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Review Article

Distal Radial Artery Access

Distal Radial Artery Access Vs. Transradial Access: Current Evidence

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Introduction: Transradial access (TRA) is currently recommended over the transfemoral (TFA) route as default, for percutaneous coronary interventions (PCI) and coronary angiography in all patients, by the European and American Guidelines, because of reduced risk of bleeding, vascular complications and mortality especially in acute and high -risk patients. **Aims and objectives:** Distal radial artery access (DRA) via the anatomical snuffbox is a safe and feasible alternative to standard transradial access (TRA). This review aims to study and discuss the endpoints in recent studies comparing DRA with TRA for coronary procedures to conclude the merits and demerits of DRA Vs. TRA. **Material and Methods:** The evidence from several randomized and non-randomized studies and meta-analyses comparing DRA with TRA is reviewed. **Results:** Though access failures and crossovers are reported to be higher with DRA compared to TRA; most studies have shown no difference in vascular complications in patients undergoing procedures via DRA or TRA. Results of some randomized controlled trials between DRA Vs. TRA for coronary procedures, including Primary Percutaneous Coronary Intervention in ST-elevation myocardial infarction (STEMI) are available and are discussed; while others are underway for evaluation of radial artery occlusion (RAO) and other end-points. **Conclusion:** DRA takes more time, and fails more often compared to TRA; though time to hemostasis is less and forearm hematoma is unreported with DRA. The Jury is still out on RAO between DRA Vs. TRA; but the meticulous application of RAO prevention practices is the key to achieving low RAO.

Keywords: Distal radial artery access (DRA), standard transradial access (TRA), radial artery occlusion (RAO), anatomical snuffbox, Primary Percutaneous Coronary Intervention, randomized and non-randomized studies, meta-analyses, distal radial artery (DRA)

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Introduction

Transradial access (TRA) is recommended as default, by the European and American Guidelines for percutaneous coronary interventions (PCI) because of the overwhelming and irrefutable evidence on reduced risk of vascular complications, bleeding and mortality, especially in acute and high-risk patients undergoing PCI using TRA [1,2].

Distal radial artery access (DRA) at the anatomical snuffbox is a safe and feasible alternative to TRA [3-12].

This review aims to study and discuss the endpoints in recent studies comparing DRA with TRA for coronary procedures to conclude the merits and demerits of DRA Vs. TRA.

Kaledin , et al first reported the use of DRA. Although the distal radial artery had previously been used for intra-arterial pressure monitoring; Babubhnashali and Dundua were the first to use DRA, a branch of the deep palmar arch, for retrograde disc-obliteration of a blocked radial artery in the forearm (RAF), following which, the feasibility and safety of performing coronary procedures via DRA were reported [3-7].

Thereafter the use of left DRA for PCI was reported, for its ergonomic advantage by Kemeneij [8].

The distal radial artery (dRA) is easily compressible over the metacarpal bone compared to RAF; thus making haemostasis easier.

Furthermore, the risk of hematoma and compartment syndrome is much lower with DRA compared to TRA because the dRA is superficial to the fascial planes of the hand.

Again, a lower rate of radial artery occlusion (RAO) was speculated with DRA, not only because of less injury to RAF; but also because of less flow limitation in the RFA with DRA.

Another complication, unique to TRA is the development of swelling with petechial haemorrhages on the dorsum of the hand following compression of forearm veins, leading to back-pressure in capillaries with a compressive haemostatic bandage or TR band™ at the wrist.

However, with no requirement for haemostatic compression at the wrist, DRA is not associated with such a complication.

Recent trials and meta-analyses on distal radial access.

Data from some randomized controlled trials (RCTs) comparing DRA with conventional transradial access (TRA) for coronary procedures are available; while results of other studies are still awaited.

DAPRAO, a randomized controlled trial (RCT) (M 76.7% Vs. 75%; 6F sheaths 92.9% Vs. 88.5%; PCI 34.5 % Vs. 36.5%; mean RAF diameter vs. Distal radial artery diameter 2.7±0.4mm Vs. 2.4±0.5mm for TRA Vs. DRA groups) reported an RAO of 8.4% and 5.65 % at 24h and 30 days for TRA vs. 0.7% and 0.7% respectively for DRA [9]. Crossover to alternate access was required in 0.71% Vs.13.3% cases in TRA Vs DRA groups respectively although vascular complications (Hematoma, radial artery spasm (RAS)) were similar between groups. The study had limitations of a selection bias, with operators choosing access and exclusion; also, females were under-represented and the study excluded patients with ST elevation MI (STEMI) and high-risk patients with haemodynamic instability.

The ANGIE (Anatomical sNuffbox for Coronary angiography and IntervEntions) and CORRECT Radial (Coronary Angiography (CAG)and Interventions via Distal vs Proximal Access) trials were designed to evaluate RAO between DRA and TRA groups as the primary end-point [10].

The single-centre, randomized ANGIE (Anatomical sNuffbox for Coronary anGiography and IntervEntions) trial (75.4% 5F coronary angiograms; 24.6% PCI excluded STEMI; only a minority of non-STEMI (NSTEMI) were included. In an intention-to-treat analysis, DRA was associated with a significantly lower risk of RAO (3.7% vs 7.9% DRA Vs. TRA; 53.2% relative risk reduction) at 46day median follow-up; although not only were the access and procedural times longer (DRA Vs. TRA: 120 vs 75 seconds and 14 vs 11 minutes, respectively), access-site crossover, mostly attributed to failure to insert the sheath wire, was also 4 times higher (DRA Vs. TRA: 21.8% Vs. 5.5%). Time to haemostasis was lower with DRA Vs. TRA (60 minutes vs 120 minutes) though significant (≥grade 2) access–site Bleeding Academic Research Consortium (BARC) bleeding, hematoma and severe RAS were similar between the groups. The ANGIE study excluded patients with ACS, those with hemodynamic

Compromise and patients undergoing PCI. Most patients underwent only diagnostic angiograms in the study; thus making any meaningful conclusions difficult [10]. Further, any conclusion on RAO was not possible, because of the heterogeneity in patient demography and procedural characteristics in the earlier studies.

The proficiency of an operator to successfully perform PCI to achieve prompt reperfusion using either access (TRA Vs. DRA) should be balanced against the benefit of lower RAO using DRA, especially for PCI in acute coronary syndromes (ACS), STEMI and NSTEMI. Since 'time is muscle'; delays, if any, on account of using DRA can be detrimental to the patient. This is important because DAPRAO and ANGIE as well as most other studies, except DATA STAR and DISCO RADIAL trials (DIStal Versus COnventional RADIAL Access for Coronary Angiography and Intervention excluded patients of ACS [9-12].

Such concerns are addressed in the ongoing RESERVE (Comparison of Distal Transradial Access and Transradial Access for Primary Percutaneous Coronary Intervention in STEMI Patients; **NCT04861389**) and the DISTAL RADIAL ACCESS MI (Comparison of success rate between distal radial approach and radial approach in STEMI) trials. The latter is a randomised study in acute myocardial infarction (AMI) patients, which is evaluating puncture success in ST-elevation AMI as the primary end-point.

The DATA STAR study was a non-randomized, retrospective registry of all-comer patients and represented a real-world population (M: F, 70.3%: 29.7%; with small diameter radial arteries (mean RAD 1.63 ± 0.27 mm; RAD≤1.6 mm in 73.5%), inclusive of diagnostic angiography and PCI. ACS, STEMI, NSTEMI and patients with hemodynamic compromise were not excluded [11]. The study showed that DRA takes more time and fails more often and the rate of RAO for DRA was the same as that for TRA. Vascular complications were no different; although minor non-vascular complications of transient localised paraesthesia over anatomical snuffbox (with full- recovery in < 6 weeks), were reported rarely (1.4%) possibly related to inadvertent trauma of sensory branches of the superficial radial nerve in the proximity during puncture.

The DISCO RADIAL (Distal versus conventional radial access for Coronary angiography and intervention) a prospective, multicentre, open-label, superiority RCT included patients of diagnostic angiography, PCI, and ACS and STEMI undergoing PCI [12]. It reported a higher crossover (7.4% vs. 3.5%; p=0.002) RAS (5.4% vs. 2.7%; p=0.015); shorter median time to haemostasis (153 vs. 180 min; DRA Vs. TRA p<0.001); and as in the DATA STAR study, not only were vascular complications similar between groups, the RAO was similar too (RAO2.4%vs 2.4%, p = 0.97 and 2.1% vs. 2.9%, p = 0.58 at day 1 and 30 for DRA vs. TRA respectively in DATA STAR Vs. 0.91 vs 0.31 TRA Vs. DRA; p 0.29 in DISCO RADIAL trial); further the RAO in DISCO RADIAL was reported to be the lowest to be ever reported in a large study, although another earlier large study reported RAO of 0.46%, attributed to the application of meticulous best practices for haemostasis and RAO prevention [11-15].

The first meta-analysis of twelve studies, with 8,605 patients (mean age 58 ± 5.6 years) (DRA n = 4,120; TRA n = 4,435; 69% M) reported no difference in vascular complications [access-site hematoma (RR: 0.92; 95% CI: 0.57-1.47; *P* = 0.72) and RAS (RR: 0.80; 95% CI: 0.50-1.30; *P* = 0.37)]; though there was a statistically non-significant trend toward more access failure with DRA (11 studies, RR: 2.63; 95% CI: 0.95-7.27; *P* = 0.06,), and DRA favoured RAO (9studies, risk ratio [RR]: 0.45; 95% confidence interval [CI]: 0.32-0.65; *P* < 0.01) [16].

Another meta-analysis of five Randomized controlled trials (RCTs) (n=1,005) reported similar cannulation success between DRA and TRA groups (RR 0.85, 95% CI 0.68 to 1.07, p = 0.16, I2 = 94%); though Radial artery spasm (RAS) significantly favoured DRA over TRA (RR 0.51, 95% CI 0.34 to 0.75, p = 0.0007, I2 = 0%) [17]. The time to haemostasis was significantly shorter in the DRA arm (mean difference -6.64, 95% CI -10.37 to -2.90, p = 0.0005, I2 = 88%); though access-site hematomas were no differences between the groups (RR 0.52, 95% CI 0.18 to 1.149, p = 0.22, I2 = 0%). There was a trend toward lower RAO in the DRA group compared to TRA (RR 0.24, 95% CI 0.05 to 1.20, p = 0.08, I2 = 46%). However, significantly more crossovers to alternate routes were reported in the DRA group.

A recent meta-analysis of 16 studies, with the largest number of patients (n= 9973; 4750 DRA; 5523 TRA) found no difference in the rate of access failure, access-site bleeding, hematoma, RAS, or cross-over; though a lower RAO was reported in patients undergoing DRA Vs. TRA (OR0.51,95% CI 0.29to 0.90 I^2 =42.6%, p=0.02) for diagnostic angiography rather than PCI [18].

Discussion

Evidence from DAPRAO, ANGIE, DATA STAR, DISCO RADIAL, and several other studies indicate a higher crossover rate and longer procedural time with DRA, compared to standard TRA; attributed mainly to failure to puncture of dRA (delay in obtaining bleed back in the needle from puncture (37%)) or for insertion of the sheath wire and/or sheath (63%) [9-12].

The major Achilles' heel of TRA is RAO; while that for DRA is a technical challenge, with failure to achieve access, as well as procedural delay and failure necessitating crossover to alternate access [9-12]. While access failures account for 20.8% of TRA failures; RAS, radial bifurcation anomalies, and tortuosities in Subclavian/Brachiocephalic arteries account for 63.4% of failures [19].

DRA fails more often because of the characteristic anatomical challenges of the distal radial artery with its angulations, bends and tortuosities and the myriad branches of the deep palmar arch; of which the distal radial artery itself is a branch. With the RAF, which is devoid of such challenges, TRA takes less time and fails less often [11].

Further, the smaller diameter of dRA, (which is reported to be 0.3 to 0.6 mm smaller) compared RAF also contributes to the higher rate of failure to puncture the dRA compared to RAF including failure to cannulate the dRA with sheath or wire, when used as default access [20]. These challenges are higher in women who have higher rates of RAO, with smaller radial artery diameters than in men, who were not included in most studies of DRA, though they were included in the DATA STAR study [11,13,19].

Again, in the MATRIX-Access (Minimising Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) trial, high–volume radial centres had better TRA PCI outcomes compared to low-volume Centres; thus expertise in TRA was related improved outcomes [21,22,37,38].

It is reasonable to believe that for the same reasons, expertise would be an important factor for success with DRA and could explain the higher access failures, with higher rates of crossover to alternate access, in DRA compared to TRA groups. In DATA STAR too, like in the ANGIE and DAPRAO studies, no significant differences were observed in the rates of severe RAS and hematomas. However, unlike the ANGIE study, the DATA STAR study included all-comers. Further, ACS, STEMI, high-risk patients, and those with hemodynamic compromise were not excluded from the DATA STAR study [9-11].

RAO was also reported to be similar between DRA and TRA groups (2.4%vs 2.4%, p = 0.97 and 2.1% vs. 2.9%, p = 0.58 at day 1 and 30 for DRA vs. TRA respectively) in the DATA STAR study. Although the RAO was comparable to that reported for TRA in the PROPHET study; it was higher compared to that in the DISCO RADIAL trial, and to that reported in PRIMA FACIE TRI due to the requirement in the study protocol of a compression elastic bandage for haemostasis, loosened at 1h and removed after 12h; without patent haemostasis [13,14].

In DISCO RADIAL, as in DATA STAR, RAO was similar between groups (DISCO RADIAL 0.91 vs 0.31, TRA Vs. DRA; p0.29; DATA STAR 2.4%vs 2.4%, p = 0.97 and 2.1% vs. 2.9%, p = 0.58 at day 1 and 30 for DRA vs. TRA respectively). In fact with strict implementation of best practices for preventing RAO, the RAO for TRA was the lowest ever-reported in a large trial, other than that reported by the authors (0.46) in PRIMA FACIE TRI in 2013; in which meticulous RAO prevention practices were applied and included: i) Pre-procedure measurement of RA size and following sheath sizing protocol to minimise RA stretch by maintaining the ratio of sheath/ catheter size(mm) to radial artery size (mm)as close to 1:1 as possible. (ii) Adequate Anticoagulation of 100 Units per kilogram; and a minimum of 5000 units for coronary angiography (iii) practice of patent haemostasis (iv) Minimising compression pressure to minimum required (feasible with TR band) and limiting Compression time to under 2 hrs for PCI while monitoring for hematoma. For angiograms, much shorter compression times (30-60 minutes) are often adequate (v) ulnar compression and

Administration of additional intravenous heparin for situations where the pulse is lost early post-procedure (vi) Avoidance of Balloon or catheter-assisted tracking [12-15].

Although patent haemostasis reduces the risk of RAO, there can be challenges in implementing it for patients Post -TRA in large volume centres because of the need for a strict vigil for early detection of the development of forearm hematomas after transradial intervention (TRI), which could potentially lead to a compartment syndrome. Some busy centres with logistical limitations for vigilant monitoring of forearm hematoma prefer a haemostatic bandage without patent haemostasis; with the trade-off of a slightly higher RAO of around 3%, similar to that reported with patent haemostasis in the PROPHET study [11,14].

Vascular complications (hematoma or RAS) are reported to be similar between DRA and TRA groups in most studies though the time for haemostasis is less and no case of compartment syndrome is reported with DRA compared to TRA. The RATATOUILLE trial reported no adverse effect on hand function with the use of DRA [23].

Ongoing Trials of distal radial access

While TENDERA is looking at late Radial artery occlusion in the DRA and TRA groups. DIPRA (DIstal vs Proximal Radial Artery access for cath) is comparing motor hand function between the DRA and TRA groups. Radiation Exposure with DRA is being studied in the DOSE trial (Randomized Comparison of Radiation Exposure in Coronary Angiography Between Right Conventional and Left Distal Radial Artery Approach;(**NCT04023838**).

Conclusion

In summary, the evidence from several Randomized and non-Randomized studies and meta-analyses comparing DRA with TRA indicate that though access failures and crossovers are reported to be higher with DRA compared to TRA; there is no difference in vascular complications in patients undergoing procedures via DRA or TRA and; though time to haemostasis is less and forearm hematoma is Unreported with DRA. However, the Jury is still out on RAO between DRA Vs. TRA; but the meticulous application of RAO prevention practices is the key to achieving low RAO.

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