Chronic total occlusion current techniques and factor related to success and failure

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Abstract

Background: Chronic total occlusions (CTOs) of coronary arteries represent a common and significant challenge to interventional cardiology. Medical therapy is often regarded as an adequate long term strategy in the management of these lesions with surgical intervention for refractory symptoms. Extensive collateralisation is used as a marker of distal coronary perfusion, further reinforcing non-invasive strategies. The aim of the study is to determine the impact of lesion age on procedural techniques and outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

Patients and methods: 66 patients with CTO having significant angina or recent acceleration of previously chronic stable angina admitted to National Heart Institute and Zagazig University Hospitals were included. The patients were divided into 3 groups: group 1 (CTO age of > than 3 to 12 months), group 2 (CTO age of 12 to 24 months) and group 3 (CTO age of >24 months). All patients were subjected to Percutaneous Coronary Intervention (PCI) for coronary chronic total occlusion.

Results: There is statistically non-significant relation between the studied groups regarding length of hospital stay. About 73%, 59% and 59% within groups of CTO from 3 to 12 months, 12 to 24 months and >24 months were discharged in the same day. All patients had successful outcome.

Conclusion: Success of CTO - PCI in the current era of new dedicated CTO equipment is unlikely to be affected by CTO lesion age.

Keywords: Lesion Age, Chronic total occlusions, Percutaneous Coronary Intervention**,**

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Introduction

Coronary artery disease is a leading cause of morbidity and mortality worldwide[1]. CAD is mainly caused by atherosclerosis plaques that progressively enlarge and cause luminal obstructions, many atherosclerotic plays become vulnerable and are precursors of acute coronary syndromes[2].

A Chronic Total Occlusion is defined as an atherosclerotic complete vessel occlusion with Thrombolysis in Myocardial Infarction (TIMI) grade 0 flow within the occluded segment, and

an estimated occlusion duration of ≥ 3 months. CTO are commonly encountered, occurring in approximately 20% of all patients referred for coronary angiography[1].

In patients who are undergoing cardiac catheterization and have a prior diagnosis of CAD, the frequency with which at least one CTO is encountered ranges from 30% to 50%[3].

CTO consists of an atherosclerotic plaque and a thrombotic component that can be homogeneous or made up of several layers of differently organized tissues as a result of multiple thrombotic episodes occurring at different times[4]. There is frequently a compelling indication to open a CTO (which is either for symptomatic and/or prognostic indication) [5].

Advances in guidewires, stents, and devices to cross chronically occluded arteries are evolving, so that more patients with Chronic Total Occlusions (CTOs) are being successfully treated percutaneously[6].

Despite progress in techniques to open CTO's and corresponding imaging modalities, either invasive or non-invasive, there still is a paucity of information regarding effect of CTO age on the success rates of PCI and the short-term outcome of the procedure[7]. This study amid to determine the impact of lesion age on procedural techniques and outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI).

Material and methods

This prospective, cross sectional cohort study enrolled Sixty six consecutive patients admitted to National Heart Institute and Ahmed Maher Teaching Hospitals with CTO having significant angina or recent acceleration of previously chronic stable angina. Institutional review board and medical ethics committee approved the study and written informed consent was taken from all participants. According to the CTO age, our study population was subdivided into 3 groups: group 1 (CTO age of > than 3 to 12 months), group 2 (CTO age of 12 to 24 months) and group 3 (CTO age of >24 months). The study was carried out in accordance to the Helsinki declaration; all patients provided written informed consent.

Inclusion criteria: Patients selection on the basis of the presence of symptoms, viability, and inducible ischemia (>10%) in the CTO artery territory, demonstrated by functional functional imaging tests. In presence of impaired LVEF, CTO re-vascularization was only considered for lesions subtending viable myocardial territory judged to be of hemodynamic importance, by LGE CMR. The decision of the revascularization strategy (PCI or CABG, and lesions to be revascularized) for each patient was left to the local heart team in the participating center. In case of surgical indication rejected by the patient, PCI was proposed if considered to be feasible by the local heart team. **Exclusion criteria included:** Patient proved by initial angiography to be non-candidate for CTO re-canalization. Patient with scarred non viable myocardium proved by viability testing modality (scar was defined as either a bright thinned out echo-reflective area of less than 6 mm thickness, which is akinetic or dyskinetic in the entire territory of CTO or an area

of scar found by other viability studies in the territory of the CTO artery). Pregnancy. Significant valvular disease. Informed consent to participation in the study was not obtained. Uncontrolled HTN. Hemodynamic instability.

All patients were investigated by history taking, clinical examination, 12-lead surface electrocardiogram (ECG) With special concern for ischemic manifestations in the form of Q waves, ST and T changes, routine pre-PCI labs were ordered shortly before procedure to rule out significant renal impairment or bleeding tendency, Echocardiography was done using Philips machines, studies were done shortly before procedure and 3 months after procedure, Angiography, angioplasty and CTO re-canalization. All patients were subjected to Percutaneous Coronary Intervention (PCI) for coronary chronic total occlusion.

Statistical analysis

Data were entered checked and analyzed using Epi-Info version 6 and SPP for Windows version 8 (Dean, 2006). P value of less than 0.1% ($p < 0.001$) was considered to be Highly significant.

Results :

Table (1): Comparison between the studied groups regarding demographic data

Parameter	CTO			Test	
	3- 12 months N=22	12 – 24 months N=22	>24 months N=22	F/χ^2	p
Age (year):					
Mean ± SD	62.09 ± 8.3	63.05 ± 6.5	64.05 ± 6.48	0.413	0.664
Range	47 – 77	53 – 74	53 – 74		
Gender:					
Male	10 (45.5%)	17 (77.3%)	18 (81.8%)	6.603	0.01*
Female	12 (54.5%)	5 (22.7%)	4 (18.2%)		
Risk factors					
Diabetes	20 (90.9%)	10 (50%)	13 (59.1%)	4.935	0.026*
Hypertension	16 (72.7%)	19 (86.4%)	17 (77.3%)	0.134	0.714

Dyslipidemia	13 (59.1%)	13 (59.1%)	14 (63.6%)	0.094	0.759
IHD	15 (68.2%)	20 (90.9%)	17 (77.3%)	0.536	0.464
Family history	12 (54.5%)	9 (40.9%)	9 (40.9%)	0.813	0.367
Smoking:					
No	13 (59.1%)	10 (45.5%)	11 (50%)	MC	0.561
Smoker	8 (36.4%)	12 (54.5%)	11 (50%)		
Ex-smoker	1 (4.5%)	0 (0%)	0 (0%)		

*p<0.05 is statistically significant χ^2Chi square for trend test

F One way ANOVA test MC Monte Carlo test

Table 1; showed that there is statistically **non-significan**t relation between the studied groups regarding age. There is statistically **significant** relation between the studied groups regarding gender. Within the group with CTO from 3 to 12 months, 54.5% were females versus 22.7% and 18.2% within the groups of 12 to 24 and >24 months respectively. There is statistically **non-significan**t relation between the studied groups regarding presence of comorbid hypertension, dyslipidemia, ischemic heart disease, family history of IHD or smoking. There is statistically **significant** relation between the studied groups regarding presence of comorbid diabetes. Within the group with CTO from 3 to 12 months, 90.9% had diabetes versus 50% and 59.1% within the groups of 12 to 24 and >24 months respectively.

Table (2): Comparison between the studied groups regarding J-CTO score

J-CTO score	CTO			Test	
	3- 12 month N=22	12 – 24 months N=22	>24 month N=22	χ^2	p
2	5 (22.7%)	4 (18.2%)	0 (0%)		
3	10 (45.5%)	5 (22.7%)	5 (22.7%)		
4	5 (22.7%)	10 (45.5%)	12 (54.5%)	MC	0.106
5	2 (9.1%)	3 (13.6%)	5 (22.7%)		

p¥	P_1 0.201	P_2 0.079	P_3 0.003*		

¥ chi square for trend test χ^2Chi square test

**p≤0.001 is statistically highly significant *p<0.05 is statistically significant

p1 the difference between group of 3 -12 months and from 12 to 24 months

p2 the difference between group of >24 months and from 12 to 24 months

p3 the difference between group of 3 -12 months and > 24 months

Table 2; showed that there is statistically **non-significant** relation between J-CTO Score and time of CTO. On comparing each two individual groups, the difference is **significant** between 3 to 12 months and >24 months and each other group.

Table (3): Comparison between the studied groups regarding collaterals and rentrop collaterals classification

Parameter	CTO			Test	
	3- 12 months N=22	12 – 24 months N=22	>24 months N=22	χ^2	p
Collaterals					
Epicardial	4 (18.2%)	7 (31.8%)	8 (36.4%)	1.922	0.383
Septal	18 (81.8%)	15 (68.2%)	14 (63.6%)		
Rentrop class					
1	8 (36.4%)	2 (9.1%)	0 (0%)		
2	11 (50%)	8 (36.4%)	5 (22.7%)	MC	<0.001**
3	3 (13.6%)	12 (54.5%)	17(77.3%)		
p¥	P_1 0.003*	P_2 0.069	P_3 <0.001**		

χ^2Chi square test ¥ chi square for trend test χ^2Chi square test

**p≤0.001 is statistically highly significant *p<0.05 is statistically significant

p1 the difference between group of 3 -12 months and from 12 to 24 months

p2 the difference between group of >24 months and from 12 to 24 months

p3 the difference between group of 3 -12 months and > 24 months

Table 3; showed that there is statistically **non-significant** relation between the studied groups regarding collaterals (septal collaterals were in 81.8%, 68.2% and 63.6% of those in groups with CTO 3 to 12 months, 12 to 24 months and >24 months). There is statistically **significant** relation between grades and time of CTO. On comparing each two individual groups, the difference is significant between 12 to 24 months and each other group.

Table (4): Comparison between the studied groups

	CTO			Test	
	3- 12 month N=22	12 – 24 months N=22	>24 month N=22	F	p
Time of PCI					
Mean ± SD	66.68 ± 25.13	88.14 ± 28.98	117.23 ± 56.21	9.171	<0.001**
Range(min)	30 – 140	45 – 150	52 – 243		
Turkey HSD	P_1 0.174	P_2 0.044*	P_3 <0.001**		
Radiation dose					
Mean ± SD	4.273 ±2.513	7.455 ± 3.019	8.405 ± 2.728		
Median	3.2	7.2	8.95	20.08	<0.001**
Range	1.7 – 10.8	2.1 – 12.9	3.2 – 13.1		
Pairwise	P_1 0.003*	P_2 <0.001**	P_3 0.944		
Contrast volume					
Mean ± SD	249.09 ± 87.17	258.18±101.07	284.55 ± 101.5	0.796	0.456
Range (ml)	120 – 410	100 – 450	120 – 490		

length of hospital stay and outcome					
LOS Median Range	 0 0 – 3	 0 0 – 5	 0 0 – 3	2.283	0.319
Same day **1 – 3** **4 – 5**	16 (72.7%) 6 (27.3%) 0 (0%)	13 (59.1%) 7 (31.8%) 2 (9.1%)	13 (59.1%) 9 (40.9%) 0 (0%)	MC	0.364
Outcome: Success	 22 (100%)	 22 (100%)	 22 (100%)	0	>0.999

F One way ANOVA test KW Kruskal Wallis test

χ^2Chi square test MC Monte Carlo test

**p≤0.001 is statistically highly significant

*p<0.05 is statistically significant

p1 the difference between group of 3 -12 months and from 12 to 24 months

p2 the difference between group of 3 -12 months and > 24 months

p3 the difference between group of >24 months and from 12 to 24 months

Table 4; showed that there is statistically **significant** relation between time for PCI and time of CTO. On doing Turkey HSD group, the difference is significant between 3 to 12 months and each other group (as in this group, time of PCI was significantly the lowest time). There is statistically **significant** difference between the studied groups regarding radiation dose. On doing pairwise comparison, the difference is **significant** between 3 to 12 months group and each other group (lowest dose was associated with recent CTO). There is statistically **non-significant** relation between contrast volume and time of CTO. It was non-significantly higher in the group of CTO>24 months. There is statistically **non-significan**t relation between the studied groups regarding length of hospital stay. About 73%, 59% and 59% within groups of CTO from 3 to 12 months, 12 to 24 months and >24 months were discharged in the same day. All patients had successful outcome.

Table (5): Comparison between the studied groups regarding cost by CTO AGE

COST BY CTO AGE	X (within normal PCI cost)	2X	>2X	P
CTO Age >3m to 12m	4	16	2	
CTO Age of 12m to 24m	2	14	6	0.164
CTO Age > 24m	0	12	10	

Table 5; showed that there is statistically **non-significant** relation between cost and age of CTO. It was non-significantly higher in the groups of CTO of 12 months and >24 months.

Table (6): Comparison between the studied groups regarding CTO technique used by CTO AGE

CTO technique used	AWE	ADR	RWE	RDR	P
CTO Age >3m to 12m	16	1	4	1	
CTO Age of 12m to 24m	8	4	6	4	0.161
CTO Age > 24m	5	6	6	5	

AWE: antegrade wire escalation

ADR: antegrade dissection re-entry

RWE: retrograde wire escalation

RDR: retrograde dissection re-entry

Table 6; showed that there is statistically **non-significant** relation between technique used and time of CTO. Regarding RDR and ADR technique, It was non-significantly higher in the groups of CTO of 12 months and >24 months.

Table (7): Comparison between the studied groups regarding complications

	CTO	Test

	3- 12 months	12 – 24 months	>24 month	χ^2	p
	N=22	N=22	N=22		
Immediate:					
No	22 (100%)	19 (86.4%)	16 (72.7%)	6.842	0.009*
Yes	0 (0%)	3 (13.6%)	6 (27.3%)		
6 weeks: no	22 (100%)	22 (100%)	22 (100%)	0	1
12 weeks: no	22 (100%)	22 (100%)	22 (100%)	0	1

*P<0.05 is statistically significant χ^2Chi square for trend test MC Monte Carlo test

Table 7; showed that there is statistically **significan**t relation between the studied groups regarding presence of immediate complications. No patients within 3 to 12 months had been complicated while 18.2% and 27.3% within 12 to 24 months and those >24 months had been complicated. There is statistically **non-significan**t relation between the studied groups regarding complications at 6 and 12 weeks as none of them had been complicated.

Discussion:

In this study, there is statistically non-significant relation between the studied groups regarding age. But, there is statistically significant relation between the studied groups regarding gender. Within the group with CTO from 3 to 12 months, 54.5% were females versus 22.7% and 18.2% within the groups of 12 to 24 and >24 months respectively. **Danek et al.**[5] determined the impact of lesion age on procedural techniques and outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in 394 patients. Mean age of the study patients was 66 ± 10 years, and 86% were men.

Regarding risk factors, there is statistically non-significant relation between the studied groups regarding presence of comorbid hypertension, dyslipidemia, ischemic heart disease, family history of IHD or smoking. But, there is statistically significant relation between the studied groups regarding presence of comorbid diabetes. Within the group with CTO from 3 to 12 months, 90.9% had diabetes versus 50% and 59.1% within the groups of 12 to 24 and >24 months respectively. **Danek et al.** [5] found high prevalence of hypertension (88%), hyperlipidemia (96%), and diabetes mellitus (43%).

Regarding J-CTO score, there is statistically non-significant relation between grades and time of CTO. On comparing each two individual groups, the difference is significant between 3 to 12 months and >24 months and each other group. **Danek et al.** [5] found that lesions of known age

tended to be more complex, with greater incidence of proximal cap ambiguity and higher J-CTO score.

In our study, there is statistically non-significant relation between the studied groups regarding collaterals (septal collaterals were in 81.8%, 68.2% and 63.6% of those in groups with CTO 3 to 12 months, 12 to 24 months and >24 months). **Danek et al.** [5] found that interventional collaterals were more common among lesions of known age (66% vs. 54%, p<0.001).

In this study, there is statistically significant relation between J-CTO scores and time of CTO. On comparing each two individual groups, the difference is significant between 12 to 24 months and each other group, looking specifically at the J-CTO score sheet criteria in our study, there is statistically **non-significant** relation between the studied groups regarding J-CTO score sheet criteria and time of CTO except for re-entry lesions, There is statistically **significant** difference between the studied groups regarding re entry CTO, which indicated that failure of CTO recanalization is more frequent CTO of more than 24 months.

Mingqiang Fu et al[8] concluded in their resent study that prior failed CTO lesions were associated with higher complexity of morphology; however, 81.1% of CTOs could be recanalized safely and effectively by experienced operators at repeat attempts. There was a definite relationship between lesion complexity and the increasing need for multiple approaches and technologies during CTO-PCI to achieve success, considering lesion complexity and prior failure, reat- tempted CTO-PCIs could still achieve an overall success rate of 81.1% by high-volume operators with acceptable complications.

Regarding time for PCI, there is statistically significant relation between time for PCI and time of CTO. On doing Turkey HSD group, the difference is significant between 3 to 12 months and each other group (as in this group, time of PCI was significantly the lowest time). **Danek et al**[5] compared 728 lesions of unknown duration with the 394 lesions of known age. Patients with known lesion age had higher incidence of prior PCI, prior CABG, prior MI, and prior failed CTO PCI as compared with those of unknown lesion age.

Regarding radiation dose, there is statistically significant difference between the studied groups regarding radiation dose. On doing pairwise comparison, the difference is significant between 3 to 12 months group and each other group (lowest dose was associated with recent CTO).

Regarding CTO revascularization cost there is statistically **non-significant** relation between cost and age of CTO. It was non-significantly higher in the groups of CTO of 12 months and >24 months.

In a recent publication by the OPEN-CTO investigators **Salisbury et al**[9], in hospital costs were measured. The authors note that the procedural costs were similar to the costs of multivessel or left main PCI in the SYNTAX trial (Synergy Between PCI With Taxus and Cardiac Surgery) and FREEDOM trial (Future Revascularization Evaluation in Patients With Diabetes Mellitus:

Optimal Management of Multivessel Disease), although the equipment requirements in this registry seem higher.

In our study, there is statistically **non-significant** relation between technique used and time of CTO. regarding RDR and ADR technique, It was non-significantly higher in the groups of CTO of 12 months and >24 months.

Emmanouil et al[10] concluded that in general, each score is only applicable to the population from which it was derived and validated. Calculating ≥1 scores can promote detailed review of the angiogram and facilitate decision making. For example, medical therapy may be preferred over CTO-PCI in mildly symptomatic patients with highly complex occlusions. Complex CTOs (such as those with J-CTO score ≥2) are more likely to require dissection reentry and retrograde crossing techniques and should be performed by experienced operators.

Regarding contrast volume, there is statistically non-significant relation between contrast volume and time of CTO. It was non-significantly higher in the group of CTO>24 months. Also, **Danek et al**[5] found that contrast volume did not differ significantly among the groups.

Regarding outcome, all patients had successful outcome with no significant difference between the studied groups, that was consistent with the study published by **Han et al**[11] who reported that the overall success rate was 88.9%. **Barlis et al**[12] showed that indeterminate CTO age independently predicts CTO PCI failure (p=0.002). **Tomasello et al**[13] showed that CTOs of longer duration (>12 months) and indeterminate duration can be treated with no impact on procedural outcomes and one-year MACE. The presence of severe calcifications, longer CTO length, and small vessel diameter were independent predictors of technical failure, suggesting that revascularization of older CTOs can be safely and effectively attempted. **Danek et al**[5] found that overall technical success was 90.1% and overall procedural success was 87.5%. There was no difference in technical or procedural success.

Regarding complications, there is statistically significant relation between the studied groups regarding presence of immediate complications. No patients within 3 to 12 months had been complicated while three patients within CTO from 12 to 24 months (13.6%) had immediate complications (one had CIN, one had hypotension with mild septal hematoma and the last one had perforation sealed with covered stent, pericardiocentesis and blood transfusion) and six patients within CTO > 24 months (27.3%) had immediate complications (one had hypotension, one had LCX, one had septal perforation, one had pulmonary edema, one had septal perforation sealed with ballon inflation and the last one had one had perforation sealed with cover stent).

Danek et al[5] found no difference in the incidence of major adverse cardiac events for older vs. more recent occlusions. There were 8 cases of MACE in the lowest tertile of lesion age: 3 perforations, 4 MIs requiring re-PCI, and 1 ischemic stroke. The middle and highest lesion age tertiles had 4 cases of MACE each. MACE in the middle tertile comprised of perforation and

ischemic stroke in 1 patient, 1 stent thrombosis requiring repeat PCI, and 2 myocardial infarctions, 1 of which was caused by donor artery damage. MACE in the highest tertile of lesion age was caused by 2 perforations causing tamponade and death, and 2 myocardial infarctions.

Prior studies have shown an association between lesion age and severity of calcification. A study of post-mortem CTO lesion morphology has shown age-related differences in occlusion histologic composition. **Srivatsa et al**[4] studied 96 CTOs from autopsies in 61 patients and found that cholesterol and foam cells were seen more frequently in younger lesions, while older lesions tended to have a greater fibrocalcific component.

Sakakura et al. [14] studied 96 CTO lesions from 82 patients with and without prior CABG; lesions from patients without CABG were stratified by occlusion duration. The prior CABG group showed the most calcification (29% calcified area at CTO segment), followed by the long-duration CTO group (17% calcified area), while the short-duration CTO group was associated with microvessels and loose fibrous tissue (12% calcified area).

An IVUS study by **Suzuki et al.** [15] also demonstrated increasing calcification with increasing CTO age (correlation between arc of calcification and lesion age r=0.445, p<0.0001; correlation between length of calcification and lesion age r=0.397, p=0.001). **Danek et al.**[5] concluded that older CTO lesions exhibit angiographic complexity and more frequently necessitate the retrograde approach or antegrade dissection/ reentry. Older CTOs can be recanalized with high technical and procedural success rates and acceptable MACE. Lesion age appears unlikely to be a significant determinant of CTO PCI success.

This study has some limitations. This study involved single team experience, multi-center studies are required to potentiate our findings. Lack of precise dating of lesion age is another potential limitation, although we only included cases with angiographic or solid clinical documentation of lesion age in our study. Determining the exact age of a CTO is very challenging, as serial coronary artery imaging is infrequently performed and even when it is performed the exact onset of the occlusion is often unclear. We relied on follow up echocardiography studies to assess evolution of systolic function and WMSI. More advanced imaging modalities would have been more accurate as CMR.

Conclusion:

Success of CTO - PCI in the current era of new dedicated CTO equipment is unlikely to be affected by CTO lesion age.

We recommendations:

Percutaneous coronary intervention (PCI) for coronary chronic total occlusion (CTO) should be performed for proved viable myocardium in the territory supplied by the occluded vessel. Proper

evaluation of the clinical and angiographic data of the patient to choose the proper plan for the intervention starting from the guiding catheter, the approach and the instruments that will be used. Larger multi-center studies, longer follow up, serial echocardiographic studies, use of CT angiography might modify patient selection and contrast amount

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