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# Clinical outcomes and risk factors of coronary artery aneurysms after successful percutaneous coronary intervention and drug-eluting stent implantation for chronic total occlusions

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ABSTRACT

*Objective:* The study aimed to analyze the risk factors and long-term outcomes associated with coronary artery aneurysms (CAAs) after successful percutaneous coronary intervention (PCI) and drug-eluting stent (DES) implantation in patients with CTOs.

*Background:* There are sporadic data available on post-procedure CAAs after transcatheter revascularization for CTOs.

*Methods and results:* A total of 141 patients with 149 CTOs who underwent successful CTO-PCI and DES implantation with angiographic follow-up from 2004 to 2010 were included. Patients were divided into CAA group and non-CAA group according to the presence of CAAs in the follow-up angiography. The independent predictors and major adverse cardiac events (MACEs) including cardiac death, myocardial infarction (MI) and target-vessel revascularization (TVR) were compared between two groups. The incidence of CAAs was 11.4% (17/149) after index procedure. Multivariate analysis showed that age (OR: 0.925, CI 0.873–0.980, P = 0.008), ostial occlusion (OR: 6.715, CI 1.473–30.610, P = 0.014), the parallel wire technique (OR: 6.167, CI 1.709–22.259, P = 0.005) and DES length (OR: 1.030, CI 1.002–1.058, P = 0.036) were the independent predictors of CAAs after successful CTO-PCI and DES implantation. MACEs were similar between two groups (adjusted hazard ratio 0.670; 95% CI 0.160–2.808; P = 0.584) during the 5-year follow-up.

*Conclusions:* The independent predictors of CAAs after successful CTO-PCI and DES implantation are age, ostial occlusion, the parallel wire technique and DES length. CAAs after index procedure are not frequently associated with adverse clinical events under dual antiplatelet therapy. Further large clinical studies are warranted to explore the clinical implications of patients with this distinct new entity.



## 1. Introduction

Approximate one third of the patients with significant coronary artery disease on angiography have at least one chronic total occlusion (CTO) [1,2]. Over the last decade, remarkable progress has been achieved in the percutaneous management of coronary artery disease. However, recanalization for CTOs of native coronary arteries is still regarded as the "last frontier" of percutaneous coronary intervention (PCI) due to its high rates of procedural complications and failure [3].

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In the 1990s, the procedural success rates of CTO-PCI were only 48%–76% [4–6]. With improved operator experience, dedicated devices and procedural techniques, the success rates have steadily increased in the past few years. In some experienced center, the procedural success rate can reach roughly 90% [7]. In spite of these improvements, many problems such as acute complications, restenosis and coronary artery aneurysms (CAAs) continue to present a challenge.

CAA is an abnormal dilatation (≥1.5-fold) of part of the coronary artery and often found coincidentally on coronary angiography. There are limited published data focused on CAA formation following PCI supported by drug eluting stent (DES) which is postulated to be associated with hypersensitivity reactions toward the stent [8,9]. As we all know, CTO-PCI has a higher probability of using longer stents and exposing the subintimal structure to the stent, or even stenting subintimally. However, not any retrospective or prospective study was designed to focus on the status and outcomes of CAAs after successful CTO-PCI and DES implantation. Therefore, we designed the current study to investigate the independent predictors and clinical outcomes for CAAs which developed after successful CTO-PCI and DES implantation.

## 2. Methods

### 2.1. Study population

We reviewed the catheterization database and medical records at the Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital of Fudan University and identified 697 patients with successful recanalization of CTOs in the native coronary arteries who presented from 2004 to 2010. All patients in the current study received follow-up angiography in the same catheterization center and were divided into CAA group and non-CAA group according to the detection of CAAs. Patients with CTOs were excluded when any of the following was encountered: (1) Procedural failure to open the CTOs; (2) PCI without DES implantation; (3) Previous attempted percutaneous transluminal coronary angioplasty (PTCA) to the target CTO; (4) In-stent restenotic occlusions (Mehran IV pattern restenosis); (5) CAAs observed in any vessel before PCI; (6) Lack of angiographic follow-up in our center; (7) Re-PCI to the target CTO vessel before detection of a CAA in the CAA group; and (8) Duration of angiographic follow-up <6 months in the non-CAA group. A retrospective chart review was performed to collect the clinical variables, history and catheterization information.

The angiographic follow-up duration of the CAA group was defined as the duration from the 1st successful CTO-PCI to the 1st diagnosis of CAA. The angiographic follow-up duration of the non-CAA group was defined as the duration from the 1st successful CTO-PCI to the final recorded angiography unless re-PCI for the target vessel. The long-term clinical follow-up duration of patients in both groups was defined as the time from the 1st successful CTO-PCI to July 31, 2013.

All the CTO-PCI procedures were performed by 10 different operators from our center. All of the operators achieved more than 200 PCI per year. The regulatory board of the Zhongshan Hospital affiliated to Fudan University approved this study. All the patients gave written informed consent before all the procedure.

### 2.2. Procedures and medications

All the percutaneous revascularizations of CTOs were performed according to the current standard guidelines. All patients were prescribed medicine prior to interventions, with administration of 300 mg aspirin and 300 mg clopidogrel as pretreatment. After operation, all patients were advised to maintain their life-long aspirin therapy, and at least a 12-month clopidogrel prescription.

Intravascular ultrasound (IVUS) was performed using iLAB (Boston Scientific, USA). After the intracoronary administration of nitroglycerin (0.2 mg), the ultrasound catheter (2.5 F Atlantis SR, 40-MHz, Boston Scientific Corporation, USA) was advanced distally to the left anterior descending artery, the left circumflex or the right coronary artery along the 0.014″ guidewire and was pulled back to the aortocoronary ostium using motorized transducer pullback at the speed of 0.5 mm/s. Continuous ultrasound images were obtained and recorded on CDs. The IVUS data were analyzed by two specially experienced cardiologists and one experienced technician.

### 2.3. Angiographic definitions

CTO is defined as thrombolysis in myocardial infarction (TIMI) grade 0 flow and the duration of coronary occlusion ≥3 months [3]. In the absence of serial angiograms, the duration of coronary occlusion is instead estimated from available clinical information related to the event that caused the occlusion (eg, acute MI or sudden change in angina pattern with ECG changes consistent with the location of the occlusion) [3]. Angiographic success was defined as a restoration of TIMI flow grade 3 in the target vessel after DES implantation and a residual stenosis <10% by visual estimation.

CAA is typically defined as a dilatation in the diameter of a coronary artery segment to more than 1.5-fold the normal size by visual estimation [10], and this CAA was closely related to the underlying DES or its edges, and the localized dilation was absent immediately after the procedure.

The angiographic indices examined were the location of the CTO, CAA, diffuse disease proximal to the occlusion (at least one stenosis of >50% proximal to the occlusion) [11], side branch at the occlusion, vessel tortuosity (the presence of at least one bend of >45° proximal to the occlusion) [11], calcium at the site of the occlusion (radio-opacity present before contrast injection), ostial occlusion (occlusion within 3 mm of the ostium), stump morphology (a blunt or tail-like stump) and grades of bridging collaterals (0 = none; 1 = filling of side branches of the artery to be dilated via collateral channels without visualization of the epicardial segment; 2 = partial filling of the epicardial segment via collateral channels; and 3 = complete filling of the epicardial segment of the artery being dilated via collateral channels) [12]. Angiographic restenosis was defined as a ≥50% diameter stenosis within the target lesion.

All the films were reviewed by two qualified interventional doctors. If there was any ambiguity in the reports or films, the films were reviewed independently by three well-qualified interventional doctors.

### 2.4. Study endpoints

The major adverse cardiac events (MACEs), including cardiac death, myocardial infarction (MI), and target-vessel revascularization (TVR), were recorded. MI was defined as elevation of the cardiac troponin with at least one value above the 99th percentile of the upper reference limit and with at least one of the following: (1) symptoms of ischemia, (2) new or presumably new significant ST–T changes or new LBBB, (3) development of pathological Q waves in the ECG, (4) imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality, and (5) identification of an intracoronary thrombus by angiography or autopsy [13]. TVR was defined as emergency or elective coronary artery bypass graft or repeat PCI in the target vessel.

### 2.5. Statistical analysis

The data were expressed as the mean ± SD for the continuous variables, and as frequencies for the categorical variables. The comparison of continuous variables was performed by the independent Student's t-test or the Mann–Whitney U test as appropriate. Statistical analysis of the categorical variables was performed using the Pearson chi-square or Fisher's exact test as appropriate.

The multivariate logistic regression model (the variables in Tables 1, 2 and 3 with $P < 0.1$ were entered into the analysis, except for the