Role of Coronary CT Angiography in Coronary Revascularization

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Since the development of computed tomography (CT) technology over the last decade, coronary CT angiography (CCTA) has become a powerful non-invasive method for evaluating coronary artery disease. Recently, CT has been used to evaluate hemodynamic status beyond anatomy by current trials such as perfusion CT, fractional flow reserve-CT, or transluminal attenuation gradient, which can help determine whether coronary revascularization occurs. Once revascularization is determined, CT can guide whether to use a stent or coronary artery bypass graft (CABG) for the reperfusion method by evaluating the nature of the lesion. In addition, CCTA helps to better define the morphological features of the occluded chronic total occlusion segment such as the occlusion length and presence of calcifications or tortuosity in its course, which are established predictors of success. Finally, CT can assess the patency of a stent or CABG in patients who previously underwent revascularization. Therefore, this review article discusses the various roles of CCTA in coronary revascularization.

Key words CT angiography · Myocardial perfusion imaging · Myocardial fractional flow reserve · Percutaneous coronary intervention · Coronary artery bypass.

INTRODUCTION

With the remarkable development of the computed tomography (CT) technique, coronary CT angiography (CCTA) has become a routine and widely accepted modality for evaluation of patients with chest pain because it shows high diagnostic accuracy, especially in terms of its high negative predictive value (NPV) [1]. In addition, CCTA can be used to visualize atherosclerotic plaques in the vessel wall in contrast to “lumenography” performed by invasive coronary angiography (ICA). Therefore, the ability to interpret CCTA images beyond visualization of the coronary lumen and stenosis is of utmost importance because it enables therapeutic interventions stratified based on plaque characteristics [2]. In addition, recent trials for evaluation of the hemodynamic status such as myocardial CT perfusion (CTP), fractional flow reserve (FFR)-CT (CT_{FFR}), and transluminal attenuation gradient (TAG) have been introduced [3-5]. Based on these current CT techniques which can provide both anatomy and functional information, cardiac CT may play an important

role in the determination of whether or not to perform coronary revascularization in patients with chest pain. Once revascularization has been determined, CT can guide whether to use a stent or coronary artery bypass graft (CABG) for the reperfusion method by evaluating lesion length, multiplicity, and complexity [6]. In cases of patients with chronic total occlusion (CTO), CT has a critical role in guiding treatment because it allows observation of the distal part beyond the occlusion, which cannot be seen by ICA [7]. Finally, CT has a potential role in the assessment of the patency of a stent or CABG in patients who previously underwent revascularization [8]. An understanding of the role of CT and keeping up to date with the evolving CT technology are both critical in coronary interventions.

STEP 1. DECISION ON WHETHER TO TREAT WITH MEDICATION OR REVASCULARIZATION

Determining the appropriate treatment strategy is very important for patients with chest pain. When deciding if myocardial revascularization should be performed, anatomical steno-

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sis as well as hemodynamic status should be considered (Fig. 1).

Quantification of the degree of stenosis

ICA is considered as the standard reference because it has a high spatial resolution of 0.3 mm and a temporal resolution of 6 msec [9]. On the other hand, the current CT equipment has a spatial resolution of 0.23 mm (Revolution CT, GE Healthcare, Waukesha, WI, USA) and temporal resolution of 66 msec at 0.25 sec rotation (dual source, SOMATOM Force, Siemens Healthcare, Forchheim, Germany) with a high NPV and sensitivity more than 95%; however, the positive predictive value (PPV) or specificity is less than 95% [10,11]. Several studies and meta-analyses have shown that CCTA is reliable for ruling out significant coronary artery disease (CAD) in patients with stable and unstable angina syndromes and in patients with low to moderate likelihood of CAD [12,13]. However, the diagnostic accuracy of CCTA can be reduced by heavily calcified coronary arteries mainly due to the so-called blooming artifact, which leads

to overestimation of the severity of atherosclerotic obstructions, thus higher coronary artery calcium score results which decreases the specificity by 35–45% [14].

Plaque burden and characteristics

The likelihood of plaque rupture has been known to be based on plaque composition. In ROMICAT I and II trials, high-risk plaques detected on CCTA predicted acute coronary syndromes independent of significant CAD and clinical risk assessment [2]. Several recent studies have reported low-attenuation, positive remodeling, the napkin-ring sign, and spotty calcifications as features of high-risk plaques [15,16] (Fig. 2). These rupture-prone plaques have been described histologically as thin cap fibroatheromas [17].

To identify low attenuated plaques (LAP), a region of interest (ROI) was set within each plaque to calculate the plaque density. On CT, lipid content correlates with lower CT attenuation values when compared with fibrotic tissue [18]. However, CT

Fig. 1. Diagram of various CT modalities for determining whether to treat with medication or revascularization. Arrow in CT perfusion image indicates areas where myocardial perfusion is reduced. CT: computed tomography, FFR: fractional flow reserve, TAG: transluminal attenuation gradient.

measurements of coronary plaques are influenced by many factors: the concentration of intraluminal iodinated contrast agent, plaque size, image noise, tube voltage, slice thickness, and reconstruction filter. Thus, reliable differentiation of the density between lipid-rich plaques and fibrous plaques is not yet feasible. Motoyama et al. [15] proposed 30 Hounsfield units (HU) as the cutoff point for the detection of lipid cores in intravascular ultrasound (IVUS) with a sensitivity of 91% and specificity

of 100%, although there is no description of the method used to identify LAPs. Otsuka et al. [19] defined a LAP when the mean value of at least 5 randomly selected points within each plaque was less than 30 HU. In an *ex vivo* study, the relative area (area>25%) of intraplaque pixels with <60 HU could accurately detect lipid-rich plaques with a sensitivity of 73% and specificity of 71% [20]. Until now, however, there are no consistent guidelines on how to measure LAPs or the appropriate cut-off

Fig. 2. Various high-risk plaques. (A) Positive remodeling (arrows): remodeling index determined for the outer vessel wall calculated by the vessel cross-sectional area at the site of maximal stenosis divided by the cross-sectional areas of the reference segments, threshold of ≥ 1.1 . (B) Low attenuated plaque: average plaque attenuation of the selected region of interest was less than 30 HU. (C) Napkin-ring sign: plaque core with low attenuation (asterisk) surrounded by a rim-like area of higher attenuation (dotted line). (D) Spotty calcification (arrow): size <3 mm with a computed tomography density of over 130 HU within the plaque. HU: Hounsfield units.

levels for their identification.

Rupture-prone plaques might not lead to significant luminal narrowing, owing to the effect of positive remodeling. Positive remodeling is the compensatory enlargement of the vessel wall that occurs at the site of an atherosclerotic lesion as the plaque size increases, resulting in preservation of the luminal area [21]. In histopathology, positive remodeling is associated with an abundance of macrophages and increased necrotic core [22]. CCTA can be used to measure the outer vessel wall as calculated by the vessel cross-sectional area at the site of maximal stenosis divided by the average of the cross-sectional areas of the proximal and distal reference segments. Usually, a remodeling index threshold of ≥ 1.1 is defined as positive remodeling [2]. A napkin-ring sign is characterized by a plaque core with low computed tomography attenuation surrounded by a rim-like area of higher attenuation [16]. Therefore, there is no cut-off value for central low attenuation and peripheral higher attenuation, but the presence of rim-like high attenuation is defined as a relatively higher attenuation compared to an adjacent plaque and no greater than 130 HU. This sign was more frequent in thin cap fibroatheroma (TCFA) compared with non-TCFA plaques defined by optical coherence tomography [23]. Napkin-ring sign seems to be a specific feature of plaques with a large necrotic core, although its sensitivity is low [22]. Spotty calcification was defined as a plaque < 3 mm in size with a CT density of over 130 HU within the plaque [2]. According to the size of a spotty calcification, small (< 1 mm) spotty calcifications have been strongly correlated with vulnerable plaque features based on virtual his-

tology IVUS [24]. However, there is controversy on whether such calcifications reflect the vulnerability of a plaque in some studies [25].

CT-based myocardial ischemic burden (CTP, CT_{FFR}, and TAG)

Although CCTA accurately assesses coronary plaques and stenosis, it is limited in evaluating the hemodynamic significance of coronary stenosis. Recently, however, three novel techniques have been demonstrated to accurately detect vessel-specific ischemia using the gold standard invasive FFR as a reference. Based on these modalities, the decision between treatment with medication and coronary revascularization can be done.

CTP

Using a pharmacologic agent such as adenosine, an acquisition image was obtained during the first pass of iodinated contrast from the arteries into the myocardium where hypoperfusion is represented by low attenuated areas. This requires both resting and stress scans, therefore additional administration of adenosine, iodinated contrast agent, and radiation exposure are required [26]. In particular, the excessive radiation dose is considered as one of the important limitations of CTP. However, the average radiation exposure from stress static CTP (6.5 mSv), stress dynamic CTP (10.0 mSv), and rest/stress dual-energy CTP (5.6/7.1 mSv) are lower compared to SPECT (11.1 mSv); furthermore, high-pitched spiral static CTP demonstrated the lowest radiation doses for stress and rest CTP (0.93 mSv

Table 1. Diagnostic accuracy of CTP imaging

Study	Number of patients/vessels	CT technique	Reference standard	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Ko et al. [30]	42/86	CCTA	FFR ≤ 0.80	93	60	68	90
		CTP		76	84	82	79
		CCTA+CTP		68	98	97	77
Bettencourt et al. [31]	101/303	CCTA	FFR ≤ 0.80	95	67	48	97
		CTP		55	95	78	87
		CCTA+CTP		71	90	68	91
Greif et al. [34]	65/195	CCTA	FFR ≤ 0.80	98	54	37	99
		CTP		95	74	49	98
		CCTA+CTP		95	75	50	98
Wong et al. [32]	75/127	CCTA	FFR ≤ 0.80	89	66	57	92
		CCTA+CTP		76	89	78	88
Choo et al. [33]	37/81	CCTA	FFR ≤ 0.80	93	83	75	96
		CTP		93	90	84	96
		CCTA+CTP		93	94	90	96
Yang et al. [28]	75/210	CCTA	FFR ≤ 0.80	97	43	88	75
		CTP		89	86	96	63
		CCTA+CTP		86	85	96	60

CT: computed tomography, PPV: positive predictive value, NPV: negative predictive value, CCTA: coronary CT angiography, CTP: CT perfusion, FFR: fractional flow reserve by invasive coronary angiography

and 0.53 mSv, respectively) [27-29]. In addition, there have been recent efforts to reduce the radiation dose of CT by using low kV, iterative reconstruction techniques, and selective acquisition of the dynamic phase. Table 1 summarizes the diagnostic accuracy of the main CTP studies [28,30-34].

Non-invasive FFR (CT_{FFR})

FFR, defined as the pressure distal to coronary stenosis relative to the pressure proximal to stenosis, has been widely used to localize ischemic lesions on ICA, and to determine the appropriate revascularization treatment [4]. It is calculated by computational fluid dynamic modeling after semiautomated segmentation of the coronary tree and left ventricular mass. CT_{FFR} can be modeled for conditions of adenosine-induced hyperemia without adenosine infusion or additional imaging. However, it is computationally complex and time-consuming requiring sever-

al hours of analysis [35]. Table 2 summarizes the diagnostic accuracy of the main CT_{FFR} studies [4,36-39].

TAG

TAG is determined by the change (measuring the reduction in HU) in the contrast opacification along coronary arteries per 10 mm length of the coronary artery (unit: HU/10 mm), and is calculated from the linear regression coefficient between CT attenuation and distance from the ostium. If there is significant stenosis, the slope of the graph obtained from the TAG will show a downward trend because the contrast attenuation in the distal artery will fall beyond the point of stenosis [27,35,40]. Table 3 summarizes the per-vessel diagnostic accuracy of TAG, CCTA, and CT_{FFR} compared with invasive FFR as a reference standard [39-42].

Table 2. Diagnostic accuracy of CT_{FFR}

Study	Number of patients/vessels	CT technique	Patient-based				Vessel-based			
			Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
DISCOVER-FLOW [4]	103/159	CCTA	94	25	58	80	91	40	47	89
		CT _{FFR}	93	82	85	91	88	82	74	92
DeFACTO [36]	252/615	CCTA	84	42	61	72	-	-	-	-
		CT _{FFR}	90	54	67	84	83	78	-	-
NXT [37]	254/484	CCTA	94	34	40	92	83	60	33	92
		CT _{FFR}	86	79	65	93	84	86	67	95
Renker et al. [38]	53/67	CCTA	94	32	38	92	90	34	37	89
		CT _{FFR}	94	84	71	97	85	85	71	93
Yoon et al. [39]	53/82	CCTA	-	-	-	-	72	68	59	79
		CT _{FFR}	-	-	-	-	81	94	90	89

CT: computed tomography, PPV: positive predictive value, NPV: negative predictive value, CCTA: coronary CT angiography, CT_{FFR}: CT-derived fractional flow reserve

Table 3. Per-vessel diagnostic accuracy of TAG, CCTA, and CT_{FFR}

Study	Number of patients/vessels	CT machine detector/slice no.	CT technique	Reference standard	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Wong et al. [41]	54/78	320/320	TAG	FFR ≤0.80	77	74	67	86
			CCTA>50%		94	66	64	94
Choi et al. [42]	63/97	64/64	TAG	FFR ≤0.80	48	91	79	71
			TAG/CCO		65	61	54	71
			CCTA>50%		95	53	58	91
			CT _{FFR}		81	94	90	89
Yoon et al. [39]	53/82	64/64	TAG	FFR ≤0.80	38	88	67	69
			CCTA>70%		72	68	59	79
			CT _{FFR}		81	94	90	89
Choi et al. [40]	85/253	128/256	TAG	FFR ≤0.80	69	44	27	83
			TAG/CCO		63	54	29	91
			CCTA>50%		95	75	54	98

CT: computed tomography, PPV: positive predictive value, NPV: negative predictive value, TAG: transluminal attenuation gradient, TAG/CCO: transluminal attenuation gradient/corrected contrast opacification, CCTA: coronary CT angiography, FFR: fractional flow reserve, CT_{FFR}: CT-derived fractional flow reserve

STEP 2. GUIDING THE REVASCUARIZATION PROCEDURE ONCE THE REVASCUARIZATION IS DETERMINED

Although CCTA can provide information about significant coronary artery stenosis and has prognostic value, only a few studies have investigated the role of CCTA in guiding patient treatment, such as determining the need for revascularization or the appropriate revascularization procedure [e.g., percutaneous coronary intervention (PCI) vs. CABG surgery]. Traditionally, CABG has been recommended in patients with multivessel disease or high- and medium-risk patients as compared to medical treatment [43]. Since the introduction of the drug eluting stent, the restenosis rate has been significantly reduced compared to the rate using the bare metal stent, thus leading to the increased confidence of interventional cardiologists for treating multivessel diseases, which had previously been the scope of thoracic surgeons. Table 4 summarize the results of the major studies comparing PCI with CABG in patients with multivessel disease [44-49].

Currently, the Synergy between PCI with TAXUS and Cardiac Surgery (SYNTAX) score has been introduced as an angiographic score to assess the extent and complexity of CAD and is known to be an independent predictor of major adverse cardiac events in populations with a varying extent of CAD [48]. The SYNTAX score demonstrates the extent and complexity of the lesion, therefore 2011 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines for CABG surgery mentioned that the SYNTAX score is a reasonable surrogate for the extent of CAD [50]. Recently, CCTA has been reported to be a feasible and reproducible modality for noninvasive estimation of the SYNTAX score and Suh et al. [51] reported that combining a CT-based SYNTAX score can be a highly specific method for selecting CABG surgery candidates.

STEP 3. ROLE OF CCTA FOR CHRONIC TOTAL OCCLUSION

CTO was defined as occlusion of a native coronary artery estimated from the clinical event to be present for at least three months or more, with no luminal continuity and a thrombolysis in myocardial infarction (TIMI) of 0 or 1 anterograde flow on angiography [52]. Because CTO territories are ischemic despite the presence of collateral channels, restoration of normal blood flow has improved symptoms and ventricular function. However, CTO lesions are the most challenging because of the high rate of complications and long-term adverse events, mostly due to failure in tracking or navigation of hardware through the occluded CTO segment, prolonged exposure to radiation, and the high dose of contrast agent used. Therefore, proper patient selection is of utmost importance. In this regard, CCTA helps to better define the morphological features of the occluded CTO segment such as the actual length of the occluded segment and any calcifications or tortuosity in its course, which are established predictors of success [53] (Fig. 3). As compared to the J-CTO score (a multicenter CTO registry in Japan), which was developed using various angiographic variables, the Computed Tomography Registry of Chronic Total Occlusion Revascular-

Fig. 3. Role of coronary CT angiography in patients with chronic total occlusion. GC: guiding catheter, CT: computed tomography, RCA: right coronary artery.

Table 4. Comparison studies between CABG and percutaneous coronary intervention in patients with multi-vessel diseases

Study	Patients (n)	Stent type	Event [CABG vs. Stent (p-value)]		Follow-up duration (yrs)
			MACE	Death	
SOS [44]	988	BMS	-	6.8% vs. 10.9% (p=0.02)	6
AWESOME [45]	142	BMS	-	21.0% vs. 20.0% (p=0.46)	3
MASS II [46]	611	BMS	-	25.1% vs. 24.1% (p=0.09)	10
ARTS II [47]	1205	BMS	21.8% vs. 41.7% (p<0.01)	7.6% vs. 8.0% (p=0.83)	5
SYNTAX [48]	1800	DES	26.9% vs. 37.3% (p<0.001)	11.4% vs. 13.9% (p=0.10)	5
CARDia [49]	510	DES	11.3% vs. 19.3% (p=0.02)	3.2% vs. 3.2% (p=0.97)	1
FREEDOM [50]	1900	DES	11.8% vs. 16.8% (p<0.01)	10.9% vs. 16.3% (p=0.05)	5

CABG: coronary artery bypass graft, BMS: bare metal stent, DES: drug eluting stent, MACE: major adverse cardiovascular and cerebrovascular events

ization (CT-RECTOR) score which is made based on CT variables has a higher success rate because CCTA can demonstrate multiple occlusions or severe calcifications [54,55] (Table 5).

STEP 4. ROLE OF CCTA FOR FOLLOW-UP OF PATIENTS WITH PREVIOUS REVASCULARIZATION

CABG

CCTA can be used to assess the patency of CABG with high

diagnostic accuracy compared to the assessment of native coronaries, because CABG have larger vessel diameters, are less movable, and have a lower propensity to develop calcified plaques compared with native coronaries [56] (Fig. 4). In meta-analysis, CCTA demonstrates high diagnostic accuracy with a sensitivity of 97.6%, specificity of 96.7%, and NPV of 98.9% [57]. CCTA can also be helpful for the evaluation of the internal mammary artery in relation to the sternum in patients considering redo-CABG (repeat coronary artery bypass grafting).

Despite the technical developments of the CT technique, non-

Table 5. Angiographic and CT predictors of failure for percutaneous coronary intervention on CTO

	Angiographic predictors (J-CTO score)	CT predictors (CT-RECTOR score)
Imaging (point)	Occlusion length ≥ 2 cm (1) Blunt stump (1) Any calcification (1) Bending ≥ 45 degrees (1)	Multiple occlusion (1) Blunt stump (1) Severe calcification* (1) Bending ≥ 45 degrees (1)
Clinical (point)	Re-try lesion (1)	Second attempt (1) Duration of CCTA > 1 yr (1)
Category of difficulty (total point)	Easy (0) Intermediate (1) Difficult (2) Very difficult (≥ 3)	Easy (0) Intermediate (1) Difficult (2) Very difficult (≥ 3)

*severe calcification means presence of any calcium involving $\geq 50\%$ of the vessel cross-sectional area at the entry or exit site or within the occlusion route. CT: computed tomography, CTO: chronic total occlusion, CCTA: coronary CT angiography, J-CTO: multicenter CTO registry in Japan, CT-RECTOR: Computed Tomography Registry of Chronic Total Occlusion Revascularization

Fig. 4. Coronary artery bypass graft in a 48-year-old male. (A) Volume rendered CT image well demonstrates two grafts (LITA-LAD and RITA-LCX) with Y-shaped anastomosis. Notes: LITA-LAD indicates bypass between the left internal thoracic artery and distal left anterior descending artery, and RITA-LCX indicates a graft between the right internal thoracic artery and left circumflex artery. (B) Curved multiplanar reconstruction image of the LITA-LAD graft shows multiple insignificant stenoses (arrows). Because multiple surgical clips (arrowheads) sometimes hampered the luminal stenosis or were confused as a calcified plaque, careful evaluation of the graft lumen is necessary. CT: computed tomography.

evaluable grafts have remained due to artifacts from surgical metal clips, mild stair-step motion artifacts, flow competition of the arterial graft, and severe calcifications of the native coronary vessels [58,59]. Another limitation of CT for evaluation of CABG is the issue of radiation exposure because the scan range should be extended for evaluation of CABG beyond the native coronary arteries. However, introduction of various radiation reduction techniques such as prospective ECG gating, iterative reconstruction, or high pitch techniques can reduce radiation exposure while maintaining image quality and high diagnostic accuracy [60,61].

In-stent restenosis

As compared to CABG, the diagnostic accuracy in patients who received stents varies because the accuracy is affected by the diameter of the stent and size of the stent struts. According to recent meta-analysis studies, the diagnostic accuracy of CCTA for stent patency is as high as 90%, with sensitivity of 89.7–90%, specificity of 91–92.2%, PPV of 72.5%, and NPV of 97.4% [62] (Fig. 5). Overall, diagnostic accuracy is significantly high-

er in stents with larger vessel diameters. CCTA demonstrated that the sensitivity, specificity, PPV, and NPV were 67, 78, 57, and 85%, respectively, for stents <3.0 mm in diameter, whereas for stents ≥3.0 mm in diameter, the sensitivity, specificity, PPV, and NPV were increased at 89, 100, 100, and 97%, respectively [63]. Moreover, the diagnostic performance of CCTA has been found to be superior in stents with thinner struts (<100 μm) compared to stents with thicker struts [63]. Due to limitations in CT technology, CCTA is not yet recommended for stents <3.0 mm in diameter [8]. However, the recent introduction of high spatial resolution CT (0.23 mm) and a calcium subtraction algorithm using dual energy CT may improve the accuracy of the evaluation of in-stent restenosis [64,65].

CONCLUSION

CCTA is now widely used as a reliable non-invasive imaging test for CAD assessment that can be performed quickly and has high diagnostic accuracy. The quantification of plaques which cannot be observed in ICA has made it possible to predict prog-

Fig. 5. Stent evaluation with coronary computed tomography angiography. (A) Curved MPR of the RCA in a 53-year-old male shows multiple stents from the proximal to distal RCA. There is no significant in-stent restenosis, although there is minimal in-stent restenosis (arrow). (B) Curved MPR of the left circumflex artery in a 62-year-old female with acute chest pain shows total occlusion within the stent (arrows), suggesting a thrombotic occlusion. RCA: right coronary artery, MPR: multiplanar reconstruction.

nosis, and the recently introduced various CT-based myocardial ischemic burden assessments can help to guide the treatment plan.

Although spatial resolution of CT is not satisfactory and radiation exposure is still considered a problem, the development of technology is expected to increasingly overcome these limitations, thus CCTA will play an important role not only in diagnosis but also in the treatment strategy for CAD management.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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