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Coronary Artery Spatial Distribution of Chronic Total Occlusions: Insights from a Large US Registry

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Abstract

Objective—To assess the spatial distribution of chronic total occlusions (CTOs) within the coronary arteries and describe procedural strategies and outcomes during CTO percutaneous coronary intervention (PCI).

Background—Acute occlusions due to plaque rupture tend to cluster within the proximal third of the coronary artery.

Methods—We examined the clinical and procedural characteristics of 1,348 patients according to lesion location within the coronary tree.

Results—A total of 1,369 lesions in 1,348 patients (mean age 66 ±10 years, 85% male) were included. CTO PCI of proximal segments (n=633, 46%) was more common than of mid (n=557, 41%) and distal segments (n=179, 13%). Patients undergoing CTO PCI of proximal segments were more likely to be smokers (p<0.01), have prior coronary artery bypass graft surgery (p=0.03)

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Compliance with Ethical Standards

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Dr. Garcia is a recipient of a career development award (1IK2CX000699-01) from the VA Office of Research and Development. Dr. Garcia is a consultant for Surmodics. Dr. Brilakis has received consulting and speaking honoraria from Abbott Vascular, Asahi, Boston Scientific,Elsevier, Somahlution, St. Jude Medical, and Terumo; and has received research support from InfraRedx and Boston Scientific; and his spouse is an employee of Medtronic. All other authors have nothing to disclose related to this manuscript.

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and lower ejection fraction (p=0.04). CTOs occurring in proximal segments had longer length (p <0.01), proximal cap ambiguity (p<0.01), and moderate/severe calcification (p<0.01) compared to mid or distally located CTOs. Interventional collaterals were more often present in CTO PCI of proximal segments (64%, 53%, 56%, p<0.01) consistent with the higher use of retrograde approach (47%, 33%, 37%, p<0.01) relative to antegrade wire escalation (67%, 82%, 82%, p<0.01). Procedural complexity was higher in CTO PCI of proximal segments (vs. mid and distal): contrast volume= 275 ml (200-375), 260 ml (200-350), 250 ml (175-350), p=0.01; fluoroscopy time 53 minutes (32-83), 39 minutes (24-65), 40 minutes (22-72), p<0.01. However, procedural success (87%, 90%, 85%, p=0.1), technical success (89%, 91%, 88%, p=0.24), and complications rates (2.8%, 2.5%, 2.2%, p=0.88) were not different.

Conclusions—The most common target vessel location for CTO PCI is the proximal coronary segment. PCI of proximal occlusions is associated with adverse clinical and angiographic characteristics and often requires use of the retrograde approach, but can be accomplished with high procedural and technical success and low complication rates.

Keywords

chronic total occlusion; percutaneous coronary intervention; coronary artery disease

Introduction

Plaque rupture of coronary atherosclerotic lesions is widely accepted to be the most common mechanism underlying acute myocardial infarction (AMI) (1-2). Most plaque ruptures occur in predictable sites within the coronary tree usually referred to as vulnerable plaques or “hot spots” (3-4). A clustering of coronary thrombosis in the proximal third of the coronary artery has been well documented in angiographic as well as pathological studies of patients with acute ST-segment elevation acute myocardial infarction (STEMI) (5-6).

In contrast, little data exists regarding the spatial distribution of chronic total occlusions (CTOs) referred for percutaneous coronary intervention (PCI) within the coronary tree. Proximally located occlusions are associated with higher myocardium at risk and lower ejection fraction and survival after AMI (7,8). Revascularization of proximal CTOs has the potential to mitigate larger areas of myocardial ischemia and improve clinical outcomes. However, these procedures can be technically challenging given adverse angiographic characteristics such as proximal cap ambiguity, blunt stump or side-branch at the site of occlusion.

The objectives of this investigation were: 1) to assess the spatial distribution within the coronary tree of CTOs in patients referred for CTO PCI and 2) to examine clinical, angiographic and procedural characteristics of CTO PCI of proximal segments relative to mid and distal locations.

Methods

We examined the baseline clinical, angiographic characteristics, and clinical outcomes of 1,369 consecutive CTO PCIs performed in 1,348 patients between 2012 and 2015 at 12 US centers: Appleton Cardiology, Appleton Wisconsin; Columbia University, New York, New York; Henry Ford Hospital, Detroit, Michigan; Massachusetts General Hospital, Boston, Massachusetts; Medical Center of the Rockies, Loveland, Colorado; Piedmont Heart Institute, Atlanta Georgia; St. Joseph Medical Center, Bellingham Washington; St. Luke's Health System's Mid-America Heart Institute, Kansas City, Missouri; Torrance Memorial Center, Torrance, California; VA Minneapolis Healthcare System, Minneapolis, Minnesota; VA North Texas Health Care System, Dallas, Texas, and VA San Diego Healthcare System, San Diego, California. Enrollment was performed during only part of the study period in some centers due to participation in other studies. Data collection was performed prospectively and retrospectively and was recorded in a dedicated online CTO database (PROGRESS CTO: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, Clinicaltrials.gov Identifier: NCT02061436) (9-12). The study was approved by the institutional review board at each site.

Coronary CTOs were defined as coronary lesions with Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow of at least 3-month duration. Estimation of the occlusion duration was based on first onset of anginal symptoms, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving ≤50% of the reference lesion diameter) and severe (involving >50% of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends >70 degrees or 1 bend >90 degrees and severe tortuosity as 2 bends >90 degrees or 1 bend >120 degrees in the CTO vessel. The Japanese Chronic Total Occlusion (*J-CTO*) score was calculated as described by Morino et al. (13). Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Occlusion length was visually estimated by the interventional cardiologist performing the procedure. Procedural success was defined as achievement of technical success with no in-hospital major adverse cardiac events (MACE). In-hospital MACE included any of the following adverse events prior to hospital discharge: death, Q-wave and all types of myocardial infarction, urgent repeat target vessel revascularization with either PCI or coronary artery bypass graft surgery (CABG), tamponade requiring either pericardiocentesis or surgery, and stroke.

Patients were classified in three groups based on the location of the CTO within the coronary tree. **Proximal** lesions were defined as those affecting the proximal segment of either the left anterior descending artery (LAD), right coronary artery (RCA), ramus intermedius (RI), left circumflex (LCX) or left main coronary artery (LMCA). **Mid** coronary lesions included the mid LAD, first diagonal (D1), mid CX, first obtuse marginal (OM) and mid RCA. **Distal** coronary lesions included the apical LAD, D2, distal CX, OM2, OM3, distal RCA, right or left PDA, and posterolateral branches (PLs). Lesion location was defined by the inteventionalist performing the CTO-PCI procedure. All procedures were performed in established CTO programs by operators that perform > 30 CTO PCIs per year. Continuous variables were presented as mean ± standard deviation or median (interquartile range) and were compared using the t-test, or Wilcoxon rank-sum test, as appropriate. Categorical data are reported as frequencies or percentages and compared using the chi square test. All statistical analyses were performed with JMP 11.0 (SAS Institute, Cary, North Carolina). Two-sided p-values of 0.05 were considered statistically significant.

Results

A total of 1,369 CTO lesions from 1,348 patients were included in the analysis. The mean age (±SD) of the population was 66 (10) years and 85% were male. Proximal lesions (n=633, 46%) were more common than mid (n=557, 41%) and distal (n=179, 13%) lesions undergoing CTO PCI. Patients with proximal CTO lesions had a higher prevalence of adverse characteristics, relative to mid and distal lesions, including smoking (proximal: 31%, mid: 22%, distal:23%, p=0.005), prior coronary artery bypass graft (CABG) surgery (proximal: 40%, mid: 28%, distal: 20%, p=0.03), heart failure (proximal: 30%, mid: 26%, distal: 20%, p=0.035) and lower ejection fraction (EF) (proximal: 49 ±14%, 51±14, 53 ±12, p=0.046) (**Table 1**).

Angiographic characteristics

A summary of angiographic characteristics is presented in **Table 2**. Proximal lesions were longer (43±28 mm) and had a larger vessel diameter (2.9±0.6 mm) relative to mid (CTO length: 28±18, vessel diameter: 2.8±0.5mm) and distal lesions (CTO length:26 ±16 mm, vessel diameter: 2.6±0.5 mm, both p <0.001). Proximal lesions also had more adverse angiographic features including proximal cap ambiguity, side branch at proximal cap, blunt or no stump, moderate or severe calcification and poor distal target vessel but had more interventional collaterals (**Figure 1 and Table 2)**. The J-CTO score was higher in proximal lesions 2.7 (±1.2) relative to mid 2.4 (±1.2) and distal 2.5 (±1.2) lesions (p<0.01).

Procedural strategies

Multiple crossing strategies were used in the overall cohort: antegrade wire escalation (75%), antegrade dissection re-entry (34%) and retrograde (40%). The use of retrograde approach was higher in proximal lesions (47%) relative to mid (33%) and distal (37%) lesions (p<0.001). Moreover, the retrograde approach was the first crossing strategy in 23% of patients with proximal lesions versus only 14% and 19% of patients with mid and distal lesions, respectively. Likewise, the retrograde approach was the successful crossing strategy in 34% of patients with proximal lesions versus 21% and 26% of patients with mid and distal lesions, respectively (**Figure 2**). CTO PCI of proximal lesions were more complex procedures requiring: a) higher contrast volume (275 ml, ±200-375) relative to procedures in the mid (260 ml,±200-350), and distal locations (250 ml,±175-350) (p=0.01), b) longer fluoroscopy time (proximal: 53 (32-83) minutes, mid:39 (24,65), and distal: 40 (22,72) (p<0.01) c) higher radiation exposure in air kerma dose (Gy) proximal: 4.0 (2.3-5.9), mid 3.2 (1.9-4.8), distal 3.4 (1.8-5.4) (p<0.01) and d) higher utilization of intraprocedural advanced imaging techniques (intravascular ultrasound use: proximal: 43%, mid: 36%, and distal: 28%, p=0.01).

Procedural success and adverse events

Overall, procedural success was 88%. Despite higher angiographic and procedural complexity, the procedural success rate for proximal CTO-PCI was high (87%) and no different than mid (90%) or distal (85%) coronary lesions (p=0.14). Likewise, the incidence of serious major adverse events was low in the overall cohort (2.6%) with no inter-group differences according to lesion location (**Figure 3)**.

Discussion

The main findings of this investigation are as follows. First, the most common target lesion location of CTO PCI within the coronary tree is the proximal third. Second, proximal lesions are associated with a higher burden of comorbidities, most notably heart failure and decreased ejection fraction. Third, proximal CTOs are associated with higher angiographic complexity, as quantified by the J-CTO score, resulting in longer and more complex procedures. Fourth, the retrograde approach was used in almost 50% of cases involving proximal CTO lesions and was the successful strategy in a third of these cases. Finally, despite increased procedural complexity associated with CTO-PCI of proximal lesions, procedural success and complications rates were similar to those of CTO-PCI of mid and distal locations.

Lesion Location and Prognosis

Most data from observational studies and randomized clinical trials suggests a relationship between myocardial ischemia and subsequent risk of death and myocardial infarction in patients with coronary artery disease (14,15). Coronary lesions located in the proximal third of the coronary artery are considered prognosticaly more important than lesions located in a more distal location due to the larger extent of myocardium at risk. This is reflected in the increased weight given to a more proximal lesion location in several angiographic scoring tools such as the Jeopardy or SYNTAX risk score (16,17). For example, the Jeopardy score (maximum number of possible points of 12) will assign 6 points to a 75% stenosis in the proximal LAD and only 2 to the same stenosis if located in the mid or distal portion of the same vessel. This has important prognostic implications; the 5-year survival of patients with single vessel disease and Jeopardy score of 2 is 97%. In contrast, the 5-year survival of patients with single vessel disease and Jeopardy score of 6 is significantly lower at 84% (16). Our analysis from the PROGRESS CTO registry show that most frequently CTO PCIs are performed to revascularize occlusions located within the proximal segment of the coronary tree, which are the ones that have the greatest potential to reduce ischemic burden, improve symptoms and clinical outcomes.

Lesion Location and Procedural Strategy

CTOs located in the proximal segment of the coronary tree had more complex angiographic features relative to distal lesions such as longer lesion length (15 mm longer on average), moderate or severe calcification, proximal cap ambiguity and a blunt stump (18). Conversely, the presence of interventional collaterals and adequate distal targets were commonly encountered in proximal stenosis all of which should be considered during pre-procedural planning. Absence of interventional collaterals is a predictor of technical failure in a recent study (19). Antegrade wire escalation and dissection re-entry have a limited role in CTO PCI of proximal coronary segments, particularly in ostial RCA occlusions where guide support and visualization can be challenging. Therefore, the presence, caliber and trajectory of interventional collaterals should be particularly considered prior to embarking in CTO PCI of proximal coronary segments. In this sub-study of PROGRESS, the retrograde approach was used in nearly half of cases involving a proximal segment and was the successful crossing strategy in one third. Experience with equipment and techniques used for retrograde CTO recanalization is essential. Despite all the procedural challenges associated with CTO PCI of proximal coronary segments, procedural success rates were high (90%) and comparable to CTO PCI in more distal locations. Procedural complications were low (2.8%) and in line with other CTO PCI procedures, highlighting the importance of adequate case selection and operator experience.

Limitations—This study has limitations. First, PROGRESS CTO is an observational registry without adjudication of clinical events by an independent committee. Second, detailed angiographic analysis was not performed by an independent core laboratory and therefore assessment of angiographic characteristics was susceptible to operator-related bias. Third, long-term follow-up of the CTO patients was not available. Finally, all procedures were performed by seasoned operators with significant CTO PCI training and extrapolation of the study results to centers with lower CTO PCI volumes should be made with caution.

Conclusions—CTO PCIs most commonly involve the proximal coronary segment and are associated with adverse clinical and angiographic characteristics. The retrograde approach is used in almost 50% of proximal CTO cases and yields high procedural and technical success rates and low complication rates.

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Study data were collected and managed using REDCap electronic data capture tools hosted at University of Texas Southwestern Medical Center.1 REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

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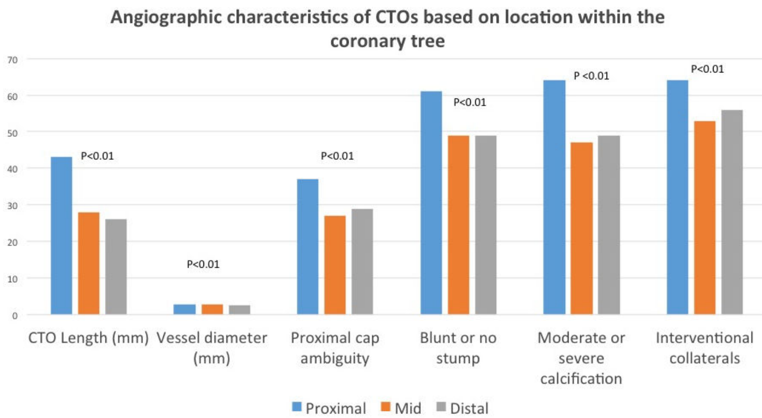

Figure 1.
Angiographic characteristics of CTOs based on location within the coronary tree. Proximal lesions had more adverse angiographic features including proximal cap ambiguity, side branch at proximal cap, blunt or no stump, moderate or severe calcification and poor distal target vessel but had more interventional collaterals

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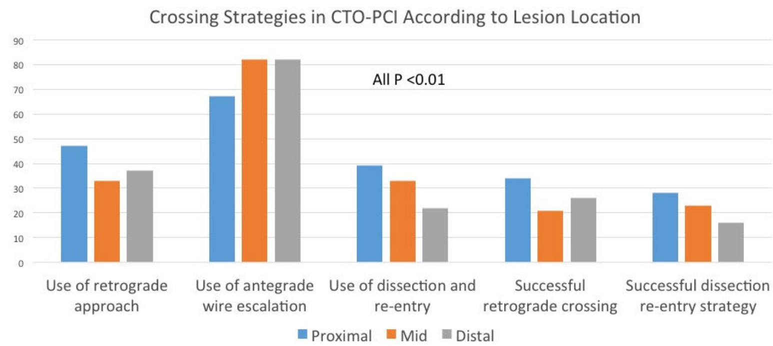

Figure 2.

Crossing Strategies in CTO-PCI According to Lesion Location. The use of retrograde approach was higher in proximal lesions relative to mid and distal lesions

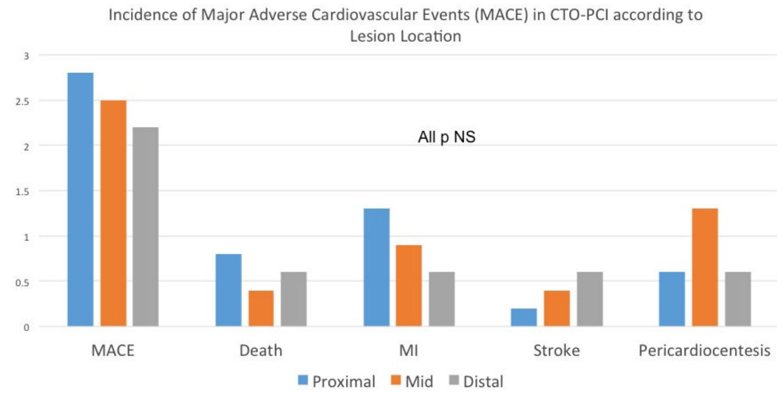

Figure 3.

Incidence of Major Adverse Cardiovascular Events (MACE) in CTO-PCI according to Lesion Location. The incidence of serious major adverse events was low in the overall cohort with no inter-group differences according to lesion location.

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Table 1

Baseline characteristics of the study cohort according to CTO location within the coronary tree

	Overall (lesions)	Proximal	Mid	Distal	p
N (%)	1369	633 (46%)	557 (41%)	179 (13%)	
Age (years)*	66±10	66±10	66±10	64±11	0.030
Male (%)	85	84	86	86	0.451
Diabetes melitus (%)	45	45	45	49	0.670
Dyslipidemia (%)	94	94	95	94	0.912
Hypertension (%)	89	91	86	89	0.019
Prior MI (%)	44	44	43	48	0.537
Smoking (%)	26	31	22	23	0.005
Prior PCI (%)	63	62	61	69	0.177
Prior failed CTOPCI (%)	18	17	19	17	0.673
Prior CABG (%)	35	40	28	37	<0.001
Heart failure (%)	27	30	26	20	0.035
History of stroke (%)	11	11	11	12	0.873
Peripheral arterial disease	16	16	16	17	0.908
Ejection fraction (%)	50±14	49±14	51±14	53±12	0.046

Table 2

Angiographic characteristics of the CTO according to lesion location

	Overall	Proximal	Mid	Distal	p
CTO length (mm)	34±24	43±28	28±18	26±16	<0.001
Vessel diameter (mm)	2.8±0.5	2.9±0.6	2.8±0.5	2.6±0.5	<0.001
Target vessel					<0.001
LAD (%)	23	19	33	9	
LCX (%)	21	20	20	28	
RCA (%)	56	61	47	63	
Proximal cap ambiguity (%)	31	37	27	29	0.008
Side branch at proximal cap (%)	48	46	50	48	0.456
Blunt/No stump (%)	54	61	49	49	<0.001
Distal cap at bifurcation (%)	32	35	29	34	0.173
Poor distal target vessel (%)	38	37	35	47	0.021
Interventional collaterals (%)	58	64	53	56	0.005
Moderate/severe calcification (%)	55	64	47	49	<0.001
Moderate/severe tortuosity (%)	35	36	32	42	0.069
In-stent restenosis (%)	13	13	13	19	0.059
J-CTO score (%)	2.6±1.2	2.7±1.2	2.4±1.2	2.5±1.2	0.002

CTO: chronic total occlusion, LAD: left anterior descending, LCX: left circumflex, RCA: right coronary artery

Table 3

Procedural Characteristic of CTO PCO according to lesion location

	Overall	Proximal	Mid	Distal	P
Contrast volume (ml)	260 (200, 360)	275 (200, 375)	260 (200, 350)	250 (175, 350)	0.01
Fluorosccopy time (min)	45 (27, 74)	53 (32, 83)	39 (24, 65)	40 (22, 72)	<0.001
Air kerma dose (Gy)	3.5 (2.1, 5.5)	4.0 (2.3, 5.9)	3.2 (1.9, 4.8)	3.4 (1.8, 5.4)	<0.001
Procedure time (min)	129 (88, 193)	145 (98, 211)	123 (83, 174)	123 (72, 191)	<0.001
VUS used (%)	37	43	36	28	0.01
Procedural success (%)	88	87	90	85	0.14
LVAD used (%)	5	7	4	4	0.10
Stent length (mm)*	66±42	61±48	69±35	74±42	<0.001
Maximal stent diameter (mm)*	3.1±0.5	3.2±0.5	3.0±0.5	3.0±0.6	<0.001

IVUS: intravascular ultrasound, LVAD: left ventricular assist device

*Values are mean +/− standard deviation or median (interquartile range)