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Impact of coronary collateral circulation on angiographic in-stent restenosis in patients with stable coronary artery disease and chronic total occlusion

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ABSTRACT

Objective: This study aimed to evaluate the relationship between coronary collateralization and in-stent restenosis (ISR) in stable coronary artery disease patients with chronic total occlusion (CTO) after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation.
Methods: The degree of coronary collaterals supplying the distal aspect of a total occlusion from the contra-lateral vessel was graded according to Rentrop classification in 216 patients with stable angina undergoing successful DES based PCI for CTO. Univariable and multivariable logistic regression analyses were performed to assess the potential factors related to angiographic ISR during follow-up.
Results: Despite similar number of diseased coronary arteries, good collateralization (Rentrop score 2 or 3) was more frequently associated with right coronary artery occlusion (60%), whereas poor collaterals (Rentrop score 0 or 1) occurred more often in left anterior descending artery occlusion (40%). Despite similar number of CTO intervened, stent length was longer in patients with good collateralization (59 ± 27 mm vs 47 ± 23 mm, $p = 0.001$). At mean 18 months, the rate of ISR did not significantly differ between patients with good collateralization and those with poor collateralization (12.7% vs 20.2%, $p = 0.148$). At multivariable analysis, age (OR 1.058, 95%CI 1.015–1.104, $p = 0.008$), history of diabetes mellitus (OR 2.382, 95%CI 1.109–5.116, $p = 0.026$) and reference CTO vessel diameter (OR 0.219, 95% CI 0.051–0.951, $p = 0.043$) were independent risk factors for ISR while Rentrop collateral grade (OR 0.795, 95% CI 0.365–1.732, $p = 0.414$) was not associated with ISR.
Conclusions: The occurrence of ISR after successful DES based PCI for CTO may be not influenced by coronary collateralization.

1. Introduction

Coronary collateral formation is a physiological accommodation during severe, gradual vessel narrowing (occlusion) in order to restore blood flow in ischemic territory [1]. Well-developed coronary collaterals serve as a natural bypass system, providing a minimum perfusion for jeopardized or hibernating myocardium, preserving left ventricular function, and improving survival after transient or permanent coronary obstruction [2,3]. In contrast to the beneficial association between coronary collateral circulation and clinical sequelae, the impact of coronary collateral circulation on angiographic prognosis has been ambiguous and rather inconsistent [4,5]. In a recent meta-analysis including seven studies mainly with plain balloon angioplasty or bare metal stent implantation, Meier et al. reported an increased risk of restenosis after percutaneous coronary intervention (PCI) in patients with good coronary collateralization [6]. Together with a relative high rate of procedural failure, peri-procedural infarction, and potential lethal complication related to revascularization [7], many physicians even feel that, since there is little room for clinical worsening in most cases with chronic total occlusion (CTO) and well-developed coronary collaterals supplying to the distal area, revascularization of these lesions could be safely avoided. Drug-eluting stents (DES) have now been frequently used for interventional treatment of CTO with lower target vessel revascularization compared with bare-metal stents [8,9], but it remains unclear whether coronary collateralization exerts a consistent effect on angiographic restenosis in era of DES. In this study, we sought

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to evaluate the impact of coronary collateral circulation on the occurrence of angiographic ISR in patients with CTO undergoing successful DES based PCI.

2. Methods

This is a prospective observational study. The protocol was approved by the Shanghai Jiao Tong University ethic committee and conducted in accordance with the Declaration of Helsinki. All patients gave written informed consent.

2.1. Patients

A total of 338 stable angina patients who underwent PCI for at least one chronic totally occluded lesion between June 2012 and December 2014 were recruited from the database of Shanghai Rui Jin Hospital PCI Outcome Program. This program utilizes clinical and angiographic information for various cardiovascular diseases to estimate risk-adjusted outcomes. Data on demographics, clinical and angiographic features, left ventricular function determined by two-dimensional echocardiography, and in-hospital management were collected retrospectively, whereas clinical outcomes during follow-up were identified prospectively. Stable angina was diagnosed according to the criteria recommended by the American College of Cardiology/American Heart Association [10]. CTO was defined as those occluded arteries with a documented duration of occlusion of at least 3 months with absolutely no flow through the lesion (TIMI 0 flow) [11]. Estimation of the duration of coronary occlusion was based on the first onset of an abrupt worsening of existing angina, a history of myocardial infarction in the target vessel territory, or information obtained from a previous angiogram.

For the purpose of this research, 52 patients (15%) who had a history of previous PCI or coronary bypass surgery were excluded. Among remaining 286 eligible patients, 232 patients (81%) were successfully revascularized for CTO with DES. The types of DES used included everolimus-eluting Xience stents (Abbott Vascular, Santa Clara, California, USA), zotarolimus-eluting Resolute stents (Medtronic Vascular, Santa Rosa, CA), and sirolimus-eluting Firebird II stents (Microport Co. Ltd., China). During follow-up, 9 patients (4%) were lost, 2 patients (1%) had sudden death, 5 patients (2%) declined to perform repeat coronary angiography due to free of symptoms. Thus, 216 patients were included in the final analysis (Fig. 1).

2.2. Coronary intervention and ISR

Coronary angiography was performed with standard techniques via the femoral or radial approach. Before the procedure, all patients received loading dose of aspirin (300 mg/d) and clopidogrel (300 mg). During the procedure, an intravenous bolus of heparin (70-100 IU/kg) was given, but the use of glycoprotein IIb/IIIa inhibitors was at the operator's discretion. PCI for CTO was performed using contemporary techniques such as bilateral injection; specialized hydrophilic, tapered tip, and stiff wires; parallel wires; microcatheters; and retrograde approach. The choice of guidewires, balloons, and DES type was left to the discretion of the operator. After the procedure, clopidogrel (75 mg/day) was prescribed for at least 12 months, and aspirin (100 mg/day) was continued indefinitely. All patients were encouraged to take guideline- recommended medications including statins, angiotensin-converting enzyme inhibitors and β-blockers unless contraindicated and to receive repeat coronary angiography at 12 months during follow-up.

Technical success was defined as a residual stenosis of <20% and restoration of TIMI flow grade 3. Procedural success was defined as technical success without death, myocardial infarction, or emergency coronary bypass grafting surgery. Complete revascularization was defined as restoration of TIMI grade 3 flow with residual stenosis <20% in all three major coronary arteries and their branches (diameter ≥ 2.0 mm). ISR was defined as recurrence of >50% luminal diameter narrowing within the stent or 5-mm proximal or distal segments adjacent to the stent at follow-up angiography.

2.3. Coronary collateral scoring

The degree of coronary collaterals supplying the distal aspect of a total occlusion from the contra-lateral vessel was graded according to Rentrop classification: 0 = no visible filling of any collateral channel, 1 = filling of the side branches of the infarct-related artery, 2 = partial filling of the epicardial vessel of the infarct-related artery, and 3 = complete collateral filling of the epicardial vessel [12]. Patients were categorized into poor (grade 0 or 1) or good (grade 2 or 3) coronary collateralization group. Visual assessments were performed off-line by 2 experienced interventional cardiologists blinded to clinical parameters. The agreement of coronary collateral classification between the two observers was 97%, and any difference in interpretation was resolved by a third reviewer. For those with more than one total coronary occlusion, the vessel with the highest collateral grade was chosen for analysis.

2.4. Statistical analysis

Continuous variables are expressed as mean ± SD and categorical data as percentages. Two-side Student's t test was used to compare continuous variables, and chi-square statistics was used to compare categorical values. Both univariable and multivariable logistic regression analyses were done to determine the factors for ISR. The following patient level candidate factors were evaluated: age, sex, hypercholesterolemia, hypertension, diabetes mellitus, current smoking, chronic renal failure, multivessel disease (number of diseased vessels), CTO located in left anterior descending artery, duration of CTO, reference CTO vessel diameter, number of implanted stents, total stent length for CTO vessel and complete revascularization. A probability level of $p < 0.05$ was considered significant. Analysis was performed using the software package SPSS, version13 (SPSS Inc., Chicago, IL, USA).

3. Results

Overall, Rentrop collateral grades 0, 1, 2, and 3 occurred in 29 (13.4%), 55 (25.5%), 59 (27.3%), and 73 (33.8%) patients, respectively. There were no significant differences in baseline clinical characteristics, medical treatment, and duration of CTO between patients with good and poor coronary collateralization. Despite similar number of diseased coronary arteries, good collateralization was more frequently associated

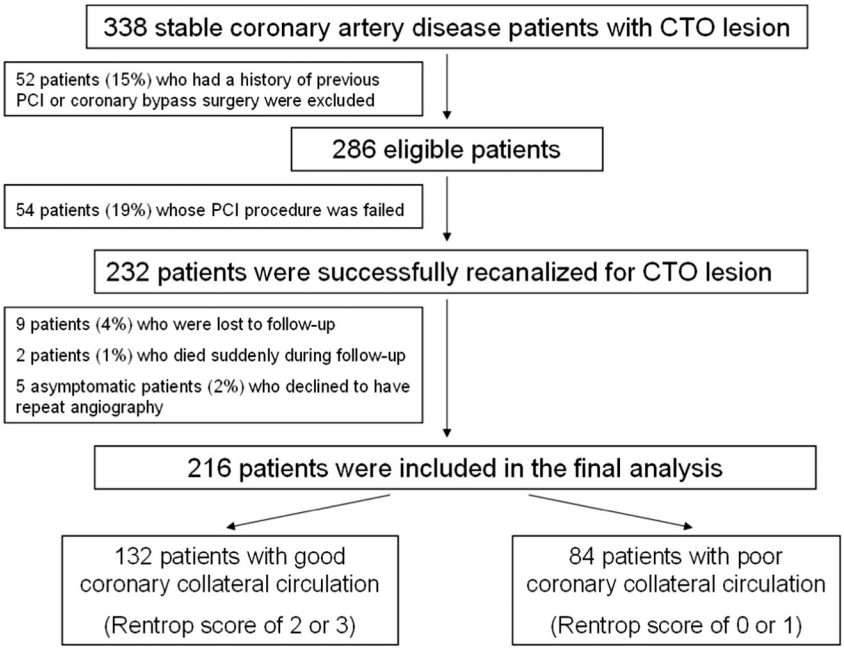

Fig. 1. Flow chart of patient enrollment. CTO: chronic total occlusion; PCI: percutaneous coronary intervention.

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