

iREVIEWS

STATE-OF-THE-ART REVIEW

Implementing Coronary Computed Tomography Angiography in the Catheterization Laboratory



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ABSTRACT

Coronary computed tomography angiography (CCTA) is now an established tool in the diagnostic work-up of patients suspected to have coronary artery disease. Yet, its usefulness beyond this phase has not been fully explored. The current review focuses on the implementation of CCTA as a tool to plan and guide coronary interventions in the catheterization laboratory. Specifically, we explore the potential of CCTA to improve patient selection for percutaneous revascularization, provide the rationale for better resource use, and present a novel approach to incorporate 3-dimensional CT guidance for percutaneous coronary interventions. (J Am Coll Cardiol Img 2021;14:1846-1855) © 2021 by the American College of Cardiology Foundation.

Over the last 2 decades, computed tomography (CT) has become an established tool in the diagnostic work-up of patients with suspected coronary artery disease (CAD). Noninvasive imaging of coronary arteries by computed tomography coronary angiography (CCTA) allows detecting atherosclerosis in its early phase, assessing for the presence of obstructive disease, and risk-stratifying patients based on plaque characteristics (1,2).

In addition, fractional flow reserve can be derived from computed tomography coronary angiography (FFR_{CT}), providing a surrogate of coronary flow and myocardial ischemia (3,4). Also, FFR_{CT} defines the severity and the functional pattern (e.g., focal or diffuse) of CAD (5). The

combination of CCTA and FFR_{CT} has increased our understanding of the interactions among luminal obstruction, plaque characteristics, and physiology at different stages of the atherosclerotic process (6).

Current guidelines emphasize the role of CCTA as a first-line test for patients with symptoms suggestive of obstructive CAD (7). Nevertheless, CCTA remains a diagnostic tool, its usefulness beyond this phase has not been yet fully explored. There is increasing awareness of the potential of CCTA to help plan and guide coronary interventions in a fashion similar to how cardiac CCTA has transformed transcatheter heart valve interventions. This state-of-the-art review summarizes the emerging role of CT in decision making about revascularization and focuses on the

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implementation of CCTA in the catheterization laboratory to guide coronary interventions.

CT-BASED EVALUATION FOR REVASCUARIZATION PROCEDURES

LUMINAL ASSESSMENT. CCTA overcomes a frequent problem of invasive angiography—that of vessel foreshortening (8). CT in the planning phase of a coronary intervention aids in providing the best angiographic projection in the cath lab, thereby minimizing foreshortening and overlapping of the segment of interest. This becomes even more relevant in the evaluation of bifurcation lesions where the visualization of the side-branch ostium is often sub-optimal with conventional angiography (9). Furthermore, angiographic foreshortening observed in 2-dimensional (2D) projection images impairs accurate evaluation of lesion length (8). This is a frequent cause of incomplete plaque coverage and geographic miss, and these latter issues are associated with adverse events after stent implantation (10). Besides, CT-derived lesion length evaluation incorporates the atherosclerotic extension that is not visible with conventional angiography; this approach mimics the evaluation obtained by intravascular imaging techniques (e.g., intravascular ultrasound [IVUS] and optical coherence tomography [OCT]).

The 2 most relevant metrics derived from CCTA analysis are minimal lumen diameter and reference vessel diameter. CT-derived quantitative coronary analysis has been shown to have a high degree of agreement with the true luminal dimensions (11). In the clinical setting, minimal lumen diameter is used to define lesion severity, whereas, for percutaneous revascularization planning, reference vessel diameter distal to the lesion is used to select stent diameter. CT-based quantitative coronary analysis has been shown to have a very high agreement concerning luminal dimensions compared to conventional angiography, and measurements based on CCTA have shown to be smaller compared with those derived from IVUS (12). The systematic differences in vessel dimensions between these methods are partially explained by the differences in spatial resolution and the physical properties of the techniques. For percutaneous coronary intervention (PCI) planning, CT-derived reference vessel diameter, obtained at healthy coronary segments, can be incorporated in the decision process concerning stent diameter selection.

PLAQUE ASSESSMENT. In addition to the lumen, CCTA allows us to visualize the atherosclerotic plaque

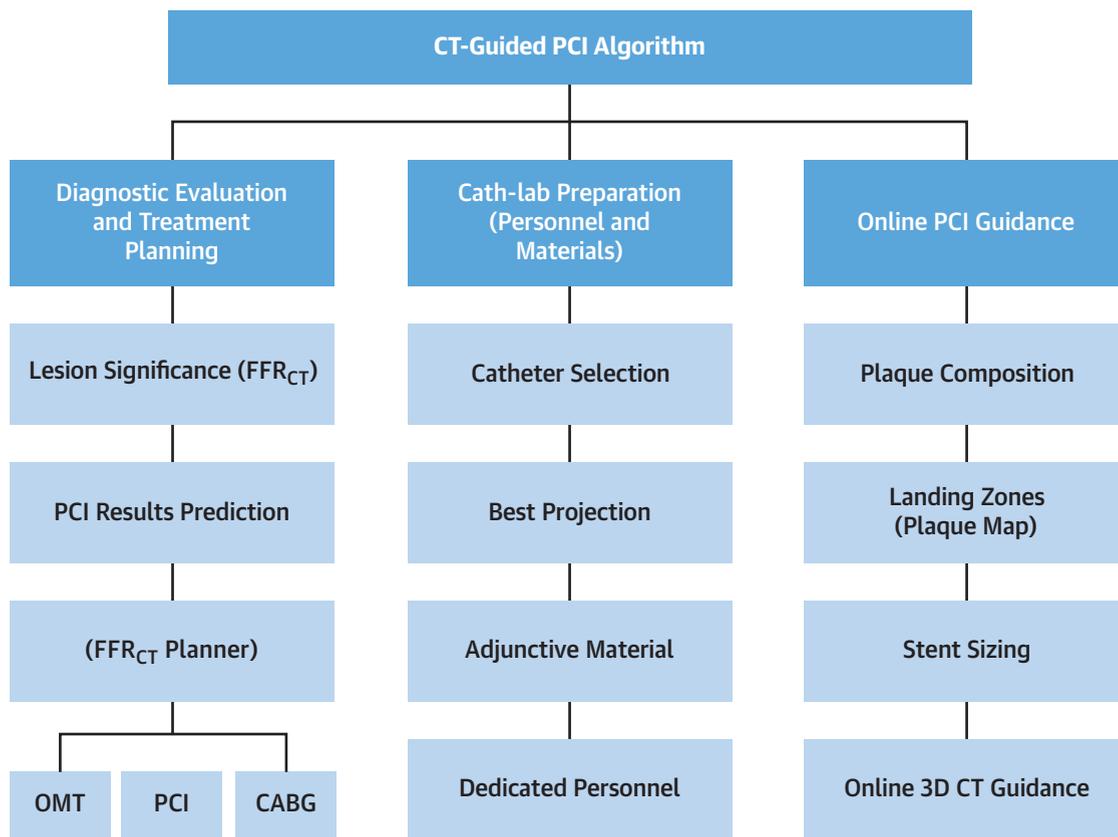
and determine its burden. Plaques can be qualitative and quantitatively characterized (13,14). It has been shown that CCTA helps identify high-risk plaques using measures of remodeling (e.g., remodeling index) and also allows the characterization of lesions through their Hounsfield units (HU) and appearances. Calcified plaques can be visualized as white structures with high HU, and their burden and circumference can be evaluated (15). High calcium burden is associated with lower stent expansion and higher rates of adverse events after PCI (16,17). Hence, visualization of high calcium burden in the planning phase of coronary intervention may prompt use of calcium modification techniques (e.g., rotational atherectomy, orbital atherectomy, excimer laser, or intravascular lithoplasty) to facilitate stent expansion (18–20). Stent expansion, which depends partially on the underlying plaque, is an independent predictor of major adverse events after PCI. On the other side of the plaque spectrum, plaques with low HU, the so-called soft plaques (i.e., HU <50) have been identified as independent predictors of acute coronary syndromes, periprocedural myocardial infarction, and no-reflow phenomenon (1,21,22). Also, identification of high-risk plaques before conventional angiography assists in the diagnostic strategy. Low-attenuation non-calcified plaques have been identified as independent predictors of low FFR (23). Therefore, the presence of high-risk plaques, even in mild to moderate stenosis, should prompt the operator to complement the invasive evaluation of the coronary lesion with invasive pressure measurements such as FFR. The assessment of plaque extension with CCTA allows extrapolating the normal-to-normal concept described with intravascular imaging (24). By “landing” the stents on healthy coronary segments, the atherosclerotic plaque is covered, mimicking the approach used with IVUS or OCT and potentially reducing the risk associated with a geographic miss.

Quantitative plaque assessment forms the basis of the 3D plaque reconstructions used during online CT guidance (as discussed later). Atherosclerotic plaque components are color-coded based on HU (e.g., white for calcified structures with >320 HU, green for plaque components between 50 and 320 HU, and red for low-attenuation plaques). This results in a 3D plaque portrayal or plaque map that facilitates imaging interpretation and the evaluation of disease extension, volume, and composition. Simultaneous plaque visualization during conventional angiography optimizes the interpretation of the images given that

ABBREVIATIONS AND ACRONYMS

- 2D** = 2-dimensional
- CAD** = coronary artery disease
- CCTA** = coronary computed tomography angiography
- CT** = computed tomography
- CTO** = chronic total occlusion
- FFR** = fractional flow reserve
- FFR_{CT}** = fractional flow reserve derived from computed tomography
- HU** = Hounsfield units
- IVUS** = intravascular ultrasound
- OCT** = optical coherence tomography
- PCI** = percutaneous coronary intervention

CENTRAL ILLUSTRATION CT-Guided PCI Algorithm



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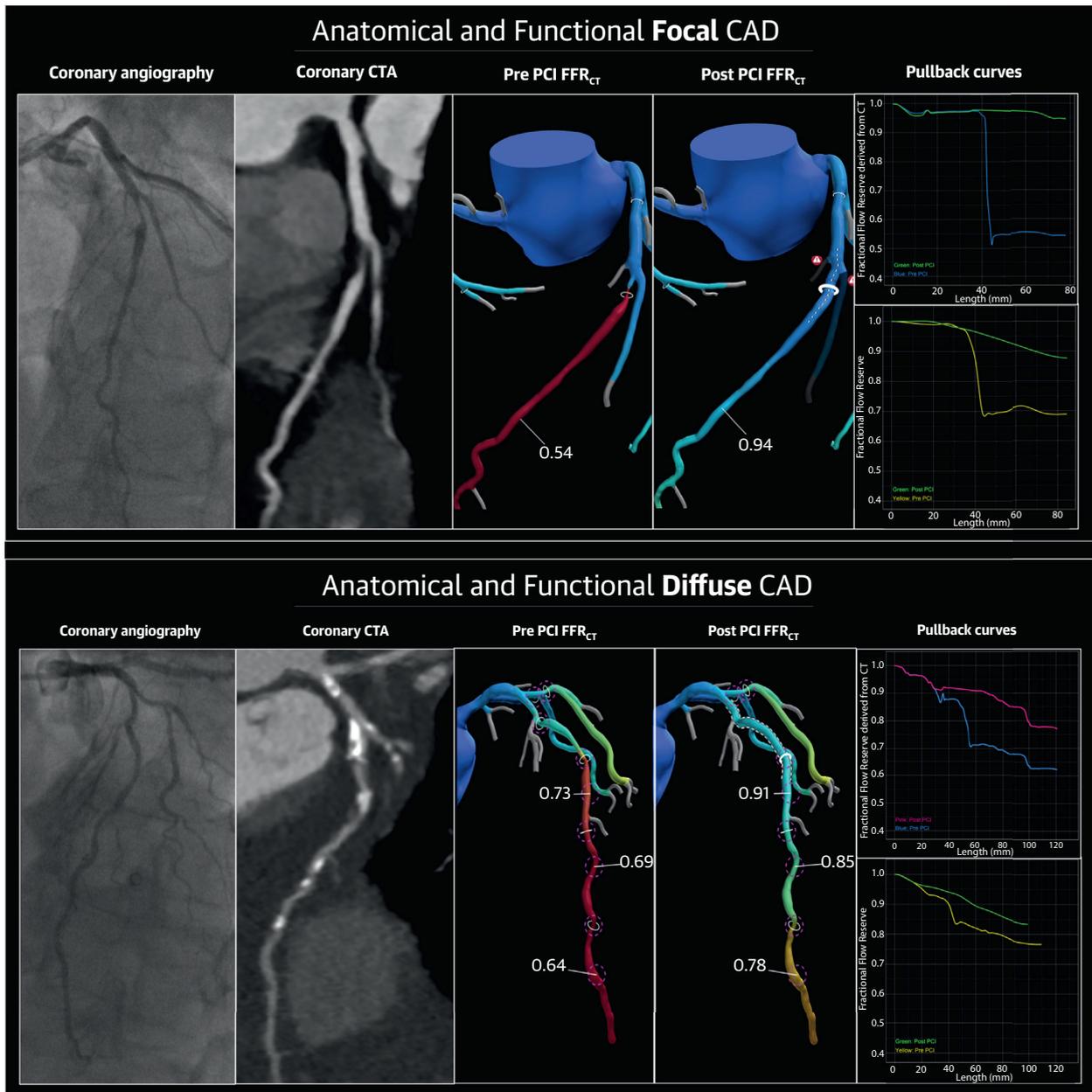
The percutaneous coronary intervention (PCI) algorithm starts with the diagnostic evaluation to ascertain hemodynamic lesion significance based on fractional flow reserve derived from computed tomography (FFR_{CT}). In this pre-cath lab phase, the results in terms of post-PCI FFR_{CT} can be predicted using the HeartFlow Planner. Based on the degree of functional revascularization assessed by virtual PCI, the clinician may opt for a given PCI strategy, coronary artery bypass graft (CABG), or medical therapy. The next step in the algorithm addresses the preparation of the cath lab based on the patient-specific characteristics. The selection of the coronary catheters is performed accounting for the position of the ostia, size of the aorta, and required support for the coronary intervention. Also, the best angulation for the visualization of the lesion can be determined. Adjunctive material and personnel corresponding to the case complexity can be prepared before starting the procedure. During the procedure, the availability of the online PCI guidance further aids in the visualization of the coronary tree. Furthermore, vessel size, extent, and composition of the atherosclerotic plaque are visualized side by side with the invasive coronary angiography helping in the selection of the diameter and length of the stent. 3D = 3-dimensional; OMT = optimal medical therapy.

apparently normal segments may be diffusely diseased. It should be highlighted that the interpretation of calcified plaques demands a special consideration given the overestimation of calcium volume due to blooming artifacts. Further research is required to determine the clinical implications of plaque features assessed by CCTA on PCI results.

FUNCTIONAL ASSESSMENT. Using CCTA, 3D coronary geometries can be extracted and used to perform fluid dynamic simulations. Assuming a normal

response of the coronary microcirculation to hyperemic stimulus, and adjusting microvascular resistance to vessel-specific myocardial mass, blood flow simulations can estimate coronary pressures, enabling us to compute FFR, the ratio of distal coronary pressure and aortic pressure during hyperemia. Clinical trials have demonstrated improved diagnostic performance of FFR_{CT} compared with a visual assessment for the detection of hemodynamically significant lesions (4). Moreover, the diagnostic performance of FFR_{CT} to detect hemodynamically

FIGURE 1 Case Examples of Focal and Diffuse CAD

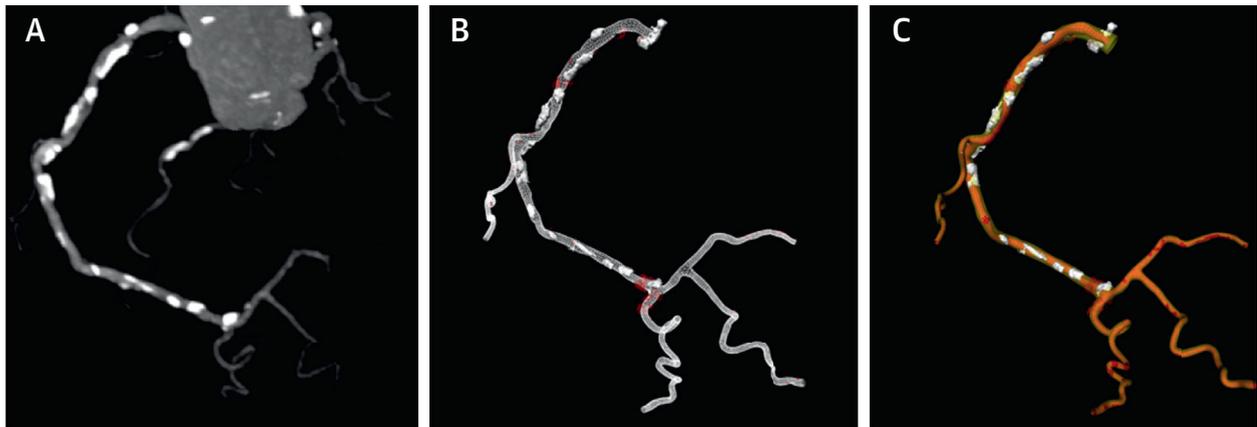


(Top) This case shows an anatomical and functional focal lesion located in the mid-left anterior descending artery. The virtual pull back curve derived from fraction flow reserve derived from computed tomography (FFR_{CT}) shows a focal pressure drop of approximately 40 FFR_{CT} units related to the lesion (**top right**). No pressure losses are observed either proximal or distal to the lesion. After virtual percutaneous coronary intervention (PCI), the predicted FFR was 0.94 and invasively measured FFR was 0.90. **(Bottom)** This case shows anatomical and functional diffuse coronary artery disease (CAD) in a left anterior descending artery. The virtual pull back curve derived from FFR_{CT} shows diffuse pressure losses along the vessel length (**bottom right**). After virtual PCI, the predicted FFR was 0.78 and invasively measured FFR was 0.82. CTA = computed tomography angiography.

significant lesions is similar to positron-emission tomography and cardiac magnetic resonance stress perfusion imaging and is significantly superior to single-photon emission computed tomography

(25,26). In the cath lab, the interpretation of the FFR_{CT} should also incorporate the agreement between the CT-derived coronary 3D anatomic model and invasive coronary angiography. By discordant

FIGURE 2 Process of 3D Lumen and Plaque Reconstruction



Computed tomography reconstruction made by QAngioCT/3D Workbench. (A) A 3-dimensional (3D) maximum intensity projection image is shown of a right coronary artery with diffuse calcifications. (B) 3D geometry reconstruction of lumen mesh and plaques. (C) Colored-coded lumen and plaques.

anatomic information, invasive FFR should be considered to confirm lesion significance. A detailed description of the principles, the different options for the calculation of FFR_{CT} , and outcome data are beyond the scope of this review. In the next section, we describe the usefulness of FFR_{CT} for patient selection for PCI.

CCTA-DERIVED 3D RECONSTRUCTION AS A GUIDE IN THE CATH LAB

PRECISE PCI AND PROCEDURAL PLANNING ALGORITHM.

The precise PCI and procedural planning algorithm is shown in the **Central Illustration**. Based on 3 mainstays—namely diagnostic evaluation, cath lab preparation and online guidance—the algorithm proposes the incorporation of CT into several phases of the management of patients with obstructive CAD.

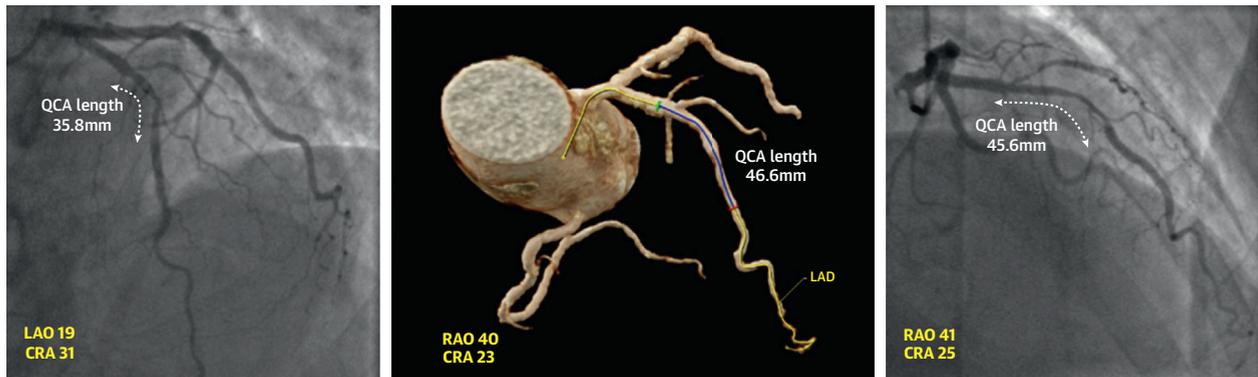
DIAGNOSTIC EVALUATION. The initial part of the algorithm extends the evaluation of the hemodynamic significance of CAD in 2 domains: 1) determination of the pattern of CAD (i.e., focal or diffuse); and 2) the prediction of PCI results. Functional evaluation with FFR_{CT} characterizes the pathophysiological pattern (e.g., focal or diffuse) of CAD noninvasively (5). This can be visualized either on the color-coded geometry or by a virtual FFR_{CT} pull back curve (27). In cases of focal functional disease, pressure losses are circumscribed to anatomic stenoses (i.e., lesion-specific ischemia), this vessel phenotype is favorable for PCI in terms of post-intervention vessel physiology. In contrast, cases of diffuse functional CAD show no focal pressure drops, these vessels often exhibit diffuse atherosclerosis on CCTA, and despite the presence of one or several vessels narrowing, PCI results are suboptimal in terms of post-PCI FFR. Therefore, the evaluation of the anatomic and physiological pattern of CAD aids predicting the likelihood of functional complete revascularization and relief from angina (27,28).

FIGURE 3 Cath Lab Setup for Online CT Guidance



The cath lab setup comprises the addition of synchronization hardware between the C-arm and CT software (black arrow) with the projection of the 3D CT-derived geometry projected side by side to the angiographic image (white arrow). Abbreviations as in Figures 1 and 2.

FIGURE 4 Impact of Optimal Projection for the Evaluation of Lesion Length



(Left) A left cranial 2-dimensional projection is shown with a lesion in the mid segment of the left anterior descending artery, and the quantitative coronary analysis (QCA) lesion length was 35.8 mm. **(Center)** Nevertheless, computed tomography showed that lesion length was longer and suggested a steep right cranial (CRA) projection to depict the true lesion length. **(Right)** The conventional angiography projection was adapted based on computed tomography-confirmed lesion length of 45.6 mm. LAO = left anterior oblique; RAO = right anterior oblique.

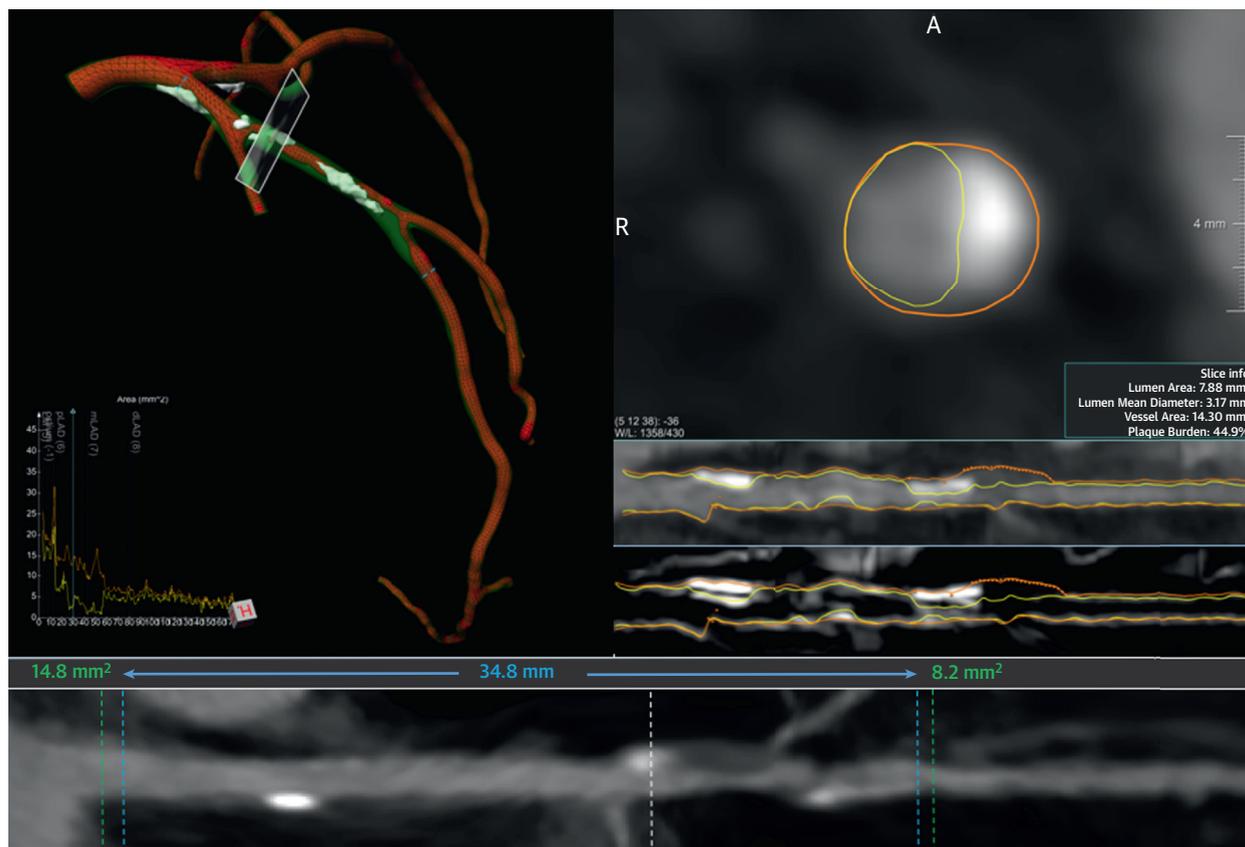
The FFR_{CT} planner (HeartFlow Planner; HeartFlow Inc., Redwood City, California) tool is a new approach to predict the results of PCI in terms of post-PCI FFR. The FFR_{CT} planner simulates luminal changes produced by PCI and recalculates coronary pressures using the modified “stented” geometry. This may assist to predict the benefit of a given PCI strategy. With the FFR_{CT} planner, the normal-to-normal can be demarcated based on coronary physiology. Two case examples of the application of the planner in cases of focal and diffuse CAD are shown in [Figure 1](#). As shown in the case example, PCI restored vessel physiology in focal functional CAD and this is likely to be translated in clinical benefit, that is, relief from angina. In contrast, in cases of diffuse functional CAD, suboptimal post-PCI results are plausibly responsible for persistent angina after PCI. Therefore, patient selection for PCI is individualized based on the potential benefit from percutaneous revascularization ([29](#)). The prospective multicenter validation of the FFR_{CT} planner is ongoing, and the results are expected by early 2021 (P3 [Precise Percutaneous Coronary Intervention Plan]; [NCT03782688](#)).

CATH LAB PREPARATION. From the evaluation of the position of the coronary ostia to the planning of complex PCI, a noninvasive stratification of the complexity of CAD aids on the organization of the cath lab. Although relatively uncommon, identification of coronary anomalies informs about the more adequate type of coronary catheters and cannulation technique ([30](#)). Moreover, CAD in the coronary ostia may change the cannulation strategy avoiding deep vessel catheterization that may conceal an obstructive lesion and

could potentially affect an FFR measurement. Furthermore, in patients with graft anastomosis in the aorta, CCTA aids in localizing conduits and expediting cannulation. In these scenarios, a CT-guided approach saves time, contrast, and reduces unnecessary radiation exposure.

Based on CCTA, complex interventions can be better planned in the cath lab. In the case of chronic coronary occlusions, CCTA helps to better identify the distal vessel and route for PCI than invasive angiography and predicts guidewire crossing and procedural success ([31](#)). The CT RECTOR (Computed Tomography Registry of Chronic Total Occlusion Revascularization) and J-CTO (Multicenter CTO Registry of Japan) score is helpful to predict the likelihood of success of chronic total occlusion (CTO) intervention integrating several CT variables allowing the planning of intervention in advance of angiography ([32,33](#)). CTO characteristics such as occlusion length, stump morphology, angulation, cross-sectional area of calcification, and the outlet morphology can all be routinely obtained from CCTA and help inform the likelihood of CTO recanalization ([33](#)). In addition to the diagnosis and characterization (e.g., calcification, tortuosity, length and stump morphology) of the CTO lesion, the 3D visualization in the cath lab allows for determining the exact vessel trajectory with accurate measurement of the occlusion (or occlusions) length. The real-time integration of 3D CCTA data and fluoroscopic images in the cath lab guides coronary wire progression in the occluded segment, reassuring the operator on the vessel-specific trajectory. Furthermore, based on the anatomic features of the CTO, for

FIGURE 5 The Prototype Software Package for Cath Lab Integration



(Top left) A 3D reconstruction of a coronary lesion located in the proximal segment of the left anterior descending artery is shown. **(Top right)** A tomographic cross-section at the level of the marker (**dashed white line**) is shown. **(Bottom)** A straight multiplanar reconstruction is shown including the measurement tool and selection of the landing zones and lesion length. Images were created using Prototype CT Workbench for Cath Lab (3D Workbench, Medis Medical Imaging Systems).

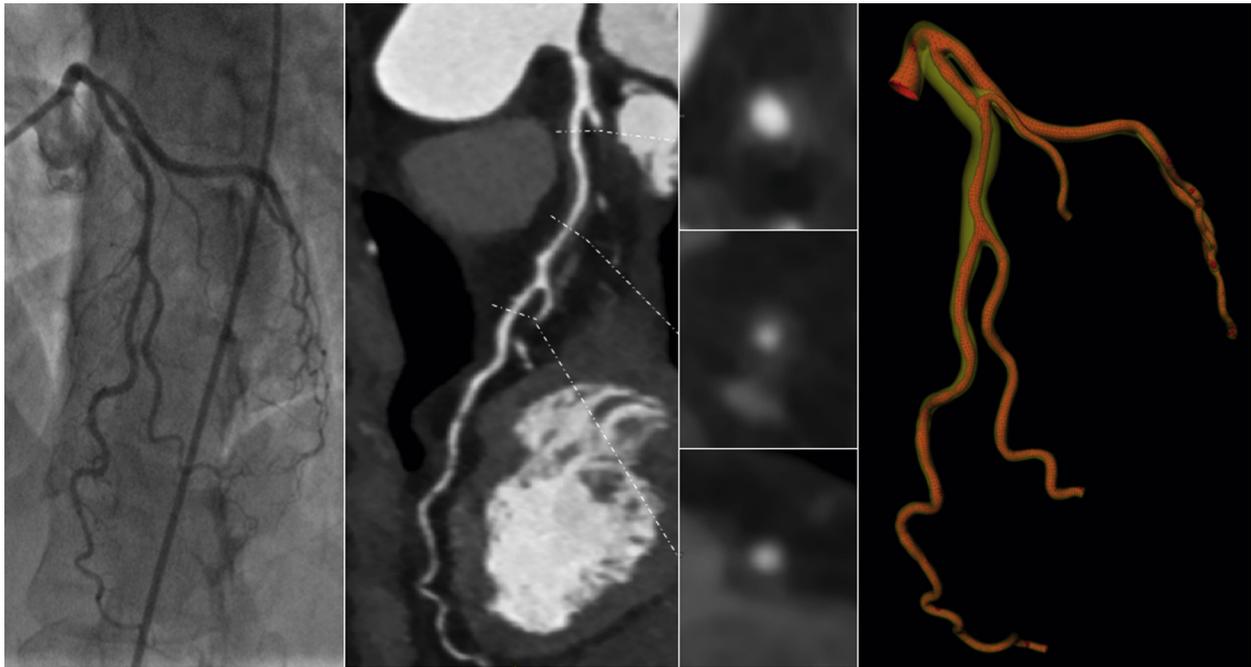
example, severe calcium in the proximal cap and good collateral circulation, an alternative CTO technique using a retrograde approach can be selected (34). Beyond CTOs, in other challenging lesion subsets such as left main disease, ostial lesions, bifurcations, or severely calcified coronary vessels, CCTA can inform upfront on the best strategy and the need for dedicated devices to increase the likelihood of success.

ONLINE PROCEDURAL AND PCI GUIDANCE. The visualization of the coronary circulation derived from CCTA provides a 3D view of the coronary tree and the plaque component during conventional angiography procedures. Both lumen and atherosclerotic plaques are reconstructed using dedicated software (QAngioCT RE/3D Workbench, Medis Medical Imaging Systems, Leiden, the Netherlands) and projected side by side with the 2D invasive angiography. To facilitate online interpretation, plaques components are

color-coded based on their HU. The process of coronary vessel reconstruction is shown in **Figure 2**. During the diagnostic procedure, the right and left coronary arteries are displayed sequentially in coordination with the invasive catheterization (**Video 1**). The movement of the C-arm is tracked in real time to synchronize the orientation of the 3D coronary tree with the projection of the fluoroscopic C-arm. A manufacturer-independent approach was accomplished by attaching an external sensor, called an inertial measurement unit to the C-arm. The inertial measurement unit is connected to a Raspberry Pi, which continuously communicates the sensor's—and therefore also the C-arm's—orientation with the 3D visualization software (**Figure 3**) (35).

During the procedure, the coronary anatomy derived from CCTA is continuously projected during changes in angiographic projections. At each projection, it is possible to assess the degree of overlapping

FIGURE 6 Atherosclerotic Disease in Apparently Normal Angiographic Vessel



(Far left) Conventional angiography shows mild disease in the proximal and mid left anterior descending (LAD) artery. (Center left) Multiplanar reconstruction image is shown of a LAD with a long noncalcified plaque from the ostial LAD until the takeoff the second diagonal branch. (Center right) The cross-sections show positive remodeling and plaque burden of 80%. (Far right) colored-coded 3D reconstruction of lumen and plaque depicting the burden and extension of the plaque. The online co-registration of coronary computed tomography angiography and angiography triggered a further invasive functional evaluation of the vessel resulting in an invasive fractional flow reserve of 0.76 (not shown).

and foreshortening without additional radiation or contrast. **Figure 4** shows a case example on the impact of patient-specific projection on lesion length assessment. Tailored angulations optimize lesion evaluation and prevent unnecessary angiographic acquisitions. Furthermore, the 3D CCTA model can be used as a 3D roadmap to assist during vessel wiring, further reducing the need for additional contrast injection while the wire is advanced.

Guidance of PCI with CCTA follows the same principles as with intravascular imaging (e.g., IVUS or OCT) (24). Pre-procedural assessment starts with the evaluation of plaque characteristics, composition, and extension. Lesion length is determined based on healthy landing zones proximal and distal to the lesion (**Figure 5**). The continuous display of CCTA and invasive angiography allows also the use of anatomic landmarks to visually co-register both modalities.

CLINICAL IMPLICATIONS. CCTA is emerging as the preferred method for noninvasive assessment of CAD. Consequently, the number of patients referred for an invasive angiography with a CCTA is expected to increase (36). Clinical decision based on the

morphological and functional component may translate to better selection of patients for percutaneous revascularization in a fashion similar to the way CTA has been used to better inform and plan structural heart disease interventions. Likewise, a pre-procedural stratification of case complexity may help to better organize time slots and personnel and, in this way, improve the cath lab workflow, efficiency, and resource use.

The integration of CCTA images in the cath lab is also likely to improve the safety of the procedure in terms of radiation dose and contrast volume. Moreover, the visualization of atherosclerotic disease in apparently normal or mild disease angiographic segments might increase the use of invasive functional and imaging assessment (**Figure 6**). Altogether, the integration of CCTA in the cath lab has the potential to improve the diagnostic performance of conventional angiography and patient management.

During PCI, CCTA provides a “live” IVUS-like imaging of the atherosclerotic plaque. The optimization of the angiographic information with plaque visualization is likely to be translated into improved PCI

technique with complete plaque coverage and might improve clinical outcomes after PCI. Nonetheless, it should be highlighted that after stent implantation, IVUS or OCT are the preferred methods to assess stent expansion and apposition.

FUTURE PERSPECTIVES

The integration of CCTA inside the cath lab represents a novel approach for the evaluation of CAD. Dedicated software has been developed that aims to simplify procedural workflow (Figure 5). This novel software solution simulates intravascular imaging tools that may facilitate adoption and image interpretation by interventionists. The Precise Procedure and PCI Planning and Guidance (P4) study will compare CT- versus IVUS-guided PCI, and the results of this study will set the foundation for the integration of CCTA in the routine of coronary interventions.

In the future, software that enables online co-registration and simulates cardiac cycle movement can further expand the synergism between these 2 techniques. Procedural planning of coronary procedures is likely to become an integral part of the percutaneous treatment of patients with CAD because most of the patients referred for invasive catheterization are evaluated with CCTA in the diagnostic phase. In the next decade, the interpretation of CCTA should become a core competency of interventional cardiologists. This would require a new training pathway focused on the guidance of coronary interventions.

CONCLUSIONS

CCTA has become the method of choice for the evaluation of CAD. Beyond the diagnostic phase, CCTA can be used to improve patient selection for PCI and to plan and guide therapeutic interventions in a fashion similar to structural heart interventions. CCTA adds 3Ds to conventional angiography and incorporates the visualization of atherosclerotic plaque in the entire coronary tree. This novel approach has the potential to enhance invasive procedures and improve clinical outcomes.

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HIGHLIGHTS

- The role of CCTA for the diagnosis and stratification of CAD is well established; however, its usefulness beyond the diagnostic phase remains to be determined.
- For patients referred to the cath lab, CCTA aids evaluating the likelihood of functional revascularization, adapting the cath lab resources to the case complexity, complementing conventional angiography based on the information of 3-dimensional model and by online real-time integration of CCTA data in the cath lab.
- Online CT-guidance for coronary procedures has the potential to improve diagnostic and therapeutic intervention.
- The clinical benefit of this CT-guided PCI warrants demonstration is a randomized trial.

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 **APPENDIX** For a supplemental video, please see the online version of this paper.