Current Cardiovascular Imaging Reports (2020) 13: 20
https://doi.org/10.1007/s12410-020-09541-3

INTRAVASCULAR IMAGING (AG TRUESDELL, SECTION EDITOR)

Role of Coronary Computed Tomography Angiography in Percutaneous Coronary Intervention of Chronic Total Occlusions

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Published online: 13 May 2020

Abstract

Purpose of Review Despite significant advances in procedural techniques for revascularization of chronic total occlusions (CTO), comprehensive procedural planning and accurate prediction of procedural success remain the Achilles' heels of CTO percutaneous coronary intervention (PCI). Understanding the unique anatomic characteristics of CTOs that may predict relative success and complication rates of revascularization is imperative. Coronary computed tomography angiography (CCTA) has evolved as an adjunct to invasive angiography to better characterize CTO lesions to improve success rates of CTO PCI.

Recent Findings Invasive angiography may be inadequate to characterize CTOs due to its inability to fully visualize the occluded segment. CCTA has evolved as a valuable adjunct to angiography, as it permits imaging of the arterial wall in the absence of luminal contrast, and thereby provides additional information regarding both the vessel course and lesion characteristics. CCTA-derived data can also be used in either standalone or combined scoring systems to assess the difficulty level of CTO PCI and has been shown to predict procedural success in clinical trials. Real-time CT fusion with X-ray angiography provides intraprocedural guidance to help resolve proximal cap ambiguity and better determine vessel course.

Summary In this review, we discuss the role of CCTA in guiding and improving outcomes of CTO PCI, both pre-procedurally and in real time.

Keywords Chronic total occlusion · Percutaneous coronary intervention · Revascularization · Coronary tomography angiography

Abbreviations

CTO	Chronic total occlusion
J-CTO	Multicenter Chronic Total Occlusion Registry of Japan
GW	Guidewire
CL	Clinical and lesion-related
ORA	Ostial location, Rentrop grade < 2, age ≥ 75 years

This article is part of the Topical Collection on *Intravascular Imaging*

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PROGRESS CTO	Prospective Global Registry for the Study of Chronic Total Occlusion Intervention
RECHARGE	Registry of CrossBoss and Hybrid procedures in France, the Netherlands, Belgium, and United Kingdom
CT-RECTOR	Computed Tomography Registry of Chronic Total Occlusion Revascularization
SVG	Saphenous vein graft

Introduction

Percutaneous coronary intervention (PCI) of chronic total occlusion (CTO) lesions is a complex procedure requiring in-depth planning and a high-degree of technical skill to achieve success. Pre-procedural assessment of both lesion characteristics and CTO anatomy may be used to predict procedural success. As contrast does not opacify the CTO segment, invasive angiography offers limited visualization of the CTO vessel, and thus little information regarding lesion composition or degree of calcification. Coronary computed tomography angiography (CCTA) can be used to plan the procedure, prognosticate success through use of risk scores, and guide the intervention in real time via CT and X-ray fusion technology. In this review, we discuss the utility of CCTA in providing information to help guide CTO PCI procedures, its use in risk stratification models that predict procedural success, and the limitations and future directions of this technology (Fig. 1).

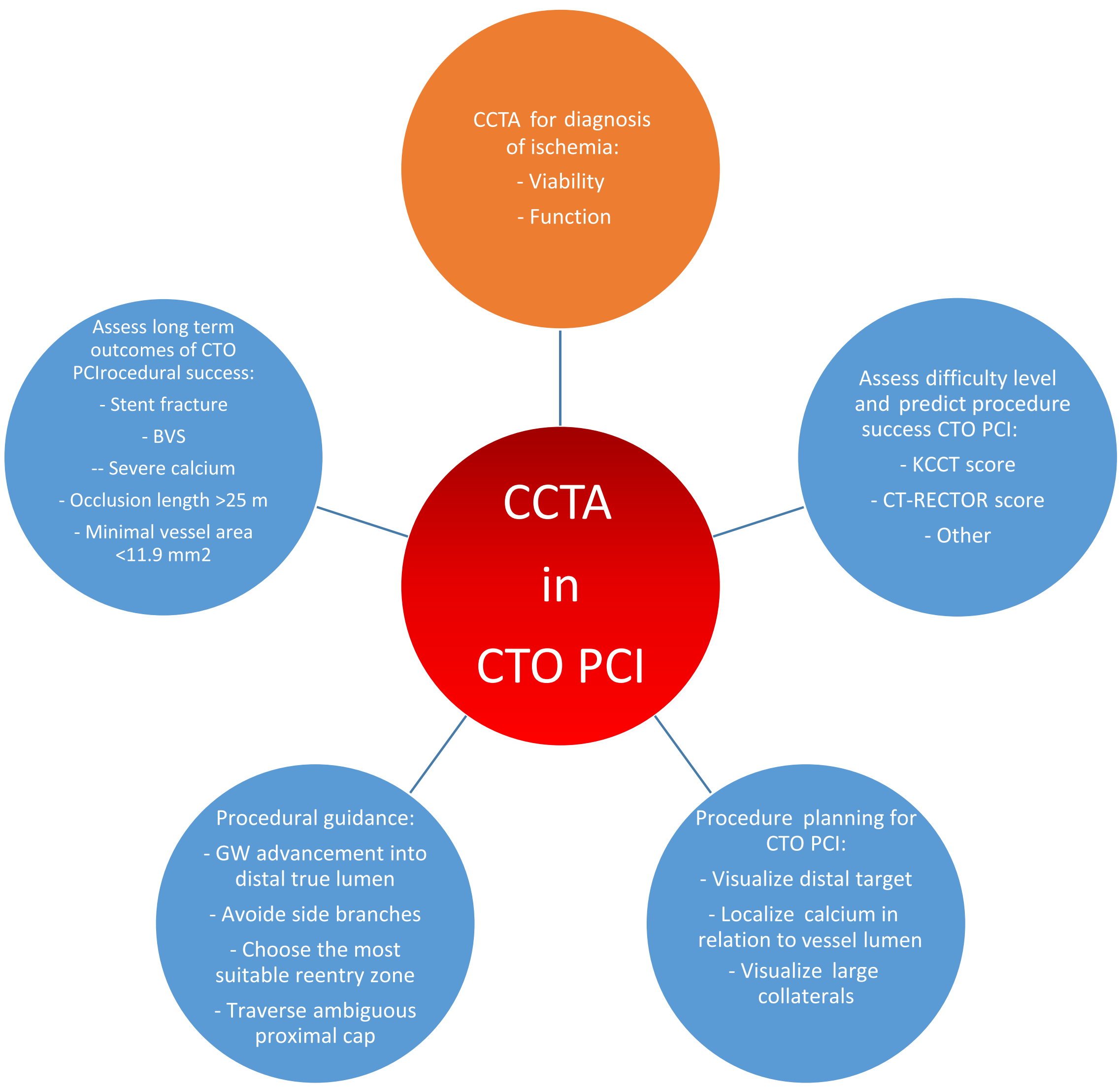

Fig. 1 Central illustration. BVS, bioresorbable scaffold; CCTA, coronary computed tomography angiography; CTO, chronic total occlusion; GW, guidewire; PCI, percutaneous coronary intervention

CTO PCI

Up to 15–30% of patients undergoing diagnostic coronary angiography have ≥ 1 CTO lesion [1–4], with a higher incidence of about 50–89% among patients who have had prior coronary artery bypass graft (CABG) surgery [2, 5]. A recent large randomized controlled trial [6] showed both a decrease in angina and improvement in quality of life (QoL) with CTO PCI in patients with CAD, while several observational studies [7, 8] have shown lower risk of major adverse cardiovascular events (MACE). Despite this data, CTO PCI represents only ~ 5% of all PCI [9] with success rates varying between 60 and 90% [9–11]. The complexity and technical challenges of the procedure, along with its associated risks, mandate a thorough evaluation of clinical, imaging, and technical factors prior to considering CTO PCI [12].

Role of CCTA in Diagnosis of Ischemia

In addition to evaluating coronary anatomy, CCTA has the ability to perform functional evaluation of wall motion, stress and rest myocardial perfusion, and assessment of scar by using appropriate scanner protocols [13–15]. However, routine use of CCTA for the assessment of myocardial perfusion and viability is not currently widely established at many institutions.

Role of CCTA to Predict Procedural Success of CTO PCI

Several risk scores derived from clinical, angiographic and CCTA CTO characteristics have been developed to evaluate the level of technical difficulty and likelihood of procedural success [16–23] (Table 1). CCTA features of CTO, including the shape of the proximal and distal stump (blunt vs. tapered), lesion length, extent of calcification in the occluded segment, presence or absence of multiple occlusions and vessel tortuosity, and course within the occluded segment, have all been used in single or combined scoring systems [24]. Scores, such as the CT-RECTOR (Computed Tomography Registry of Chronic Total Occlusion Revascularization) [22] and KCCT (Korean Multicenter CTO CT registry) [23], have been developed using CCTA features to estimate difficulty level and predict procedural success of CTO PCI.

CT-RECTOR Score Opolski et al. [22] noted multiple occlusions, blunt stump within the CTO, severe calcification ≥ 50% cross sectional area (CSA) within the CTO, bending ≥ 45 degrees within the CTO, duration of CTO ≥ 12 months, and previous failed PCI attempt as independent predictors for guidewire (GW) crossing within 30 min, and assigned 1 point for each predictor to develop the CT-RECTOR score. This score classifies CTOs into easy (score 0), intermediate (score 1), difficult (score 2), and very difficult (score ≥ 3) using the aforementioned predictors. Multiple occlusions (22% vs. 7%, $p < 0.001$) and severe calcification (34% vs. 21%, $p < 0.001$) were detected more often by CCTA than by coronary angiography, while blunt stump (47% vs. 46%, $p = 0.927$) and bending (23% vs. 25%, $p = 0.749$) were detected equally by both modalities. The probability of GW crossing of CTO in ≤ 30 min for easy to very difficult groups was 95%, 88%, 57%, and 22%, respectively.

KCCT Score Yu et al. [23] developed the KCCT score using CCTA-derived independent predictors for GW crossing ≤ 30 min, including proximal blunt entry, proximal side branch, bending > 45°, occlusion length ≥ 15 mm, severe calcification in the occluded segment, whole luminal calcification, reattempt of previously failed CTO PCI, and ≥ 12 months or unknown duration of occlusion. A KCCT score < 4 had a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for GW crossing ≤ 30 min of 70%, 68%, 72%, 73%, and 70%, respectively [23].

Fujino et al. demonstrated that CCTA-derived Multicenter Chronic Total Occlusion Registry of Japan (J-CTO) scores had greater area under the receiver operating characteristic curve (AUC) compared with angiography-derived scores for predicting procedural success of CTO PCI (0.855 vs. 0.698; $p < 0.001$) and 30-min wire crossing (0.812 vs. 0.692; $p < 0.001$) [25]. Thus, CCTA may be superior to angiography in predicting procedural success of CTO PCI.

Role of CCTA to Assess CTO Lesion Characteristics

Conventional invasive angiography with dual guide catheter injections through both donor and recipient vessels is used to better characterize CTOs but is limited in its ability to define either vessel morphology within the occlusion or vessel trajectory during wire manipulations, and offers often insufficient definition of the distal target zone due to inadequate collateral filling [26]. More recently, CCTA has emerged as an adjunctive imaging modality to more completely characterize CTOs. Unlike selective invasive coronary angiography, CCTA uses a larger volume of contrast which is injected simultaneously throughout the heart. Moreover, image acquisition occurs several seconds after the contrast reaches the coronary arteries. As a result, there may be more time for filling of distal vessels (via collaterals). CCTA can better define CTO lesion morphology—by providing information on soft tissues surrounding the occluded

Table 1 Scores to predict procedural success of CTO PCI

Name of score	Year published and number of patients	Components included in the score	End point/interpretation	C-statistic in validation model
CT-RECTOR score [22]	- 2015 - 229 patients - 240 CTO lesions	- Multiple occlusion—1 point - Blunt stump within CTO—1 point - Calcification ≥ 50% CSA within CTO—1 point - Bending ≥ 45 degrees within CTO—1 point - Previous attempt of PCI at CTO—1 point - Occlusion duration ≥ 12 months or unknown—1 point	GW crossing ≤ 30 min 0 points—easy 1 point—intermediate 2 points—difficult ≥ 3 points—very difficult	0.56 vs. J-CTO
KCCT score [23]	- 2017 - 643 patients - 684 CTO lesions	- Proximal blunt entry —1 point - Proximal side branch —1 point - CTO segment bending > 45°—1 point - CTO segment length ≥ 15 mm—1 point - Peripheral calcification: maximal encircling—1 point - ≥ 180° and CSA ≥ 50%—1 point - Central calcification (CSA = 100%)—1 point - Reattempt of previously failed CTO PCI—1 point - CTO duration ≥ 12 months or unknown—1 point	GW crossing < 30 min 0 points—easy 1 point—intermediate 2 points—difficult 3 points—very difficult 4 points—extremely difficult	0.809 vs. 0.75 (J-CTO) vs. 0.603 (PROGRESS CTO) vs. 0.73 (CL score) vs. 0.76 (CT-Rector)
J-CTO score [17]	- 2011 - 436 patients	- Proximal cap (blunt—1 point) - Tortuosity (> 45° bend—1 point) - Calcification (present—1 point) - Lesion length (≥ 20 mm—1 point)	GW crossing < 30 min 0 points—easy 1 point—intermediate 2 points—difficult ≥ 3 points—very difficult	0.76 (validation cohort) vs. 0.82 (derivation cohort)
CL score [16]	- 2015 - 1657 patients	- Proximal cap (blunt—1 point) - Calcification (severe—2 points) - Lesion length (≥ 20 mm—1.5 points) - Target vessel (non-LAD—1 point) - Other (prior MI—1 point; prior CABG—1.5 points)	Technical success 0 to 1—high probability > 1 and < 3—intermediate ≥ 3 and < 5—low ≥ 5—very low probability	0.68 vs. 0.60 (J-CTO)
ORA score [19]	- 2016 - 1073 patients	- Ostial location (yes—1 point) - Collateral filling (Rentrop 0 to 1—2 points, Rentrop 2 to 3—0 points) - Age (< 75—0 points, ≥ 75—1 point)	Technical success 0—easy 1—intermediate 2—difficult ≥ 3—very difficult	0.77 (validation cohort) vs. 0.72 (derivation cohort)
PROGRESS CTO score [20]	- 2016 - 781 CTO PCI procedures in 762 patients	- Proximal cap ambiguity—1 point - Absence of interventional collaterals—1 point - Moderate to severe tortuosity (2 bends > 70° or 1 bend > 90°)—1 point - Circumflex CTO—1 point	Technical success	0.72 vs. 0.74 (J-CTO)
RECHARGE score [21]	- 2017 - 880 patients	- Blunt proximal cap—1 point - Visible calcification on angiography—1 point - Tortuosity ≥ 45° within CTO segment or at CTO entry—1 point - Lesion length ≥ 20 mm—1 point - Diseased distal landing zone—1 point - Previous bypass graft on CTO vessel—1 point	Technical success	0.71 vs. 0.67 (J-CTO)
Ellis score [18]	- 2017 - 456 lesions in 436 patients	- Proximal cap - Distal target - Lesion length - Ostial lesion - Operator G - Collateral score - Tortuosity > 90° bend - Moderate to severe calcium	Technical success	0.73 vs. 0.55 (J-CTO) and 0.61 (PROGRESS CTO)

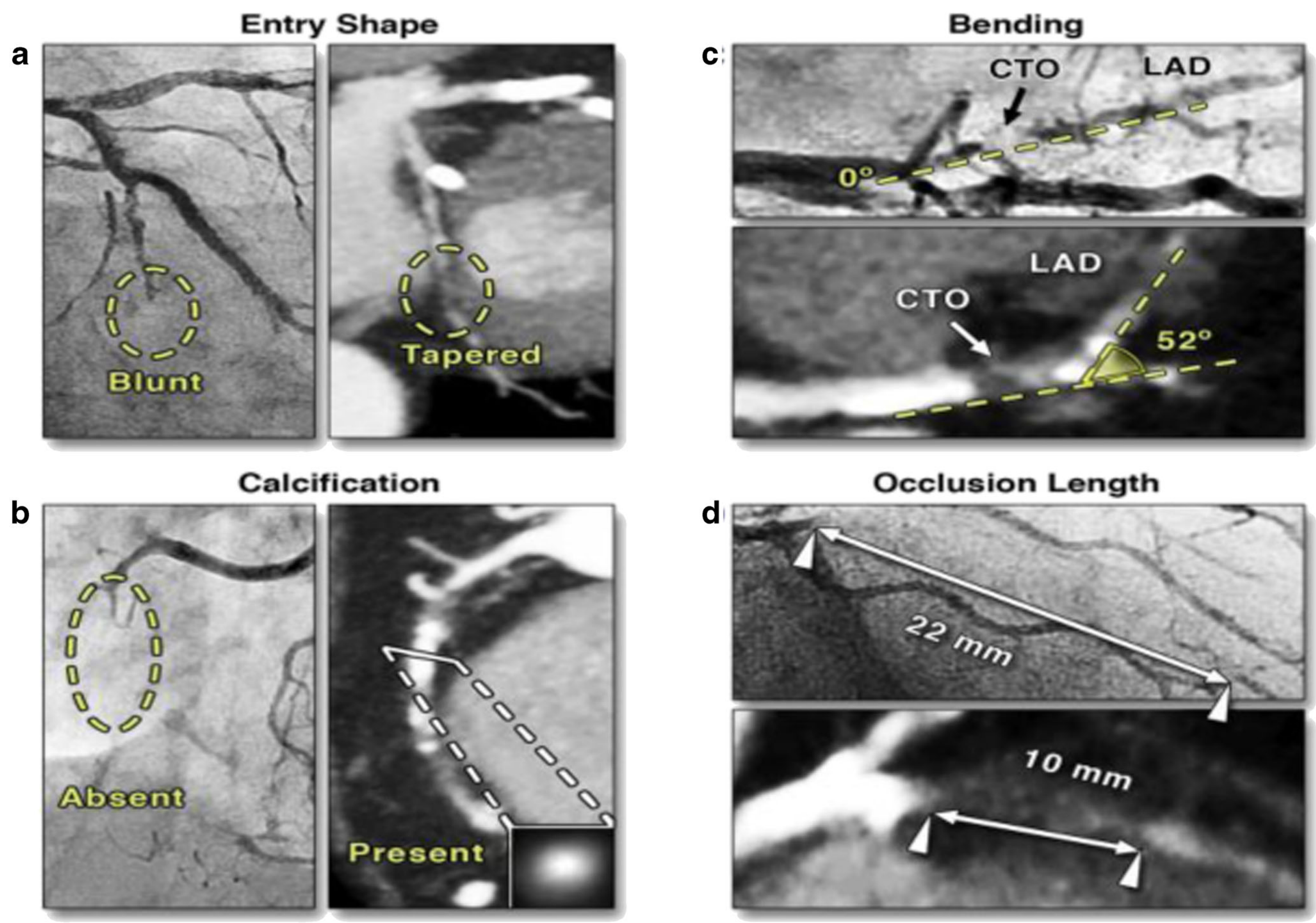

Fig. 2 CTO characteristics by coronary angiography versus CCTA. **a** Conventional angiography demonstrated a blunt entry shape; CTA revealed a microchannel. **b** An unsuccessful CTO case in which the guidewire did not pass the lesion because of severe calcification throughout the entire circumference as revealed by CTA. **c** A CTO lesion that appeared straight with conventional angiography. However, CTA clearly showed bending of the CTO segment. **d** Even though the occlusion length of the CTO measured using conventional angiography was 22 mm, the length measured by CTA was only 10 mm. CTA, coronary tomography angiography; CTO, chronic total occlusion. Adapted with permission from Fujino A et al. Accuracy of J-CTO score derived from computed tomography versus angiography to predict successful percutaneous coronary intervention. JACC Cardiovasc Imaging. 2018 Feb;11(2 Pt 1):209-217

vessel segment—and can better characterize predictors of CTO PCI success, including degree of calcification, extent of tortuosity, occlusion length [26], and distal vessel trajectory [27–29] (Fig. 2). CCTA can also identify ostial lesions that may be missed on angiography [24] (Fig. 3). A drawback of CCTA compared with angiography is its inability to differentiate total from high-grade stenosis/sub-total occlusions due to lower spatial resolution as well as the need for additional contrast and radiation exposure [30]. Table 2 compares invasive angiography with CCTA in evaluating CTOs.

Role of CCTA for Procedural Planning of CTO PCI and Procedure Guidance Through Real-Time Fusion of CT-Fluoroscopic Imaging

Information obtained by CCTA can assist in the procedural planning of CTO PCI. CCTA can better visualize distal targets compared with coronary angiography, given the impaired contrast filling of the distal bed during angiography secondary to negative remodeling in longstanding CTOs [28]. Upfront knowledge of distal target characteristics can help operators plan the direction of GW advancement during CTO PCI. CCTA can identify the extent of calcium and its location in relation to the lumen [26]. Central calcification is more challenging to wire than circular wall calcification, and knowing the location of calcium can help operators assess the difficulty of CTO PCI and plan their choice of guidewires and devices more appropriately [23, 30]. CCTA has a low spatial resolution compared with coronary angiography (~ 0.5–0.6 mm for contemporary scanners) and hence cannot visualize small collaterals with diameters below that size [31]. However, larger collaterals can be visualized and this information can be used to plan approach strategies for CTO crossing [32]. Thus, CCTA imaging is a helpful tool in procedure planning of CTO PCI and also has the potential to reduce contrast use

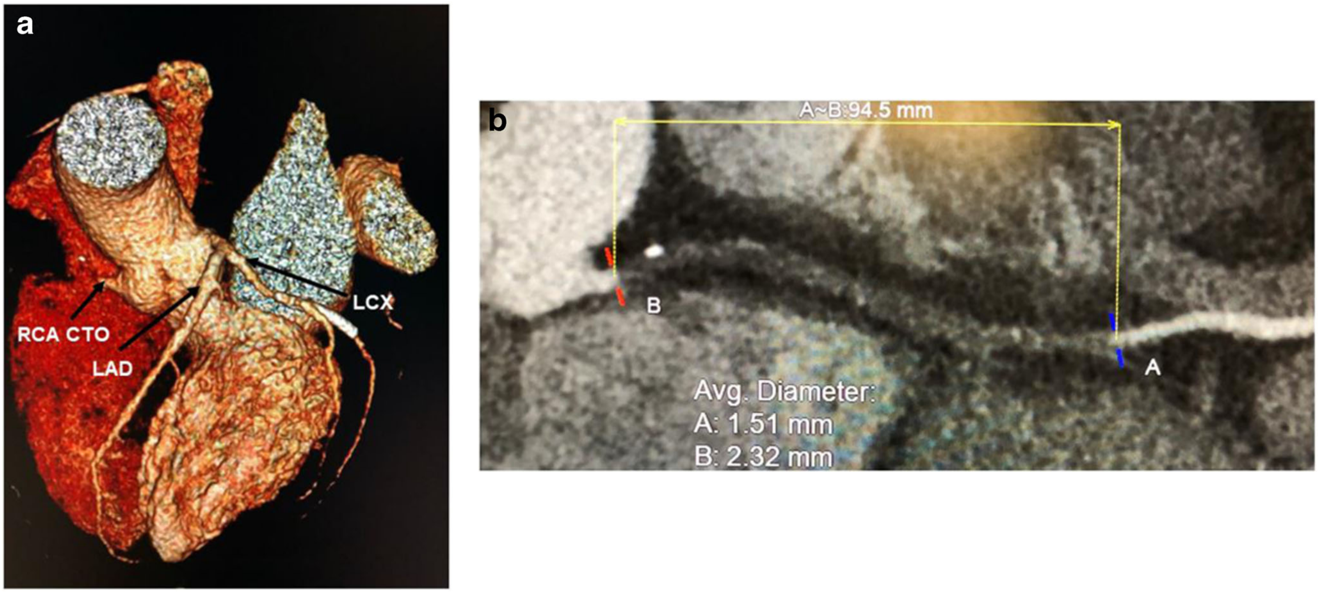

Fig. 3 CCTA showing ostial right coronary artery (RCA) CTO. **a** 3-dimensional rendered view. **b** Curved multiplanar reformatted view showing the length of the CTO and the size of the distal and proximal cap

and radiation exposure during CTO PCI and increase the chance of procedural success [30, 33].

CCTA can be a helpful tool for comprehensive evaluation of the anatomy of suitable occluded saphenous venous grafts and the distal vasculature to help plan CTO PCI of the vein graft or for retrograde CTO PCI of native vessel through the vein graft in post-CABG patients. Hajek et al. [34] used CCTA imaging to plan and successfully perform PCI of an ostial saphenous vein graft (SVG) to LAD CTO demonstrating superiority of CCTA compared with invasive coronary angiography to image the distal segment of the occluded SVG. Several studies since have shown high sensitivity and specificity, both greater than 90% of CCTA in imaging saphenous vein grafts [35, 36].

CCTA can be used for live procedure guidance using real-time integration of three-dimensional CCTA with fluoroscopic images [37]. By creating center lines of vessels, this fusion technology helps operators to see the path of the GW in relation to the vessel lumen, thereby providing a live roadmap for GW advancement into the distal true lumen, avoidance of side branches, and selection of the most suitable reentry zone [29] (Fig. 4). Ghoshhajra and Jaffer et al. showed that fusion of CCTA-derived centerline of a CTO on fluoroscopic images was feasible

Table 2 Comparison of evaluation of CTO morphology by coronary angiography and CCTA

Imaging modality	Advantages	Disadvantages
Invasive angiography	- Can differentiate CTO from high-grade stenosis/sub-total occlusion - Commonly used scores to evaluate difficulty of CTO PCI are based on coronary angiography-derived CTO characteristics	- Does not provide information on the vessel wall - Cannot visualize vessel morphology and course within CTO segment - Less effective in characterizing distal vessel beyond CTO due to negative remodeling and underfilling of collaterals - May miss ostial CTOs
CCTA	- Can provide information on the vessel wall - Can detect presence and degree of coronary calcifications in the occluded segment - Can provide information about vessel morphology within occlusion - Can characterize distal vessel beyond CTO - Provides information on ostial occlusions - May provide information on myocardial scar/viability (e.g., wall thinning, myocardial calcifications, resting perfusion defects)	- Additional radiation and contrast exposure to the patient - Cannot distinguish CTO from high-grade stenosis/sub-total occlusion, particularly in heavily calcified vessels, due to lower spatial resolution

CTO, chronic total occlusion; *PCI*, percutaneous coronary intervention; *CCTA*, coronary computed tomography angiography

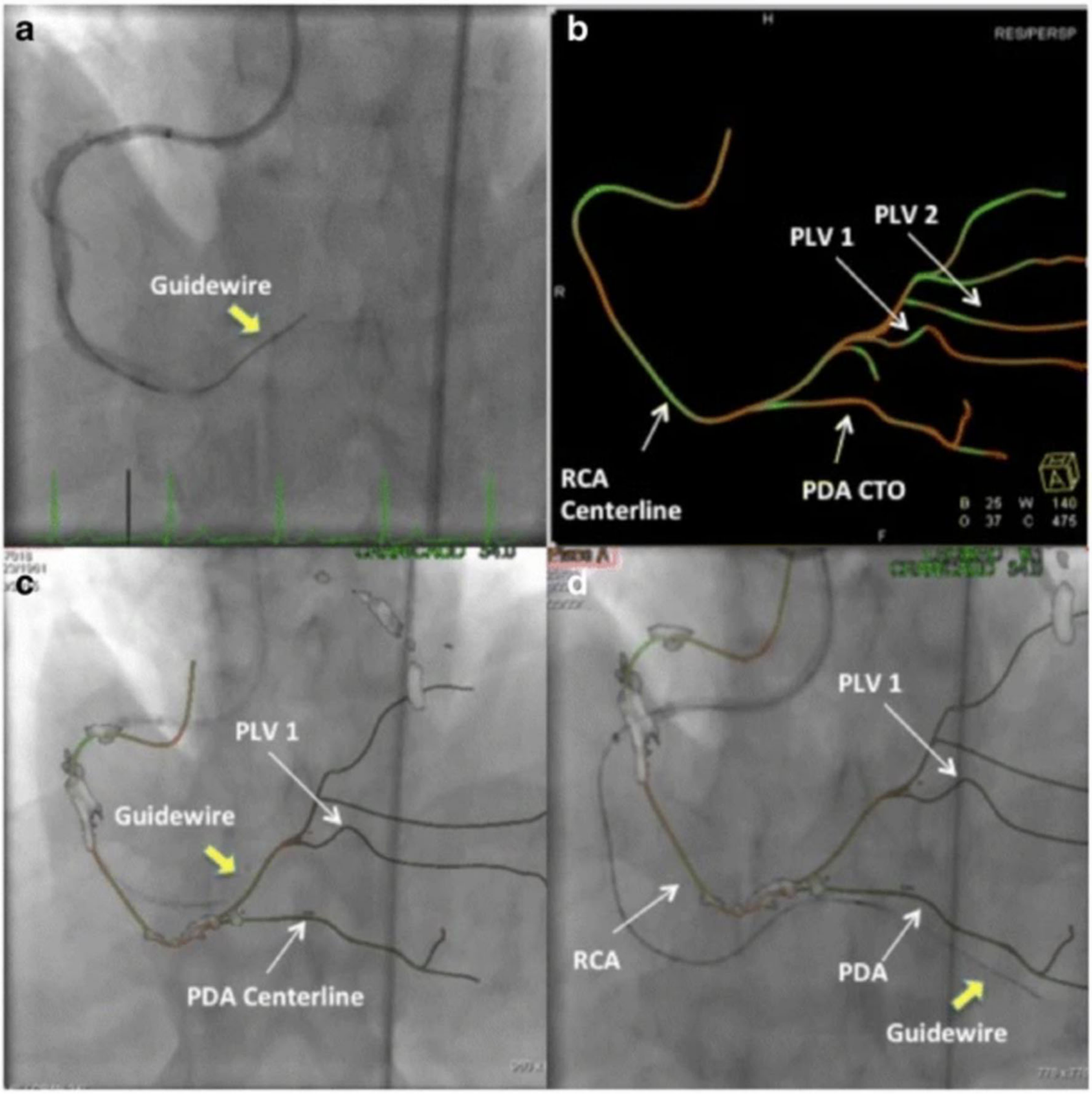

Fig. 4 Wiring target vessel without contrast injection. In this example, the operators were attempting to place the guidewire (*thick yellow arrow*) into the right posterior descending artery (PDA) to attempt opening an RPDA CTO. **a** RCA cineangiogram showing the antegrade wire in the distal vessel. **b** Centerline display of the PDA and PLV branches. **c** CTA/fluoroscopy fusion, without contrast, reveals that the wire has advanced past the entrance to the RPDA. The wire was pulled back and then advanced into the PDA without the use of contrast. **d** CTA/fluoroscopy fusion showing wire in the PDA after crossing of the CTO. PDA, posterior descending artery; RPDA, right posterior descending artery; CTO, chronic total occlusion; RCA, right coronary artery; PLV, posterior left ventricular artery; CTA, computed tomography angiography. Adapted with permission from Ghoshhajra BB et al. Real-time fusion of coronary CT angiography with X-ray fluoroscopy during chronic total occlusion PCI. Eur Radiol. 2017 Jun;27 (6):2464-2473

and particularly useful to understand mechanisms of success and failure in controlled antegrade dissection reentry (CART) [37] (Fig. 5). In particular, successful reentry occurred in zones devoid of calcium on CT overlay, which were not easily appreciated on fluoroscopy. Future applications of this approach may be to resolve proximal cap ambiguity, a marker of CTO lesion complexity that often necessitates primary retrograde CTO PCI approaches which are associated with higher adverse event rates [38]. In addition, CT fusion overlay is anticipated to help safely guide subintimal dissection of long right coronary artery occlusions with little calcium, and for side branch identification [33]. Future trials to evaluate the procedural benefits of routine use of co-registration of CCTA and fluoroscopic images in CTO PCI are warranted.

Use of CCTA to Assess Long-Term Outcomes After CTO PCI

CCTA can play a role in monitoring long-term outcomes after CTO PCI with some caveats. Due to blooming artifact

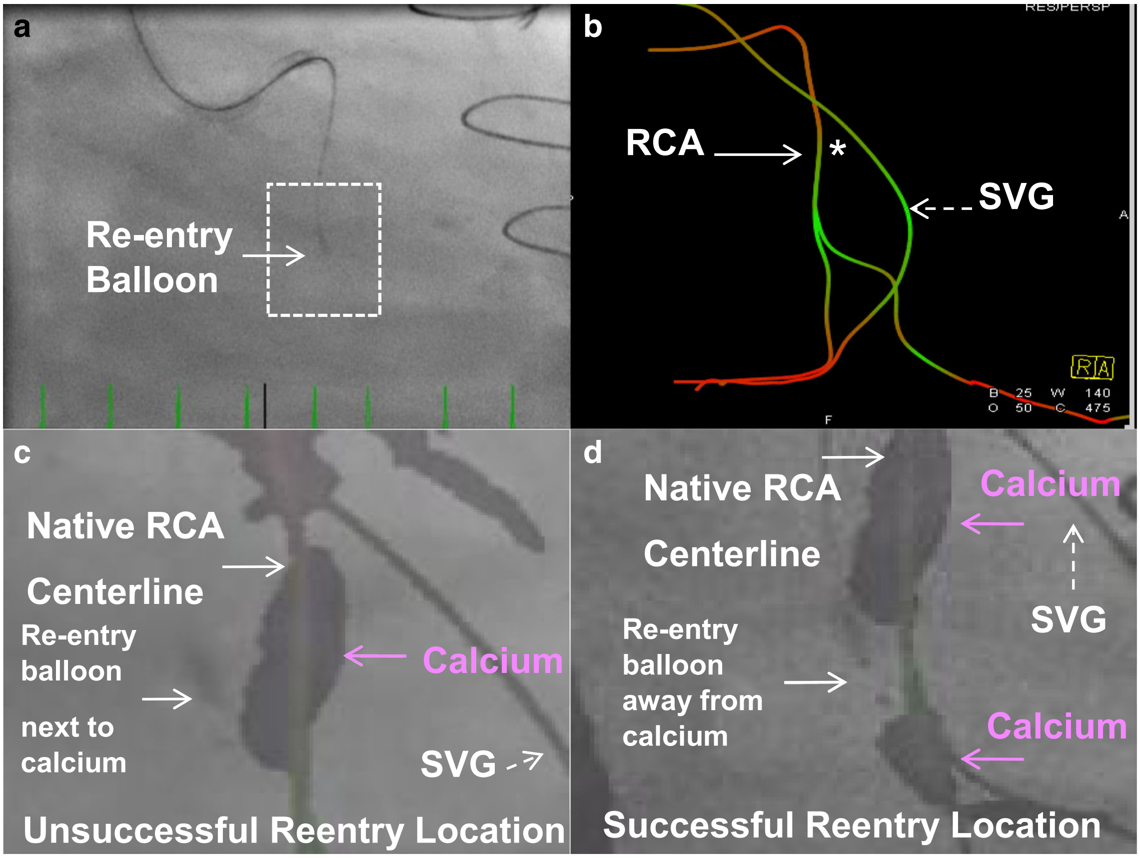

Fig. 5 Analysis of unsuccessful then successful antegrade dissection reentry during CTO PCI. In this example, coronary CTA fusion data display was chosen to show both the centerline and the arterial calcium. **a** Fluoroscopic image showing a reentry balloon placed distal to an RCA CTO (as confirmed by contralateral contrast injection; image not shown). The initial attempt at reentry from this location was unsuccessful. **b** Centerlines from CTA segmentation showing the RCA and SVG. **c** Magnified CTA/fluoroscopy fusion of the initial unsuccessful reentry site showing that the reentry balloon resided next to a large zone of calcium (*yellow arrow*). The reentry balloon was then advanced more distally approximately 1 cm, and successful reentry was performed using a stick-and-swap technique. **d** Magnified CTA/fluoroscopy fusion revealed that the successful reentry zone was between two areas of calcification. Adapted with permission from Ghoshhajra BB et al. Real-time fusion of coronary CT angiography with X-ray fluoroscopy during chronic total occlusion PCI. Eur Radiol. 2017 Jun;27 (6):2464-2473

produced by some coronary stents, CCTA may have limited ability to assess stent patency after PCI [33]. Stent fracture can however be detected and has been shown to be associated with higher MACE [39]. Non-metallic bioresorbable scaffolds can be well visualized by CCTA and monitored for disease progression with studies showing good patency of these stents for up to 5 years of follow-up post-CTO PCI [40, 41]. Finally, CCTA-derived parameters can be used to predict long-term outcomes. Ito et al. showed that the presence of ≥ 2 risk factors of severe calcification, occlusion length > 25 mm, and minimal vessel area < 11.9 mm^2 was associated with a higher rate of restenosis, re-occlusion, and MACE compared with 0 or 1 risk factor [42].

Limitations of CCTA in CTO PCI

First, performing a CCTA prior to CTO PCI adds additional contrast and radiation exposure for the patient. The typical dose for a gated scan is ~3–5 mSv, which is similar to a diagnostic coronary angiogram [43, 44]. This dose can be reduced further using an axial acquisition with prospective ECG-triggered scan [30, 45]. Second, patient preparation with coronary vasodilators (sublingual or topical nitroglycerin) and beta-adrenergic blockage to maintain a relatively slow heart rate (e.g., < 65 beats per minute) is often necessary to obtain good-quality CCTA images. Last but not least, one must weigh the benefits of a pre-procedural CCTA with the additional financial expense of this procedure [24]. For now, pre-procedural CCTA may be reserved for challenging CTO lesions (e.g., presence of proximal cap ambiguity, long CTO lesion lengths) more likely to benefit from additional imaging details.

Conclusions

CCTA evaluation of CTO coronary lesions can assist in guiding and improving the outcomes of CTO PCI, both pre-procedurally and in real time. Operators now have a promising opportunity to incorporate this imaging modality in conjunction with invasive angiography to optimize PCI treatment plans for CTO. Future studies evaluating the use of CCTA for pre-planning and intraprocedural guidance of CTO PCI are needed to determine whether CCTA can routinely improve procedural efficacy and safety.

Compliance with Ethical Standards

Conflict of Interest Poonam Velagapudi: None.

J Dawn Abbott: Research grants: Abbott Vascular, Sinomed, Biosensors Research USA.

Mamas Mamas: None.

Ron Blankstein: Research support from Amgen Inc. and Astellas Inc.

Yiannis Chatzizisis: Speaker honoraria, consultation fees, research grant by Boston Scientific, and research support by Medtronic.

Emmanouil S. Brilakis: Consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor Circulation), Biotronik, Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), CSI, Elsevier, GE Healthcare, InfraRedx, Medtronic, Siemens, and Teleflex; research support from Regeneron and Siemens. Shareholder: MHI Ventures.

Farouc Jaffer: Sponsored research from Canon, Siemens, and Shockwave; consultant for Boston Scientific, Abbott Vascular, Siemens, Philips, Biotronik, and Acrostak; equity interest, Intravascular Imaging, Incorporated. Massachusetts General Hospital has a patent licensing arrangement with Canon; FAJ has the right to receive royalties.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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