Journal of the American College of Cardiology
© 2013 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 61, No. 5, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2012.10.036

Predictors of Reocclusion After Successful Drug-Eluting Stent–Supported Percutaneous Coronary Intervention of Chronic Total Occlusion

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Objectives This study sought to assess the incidence of reocclusion and identification of predictors of angiographic failure after successful chronic total occlusion (CTO) drug-eluting stent–supported percutaneous coronary intervention (PCI).

Background Large registries have shown a survival benefit in patients with successful CTO PCI. Intuitively, sustained vessel patency may be considered as a main variable related to long-term survival. Very few data exist about the angiographic outcome after successful CTO PCI.

Methods The Florence CTO PCI registry started in 2003 and included consecutive patients treated with drug-eluting stents for at least 1 CTO (>3 months). The protocol treatment included routine 6- to 9-month angiographic follow-up. Clinical, angiographic, and procedural variables were included in the model of multivariable binary logistic regression analysis for the identification of the predictors of reocclusion.

Results From 2003 to 2010, 1,035 patients underwent PCI for at least 1 CTO. Of these, 802 (77%) had a successful PCI. The angiographic follow-up rate was 82%. Reocclusion rate was 7.5%, whereas binary restenosis (>50%) or reocclusion rate was 20%. Everolimus-eluting stents were associated with a significantly lower reocclusion rate than were other drug-eluting stents (3.0% vs. 10.1%; $p = 0.001$). A successful subintimal tracking and re-entry technique was associated with a 57% of reocclusion rate. By multivariable analysis, the subintimal tracking and re-entry technique (odds ratio [OR]: 29.5; $p < 0.001$) and everolimus-eluting stents (OR: 0.22; $p = 0.001$) were independently related to the risk of reocclusion.

Conclusions Successful CTO-PCI supported by everolimus-eluting stents is associated with a very high patency rate. Successful subintimal tracking and re-entry technique is associated with a very low patency rate regardless of the type of stent used. (J Am Coll Cardiol 2013;61:545–50) © 2013 by the American College of Cardiology Foundation

Large registries have shown a survival benefit in patients with successful chronic total occlusion (CTO) percutaneous coronary intervention (PCI) as compared to unsuccessful or unattempted CTO PCI (1–4). Intuitively, sustained vessel patency may be considered as a main variable related to long-term survival. Very few data exist about the angiographic outcome of successful CTO PCI, because randomized studies comparing different types of stents had small sample sizes; most registries did not include angiographic follow-up; and sparse data are available from a few small registries with a very low angiographic follow-up rate (4–12). The aim of this study was to assess the incidence of reocclusion and identification of predictors of angiographic failure after successful drug-eluting stent (DES)–supported CTO PCI.

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Methods

Patients and treatment. The Florence CTO PCI registry, started in 2003, includes consecutive patients treated with DES for at least 1 CTO. Details on this registry have been previously published (4,10). CTO was defined as a coronary obstruction with TIMI (Thrombolysis in Myocardial Infarction) flow grade 0 with an estimated duration >3 months. The duration of the occlusion was determined by the interval from the last episode of acute coronary syn-

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Manuscript received July 3, 2012; revised manuscript received September 28, 2012, accepted October 23, 2012.

JACC Vol. 61, No. 5, 2013
February 5, 2013:545–50

Abbreviations and Acronyms

CI = confidence interval(s)
CTO = chronic total occlusion
DES = drug-eluting stent(s)
EES = everolimus-eluting stent(s)
HR = hazard ratio(s)
OR = odds ratio(s)
PCI = percutaneous coronary intervention
STAR = subintimal tracking and re-entry
TIMI = Thrombolysis In Myocardial Infarction

drome, or in patients without a history of acute coronary syndromes, from the first episode of effort angina consistent with the location of the occlusion or by a previous coronary angiography. In patients without a history of angina and who were admitted for an acute coronary syndrome or ST-segment elevation acute myocardial infarction with a definite identification of the culprit vessel, associated total occlusion of a nonculprit vessel was considered as a chronic occlusion if there was angiographic evidence of filling the vessel through collaterals. The indication for the percutaneous treatment of CTO was the demonstration of viable myocardium in the territory of the occluded vessel by echographic or scintigraphic provocative tests, whereas no CTO angiographic characteristic was considered as an absolute contraindication to PCI attempt. Thus, patients with long occlusions, extensive calcification, bridging collaterals, a nontapered stump, or a side branch at the occlusion site were included. Occlusion length was assessed from the beginning of the occlusion to the distal antegrade or retrograde vessel by filling from bridge collaterals or collaterals provided by a coronary artery other than the CTO vessel and using simultaneous contrast medium injection in both right and left coronary arteries. All occlusions were attempted using the anterograde or retrograde approach and dedicated coronary wires (hydrophilic and nonhydrophilic) and devices. The anterograde approach was the first option treatment in all but right coronary ostium CTO. Subintimal tracking and re-entry (STAR) technique was used only after failed anterograde and retrograde approaches. Three types of DES were used during the study period: first-generation sirolimus-eluting stent (Cypher, Cordis Corp., Miami Lakes, Florida), first-generation paclitaxel-eluting stent (Taxus Express or Taxus Liberté, Boston Scientific, Natick, Massachusetts), and everolimus-eluting stent (EES) (either Xience V, Abbott Vascular, Santa Clara, California; or Promus, Boston Scientific). Standard stent implantation techniques, including minimum overlap between stents and routine post-dilation using final high balloon pressure (≥16 atm) were used. All patients were pre-treated with aspirin (300 mg/day) and clopidogrel (loading dose 600 mg). Aspirin (300 mg/day) was continued indefinitely and clopidogrel (75 mg/day) for at least 12 months.

Procedural success was defined as a final diameter stenosis <30% with a TIMI flow grade 3 of the CTO vessel without death, or Q-wave myocardial infarction, or emergency coronary surgery. A Q-wave myocardial infarction was defined as new Q waves in 2 or more contiguous leads in addition to creatine kinase-myocardial band elevation. Creatine kinase-myocardial band fraction was routinely assessed 12 h after PCI in all patients or at least 3 times every 6 h in patients with recurrent chest pain.

All patients had scheduled clinical and electrocardiographic examinations at 6 months and at 1 and 2 years. All other possible information derived from hospital readmission or by the referring physician, relatives, or municipality live registries were entered into the prospective database.

All patients with successful CTO PCI and without moderate or severe renal insufficiency were scheduled for angiographic follow-up at 6 to 9 months. Unscheduled angiography was allowed based on clinical indication. Angiographic parameters were assessed using a computer analysis system (Innova 2100IQ, General Electric Healthcare Technologies, Little Chalfont, Buckinghamshire, United Kingdom).

Endpoints. The primary endpoint of the study was reocclusion of the CTO vessel at the scheduled or unscheduled angiographic follow-up. The secondary endpoints were: 1) binary angiographic restenosis; 2) 1-year major adverse cardiac events including death, myocardial infarction, and target CTO vessel revascularization; and 3) definite CTO stent thrombosis. Reocclusion was defined as a TIMI flow grade 0 to 1 in the target vessel, whereas restenosis was defined as >50% luminal narrowing at the segment site including the stent and 5 mm proximal and distal to the stent edges. For patients with multiple treated CTO, only the first CTO attempted was considered for the analysis. All deaths were considered cardiac unless otherwise documented. Stent thrombosis was defined according to the Academic Research Consortium criteria (13).

Statistical analysis. Discrete data are summarized as frequencies and continuous data as mean ± SD or median and interquartile range. Chi-square test or Fisher exact test analyses were used for comparison of categorical variables. The multivariable analysis to evaluate the independent contribution of clinical, angiographic, and procedural variables to reocclusion and in-segment restenosis was performed by forward stepwise logistic regression analysis. The following variables were tested: diabetes mellitus; renal insufficiency; CTO stent length >40 mm; STAR technique; EES; year of the index procedure. Cumulative survival analyses were performed using the Kaplan-Meier method, and the difference between curves was assessed by log-rank test. A multivariable analysis by forward stepwise Cox proportional hazards model was performed to evaluate the independent predictors of death, myocardial infarction, and target CTO vessel revascularization. The following variables were tested: age >75 years; diabetes mellitus; previous myocardial infarction; renal insufficiency; acute coronary syndrome at admission; left ventricular ejection fraction <0.40; 3-vessel disease; CTO vessel; CTO stent length >40 mm; STAR technique; EES; completeness of revascularization; year of the index procedure. Interaction between EES and year of the index procedure was tested