015) but the rate of non-CABG related major bleeding was similar in both radial access group and femoral access group (0.7 vs 0.9%; HR: 0.73; 95% CI: 0.43-1.23; p = 0.23). However, an exploratory analysis on RIVAL study using the acute catheterization and urgent intervention triage strategy (ACUITY) definition of major bleeding revealed a 57% significant reduction in major bleeding as well as a 47% significant reduction in non-CABG related major bleeding and major vascular complications in the radial access arm [49]. A recent retrospective study of 439,947 patients using the British Cardiovascular Intervention Society (BCIS) database suggest transradial access was independently associated with lower bleeding rate regardless of presenting syndromes (stable OR: 0.24; NSTEACS OR: 0.35; STEACS OR: 0.47; all p < 0.001) as well as access site complications (stable OR: 0.21; NSTEACS OR: 0.19; STEACS OR: 0.16; all p < 0.001) with significant reductions in 30-day mortality observed across all indications for PCI associated with adoption of the transradial access site [24].

Whilst reductions in major access site related bleeding complications contribute in part to the decreased mortality associated with radial access site adoption, other unmeasured confounders may also contribute. Radial operators may be more experienced/higher volume operators which may drive their favorable outcomes, rather than just access site choice. Furthermore, in many registry datasets, older and frailer patients with a greater prevalence of comorbid conditions often have their PCI undertaken through a femoral approach and this may in part contribute to the worse outcomes associated with femoral access site choice. Finally, other mechanisms such as reduced incidence of acute kidney injury following PCI through the radial artery when compared with the femoral artery, may mediate some of the more favorable outcomes reported [50].

Transradial access & its growth in national populations

National registry data from North American and European databases have reported changes in access site selection over the last few years, with increasing adoption of the transradial access site as the default choice for PCI in recent years in several countries [24,51-52]. The National Cardiovascular Data Registry (NCDR) analyzed data from over 2.5 million PCI cases and reported the proportion of transradial access procedure increased from 1.2% from beginning of 2007 to 16.1% at end of 2012, in contrast to the previously reported rates of 1.32% between 2004 and 2007 [51]. Hannan et al. reported the use of transradial access in STEMI patients increased from 4.9 to 11.9% in NY, USA over a period of 24 months [52]. More impressively, the BCIS registry reported an increased in transradial utilization from 24.3% in 2007 to 61.6% in 2012, with data from 2013 suggestion radial access rates of over 70% [24].

Observational data in STEMI

National registry data suggested that transradial access is independently associated with lower mortality and major bleeding complications in high-risk ACS patients. A recent report from NCDR analyzed 90,879 patients presented with primary or rescue PCI from 2007 to 2011 showed that transradial access was associated with a 24% relative reduction in in-hospital mortality and a 38% relative reduction in bleeding in comparison with femoral approach [53]. Data derived from the BCIS dataset in 46,128 STEMI patients over a 5-year period demonstrated that the transradial access was independently associated with lower 30-day mortality (HR: 0.71; 95% CI: 0.52-0.97; p < 0.05), in-hospital MACCE (major adverse cardiac and cerebrovascular events; HR: 0.73; 95% CI: 0.57-0.93; p < 0.05), major bleeding (HR: 0.37; 95% CI: 0.18-0.74; p < 0.01) and access site complications (HR: 0.38; 95% CI: 0.19-0.75; p < 0.01) [54]. Patients who required intraaortic balloon pump, in cardiogenic shock or those had previous CABG were less likely to have transradial access for PCI in this registry suggesting a selection bias toward higher risk procedures being undertaken through the femoral approach which may account for some of the apparent decreased mortality risk observed in the radial cohorts in this and other registries. Nevertheless even after adjustment for differences in baseline covariates and following propensity score matching to minimize the effects of unmeasured confounders and selection bias, the reduction in mortality observed in the radial cohort persisted. Similar data derived from the UK in a retrospective cohort study in Scotland also demonstrated the use of transradial access in primary or rescue PCI (n = 4534) significantly reduced 30-day mortality (OR: 0.51; 95% CI: 0.04–0.52; p < 0.001), in-hospital myocardial infarction (OR: 0.66; 95% CI: 0.51-0.87; p = 0.003) and access site bleeding complications (OR: 0.21; 95% CI: 0.08-0.56; p = 0.002) [55]. All these observational studies demonstrated that transradial access in high bleeding risk ACS patients (STEMI) is associated with improved clinical outcomes, reduced mortality and complications. Such reductions in mortality observed in STEMI through changes in access site are similar to those observed following a change in practice from thrombolysis to primary PCI [56].

Randomized controlled trials in STEMI

Registry data provides important information regarding access site choice and clinical outcome in realworld setting. However, it is limited by selection bias in which higher risk patients that require PCI are being performed via femoral access. Moreover, despite the use of propensity score matching in comparing two different treatment modalities using observational data, there are still inherent limitations due to unmeasured variables which might have influenced the treatment patient received. Randomized controlled trials (RCTs) overcome those limitations around unmeasured variables and selection bias, although are limited by reporting outcomes in highly selected populations.

A number of contemporary RCT have been published comparing transradial to femoral access in STEMI patients [33,57-58]. These are summarized in Table 1. The RIVAL trial which randomized >7000 patients is the largest trial comparing transradial and femoral access [33]. It included patients with ACS but excluded patients in cardiogenic shock, previous bypass grafting or patient with severe peripheral vascular disease that precluding femoral approach. In the prespecified STEMI subgroup of RIVAL trial (n = 1958), the transradial access was associated with reduced mortality (12 vs 32%; p = 0.006), MACCE (26 vs 46%; p = 0.031) and major vascular complications (12 vs 35%; p 0.002), but not in patients with non-ST-segment elevation ACS [33]. The RIFLE-STEACS trial of patients undergoing PCI for STEMI also included higher risk group of patients with cardiogenic shock and patients who failed thrombolysis (rescue PCI) [57]. The transradial access in comparison with femoral access demonstrated a significant reduction in cardiac mortality (OR: 0.57; 95% CI: 0.36–0.90) and bleeding (OR: 0.64; 95% CI: 0.44–0.94).

Patients in other high-risk categories

Patients with myocardial infarction complicated by cardiogenic shock have an in-hospital mortality rate as high as 60% [59]. Major bleeding complications commonly occur and contributed up to 14% of the 30-day noncardiac mortality in the SHOCK trial [60]. Few observatory studies have suggested that transradial access was associated with independent reduction in mortality and favorable outcomes in patient presenting with cardiogenic shock, mainly due to lower access related bleeding complications, although many of these report outcomes from expert transradial centers [61–64].

Mamas et al. recently published the BCIS registry data of 7231 patients presented with cardiogenic shock over a 7-year period within the UK who underwent PCI [65]. The transradial access was used in 1877 patients and was independently associated with a reduction in 30-day mortality (HR: 0.56; 95% CI: 0.46-0.69; p < 0.001), in-hospital MACCE (HR: 0.64; 95% CI: 0.53-0.76; p < 0.001) and major bleeding (HR: 0.37; 95% CI: 0.18-0.73; p = 0.004) in comparison to femoral access. Interestingly this mortality reduction was not observed in low volume radial centers with radial rates of < 25%. Patients who were more likely to be treated via the femoral access were more likely to be diabetic, female, receive an intra-aortic balloon pump and inotropic support or be ventilated suggesting that femoral access is favored in hemodynamically unstable patients complicating the interpretation of such analyses. Nevertheless, even after adjustment for differences in baseline characteristics, the mortality benefit associated with radial access site choice persists. Transradial access in cardiogenic shock patient represents a viable alternative in experienced centers to femoral access site and may be associated with reduced mortality.

Transradial access had been used in complex PCI setting. Yang *et al.* demonstrated that transradial access has similar procedural success rate and total procedure time as well as comparable late-term clinical safety and efficacy in patients with unprotected left main disease PCI when compare with femoral access [66]. Another study showed transradial access in chronic total occlusion PCI can be performed as successful as femoral

Table 1. d	Contemporary	Table 1. Contemporary randomized controlled		trials comparing transradial and femoral access in ST-elevation myocardial infarction patients.	/ation myocardi	al infarction p	atients.	
Study (year)	Trial name	Sample size, n (number of radial/femoral in sample size)	Inclusion and exclusion criteria	End points	Major bleeding	MACE	Mortality	Ref.
Mehta e <i>t al.</i> (2012)	RIVAL⁺	1958 (955/1003)	Inclusion: patients with ischemic symptoms >20 min with ST-segment elevation of >2 mm in 2 continuous precordial leads or >1 mm in two continuous limb leads or new left bundle branch block Exclusion: patients with cardiogenic shock, severe peripheral vascular disease precluding a femoral approach, or previous CABG with an internal mammary artery graft	Primary: composite of death, myocardial infarction, stroke, or non-CABG-related major bleeding within 30 days Secondary: death, myocardial infarction, or stroke; and non- CABG-related major bleeding at 30 days; major vascular access site complications	(a) 0.8 vs 0.9%; p = 0.87	3.1 vs 5.2%; p = 0.026	1.3 vs 3.2%; p = 0.006	[33]
Romagnoli et al. (2012)	i RIFLE- STEACS	1001 (500/501)	Inclusion: all comers with STEMI, including patients with cardiogenic shock or hemodynamic instability Exclusion: patients with abnormal Allen's test or known severe peripheral vascular disease, recent stroke (within 4 weeks), an international normalized ratio >2, or other severe bleeding diathesis	Primary: 30-day incidence of NACEs which include composite of cardiac death, myocardial infarction, stroke, target lesion revascularization, and noncoronary artery bypass graft-related bleeding graft-related bleeding Secondary: 30-day individual components of NACEs and hospital stay	(b) 7.8 vs 11.4%; p = 0.029	7.2 vs 11.4%; p = 0.029	5.2 vs 9.2%; p = 0.02	[57]
Values are rac Major bleedin disabling seq. physician and intrapericardis the HORIZON: without an ov 'Pre-specific si CABG: Corona	Values are radial vs femoral in number/1 Major bleeding classification: (a) Bleedin disabling sequel: was intracranial and sy physician and fulfilling the following ble intrapericardial with cardiac tamponade tintrapericardial with cardiac tamponade withe HORIZONS-AMI criteria, defined as without an overt bleeding source or >3 Pre-specific subgroup of STEMI results. CABG: Coronary artery bypass graft; M	Values are radial vs femoral in number/number or percentage (%/%) format. Major bleeding classification: (a) Bleeding that was fatal; resulted in transfusi disabling sequel; was intracranial and symptomatic or intraocular and led to s physician and fufilling the following bleeding requiring blood transfusion; blic intrapericardial with cardiac tamponade;fatal bleeding; any of the above lead the HDRZONS-AMI criteria, defined as intracranial or intraocular hemorrhage without an overt bleeding source or >3g/dl with an overt bleeding source; re "Pre-specific subgroup of STEMI results. CABG: Coronary artery bypass graft; MACE: Major adverse cardiovascular ev	tage (%/%) format. resulted in transfusion of 2 units of blood; caused substantial traocular and led to significant visual loss; or led to a decrease i blood transfusion; bleeding requiring surgical repair, cerebral bl any of the above leading to unplanned diagnostic examinations rancular hemorrhage; bleeding at the access site, with a hemor t bleeding source; reoperation for bleeding; blood transfusion. t scardiovascular events; NACE: Net adverse clinical event; STF	Values are radial vs femoral in number/number or percentage (%/%) format. Major bleeding classification: (a) Bleeding that was fatal; resulted in transfusion of 2 units of blood; caused substantial hypotension with the need for inotropes; needed surgical intervention; caused severely disabling sequel; was intracranial and symptomatic or intraocular and led to significant visual loss; or led to a decrease in hemoglobin of at least 50g/l. (b) Overt and actionable bleeding needing evaluation by physician and fulfilling the following bleeding requiring blood transfusion; bleeding requiring surgical repair, cerebral bleeding; intracranial or retroperitoneal bleeding; derease in hemoglobin level >3g/dl; physician and fulfilling the following bleeding; any of the above leading to unplanned diagnostic examinations and/or prolonged hospitalization and/or lifesaving drug discontinuation. (c) Based on the RIZONS-AMI criteria, defined as intracranial or intraocular hemotypes; bleeding at the access site, with a hematoma that was >5cm or that required intervention; a decrease in hemoglobin level >4g/dl; the nover bleeding source or >3g/dl with an overt bleeding source; reoperation for bleeding; blood transfusion. Pre-specific subgroup of STEMI results. CABG: Coronary artery bypass graft; MACE: Major adverse cardiovascular events; NACE: Net adverse clinical event; STEMI: ST-elevation myocardial infarction.	d for inotropes; neede 50g/l. (b) Overt and ac roperitoneal bleeding, alization and/or lifesav at required interventi lial infarction.	d surgical intervent ctionable bleeding r c decrease in hemo ing drug discontint an; a decrease in he	ion; caused severel reeding evaluation Jobin level >3/dl; ation. (c) Based on ation. (c) Based on timoglobin level >4(y by 3/dl

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Study (year)	Trial name	Sample size, n (number of radial/femoral in sample size)	Sample size, n Inclusion and exclusion criteria End points (number of radial/femoral in sample size)	End points	Major bleeding	MACE	Mortality	Ref.
Bernat et al. (2014)	STEMI- RADIAL	707 (348/359)	Inclusion: Patients with STEMI <12 h of onset of symptoms Exclusion: patients with cardiogenic shock, Killip IV class or unable to consent, known prior aortobifemoral bypass, no radial or femoral artery pulse, participation in artery pulse, participation in another clinical trial, negative Allen's test	Primary: cumulative incidence of major bleeding and vascular access site complications at 30 days Secondary: composite of death, myocardial infarction, stroke, and major bleeding/ vascular complications, access site crossover, contrast volume, duration of intensive care stay, and death at 6 months	(c) 1.4 vs 11.0%; p = 0.0001	3.5 vs 4.2%; p = 0.7	2.3 vs 3.1%; p = 0.64	[58]
Values are Major blee disabling si physician a intraperica the HORIZC without an *Pre-specifi CABG: Cor	Values are radial vs femoral in number/ Major bleeding classification: (a) Bleedi disabling sequel; was intracranial and sy physician and fulfilling the following bli physician and fulfilling the following bli the HORIZONS-AMI criteria, defined as without an over bleeding source or >3 Pre-specific subgroup of STEMI results CRBG; Coronary artery bypass graft; N	Values are radial vs femoral in number/number or percentage (%/%) format. Major bleeding classification: (a) Bleeding that was fatal; resulted in transfusi disabling sequel; was intracranial and symptomatic or intraocular and led to s physician and fulfilling the following bleeding requiring blood transfusion; bli intrapericardial with cardiac tamponade; fatal bleeding; any of the above lear the HORIZONS-AMI criteria, defined as intracranial or intraocular hemorrhage without an overt bleeding source; or >3g/dl with an overt bleeding source; re Pre-specific subgroup of STEMI results.	ntage (%/%) format. ; resulted in transfusion of 2 units of blood; caused substantial traocular and led to significant visual loss, or led to a decrease i blood transfusion; bleeding requiring surgical repair, cerebral b any of the above leading to unplanned diagnostic examinations traocular hemorrhage; bleeding at the access site, with a hema t bleeding source; reoperation for bleeding; blood transfusion.	Values are radial vs femoral in number/number or percentage (%/%) format. Major bleeding classification: (a) Bleeding that was fatal; resulted in transfusion of 2 units of blood; caused substantial hypotension with the need for inotropes; needed surgical intervention; caused severely disabling sequel; was intracranial and symptomatic or intraocular and leading to real or extoneopien of at least 509/L. (b) Overt and actionable bleeding needing evaluation by physician and fuffiling the following bleeding requiring blood transfusion by anging requiring surgical repair; cerebral bleeding; intracranial or retroperitoneal bleeding; devaluation. (c) Based on the NRT and actionable bleeding; any of the above, the above unplanned diagnostic examinations and/or proportioneal bleeding; derease in hemoglobin level >39/dl; intrapreticardial with cardiac tamponade; fatal bleeding; any of the above leading to unplanned diagnostic examinations and/or prolonged hospitalization and/or lifesaving drug discontinuation. (c) Based on the HORIZONS-AMI criteria, defined as intracranial or intraocular hemorrhage; bleeding at the access site, with a hematoma that was >5cm or that required intervention; a decrease in hemoglobin level >49/dl. Pre-specific subgroup of 5TEMI results. (A mode diagnostic examinations and/or profonged of profit diresaving drug discontinuation. (c) Based on the HORIZONS-AMI criteria, defined as intracranial or intraocular hemorrhage; bleeding at the access site, with a hematoma that was >5cm or that required intervention; a decrease in hemoglobin level >49/dl. Pre-specific subgroup of 5TEMI results.	509/L (b) Overt and a 509/L (b) Overt and a troperitoneal bleeding talization and/or lifesa hat required interventi dial infarction.	led surgical intervent tettonable bleeding r 3; decrease in hemoc ying drug discontinu ion; a decrease in he	ion; caused severely needing evaluation i Jobin Jevel >3g/dl; Jation. (c) Based on moglobin level >4g	y by J/dl

access with comparable in hospital MACE but with less access site complications with radial access (3.5 vs 11.3%; p < 0.001) [67].

This growing body of evidence supporting the use of transradial access for percutaneous coronary intervention as the preferred access site for the treatment of high-risk as well as low-risk patients. Hence, the transradial access is now recommended by both the Society for Cardiovascular Angiography and Intervention (SCAI) and European Society of Cardiology (ESC) guidelines as the primary access site for PCI when performed by experienced radial operators in a timely fashion (class IIa, level B evidence) [68,69]. Despite the evidence and guidance in favor of transradial access, the femoral artery remains the preferred access site in 83% of cases based on a survey in America [70].

Recent data suggests the magnitude of mortality benefit from transradial approach relates to the baseline bleeding risk of individual patient [71]. This study was based on BCIS database, using the 'modified Mehran risk score' to define the baseline risk of bleeding complications in patients (n = 348,689)who underwent PCI. As the modified Mehran score increased, the risk of significant bleed and mortality rose substantially. Each unit increase in the baseline bleeding score was associated with a 10% additional risk of in-hospital major bleed (OR: 1.10; 95% CI: 1.09-1.11; p < 0.0001) and 18% additional risk of 30-day mortality (OR: 1.18; 95% CI: 1.17-1.18; p < 0.0001). The baseline bleeding risk was the strongest independent predictor of in-hospital major bleeding complications and 30-day mortality [71]. Patients with highest risk of bleeding complications in this study were shown to have the greatest mortality benefit from the transradial access for their PCI compare to those at lower risk of bleeding. Paradoxically, those patients at highest risk of bleeding complications who had most to benefit from adoption of the transradial access site were also more likely to receive PCI through the femoral approach in this retrospective study. This observational study supports the radial paradox, in which patients at highest risk of bleeding complications who potentially derive the greatest benefit from the transradial approach are least likely to receive it.

Conclusion

Available evidence indicates that the rates of transradial access have improved over the years. Transradial access is the optimal treatment approach for high-risk patients due to lower rates of major bleeding, MACE and mortality compared with femoral access. Where possible, the radial access site should be considered the default access site for PCI.

Future perspective

Transradial access has been shown to reduce mortality and major bleeding complication in PCI in both RCT and real world registry studies. This has important implications for interventional cardiology training programs on both sides of the Atlantic. Education programs, access site courses and operator mentorship schemes have driven the changes observed in access site practice across many European countries and adoption of such educational programs, meetings and mentorship schemes has already began to improve penetrance of TRI in the USA. It will remain challenging to achieve a change in access site practice in low volume operators particularly within the USA who may not undertake sufficient numbers of PCIs annually to enable them to successfully negotiate the transradial learning curve. Access site choice is only one determinant of major bleeding complications, antiplatelet and anticoagulant choices are also important determinants of major bleeding complications. The synergy between access site and contemporary antithrombotic and antiplatelet therapy in reducing event rates will need to be explored further.

One important component of the radial procedure is the maintenance of radial patency post procedure, particularly given that contemporary studies have suggested radial occlusion rates of between 5 and 20% [30]. Radial occlusions can be minimized through the use of anticoagulation postprocedure, patent hemostasis and smaller French guide catheters [30]. An evolving technique named 'Slender' is being proposed in Japan and Europe to reduce radial artery trauma. This includes the downsizing of the vascular access sheath (<6 French), sheathless systems, balloon-assisted tracking and back-up techniques such as anchor wire, anchor balloon and parallel wire with previous studies derived from Japan reporting complex PCI procedures undertaken through 5-French compatible and virtual 4 French systems [72]. A movement toward such Slender techniques, with the development of slender compatible equipment may serve to minimize radial trauma and ensure the patency of the radial artery enabling use of the transradial access site for repeated procedures.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending or royalties.

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Executive summary

Radial artery as an access site for percutaneous coronary intervention

• The transradial access site has grown to be the default access site for percutaneous coronary intervention (PCI) for all indications of PCI in several European and Asian countries, although its adoption in the USA has lagged behind.

Major bleeding complications & their prognostic impact

- Major bleeding complications post PCI are independently associated with increases in major adverse cardiovascular events and mortality.
- Major bleeding complications can be derived from both access site and nonaccess site sources and both are associated with adverse major adverse cardiovascular events and mortality outcomes.

Influence of access site choice on clinical outcomes in PCI setting

- Adoption of the radial artery as is associated with marked reductions in major access site related bleeding complications, which may in part account for the improved clinical outcomes associated with transradial access, although other mechanisms may contribute in addition.
- Data derived from both national registries and randomized controlled trials suggest that transradial access is independently associated with lower mortality and major bleeding complications in high-risk patients undergoing PCI.

Conclusion

- Adoption of the radial artery is associated with decreased mortality and major adverse cardiovascular events outcomes in high-risk patients undergoing PCI.
- Transradial access is now recommended by both the American (SCAI) and European (ESC) guidelines as the primary access site for PCI.
- Maintaining radial patency represents an important aim for all procedures undertaken through the radial approach.

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