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Further validation of the hybrid algorithm for CTO PCI; difficult lesions, same success $^{\bigstar, \bigstar, \bigstar}$

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ABSTRACT

Objectives: To evaluate the success rates and outcome of the hybrid algorithm for chronic total occlusion (CTO) percutaneous coronary intervention (PCI) by a single operator in two different clinical settings. *Methods:* We compared 279 consecutive CTO PCIs performed by a single, high-volume operator using the hybrid algorithm in two different clinical settings. Data were collected through the PROGRESS CTO Registry. We com-

algorithm in two different clinical settings. Data were collected through the PROGRESS CTO Registry. We compared 145 interventions performed in a community program (cohort A) with 134 interventions performed in a referral center (cohort B). *Results:* Patient in cohort B had more complex lesions with higher I-CTO (3.0 vs. 3.41; p < 0.001) and Progress CTO

(1.5 vs.1.8, P = 0.003) scores, more moderate to severe tortuosity (38% vs. 64%; p < 0.001), longer total orclusion length (25 vs. 40 mm; p < 0.001) and higher prevalence of prior failed CTO PCI attempts (15% vs. 35%; p = 0.001). Both technical (95% vs. 91%; p = 0.266) and procedural (94% vs. 88%; p = 0.088) success rates were similar between the two cohorts despite significantly different lesion complexity. Overall major adverse cardiovascular events were higher in cohort B (1.4% vs. 7.8%; p = 0.012) without any significant difference in mortality (0.7% vs. 2.3%, p = 0.351).

Conclusions: In spite of higher lesion complexity in the setting of a quaternary-care referral center, use of the hybrid algorithm for CTO PCI enabled similarly high technical and procedural success rates as compared with those previously achieved by the same operator in a community-based program at the expense of a higher rate of MACE. © 2017 Elsevier Inc. All rights reserved.

1. Introduction

The hybrid algorithm for chronic total occlusion percutaneous coronary intervention (CTO PCI) emphasizes critical review of prior angiograms and the use of a two-guide catheter intervention to allow for seamless transition between multiple antegrade and retrograde approaches [1]. The decision on the best subsequent approach is determined by an analysis of 4 major angiographic parameters; 1) the location of the proximal cap, 2) the lesion length, 3) the quality of the distal vessel, and 4) the suitability of collaterals for retrograde

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http://dx.doi.org/10.1016/j.carrev.2017.02.014 1553-8389/© 2017 Elsevier Inc. All rights reserved. techniques. Thus the hybrid approach serves to demystify the treatment of CTOs by creating a uniform method for CTO PCI planning, allowing for a standardized and reproducible approach for crossing CTOs.

The hybrid algorithm has been adopted by several operators and has resulted in a significant improvement in success rates without a difference in major complications [2,3]. We therefore sought to investigate if use of the hybrid algorithm was reproducible across two distinct practice settings. One operator (KA) moved from a community-based program to an urban quaternary referral center. We hypothesized that despite treating more angiographic complex lesions in a patient population with greater clinical morbidity use of the hybrid algorithm for CTO PCI would allow for similar success rates without differences in major complications.

2. Methods

Using the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention ([PROGRESS CTO Registry, Clinicaltrials.gov ID:NCT02061436] [3–14]) we analyzed 279 consecutive CTO PCIs performed by a single, high-volume operator using the hybrid algorithm. Clinical and angiographic characteristics were compared between 145

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interventions performed in a 147 bed community hospital (cohort A) and 134 interventions performed in an 877 bed quaternary-care referral center (cohort B).

Chronic total occlusions were defined as coronary obstructions with thrombolysis in myocardial infarction (TIMI) flow grade 0 for at least three months duration. Estimation of the occlusion duration was based on the first onset of anginal symptoms, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. Technical success was defined as angiographic evidence of <30% residual stenosis with restoration of TIMI 3 antegrade flow in the CTO target vessel. Procedural success was defined as technical success with no procedural major adverse cardiovascular events (MACE), including death, Q-wave myocardial infarction (troponin or creatine kinase leak was not classified as a major complication as it often occurs transiently post CTO-PCI and resolves spontaneously), recurrent cardiac symptoms requiring repeat target vessel PCI or coronary artery bypass surgery (CABG), cardiac tamponade requiring pericardiocentesis or surgery, and stroke before hospital discharge. Major bleeding was defined as bleeding causing hemoglobin drop >3 g/dl or bleeding requiring transfusion or surgical intervention. Vascular access complications included major bleeding from the access site or other complication requiring surgical intervention.

Continuous data were summarized as mean \pm standard deviation for normally distributed data or median and interquartile range (IQR) for non-normally distributed data, and compared using t-test. Categorical data were presented as frequencies or percentages and compared using chi square or Fisher's exact test, as appropriate. A two-sided pvalue of <0.05 was considered statistically significant.

3. Results

Between December 2011 and December 2015 a total of 279 consecutive CTO-PCIs were performed at two institutions by the same operator. Mean age was 65.7 ± 10.1 years and 79.8% were men. Patients in cohort B had more prior myocardial infarctions (29.9% vs. 49.2%, p = 0.002), and higher creatinine levels (1.0 vs. 1.07, p = 0.045). Left ventricular ejection fraction (LVEF) in cohort B was numerically lower, though the difference did not reach statistical significance (50.6 \pm 12.4 vs. 47.2 \pm 14.5, p = 0.063). Similarly, there was a trend toward increased diabetes mellitus in cohort B (46.4 vs. 58.1%, p = 0.055). Baseline characteristics were otherwise similar in both groups and are summarized in Table 1.

When comparing lesion complexity, cohort B lesions were more complex lesions with higher J-CTO (3.0 ± 1.1 vs. 3.41 ± 1.1 ; p < 0.001) and Progress CTO (1.5 ± 1.0 vs. 1.8 ± 1.0 p = 0.003) scores, more moderate to severe tortuosity (37.8% vs. 63.9%; p < 0.001), longer total occlusion length (25 vs. 40 mm; p < 0.001) and a higher frequency

Table 1

Baseline Patient Characteristics Classified According to CTO Center.



Fig. 1. Right panel: The overall technical success rate in a community based cohort compared with a referral center cohort. Left panel: mean J-CTO score compared between centers.

of prior failed CTO PCI attempts (15% vs. 35%; p < 0.001). Despite the complex lesion characteristics, both technical (94.5% vs. 91.0%; p = 0.266) and procedural (93.6% vs. 87.6%; p = 0.088) success rates were similar in the two study cohorts (Fig. 1). Retrograde crossing (26.3% vs. 49.2%) and antegrade dissection and re-entry (14.6% vs. 23%) (p < 0.0001 for both) were more commonly used in cohort B. Angiographic features of the CTO target vessel are summarized in Table 2.

MACE were higher when treating more difficult lesions in a more morbid cohort (1.4% vs. 7.8%; p = 0.012), but there was no significant difference in mortality (0.69% vs. 2.3%, p = 0.351). Mortality in cohort B included one patient in cardiogenic shock and another with acute coronary syndrome. Table 3 summarizes MACE by center.

4. Discussion

Our study demonstrates that an operator can maintain high success rates when using the hybrid algorithm despite significant differences across practice settings. We compared outcomes between two distinct patient populations, a community-based practice (cohort A) and a referral center (cohort B) in which patients presented with significant morbidity associated with complex angiographic lesions. The similar success rates between multiple operators (demonstrated in prior studies) and between two institutions with the same operator (demonstrated in our study) provide further evidence that the application of the hybrid algorithm allows for procedural reproducibility, thus making it more teachable at the operator and institutional level [4].

A key factor for operators and institutions to achieve high success rates in patients with complex lesion characteristics is to adopt the

Variable	Overall ($N = 270$)	Community program (N = 141)	Referral center ($N = 129$)	p-value
Age (years)	65.7 ± 10.1	66.5 ± 8.9	65.4 ± 10.5	0.521
Male, sex, %	79.8	81.2	78.3	0.56
Diabetes mellitus, %	52.0	46.4	58.1	0.055
Hypertension, %	87.3	87.1	87.6	0.893
Dyslipidemia, %	93.3	92.9	93.8	0.758
Smoking (current or quit within 1 year), %	21.1	26.1	15.5	*0.035
LVEF %	49.1 ± 13.5	50.6 ± 12.4	47.2 ± 14.5	0.063
Heart failure %	27.6	25.0	30.2	0.348
Prior myocardial infarction, %	39.5	29.9	49.2	*0.002
Family history of premature CAD	32.6	27.2	40.1	0.066
Prior CABG, %	41.5	36.9	46.5	0.109
Prior PCI, %	81.9	94.3	68.2	*<0.001
CVD, %	9.7	8.5	10.9	0.501
PAD, %	10.4	8.5	12.4	0.295
Baseline creatinine	1.03 (0.87, 1.30)	1.0 (0.84, 1.23)	1.07 (0.91, 1.40)	0.045

* Statistically significant value (p < 0.05).

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Table 2

Angiographic Features of CTO Target Vessel Classified According to CTO Center.

Variable	Overall	Community program ($N = 145$)	Referral center ($N = 134$)	p-value			
CTO target vessel							
RCA	60.4%	56.9%	64.2%				
LAD	20.1%	24.3%	15.7%	0.235			
LCX	19.1%	18.8%	19.4%				
Prior attempt to open CTO?	24.8	15.3	35.1	*<0.001			
Previously treated lesion/in-stent Restenosis	14.4	8.4	20.9	*0.003			
Successful crossing strategy (shown for lesions with technical success)							
Antegrade wiring	44.4	59.1	27.9				
Retrograde	37.1	26.3	49.2	*<0.001			
Antegrade dissection and re-entry	18.5	14.6	23.0				
J-CTO score (mean \pm SD)	3.2 ± 1.1	3.0 ± 1.1	3.4 ± 1.1	*<0.001			
Progress Score (mean \pm SD)	1.6 ± 1.0	1.5 ± 1.0	1.8 ± 1.0	*0.003			
Calcification (moderate/severe), %	74.9	71.0	79.1	0.12			
Tortuosity (moderate/severe), %	50.4	37.8	63.9	*<0.001			
Proximal cap ambiguity, %	46.6	41.4	52.2	0.069			
Side branch at proximal cap, %	50.5	46.5	54.9	0.164			
Distal cap at bifurcation, %	34.1	31.0	37.3	0.269			
Interventional collaterals	51.6	50.3	53.0	0.655			
Occlusion length, mm	30 (20,50)	25 (16, 30)	40 (25, 60)	< 0.001			
In-stent restenosis, %	12.34	15.81	11.04	0.07			

* Statistically significant value (p < 0.05).

hybrid CTO PCI algorithm while being well versed in both retrograde and antegrade dissection and re-entry techniques. In cohort A over 59% of CTO PCIs were successfully revascularized using only antegrade techniques (59 vs. 27.9%; p < 0.001). However, in cohort B, in which 35% of cases had a previously failed CTO PCI attempt, retrograde and antegrade dissection and re-entry techniques were used in 72% of cases (40.9 vs. 72.2%, p < 0.001). This suggests that the high success rate associated with the hybrid algorithm is at least in part due to the transition between antegrade and retrograde techniques. Longer occlusions may dictate increase use of antegrade dissection and reentry, and an ambiguous proximal cap may dictate increased use of retrograde techniques. The ability of an operator to use multiple CTO PCI techniques as dictated by lesion characteristics is essential in maintaining high success rates despite changes in the lesion complexity. This also indicates that to achieve high success rates CTO PCI operators should be familiar with antegrade dissection and reentry, and the retrograde techniques in addition to antegrade wire skills. Operators and institutions that adopt only parts of the hybrid algorithm may be unable to achieve high success rates and may select to refer patients with high morbidity and angiographic complex lesions to centers where operators are well versed in the techniques required within the hybrid algorithm.

Evaluating the outcomes of CTO PCI by the same operator in two practice settings allows for comparisons not subject to inter-operator variability. For example, use of mechanical circulatory support devices was significantly higher in cohort B. The higher use of mechanical circulatory support devices provides a unique variable to assess how truly "sick" and "high risk" patients in in cohort B were. As opposed to other studies in which many operators have different "thresholds" for the use of hemodynamic support devices, all of the above procedures were performed by a single operator hence eliminating such a bias.

High success rates can be achieved in community-based programs using the hybrid algorithm with an expedited learning curve. Shammas and colleagues reported CTO PCI procedural success rate >90% using the hybrid algorithm by a prior non-CTO operator [15]. As the scope of interventional cardiology changes and becomes even more subspecialized the above study demonstrates the ability of operators who use the hybrid algorithm for CTO PCI to develop successful CTO PCI programs in varying practice settings, including community programs.

Our study does have important limitations. There is a temporal bias, as patients treated in cohort A included the early experience of the operator after his adoption of the hybrid algorithm, while patients in cohort B included patients after the operator's introduction of the hybrid algorithm. Similarly, it is difficult to isolate the effects of the operator's learning curve versus institutional learning curve.

5. Conclusions

In spite of higher lesion complexity in the setting of a quaternarycare referral center, use of the hybrid approach for CTO-PCI enabled

Table 3

Procedural Efficiency and Clinical Outcomes Classified According to CTO Center.

Overall, $N = 270$	Community program, $N = 145$	Referral center, $N = 134$	p value (Fisher's exact test)				
152 (98, 219)	116 (91, 177)	179 (130,246)	*<0.001				
57 (32,94)	38 (26, 78)	76 (45, 105)	*<0.001				
246 (183, 310)	240 (170, 300)	248 (186, 327)	0.14				
15.0	4.4	26.4	*<0.001				
92.8	94.5	91	0.266				
90.7	93.6	87.6	0.088				
4.4	1.4	7.8	*0.012				
1.5	0.7	2.3	0.351				
0.7	0	1.6	0.227				
1.1	0	2.3	0.108				
0.7	0	1.6	0.227				
1.9	1.4	2.3	0.672				
	$\begin{aligned} & \text{Overall, N} = 270 \\ & \text{152 (98, 219)} \\ & \text{57 (32,94)} \\ & \text{246 (183, 310)} \\ & \text{15.0} \\ & \text{92.8} \\ & \text{90.7} \\ & \text{4.4} \\ & \text{1.5} \\ & \text{0.7} \\ & \text{1.1} \\ & \text{0.7} \\ & \text{1.9} \end{aligned}$	Overall, N = 270 Community program, N = 145 152 (98, 219) 116 (91, 177) 57 (32,94) 38 (26, 78) 246 (183, 310) 240 (170, 300) 15.0 4.4 92.8 94.5 90.7 93.6 4.4 1.4 1.5 0.7 0.7 0 1.1 0 0.7 0 1.9 1.4	Overall, N = 270 Community program, N = 145 Referral center, N = 134 152 (98, 219) 116 (91, 177) 179 (130,246) 57 (32,94) 38 (26, 78) 76 (45, 105) 246 (183, 310) 240 (170, 300) 248 (186, 327) 15.0 4.4 26.4 92.8 94.5 91 90.7 93.6 87.6 4.4 1.4 7.8 1.5 0.7 2.3 0.7 0 1.6 1.1 0 2.3 0.7 0 1.6 1.9 1.4 2.3				

MACE according to our definition: 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.

* Indicates statistical significance.

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similarly high technical and procedural success rates as compared with those previously achieved by the same operator in a community-based program. MACE rate was higher in the more complex patient population without a significant difference in mortality.

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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.

References

- Brilakis ES, Grantham J, Rinfret S, Wyman M, Burke N, Karmpaliotis D, et al. A percutaneous treatment algorithm for crossing coronary chronic total occlusions. J Am Coll Cardiol Intv 2012;5(4):367–79.
- [2] Pershad A, Eddin M, Girotra S, Cotugno R, Daniels D, Lombardi W. Validation and incremental value of the hybrid algorithm for CTO PCI. Catheter Cardiovasc Interv 2014;84:654–9.
- [3] Christopoulos G, Menon RV, Karmpaliotis D, Alaswad K, Lombardi W, Grantham A, et al. The efficacy and safety of the "hybrid" approach to coronary chronic total occlusions: insights from a contemporary multicenter US registry and comparison with prior studies. J Invasive Cardiol 2014;26(9):427–32.
- [4] Christopoulos G, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Wyman RM, et al. Application and outcomes of a hybrid approach to chronic total occlusion percutaneous coronary intervention in a contemporary multicenter us registry. Int J Cardiol 2015;198:222–8.
 [5] Alaswad K, Menon RV, Christopoulos G, Lombardi WL, Karmpaliotis D, Grantham JA,
- [5] Alaswad K, Menon RV, Christopoulos G, Lombardi WL, Karmpaliotis D, Grantham JA, et al. Transradial approach for coronary chronic total occlusion interventions: insights from a contemporary multicenter registry. Catheter Cardiovasc Interv 2015;85:1123–9.

- [6] Christopoulos G, Kandzari DE, Yeh RW, Jaffer FA, Karmpaliotis D, Wyman MR, et al. Development and validation of a novel scoring system for predicting technical success of chronic total occlusion percutaneous coronary interventions: the progress CTO (prospective global registry for the study of chronic total occlusion intervention) score. JACC Cardiovasc Interv 2016;9:1–9.
- [7] Christopoulos G, Karmpaliotis D, Alaswad K, Lombardi WL, Grantham JA, Rangan BV, et al. The efficacy of "hybrid" percutaneous coronary intervention in chronic total occlusions caused by in-stent restenosis: insights from a us multicenter registry. Catheter Cardiovasc Interv 2014;84:646–51.
- [8] Christopoulos G, Karmpaliotis D, Wyman MR, Alaswad K, McCabe J, Lombardi WL, et al. Percutaneous intervention of circumflex chronic total occlusions is associated with worse procedural outcomes: insights from a multicentre us registry. Can J Cardiol 2014;30:1588–94.
- [9] Christopoulos G, Menon RV, Karmpaliotis D, Alaswad K, Lombardi W, Grantham JA, et al. Application of the "hybrid approach" to chronic total occlusions in patients with previous coronary artery bypass graft surgery (from a contemporary multicenter us registry). Am J Cardiol 2014;113:1990–4.
- [10] Christopoulos G, Wyman RM, Alaswad K, Karmpaliotis D, Lombardi W, Grantham JA, et al. Clinical utility of the Japan-chronic total occlusion score in coronary chronic total occlusion interventions: results from a multicenter registry. Circ Cardiovasc Interv 2015;8:e002171.
- [11] Sapontis J, Christopoulos G, Grantham JA, Wyman RM, Alaswad K, Karmpaliotis D, et al. Procedural failure of chronic total occlusion percutaneous coronary intervention: insights from a multicenter us registry. Catheter Cardiovasc Interv 2015;85: 1115–22.
- [12] Danek BA, Karatasakis A, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, et al. Use of antegrade dissection re-entry in coronary chronic total occlusion percutaneous coronary intervention in a contemporary multicenter registry. Int J Cardiol 2016;214: 428–37.
- [13] Karacsonyi J, Karatasakis A, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, et al. Effect of previous failure on subsequent procedural outcomes of chronic total occlusion percutaneous coronary intervention (from a contemporary multicenter registry). Am J Cardiol 2016;117(8):1267–71.
- [14] Nguyen-Trong PJ, Rangan BV, Karatasakis A, Danek BA, Christakopoulos GE, Martinez-Parachini JR, et al. Predictors and outcomes of side-branch occlusion in coronary chronic total occlusion interventions. J Invasive Cardiol 2016;17(1):15–8.
- [15] Shammas NW, Shammas GA, Robken J, Harris T, Madison A, Dinklenburg C, et al. The learning curve in treating coronary chronic total occlusion early in the experience of an operator at a tertiary medical center: the role of the hybrid approach. Cardiovasc Revasc Med 2016;17(1):15–8.

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¹ Paul A. Harris, Robert Taylor, Robert Thielke, Jonathon Payne, Nathaniel Gonzalez, Jose G. Conde, Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support, J Biomed Inform. 2009 Apr.; 42(2):377–81.