BMJ Open

ULTrasound-guided TRAnsfemoral puncture in COmplex Large bORe PCI: study protocol of the UltraCOLOR trial

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ABSTRACT

Introduction Although recently published evidence favours transradial access (TRA) when using large-bore guiding catheters for percutaneous coronary intervention (PCI) of complex coronary lesions, the femoral artery will still be used in a considerate proportion of patients undergoing complex PCI, especially in PCI of chronic total occlusions (CTO). Ultrasound-guided puncture of the femoral artery may reduce clinically relevant access site complications, but robust evidence is lacking up to date.

Methods and analysis A total of 542 patients undergoing complex PCI, defined as PCI of CTO, complex bifurcation, heavy calcified lesion or left main, in which the 7-F or 8-F transfemoral access is required, will be randomised to ultrasound-guided puncture or fluoroscopy-guided puncture. The primary outcome is the incidence of the composite end-point of clinically relevant access site related bleeding and/or vascular complications requiring intervention. Access site complications and major adverse cardiovascular events up to 1 month will also be compared between both groups.

Ethics and dissemination Ethical approval for the study was granted by the local Ethics Committee ('Medisch Ethische Toetsing Commissie Isala Zwolle') for all Dutch sites, 'Comité Medische Ethiek Ziekenhuis Oost-Limburg' for Hospital Oost-Limburg, 'Comité d'éthique CHU-Charleroi—ISPPC' for Centre Hospitalier Universitaire de Charleroi and 'Ethik Kommission de Ärztekammer Nordrhein' for Elisabeth-Krankenhaus). The trial outcomes will be published in peer-reviewed journals of the concerned literature. The *ul*trasound guided *tra*nsfemoral access in *co*mplex *l*arge b*or*e PCI trial has been administered in the ClinicalTrials.gov database, reference number: NCT03846752.

Registration details ClinicalTrials.gov identifier: NCT03846752.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The design as a randomised 1:1 open-label study and the vast experience with large bore transfemoral access in complex percutaneous coronary intervention of the participating centres

⇒ Clinical Event Committee adjudicated and clinically relevant primary endpoint.

⇒ As a limitation, bias could be derived from the unblinded nature of the study for the treating interventional cardiologist.

⇒ As a limitation, experience and proficiency using ultrasound may vary among operators and centres, although mitigated by thorough on-site or online instruction in addition to use of a step-by-step instruction manual.

BACKGROUND

For complex percutaneous coronary intervention (PCI), transfemoral access (TFA) remains frequently used when large bore guiding catheters are considered necessary.[1] [2] However, femoral access is strongly associated with increased bleeding and vascular complications, especially when large-bore guiding catheters are used.[3–5] The recently published Complex Large Bore Radial access (COLOR) and Femoral or Radial Approach in the Treatment of Chronic Total Occlusion (FORT CTO) trials support the use of large bore transradial access (TRA) for complex PCI, leading to significantly less access site complications and similar procedural success rates as compared with TFA.[6] [7] A considerate proportion of patients will not be suitable for large bore TRA, though, for example, in case of anticipated small radial artery size, previous radial artery harvesting for coronary artery bypass grafting, arteriovenous shunts for haemodialysis, radial artery occlusion or spasm. In addition, when dual arterial access is applied in case of CTO PCI, large bore radial combined with large bore femoral artery access is predominantly used, as demonstrated in both the COLOR and FORT CTO trials. Improvement and refinement of femoral access site management are therefore of the utmost importance.
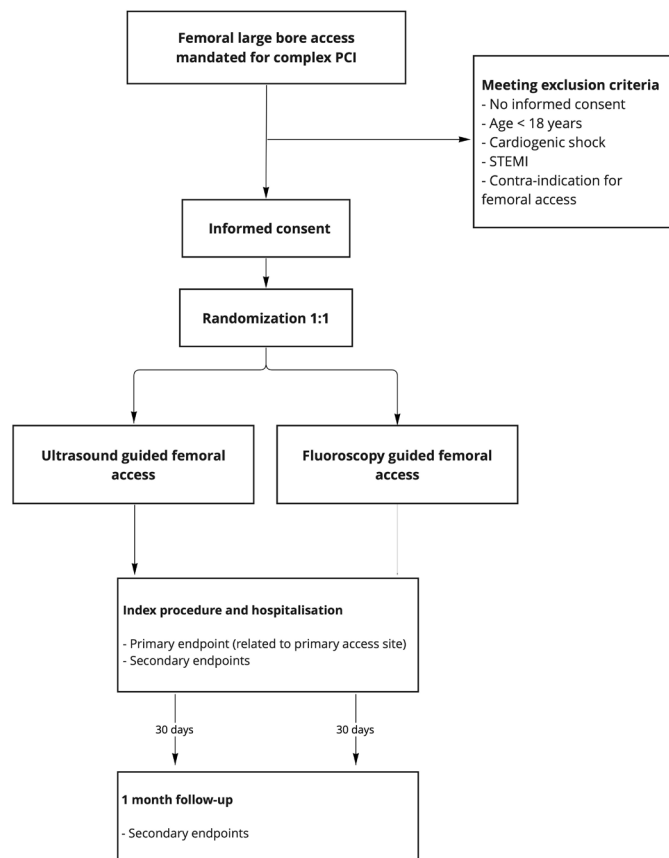
Figure 1 Study flow chart. Graphic representation of inclusion for the *ul*trasound guided *tra*nsfemoral access in *co*mplex *l*arge *bo*re PCI trial. PCI, percutaneous coronary intervention; STEMI-ST, segment elevation myocardial infarction.

Ultrasound-guided puncture of the femoral artery might reduce bleeding or vascular complications. By direct visualisation of the puncture site, the use of ultrasound may prevent a too high or too low puncture, both associated with clinically significant bleeding and vascular complications.[8–10] Additionally, it can prevent puncture into calcified lesions and may decrease the risk of vascular closure device (VCD) failure, which occurs in about 3% of cases.[11 12] Accidental puncture or even damage of adjacent structures, such as the femoral nerve or femoral vein, can also be avoided by using ultrasound-guided puncture.

Data regarding the benefit of ultrasound-guided femoral artery puncture is scarce. For transfemoral transcatheter aortic valve replacement, limited non-randomised evidence shows substantial reductions in access-related vascular and bleeding complications when using ultrasound-guided femoral puncture for large-bore cannulation.[13] Ultrasound-guided access of the femoral artery for coronary procedures, however, is not common practice and is not recommended in current international guidelines. In experienced complex PCI centres ultrasound was used for large-bore TFA in the minority of patients (40% in the COLOR trial).[6] It was previously shown that ultrasound-guided puncture of the femoral artery in patients undergoing coronary

catheterisation or intervention with standard 5-F or 6-F sheaths might reduce vascular complications. However, this was mainly driven by large haematomas which proved not to be associated with increased morbidity or mortality.[14–16] A recently published meta-analysis of randomised trials addressing ultrasound-guided cannulation of the femoral artery showed no significant difference in major bleeding, possibly because of the small sample size of most studies and variable endpoint definitions.[17] In 2022, a retrospective trial including 418 patients requiring femoral access showed clear reduction of access site complications using ultrasound-guided access combined with VCD.[18]

The primary aim of this trial will be to assess if application of ultrasound guidance for complex PCI with large-bore access ($\geq 7\,F$) reduces the occurrence of clinically relevant bleeding and vascular complications.

METHODS
Study design
The *ul*trasound guided *tra*nsfemoral access in *co*mplex *l*arge *bo*re PCI (UltraCOLOR) trial is an investigator-initiated international multicentre study with a prospective, randomised controlled design. Participating centres are the Isala Heart Center (Zwolle, the Netherlands), Catharina Hospital (Eindhoven, the Netherlands), Radboud University Medical Center (Nijmegen, The Netherlands), Elisabeth-Krankenhaus (Essen, Germany), Centre Hospilatier Universitaire de Charleroi (Charleroi, Belgium), St. Antonius Hospital (Nieuwegein, the Netherlands), Utrecht University Medical Center (Utrecht, the Netherlands) Hospital Oost-Limburg (Genk, Belgium), Amsterdam University Medical Center (Amsterdam, The Netherlands) and Jessa hospital (Hasselt, Belgium). All centres have been selected based on their experience with complex PCI and ultrasound-guided access.

Trial organisation
The trial is approved by the appropriate ethics review board at each clinical site. Written informed consent will be obtained from all patients before enrollment (patient information file/informed consent form can be found under online supplemental material I). The trial was designed in accordance with the declaration of Helsinki. All data will be collected in an electronic data capturing system, the eDREAM (electronic case record form Diagnostic REsearch And Management). Diagram BV, Zwolle, the Netherlands will be responsible for overall trial and data management, as well as monitoring of the study. Evaluation of serious adverse events (AEs) is being performed by an independent Data Safety Monitoring Board (DSMB). A Clinical Events Committee (CEC) will review and adjudicate all end-point related AEs. The UltraCOLOR trial has been administered in the Clinical-Trials.gov database, reference number: NCT04837404
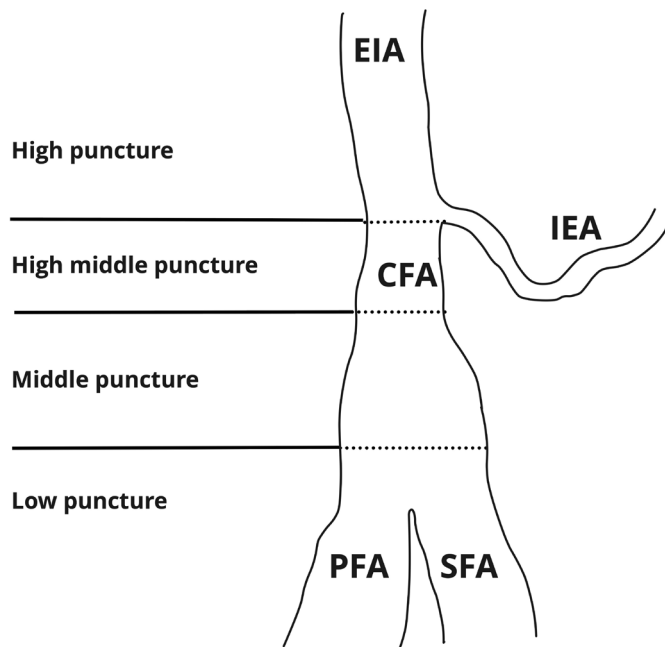
Figure 2 Puncture height classification for femoral artery access. CFA, common femoral artery; EIA, external iliac artery; IEA, inferior epigastric artery; PFA, profunda femoral artery; SFA, superficial femoral artery.

Objectives
The primary objective of this study is to confirm the hypothesis that ultrasound-guided puncture for complex PCI with large-bore access (≥ 7 F) is superior to fluoroscopy-guided puncture with regard to clinically relevant bleeding (Bleeding Academic Research Consortium (BARC) 2, 3 or 5) and/or vascular access-site complications.

As secondary objectives, ultrasound-guided and fluoroscopy-guided TFA will be compared with regard to procedural duration, first pass puncture, accidental venous puncture and VCD failure. MACE at discharge and 1-month follow-up will be compared between both randomised groups. Clinically relevant complications of the additional access site (if applicable) will also be studied.

Inclusion
All patients of 18 years or older, presenting with stable coronary artery disease, unstable angina or non-ST elevation myocardial infarction and planned for PCI of the following complex coronary lesions: CTO, left main, heavily calcified lesions which may require calcium modification techniques (rotational atherectomy or intravascular lithotripsy) and complex bifurcations in whom the operator anticipates the use of at least one 7-F or 8-F femoral access site, are screened for inclusion. See figure 1 for study flow chart. CTO is defined as a lesion exhibiting TIMI 0–1 flow in a native coronary artery with an occlusion duration of≥3 months.[19] Heavily calcified lesions are characterised by multiple persisting opacifications of the coronary wall visible in more than one projection surrounding the complete lumen of the coronary

artery at the site of the lesion.[20] Complex bifurcation includes lesions with Medina classification 0.1.1, 1.1.1 or 1.0.1.[21] Patients with ST elevation myocardial infarction or cardiogenic shock will be excluded. Patients with contraindications for large bore femoral access, such as occlusive peripheral artery disease, will be excluded as well.

Randomisation
After providing written informed consent, eligible subjects are randomly assigned to receive one of the two study treatments in a 1:1 ratio. Treatment assignments are performed centrally through a dedicated website as part of the electronic Case Report Form according to a computer-generated random schedule in random permuted blocks with stratification by site.[22] There will be no blinding of the randomisation assignment.

Endpoints
Primary endpoint is defined as
► Clinically relevant access site related bleeding or vascular complication requiring intervention of the primary femoral access site during hospitalisation. Bleeding will be classified according to the BARC criteria,[23] and considered clinically relevant when the score is≥2 (CEC adjudicated).[24] Severity and type of intervention of vascular complications is specified in the CEC manual.

Secondary endpoints are defined as
► BARC 2, 3 or 5 access-site related bleeding or vascular complication requiring intervention of the primary femoral access site at 1 month.
► MACE (hospitalisation and 1 month).
► Procedural duration.
► First pass puncture.
► Number of access attempts.
► Accidental venepuncture.
► Cross-over (fluoroscopy guided to ultrasound guided or vice versa).
► Suboptimal femoral artery puncture, based on the ileofemoral angiogram (scored by operator according to figure 2).
► Vascular complication not requiring intervention of the primary femoral access site (hospitalisation and 1 month).
► Vascular complication not requiring intervention of the secondary femoral or radial access site (hospitalisation and 1 month).
► BARC 2, 3 or 5 access-site related bleeding or vascular complication requiring intervention of the secondary femoral or radial access site (hospitalisation and 1 month).

Index PCI and hospitalisation
Femoral access will be performed according to the randomised strategy. After sheath placement, a bolus of unfractionated heparin will be given, adapted to the patient's body weight. The need for additional arterial
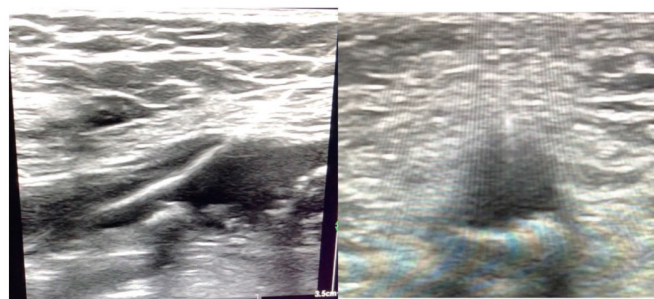
Figure 3 Long axis (left) and short axis (right) view of guidewire entering the common femoral artery at the correct position.

access is left to the discretion of the operator. In case of dual large-bore femoral access, the operator decides which access site (right or left femoral artery) will be used for the primary endpoint (this is defined as primary access) and which access site for the secondary endpoint (this is defined as secondary access) before application of local anaesthetics. In case of secondary radial access site, the application of ultrasound for radial access will be left to the discretion of the operator. In case of bifemoral access, the application of the randomised strategy (ultrasound or angio based) for the secondary femoral access is highly recommended. PCI strategy and choice of materials will be left to the discretion of the operator as well. The activated clotting time during and at the end of the procedure will be obtained before removal of the arterial sheath(s). Active anticoagulants during procedure will be reported. An ileofemoral angiogram is mandated before closure device placement to check for complications and access location, in which adequate projection of the C-arc to clearly identify the bifurcation is important. It is recommended to perform this angiogram right after sheath placement, and before administration of intra-arterial heparin. Haemostasis will be achieved according to the local protocol using a closure device unless contraindicated, in the latter case manual compression with bandage will be applied for hemostasis. Failure of VCD will be documented. Pain score related to the primary femoral access site directly after haemostasis will be collected according to the numerical rating scale (NRS). Before discharge, all access sites should be checked for potential complications including haematoma (haematoma size is documented). Additional ultrasound should be performed within 1 month in case of suspected femoral artery occlusion or other vascular complications of the (additional) femoral or radial artery.

Fluoroscopy-guided femoral access
A detailed step-by-step approach of fluoroscopy-guided femoral puncture is provided to all participating centres. Step 1 comprises disinfection of the groin and identification of the course of the femoral artery by palpation. The X-ray tube is placed in anterior–posterior position at the level of the groin. In step 2, fluoroscopy is used to identify the ideal site of femoral artery puncture, which

is a point~1 cm lateral to the most medial aspect of the femoral head, midway between its superior and inferior borders (Rupp's rule[9]). The lower border of the femoral head is marked with a metal clamp or haemostat. In step 3, a local anaesthetic is administered subcutaneously, followed by skin puncture at the lower border of the femoral head (marked at step 2) with the needle entering the skin at a 30°–45° angle while palpating the femoral artery (with a steeper angle in more obese patients). Use of micropuncture and/or skin nick is optional and according to operators' experience and preference.[25] Finally in step 4, once the femoral artery is cannulated, good pulsatile blood flow should be ensured before advancing the guidewire through the needle into the femoral artery, iliac artery and descending aorta under fluoroscopic guidance followed by sheath placement. It is recommended to perform the obligated femoral artery angiogram right after sheath placement (in order to detect possible complications before administration of intra-arterial heparin). Height of femoral artery access is checked and scored according to figure 2 (groups 1–4). Use of ultrasound in the fluoroscopy-guided group (in case of failure to cannulate the femoral artery) is considered cross-over.

Ultrasound-guided femoral access
For the ultrasound-guided group, 2-dimensional real-time ultrasound will be used to identify the optimal location for puncture of the femoral artery.[14] A full description of a step-by-step approach of ultrasound-guided femoral puncture is provided to all participating centres. Step 1 comprises disinfection of the groin and identification of the course of the femoral artery by palpation. Use of fluoroscopy to identify the femoral head is optional in the ultrasound-guided group. Next, a 5–12 MHz lineair (vascular) ultrasound probe is inserted into a sterile cover after application of non-sterile ultrasound gel inside the cover. The operator should ensure that there is no air between probe and cover. Sterile ultrasound gel is used on the skin. In step 2, settings for the ultrasound device visualisation (depth and gain) should be optimised. In step 3, the common femoral artery (CFA) trajectory and bifurcation should be both visualised in short and long axes (figure 3). A reasonable calcium-free spot should be identified for the puncturing the CFA. Local anaesthetic is administered subcutaneously under direct visualisation with ultrasound. In step 4, an 18-gauge needle is used for arterial puncture at a 30°–45° angle under continuous ultrasound visualisation. Use of micropuncture with an 21-gauge needle and/or skin nick is optional and according to operators' experience and preference.[25] The needle entry in the designated CFA location is monitored first by 'tenting' of the CFA in the middle of the 'dome' of the artery (figure 3). The correct height and freedom of calcification may be additionally confirmed in the longitudinal view. Puncture can then be performed with subsequent appearance of pulsatile arterial blood from the needle. In step 5, good pulsatile blood flow should

be ensured before advancing the guidewire through the needle into the femoral artery, iliac artery and descending aorta. Verification of correct entrance location and guide-wire position may be confirmed with ultrasound in both short and long axis views before sheath placement. It is recommended to perform the obligated femoral artery angiogram right after sheath placement (in order to detect possible complications before administration of intra-arterial heparin). Height of femoral artery access should also be checked and scored according to figure 2 (groups 1–4).

Follow-up

Follow-up will be performed 1 month after index PCI by either phone call or outpatient clinic visit. MACE and access site bleeding or vascular complications will be documented. Residual pain of the primary femoral access site will be scored according to the NRS. AEs will be monitored from inclusion to 1-month follow-up and will be assessed by an independent DSMB, composed of two experienced cardiologists and one statistician, reviewing patient safety and study integrity.

Sample size calculation and statistics

The appropriate sample size was estimated at n=271 subjects, based on a type 1 error rate of 5% and a power of 80%, assuming a 16% complication rate in the compar-ator group and 49% reduction (7.84% complication rate) in the ultrasound-guided group.[6 15] A total of 542 subjects (271 subjects in each group) will need to be randomised in this trial.

The primary analysis will take place after last subject follow-up. An intention-to-treat analysis will be performed. Demographics and baseline characteristics, primary and secondary outcomes per group will be anal-ysed using descriptive statistics. Categorical variables will be summarised by frequency and percentages. Contin-uous variables will be summarised by mean, SD as well as median and IQR. A subject reaches the primary endpoint when at least one complication according to the defini-tion has occurred. The primary outcome is the incidence of access-site related BARC 2, 3 or 5 or vascular complica-tion requiring intervention during index hospitalisation. In case of double arterial access (eg, in CTO procedures), the primary endpoint will only be scored for the primary access site. For our primary objective we will use the Pearson Chi-Square test. To account for confounding variables, the main analysis will be performed using logistic regression with treatment allocation and use of additional antiplatelets as fixed effects. The effect of the intervention will be presented as the OR of access-site related BARC 2, 3 or 5 or vascular complication requiring intervention during index hospitalisation and its 95% CI. Crude proportions by treatment arm will also be reported with an unadjusted OR and 95% CI, and a χ^2 (or Fisher exact) test p value. For secondary endpoints, differences in incidences will be statistically tested between groups by using Fisher's exact test or Pearson's χ^2 test. Differences

in means of continuous data will be statistically tested by performing Student's t-test or, in case the data are not normally distributed, the Mann-Whitney-Wilcoxon test. The time to event for MACE will be plotted by means of Kaplan-Meier survival curves. In case a patient is lost to follow-up or the outcome variable is missing, we will use the latest time available if the event of interest did not occur during the observation period (censoring). We will test for differences between the survival distributions in the two treatment groups by means of the logrank test. All statistical tests will be two tailed. A p-value<0.05 is consid-ered to be statistically significant.

Ethics and dissemination

Ethical approval for the study was granted by the local Ethics Committee ('Medisch Ethische Toetsing Commissie Isala Zwolle' for all Dutch sites, 'Comité Medische Ethiek Ziekenhuis Oost-Limburg' for Hospital Oost-Limburg, 'Comité d'éthique CHU-Charleroi—ISPPC' for Centre Hospilatier Universitaire de Charleroi, 'Ethik Kommission de Ärztekammer Nordrhein' for Elisabeth-Krankenhaus and (insert METC Hasselt) after reviewing the protocol, site-specific informed consent forms (local language and English versions), participant education and recruitment materials, other requested documents and any subse-quent modifications. Trained research nurses or physi-cians directly involved in the trial will introduce the trial to eligible patients. Patients will also receive patient infor-mation form (PIF). The research nurse or physician will discuss the trial with patients in light of the information provided in the PIF and will obtain written consent from patients willing to participate in the trial. No reimburse-ment is provided to study participants.

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with limited access. All reports, data collection, process and administrative forms will be identified by a coded identification-number only to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number. All local databases will be secured with password-protected access systems. Safety and progress reports to the ECs will be made at least annually and within 3 months of study termination or completion. These reports will include the total number of participants enrolled and summaries of the DSMB. Any modifications to the protocol which may have impact on the conduct of the study, potential benefit of the patient or may affect patient safety, including changes of study objectives, study design, patient popula-tion, sample sizes, study procedures, or significant admin-istrative aspects will require a formal amendment to the protocol. Such amendment will have to be approved by the Ethics Committee prior to implementation. The study findings will be disseminated via publication of peer-reviewed manuscripts and presentations at interna-tional conferences, as well as through media publications.

Results will be published irrespective of whether the findings are positive or negative. The Standard Protocol Items: Recommendations for Interventional Trials checklist of this trial can be found under online supplemental material II).

Patient and public involvement
No patients or public involved in the design of the study.

DISCUSSION
Although several observational trials and, more recently, two randomised controlled trials have shown that complex PCI performed through large bore TRA reduces access site complications without compromising on procedural efficacy, large bore TFA will still be applied in a considerate amount of patients. This will especially be true when dual arterial access is used in CTO PCI. Dual arterial access as part of the hybrid algorithm is used for distal target visualisation and retrograde access.[26 27] In both the COLOR trial and the FORT trial, biradial access was used only in a minority of patients regardless of randomised access site (21% and 30%, respectively).[6 7] In a substudy of the RECHARGE registry, full transradial access (single TRA or dual TRA) was compared with TFA (either single TFA, dual TFA or TFA combined with TRA) using propensity matching.[28] Although procedural success was comparable between both groups, only a minority (48%) of the full TRA group had dual arterial access. Comparable procedural success rates were also noted in an observational study by Meah et al, comparing biradial with femoral (either radial/femoral or bifemoral) access.[29] Next to patients requiring dual arterial access, patients with contraindications for large bore radial access or failed attempt to TRA also need to be treated by large bore TFA. In the COLOR trial, almost 10% of screened patients were not eligible for large bore TRA. The need for additional measures to reduce large bore femoral access bleeding and vascular complications is therefore still of paramount importance.

Ultrasound-guided puncture is widely accepted and used in central venous access. It is endorsed by American Institute of Ultrasound in Medicine guidelines mainly because of less access site related complications, shorter procedural time and time to cannulation.[30–32] For large bore TFA, guidelines regarding ultrasound-guided puncture are lacking up to now due to gaps in scientific evidence. Possible advantages are numerous though. Ultrasound-guided puncture prevents puncture above the inguinal ligament, which is associated with retroperitoneal haemorrhage[33–35] and also prevents puncture below the CFA bifurcation, which is associated with pseudoaneurysm and arteriovenous fistula.[8 10] The ideal puncture site is therefore defined above (proximal to) the CFA bifurcation and below the inferior margin of the inferior epigastric artery ('middle puncture' as depicted in figure 2). Up to 30% of patients have a high or very high CFA bifurcation.[36] In these patients, fluoroscopy-guided femoral artery puncture using the margins of the femoral head as markers does not prevent puncture in or below the bifurcation. Ultrasound-guided puncture circumvents these limitations and may therefore be superior to fluoroscopy-guided puncture. In addition, the diameter of the superficial and profunda femoral arteries are usually smaller than the CFA, limiting the use of a VCD. For example, the use of an Angioseal (Terumo, Japan) closure device in vessels with a diameter of less than 5 mm is not recommended.[37 38] Ultrasound-guided puncture may prevent cannulation in the profunda or superficial femoral arteries and therefore prevent VCD failure.

Several studies have been performed regarding ultrasound-guided puncture in regular coronary angiography or PCI using regular 5-F or 6-F sheaths. The Femoral Arterial Access with Ultrasound Trial by Seto et al compared fluoroscopy-guided puncture with ultrasound-guided puncture using standard sized sheaths (average 5.6 F) and showed a reduction in vascular complications, mainly driven by reduction in large haematomas (>5 cm).[14] More recently, Katirsibasi et al reported lower rates of haematomas, pain and arteriovenous fistulae in patients randomised to ultrasound-guided puncture compared with manual technique.[39] Both trials were included in a meta-analysis by Sorrentino et al in 2020, showing significant reduction in any access site complications with ultrasound-guided access, but no clinically significant reduction in major access-site related bleeding events.[17] In 2022, Iannopolli et al retrospectively analysed access site related bleeding in 418 patients receiving femoral access (median sheath size 6 F) for multiple combinations of puncture and closure techniques. Access site complications were classified using the BARC criteria. Incidence of bleeding was significantly lower in patients treated with ultrasound-guided access combined with a suture-based VCD.[18] Heterogeneity in safety endpoint definitions and study designs hampers comparability of previous trials, though. The UltraCOLOR trial uses the standardised BARC criteria to classify bleeding complications of the access site.[23] BARC bleeding≥2 has shown to independently predict 1-year mortality and capture more clinically significant bleeding than TIMI minor/major and GUSTO moderate/severe criteria.[23 24] Importantly, haematoma size alone, not meeting criteria for other bleeding outcome measures, has not been shown to have an association with clinically relevant endpoints.[16] Randomised controlled trials adequately powered to detect a significant difference in clinically relevant bleeding or vascular complications are lacking, especially for large bore TFA. Since the risk for access site complications is the greatest in patients requiring large bore access for complex PCI, the UltraCOLOR trial was designed to test the advantage of ultrasound-guided puncture in this group of patients.

One of the potential limitations in performing a trial assessing ultrasound-guided puncture is the heterogenic proficiency of operators in using ultrasound for femoral access and variable puncture techniques.

Therefore, participation was limited to high volume complex PCI centres and operators with ample experience in ultrasound-guided access and large bore femoral access site management. In addition, all participating centres received on-site or online training through a prerecorded demonstration video. As for the control group, extensive instructions regarding fluoroscopy-guided puncture were provided as well. These measures should limit the intra-operator variability. Another possible limitation is that the operator is inevitably unblinded to the randomised strategy. This has been countered by establishing an independent and blinded Clinical Event Committee which will adjudicate all safety endpoints of this trial.

In conclusion, the UltraCOLOR trial is the first prospective multicentre randomised trial comparing ultrasound guided with fluoroscopy-guided TFA using large-bore guiding catheters for complex PCI. Currently, 300 patients have been randomised. The results of this trial will provide important insights in the role of ultrasound guidance for large bore TFA. If this trial can show that the use of ultrasound has clear benefits regarding access site complications, it will have a significant impact on daily practice.

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