

Computed tomography angiography for the interventional cardiologist

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In recent years, coronary CT angiography (CCTA) has become a widely adopted technique, not only due to its high diagnostic accuracy, but also to the fact that CCTA provides a comprehensive evaluation of the total (obstructive and non-obstructive) coronary atherosclerotic burden. More recently, this technique has become mature, with a large body of evidence addressing its prognostic validation. In addition, CT angiography has moved from the field of 'imagers' and clinicians and entered the interventional cardiology arena, aiding in the planning of both coronary and structural heart interventions, being transcatheter aortic valve implantation one of its most successful examples. It is therefore of utmost importance that interventional cardiologists become familiar with image interpretation and up-to-date regarding several CTA features, taking advantage of this information in planning the procedure, ultimately leading to improvement in patient outcomes. On the other hand, the increasing use of CCTA as a gatekeeper for invasive coronary angiography is expected to lead to an increase in the ratio of interventional to diagnostic procedures and significant changes in the daily cath-lab routine. In a foreseeable future, cath-labs will probably offer an invasive procedure only to patients expected to undergo an intervention, perhaps becoming in this change true interventional-labs.

Keywords CT angiography • Coronary artery disease • Structural heart interventions

Come gather 'round people, wherever you roam
And admit that the waters, around you have grown...
...Then you better start swimmin', or you'll sink like a stone
For the times they are a-changin'.

Bob Dylan

Introduction

Advances in the field of computed tomography (CT) have made possible the non-invasive evaluation of coronary artery disease (CAD) and in recent years coronary CT angiography (CCTA) has become a widely adopted technique. This was due not only to its high diagnostic accuracy, but also to the fact that CCTA provides a comprehensive evaluation of both obstructive and non-obstructive CAD and, more recently, its prognostic information has been validated.

The initial studies of CCTA addressed mainly its diagnostic accuracy. This was done both by comparison with the gold standard invasive coronary angiography (ICA) and with intravascular ultrasound (IVUS).

As the technique became more robust and widely adopted in clinical practice, data were gathered regarding cardiovascular outcomes and this opened a second phase of studies addressing its prognostic value.

The latest technological advances have significantly improved CCTA temporal resolution and volume coverage, leading to a decrease in radiation and contrast dose, and improvements in image quality, that will further reinforce the role of CCTA for the evaluation of patients with possible CAD and potentially for making clinical decisions based on these findings (e.g. CT-based coronary atherosclerotic burden scores and functional assessment of coronary lesions).

Correlation with ICA: cardiac CT diagnostic accuracy

Many studies have been published evaluating the diagnostic accuracy of CCTA, by comparing with the gold standard ICA. These were initially done with four-detector row,^{1–4} followed by 16-detector row scanners,^{5–9} but by that time significant limitations existed related to the dose of contrast, long breath-hold times, and high percentage of

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segments excluded from analysis due to insufficient image quality. In a meta-analysis of 27 studies comparing CCTA (with scanners of at least 16-detector row) with ICA, the per-patient sensitivity was very high (96%), but the specificity was only modest (74%), leading to a positive predictive value (PPV) of 68%.¹⁰

The 64-detector row scanners are now considered to be the minimum requirement for CCTA.¹¹ In a more recent meta-analysis, including only studies with 64-detector row scanners, the reported per-patient sensitivity was 99%, specificity 89%; PPV was 93% and negative predictive value (NPV) was 100%.¹²

Nevertheless, even with 64-detector row scanners, some multi-centre trials, have reported low specificity and PPV when evaluating consecutive non-selected patients. In the assessment by coronary computed tomographic angiography of individuals undergoing invasive coronary angiography (ACCURACY) trial, a prospective multi-centre evaluating stable patients without known CAD who underwent CCTA before clinically indicated ICA, CCTA had a diagnostic sensitivity, specificity, PPV, and NPV of 94, 83, 48, and 99%, respectively.¹³ The low specificity and PPV reported in this trial could be related to the fact that patients were consecutively included irrespective of the baseline coronary calcium score, body mass index, or heart rate, variables that are well known to influence image quality.

In another multicentre study, Meijboom *et al.*¹⁴ evaluated the diagnostic performance of CCTA in a population including both stable and acute chest pain patients without known CAD referred for ICA. No patients or segments were excluded because of impaired

image quality attributable to either coronary motion or calcifications and the prevalence of obstructive CAD was 68%, factors that could explain the low per-patient specificity of 64% for CCTA found in this study, leading to a PPV of 86%. Once again, the per-patient sensitivity was 99% and the NPV was 97%.

With the development of dual source scanners, there was a significant increase in temporal resolution, leading to a less dependence on heart rate control.¹⁵ The introduction of new acquisition protocols with prospective ECG-triggering¹⁶ lead to a significant reduction in radiation dose, which was further reduced to <1 mSv doses with high-pitch spiral acquisitions, without compromising diagnostic accuracy^{17,18} (Figure 1).

Likewise, 320-detector row scanners also lead to significant improvements, reducing the radiation dose and amount of contrast while maintaining high diagnostic accuracy.^{19,20}

Addressing another important technical issue in CCTA, the improved spatial resolution of the high-definition scanners are also expected to lead to significant improvements, especially in the evaluation of calcified lesions, in-stent restenosis, lesions stenosis, and plaque composition, without increasing radiation dose.^{21,22}

The possibility of extracting both anatomical and functional information from CT data sets could ultimately lead to significant improvements in specificity and PPV, especially in the setting of lesions with intermediate stenosis. This concept has been recently reinforced by the DISCOVER-FLOW,²³ DeFACTO,²⁴ and NXT²⁵ studies that demonstrated a significant improvement in CCTA diagnostic

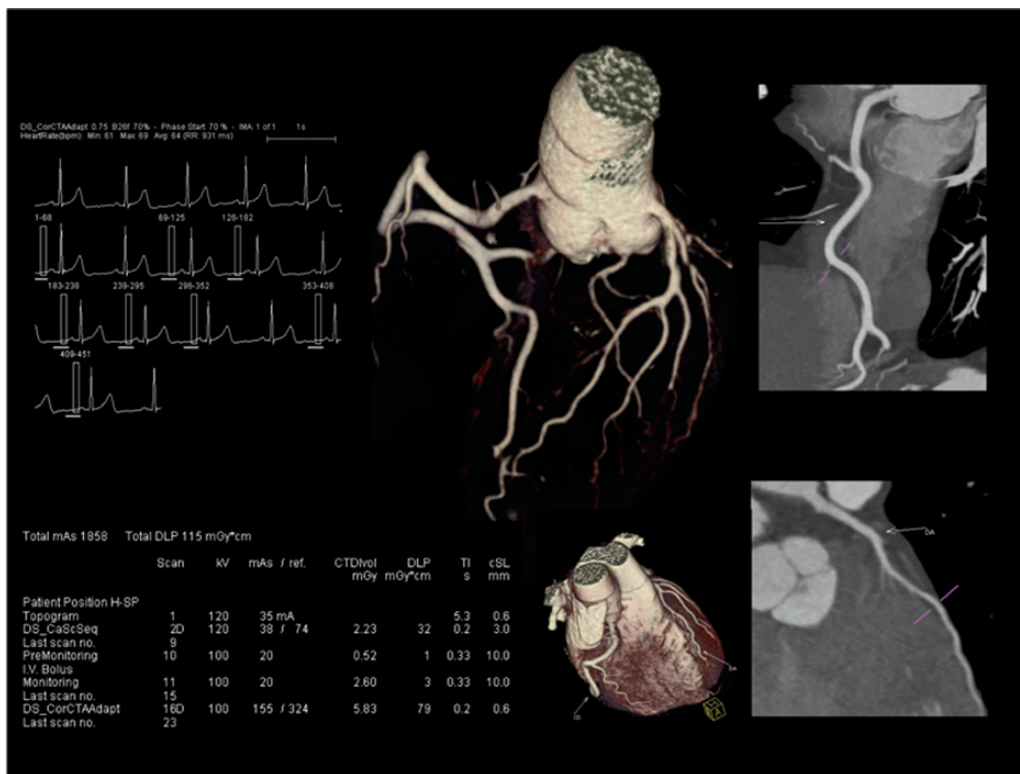


Figure 1: CCTA with prospective triggering with an estimated radiation dose of 1.1mSv (79DLP, conversion factor of 0.014), in a patient with normal coronary arteries.

performance when combined with non-invasive fractional flow reserve (FFR_{CT}). This novel method derives the physiological significance of CAD by applying the principles of computational fluid dynamics, taking in consideration not only CAD severity, but also left ventricular mass.

Summing up the different multicentre trials and meta-analysis addressing this issue, it has become clear now that this non-invasive imaging technique has a very high sensitivity for detecting patients with significant CAD, leading to a very high (virtually 100%) NPV, which makes CCTA a perfect gatekeeper for invasive angiography.

The selection of patients for ICA is traditionally based on non-invasive stress testing aimed at identifying patients with obstructive CAD who could benefit from revascularization. Nevertheless, many patients undergoing ICA have normal coronary arteries or non-obstructive lesions, which decrease its diagnostic yield. In a large contemporary registry, with data from almost 400 000 patients referred for ICA, obstructive CAD was found in only 37.6% of the patients, reflecting the low diagnostic yield in routine clinical practice.²⁶ This way, better strategies for the identification of patients in need for ICA are needed and in this regard CT angiography (CTA), by having a high NPV, can be a useful gatekeeper.

In a recent analysis of the large CONFIRM registry, the rates of ICA and revascularization after a CCTA with no CAD (2.5 and 0.3%, respectively) or mild CAD (8.3 and 2.5%, respectively) were very low. On the other hand, in this registry, obstructive CAD ($\geq 50\%$

stenosis) by CCTA was associated with a high percentage of revascularization, ranging from 28% for 1 vessel to 66.8% for 3 vessel CAD, supporting the concept of CCTA as a gatekeeper for ICA.²⁷

Presently, some patients are referred for ICA for pure diagnostic purposes, like the evaluation of possible CAD in patients scheduled to undergo non-coronary cardiac surgery, to evaluate the need of concomitant myocardial revascularization. In those patients, CCTA seems to be a valid alternative^{28,29} and is considered to be appropriate when the pre-test probability of CAD is not high^{11,30} (Figure 2).

CCTA might also become an alternative to ICA for a routine evaluation of coronary arteries following heart transplantation,³¹ although this can be difficult in the setting of more advanced diffuse disease of chronic transplant arteriopathy, in face of the current limitations of CCTA spatial resolution.

Patients with new-onset or newly diagnosed heart failure and no prior CAD are recommended to undergo the evaluation of possible CAD and are frequently referred for ICA.^{11,32,33} In this setting, CCTA might be a valid alternative to exclude CAD as the underlying aetiology for dilated cardiomyopathy, with the advantage of providing in the same scan information on cardiac vein anatomy that might be potentially relevant in candidates for cardiac resynchronization therapy.^{34,35}

Owing to its non-invasive nature and the ability to evaluate the coronary wall, CCTA has also been considered as a valuable imaging modality for coronary dissections and intramural haematomas, especially in the follow-up of patients managed conservatively.³⁶

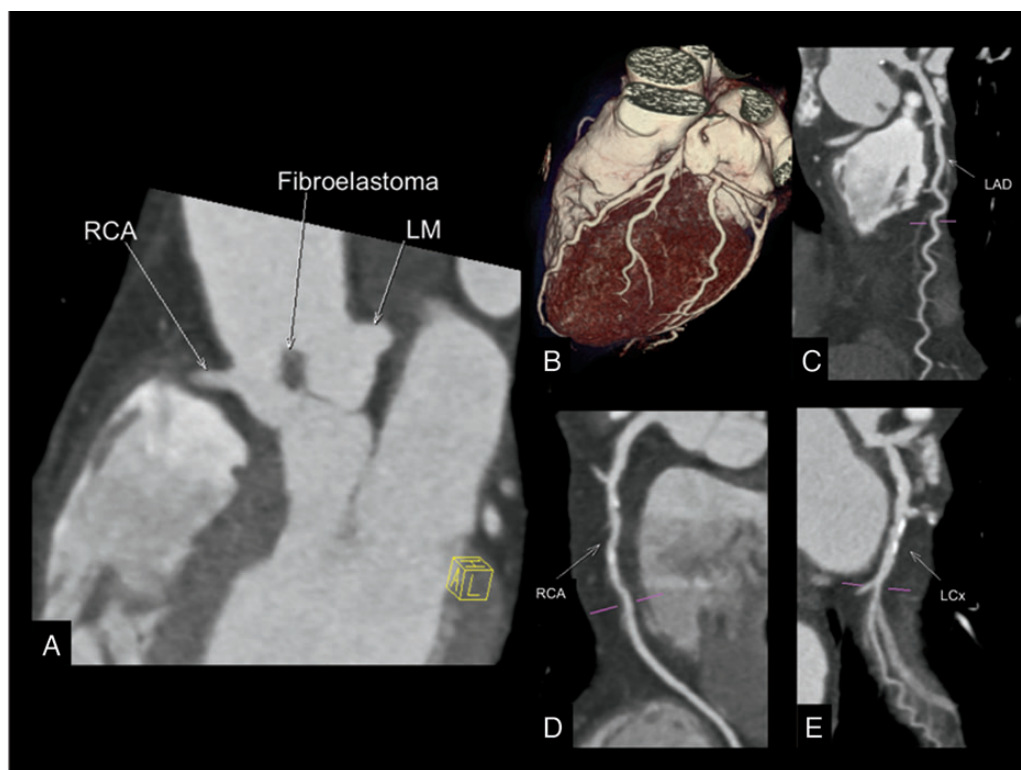


Figure 2: CCTA for the exclusion of obstructive CAD prior to valvular surgery, in a patient with a fibroelastoma of the aortic valve. Multiplanar (A, C, D, and E) and volume-rendering technique (B) reconstructions showing the mass attached to the aortic cusps and predominantly calcified non-obstructive coronary lesions in the RCA and LCx. This 66-year-old female patient underwent surgery without the need for invasive coronary angiography.

The use of CCTA in these purely diagnostic indications, coupled with a better selection of patients for ICA using CCTA as a gatekeeper, are expected to lead to an increase in the ratio of interventional to diagnostic procedures in the catheterizations laboratories.

In conclusion, when evaluating the diagnostic accuracy of CCTA, some factors have to be considered, that could influence the performance of the exam, and could explain the differences between different studies:

- type of scanner technology (64-detector row scanners are now considered to be the typical minimum standard).
- population studied, regarding expected prevalence of obstructive CAD (can be calculated with pre-test CAD probability scores—CCTA is indicated in low-to-intermediate CAD probability).
- inclusion of non-evaluable segments in the analysis (considering non-evaluable segments as positive improves sensitivity but reduces specificity).
- inclusion of patients with a high body mass index, high calcium score or high heart rates, factors known to negatively affect image quality.

Evaluation of patients with previous revascularization

The evaluation of patients with previous revascularization procedures can be challenging for CCTA and these patients are usually recommended to undergo stress imaging.³⁷

In the evaluation of patients after PCI, there are two sets of difficulties faced by CCTA. Metallic artefacts caused by the struts (influenced by the type of alloy and strut thickness), impairing the assessment of stents with a diameter <3 mm and/or stents with thick struts (≥ 140 μm).^{38,39} In a meta-analysis of studies with 64-rows scanners including 1398 stents, the sensitivity and specificity for the detection of in-stent restenosis was only 79 and 81%, respectively.⁴⁰ The increasing adoption of bioresorbable scaffolds in clinical practice might lead to an improvement in the diagnostic accuracy of CCTA for stent evaluation, since the metallic artefacts are only limited to the radio-opaque markers at scaffold margins.⁴¹

Besides the aforementioned difficulties imposed to the evaluation of the stented lesions, these patients frequently have other lesions in the coronary tree, some of them of intermediate degree of stenosis, that could impair specificity on a patient-based level, since specificity and/or PPV of CCTA has been shown to be lower in cohorts with higher disease prevalence^{13,14,24} (Figure 3). This last limitation is also true regarding the evaluation of the native vessels in patients with prior coronary artery bypass grafts, because of the extent of CAD, often associated with severe calcifications and small vessel calibre, leading to a decrease in CCTA accuracy in this setting.^{42,43}

In contrast, CCTA has a high accuracy for the evaluation of graft patency, due to the larger diameter, less motion and less frequently calcified, when compared with the native arteries (Figure 4). In addition, disease in grafts more often presents as occlusion rather than stenosis, which are easy to depict in CCTA. In a meta-analysis including studies with both 16- and 64-rows scanners, the sensitivity and

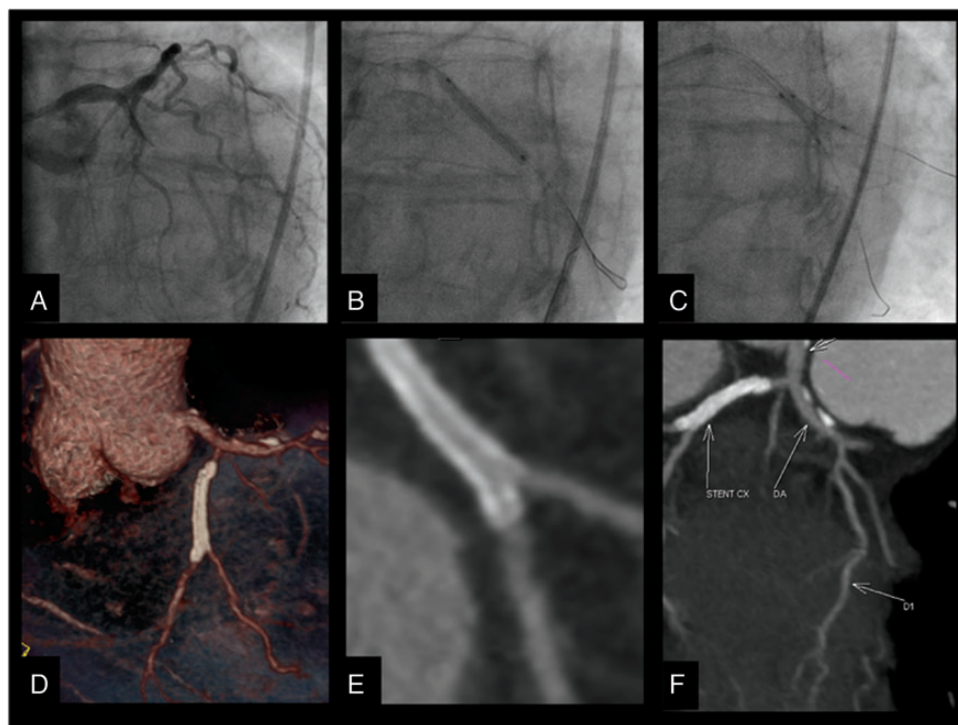


Figure 3: CCTA evaluation of a patient with previous PCI. (A) Chronic total occlusion of the proximal circumflex; (B) implantation of a Xience 2.5/23 mm stent; (C) final kissing-balloon; (D) CCTA with volume-rendering technique reconstruction; (E) multiplanar reconstruction with a detail of the ostial scaffolding to the first obtuse marginal; (F) mixed plaque in proximal LAD with intermediate stenosis.

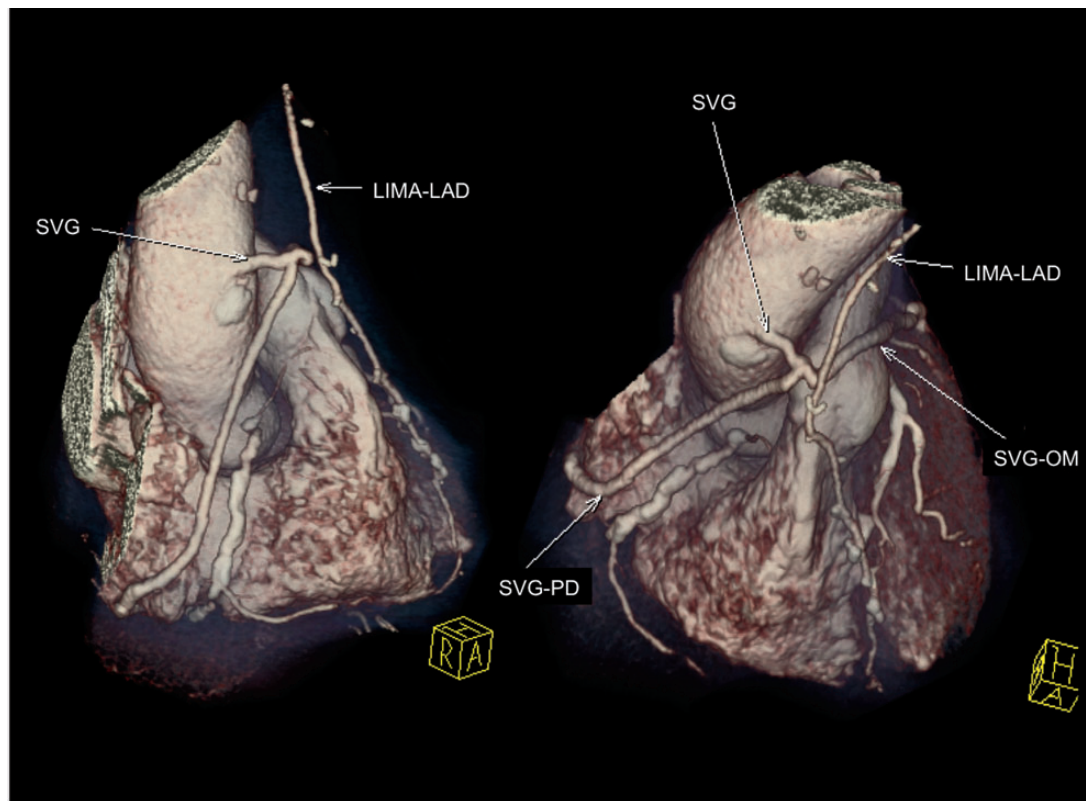


Figure 4: Evaluation of bypass grafts by CCTA. Volume-rendering technique reconstructions showing saphenous vein grafts (SVG) to the posterior-descending (PD) and obtuse marginal (OM) branches and a left internal mammary artery to the left anterior descending artery (LIMA-LAD).

specificity for the detection of significant ($\geq 50\%$) graft stenosis was 96 and 97%,⁴⁴ documenting a high overall performance for non-invasive graft assessment.

Plaque characterization and correlation with other imaging modalities: pushing the limits of spatial resolution

Since many myocardial infarctions present in previously asymptomatic patients and not infrequently the first manifestation of CAD is sudden cardiac death, the main challenge that we face today is to identify patients at risk before those events occur. In this regard, clinical evaluation alone might be insufficient, since only a minority of patients experiencing an acute myocardial infarction would have been identified as high risk by the available risk factors based scores, prior to the event.⁴⁵

Coronary plaque characterization, namely the identifications of features of vulnerability, has been the focus of extensive research by different coronary imaging modalities such as IVUS, IVUS-virtual histology (IVUS-VH), and optical coherence tomography (OCT). These imaging modalities, although providing the highest possible

spatial resolution, have their applicability limited by their invasive nature, and are usually employed in patients already referred for invasive angiography because of suspected CAD or with acute coronary syndromes (ACS). Many of these patients will be (independent of the result of the imaging modality) under secondary prevention of CAD, which changes natural history and reduces the risk of subsequent cardiovascular events.^{46,47}

In the multicentre PROSPECT study,⁴⁷ a large plaque burden, a small lumen area and the presence of a thin cap fibroatheroma (TCFA) assessed by IVUS-VH in non-culprit lesions, were independent predictors of future major adverse cardiac events. In this study, lesions that led to major adverse cardiac event had a high plaque burden by IVUS, but were mild by baseline angiography, with a mean diameter stenosis of only 32%.

On the other hand, *ischaemia based imaging modalities* have also some limitation in this regard, especially related to the fact that non-obstructive lesions are not associated with ischaemia, but can also be the culprit of coronary events⁴⁷⁻⁵⁰ (Figure 5).

Several studies have reported on the correlation between CCTA plaque features with invasive coronary imaging modalities like IVUS, IVUS-VH, and OCT. In a meta-analysis published in 2011, CCTA had a good diagnostic accuracy to detect coronary plaques compared with the gold standard IVUS, with an area under the curve for the receiver operating characteristics analysis of 0.94, a sensitivity of 90%, and a

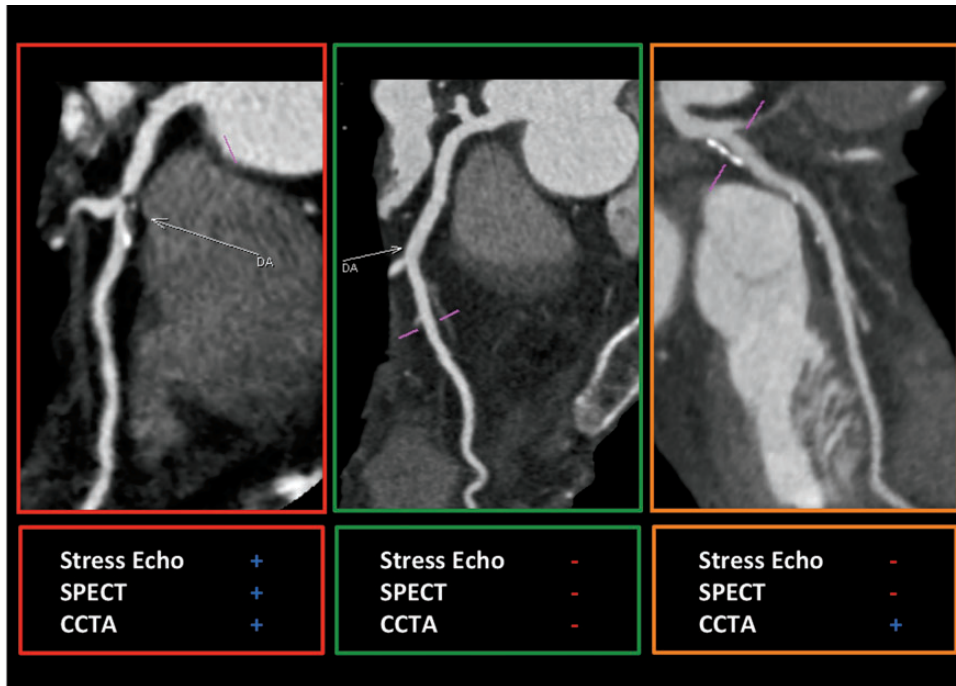


Figure 5: Identification of non-obstructive CAD as a unique feature of CCTA as a non-invasive CAD imaging modality.

specificity of 92%, with small differences in the assessment of plaque area and volume, percent area stenosis, and a slight overestimation of lumen area.⁵¹

Several CCTA plaque characteristics have now been shown to be more prevalent in culprit lesions in the setting of ACSs. In a study done by Hoffman *et al.*⁵², a significantly larger plaque area and positive remodelling were found in culprit lesions of ACS patients, compared with patients with stable CAD. Positive remodelling has been considered for many years a surrogate marker of plaque vulnerability, and many of these lesions have a high plaque burden, that is, underestimated by luminal angiograms because they undergo expansive or positive outward enlargement and are frequently non-stenotic⁴⁹ (Figure 6). In another small study, Motoyama *et al.*⁵³ found that culprit lesions of patients with ACS had more frequently positive remodelling, low-density plaque [<30 Hounsfield units (HU)] and spotty calcifications.

Extending on these results, the same authors conducted a large prospective trial including 1059 patients who underwent CCTA, and demonstrated that positive remodelling and low-attenuation plaques were associated with the subsequent development of ACSs.⁴⁸ In this study, the percentage of patients with these two features that subsequently developed an ACS was 22.2%, compared with only 3.7% for patients with only one feature and 0.5% for patients with neither positive remodelling nor low-attenuation plaques.

In a study by Kashiwagi *et al.*,⁵⁴ evaluating 105 patients with CAD, CCTA findings have been also validated against OCT. In this study, TCFA had higher remodelling indexes, lower CT attenuation values and more often ‘ring-like’ enhancement by CCTA (44% in the TCFA group vs. 4% for the non-TCFA group).

In a recent study, Papadopoulou *et al.*⁵⁵ evaluated the distribution and composition of coronary plaques at bifurcations with both

CCTA and IVUS-VH. They found that plaques with a high-risk phenotype as assessed by IVUS-VH were more commonly found in segments proximal to the bifurcation, rather than in the bifurcation or distal to the bifurcation. Interestingly, by evaluating the geometry of the bifurcation, a feature easily assessed with CCTA, they found that a wide angle was more often associated with high-risk plaques.

As a group, these studies provide evidence on how CCTA can non-invasively provide information on several plaque characteristics—like plaque volume, remodelling, plaque composition, distribution, and geometry of the coronary tree—that can be associated with the development of future coronary events.

Limitations of CCTA for plaque characterization

Despite significant improvements in image quality, spatial resolution has not seen significant improvements and remains presently one of the major technical limitations of CCTA. The spatial resolution of currently available scanners (in the range of 400–600 μm) prevents the detailed assessment of several features associated with vulnerable plaques, as is the case of the evaluation of a thin fibrous cap.⁵¹ This spatial resolution is significantly worse than that of IVUS (200–250 μm) or OCT (10–15 μm)⁵⁶ and this has to be taken in consideration and should temper our expectations regarding the potential of CCTA for plaque assessment in face of the limitations already faced by other invasive imaging modalities regarding the identification of the vulnerable plaque.

Another limitation faced by CCTA plaque characterization is related to the fact that coronary plaque attenuation values are significantly modified by differences in lumen contrast densities, as has been

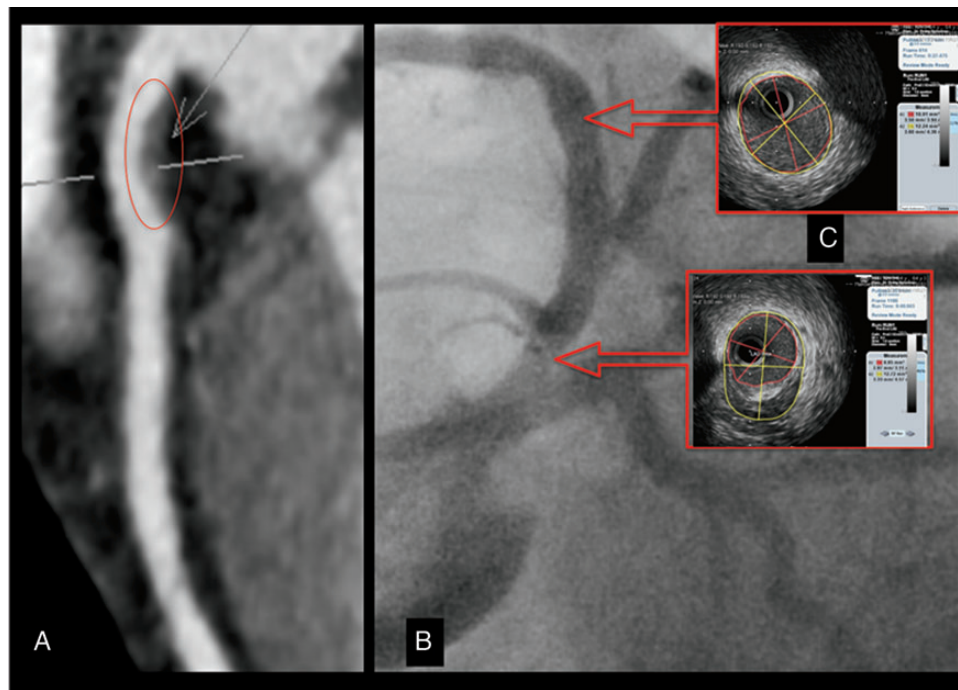


Figure 6: CCTA depicting a non-calcified plaque in the proximal left anterior descending artery without significant stenosis (A). In invasive angiography (B), this lesion was not apparent but was confirmed with IVUS (C).

demonstrated both *ex vivo* and *in vivo*.^{57,58} This is important because lumen attenuation can be influenced by different contrast and scanning protocols and therefore makes it difficult to establish thresholds for the definition of low-attenuation plaque as a surrogate of vulnerable plaque that can be widely adopted.

One last important limitation in this regard is related to the reproducibility of CCTA plaque measurements, as many previous studies have reported significant inter-observer variability in the assessment of several CCTA plaque characteristics.^{59,60} This is dependent on image quality, vessel size and degree of calcification, features that are dependent again on spatial resolution. In the future, improvements in spatial resolution and the development of robust dedicated automated quantification software could contribute to overcome these difficulties.

Prognostic value: cardiac CT reaching adulthood

As the technique became more robust and more data become available, CCTA proved also to be a strong prognostic tool for the evaluation of patients with suspected CAD.^{61–66}

Pundziute et al.⁶¹ in 100 patients with known or suspected CAD, showed that there were no major cardiac events on the subset of patients without CAD, contrasting with the 30% event rate of patients with CCTA documented CAD upto 16 months. More importantly, the cumulative event rate of patients with non-obstructive CAD was higher and different from the excellent prognosis of

patients without plaques on CCTA. This earlier study had some limitations, both related to the small sample size and the fact that some of the included cardiovascular events (revascularization and unstable angina requiring hospitalization) are not 'hard' endpoints and could be influenced by the CCTA result.

Min et al.⁶² evaluated the prognostic value of identifying CAD with CCTA in a single-centre cohort of 1127 patients with stable chest symptoms. A negative CCTA was associated with an excellent prognosis and some CCTA-derived CAD indexes were developed and prognostically validated. Some of those indexes were expected to convey prognostic information, as these observations extend on what was previously documented for ICA, as was the case of number of diseased vessels, degree of stenosis and more proximal location. More importantly was the fact that they were able to demonstrate the prognostic value of more CCTA-specific indexes derived from the comprehensive information of both obstructive and non-obstructive plaque: the segment involvement score (SIS), obtained as the total number of segments with plaque (1 point for each segment with plaque, irrespective of the degree of luminal stenosis) and the segment stenosis score (SSS), obtained by grading the stenosis severity of each segment with plaque (segments graded from 0 to 3 according to the degree of stenosis). For both SIS and SSS, a value of 5 was identified as the best cut-off to predict all-cause mortality.

In 2011, two meta-analyses were published^{63,64} evaluating the prognostic value of CCTA and (not surprisingly) had the same two main conclusions: (i) that the presence and extent of CAD on CCTA are strong and independent predictors of future

cardiovascular events; (ii) the absence of CAD on CCTA is associated with an excellent prognosis. Of note, in both meta-analysis, it was possible to distinguish between the excellent prognosis of patients in the absence of CAD from that of patients with non-obstructive CAD, as documented by CCTA.

In the CCTA registry CONFIRM (Coronary Computed Tomography Angiography Evaluation for Clinical Outcomes: an International Multicentre Registry),⁶⁵ which included >20 000 patients, the absence of CAD was associated with an excellent prognosis (annualized death rate of 0.28%). At 2.3 years follow-up, both obstructive and non-obstructive CAD conferred an increased mortality risk with hazard ratios of 2.6 and 1.6, respectively.

In another report of the CONFIRM database, it was demonstrated that CCTA measures of CAD severity yield independent and incremental prognostic value to that of left ventricle ejection fraction (LVEF) and routine clinical predictors.⁶⁶ In this report, all-cause mortality occurred in 0.65% of patients without CAD, in 1.99% of patients with non-obstructive CAD, 2.90% of patients with non-high-risk CAD, and 4.95% with high-risk CAD.

In what concerns the incremental prognostic value of CCTA over other CAD imaging modalities, Werkhoven *et al.*⁶⁷ have evaluated the potential synergistic effect of a functional test (single-positron emission CT-SPECT) and CCTA (as an anatomical test). They found CCTA to be an independent predictor of cardiovascular events and its prognostic information was incremental to that of SPECT, in line with previous studies that showed an incremental value over exercise ECG testing.⁶⁸ Nevertheless, although the potential synergistic role of both anatomical and functional imaging modalities can be appealing, for both diagnostic and prognostic purposes, this concept might be difficult to prove as a cost-effective strategy and probably not desirable to perform both exams in the same patient. In addition, some studies evaluating the relative prognostic value of CCTA and exercise ECG testing suggested that CCTA may be used as a first line exam, since a normal CCTA is always associated with a good prognosis, independent of the results of exercise ECG, and a non-negligible percentage of patients with a normal exercise ECG are found to have significant stenosis on CCTA, a finding associated with worse outcomes.^{69,70}

This way, more research is needed to further evaluate the role and relative position of the different imaging modalities in the algorithm for the evaluation of patients presenting with possible CAD. One proposed approach is to select the type of exam according to the patient CAD probability, favouring functional exams in the intermediate probability and CCTA for the lower probability patient, as recommended by the National Institutes of Clinical Excellence (NICE) Clinical guidelines on 'chest pain of recent onset'.⁷¹

The prognostic evaluation of CCTA data (as is the case for other CAD imaging modalities) is dependent on the baseline risk of the population included and the outcomes evaluated. Studies including a higher percentage of patients with intermediate-to-high CAD probability and/or risk, or even with known CAD, can more easily document the prognostic power of CCTA. This is also the case for studies evaluating the impact on total cardiovascular events (instead of only 'hard' CV events). This is especially true regarding the inclusion of revascularizations after CCTA, as the result of this anatomical test could influence and increase subsequent procedures.

For this reason, many studies addressing this issue have now excluded earlier revascularizations from the outcome analyses.^{63,72}

In another recently published study, Andreini *et al.* evaluated the long-term (>4 years follow-up) prognostic value of CCTA in a cohort of 1304 patients with suspected CAD.⁷² Although the authors excluded patients with known CAD, the mean pre-test probability of CAD in the study population was high (42.5%, with one-quarter of the patients having a high CAD probability) and they also included patients with possible ACSs. This led to a higher than expected hard event rate for a stable CAD population (event-free survival of 54% for patients with obstructive CAD). Therefore, the design of studies to address the prognostic value of CCTA can be influenced by these two important aspects: inclusion of many high-risk/high-CAD probability patients and of revascularization as a cardiovascular event can lead to an overestimation of the prognostic power of CCTA.

When comparing the prognostic information conveyed by CCTA with that of other non-invasive imaging modalities such as SPECT or stress echo, it is remarkable that the excellent prognosis of a normal CCTA—no plaque—0.17% annual event rate in a CCTA meta-analysis⁶⁴ is even lower than what was previously demonstrated for patients with normal perfusion on SPECT (0.6% annual event rate) or normal wall motion on stress echo (1.0% annual event rate) in previous meta-analysis.^{73,74}

This difference could be explained by the fact that CCTA identifies non-obstructive CAD (usually negative of stress-based exams) and in this way provides a more comprehensive evaluation of the total coronary atherosclerotic burden that has a stronger prognostic meaning (Figure 7).

Scores that reflect the comprehensive information provided by CCTA have already been developed and they can be useful tools to quantify the coronary atherosclerotic burden. One of these is the *CT-SYNTAX* score, a CCTA adaptation of its angiographic counterpart, known to reflect the severity of CAD which has prognostic implications and is a useful tool for decision-making on myocardial revascularization. The score calculated with CCTA data acquired with last generation scanners has been shown to correlate well with the invasive SYNTAX and to have a high reproducibility.⁷⁵ This way it is also expected to be a useful prognostic tool for risk stratification of patients with obstructive CAD. In addition, this information can be made available in advance, which could help in the planning of the revascularization procedure.

Another CCTA score that was recently described is the *CT-Leaman* score, in which all the atherosclerotic lesions are taken in consideration (both obstructive and non-obstructive) in a comprehensive score that has three sets of weighting factors: lesion localization (taking in consideration the anatomical dominance), degree of stenosis (obstructive and non-obstructive), and type of plaque (calcified, non-calcified, and mixed plaques).⁷⁶ This score can become a useful tool to quantify a total coronary atherosclerotic burden and is expected to convey the strong prognostic information of CCTA. This could even be more useful in patients with non-obstructive lesions, whose prognosis has been shown to be worse than that of patients without coronary plaques,^{65,72} and is a very prevalent subset,^{77,78} for whom risk stratification will be of utmost importance.

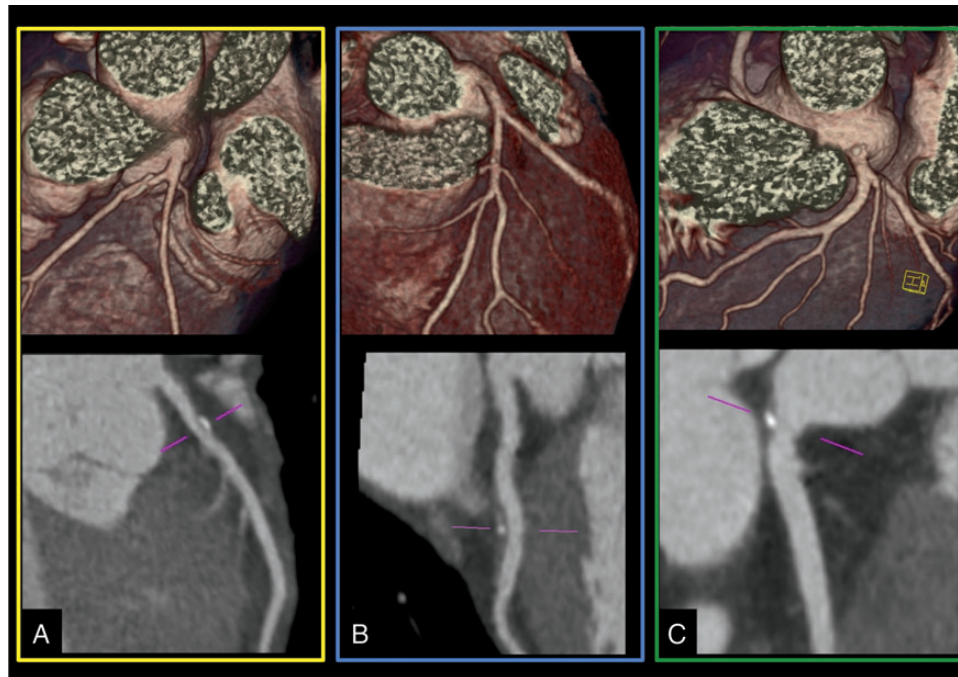


Figure 7: Non-obstructive (but probably not non-significant!) coronary lesions identified with CCTA. Upper panel with a volume-rendering technique and lower panel with multiplanar reconstructions. (A) Mixed plaque in the proximal LAD with 25–50% stenosis in a 54-year-old female with dyslipidaemia and smoking habits; (B) mixed plaque in the proximal LAD with <25% stenosis in a 31-year-old male with a family history of premature CAD; (C) mixed plaque in the left main with <25% stenosis in a 51-year-old male with hypertension and dyslipidaemia. None of these patients had a high ($\geq 5\%$) 10-year risk of cardiovascular death, as estimated by the HeartScore.

CTA as a tool in the planning of interventional procedures

CTA can also be used as a tool for the appropriate selection and planning of interventional procedures, and has been routinely used in this setting in chronic total occlusions (CTOs), transcatheter aortic valve implantation (TAVI), and potentially many other coronary and structural heart procedures.

Regarding CTOs, which still remain a challenging subset of lesions for percutaneous revascularization, appropriate selection of the cases is of utmost importance, since PCI in this setting is not only associated with higher contrast and radiation dosages, but also with a non-negligible rate of procedural complications. In this regard, several CTA features have been associated with success of PCI for CTOs like the length of the occluded segment, the amount of calcification, the presence of a blunt stump and bending and tortuosity of the proximal vessel and/or occluded segment.^{79,80} The evaluation of myocardial perfusion by CT is also becoming a reality^{81,82} and patients with CTOs might be an important subset to benefit from this combined anatomic and viability assessment for decision-making regarding intervention.⁸³

CTA plays also an important role in the evaluation of the candidate for implantation of a catheter-based aortic valve. CTA provides information in correct sizing of the prosthesis since it is acknowledged that 3D imaging techniques, with a greater extent of evidence for CTA, yield larger aortic annulus dimensions than echocardiography.^{84,85}

The improved accuracy of aortic annular sizing by CT can influence patient outcomes. In a study of 133 patients who underwent CTA before TAVI/TAVR, it was reported that, in comparison with TEE-based sizing, the use of CTA-based aortic annulus dimensions led to a significantly lower rate of ‘worse-than-mild’ paravalvular regurgitation after TAVI (7.5 vs. 21.9%).⁸⁶

Besides aortic annulus size, distance of the coronary ostium to the aortic valve plane, aortic cusp length, width of the aortic sinus, width of the sinotubular junction, and width of the ascending aorta are important measures for TAVI planning.⁸⁵ Unlike surgery for aortic valve replacement, in TAVI the cusps are not resected but instead they are crushed by the endoprosthesis. This way, the distance of the coronary ostia to the aortic valve plane and aortic cusp length is important to evaluate the potential risk of coronary occlusion, a rare but menacing complication.⁸⁷ The width of the aortic sinus, the sinotubular junction, and the ascending aorta are also important measurements for the self-expandable TAVI, since it extends beyond the sinotubular junction into the ascending aorta. The evaluation of CAD in these patients might be challenging especially in the presence of advanced coronary calcification, although some authors have reported a good accuracy in this setting.⁸⁸

CTA also provides information on the suitability of access site, taking in consideration the minimum vessel lumen required for each TAVI system (Table 1). Small vessel diameter, severe atherosclerotic disease, bulky calcification, and tortuosity are the main determinants of vascular complications in TAVI procedures.^{89,90}

Table 1 Manufacturer-suggested anatomic evaluation for TAVI

	Aortic annulus diameter, mm	Ascending aorta diameter, mm	Sinus of Valsalva width, mm	Sinus of Valsalva height, mm	Distance aortic annulus to left main ostium, mm	Minimal iliofemoral diameters, mm
CoreValve™ Evolut™ Bioprosthesis 23 mm	18–20	≤34	≥25	≥15	–	6
CoreValve™ Bioprosthesis 26 mm	20–23	≤40	≥27	≥15	–	6
CoreValve™ Bioprosthesis 29 mm	23–27	≤43	≥29	≥15	–	6
CoreValve™ Bioprosthesis 31 mm	26–29	≤43	≥29	≥15	–	6
Edwards SAPIEN XT 23	18–21	–	–	–	≥10	6
Edwards SAPIEN XT 26	22–24	–	–	–	≥10	6.5
Edwards SAPIEN XT 29	25–28	–	–	–	≥10	7

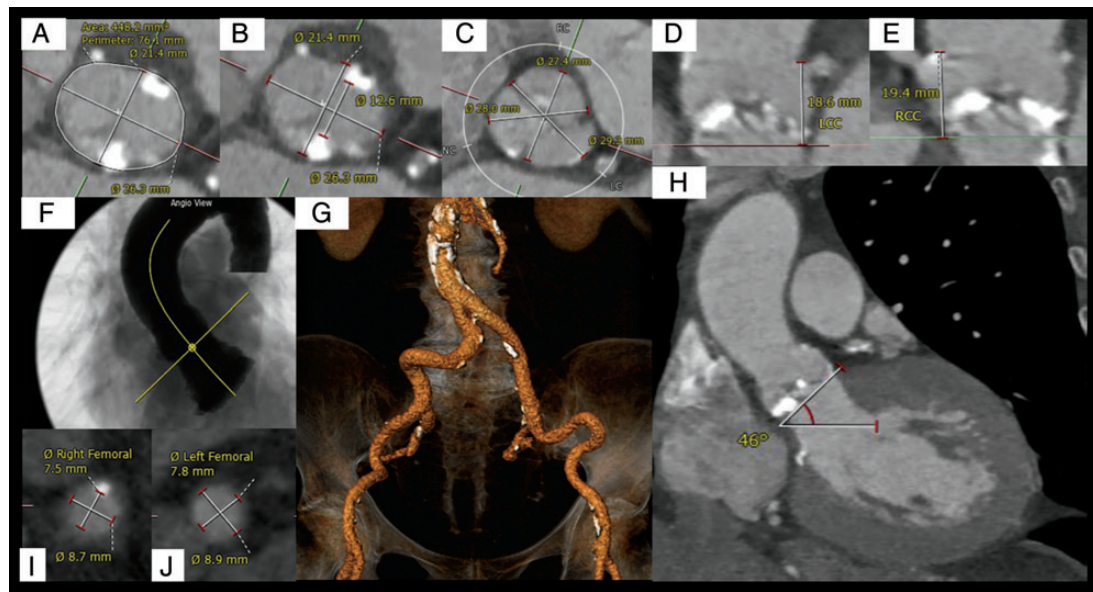


Figure 8: CTA evaluation for TAVI. (A) and (B) Aortic annulus measurements; (C) Aortic cusps lengths; (D) and (E) Aortic sinus heights for left coronary cusp (LCC) and right coronary cusp (RCC); (F) CTA simulation of an optimal viewing projection for valve implantation; (G) Three-dimensional reconstruction of the abdominal aorta showing severe iliofemoral tortuosity; (H) aortic root angulation measurement; (I) and (J) right and left femoral mensuration.

Not only the iliac and femoral artery, but also the entire aorta should be examined by CTA, since it can identify tortuosity, dissections or thrombus, all increasing the risk of procedure-related complications, which can be anticipated with CTA (Figure 8). In addition, the assessment of left ventricle and chest wall may influence the feasibility, safety, and effectiveness of the procedure. CTA data sets should be evaluated for the presence of LV thrombi as a source of embolic complications. The disposition of the LV apex relative to the chest wall and alignment of the LV-axis with LV outflow tract orientation may be useful information for transapical procedures. The optimal viewing projections for TAVI implantation can also be virtually simulated by CTA, with potential reductions in contrast dose and procedure time.

Percutaneous valvular interventions are not limited to TAVI, and mitral interventions are becoming a reality. CTA can be useful in this setting, especially for coronary sinus annuloplasty techniques, since CTA can provide information on the relation between the coronary sinus and the left circumflex and also between the coronary sinus and the level of the annulus and these anatomical relations have been linked to the success and safety of the procedure.⁹¹ The role of CTA for mitral interventions aimed at the leaflets, like edge-to-edge repair technologies, has yet to be defined, and presently echocardiography plays a central role in the selection and guidance of these procedures.

Other structural heart interventions can benefit from the detailed anatomical evaluation prior to the procedure, like the evaluation of

the left atrial appendage in patients candidate for closure devices.⁹² In addition, left atrial appendage morphology has been correlated with the risk of stroke in patients with atrial fibrillation, suggesting CTA as a potential tool for risk stratification regarding anticoagulation management in these patients.⁹³

The detailed morphological characterization of coronary anatomy and plaque distribution provided by CCTA might also be useful in the evaluation of *bifurcation lesions*, and can have some implications regarding selection of the PCI bifurcation technique.^{94,95} In a recent study, plaque distribution and morphology assessed by CCTA was associated with side branch compromise after left main PCI.⁹⁶ The development of some complications during PCI has also been linked to CCTA plaque characteristics. In one study, the presence of low-attenuation plaque and napkin ring-like appearance of culprit lesions on CCTA were associated with the development of slow-flow or no-reflow phenomenon during PCI.⁹⁷

Another condition easily identified with CCTA is *myocardial bridging*, and this explains the higher prevalence in CCTA reports, in line with classic autopsy series and much higher than in ICA studies.⁹⁸ In most of the cases this is a benign finding, although it has been associated with the development of myocardial ischaemia and found to be more prevalent in patients with apical ballooning syndrome.⁹⁹ Additionally, bridging of the left anterior descending imposes a higher technical difficulty for bypass surgery and has been associated with higher rates of complications, including perforation of the right ventricle, and therefore its preoperative identification can potentially help planning the revascularization procedure.⁹⁸

In summary,

- (1) CCTA is becoming an alternative for ICA in many purely diagnostic procedures that are becoming less often referred to the cath lab.
- (2) The performance of CCTA as a gatekeeper for ICA is expected to lead to an increase in the ratio of interventional to diagnostic procedures.
- (3) CCTA can potentially be useful in planning PCI especially more complex interventions like CTOs and bifurcations.
- (4) CTA is routinely used in the selection process of percutaneous valvular interventions as is the case of TAVI, especially for correct annular sizing.
- (5) Lastly, some CCTA plaque features can also be useful as predictors of potential complications during PCI and the operator can take advantage of this information in planning the procedure.

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