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REVIEW ARTICLE

Ulnar artery: The Ulysses ultimate resort for coronary procedures

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Abstract Despite the increasing worldwide adoption of the transradial access site, the ulnar artery (UA) only very infrequently serves as a primary option for coronary procedures. In contrast to the uncertainty surrounding previous reports regarding the feasibility and safety, recent data from larger registries and randomized trials provide more conclusive evidence that the transulnar route may be safely selected as an alternative arterial access approach. However, a default transulnar strategy appears time-consuming and is associated with higher crossover rates compared with the radial artery (RA). Once arterial access is obtained, the likelihood of a successful coronary procedure is high and similar between the two forearm arteries. The UA has similar flow-mediating vasodilating properties with and seems at least as vulnerable as the RA with regard to incident occlusion, with UA occlusion (UAO) rates being probably higher than previously anticipated. A learning curve effect may not be apparent for crossover rates among experienced radialists, but increasing experience is associated with reduction in the fluoroscopy time, contrast volume and frequency of large hematoma formation. The UA may represents an important alternative access site for coronary procedures, and experienced radial operators should obtain additional skills to perform the transulnar approach. Nevertheless, in view of this method's lower feasibility compared to the RA, an initial ulnar access strategy should be reserved for carefully selected patients to ensure satisfactory cannulation rates.

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More than two decades since publication of transradial coronary angiography[1] and percutaneous coronary interventions (PCI),[2] there is growing interest worldwide in adopting the transradial approach over the transfemoral approach for coronary procedures.[3–5] Although technically more challenging, the radial artery (RA) possesses a cardinal advantage over the femoral artery: it is easily compressible, minimizing the hemorrhagic risk and allowing for earlier patient ambulation.[3] These benefits are of considerable clinical relevance compared with the minor drawbacks of RA catheterization, including 4-8% crossover rates to another artery[4,5] and 6-8% incidence of asymptomatic radial artery occlusion (RAO).

Surprisingly, an alternative forearm route, namely the use of the ulnar artery (UA), has been scarcely investigated in the past, although more than 15 years have elapsed since the first publication of transulnar coronary angiography.[6] In everyday practice, the UA is rarely selected as a first-line angiographic strategy despite the following potential advantages. First, it may enable the operator to circumvent possible vascular trauma and ensure an intact RA for subsequent coronary-artery bypass grafting.[7,8] Second, the UA may serve as an alternative access site for repeated angiographies and PCI in patients with an abnormal Allen's test, but normal reversed Allen's test, should this practice be an integral part of procedural decision-making. Third, the transulnar access could be viewed as part of a patient-friendly angiographic strategy for minimizing transfemoral use, serving either as a primary access site if the RA pulse quality is poor or as a crossover resort after RA failure.[9,10] Forth, some have advocated for the use of the UA as an alternative to the RA in hemodialysis patients. In a recent survey for example, 3.3% of the interventionalists preferred the ipsilateral UA after failing the radial attempt.[11]

The initial experience with the UA at our institution was similar to the prevailing belief of other interventionalists that it is a cumbersome technique with a high crossover rates, which possibly justifies the limited adoption of transulnar coronary procedures by the interventional community. What is the scientific evidence thus far on the feasibility and safety of the transulnar approach? (Table 1).

1. Nonrandomized studies

A synthesis of 10 small studies, which were published before 2007 and included 483 coronary procedures in 463 patients, described an average crossover frequency of 9%,[10] 2 pseudo-aneurysms, 1 perforation and 1 occlusion. Follow-up ultrasonography was given in only half of the trials.[10] According to recent reports,[12–21] the crossover rate appears variable, ranging from 1.5%[15] to 36%.[12] Considering the exclusion of 22% of patients for a weak or absent ulnar pulsation, the feasibility of the transulnar approach may be as low as 45%.[12]

In a registry from Brazil involving 387 patients and 410 procedures (70% of which were coronary angiographies), the rate of procedural success was 98.5% and of crossover 1.5%.[15,18] The most common reason for UA selection was the stronger ulnar pulse compared to the radial pulse. There were no access site complications, except for minor bleeding. The UA approach, compared with 10108 transradial procedures, was associated with a 20% longer fluoroscopy time, but it had a similar incidence of asymptomatic occlusions (0.7% versus 0.9%, p = ns).[18]

A preliminary report from Spain analyzed 1635 attempted transulnar coronary procedures in 1403 patients over an 11-year period.[19] Procedural success was 91% and puncture failure was the main reason for crossover. The median nerve was traumatized in 9.4% of the patients and one temporary nerve compression was noticed due to hematoma formation; however, no permanent nerve damage was found. The investigators reported a learning curve effect over time in which the formation of large hematomas decreased from 12% to 3.1% after the first 100 cases.[19]

A retrospective comparison found no difference between 317 transulnar and 317 transradial PCI with respect to the success rate of first puncture, procedural duration and entry-site complications; however, the hematoma and spasm rates were lower, favoring the UA.[20]

2. Randomized studies

These trials deliver a more ambiguous view on the feasibility of the transulnar approach. Aptecar et al.[22] randomized 441 patients to either an UA or RA coronary procedure. They excluded 2.3% of subjects after randomization, due to abnormal Allen's or reversed Allen's tests. Among the remaining patients, the authors demonstrated a 93% versus 95.5% success rate in the UA and RA patient groups, respectively (p = ns). The number of attempts slightly favored the transradial route (1.6 vs. 1.4, $p = 0.02$), while the procedural duration (14.0 vs. 12.7 min, $p = 0.06$) and fluoroscopy time (5.6 vs. 5.2 min, p = ns) was similar between the 2 groups. Entry-site complications were notably very low and summarized as follows: one trivial arteriovenous fistula, no pseudo-aneurysm and 5.7% incident occlusion among the PCI patients with echocardiographic follow-up.[22]

In the study by Li et al, 240 patients were randomized to either forearm artery. Successful coronary angiographies or PCI were achieved in 98,3% and 100% of the patients in the UA and RA artery group, respectively.[23] However, patients with an artery diameter smaller than 1.5 mm as well as those with failure of either the UA or RA access puncture were excluded from that study.[23] The rates of UA occlusion or restenosis at 30 days reached 6.8% (incident occlusions: 1.7%) among the 118 patients with ultimate transulnar procedure. On Doppler echocardiography and similar to the study by Aptecar et al,[22] the UA appeared to be as large as the RA.[23]

In the recent randomized AURA of ARTEMIS (Transulnar or Transradial Instead of Coronary Transfemoral Angiographies) trial, we included 902 patients and compared the transulnar and transradial approach as a default strategy for coronary angiography and PCI, including primary PCI.[24] The inclusion criteria were broad, allowing the participation of 96% of the screened patients, including those with faint ulnar pulsation, irrespective of the Allen's and reverse Allen's test outcome. The UA exhibited a threefold higher number of attempts before successful arterial access ($p < 0.001$) than the RA group as well as a twofold longer arterial access time ($p < 0.001$) and 12% larger amount of contrast volume. There were high cross-over rates of the UA (32.3%) compared with

Table 1 Studies reporting the feasibility and safety of the transulnar approach for coronary procedures.

Author, Year	Patient (n)	Procedures (n)	UA vs. RA size (mm)	Catheter size (Fr)	Success rate (%)	Crossover rate (%)	UAO rate (%)	Study design, entry-site complications & comments
17 studies[18], 2001–2011*	922	1028	NA	4–7	75–100	0–25	1.0	*Synthesis of previous studies* • Large hematomas:4 (<1%) • Pseudoaneurysms:2 • Arteriovenous fistula:1
Aptecar[22] 2006	431	450	2.83 ± 60.9 vs. 2.87 ± 60.6 (p = ns)	4–6	93.1	6.9	5.7%	*Randomized single-center trial of TUA vs. TRA* • Spasm incidence: 7.3% • Large hematoma:1 • Arteriovenous fistula: 1
Vassilev[12], 2008	92	59	2.76 ± 0.08 vs. 3.11 ± 0.12 (p = ns)	NA	64	36	NA	*Feasibility single-center study as a primary access approach* • No complications • Crossover rates 55% for the whole population & lower for patients with palpable UA • High spasm incidence (13.6%) • Anatomical abnormalities: 11.9%
Knebel[14], 2008	28	26	NA	5 & 6	93	7	0.0	*Observational study* • No complications • UA patency assessed by palpation
Li[23], 2010	120	120	2.36 ± 0.44, vs. 2.27 ± 0.47 (p = ns)	5–7	98	2	6.8†	*Randomized trial of TUA vs. TRA* • Exclusion of patients with UA diameter of <1.5 mm or failed UA puncture • No UA vs. RA difference in procedural duration and success rate • No complications • Anatomical abnormalities: 5.4% • Intimal thickening of the UA at 30 days:18.6%
de Andrade[18], 2012	387	410	NA	5–7	98.5	1.5	<1.0	*Prospective single center registry* • Large hematomas, grade III & IV:4 (1% of the procedures) • 20% longer fluoroscopy time over TRA
Agostoni[16], 2013‡	42	36	NA	5–7	86	14	12.0	*Part of a multicenter registry* • No complications • UAO estimated by palpation
Hahalis[24], 2013	462	462	NA	5–7	67.7	32.3	10.4	*Randomized multicenter trial of TUA vs. TRA as a*

Table 1 (*continued*)

Author, Year	Patient (n)	Procedures (n)	UA vs. RA size (mm)	Catheter size (Fr)	Success rate (%)	Crossover rate (%)	UAO rate (%)	Study design, entry-site complications & comments
								default arterial access strategy • Much higher crossover rates for TUA over TRA • No learning curve for the TUA • Large hematomas:15 (3.2%) • Pseudoaneurysms:1 • Arteriovenous fistula:1
Valdesuso[19] 2013	1405	1635	NA	NA	91	9	NA	*Preliminary two-center report* • Large hematomas:53 (3.2% of the procedures) • Ulnar nerve compression:1 • Transient ulnar nerve damage:137 (8% of the procedures)
Kwan[42], 2013‡	17	17	NA	5 & 7	100	0	0.0	*PCI in ipsilateral RAO* • No complications • Interosseous artery served as feeding collateral vessel in RAO
Liu[20], 2014	317	317	3.62 ± 0.28 vs. 3.26 ± 0.22 (p = NA)	6	100	0	6.3	*Retrospective analysis of PCI* • Large hematoma13 (4%)
Deshmukh[21] 2014	81	81	NA	5–7	93.8	6.2	NA	*Retrospective analysis* • Large hematomas:1 (1.4%)
Kedev[43], 2014	474	462	NA	5–8	97	3§	*3.1*	*Prospective registry (including a subgroup with ipsilateral RAO)* • Large hematomas, grade III & IV:11 (2.3%)
Kedev[43], 2014‡	240	240	NA	5–7	100	0	*0.0*	• Large hematomas: 5 (2.1%)
Gokhroo[25], 2015‡	410	410	UA: 2.11 ± 0.49	5 & 6	97.8	2.2	*<1%*	Non-randomized observational study of TUA compared with retrospectively analyzed patients with TRA • UA spasm: 8% • Absent UA at wrist level: 2.5% • No difference in the number of attempts for successful puncture, procedural and fluoroscopy time for an experienced operator • Learning curve evident • Measures worse for the UA vs. RA among inexperienced operators

(*continued on next page*)

Table 1 (*continued*)

Author, Year	Patient (n)	Procedures (n)	UA vs. RA size (mm)	Catheter size (Fr)	Success rate (%)	Crossover rate (%)	UAO rate (%)	Study design, entry-site complications & comments
Gokhroo[45], 2016	2352	2352	NA	NA	95.6	4.4	NA	Largest randomized trial of TUA vs. TRA • non-inferiority of the UA regarding the primary end-point (major adverse cardiac events, major vascular events during hospital stay and cross-over rates) as well as frequency of crossover, spasm and UAO vs. RAO (6.14% vs. 6.4%)

* Summarized by de Andrade PB, et al.[18]; † At 30 days including both UAO and UA stenosis; ‡ In patients with ipsilateral radial artery access failure or occlusion; § Additional 3% crossovers to the contralateral ulnar artery.
RA denotes radial artery; TRA denotes transradial approach; RAO denotes radial artery occlusion; TUA denotes transulnar approach; UA denotes ulnar artery; and UAO denotes ulnar artery occlusion.

the RA (5.9%) route ($p_{inferiority}$:0.001). Regarding vagal reactions, the formation of large hematomas and frequency of forearm artery occlusions (10.4% vs. 8.9%) for the UA was not inferior to the RA in the intention-to-treat analysis. However, we noted a doubling of the ulnar occlusion rates[24] compared with the previously randomized studies[22,23] and with our unpublished meta-analysis results. In the per protocol analysis, by only including patients who adhered to the initial assigned access route, the transulnar was noninferior to the transradial approach in most components of the secondary outcomes. We found two access-site, non-hemorrhagic complications in the UA group (incidence: 0.43%): one pseudoaneurysm and one arterio-venous fistula. Notably, fluoroscopy, coronary angiography and the PCI time was similar between the groups, indicating no visible post-cannulation UA disadvantage. The crossover likelihood was higher in female patients, those randomized in the transulnar strategy and those requiring at least 3 attempts for artery cannulation.[24] A learning curve for the frequency of crossovers was not found in the UA patient group, indicating that improvement in the UA access rates over time is unlikely among operators with established radial experience. However, there was a learning curve regarding the fluoroscopy time and contrast level used. In accordance with the other randomized trials, we did not find any persistent median nerve damage despite the initial nerve trauma in approximately 10% of the index procedures.[24]

Recently, a non-randomized observational report comparing 410 patients who underwent transulnar coronary procedures with retrospectively analyzed patients having had undergone transradial interventions performed by a single experienced operator demonstrated no differences in the procedural and fluoroscopy time and contrast volume as well as the very low cross-over and UAO rate (Table 1).[25] A meta-analysis of 5 RCTs in 2744 patients not including the largest and latest RCT as shown in Table 1 showed higher rates for the UA over the RA with regard to access cross-over [relative risk: 2.31 (confidence intervals: 1.07-4.98); $p = 0.003$] and the number of punctures ($p = 0.0002$) without a difference in the arterial access time, fluoroscopy time, or contrast volume.[26]

The reasons for the discrepancy between the AURA of ARTEMIS[24] and the aforementioned randomized trials include unknown factors and pre-randomization selection bias of the older studies.[22,23,25] For example, Li et al. included optimal candidates with larger forearm arteries and successful arterial cannulation; otherwise, patients were excluded from study participation.[23] As in the study by Gokhroo et al.[25] and according to the initial abstract presentation and the final publications, patients with an RA or UA that was nonpalpable were excluded from study enrollment, whereas RA patients were either retrospectively or in a randomized fashion (see below and Table 1) compared with those enrolled in the UA observational and randomized study, respectively.

3. Anatomic and physiologic considerations (Figure 1)

The brachial artery gives rise to the superior and inferior ulnar collateral arteries on the ulnar side of the upper arm. The UA takes a medial course after its origin on the lateral side of the ulnar nerve until it is very distal. A line joining the medial epicondyle of the humerus to the lateral side of the pisiform bone mirrors its course in the distal forearm half.[27,28] The UA lies deep to the flexor carpi ulnaris and flexor digitorum sublimis in the middle third of the forearm and lateral to the tendon flexor carpi ulnaris in the distal third, which is only covered by fascia and skin. The proximal large branch of the UA, the common interosseus artery, divides into the anterior and posterior interosseous arteries, supplies myo-skeletal tissues and serves as a collateral vessel for forearm artery occlusion. The long median artery arises from the anterior interosseous artery, courses along the median nerve and sometimes reinforces the superficial

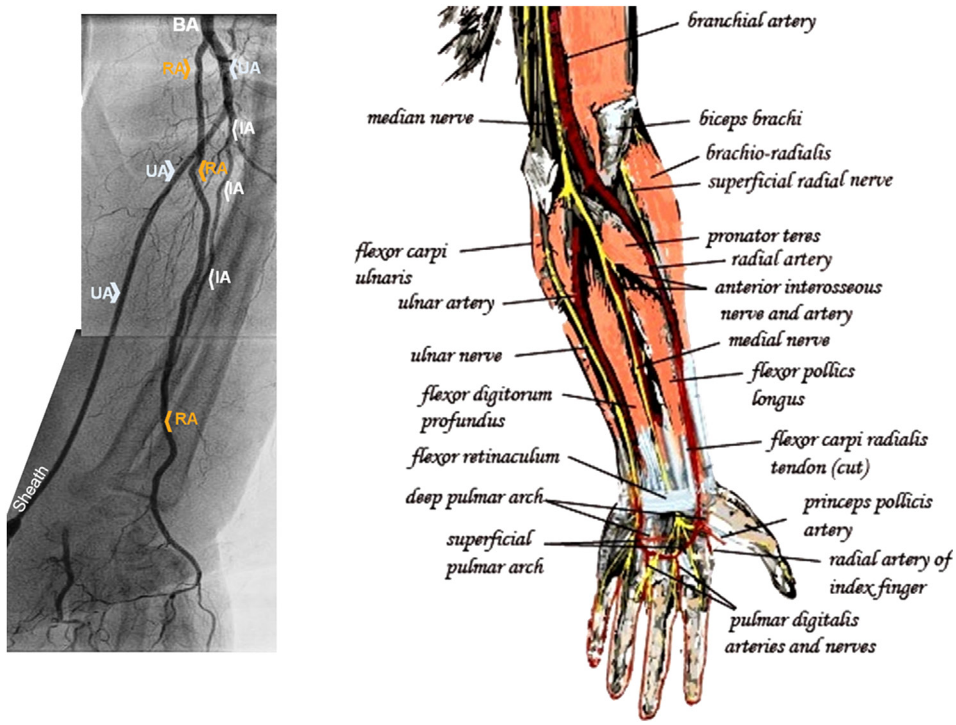

Figure 1 Transulnar arteriography and anatomy of the forearm. The angiographic frame depicts the brachial artery (BA) dividing in the UA (light blue arrows) and the RA (brown arrows) as well as the interosseous artery (IA), a branch of the UA (white arrows). Bone back-up is broader for the RA rather than that of the UA ensuring better stability during the RA over the UA puncture. For details of forearm anatomy see text.

palmar arch.[27,28] The UA provides small branches to the ulnar nerve (arteriae nervorum) that are capable of additionally securing UA attachment.[27] Immediately beyond the pisiform bone, the UA divides into two branches, which enter into the formation of the superficial and deep palmar arches. The UA is the main contributor to the superficial palmar arch, which is formed together with the superficial branch of the radial artery. The deep branch of the UA accompanies the deep branch of the ulnar nerve and completes the deep palmar arch together with the deep radial and dorsal interosseous artery branches.[27,28] In men, a complete superficial palmar arch, i.e., supplying the fingers and ulnar side of the thumb, is found in 66-96%. In the remaining cases, an incomplete superficial palmar arch is encountered, i.e., an UA supplying the little, ring, and middle fingers without metacarpal thumb-supplying branches.[29] Moreover, a complete deep palmar arch, indicating direct deep branches, that anastomoses between the UA and RA has a prevalence of 67—97%.[29] In one study, the thumb, index and fifth fingers lost pulsatile blood flow 4 times more often with radial instead of ulnar artery compression, indicating more clinical relevance of the RA for digital blood flow.[30]

Unlike the internal thoracic, but similar to the RA and coronary arteries, the UA is a muscular artery with ageing-dependent alterations[31] that is prone to spasm at least as frequently as the RA.[24] This tendency is associated with the nitric oxide bio-availability level with lower flow-mediated dilatation resulting in a developing ageing-dependent UA spasms.[32]

Some have demonstrated the feasibility of using the UA as a coronary artery bypass graft when the RA was dominant and could not be removed without risk.[27] In this regard, either the RA, as shown in cadavers[33] and echocardiography,[12,34] or UA[20,28,35] has been reported as the dominant forearm artery, while a similar anatomic size in some studies[22,23,35,36] is not synonymous with functional non-dominance.[35,37] Results that are based on pre-procedural ultrasonographic measurements may undergo selections bias in favor of the UA by only including patients with good ulnar pulsation.[20,28,34] Even a large originating UA may become of equal size, or even smaller; as a result, the non-dominant artery is compared with the radial artery near the wrist.[37] The UA is capable of increased compensatory blood flow and providing recruitable collaterals, even in hands with RAO or poor collateral circulation at baseline, i.e., with abnormal Allen's test results.[38,39] Whether the size of the two forearm arteries is similar or different, the deeper location of the UA renders its pulsation almost invariably weaker than that of the RA, reducing the likelihood of a successful ulnar puncture. Furthermore, anatomic abnormalities that are present in approximately 6-12%[12,23] may prolong the duration and increase the failure rates of transulnar coronary procedures.

4. Tips and tricks

Operators already experienced on transradial angiography should expand his/her repertoire with transulnar procedures. In general, the transulnar approach has to be reserved for patients with satisfactory ulnar pulsation in a non-busy catheterization laboratory. Access difficulties are usually exaggerated in patients with hypotension, rapid atrial fibrillation and severe aortic stenosis. In contrast to transradial cannulation failure, which is largely due to spasm,[24] ulnar access failure usually results from inability to puncture the artery and less often to advance the wire despite obtaining satisfactory blood flow.[12,24]

Selection of an UA based on an abnormal Allen's test may further increase the frequency of access failure because of its smaller average diameter compared to vessels in patients with normal Allen's tests.[40]

The requirements for optimal transulnar access include minimal anesthesia, 40-70° arm abduction, slight wrist hyperreflexion, simultaneous palpation of the RA if the ulnar pulse is faint and an alternative, more proximal access site (> 3 cm) if a distal attempt in the proximity to the pisiform bone has failed.[30] Some strongly suggest the wrist fold as a preferable access site because proximal UA puncture has been associated with hematoma formation.[19] Furthermore, lateral to medial puncture attempts may minimize unintentional trauma of the ulnar nerve.[19] Because of a tendency for more UA spasms than RA spasms,[24] we recommend maximized pharmacological vessel protection, such as anticoagulation with at least 5000 units of unfractionated heparin, a vasodilating intraarterial cocktail, avoidance of excessive manipulation and mild sedation. Following careful selection, and once cannulated, the UA appears to be as safe and feasible as the RA without difficulties in wire insertion or catheter advancement, resulting in a similar rate of successful coronary procedures.[13–27] At the end of each procedure, an hemostatic device according to the patent hemostasis technique should be applied over the UA and removed as soon as hemostasis is achieved.

5. Radial-to-ulnar artery switching: Is it feasible? Is it safe?

The rationale of this strategy would be to save time after failure in cannulating the RA instead of preparing the contralateral wrist or femoral artery. Agostoni P, et al. showed that this approach was feasible and safe in 86% of the patients, as no hand ischemia developed in the 42 study patients.[16] In the AURA-of-ARTEMIS study, we attempted an ipsilateral crossover in 134 cannulation failures of either forearm artery.[24] Sheath insertion was an exclusion criterion for ipsilateral crossover. Although the incidence of RAO was 14%, no hand ischemia was observed. Furthermore, the ultimate femoral artery use was low (3.5%), which is in keeping with other investigators[41] and supports a patient-friendly angiographic approach of alternative crossover to another forearm, rather than to the femoral artery, after failed radial access. In the registry of de Andrade et al, 81 transulnar procedures were performed due to an absent radial pulse or RA spasm (bail-out due to RA failure was observed in 46 patients). Incident UA occlusion was as low as 0.7%, and none of the 7 patients experienced hand ischemia.[18]

Switching becomes more complex when documented RA occlusion already exists. Recent data in 257 such patients suggest that this approach appears safe, even after subsequent UA occlusion in 7 patients.[42,43] It is likely that the anterior interosseous branch ensures adequate collaterals to the occluded wrist arteries. Moreover, the compensatory enlargement and hyperperfusion of the UA[38,39] renders the vessel easily accessible and less prone to occlusion.[43] Nonetheless because of the observational nature of these studies and small number of patients, we advise against routine ipsilateral ulnar crossover in RAO cases to avoid possible hand ischemia. This risk may not be negligible considering that hand ischemia has been described following UA use and antecedent unsuccessful RA catheterization.[44] If there is no option for transfemoral access as a result of peripheral artery disease, transulnar access can be selected by very experienced operators, even in the case of RAO after previously administering prophylactic high-intensity anticoagulation (e.g., 100 IU/kg heparin) and performing transulnar forearm arteriography through a cannula or a previously inserted small sheath to elucidate UA anatomy.

6. Summary and Conclusions

A routine, default UA primary approach for coronary interventions may become time-consuming and inconvenient for patients when used by inexperienced operators. This approach is further associated with a high incidence of crossover to another artery and requires additional skills from experienced interventionalists. Therefore, the RA should remain the first option for coronary interventions. Because the UA offers the potential of an important alternative access site for coronary procedures, experienced radial operators should obtain adequate expertise for the transulnar approach. In fact, if the ulnar pulse is of adequate quality or is even better than that of the radial artery, an UA primary access strategy appears to be a reasonable alternative to the RA approach. A gradual learning curve is, in our experience, not apparent for crossover rates, but increasing experience may lead to a shorter fluoroscopy time, lower contrast volume used and reduction of incident large hematomas. The adoption of a convenient "bail-out" ipsilateral crossover from the RA to UA access site, and vice versa, is possible if no vascular damage has occurred after failed attempts, but has to be balanced against the risk for possible hand ischemia. The UA may be very cautiously used for coronary procedures if a RAO is present and no femoral access option is available. Notably, a recently published RCT comparing the UA with the RA for coronary procedures showed similar rates for cross over (4.4% for the UA vs 3.8% for the RA; $p = 0.44$); for large hematoma (1.0% vs 0.9%; $p = 0.69$); for vessel spasm (6.9% vs 8.7%; $p = 0.09$); and for the primary endpoint (a composite of major adverse cardiac events such as death, myocardial infarction, stroke, or urgent target-vessel revascularization as well as major vascular events during hospital stay and crossover rates).[45]

Disclosures

The authors have nothing to disclose. George Hahalis contributed to, reviewed and edited the manuscript; Spyridon Deftereos reviewed and edited the manuscript;

Olivier Bertrand contributed to the manuscript, provided advice, and reviewed and edited the manuscript. The authors are solely responsible for drafting and editing the manuscript as well as for the final manuscript contents.

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