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Retrograde Coronary Chronic Total Occlusion Revascularization

Procedural and In-Hospital Outcomes From a Multicenter Registry in the United States

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Objectives This study sought to examine the contemporary outcomes of retrograde chronic total occlusion (CTO) interventions among 3 experienced U.S. centers.

Background The retrograde approach, pioneered and developed in Japan, has revolutionized the treatment of coronary CTO, yet limited information exists on procedural efficacy, safety, and reproducibility of outcomes in other settings.

Methods Between 2006 and 2011, 462 consecutive retrograde CTO interventions were performed at 3 U.S. institutions. Patient characteristics, procedural outcomes, and in-hospital clinical events were ascertained.

Results Mean patient age was 65 ± 9.7 years, 84% were men, and 50% had prior coronary artery bypass surgery. The CTO target vessel was the right coronary artery (66%), circumflex (18%), left anterior descending artery (15.5%), and left main artery or bypass graft (0.5%). The retrograde approach was used as the primary method in 46% of cases and after failed antegrade recanalization in 54%. Retrograde collateral vessels were septal (68%), epicardial (24%), and bypass grafts (8%). Technical and procedural success was 81.4% (n = 376) and 79.4% (n = 367), respectively. The mean contrast volume and fluoroscopy time were 345 ± 177 ml and 61 ± 40 min, respectively. A major complication occurred in 12 patients (2.6%). In multivariable analysis, years since initiation of retrograde CTO percutaneous coronary intervention (PCI) at each center, female sex, and ejection fraction ≥40% were associated with higher technical success.

Conclusions Among selected U.S. programs, retrograde CTO PCI is often performed in patients with prior coronary bypass graft surgery and is associated with favorably high success and low complication rates. (J Am Coll Cardiol Intv 2012;5:1273–9) © 2012 by the American College of Cardiology Foundation

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The introduction of coronary chronic total occlusion (CTO) recanalization through retrograde collaterals has offered incremental procedural success and clinically meaningful benefit to traditional antegrade methods (1,2). Initially developed in Japan (1–6) and advanced throughout other Asian countries and Europe (7,8), limited experience regarding the performance and outcomes of retrograde CTO percutaneous coronary intervention (PCI) has been reported from North American centers (9,10). The present study describes the practice patterns, procedural outcomes, and in-hospital clinical events associated with retrograde CTO PCI among 3 selected programs within the United States, each representing a varied operator group and hospital structure.

Methods

Patient population. Between January 2006 and November 2011, consecutive patients undergoing retrograde CTO PCI were prospectively identified and outcomes were retrospectively examined at 3 centers within the United States: St. Joseph Medical Center, Bellingham Washington; Piedmont Heart Institute, Atlanta Georgia; and Veterans Affairs North Texas Health Care System, Dallas, Texas. The study was approved by the Institutional Review Board of each institution.

Abbreviations and Acronyms

CABG = coronary artery bypass graft

CART = controlled antegrade and retrograde tracking

CTO = chronic total occlusion

PCI = percutaneous coronary intervention

TIMI = Thrombolysis In Myocardial Infarction

Study endpoints and definitions. Coronary CTO were defined as angiographic evidence of a total occlusion with TIMI (Thrombolysis In Myocardial Infarction) flow grade 0 or 1 and estimated duration of at least 3 months. Estimation of occlusion duration was based on the following: first onset of anginal symptoms; prior history of myocardial infarction in the target vessel territory; or comparison with a prior angiogram. Patients were considered to have had retrograde CTO PCI if a guidewire was introduced into a collateral channel that supplied the target CTO vessel distal to the lesion.

Technical success was defined as successful CTO recanalization by any method (either retrograde and/or antegrade), with achievement of <50% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Procedural success was defined as achievement of technical success without in-hospital major adverse cardiac events. In-hospital major adverse cardiac events included any of the following adverse events before hospital discharge: death from any cause; Q-wave myocardial infarction; recurrent angina requiring urgent repeat target vessel revascularization with PCI or coronary bypass surgery; or tamponade requiring pericardiocentesis or surgery.

Statistical analysis. Clinical characteristics, angiographic measures, and in-hospital outcomes were reported using descriptive statistics. Continuous variables are presented as mean ± SD and were compared using the Student *t* test or Wilcoxon rank-sum test. Categorical variables are expressed as percentages and were compared using the chi-square or the Fisher exact test, as appropriate. Logistic regression analysis was performed to identify predictors of technical success. Variables with $p < 0.25$ on univariable analysis (age, sex, years since initiation of retrograde CTO PCI at each center, ejection fraction <40%, and prior PCI) were included in the model as well as diabetes, history of myocardial infarction, and prior coronary artery bypass graft surgery (CABG), variables known to be associated with more advanced coronary artery disease and more challenging PCI. All statistical analyses were performed with JMP (version 9.0, SAS Institute, Cary, North Carolina).

Results

Patient characteristics. During the study period, retrograde CTO PCI was performed in 462 of 1,374 (34%) consecutive patients undergoing CTO PCI among 3 CTO programs in the United States: St. Joseph Medical Center, Bellingham, Washington (n = 270); Piedmont Heart Institute, Atlanta, Georgia (n = 127); Veterans Affairs North Texas Health Care System, Dallas, Texas (n = 65). A single operator (W.L.) performed all retrograde CTO PCI cases at St. Joseph's, 5 operators (D.K., N.L., A.K., H.C., D.K.) at Piedmont Heart Institute, and 2 operators (E.S.B., S.B.) at Veterans Affairs North Texas Health Care System. Table 1 represents the clinical and angiographic characteristics of the study population. Overall, most patients were men with mean age of 65 ± 9.7 years. Notably, one-half of the patients had prior CABG, and nearly one-half of all patients were diabetic (45%), had experienced prior myocardial infarction (48%), or had prior PCI (45%).

The target vessel in most patients was the right coronary artery (66%), followed by nearly equal proportions of the left circumflex and left anterior descending arteries. Prior failed attempted CTO at recanalization had occurred in 18% of the patients.

Procedural characteristics and outcomes. A procedural strategy involving primary retrograde CTO recanalization was employed in 46% of cases with a retrograde method used after failed initial antegrade crossing in the remaining (Table 1). The retrograde vessel was most commonly a septal collateral channel, followed by epicardial vessels, and, least commonly, bypass grafts (Table 1). Success in collateral wire crossing was 81% for septal collaterals, 78% for epicardial collaterals, and 75% for bypass grafts. Subintimal dissection techniques (controlled antegrade and retrograde

Table 1. Baseline Characteristics of the Study Patients, Classified According to Whether Technical Success Was Achieved

Variable	Overall (n = 462)	Technical Success (n = 376)	Technical Failure (n = 86)	p Value
Clinical characteristics				
Age, yrs	65 ± 9.7	65 ± 9.9	68 ± 8.8	0.138
Men	84.2	83	89.5	0.086
Hypertension	92	92	92	0.769
Hyperlipidemia	97.6	97.9	95.8	0.304
Diabetes	45	45.5	42.5	0.449
Heart failure	22.8	21.5	29.9	0.129
Ejection fraction <40%	18	16.3	26.9	0.006
History of MI	47.7	48.7	44.1	0.287
History of CABG	50	48.3	55.3	0.493
History of stroke	7.2	7	7.6	0.615
Prior PCI	45	45.9	40	0.66
Treatment center				0.001
Piedmont Heart Institute	27.5 (127)	25.0 (94)	38.4 (33)	
St. Joseph Medical Center	58.4 (270)	62.7 (236)	39.5 (34)	
Dallas Veterans Affairs Medical Center	14.1 (65)	12.2 (46)	22.1 (19)	
Angiographic characteristics				
CTO target vessel				
RCA	66	66.2	62.8	0.27
LCX	18	18.1	17.4	
LAD	15.5	15.2	17.4	
LM/graft*	0.5	0.3	2.3	
Prior failed attempt for CTO PCI	18	19	13	0.107
Retrograde crossing technique				NA
Retrograde wire cross or kissing wire or antegrade wire cross	41.3	42.7		
CART	11.5	11.5		
Reverse CART	47.2	46		
Indications for retrograde approach				0.304
Complex lesion morphology (primary retrograde)	46	47	39.4	
Failed antegrade approach	54	53	60.6	
Collateral used				0.108
Septal	68	69	66	
Epicardial	24	24	25	
Bypass graft	8	7	9	
Technical success	81.4	100		NA
Procedural success	79.4	97.6		NA
Intravascular ultrasound use	10	10		NA
Total stent length, mm*		72 ± 35	NA	NA
Number of stents implanted*	NA	3.1 ± 1.2	NA	NA
Drug-eluting stents	NA	96	NA	NA
Bare-metal stents	NA	4	NA	NA
Balloon angioplasty only	NA	4.6	NA	NA
Total procedure time, min*	150 ± 65	147 ± 67	161 ± 57	0.139
Total fluoroscopy time, min*	61 ± 40	58 ± 40	72 ± 36	0.003
Total contrast volume, ml, median (IQR)	300 (220, 430)	300 (200, 424)	375 (270, 520)	0.003

Values are mean ± SD, %, or % (n). *mean ± standard deviation.

CABG = coronary artery bypass graft; CART = controlled antegrade and retrograde tracking; CTO = chronic total occlusion; IQR = interquartile range; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main; MI = myocardial infarction; NA = not applicable; PCI = percutaneous coronary intervention; RCA = right coronary artery.

tracking [CART] and reverse CART) were used in 53% of successful cases, whereas in the remaining cases, retrograde wire crossing, kissing wire, or antegrade wire crossing was performed (3,11–13).

The overall technical and procedural success rates were 81.4% (n = 376) and 79.4% (n = 367), respectively (Table 1). The technical success rate for primary retrograde approach was 83.4% versus 79.7% for retrograde attempts after antegrade crossing failure (p = 0.34). Compared with successful lesion treatment, technical failure was associated with reduced left ventricular function (Table 1). Contrast volume and fluoroscopy time were significantly higher among technical failure cases (Table 1). The air kerma radiation exposure was available in 270 patients and was 6.0 ± 2.9 Gy in technical success versus 7.2 ±3.1 Gy in technical failure cases (p = 0.036). Among 2 of the 3 centers, a temporal relationship in success was observed (Table 2, Fig. 1). On multivariable analysis, years since initiation of retrograde CTO PCI at each center, female sex, and ejection fraction ≥40% were the only variables that were independently associated with technical success (Table 3).

Table 4 details procedural-related complications. A major adverse event occurred in 12 patients (2.6%), including 1 death and 6 instances of cardiac perforation requiring either pericardiocentesis or emergency surgery.

Discussion

The major findings of our study is that retrograde CTO PCI can be performed in selected contemporary U.S. centers with high success and low complication rates. Moreover, retrograde CTO PCI was frequently performed in patients with prior bypass surgery and increasing experience with retrograde CTO PCI was associated with incremental procedural success rates.

Technical success in the present study is comparable to the rates from established CTO centers that range from approximately 80% to nearly 100% and is more similar to outcomes demonstrated in larger studies (Table 5). Given that the retrograde approach was often performed in instances of failed prior antegrade attempt or cases in which CTO anatomy was unfavorable for antegrade recanalization, the incremental contribution to overall CTO program success is a clinically meaningful improvement. However, unlike previous studies that describe the relative proportion of retrograde procedures (26% in Japan (11) and 12% in Europe (12)), the frequency of retrograde PCI in the present study (34%) is higher, in part reflecting a high frequency of failed antegrade crossing, but also suggesting more common use of this approach as a primary method (12).

Another distinction from previous studies performed outside the United States is the considerably higher representation of patients with prior coronary bypass surgery, an observation that previously has been associated with a higher likelihood of procedural failure (11). In particular, the observed incidence of previous CABG was approximately 2- to 5-fold higher in the U.S. centers compared with reports from Asia and Europe (14) (Table 5). Although not identified as a predictor of procedural failure in multivariable analysis in the present study, prior surgical

Table 2. Frequency and Technical Success of Retrograde CTO Interventions, Classified According by Center and Calendar Year During Which the Procedures Were Performed

Center	Year	Total CTO PCI, n	Retrograde PCI, n	Retrograde CTO PCI, %	Technical Success Rate for Retrograde CTO PCI, % (n/N)
St. Joseph Hospital	2006	100	9	9	44.4 (5/9)
	2007	127	26	20	85 (22/26)
	2008	108	40	37	77.5 (31/40)
	2009	129	67	52	82 (55/67)
	2010	138	67	49	98.5 (66/67)
	2011	125	61	49	93.5 (57/61)
	2006–2011	728	270	37	87.4 (236/270)
Piedmont Heart Institute	2010	154	61	40	73.7 (45/61)
	2011	207	66	32	74.4 (49/66)
	2010–2011	367	127	35	74 (94/127)
Veterans Affairs North Texas Healthcare System	2008	39	6	15	17 (1/6)
	2009	70	11	16	100 (11/11)
	2010	95	28	29	61 (17/28)
	2011	75	20	27	85 (17/20)
	2008–2011	279	65	23	71 (46/65)
Total	2006–2011	1,374	462	34	81.4 (376/470)

Abbreviations as in Table 1.

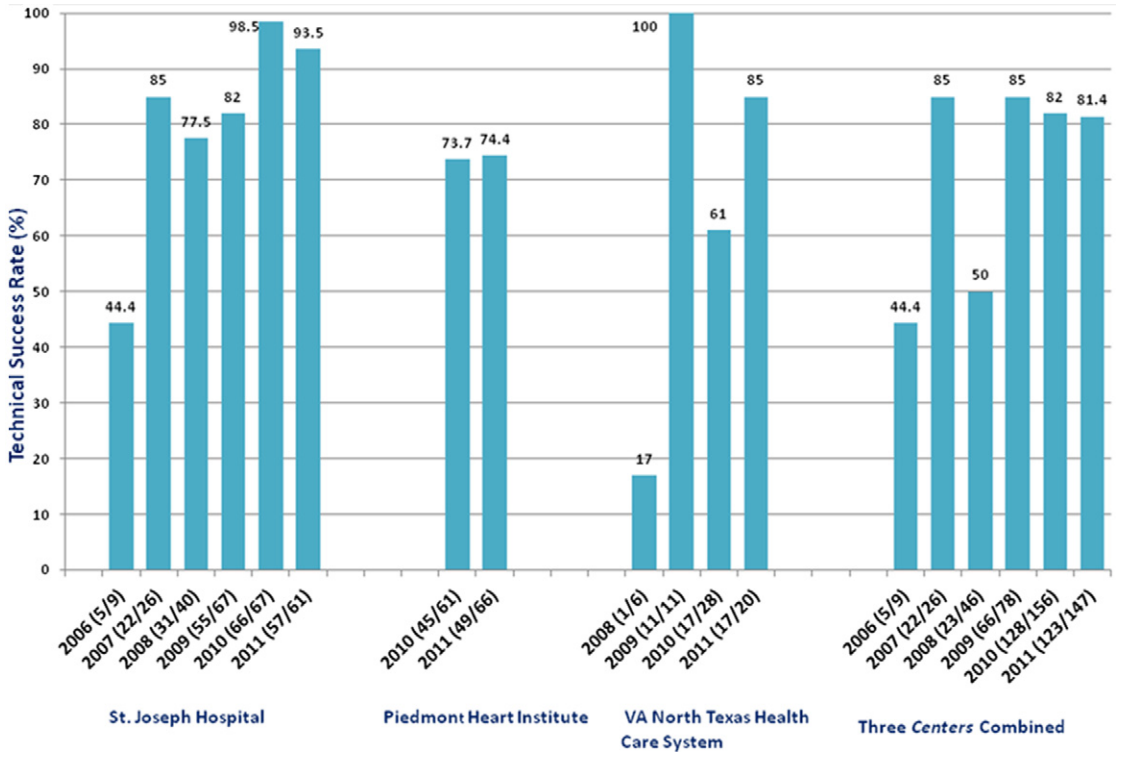

Figure 1. Temporal Trends in Technical Success of Retrograde Chronic Total Occlusion Interventions Among the 3 Study Centers. The Technical Success Rate is Presented For Each Year For Each Participating Center and For All 3 Centers Combined

Temporal trends in technical success of retrograde chronic total occlusion interventions among the 3 study centers.

revascularization may confer greater lesion complexity due to anatomical distortion of the native anatomy and acceleration of native coronary artery atherosclerosis (15). The observation also underscores an important role of CTO PCI among patients with prior CABG who require repeat coronary revascularization, commonly due to saphenous vein graft failure. Repeat surgical coronary revascularization can sometimes carry prohibitive risk (14) or is oftentimes unsuitable given occlusion of a vein graft to the CTO target vessel with preserved patency of the internal mammary graft. In some instances, native coronary CTO PCI may be preferred in the setting of patent but degenerative saphenous vein bypass grafts (16). Considering the risk of periprocedural complications and eventual vein graft failure, native coronary PCI may be associated with more favorable outcome than bypass graft PCI (15).

Table 3. Multivariable Logistic Regression Analysis of Variables Associated With Technical Success

Variable	OR	95% CI	p Value
Age, per 10-yr increase	0.73	0.52–1.01	0.061
Years since retrograde PCI started, per 1-yr increase	1.63	1.32–2.04	**<0.001**
Men	0.34	0.01–0.92	**0.034**
Diabetes	1.06	0.59–1.89	0.855
Ejection fraction <40%, %	0.43	0.21–0.87	**0.019**
History of MI, %	1.10	0.62–1.97	0.738
History of CABG, %	0.99	0.54–1.79	0.976
Prior PCI, %	1.28	0.70–2.38	0.414

Bold values signify statistical significance.
CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

There is currently controversy on whether "true to true" lumen crossing should be used in all cases, with subintimal dissection re-entry techniques only used as a last resort (11,16). In the present series, wire crossing was achieved using the CART or reverse CART technique in approximately one-half of the patients (Table 1).

In the present study, procedures were performed in 3 very different hospital settings, including a rural hospital, a metropolitan hospital, and a Veterans Affairs hospital, suggesting that high success rates can be achieved across varied institutional, administrative, and geographic backgrounds. Importantly, as a measure of quality assurance, all participating institutions adopted careful CTO PCI performance guidelines, including careful attention to contrast and fluoroscopy use, patient selection, and post-procedural

Table 4. Procedural Complications and In-Hospital Adverse Events

Complication	n (%)	Description
Any major procedural complication	12 (2.6)	
Death	1 (0.2)	Due to intracranial bleeding
Q-wave MI	2 (0.4)	Treated conservatively
Donor vessel dissection	2 (0.4)	1 required emergent CABG, and 1 was treated by stenting
Equipment entrapment	1 (0.2)	Required coil occlusion of a fistula between a septal branch and the right ventricle that was created during retrieval
Coronary artery perforations	6 (1.3)	4 required pericardiocentesis and 2 emergent surgery
Emergency cardiac surgery (included in the categories above)	3 (0.6)	Due to perforation in 2 cases and due to donor vessel dissection in 1 case, as described above

Abbreviations as in Table 1.

follow-up (16,17). Consistent with prior description of CTO PCI (9), temporal assessment of procedural outcomes suggests a learning curve to retrograde PCI that depends on case volume (Tables 2 and 3, Fig. 1). In particular, improved technical success parallels annual experience and cumulative procedural volume.

Despite a larger sample size and inclusion of early experience, the procedural complication and in-hospital adverse event rate of 2.6% is also consistent with published series (Table 5). Although the perceived risk of complications is a common deterrent to attempted CTO revascularization, the overall complication rates appear to be similar for CTO versus non-CTO PCI (18). Nevertheless, there are complications unique to retrograde CTO PCI, such as injury of the donor vessel, which can be a life-threatening complication (12). Global ischemia may also occur, related to simultaneous interruption of collateral supply to the target vessel and impairment of blood flow or injury in the donor vessel. Donor vessel dissection occurred in 2 patients in our series (0.5%) and was treated conservatively in 1 patient, but required urgent CABG in the other patient. Another retrograde CTO-specific complication is perforation of the collateral vessel that may result in septal hematoma and tamponade (19). Overall, perforation requiring pericardiocentesis or surgery occurred in 6 cases (1.3%), all of whom survived to hospital discharge. Another complication unique to retrograde CTO PCI is equipment entrapment within a collateral vessel (20,21). This event occurred in 1 patient (0.2%) causing a coronary-ventricular fistula that was successfully treated with coil embolization.

Study limitations. As with other retrograde CTO reports, this analysis is limited by the retrospective and observational design, in which unmeasured variables and potential for treatment bias may influence the results. Angiographic core laboratory quantitative coronary analyses were not performed. Heterogeneity with regard to procedural outcome and institution could indicate variability among individual operators and case selection. Procedures were performed over a period amid changes in operator experience and techniques and in different institutions; however, these findings also imply the generalizability of the study findings. The 3 centers included in the present study have demonstrated commitment to performing CTO PCI and have gone through intensive and continuous training of the operators and the cardiac catheterization laboratory personnel, and in each center, a single operator is involved in all or in most CTO PCI cases. Finally, post-procedural biomarkers were not systematically ascertained, and angiographic-dependent and clinical outcomes were not independently adjudicated.

Conclusions

In summary, our series shows that among selected U.S. programs, retrograde CTO PCI is often performed in patients with prior coronary bypass graft surgery and is

Table 5. Summary of Published Retrograde CTO PCI Series, Including >90 Patients

Study	Year	N	Prior CABG, %	Septal Collaterals Used, %	Reverse CART, %	Technical Success, %	Major Complications, %	Fluoroscopy Time, min, mean ± SD	Contrast Use, ml, mean ± SD
Sianos et al. (8)	2008	175	10.9	79.4	NR	83.4	4.6	59 ± 29	421 ± 167
Rathore et al. (4)	2009	157	17.8	67.5	NR	84.7	4.5	NR	NR
Kimura et al. (5)	2009	224	17.6	79	14	92.4	1.8	73 ± 42	457 ± 199
Tsuchikane et al. (6)	2010	93	10.8	82.8	60.9	98.9	0	60 ± 26	256 ± 169
Morino et al. (21)*	2010	136	9.6	63.9	NR	79.2	NR*	NR*	NR*
Present study	2012	462	50.0	71	41	81.4	2.6	61 ± 40	345 ± 177

*Multicenter CTO registry in Japan: 136 of 529 procedures (25.7%) were retrograde.
NR = not reported; other abbreviations as in Table 1.

associated with favorably high success and low complication rates.

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Key Words: chronic total occlusion ■ outcomes ■ percutaneous coronary intervention ■ retrograde technique.