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Outcomes of chronic total occlusion percutaneous coronary intervention from the RAIAN (RAjaie - Iran) registry☆

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ABSTRACT

Objective: While most of the evidence in CTO interventions emerge from Western and Japanese studies, few data have been published up today from the Middle East. Objective of this study was to evaluate technical success rates and clinical outcomes of an Iranian population undergoing CTO PCI in a tertiary referral hospital. Moreover, we sought to evaluate the efficacy of our CTO teaching program.

Methods: This is a retrospective single-center cohort study including 790 patients who underwent CTO PCI performed by operators with different volumes of CTOs PCI performed per year. According to PCI result, all patients have been divided into successful ($n = 555$, 70.3 %) and unsuccessful ($n = 235$, 29.7 %) groups. Study endpoints were Major Adverse Cardiovascular Events and Health Status Improvement evaluated using the Seattle Angina Questionnaire at one year.

Results: A global success rate of 70 % for antegrade and 80 % for retrograde approach was shown despite the lack of some CTO-dedicated devices. During the enrollment period, the success rate increased significantly among operators with a lower number of CTO procedures per year. One-year MACE rate was similar in both successful and unsuccessful groups (13.5 % in successful and 10.6 % in unsuccessful group, $p = 0.173$). One year patients' health status improved significantly only in successful group.

Conclusions: No significant differences of in-hospital and one-year MACE were found between the successful and unsuccessful groups. Angina symptoms and quality of life significantly improved after successful CTO PCI. The RAIAN registry confirmed the importance of operator expertise for CTO PCI success.

1. Introduction

Percutaneous coronary intervention (PCI) of chronic total occlusions (CTOs) represents one of the most technically challenging procedure in contemporary coronary interventional cardiology. CTO PCI success rate in experienced centers ranges between 85 and 90 %.[1,2] These results can

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be explained by three main factors: first, skill acquisition in CTO interventions by dedicated operators; second, the development of new recanalization techniques; third, a large number of dedicated devices for CTO PCI available in the market.[3]

Many studies conducted in Western Countries have proven that quality-of-life variables improve after successful CTO PCI, including angina relief, heart failure symptoms, physical activity, and overall treatment satisfaction.[4] Successful CTO PCI, especially in presence of myocardial viability, leads other cardiovascular benefits like increase in left ventricular ejection fraction (LVEF) and reduction in myocardial arrhythmic vulnerability.[5,6]

Regional variations in patient characteristics and outcomes, due to demographics, socioeconomic status, access to healthcare, treatment patterns and culture issues could not permit a generalization of above-mentioned results.[7,8] Most of large registries and randomized trials come from Europe, North America and Japan, but there is a lack of data about CTO PCI in other regions as Middle East.[3,9]

In the present study, clinical, procedural and outcomes data of a large cohort of Iranian population underwent CTO interventions in a single high-volume referral teaching hospital will be reported.

2. Methods

2.1. Study population and procedures

PCI registry was retrospectively reviewed to identify patients who underwent Chronic Total Occlusion (CTO) PCI between September 2016 and September 2019. The study was approved by the local Ethics Committee. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee.

A total of 790 CTO patients were enrolled consecutively. According to PCI result, all patients were divided into successful ($n = 555$, 70.3 %) and unsuccessful procedure group ($n = 235$, 29.7 %).

CTO interventions were performed by dedicated CTO operators with different volume of CTO procedures per year. To measure the performance of our teaching hospital model, as the procedural success was previously demonstrated to be linearly related to the operator volume of CTO procedures/year[2], we used a number of 50 procedures/year/operators as cut-off to identify **low-volume operators (LVOs) if they perform < 50 CTO PCIs/year and high-volume operators (HVOs) if they perform > 50 CTO/PCIs/year.** Technical success rates have been evaluated and compared as long as the three years of patient's enrollment.

Indication for angioplasty was given by the Heart Team within the Hospital's standard protocol of care. Some operators were interventional cardiologist non-European affiliated members or engaged in a training-program of the Euro-CTO Club. All PCI procedural angiograms and reports were reviewed by two interventional cardiologists to identify lesion characteristics and technical success. In case of disagreement, a third operator reviewed angiograms and reports. CTO was defined as a total occlusion of epicardial coronary arteries with Thrombolysis in Myocardial Infarction (TIMI) flow grade 0 for at least 3 months; technical success was defined as a residual stenosis <30 % with antegrade TIMI flow grade 3 in the CTO target vessel.

Minimal distal disease was defined as the absence of lesions more than mild, distally to the CTO; proximal tortuosity was considered as the presence of ≥3 consecutive curvatures of 90°–180° measured at end-diastole in a major epicardial coronary artery ≥2 mm in diameter; calcifications were defined when readily apparent radiopacities within the vascular wall at the site where the stenosis were detected: it was classified as none/mild, moderate (radiopacities noted only during the cardiac cycle before contrast injection), and severe (radiopacities noted without cardiac motion before contrast injection generally compromising both sides of the arterial lumen); stent loss was defined as under-deployment of stent unintentionally dislocated partially or completely from the balloon with or without the guidewire in place. Wire loss was the unintentional disconnection and dislocation of the distal portion of the guidewire.[10,11]

The J-CTO Score, the CASTLE Score and the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) Score, were calculated for each lesion.[12–17]

For each patient, demographic data, risk factors for coronary artery disease (CAD), clinical information such as Left Ventricle Ejection Fraction (LVEF), baseline laboratory data and angiographic data were collected in a dedicated database.

One-year clinical follow-up was performed using call interviews. In case of adverse cardiovascular events, the patients underwent clinical evaluation performed by the study team. Population health status was evaluated using the Seattle Angina Questionnaire (SAQ).[18]

2.2. Clinical and functional status endpoints

Clinical endpoints were procedural complications, in-hospital and one-year-follow-up major adverse cardiovascular events (MACE). Functional status endpoint was SAQ Score variation through the follow-up.

MACE was defined as a composite of cardiovascular death, cerebrovascular accidents (CVA), periprocedural myocardial infarction (MI), or target-lesion revascularization (TLR).

Periprocedural (type 4a) myocardial infarction was defined according to the "Fourth definition of myocardial infarction".[19]

TLR was defined as repeat revascularization of a CTO vessel, including redo-PCI or CABG surgery.

2.3. Statistical analysis

For statistical analysis, quantitative variables were presented as mean ± standard deviation (SD) and were presented as frequency (percentage) for categorical variables. Continuous variables were compared between groups using Student's *T*-test or Mann–Whitney test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using Chi-square test. Considering the binary nature of the response variables we adapted a logistic regression model. Significant variables at univariable analysis were included in the multivariable analysis. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

3. Results

3.1. Baseline population characteristics

Out of 790 patients included in the study, 555 (70.3 %) were assigned to the successful group and 235 (29.7 %) to the unsuccessful group. The two groups were homogeneous for all clinical characteristics except LVEF values that were significantly higher in successful group (43.03 ± 9.56 vs 41.03 ± 10.08; $p = 0.010$).

No significant differences were found in baseline SAQ values between success and unsuccessful group (47.8 ± 11.3 vs 46.4 ± 14.5, $p = 0.643$). Table 1.

3.2. Lesion characteristics

All the details are reported in Table 2. There were no differences in target CTO vessel revascularization involvement between successful and unsuccessful groups, respectively: LAD 37.1 % and 31.9 % ($p = 0.163$), LCX 18.4 % and 22.6 % ($p = 0.177$), RCA 44.5 % and 45.5 % ($p = 0.791$). CTO complexity scores were lower in successful than unsuccessful group (J-CTO Score: 1.59 ± 1.060 vs 1.82 ± 1.005; $p = 0.002$. CASTLE Score:

Table 1
Baseline population characteristics.

Clinical variable	Overall (n = 790)	Successful (n = 555)	Unsuccessful (n = 235)	p value
Age (years)	58.99 ± 10.65	58.63 ± 10.75	59.85 ± 10.3	0.140
Male gender % (n)	79.6 (629)	78.2 (434)	83 (195)	0.127
Diabetes mellitus % (n)	24.8 (196)	25.0 (139)	24.3 (57)	0.814
Hypertension % (n)	58.2 (460)	58.6 (325)	57.4 (135)	0.772
Hyperlipidemia % (n)	38.1 (301)	38.2 (212)	37.9 (89)	0.931
Family history % (n)	16.6 (131)	17.7 (98)	14.0 (33)	0.212
Smoking % (n)	23.7 (187)	23.8 (132)	23.4 (55)	0.909
LVEF %	42.45 ± 9.75	43.03 ± 9.56	41.03 ± 10.08	0.010
Creatinine (mg/dL)	1.12 ± 0.75	1.12 ± 0.72	1.11 ± 0.83	0.908
Previous PCI % (n)	25.3 (200)	26.1 (145)	23.4 (55)	0.421
Previous CABG surgery % (n)	15.4 (122)	14.4 (80)	17.9 (42)	0.291
Previous PCI and CABG surgery % (n)	3.3	3.1	3.8	0.581
SAQ % (n)	70.0 (553)	63.4 (346)	36.6 (207)	0.212
SAQ score	46.1 ± 10.9	47.8 ± 11.3	46.4 ± 14.5	0.643

Abbreviations: CABG: Coronary Artery Bypass Graft; LVEF: Left Ventricular Ejection Fraction; PCI: Percutaneous Coronary Intervention; SAQ: Seattle Angina Questionnaire.

1.80 ± 1.14 vs 2.25 ± 1.22, $p < 0.001$. PROGRESS score: 2.07 ± 1.61 vs 2.39 ± 1.71; $p = 0.020$).

Successful group had significantly lower prevalence of occlusion length ≥20 mm (62.7 % vs 74.5 %, $p = 0.002$), blunt or ambiguous stump (55.6 % vs 70.2 %, $p = 0.001$), calcifications (12.8 % vs 19.6 %, $p = 0.015$), proximal tortuosity (28.6 % vs 38.6 %, $p = 0.024$) and minimal distal vessel disease (76.5 % vs 59.2 %, $p = 0.001$). No differences in Syntax Score, number of ostial CTO lesions, number of in-stent restenosis (ISR), presence of side branch at proximal cap, use of double arterial access, use of radial artery access, use of supportive guiding catheter or micro-catheter, use of atherectomy devices and IVUS were found.

3.3. Procedural characteristics

All the details are reported in Table 2. A primarily antegrade approach was chosen in 752 patients (95.2 %), while a primarily retrograde approach was used in 38 patients (4.8 %). In 13 patients (1.6 %) a switching from antegrade to retrograde or vice versa was required.

The overall CTO PCI success rate was 70.3 %, respectively 70.6 % in antegrade cases and 63.1 % in retrograde ones. Success rate was 73.3 % for LAD, 65.8 % for LCX and 69.8 % for RCA CTOs (p value = 0.251).

Antegrade wire escalation was the most frequent crossing strategy; a retrograde approach was used similarly in both groups, in a small proportion of patients (4.3 % vs 6.0 %, $p = 0.327$).

The total stented segment length (mean ± standard deviation) was 52.14 ± 23.97 mm in left anterior descending (LAD) artery, 45.54 ± 21.99 mm in left circumflex (LCA) artery, and 70.95 ± 30.82 mm in Right coronary artery (RCA) (p value: 0.002).

A total of 252 (31.9 %) CTO-PCI were performed by **HVOs**, 64 in the first year, 106 in the second year and 82 in the third year; a total of 538 (68.1 %) CTO-PCI were performed by **LVOs**, **171** in the first year, 182 in the second year and 185 in the third year.

Technical success was significantly higher in the sub-group of procedures performed **by HVOs** than in the subgroup of procedures performed **by LVOs** (83.3 % vs 64.1 %; $p = 0.036$). Moreover, during the three years of enrollment, technical success increased significantly for **LVOs** (first vs third year technical success was 60.8 % vs 68.1 %; $p = 0.048$) while in the subgroup of procedure performed by **HVOs** the success rate remains stable (first vs third year technical success was 81.3 % vs 84.1 %; $p = 0.067$) **(Table 3 and Fig. 2).**

Table 2
Lesion and procedural characteristics.

	Overall (n = 790)	Successful (n = 555)	Unsuccessful (n = 235)	p value
J-CTO Score	1.64 ± 1.264	1.59 ± 1.060	1.82 ± 1.005	0.002
CASTLE Score	1.91 ± 1.5	1.80 ± 1.14	2.25 ± 1.22	<0.001
PROGRESS CTO	2.13 ± 1.7	2.07 ± 1.61	2.39 ± 1.71	0.020
Syntax Score	16.390 ± 7.2145	16.394 ± 7.3683	16.382 ± 7.1024	0.944
Lesion Location % (n)				0.590
Ostial	1.6	1.4	2.1	–
Proximal	46.1 (364)	45.8 (254)	46.8 (110)	–
LAD % (n)	35.6 (281)	37.1 (206)	31.9 (75)	0.163
LCA % (n)	19.6 (155)	18.4 (102)	22.6 (53)	0.177
RCA % (n)	44.8 (354)	44.5 (247)	45.5 (107)	0.791
Length ≥ 20 mm % (n)	66.1 (496/750)	62.7 (335/534)	74.5 (161/216)	0.002
Side branch at proximal cap % (n)	53.2 (410/770)	51.9 (282/543)	56.4 (128/227)	0.268
Minimal Distal Vessel Disease % (n)	71.7 (523/729)	76.5 (404/528)	59.2 (119/201)	0.001
Blunt or Ambiguous Stump % (n)	59.9 (463/773)	55.6 (303/545)	70.2 (160/228)	0.001
Calcification % (n)	14.8 (113/763)	12.8 (69/539)	19.6 (44/224)	0.015
Proximal tortuosity % (n)	31.6 (243/770)	28.6 (155/542)	38.6 (88/228)	0.024
Antegrade Approach	95.2 (752)	70.6 (531)	29.4 (221)	0.452
Retrograde Approach	4.8 (38)	63.1	36.9	0.327
Overall Success rate	70.3 (555)	–	–	–
LAD	73.3 (579)			0.251†
LCA	65.8 (520)			
RCA	69.8 (551)			
Approach Switching	1.6	11 (61)	2	0.45
Radial PCI % (n)	22.0 (174)	20.4 (113)	26 (61)	0.083
Double arterial access % (n)	71.1 (562)	70.6 (392)	72.3 (170)	0.734
Use of Rotablator % (n)	0.8	0.9	0.4	0.675
ISR % (n)	1.4	1.6	0.9	0.521
Use of Microcatheter % (n)	48.6 (384)	50.5 (280)	44.3 (104)	0.111
Extra back-up Guiding Catheter % (n)	4.4 (35)	4.5	4.3	0.876

Abbreviations: CASTLE=Coronary Artery Bypass Grafting History, Age, Stump anatomy, Tortuosity degree, Length of occlusion and Extent of calcification; ISR: In-Stent Restenosis; J-CTO = Japanese Multicenter CTO Registry; LAD: Left Anterior Descending Artery; LCX: Left Circumflex Artery; LVEF: Left Ventricular Ejection Fraction; PCI: Percutaneous Coronary Intervention; PROGRESS=Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA: Right Coronary Artery.

3.4. Procedural and in-hospital complications

All the details are reported in Table 4. Overall coronary perforations rate was 3.2 %; it was significantly higher in the unsuccessful group as compared with successful (8.1 vs 1.1 %; $p < 0.001$). All the other procedural complications did non differ significantly between the two groups. In-hospital death occurred in 0.8 % ($n = 6$) patients, 0.7 % ($n = 4$) in successful and 0.9 % ($n = 2$) in unsuccessful group ($p = 0.847$). All deaths were cardiovascular in nature, respectively: two cases secondary to coronary perforation, four cases caused by cardiac arrest not responsive to cardiopulmonary resuscitation.

Table 3
Technical success according to operators' annual procedural volume.

	Overall	Year 1	Year 2	Year 3	*p* value
CTO attempted n (%)	790	235 (29.7 %)	288 (36.5 %)	267 (33.8 %)	ns
LVOs n	538 (68.1 %)	**171 (31.8 %)**	182 **(33.9 %)**	185 **(34.4 %)**	**0.039/ °0.030
HVOs	252 (31.9 %)	64 (25.4 %)	106 (42.1 %)	82 (32.5 %)	§0.042
Technical Success n (%)	555/790 (70.3 %)	156/235 (66.4 %)	204/288 (70.8 %)	195/267 (73.0 %)	+0.048
LVOs n	345/538 (64.1 %)	104/171 (60.8 %)	115/182 (63.2 %)	126/185 (68.1 %)	*0.041
HVOs	210/252 (83.3 %)	52/64 (81.3 %)	89/106 (84.0 %)	69/82 (84.1 %)	0.067

Abbreviations: LVOs = Low-volume operators; CTO: Chronic Total Occlusions; ns: not significant; HVOs = high-volume operators.
Note: *** and § calculated from the comparison between year 1 and year 2.*
°, + and * calculated from the comparison between year 1 and year 3.

3.5. Follow-up outcomes

One-year follow-up data (mean 22.2 ± 11.6 months) were available for all patients. After hospital discharge, cardiovascular death occurred in 3.2 % of overall population ($n = 25$): 3.0 % ($n = 17$) in successful and 3.4 % ($n = 8$) in unsuccessful group ($p = 0.151$). At one year follow-up there were no significant differences in MACE between the two groups. Overall population MACE rate was 12.7 % ($n = 100$ events), respectively 13.5 % ($n = 75$) in successful and 10.6 % ($n = 25$) in unsuccessful group ($p = 0.173$).

CVA occurred in 11 patients (1.4 %), respectively in 6 (1 %) successful patient and in 5 (2.1 %) in unsuccessful ($p = 0.038$). Conversely, myocardial infarction occurred in 52 patients (6.6 %), respectively in 43 patients in successful group (7.7 %) versus 9 patients (3.8 %) in the unsuccessful group ($p = 0.031$).

Overall TLR rate was 1.5 % ($n = 12$): CABG 1.0 % ($n = 4$) and redo-PCI 0.5 % ($n = 8$). Repeated revascularization rates were respectively: 1.6 % ($n = 9$) in successful group and 1.4 % ($n = 3$) in unsuccessful group ($p = 0.123$). Table 4.

3.6. Longitudinal health status outcomes

Data from Seattle Angina Questionnaire were available in 70.0 % ($n = 553$) of the entire population at baseline and in 65.0 % ($n = 513$) at one-year follow-up.

At one-year follow-up, only patients in the successful group showed a statistically significant health status improvement according to the longitudinal evaluation of SAQ (baseline 47.8 ± 11.3 vs 1 year follow-up 69.1 ± 10.5; $p = 0.020$) (Fig. 1).

4. Discussion

The RAIAN registry reports data from a large Iranian cohort of patients who underwent CTO interventions between the years 2016–2019 in a single high-volume center in the middle east area. It has been shown that CTO interventions has reached a rather satisfactory procedural success rate and few complications in one of the highest volume Iranian Centers. At one-year follow-up the health status has significantly improved after successful revascularization, while MACE rate was similar in both groups.

4.1. Procedural success rate and technical issues

Data about CTO PCI from North America, Europe and Japan have been extensively reported in literature during recent years, but real-world data from other Countries such as the Middle East area lacking.[3,4,9] The technical success rate in our study was 70 %. This data is slightly lower than European, Japanese or US experiences[20–22] but seem to be like a registry from other new emerging countries such as Latin America (LATAM Registry) which success rates was quoted as high as 81 %.[23]

Another observational study with a retrospective data analysis on an Indian cohort, the CTO PCI success rate was 89 %. However, the percentage of retrograde approach was not specified and the overall population JCTO score was slightly lower than how reported in our study.[24]

Even if the success rate of our study population has shown to be 70

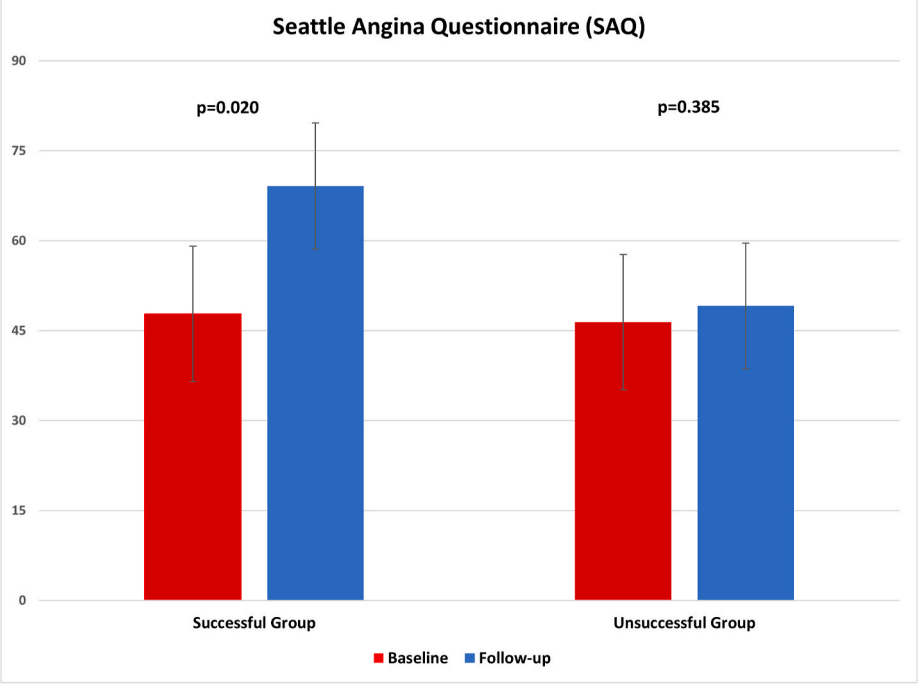

Fig. 1. Unadjusted Seattle Angina Questionnaire (SAQ) Score at baseline and one year follow-up in both successful and unsuccessful groups.

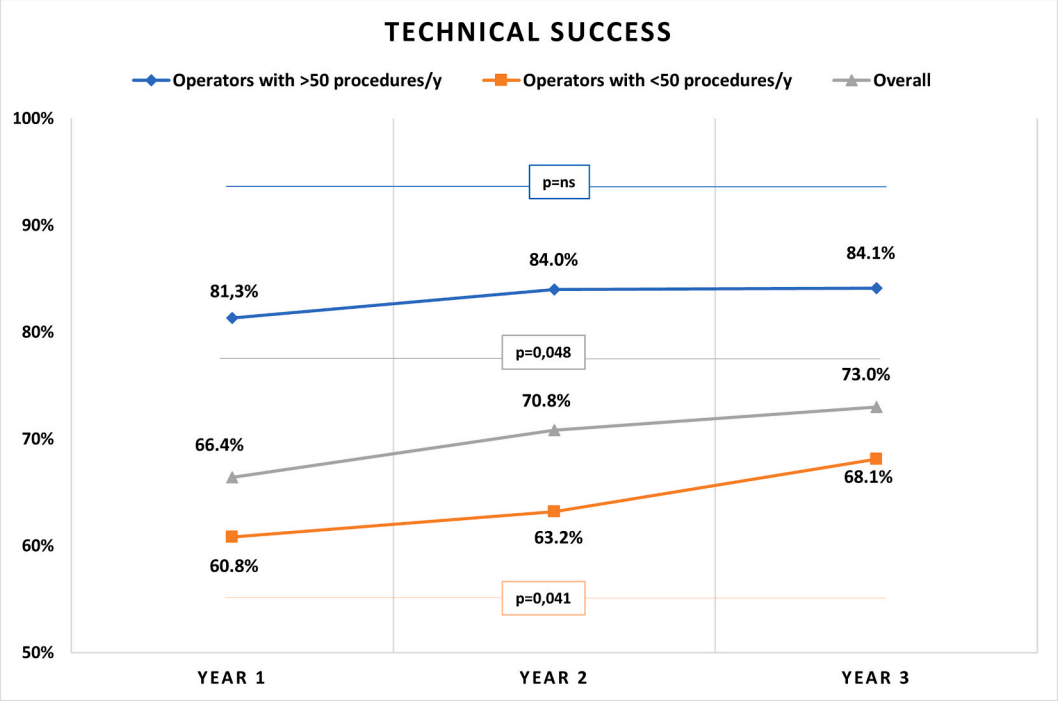

Fig. 2. Technical success rates throughout the study period for **HVOs and LVOs**.

Table 4
Complications.

% (n)	Overall (790)	Successful 70.3 (555)	Unsuccessful 29.7 (235)	*p* value
PROCEDURAL AND IN-HOSPITAL				
Perforations	3.2	1.1	8.1	0.001
Conservative management	1.9	0.5	5.1	
Coil embolization alone	0.1	0	0.4	
Covered stent	0.4	0.4	0.4	
Pericardiocenthesis alone	0.3	0	0.9	
Pericardiocenthesis with Coil embolization	0.5	0.2	1.3	
CPR	0.4	0.4	0.4	0.426
No Reflow	0.3	0.4	0	
LM/LAD dissection in Retrograde approach	0.4	0.5	0	
Stent Loss	0.4	0.4	0.4	
Wire Loss	0.1	0	0.4	
Emergent CABG	0.3	0	0.9	
Packed Cell transfusion	10.2 (80)	6.4 (35)	19.1 (45)	0.001
In hospital death	0.8	0.7	0.9	0.847
FOLLOW-UP				
MACE	12.7 (100)	13.5 (75)	10.6	0.173
Rehospitalization	16.8 (133)	18.9 (105)	11.9	0.016
Cardiovascular death	3.2	3.0	3.4	0.151
CVA	1.4	1.0	2.1	0.038
Myocardial infarction	6.6 (52)	7.7 (43)	3.8	0.031
TLR (redo-PCI or CABG)	1.5	1.6	1.4	0.123
Redo-PCI	1.0	1.2	0.4	0.151
CABG	0.5	0.3	0.8	0.207

Abbreviations: CABG: Coronary Artery Bypass Graft; CPR: Cardiopulmonary Resuscitation; LAD: Left Anterior Descending Artery; LCA: Left Circumflex Artery; LM: Left Main; RCA: Right Coronary Artery.
Note: †*p* value related to the comparison among LAD, LCA and RCA success rates.

%, that is lower than other best in class CTO studies, **most of them from western countries and others from east regions**, however, **this result is** significantly higher than the 57 % reported years ago in the same community.[24,25] This data could be explained, at least in part, by the teaching nature of a such tertiary hospital where CTO PCI are performed by resident operators, fellow operators and also with the cooperation with master Euro CTO club operators; furthermore, the low retrograde approach rate might have reduced the chance to succeed when the antegrade approach failed.

As expected, patients who had unsuccessful revascularization were more likely to have complex lesions as classified by J-CTO, CASTLE and PROGRESS-CTO Scores. These findings could be interpreted as a main bias in the comparison process of the two study groups (successful versus unsuccessful). However, the finding that operators in their learning curve could achieve less percentage of success even in "simpler" cases (J-CTO score 0 or 1), while performing successfully those judged to be more difficult (J-CTO $\geq$2) with the proctor's guidance was already described in literature.[26–28]

Our paper faced off the CTO interventions trends in middle-incoming Countries and examined some issues regarding financial cost restriction and equipment limitations which might have affected the final success rate. Indeed, the lack of dedicated tools due to embargo restriction in the Iranian area such as dedicated retrograde wires, new microcatheters with excellent penetration power and torquability, dual lumen microcatheters and ADR dedicated devices, might have contributed to a less effective CTO intervention results even in the hands of very expert operators. Although, this is not always true in new emerging Countries as well as recently shown in the LATAM registry due to a lack of newer products[23], we believe that in some of our cases this issue could have played a crucial role.

4.2. Clinical outcome and follow-up

Our study confirmed that successful CTO revascularization leads to significant improvements in angina symptoms, physical performance and quality of life evaluated by SAQ questionnaire after revascularization and at one-year follow-up.

Two previous registries showed significantly greater improvement of physical limitation, angina frequency, and quality of life in patients with successful PCI of a CTO as opposed to failed procedures.[29,30] The comparison with medical management in a Canadian registry showed also a considerable benefit of a CTO revascularization either by PCI or surgery, especially in case of multi-vessel disease.[31] Similarly, the OPEN-CTO Registry demonstrated that successful CTO PCI determines early significant health status benefits.[4]

More recently, two open label controlled clinical trials, the Euro CTO trial and the IMPACTOR-CTO trial showed for the first time, in a randomized fashion, that CTO intervention is a feasible and more effective treatment option to improve anginal symptoms and quality of life of the patients than medical therapy alone.[28,32]

Furthermore, also in patients with refractory angina, Hirai and colleagues demonstrated that successful CTO PCI led to a persistent health status improvement at 12 months follow-up.[17]

While no doubts exist about the efficacy of successful CTO interventions in reduction of angina symptoms and quality of life improvement, a clear benefit of this challenge procedure in terms of hard outcomes reduction as cardiovascular mortality or other cardiovascular events has not been definitively proven yet.

Observational studies, in a propensity matched analysis, have demonstrated lower incidence of major adverse events with CTO PCI (15) as compared to medical therapy alone, even among patients with well-developed collateral circulations.[16]

Conversely, a recent randomized study[33] did not demonstrate any additional benefit of CTO PCI to medical therapy alone; however, this trial carried many caveats such as nearly 20 % of patients in the no-CTO PCI group crossed over to CTO PCI within 3 days after randomization.

Similarly, in our study, one-year MACE rate did not differ between patients with successful and unsuccessful CTO PCI (13,5 % vs 10,6 %; $p = 0{,}173$). **However, in a previous study, long-term outcomes of patients underwent CTO-PCI were related more likely to the completeness of revascularization rather than to the procedural result alone[24].**

The “vexata quaestio” concerning long term outcomes after successful CTO intervention is still debated and although dedicated large randomized trials would be needed, it is also to be remarked that in the interpretation of randomized CTO PCI trials, frequently, most symptomatic patients are excluded as well as patients with low ejection fraction that are definitely those whom revascularization benefits and improvements in long-term outcomes could be higher. **However, it is encouraging to observe that the long-term MACE rate of patients underwent unsuccessful procedures is not worse as compared to that of patients receiving a successful CTO PCI.**

5. Study limitations

This study is mainly limited by its single center retrospective not-randomized design. Second, one-year follow-up might have been too brief to draw powerful meaningful prognostic data. Third, angiographic and procedural characteristics were not evaluated by a central core lab. Fourth, clinical outcomes were not centrally adjudicated by a central events committee.

6. Conclusions

The success rate of CTO PCI in Iran has greatly improved in the last decade, becoming consistent with literature data from different international studies.

Successful CTO PCI is associated with a significant improvement in post-procedural and one-year health status evaluated by Seattle Angina Questionnaire.

Operators early in their learning curve improved significantly their skills during the three years of patient’s enrollment thanks to dedicated training.

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None.

‘What is Already Known?

- Successful CTO PCI is associated with a significant improvement in one-year health status evaluated by Seattle Angina Questionnaire.
- Success rate of CTO intervention in Iran has improved consistently with literature data despite several dedicated devices availability.

What this Study Adds?

- Dedicated training programs play a pivotal role in CTOs skill acquisition of operators with lower volume of yearly performed procedures.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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