



THE BIOLOGICAL COST OF CTO INTERVENTION: INSIGHT FROM A PROSPECTIVE STUDY

Gopakumar K S., Mathew Iype., Sunitha Viswanathan and A. George Koshy

From the CTO Investigators- Kerala (CTOI-K) Group

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ABSTRACT

Objectives: Chronic Total Occlusion (CTO) intervention is a challenging area in interventional cardiology. Presently about 70% of CTO interventions are successful. This study aims to look at the biological costs of CTO interventions in the current era in a teaching hospital in South India

Materials and methods: It was a prospective study of a cohort of all patients undergoing Percutaneous coronary intervention (PCI) for CTO. Only antegrade CTO interventions were included.

Results: A total of 210 (8.9% of total PCI (2353) during the study period) CTO patients were followed up. The mean age of the patients was 56.54 +/- 8.9 %. In the cohort 32.9% (n=69) had chronic stable angina, 22.9 % (n= 48) had unstable angina (UA) or non ST elevation myocardial infarction (NSTEMI) and 44.2% (n= 93) had (ST Elevation Myocardial Infarction (STEMI). Immediate cardiac complications in the first attempt CTO PCI were peri- procedural myocardial infarction in 10 patients (4.8%) and Coronary perforations in 17 patients (8.1%) and heart failure in 3 patients (1.5). There was no in hospital death /stent thrombosis/ need for urgent revascularization. Majority of coronary perforations were seen in failed cases (15/17 cases of perforation). Contrast nephropathy was seen in 5.7 % of cases

Conclusions: Biological costs of CTO interventions were immediate complications like periprocedural MI, cardiac perforation, contrast induced nephropathy, TIMI major and minor bleed, and AF and radiation exposure. Failed CTO interventions significantly had more biological costs compared to successful ones

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INTRODUCTION

Coronary Chronic Total Occlusion (CTO) is defined as an occluded coronary segment with Thrombolysis In Myocardial Infarction (TIMI) flow 0 for ≥ 3 months duration^{1,2}. Coronary CTOs are commonly encountered in clinical practice, with a prevalence rate of 18–52% among patients undergoing coronary angiography^{3,4}. The field of percutaneous coronary intervention (PCI) for CTO has enjoyed significant innovations in the recent years. Novel techniques and technologies have revolutionized the field and have resulted in considerably higher success rates even in patients with high anatomical complexity... The clinical benefit of CTO revascularization is still a hot topic in current literature. Several observational studies have shown that successful CTO revascularization improves cardiovascular outcomes.^{5,6} A meta-analysis by

Hoebbers *et al.* Found that successful revascularization of CTO improved the Left Ventricular ejection fraction.⁷

Intervention a lists and patients are interested in “opening-up” a CTO. But what are its biological costs to the patient and interventionist? However, complex CTO procedures often require prolonged x-ray exposure which have been associated with adverse long term outcomes. There are no studies in this direction. The present study gives some interesting observations.

MATERIALS AND METHODS

It was a prospective study of a cohort of all patients undergoing antegrade CTO intervention in the department of Cardiology Government Medical College, Thiruvananthapuram from August 1st 2014 to June 30th 2015

*Corresponding author: Gopakumar K S

Inclusion criteria

All patients undergoing antegrade CTO intervention in the department of Cardiology Government Medical College, Thiruvananthapuram from August 1st 2014 to June 30th 2015 were included in the study. CTO is defined as a high-grade coronary occlusion with reduced antegrade flow (Thrombolysis in Myocardial Infarction [TIMI] grade 0 flow) with estimated duration of at least 3 months

Exclusion criteria

Exclusion criteria included patients with an estimated CTO duration less than 3 months, CTO vessel size \leq 2.5 mm, in-stent total occlusion, status post Coronary Artery Bypass Graft surgery (CABG), Chronic Kidney Disease (CKD) with a baseline e GFR $<$ 30 ml/min/1.73 m², retrograde approach for CTO, inability to take antiplatelets and left ventricular ejection fraction less than 30 %.

Procedure

All patients was pre-treated with aspirin and clopidogrel (a loading dose of 300 mg at least 6 h before the procedure). After the procedure, all patients were on dual antiplatelet therapy with aspirin and one of clopidogrel or prasugrel or ticagrelor. Baseline characteristics procedural and angiographic characteristics were recorded.

Peri-procedural complications were like coronary perforation with or without tamponade), heart failure (requiring NTG and diuretic), cardiogenic shock and arrhythmias.

Immediate outcomes were recorded before the discharge of the patient which included death, ACS – STEMI, NSTEMI, unstable angina, arrhythmias, stroke (ischemic/hemorrhagic), renal failure, need for urgent revascularization (PCI/ CABG) and stent thrombosis.

Data analysis

The statistical significance is calculated by chi square test and paired ANOVA test where applicable

RESULTS**Baseline demographics**

We had a total of 210 (8.9% of total PCI (2353) during the study period) CTO patients were followed up. The mean age of the patients was 56.54 +/- 8.9 % 32.9% (n=69) had Chronic stable Angina, 22.9 % (n= 48) had UA/NSTEMI and 44.2% (n= 93) had STEMI. In those with history of ACS, 64.78% (n=92) had ACS during the previous year and remaining 35.22% (n=49) had ACS prior to that.

Immediate cardiac complications

Immediate cardiac complications in the first attempt CTO PCI were peri procedural myocardial infarction in 10 patients (4.8%) and Coronary perforations in 17 patients (8.1%) and heart failure in 3 patients (1.5%). There was no in hospital death /stent thrombosis/ need for urgent revascularization. Majority of coronary perforations were seen in failed cases (15/17 cases of perforation). The operator stopped the procedure due to the perforation. Pericardiocentesis was needed in 2 cases. See table

Table 1 Coronary perforations in successful and failed CTO interventions

	Successful CTO intervention	Failed CTO intervention	P value
Conservative management	0	12	<0.001
Prolonged balloon inflation	2	1	
Pericardiocentesis	0	2	

Contrast nephropathy and stroke

Contrast nephropathy was seen in 5.7 % of cases. None of the cases developed stroke/transient ischemic attack (TIA). See table 2.

Table 2 Contrast nephropathy and stroke

	Number	Percentage
Renal failure	12	5.71
Stroke / TIA	0	0

Complications in successful cases vs failed cases

The incidence of heart failure and contrast nephropathy were not significantly different in successful and failed cases. Two failed cases has atrial fibrillation during the procedure. Cardiac perforations were significantly more in the failed group and the indication for stopping the intervention was perforation.

Table 3 Complications in successful cases vs failed cases

	Successful cases	Failed cases	P value
Heart failure	7	5	0.455
Atrial fibrillation/	0	2	0.038
Cardiac perforation	2	15	<0.001
Contrast nephropathy	7	5	0.455

Access site complications

The main access site complication was TIMI minor bleed. There was no TIMI major bleed. Two cases of femoral pseudoaneurysm occurred. See table 5.

Table 4 Access site complications

	Number	percentage
TIMI major bleed	0	0
TIMI minor bleed	16	6.7%
Pseudoaneurysm	2	1%

Fluoroscopy time

The mean fluoroscopy time was 24.3 minutes. However, the fluoroscopy time by itself is much less specific than the air kerma dose expressed in Gy.

Table 5 Fluoroscopy time

	Number	Percentage
< 20 mins	93	44.3
20-40 mins	90	42.8
>40 mins	27	12.8

Quantity of radiographic contrast

The mean contrast volume used was 243 ml.

Table 6 Quantity of radiographic contrast

	Number	percentage
<200 ml	70	33.3
200-400 ml	122	58.1
400 ml	18	8.5

DISCUSSION

CTO interventions though beneficial to the patients in most cases, the biological cost to the operator and to the patient are not insignificant.

Radiation is an important factor, in the sense that modern interventionists in their thirties are expected to continue to their sixties resulting in a high cumulative radiation dosage. CTO PCI, typically due to longer time involved, has a radiation injury potential⁸. This can lead to skin injury. However it should be kept in mind that radiation is mutagenic and is considered an important causative factor for some tumors.

The incidence of coronary perforations in the present study is higher compared to published studies. Patel *et al* in a meta-analysis of 65 studies noted a coronary perforation rate of 2.9%⁹. CTO intervention in general involves the use of stiffer wires compared to routine PCIs. An important point to remember is that device perforations are more catastrophic, than just a wire perforation. Balloon dilation or following a wire with a micro catheter should be avoided unless the operator is confident that the wire is in the vessel.

Contrast induced nephropathy (CIN) can occur during PCI. This has adverse consequences on long-term prognosis¹⁰. Scoring systems such as the Mehran score are useful in predicting contrast induced nephropathy¹¹.

Table 7 Major complications of CTO intervention-present study vs meta-analysis by Patel *et al*.

	Present study	Meta-analysis (Patel <i>et al</i>)
Peri-procedural myocardial infarction	4.8%	3.1% (95% CI 2.4%-3.7%)
Cardiac perforation	8.1%	2.9% (95% CI 2.2%-3.6%)
Contrast nephropathy	5.7%	3.8% (95% CI 2.4% - 5.3%)

CONCLUSIONS

Biological costs of CTO interventions were immediate complications like periprocedural MI, cardiac perforation, contrast induced nephropathy, TIMI major and minor bleed, and AF and radiation exposure.

Failed CTO interventions significantly had more biological costs compared to successful ones and with the current available evidences the beneficial long term outcomes of CTO interventions with these high biological costs need to be further investigated

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