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Computed tomography angiography-guided percutaneous coronary intervention in chronic total occlusion*

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Abstract: Objective: The aim of this study is to investigate if dual-source computed tomography (DSCT) could guide the percutaneous coronary intervention (PCI) of chronic total occlusion (CTO). Methods: We enrolled patients who were confirmed to have at least one native coronary artery CTO by DSCT before they underwent selective PCI in the period from December 2007 to October 2008. A CTO was defined as an obstruction of a native coronary artery with no luminal continuity. The CT-guided PCI procedure involved placing CT and fluoroscopic images side-by-side on the screen. DSCT images were analyzed for location, segment, plaque characteristics, calcification, and proximal lumen diameter of the CTO before PCI. The guidewire was advanced and manipulated under CT guidance. The PCI was carried out and the results were compared. Results: Seventy-four CTOs were assessed. PCI was successful in 57 cases of CTOs (77.0%). According to the results, CTOs were divided into two groups: successful-PCI and failed-PCI. All coronary artery paths of CTOs were clearly recognized by DSCT. In the successful-PCI group, soft plaques were detected much more often than those in the failed-PCI group, but fibrous and calcified plaques were seen more often in the failed-PCI group. Calcification severity in CTO segments showed a significant difference between the groups (P=0.014). Calcified plaques were detected in 20 (35.1%) lesions in the successful-PCI group. More than 70% of the failures were calcified plaques, of which there were two arc-calcified and one circular-calcified lesions. Occlusions were longer in the failed-PCI group than those in the successful-PCI group [(38.8±25.0) vs. (18.0±15.3) mm, respectively, P<0.01]. Fewer guidewires were used in the successful-PCI group compared with the failed-PCI group (1.7±1.0 vs. 2.5±0.9, respectively, P<0.01). The logistic regression analysis indicated that predictors of recanalization of CTOs included occlusion length (P=0.0035, risk ratio (RR)=0.93) and calcification severity (P=0.05, RR=0.27). Multi-linear trends analysis showed that the factors affecting procedural time were CTO location (P=0.0141) and occlusion length (P=0.0035). Conclusions: DSCT could delineate the path of CTOs and characterize plaques. The outcomes of PCI were related to thrombolysis in myocardial infarction (TIMI) flow grade, CTO characteristics, severity of calcified plaques, and the length of occlusive segments. Occlusion length and calcification severity were independent predictors of CTOs. Occlusion length and CTO segments could also help to estimate the duration of interventional procedures.

Key words: Dual-source computed tomography (DSCT), Chronic total occlusion (CTO), Angiography, Recanalization
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1 Introduction

Multi-slide 64 computed tomography (CT) has been widely used for diagnosing coronary heart disease, which is reasonably accurate. However, it is unknown if it can also be used to guide interventions in the treatment of chronic total occlusion (CTO). CTO is readily identified using cineangiography as an abrupt termination of epicardial vessels (flush occlusion). The length of the occlusion can be determined by the presence of anterograde or retrograde collaterals (Libby *et al*., 2007). It was reported that CTOs account for 5%–15% of patients who undergo coronary angiography (Ruocco *et al*., 1992; Puma *et al*., 1995). A multi-center and prospective study confirmed that successful percutaneous coronary intervention (PCI)

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of CTO produces a better outcome than if PCI not carried out (Olivari *et al*., 2003). However, the success rate of CTOs is often low, whereas costs and the prevalence of restenosis are high (Safian *et al*., 1988). Data from transcatheter cardiovascular therapeutics (TCT) 2006 indicated that the mean prevalence of failure was about 32%. One of the reasons is that traditional coronary angiography (CAG) is a type of "lumenography". It cannot provide information on the plaque composition of CTO, lesion length, or access. Studies suggested that younger CTO lesions were predominantly soft or lipid-laden, whereas older lesions were typically hard or fibro-calcific, which resulted in resistance to guidewire crossing and a lower success rate for the procedure (Srivatsa *et al*., 1997). The time of onset of CTOs can be determined according to the history of myocardial infarction. However, this is not always reliable because the occlusive vessel could be thrombolytic after myocardial infarction or due to multi-vessel disease. At least one quarter of the CTO lesions at the time of the occlusion cannot therefore be further discerned. Moreover, using CAG to analyze plaque composition and determine the lengths of the plaques in occlusion segments is difficult.

Conventional invasive CAG has been the "gold standard" for the diagnosis of coronary artery disease. However, CAG shows only luminal stenosis and the extent of coronary atherosclerosis. It does not provide information on plaque composition. Non-invasive coronary multi-detector computed tomography (MDCT) can visualize the coronary artery lumen, artery wall, and atherosclerotic plaque; even the lipid pool can be visualized, which is fibrous, calcified, and heavily laden with cholesterol. Leber *et al*. (2004) and Schroeder *et al*. (2007) confirmed that contrast-enhanced MDCT permits accurate identification of coronary plaques, and that CT density values within plaques reflect echogenicity and plaque composition. Dual-source computed tomography (DSCT) equipped with two tubes and corresponding detectors in 90° geometry provides temporal resolution of approximately one quarter of its 330-ms gantry rotation time. Its spatial and temporal resolutions are much higher than those of MDCT (Brodoefel *et al*., 2008). However, studies focusing on the ability of DSCT to identify the route and plaque characteristics in CTOs (as well as the relationship between CT parameters and the outcomes of PCI) are lacking.

The aim of the present study was to investigate (1) if the route and plaque components of CTOs detected by DSCT could help guide PCI, and (2) which factors affect the outcome of PCI or the duration of the procedure.

2 Patients and methods

The study protocol was approved by the Ethics Committee of Chinese PLA General Hospital. All patients were provided with written informed consent to be included in this study.

2.1 Study population

Patients were selected if at least one native coronary artery was confirmed to be chronically occluded by DSCT before selective PCI was carried out from December 2007 to October 2008.

Exclusion criteria were: estimated duration of CTO <30 d, arrhythmia, acute myocardial infarction, contraindication to β-blockers, known allergic reactions to iodinated contrast media, inability to follow breath-hold commands, renal insufficiency (serum creatinine >1.5 mg/dl), hyperthyroidism, or advanced heart failure (New York Heart Association Grades III–IV).

2.2 Criteria for diagnosis

1. CTO diagnostic criteria: A CTO was defined as an obstruction of a native coronary artery with no luminal continuity and with thrombolysis in myocardial infarction (TIMI) flow grade 0 or 1.

2. Classification system for coronary arteries: The nomenclature usually employed to describe the coronary anatomy was used. That was, the 27 segments in three major coronary arteries defined by the coronary artery surgery study (CASS) investigators were used.

3. Successful PCI: Successful PCI was defined as attainment of a residual diameter stenosis of <20% and TIMI flow grade 3.

4. TIMI flow grade: grade 0, no perfusion; grade 1, penetration with minimal perfusion into the artery; grade 2, partial reperfusion; grade 3, complete reperfusion.

5. Hypertension and diabetes mellitus: Hypertension and diabetes mellitus were diagnosed

according to the World Health Organization (WHO) criteria.

2.3 CT coronary angiography and reconstruction

CT was carried out on a DSCT machine (Somatom Definition, Siemens Medical Solutions, Germany). Subjects received glycerol trinitrate spray before imaging. Estimation of individual circulation time was based on the test bolus technique using a 20-ml bolus contrast. Vessel opacification was achieved through automated injection by a power injector (Medrad Stellant®) of 60–80 ml iohexol (350 mg I/ml Omnipaque, GE Healthcare, USA) at a flow rate of 5 ml/s plus a 40–60 ml saline flush. Collimation was 32 mm×0.6 mm; slice acquisition was 64 mm×0.6 mm using the z-flying focal spot technique; the gantry rotation time was 330 ms; the pitch was 0.20–0.43 and was adapted to heart rate; tube voltage was 120 kV; and, the maximum tube current was 400 mA per rotation. Electrocardiography (ECG) was digitized and continuously monitored during the scanning period. Electrocardiographically gated datasets were reconstructed at 70%, 75%, and 80% of the cardiac cycle after the QRS complex to identify central diastole, and additional datasets were reconstructed at 40%, 45%, and 50% of the cardiac cycle to identify central early diastole.

Acquired datasets were reconstructed by three dimensional (3D) volume-rendered (VR), thin-slab maximum-intensity projections (MIPs), and multiplanar-reformatted (MPR) images. The region of interest was placed on axial or cross-sectional MPR images.

Occlusion coronary artery routes were visualized by MIP and VR imaging. The location (left anterior descending artery (LAD), left circumflex artery (LCX), or right coronary artery (RCA)) and the segment (proximal, middle, or distal) of CTOs were accessed by MIP and MPR images. Plaque characteristics in the CTO segment were classified as “soft”, “fibrous”, and “calcified” by CT density in cross-sectional MPR images. Calcified plaques were defined as >120 Hounsfield units (HU), whereas the mean density measured within “lipid-rich” or “soft” plaques was <50 HU, and intermediate (fibrous) plaques were 50–120 HU (Schroeder *et al*., 2007). Each lesion was classified as “non-calcified”, “spot-calcified”, “arc-calcified”, and “circular-calcified”. Distal perfusion from the occlusion segment was judged as TIMI grade 0 or 1 by MPR images. The length of the occlusion segment was measured using MPR images.

2.4 Percutaneous coronary intervention (PCI)

By studying CT images, each operator evaluated the route of the occlusive vessel, as well as its branches, plaque characterization, and severity of calcification. In view of the information on the CTO segment provided by DSCT, the operator was permitted to select an appropriate projection to show the occluded segment, without having to carry out conventional CAG. PCI was then carried out by reference to these CT images. The choice of devices, as well as procedural and technical details, was determined by the operator. The guidewire was advanced and manipulated under CT guidance. The entry point had to be determined to cross the occlusion. When focusing on the target lesions, it is advisable to obtain a 3D CT angiogram by volume rendering to visualize the undistorted course of the coronary artery. Once the target vessel was identified, the operator used the MIPs to find the entry point. The occlusion point and the length of the occlusions could be clearly identified on the DSCT coronary angiogram. The operator was then instructed to align the CT and the “frozen” coronary angiogram. This was called the “CT image-adjusted technique” (Gai *et al*., 2008). The next stage was to push the guidewire forward. Adjustment of the direction of the guidewire was necessary. Some of the occlusions were very long (particularly in the RCA). The risk of perforation was low as long as the artery was not dilated. Perforation occurred in one patient, but there were no adverse consequences. PCI was then carried out and the results compared. Anatomically successful PCI was defined as attainment of a residual diameter stenosis <20% and a TIMI flow rate of grade 2 or 3.

2.5 Statistical analyses

Data analyses were carried out using SAS 9.1 statistical software (SAS Institute, Incorporated, Cary, North Carolina, USA). Continuous data were expressed as mean±standard deviation (SD) or median with interquartile ranges. Categorical data were reported as percentages. For continuous variables, the Student’s *t*-test or analysis of variance (ANOVA) was used to identify if inter-group differences were significant. Tests for multi-linear trends and logistic regression were computed for these analyses. $P<0.05$ was considered significant.

3 Results

3.1 Baseline characteristics of patients

DSCT and CAG were undertaken in 567 cases from December 2007 to October 2008. One hundred and two (18%) cases had at least one CTO, of which 68 (67%) patients had PCI. After PCI, 77.9% (53/68) patients with CTOs and 77.0% (57/74) CTO lesions were successfully treated. CTOs were divided into two groups (successful-PCI and failed-PCI groups) according to the results. Patient characteristics are summarized in Table 1. The parameters of the two groups were similar.

There were no in-hospital major adverse cardiac events (MACEs), i.e., death, acute myocardial infarction, urgent repeat PCI, and urgent coronary artery bypass graft (CABG). Intravascular ultrasound (IVUS) was completed in two cases, which was consistent with DSCT.

3.2 Characteristics of CT angiography

All CTOs were correctly identified by MIP images. Most of the CTOs were located in the proximal LAD. Plaque compositions between the two groups were significantly different ($P=0.022$). In the successful-PCI group, there were more soft plaques (Fig. 1).

Table 1 Baseline characteristics of patients

Parameter	Value*		*P*
	Successful-PCI (*n*=57)	Failed-PCI (*n*=17)	
Age (year)	60.0±10.2	57.7±9.9	>0.05
Females	9 (15.8%)	2 (11.8%)	>0.05
History of tobacco use	27 (47.4%)	7 (41.2%)	>0.05
Diabetes mellitus	17 (29.8%)	7 (41.2%)	>0.05
Hypertension	33 (57.9%)	11 (64.7%)	>0.05
Hyperlipidemia	27 (47.4%)	7 (41.2%)	>0.05
History of CABG	0 (%)	0 (%)	>0.05
History of PCI	10 (17.5%)	7 (41.2%)	>0.05
History of MI	7 (12.3%)	2 (11.8%)	>0.05

* Values are mean±SD for age, and number (percentage of group) for other parameters. CABG: coronary artery bypass graft; PCI: percutaneous coronary intervention; MI: myocardial infarction

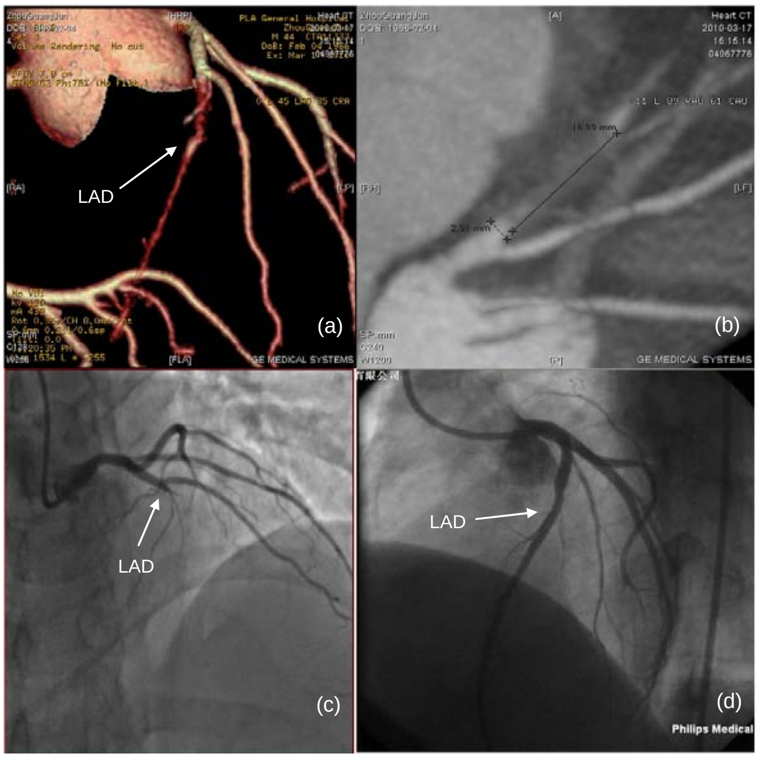

Fig. 1 Computed tomography angiography-guided percutaneous coronary intervention
The lumen of soft tissue was clearly visualized by both volume-rendered (VR) (a) and multiplanar-reformatted (MPR) (b). Coronary angiography (CAG) was performed before (c) and after (d) PCI

In the failed-PCI group, there were more fibrous and calcified plaques. There was more calcification in the CTO segments (*P*=0.014). Only 20 (35.1%) calcified plaques were successfully recanalized. More than 70% failures were calcified plaques, in which two arc-calcified and one circular-calcified lesions were identified. This indicated that few calcified plaques could be recanalized. CTOs presenting with TIMI grade 1 were recanalized much easier (*P*=0.044). The location of CTOs between the two groups did not show a significant difference. However, the occlusion length was longer in the failed-PCI group than in the successful-PCI group [(38.8±25.0) vs. (18.0±15.3) mm, respectively, *P*<0.01] (Table 2).

Table 2 CT angiography characteristics

Parameter	Value[#] Successful-PCI group (*n*=57)	Value[#] Failed-PCI group (*n*=17)	*P*
Plaque characteristics			
Soft	35 (61.4%)	5 (29.4%)	0.022*
Fibrous	15 (26.3%)	6 (35.3%)	
Calcified	7 (12.3%)	6 (35.3%)	
Severity of calcification			
Non-calcified	37 (64.9%)	5 (29.4%)	0.014*
Spot-calcified	18 (31.6%)	9 (52.9%)	
Arc-calcified	2 (3.5%)	2 (11.8%)	
Circular-calcified	0 (0%)	1 (5.9%)	
TIMI flow grade			0.044*
0	5 (8.8%)	7 (41.2%)	
1	52 (91.2%)	10 (58.8%)	
Location of CTOs			>0.05
LAD	24 (42.1%)	7 (41.2%)	
LCX	13 (22.8%)	4 (23.5%)	
RCA	20 (35.1%)	6 (35.3%)	
Segment of CTOs			>0.05
Proximal	27 (47.4%)	8 (47.1%)	
Middle	25 (43.8%)	6 (35.3%)	
Distal	5 (8.8%)	3 (17.6%)	
Proximal lumen diameter (mm)	2.3±0.8	1.9±0.9	>0.05
Length of occlusion (mm)	18.0±15.3	38.8±25.0	0.0039**

* *P*<0.05; ** *P*<0.01. # Values are number (percentage) of subjects or mean±SD. CT: computed tomography; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction; CTO: chronic total occlusion; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery

3.3 PCI procedure

There was no significant difference in procedural time, irrespective of whether the procedure was successful or not [(32.8±23.0) vs. (46.8±38.5) min, respectively, *P*>0.05]. Fewer guidewires were used in the successful-PCI group compared with the failed-PCI group (1.7±1.0 vs. 2.5±0.9, respectively, *P*<0.01).

In the logistic regression analysis to determine the predictors of recanalized CTOs, we included the occlusion length (*P*=0.0035, risk ratio (RR)=0.93) and the severity of calcification (*P*=0.05, RR=0.27).

In the multi-linear trends analysis to determine the predictors of procedure time, we included the CTO segment (*P*=0.0141) and the occlusion length (*P*=0.0035).

4 Discussion

MDCT is a non-invasive tool for imaging the coronary artery. MDCT has been repeatedly used to identify and classify the compositions of coronary plaques, such as calcium, fibers, or large lipid pools. DSCT holds the promise of providing more accurate classification and quantification of plaque components than coronary angiography.

We found that the advantage of DSCT was its ability to visualize the occluded coronary artery. Under conventional coronary angiography, the occlusion was seen as a discontinuity of the contrast. However, on DSCT the occluded artery was seen as soft tissue containing no contrast. The ‘lumen’ of soft tissue forms the basis of the CT-guided PCI procedure. Conventional CAG has been the gold standard for the diagnosis of coronary artery disease, but it has limitations. It shows the stenotic lumen at a given time. In particular, visualizing the exact course of CTO segments is difficult. Therefore, the experience of the operator was needed to estimate the path of the CTO in the course of the procedure. DSCT, however, can accurately show the anatomy of CTO lesions. Operators can readily and accurately ‘see’ the routes of CTOs. Even in complex and tortuous vessels, the guidewire can reach the real lumen under DSCT guidance (Roguin *et al*., 2009).

The present study confirmed that DSCT and prospective HU-based analysis software indicated a moderate, but reproducible, correlation of volumes for the total plaque and its components with intravascular ultrasound-virtual histology (IVUS-VH) (Brodoefel *et al*., 2008). We also found that DSCT could visualize plaques in the CTOs. Despite advances in the development of angioplasty equipment (Saito *et al*., 2003), such as novel guidewires, as well as various complex techniques (Ng *et al*., 2003; Orlic *et al*., 2005), the success rate of PCI in CTOs remains low. Moreover, we found that successful PCI was often obtained in CTOs with a TIMI flow grade 1. TIMI flow grade in the CTO is dependent upon bridging collaterals, and occlusion duration (new micro-channels are generated in the CTO segment). Whatever the reason, CAG cannot observe these aspects clearly and accurately in a short period of time.

Typical atherosclerotic plaques of CTOs consist of intracellular and extracellular lipids, smooth muscle cells, the extracellular matrix, and calcium. CTO characteristics and the severity of calcified plaques significantly influenced the PCI outcome. For a CTO lesion composed of a soft plaque, the guidewire passed through and balloon expanded easily. In the case of severe calcification (e.g., circular-calcified), it was “like drilling holes in a stone”. Olivari *et al*. (2003) identified calcification to be a significant predictor of PCI failure.

In some cases, measuring the length of CTOs using conventional angiography is very difficult. Conversely, DSCT angiography allows a reliable 3D measurement of the length of an occlusive segment. DSCT not only showed the “lumenography”, but also detailed plaque morphology. In the present study, the long occlusive segment often predicted a low success rate. Puma *et al*. (1995) showed that an occlusion length >15 mm detected by conventional angiography was associated with procedural failure. The mean length of occlusions in the present study was >15 mm, even in the successful-PCI group. This may be due to foreshortening, calibration limitations, or a lack of visualization of the distal vessel in the absence of collateral filling measured by conventional angiography. Nevertheless, the length of occluded segment was an important predictor of failed PCI, in accordance with the previously mentioned study.

In addition, due to the complex procedure and vague route of CTO segments, the procedure often needed a long exposure time and a large amount of contrast. It was also associated with an increased prevalence of complications. Saito *et al*. (2003) recommended the following guidelines for termination of the procedure: time from arterial access to successful penetration of a guidewire through the occlusion ≤30 min, total procedure time ≤90 min, and total dye volume ≤300 ml. The CTO segment was a predictor of procedure duration. We believed that higher successful PCI rate obtained in distal vessels was due to better support than in proximal artery. Also, the length of the occlusive segment can result in the difference in procedure duration. That is, guidewires readily penetrated into the false lumen in long occlusions, and fewer guidewires were used in the successful-PCI group compared with the failed-PCI group.

5 Conclusions

DSCT can delineate the routes of CTOs and clearly characterize plaques. The outcome of PCI is related to TIMI flow grade, CTO characteristics, severity of calcified plaques, and the length of the occlusive segment. Occlusion length and calcification severity are independent predictors of recanalized CTOs. Occlusion length and CTO segments can also predict the duration of the interventional procedure.

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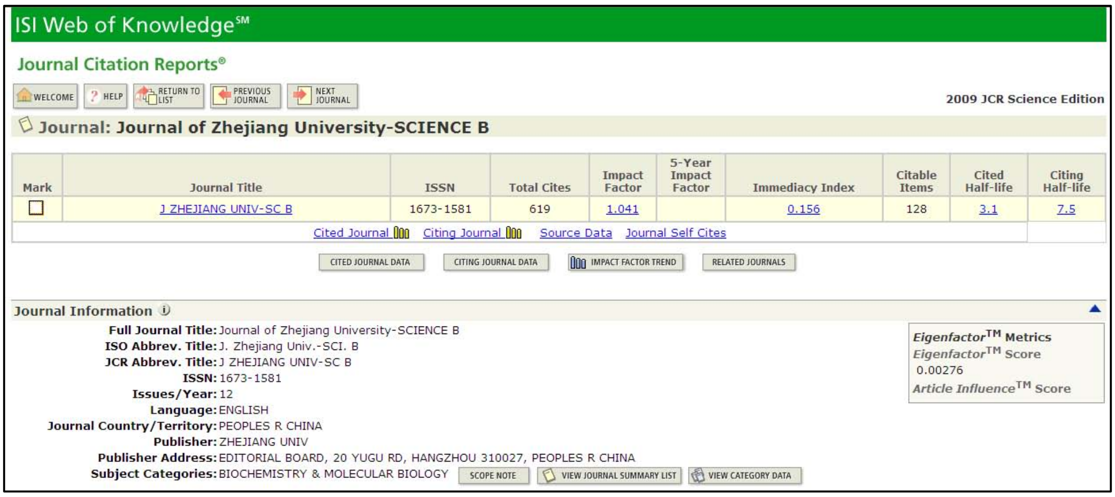

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