Fully Transradial Versus Transfemoral Approach for Percutaneous Intervention of Coronary Chronic Total Occlusions Applying the Hybrid Algorithm Insights From RECHARGE Registry

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Original Research

Fully-transradial versus transfemoral approach for percutaneous intervention of coronary chronic total occlusions applying the hybrid algorithm: insights from RECHARGE registry.

Bakker. Fully transradial approach in chronic total occlusion recanalization.

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Abstract

Background

Small observational studies demonstrate the feasibility of transradial approach (TRA) for chronic total occlusion (CTO) percutaneous coronary intervention (PCI). The aim of the current study is to assess technical success, complication rates and procedural efficiency in fully-TRA (fTRA) and transfemoral approach (TFA) in a large prospective European registry adopting the hybrid algorithm for CTO PCI (RECHARGE).

Methods and Results

We analyzed 1253 CTO PCI procedures performed according to the hybrid protocol in 17 European centers, comparing fTRA (single or bi-radial access) and TFA (single or bi-femoral or combined radial and femoral access). Fully-TRA was applied in 306 (24%) and TFA in 947 (76%) cases. The average J-CTO score was 2.1±1.2 in fTRA and 2.3±1.1 in TFA (p=0.06). Technical success was achieved in 85% in fTRA and 86% in TFA (p=0.51). Technical success was comparable for fTRA and TFA in different J-CTO score subgroups, after multivariable analysis and after propensity adjustment. In-hospital major adverse cardiac and cerebral events (MACCE) occurred in 2.0% in fTRA and 2.9% in TFA (p=0.40). Major access-site bleeding occurred in 0.3% in fTRA and 0.5% in TFA (p=0.66). Fully-TRA compared with TFA had similar procedural duration (80 [54-120] vs 90 [60-121] min, p=0.07), similar radiation dose (DAP 89 [52-163] vs 101 [59-171] gray*cm2, p=0.06) and lower contrast agent use (200 [150-310] vs 250 [200-350] ml, p<0.01).

Conclusions

Fully-TRA CTO PCI is a valid alternative to TFA with a high rate of success, low complication rates and no decrease in procedural efficiency.

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Chronic Total Occlusion; Percutaneous Coronary Intervention; Transradial approach.

INTRODUCTION

The transradial approach (TRA) for percutaneous coronary intervention (PCI) has gained widespread acceptance over the last decades. The radial artery is easily compressible, not surrounded by major venous and nervous structures, and an adequate collateral arterial network is present. As a result, the risk of vascular complications after TRA is negligible[1]. Multiple randomized trials demonstrated that a transfemoral approach (TFA) is associated with a significantly higher risk of bleeding, pseudo-aneurysm and arteriovenous fistula formation, cardiac events and mortality after PCI[1,2]. This has been demonstrated in PCI for stable coronary artery disease and acute coronary syndromes both with and without persistent ST-segment elevation. Moreover, vascular complication rates after TFA are only modestly reduced with the use of vascular closure devices[3].

However PCI of chronic total occlusion (CTO) is mostly performed with (bilateral) femoral access to facilitate the use of large-bore guiding catheters for optimal support and freedom in technique selection. Nevertheless, previous reports suggest that TRA CTO PCI is feasible [4-6]. The aim of the current study is to compare a fully-TRA (fTRA) versus a TFA (including combined transradial-transfemoral approaches) regarding technical success, procedural characteristics and complications in the RECHARGE registry[7], a large prospective multicentre cohort of CTO PCI procedures performed according to the state-of-art hybrid algorithm[8].

METHODS

A total of 1253 CTO PCI procedures in 1177 patients in 17 centres in France, Belgium, the Netherlands, and the United Kingdom were prospectively and consecutively included in the RECHARGE registry between January 2014 and October 2015. The study complies with the Declaration of Helsinki, ethical approval was obtained in all centres and all patients provided written informed consent. All operators had performed a minimum of 25 hybrid procedures before starting enrolment and they were all certified operators for the controlled antegrade dissection re-entry (ADR) technique with CrossBoss and Stingray devices (Boston Scientific, Marlborough, Massechusetts).

Case selection was based on symptoms, ischemia and/or viability rather than perceived likelihood of success. All CTO PCIs were presumed to be treated according to the hybrid algorithm. The choice of techniques, materials and access site was left at the discretion of the operator.

Arterial access

Selection of arterial access site was made on a case-to-case basis, reflecting the operators' considerations. Arterial access was categorized as either fTRA (single radial or biradial) or TFA (single femoral, bifemoral or combined radial and femoral).

Baseline characteristics

Demographics, medical history and lesion characteristics were obtained prior to CTO PCI in all patients. The Japanese chronic total occlusion (J-CTO) score and the PROGRESS CTO score were used to assess CTO lesion complexity[9,10].

Outcome measures and definitions

Technical success was defined as CTO revascularization with <30% residual stenosis within the treated segment and restoration of antegrade TIMI flow grade 3. In-hospital Major Adverse Cardiac and Cerebral Events (MACCE) included death, stroke, periprocedural myocardial infarction (MI, ongoing chest pain with both electrocardiogram changes and elevated cardiac markers), urgent target vessel (TV) revascularization (TVR) or target vessel failure (TVF, TV occluded at follow-up). Major bleeding was defined as bleeding leading to death, severe hypotension, a drop in haemoglobin of ≥3 g/dl, ≥2 units of whole blood packed cells transfusion, prolonged hospitalization, permanent injury or need for vascular surgery. Procedural time, exposure to radiation and contrast agent were also documented.

Statistical analysis

Categorical data are presented as numbers and percentages and compared using Chi-Square tests. Continuous data are presented as mean ± standard deviation or median ± interquartile range and compared using ANOVA or Mann-Whitney U tests as appropriate. Multivariable logistic regression analysis was used to identify predictors of technical success. Arterial access site and all demographic and angiographic characteristics with a significantly different prevalence between fTRA and TFA groups in univariable analysis were included in the multivariable model. A propensity analysis was carried out by use of a non-parsimonious logistic regression model for fTRA versus TFA. All variables listed in table 1 and 2 were included in this model, along with significant interactions. In patients with missing values, the multiple imputation method was adopted to obtain a value to generate the propensity score, in order not to lose patients for the analysis. The score was then incorporated into subsequent proportional-hazards models as a covariate and was used to divide the population according to quintiles of propensity score. We also performed a 1:1 matched analysis without replacement on the basis of the estimated propensity score of each patient. The log odds of the probability that a patient received fTRA (the "logit") was modelled as a function of the confounders that we identified and included in our dataset. Using the estimated logits, we first randomly selected a patient in the group receiving fTRA and then matched that patient with the patient in the TFA group with the closest estimated logit value (nearest neighbor matching method, caliper 0,2 SD). If more than one patient in the group receiving TFA met this criterion, we randomly selected one patient for matching. A

2-sided p-value of <0.05 was considered significant for all tests. All analyses were performed using SPSS version 22 (IBM SPSS Inc.). Additional statistical analyses (including more details about the propensity score and inverse probability of treatment weight analysis) have been added in Supplemental file 1.

RESULTS

Of the 1253 cases enrolled, fTRA was applied in 306 (24%) cases and TFA in 947 (76%) cases. In the fTRA group, 159 cases were performed with unilateral and 147 with bilateral radial access. In the TFA group, unilateral femoral access was applied in 126, bilateral femoral access in 271 and combined radial and femoral access in 550 patients.

Demographic characteristics

Mean age was 66 ± 11 years. Fully-TRA and TFA groups differed significantly regarding gender (89% vs 85% male, p = 0.04), history of hypertension (69% vs 59%, p < 0.01) and peripheral vascular disease (18% vs 13%, p = 0.02). The prevalence of other cardiovascular comorbidities was high but well-balanced between groups as presented in Table 1.

Angiographic characteristics

The most common CTO-target vessel was the right coronary artery (61%), followed by the left anterior descending (23%), the circumflex (16%) and the left main (0.3%) coronary arteries as presented in Table 2. Lesion length >20mm (49% vs 62%, p <0.01), a blunt stump (41% vs 53%, p < 0.01), proximal cap ambiguity (30% vs 38%, p = 0.02), and a diseased distal landing zone (40% vs 47%, p = 0.04) were more common in the TFA group, and significant calcification (66% vs 56%, p < 0.01) and lack of 'interventional' collaterals (50% vs 29%, p < 0.01) were found more frequently in the fTRA group. As a result, the J-CTO score was lower in the fTRA group without reaching statistical significance (2.1 ± 1.2 vs 2.3 ± 1.1, p = 0.06), meanwhile the PROGRESS CTO was significantly higher in the fTRA group (1.4±1 vs 1.1±0.9, p<0.001).

Procedural outcomes

Overall technical success was 85% (259 out of 306 patients) in the fTRA group and 86% (816 out of 947) in the TFA group (p = 0.51). Fully-TRA and TFA procedures were equally successful in all strata of the J-CTO score with success rates of 100% vs 99% (p = 0.99) in easy, 97% vs 94% (p = 0.52) in intermediate, 85% vs 88% (p = 0.47) in difficult, and 72% vs 79% (p = 0.17) in very difficult lesions (see Figure 1).

The successful crossing technique was antegrade wire escalation in 198 (76%) of fTRA patients and 425 (52%) of TFA patients, antegrade dissection and re-entry in 33 (13%) of fTRA and 159 (19%) of TFA, and a retrograde techniques in 28 (11%) of fTRA and 232 (28%) of TFA. The average number of approaches required was 1.5 ± 0.7 and was similar in both groups as demonstrated in Table 3. A retrograde technique was less frequently planned and/or applied in the fTRA group (42% vs 61%) compared with the TFA group. Antegrade dissection and re-entry as a planned and/or applied strategy was similar between groups (49% vs 51%).

In the fTRA group, we observed similar procedure duration times (80 vs 90 min, p = 0.07) compared with the TFA group. The Air Kerma radiation dose was significantly higher (1.7 [1.1 – 2.9] vs 1.5 [0.9 - 2.6] Gray, p < 0.01) in the fTRA group, without difference in Dose Area Product dose (89 [52 – 163] vs 101 [59 – 171] Gray*cm2, p = 0.06). On average, less contrast agent was used in the fTRA group (200 [150 – 310] vs 250 [200 – 350] ml, p < 0.01). A higher average number of balloons, guidewires, stents and microcatheters were used in TFA. A ≥7F guide catheter was used in 42% of fTRA and 91% of TFA patients.

MACCE occurred in 33 patients (2.6%), including 3 deaths (1 aortic dissection, 1 sudden death, 1 shock after staged non-target vessel PCI), 3 strokes, and 27 myocardial infarctions (one of which was due to TVF requiring immediate TVR). Of these, 6 (2.0%) occurred in the fTRA group and 27 (2.9%) in the TFA group (p = 0.40). Major bleeding occurred in 24 (1.9%) patients. Of these, 16 were cardiac tamponades. Retroperitoneal bleeding occurred in 2 patients in the TFA group. Major access-site related bleeding occurred in 1 (0.3%) patient in the fTRA group and 5 (0.5%) in the TFA group (p = 0.66).

Multivariable analysis

On multivariable analysis, previous CABG on the CTO target vessel, CTO length >20mm, a blunt stump, significant calcification, moderate to severe tortuosity, lack of 'interventional' collaterals, a diseased distal landing zone, and planned and/or applied retrograde approach were associated with technical failure. There was no statistically significant association between arterial access site and technical success, as presented in Table 4.

Propensity-score Analysis

The propensity-score model included 34 baseline and angiographic variables (table 1 and 2). Mean standardized differences of these variables between the two groups before and after propensity matching are available in Supplemental Figure A. In fTRA patients the median propensity score (0=TFA; 1=fTRA) was 0.33 (interquartile range, 0.21 to 0.51) while in TFA patients the median score was 0.16 (interquartile range, 0.10 to 0.26, see also Supplemental File 1 and Supplemental Figure B). The C-statistic for the propensity score model was 0.75, indicating acceptable discrimination. Procedural success according to propensity score quintiles is shown in figure 2, which highlights broadly comparable results in the different sub-groups. Propensity-score was also introduced in a bivariate analysis model together with access site, showing no statistically significant association between arterial access site and procedural success (see Table 4). The matching of patients performed in the study population yielded 144 patients treated via fTRA matched with 144 patients treated via TFA. After propensity-score matching, comparisons in procedural outcomes were repeated according to the arterial approach. Comparable success rates were observed also in the matched cohort. However, a significantly higher rate of retrograde techniques and a significantly higher number of microcatheters were used in the TFA group. In fact, adoption of antegrade wire escalation technique was more common in the fTRA group, with a lower use of dual-catheter injection (see Table 5). After calculation of the IPTW, generalized estimation equations for procedural success in the two access groups generated an expected odd ratio for Procedural Success of 0,847 (Confidence Interval: 0,526 – 1,363) statistically non-significant (p-value=0.49), thus supporting results deriving from the PS-matching and PS-stratified analyses (see Supplemental File 1 for more details).

Single-Catheter Access Sub-group Analysis

An additional analysis on single-catheter access in the two vascular approach was carried to further analyse the performance of fTRA and TFA in this specific subset of CTO-PCI. A single guiding catheter access was adopted in 159 of the fTRA cases and 126 of the TFA cases. Previous MI, in-stent occlusion, blunt stump, and lesion length > 20mm were significantly more common in the TFA group, while severe calcification was more common in the fTRA group. Other demographic and angiographic characteristics (as listed in Tables 1 and 2) did not differ significantly between groups. The J-CTO score was 1.5 ± 1.0 in fTRA and 1.7 ± 1.1 in TFA ($p = 0.16$). The PROGRESS score was 1.6 ± 1.1 in both groups ($p = 0.94$). Procedure time, fluoroscopy time and contrast use were not significantly different between groups. AWE was more common as the final successful crossing technique in fTRA (88 vs 68 percent, $p < 0.01$) and ADR was less common (1 vs 13 percent, $p < 0.01$). Technical success was achieved in 92% in fTRA and 86% in TFA ($p = 0.13$). Four major complications including 3 MI and 1 cardiac tamponade occurred in the TFA group, none in the fTRA group.

DISCUSSION

This study supports that technical success rates in PCI for CTO using the hybrid algorithm with a fully transradial approach are high and similar to transfemoral CTO PCI.

No randomized trials comparing TRA and TFA for CTO PCI have been published to our knowledge, but several observational studies have shown promising results of TRA CTO PCI. In early reports by Rathore et al. and Yang et al., where most probably only antegrade techniques were adopted, transradial CTO PCI yielded technical success in 82% and 69% of cases, respectively[4,11]. On the other hand, Alaswad et al. described a contemporary cohort of CTO PCI applying the hybrid protocol with success in 93% of both TRA and TFA cases[5]. Of note, this cohort included only 73 purely transradial procedures. Our cohort with more than 300 fully-transradial CTO PCI procedures is to our knowledge the largest published in the literature.

A recent report from Tanaka et al has investigated the procedural success of 280 TRA against 305 TFA CTO PCIs, with particular focus on CTO complexity. The authors reported relatively low and comparable procedural success rates in the TRA and TFA groups in all-comers CTO (74.6% vs. 72.5% respectively, $p = 0.51$), which even worsened when considering complex CTO lesions (J-CTO ≥3; 35.7% vs. 58.2% respectively, $p = 0.04$)[12]. Of note, patients with combined radial and femoral approaches were included in both groups, depending on where the antegrade catheter was inserted, i.e. the access site for the antegrade catheter was determining the TRA or TFA. Their findings resulted worse than those described in our analysis, a fact that can be explained by the wider enrolment period in Tanaka's work, ranging from January 2005 to December 2014. In our opinion, the most recent evolutions in the materials and technologies, as well as advanced techniques including the development of the hybrid approach, allow for improved procedural outcomes in the current practice.

TRA has been widely adopted over the last years in both elective and primary PCI. There are robust data from randomized trials demonstrating a significantly lower risk of vascular complications, cardiac events, bleeding and mortality after both elective and primary TRA PCI[2]. No data on this matter from randomized studies or large registries exist in CTO PCI, but a significant effect is to be expected given the prolonged time of periprocedural anticoagulation with an activated clotting time usually maintained between 300 and 350 seconds in the presence of large-bore femoral arterial sheaths[13]. Major bleedings were rare in the current study with no significant difference between radial and femoral groups. However, considering the relevant advantage in terms of major bleeding conferred by TRA in all patients undergoing PCI, particularly pronounced in those with stable coronary syndrome as shown by a recent metanalysis by Ferrante et al.[2], similar benefits have to be expected with higher number of patients also in the settings of CTO PCI. Moreover, an even greater difference would potentially be observed if also minor bleedings were taken into account, which however was not done for the present analysis. Of note, such potential benefits of fTRA in terms of safety are not counterbalanced by an expense in procedural success rates. In fact, in our analysis these were maintained high and comparable with the TFA group in different settings of technical difficulty, as reflected by J-CTO score (Figure 1). Furthermore, after propensity score adjustment and matching, our observations confirmed that fTRA had no significant impact on procedural success, which was maintained over 80% in the fTRA group (see table 4 and 5).

At present, CTO PCI is still mostly performed with transfemoral or combined radial and femoral approach, and we identify as primary reason for this phenomenon the frequent choice of 8 French guiding catheters for both optimal support and optimal freedom in technique selection. However, the radial use of conventional 8 French sheaths has been demonstrated feasible.[14] In addition, ongoing developments such as miniturization of endovascular devices (for example Stingray Low Profile for ADR and TrapLiner catheter allowing the trapping technique in 6 French guiding catheters) and the use of thin-walled sheaths (for example Glidesheath Slender, Terumo) or sheathless techniques to minimize the number of cases requiring large-bore arterial sheaths, make fTRA CTO PCI feasible in the majority of patients[15]. Indeed, the TRA in CTO PCI should not be directly perceived as a limitation to materials and techniques choices any longer, and the broadly promoted adoption of TFA for CTO PCI is, in our opinion, relatively overestimated. When performed in the hands of expert operators, with proper experience in radial access management and high confidence with TRA PCI, we believe that fTRA can be a valid and effective alternative to TFA even in the CTO setting. Finally, even if limited by the lower number of patients analysed, our findings were confirmed also in the sub-set of single-catheter access, where the absence collaterals for interventional techniques or visualization of the distal vessel furthermore hinder the success of CTO-PCI.

Our study has several limitations. First of all, despite extensive and careful statistical modelling, residual confounding related to selection bias cannot be completely excluded and should be kept in mind interpreting these results. Because of the observational study design, no causal relationship between arterial access site selection and technical success can be established. This relationship may be influenced by operator based predicted CTO lesion difficulty. Differences in the angiographic characteristics of the CTO lesions in the transradial and transfemoral group are observed with a trend towards a lower J-CTO score in the fTRA group, with a higher average number of wires, microcatheters, balloons, stents and dual catheter injection required in the TFA group. Technical success rates were similar in fTRA and TFA groups also after stratification for J-CTO class, correction for angiographic characteristics in multivariable regression and in the propensity score analysis. The need for multiple imputation in calculating propensity score in almost all patients is a statistical expedient that, although widely accepted, might have underestimated confounding factors. Of note, caution should be paid when interpreting the comparison in procedural success between fTRA and TFA in the group with lowest propensity for radial approach (see Figure 2), where we disclosed a statistically non-significant, but numerically relevant, difference between the two approaches. In addition, the fact that the J-CTO score was lower and the PROGRESS-CTO was higher in fTRA compared to TFA is puzzling. It seems that TFA occlusions had more complexity features than fTRA, and the major adverse characteristic in fTRA was a higher absence of interventional collaterals, which drove the difference in PROGRESS-CTO score. These findings might be correlated to the fact that the prevalence of circumflex CTO was double in fTRA compared with TFA. The circumflex has less collaterals than other coronary arteries, and when there are, they are mainly epicardial and tortuous, hence non-interventional. Regardless of the explanation, this may introduce additional bias in the study. Lesion difficulty however does not seem to be a major confounding factor in the current study. Operators in our study have a minimum experience of 25 hybrid CTO PCI cases but are overall well experienced. This limits the generalizability of our findings to less experienced operators but supports the hypothesis that fTRA and TFA are equally technically demanding and thus equally successful in the hands of experienced CTO PCI operators. This is also supported by the fact that the current study does not confirm the previously raised concerns about lower efficiency of TRA for CTO PCI, as represented by more changes in CTO crossing strategies, longer procedure and fluoroscopy times, higher radiation doses and higher contrast agent requirement and the previously observed relationship between experience and procedural success in TRA CTO PCI[1,3,9,13]. Moreover, the current study is not powered to detect differences in relatively rare adverse events such as major bleedings. Even with the aforementioned limitations, the present analysis supports the use of a fully-transradial approach, which proved feasible and with relatively high success rate, low complication rate and no decrease in procedural efficiency when compared to conventional fully transfemoral or combined transradial-transfemoral approaches.

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References

1. Agostoni P, Biondi-Zoccai GG, de Benedictis ML, Rigattieri S, Turri M, Anselmi M, Vassanelli C, Zardini P, Louvard Y, Hamon M. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures; Systematic overview and meta-analysis of randomized trials. J Am Coll Cardiol. 2004;44:349-56.

2. Ferrante G, Rao SV, Jüni P, Da Costa BR, Reimers B, Condorelli G, Anzuini A, Jolly SS, Bertrand OF, Krucoff MW, Windecker S, Valgimigli M. Radial Versus Femoral Access for Coronary Interventions Across the Entire Spectrum of Patients With Coronary Artery Disease: A Meta-Analysis of Randomized Trials. JACC Cardiovasc Interv. 2016;9:419-34.

3. Wimmer NJ, Secemsky EA, Mauri L, Roe MT, Saha-Chaudhuri P, Dai D, McCabe JM, Resnic FS, Gurm Hs, Yeh RW. Effectiveness of arterial closure devices for preventing complications with percutaneous coronary intervention: an instrumental variable analysis. Circ Cardiovasc Interv. 2016;9:e003464.

4. Rathore S, Hakeem A, Pauriah M, Roberts E, Beaumont A, Morris JL. A comparison of the transradial and the transfemoral approach in chronic total occlusion percutaneous coronary intervention. Catheter Cardiovasc Interv. 2009;73:883-887.

5. Alaswad K, Menon RV, Christopoulos G, Lombardi WL, Karmpaliotis D, Grantham JA, Marso SP, Wyman MR, Pokala NR, Patel SM, Kotsia AP, Rangan BV, Lembo N, Kandzari D, Lee J, Kalynych A, Carlson H, Garcia SA, Thompson CA, Banerjee S, Brilakis ES. Transradial approach for coronary chronic total occlusion interventions: Insights from a contemporary multicenter registry. Catheter Cardiovasc Interv. 2015;85:1123-1129.

6. Rinfret S, Joyal D, Nguyen CM, Bagur R, Hui W, Leung R, Larose E, Love MP, Mansour S. Retrograde recanalization of chronic total occlusions from the transradial approach; early Canadian experience. Catheter Cardiovasc Interv. 2011;78:366-374.

7. Maeremans J, Walsh S, Knaapen P, Spratt JC, Avran A, Hanratty CG, Faurie B, Agostoni P, Bressollette E, Kayaert P, Bagnall AJ, Egred M, Smith D, Chase A, McEntegart MB, Smith WH, Harcombe A, Kelly P, Irving J, Smith EJ, Strange JW, Dens J. The Hybrid Algorithm for Treating Chronic Total Occlusions in Europe: The RECHARGE Registry. J Am Coll Cardiol. 2016;68:1958-1970.

8. Azzalini L, Vo M, Dens J, Agostoni P. Myths to Debunk to Improve Management, Referral, and Outcomes in Patients With Chronic Total Occlusion of an Epicardial Coronary Artery. Am J Cardiol. 2015;116:1774-80.

9. Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, Hiasa Y, Doi O, Yamashita T, Hinohara T, Tanaka H, Mitsudo K; J-CTO Registry Investigators. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: the J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. JACC Cardiovasc Interv. 2011;4:213-221.

10. Danek BA, Karatasakis A, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Patel MP, Mahmud E, Lombardi WL, Wyman MR, Grantham JA, Doing A, Kandzari DE, Lembo NJ, Garcia S, Toma C, Moses JW, Kirtane AJ, Parikh MA, Ali ZA, Karacsonyi J, Rangan BV, Thompson CA, Banerjee S, Brilakis ES. Development and Validation of a Scoring system for predicting periprocedural complications during percutaneous coronary interventions of chronic total occlusions: the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS CTO) Complications Score. J Am Hear Assoc 2016;5. doi: 10.1161/JAHA.116.004272

11. Yang CH, Guo GB, Chen SM, Yip HK, Hsieh K, Fang CY, Chen CJ, Hang CL, Chen MC, Wu CJ. Feasibility and safety of a transradial approach in intervention for chronic total occlusion of coronary arteries: a single-center experience. Chang Gung Med J. 2010;33:639-645.

12. Tanaka Y, Moriyama N, Ochiai T, Takada T, Tobita K, Shishido K, Sugitatsu K, Yamanaka F, Mizuno S, Murakami M, Matsumi J, Takahashi S, Akasaka T, Saito S. Transradial Coronary Interventions for Complex Chronic Total Occlusions. JACC Cardiovasc Interv. 2017;10:235-243.

13. Hoye A. Management of chronic total occlusion by percutaneous coronary intervention. Heart. 2012;98:822-828.

14. Burzotta F, De Vita M, Lefevre T, Tommasino A, Louvard Y, Trani C. Radial approach for percutaneous coronary interventions on chronic total occlusions: technical issues and data review. Catheter Cardiovasc Interv. 2014;83:47-57.

15. Dautov R, Ribeiro HB, Abdul-Jawad Altisent O, Nombela-Franco L, Gibrat C, Nguyen CM, Rinfret S. Effectiveness and Safety of the Transradial 8Fr Sheathless Approach for Revascularization of Chronic Total Occlusions. Am J Cardiol. 2016;118:785-789.

Figure Legends

Figure 1: Procedural success in fully transradial approach (fTRA) and transfemoral approach (TFA) groups according to the Japanese – Chronic Total Occlusion (J-CTO) score.

Figure 2: Procedural success in fully transradial approach (fTRA) and transfemoral approach (TFA) groups according to propensity-score quintiles.

Tables

Table 1: Demographic characteristics of the RECHARGE study population.

	fTRA (n=306)	TFA (n=947)	p-value
Age; mean ± SD (years)	66 ± 11	65 ± 10	0.262
BMI; mean ± SD (kg/m^2)	28 ± 5	28 ± 5	0.981
Male (%)	273 (89)	800 (85)	0.040
Current smoker (%)	62 (20)	209 (22)	0.507
Hypertension (%)	213 (69)	558 (59)	0.001
Dyslipidemia (%)	203 (68)	631 (67)	0.621
Diabetes mellitus (%)	91 (30)	241 (26)	0.136
Heart failure (%)	29 (10)	84 (9)	0.585
Previous MI (%)	106 (35)	384 (41)	0.066
Previous CABG (%)	48 (16)	169 (18)	0.366
Previous CABG on target vessel (%)	36 (12)	131 (14)	0.355
Previous PCI (%)	172 (56)	542 (57)	0.725
Previous stroke (%)	21 (7)	53 (6)	0.416
Peripheral vascular disease (%)	54 (18)	118 (13)	0.023
Chronic Kidney Insufficiency (%)	42 (14)	102 (11)	0.164
LVEF ≥50% (%)	155 (51)	533 (56)	0.140

BMI: body mass index; CABG: coronary artery bypass graft; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention; SD: standard deviation; fTRA: fully-transradial access; TFA: transfemoral access.

Table 2: Angiographic characteristics of the RECHARGE study population.

	fTRA (n=306)	TFA (n=947)	p-value
CTO target vessel			<0.001
RCA (%)	149 (49)	610 (64)	
LAD (%)	75 (25)	215 (23)	
LCX (%)	81 (27)	119 (13)	
LMCA (%)	1 (0.3)	3 (0.3)	
Ostial lesion (%)	29 (10)	17 (8)	0.286
In-stent occlusion (%)	30 (10)	96 (10)	0.862
Lesion length ≥20mm (%)	150 (49)	585 (62)	<0.001
Clear stump (%)	223 (73)	671 (71)	0.497
Blunt stump (%)	125 (41)	499 (53)	<0.001
Calcification (%)	203 (66)	526 (56)	0.001
Tortuosity ≥45° (%)	112 (37)	314 (33)	0.253
Re-attempt (%)*	53 (17)	215 (23)	0.050
J-CTO score, mean ± SD	2.1 ± 1.2	2.3 ± 1.3	0.058
PROGRESS score, mean ± SD	1.4 ± 1	1.1 ± 0.9	<0.001
Proximal cap side-branch†	115 (38)	373 (39)	0.591
Proximal cap ambiguity (%)	92 (30)	355 (38)	0.018
Lack of “interventional” collaterals (%)	154 (50)	278 (29)	<0.001
Diseased distal landing zone (%)	122 (40)	442 (47)	0.038
Distal cap at bifurcation (%)	77 (25)	268 (28)	0.286

*Re-attempt defined as patient which were included for a second or third attempt of their CTO (i.e. already had a previous failed procedure). † Side-branch with a diameter >2mm, within <5mm of the proximal CTO cap. CTO: chronic total occlusion; LCx: circumflex; J-CTO: Japanese-CTO; LAD: left anterior descending; LMCA: left main coronary artery; RCA: right coronary artery; SD: standard deviation; fTRA: transradial access; TFA: transfemoral access.

Table 3: Procedural characteristics.

	fTRA (n=306)	TFA (n=947)	p-value
Dual catheter injection (%)	48	86	<0.01
Procedure time* (min)	80 (54-120)	90 (60-121)	0.07
Fluoroscopy time* (min)	28 (17-50)	38 (22-56)	<0.01
Air Kerma dose* (Gray)	1.7 (1.1-2.9)	1.5 (0.9-2.6)	<0.01
Dose area product* (Gray*cm2)	89 (52-163)	101 (59-171)	0.06
Contrast volume* (ml)	200 (150-310)	250 (200-350)	<0.01
Guidewires† (n)	4.4 ± 2.9	5.4 ± 4.0	<0.01
Balloons† (n)	3.0 ± 2.4	3.6 ± 2.9	<0.01
Stents† (n)	2.0 ± 1.0	2.5 ± 1.1	<0.01
Stent length† (mm)	62 ± 31	76 ± 34	<0.01
Microcatheters† (n)	1.0 ± 0.6	1.2 ± 0.6	<0.01
Antegrade wire escalation ¥(%)	288 (94)	709 (75)	<0.01
Antegrade dissection/re-entry¥ (%)	51 (17)	241 (25)	<0.01
Retrograde¥ (%)	54 (18)	367 (39)	<0.01
Final successful technique for CTO crossing			<0.01
Antegrade wire escalation (%)	198 (76)	425 (52)	
Antegrade dissection/re-entry (%)	33 (13)	159 (19)	
Retrograde (%)	28 (11)	232 (28)	
Number of approaches†	1.4 ± 0.6	1.5 ± 0.6	<0.01

*Median (interquartile range). †Mean ± standard deviation. ¥Applied as primary or secondary strategy. CTO: Chronic Total Occlusion; fTRA: fully-transradial access; TFA: transfemoral access.

Table 4: Predictors of technical success in CTO PCI in multivariable analysis.

	Odds Ratio	95%-CI	p-value
Covariate Adjusted			
Radial access	0.88	0.58 – 1.34	0.56
Male sex	0.95	0.57 – 1.57	0.84
Peripheral vascular disease	0.89	0.56 – 1.41	0.62
CTO target vessel			
LAD vs RCA	1.08	0.68 – 1.73	0.75
LCx vs RCA	0.89	0.53 – 1.48	0.64
Previous CABG on target vessel	0.50	0.32 – 0.80	<0.01
CTO length >20mm	0.48	0.32 - 0.73	<0.01
Blunt stump	0.62	0.40 – 0.96	0.03
Severe calcification	0.57	0.39 – 0.84	<0.01
Bending >45 degrees	0.60	0.42 – 0.87	<0.01
Re-attempt	0.77	0.52 – 1.13	0.18
No ‘interventional’ collaterals	0.40	0.25 – 0.63	<0.01
Side branch >2mm	0.83	0.57 – 1.20	0.32
Diseased distal landing zone	0.65	0.45 – 0.95	0.03
Proximal cap ambiguity	0.64	0.42 – 0.99	0.04
ADR planned or applied	0.88	0.60 – 1.09	0.51
Retrograde planned or applied	0.49	0.31 – 0.77	<0.01
Propensity Adjusted			
Fully-Radial access	0.90	0.60 – 1.35	0.62
Propensity score (0.1 increase)	0.84	0.31 – 2.27	0.73

ADR: Antegrade Dissection and Re-Entry; CABG: coronary artery bypass graft; CI: Confidence Interval; CTO: Chronic Total Occlusion; LCx: Circumflex Artery; LAD: Left Anterior Descending artery; PCI: Percutaneous Coronary Intervention; RCA Right Coronary Artery.

Table 5: Procedural results of the study population after propensity score matching.

	fTRA (n=144)	**TFA (n=144)**	**p-value**
J-CTO score*	2.1±1.3	2±1.2	0.39
PROGRESS Score*	1.2±0.9	1±0.8	0.15
Procedural Success (%)	120 (83)	128 (89)	0.23
Procedural Time (min)*	101 ± 68	91 ± 45	0.15
Fluoroscopy Time (min)*	38 ± 28	40 ± 25	0.39
Dual catheter injection (%)	72 (50)	121 (84)	<0.0001
Stents* (n)	2.1 ± 1.1	2.4 ± 1.2	0.04
Microcatheters* (n)	1.0 ± 0.6	1.2 ± 0.6	<0.01
Antegrade wire escalation† (%)	136 (94)	122 (84)	0.01
Antegrade dissection/re-entry† (%)	25 (17)	33 (23)	0.30
Retrograde† (%)	29 (20)	45 (31)	0.04
Final successful technique for CTO crossing			0.14
Antegrade wire escalation (%)	87 (72)	80 (62)	
Antegrade dissection/re-entry (%)	18 (15)	22 (17)	
Retrograde (%)	15 (12)	26 (10)	
Number of approaches†	1,4 ± 0,6	1,5 ± 0,7	0.39

*Mean ± standard deviation. †Applied as primary or secondary strategy. CTO: chronic total occlusion; J-CTO: Japanese-CTO. fTRA: fully-transradial access; TFA: transfemoral access;