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Outcomes of chronic total occlusion percutaneous coronary intervention in patients with reduced left ventricular ejection fraction

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Abstract

Background: The relationship between left ventricular ejection fraction (LVEF) and the success and safety of coronary chronic total occlusion (CTO) percutaneous coronary intervention (PCI) has received limited study.

Methods: We examined the clinical characteristics and outcomes of CTO PCI in the Prospective Global Registry for the Study of CTO Intervention (PROGRESS-CTO) after stratifying patients by LVEF ($\leq 35\%$, 36%–49%, and $\geq 50\%$).

Results: A total of 7827 CTO PCI procedures with LVEF data were included. Mean age was 64 ± 10 years, 81% were men, 43% had diabetes mellitus, 61% had prior PCI, 45% had prior myocardial infarction, and 29% had prior coronary artery bypass graft surgery. Technical success was similar in the three LVEF strata: 85%, 86%, and 87%, $p = 0.391$ for LVEF $\leq 35\%$, 36%–49%, and $\geq 50\%$, respectively. In-hospital mortality was higher in lower LVEF patients (1.1%, 0.4%, and 0.3%, respectively, $p = 0.001$). In-hospital major adverse cardiovascular events (MACE) were numerically higher in lower EF patients (2.7%, 2.1%, and 1.9%, $p = 0.271$). At a median follow-up of 2 months (interquartile range: 19–350 days), patients with lower LVEF continued to have higher mortality (4.9%, 3.2%, and 1.4%, $p < 0.001$) while the MACE rates were similar (9.3%, 9.6%, and 7.4%, $p = 0.172$).

Conclusion: CTO PCI can be performed with high technical success in patients with reduced LVEF but is associated with higher in-hospital and post-discharge mortality.

KEYWORDS

chronic total occlusion, clinical outcomes, left ventricular ejection fraction, percutaneous coronary intervention

1 | INTRODUCTION

Coronary artery chronic total occlusion (CTO) percutaneous coronary intervention (PCI) can be more challenging in patients with decreased left ventricular ejection fraction (LVEF), potentially requiring the use of mechanical circulatory support (MCS).^{1,2} Patients who have impaired LVEF and have a concomitant CTO have a high risk of sudden death and ventricular arrhythmias as well as poor quality of life.³ Some pilot studies demonstrated that CTO PCI can be safely performed in patients with low LVEF and can provide good outcomes with improvements in LVEF, global longitudinal strain, and decreased LV end-systolic volume.^{4–7} We evaluated the contemporary outcomes of patients with decreased LVEF who underwent CTO PCI in a large multicenter CTO PCI registry.

2 | METHODS

We examined in-hospital outcomes of CTO PCI in the Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO registry, NCT02061436) after stratifying patients into three groups based on LVEF ($\leq 35\%$, 36%–49%, and $\geq 50\%$).⁵ PROGRESS-CTO includes CTO PCI procedures performed at 53 centers from the United States, Canada, Greece, Turkey, Egypt, Russia, and Lebanon.⁸

2.1 | Definitions

CTOs were defined according to the definition of CTO Academic Research Consortium, with the absence of antegrade flow through

the lesion with a presumed or documented duration of ≥ 3 months with Thrombolysis in Myocardial Infarction (TIMI) grade 0 flow.⁹

Technical success was defined as the successful canalization of the CTO vessel with $<30\%$ residual stenosis and final TIMI 3 flow. Major adverse cardiovascular events (MACE) were defined as the composite of death, myocardial infarction (MI), stroke, urgent repeat revascularization (re-PCI or surgery), or pericardiocentesis. Procedural success was defined as technical success in the absence of in-hospital MACE.

The study was approved by an institutional review board of each site.

2.2 | Statistical analysis

Continuous variables were presented as mean \pm standard deviation and median (interquartile range) and compared using the independent *t*-test or Mann–Whitney *U* test, as appropriate. Categorical variables were presented as absolute numbers and percentages and compared using χ^2 or Fisher's exact test, as appropriate. Multivariable logistic regression was performed to identify parameters associated with in-hospital death; variables with $p < 0.10$ on univariable analysis were included in the multivariable model. Statistical analysis was performed using Stata v17.0 (StataCorp).

3 | RESULTS

After excluding centers with <40 case entries to the registry and cases with missing LVEF information (2251), this analysis included 7827 patients who underwent CTO PCI at 38 centers in

TABLE 1 Baseline characteristics and CTO crossing strategies stratified by left ventricular ejection fraction

Characteristics/variables	EF ≤35% N = 1239	EF 36%–49% N = 1617	EF ≥50% N = 4971	p value
Mean age	65 ± 10	65 ± 10	64 ± 1.3	0.563
Men, n (%)	1024 (85%)	1295 (83%)	3747 (79%)	<0.001
Mean LVEF (%)	27 ± 6.6	43 ± 3.3	58 ± 6.0	
Technical (angiographic) success, n (%)	1051 (86)	1381 (86)	4273 (87)	0.391
J-CTO	2.4 ± 1.2	2.4 ± 1.3	2.3 ± 1.3	0.002
PROGRESS-CTO	1.3 ± 1.0	1.3 ± 1.0	1.2 ± 1.0	0.942
HTN, n (%)	1055 (89)	1408 (91)	4169 (89)	0.034
DM, n (%)	605 (51)	704 (46)	1827 (39)	<0.001
Smoking				<0.001
Current, n (%)	357 (31)	430 (28)	1128 (24)	
Past (>1 year year), n (%)	434 (38)	521 (34)	1700 (37)	
Never, n (%)	362 (31)	570 (37)	1767 (38)	
Baseline creatinine	1.37 ± 1.24	1.21 ± 0.99	1.11 ± 0.76	<0.001
Atrial fibrillation, n (%)	152 (19)	154 (14)	374 (11)	<0.001
Prior HF, n (%)	952 (81)	657 (44)	600 (13.0)	<0.001
Prior MI, n (%)	656 (58)	862 (58)	1730 (38)	<0.001
Prior PCI, n (%)	717 (60)	1012 (65)	2915 (60)	0.006
Prior CABG, n (%)	328 (27)	542 (34)	1346 (28)	<0.001
Dyslipidemia, n (%)	1046 (88)	1348 (87)	3992 (85)	0.021
RHC during CTO PCI, n (%)	85 (12)	44 (4.6)	74 (2.5)	<0.001
LV assist device used, n (%)	176 (16.3)	66 (4.7)	62 (1.5)	<0.001
Prophylactic use of LV assist device, n (%)	151 (12)	48 (3.0)	31 (0.6)	<0.001
Urgent use of LV assist device, n (%)	16 (1.3)	17 (1.1)	22 (0.4)	0.001
Cerebrovascular disease, n (%)	143 (12)	163 (11)	455 (10)	0.06
Chronic lung disease, n (%)	215 (18)	214 (14)	625 (14)	<0.001
On dialysis at baseline, n (%)	56 (4.8)	47 (3.1)	77 (1.7)	<0.001
Length of hospital stay	2.3 ± 3.9 (906)	1.7 ± 3.1 (1,231)	1.4 ± 2.3 (3,693)	<0.001
CTO target vessel				<0.001
Left main, n (%)	5 (0.43)	9 (0.58)	20 (0.42)	
LAD, n (%)	389 (33)	408 (26)	1196 (25)	
LCx, n (%)	246 (21)	321 (21)	864 (18)	
RCA, n (%)	511 (44)	781 (51)	2601 (55)	
SVG, n (%)	0 (0)	3 (0.2)	6 (0.1)	
Other, n (%)	17 (1.5)	19 (1.2)	55 (1.2)	
CTO lesion length >20 mm, n (%)	763 (74)	925 (68)	2582 (63)	<0.001
Moderate or severe calcification (CTO lesion), n (%)	582 (50)	728 (48)	2,087 (44)	<0.001

(Continues)

TABLE 1 (Continued)

Characteristics/variables	EF ≤35% N = 1239	EF 36%–49% N = 1617	EF ≥50% N = 4971	p value
Orbital atherectomy, n (%)	12 (0.9)	19 (1.2)	40 (0.8)	0.375
Rotational atherectomy, n (%)	52 (4.1)	59 (3.6)	174 (3.5)	0.506
Atherectomy for a last remaining vessel	7 (0.6)	3 (0.2)	19 (0.4)	0.258
Successful crossing strategy				0.329
AWE, n (%)	669 (55)	852 (54)	2746 (56)	
ADR, n (%)	154 (13)	192 (12)	607 (12)	
Retrograde, n (%)	241 (20)	331 (21)	895 (18)	
None, n (%)	156 (13)	217 (14)	619 (13)	

Abbreviations: CABG, coronary artery bypass graft surgery; CTO, chronic total occlusion; DM, diabetes mellitus; HF, heart failure; HTN, hypertension; J-CTO, The Japanese Multicenter CTO Registry score; LAD, left anterior descending; LCx: left circumflex; LV, left ventricle; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PROGRESS-CTO, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention score; RCA, right coronary artery; RHC, right heart catheterization; SVG, saphenous vein graft; PCI, percutaneous coronary intervention.

five countries (mainly the United States followed by Russia, Turkey, Greece, and Egypt). Mean age was 64 ± 10 years, and 81% of patients were men with high prevalence of hypertension (90%), diabetes mellitus (43%), dyslipidemia (87%), prior coronary artery bypass graft surgery (CABG) (29%), prior PCI (62%), current smoking (26%), and prior MI (45%).

3.1 | LVEF stratification

Of the 7827 patients; 1239 had LVEF ≤35%, 1617 had LVEF 36%–49%, and 4971 had LVEF ≥50%. The baseline clinical characteristics and CTO crossing strategies are presented in Table 1. Patients with lower LVEF had higher J-CTO scores ($p = 0.002$) but similar PROGRESS-CTO scores ($p = 0.942$). They were also more likely to have multiple comorbidities, such as hypertension, dyslipidemia, diabetes mellitus, current smoking, high creatinine, coexisting atrial fibrillation, prior heart failure, and prior MI. Patients with lower LVEF (≤35%, 36%–49%, and ≥50%) were more likely to undergo PCI of left anterior descending artery CTOs (33%, 26%, and 25%, respectively, $p < 0.001$) and more likely to have longer CTO lesion length (average lesion length, 32.5 mm, 32.1 mm, and 29.6 mm, respectively, $p < 0.001$).

MCS was used in 3.6% of the overall cohort, more frequently in lower LVEF groups (16%, 5%, and 1.5%, $p < 0.001$), respectively for LVEF ≤35%, 36%–49%, and ≥50%. Prophylactic use of MCS (defined as before CTO PCI) was also more common in the lower LVEF groups (12%, 3%, and 0.6%, $p < 0.001$), as was the urgent use of MCS (1.3%, 1.1%, and 0.4%, $p = 0.001$). Technical success was similar in all LVEF groups (86%, 86% and 87%, $p = 0.391$).

3.2 | Complications

Patients with LVEF ≤35% had significantly higher in-hospital mortality ($p = 0.001$) and contrast-induced nephropathy ($p = 0.002$) compared with other groups. A total of 163 MACE were reported. Baseline LVEF was not associated with MACE (2.7%, 2.1%, and 1.9%, $p = 0.183$), respectively for LVEF ≤35%, 36%–49%, ≥50%; acute MI, stroke, re-PCI, or emergency CABG (Table 2). Procedural success was similar across the LVEF groups (84%, 84%, and 85%, respectively, $p = 0.442$).

A total of 45 in-hospital deaths were reported. For 44/45 deaths (98%), the cause of death was cardiovascular (Supplementary Online Material). Compared with patient who survived CTO PCI, patients who died were older (72 ± 8 , 64 ± 10 , $p < 0.001$), had lower LVEF ($42 \pm 17\%$ vs. $50 \pm 13\%$, $p < 0.001$), higher J-CTO score (2.8 ± 1.2 vs. 2.4 ± 1.3 , $p = 0.04$), and were more likely to have had prior CABG (55% vs. 29%, $p < 0.001$). They also had higher baseline creatinine (1.5 ± 1.2 vs. 1.2 ± 0.9 , $p = 0.03$), and more often received MCS: 13%, 4%, and 1%, $p < 0.001$ respectively for LVEF ≤35%, 36%–49%, and ≥50%.

On multivariable logistic regression that included successful crossing strategy, J-CTO score, age, and LVEF (that all had $p < 0.10$ in univariable analysis), the association between these variables and mortality was as follows: successful retrograde crossing strategy odds ratio (OR): 2.83 (95% confidence interval [95% CI], 1.14–7.02), $p = 0.025$; J-CTO score OR: 1.10 (95% CI, 0.80–1.54), $p = 0.537$; age (for every 10 year increase) OR: 2.13 (95% CI, 1.45–3.13), $p < 0.001$; LVEF (for every 10% decrease) OR: 1.38 (95% CI, 1.08–1.76), $p = 0.01$. Complications during the follow-up period are reported in Supplementary Online Material.

TABLE 2 In-hospital clinical events stratified by left ventricular ejection fraction

In-hospital events	LVEF ≤35% n = 1239	LVEF 36-49% n = 1617	LVEF ≥50% n = 4971	p value
Death, n (%)	14 (1.13)	6 (0.37)	16 (0.32)	0.001
MACE, n (%)	33 (2.66)	34 (2.10)	96 (1.93)	0.183
Acute MI, n (%)	8 (0.65)	16 (0.99)	26 (0.52)	0.123
Stroke, n (%)	3 (0.24)	4 (0.25)	6 (0.12)	0.362
re-PCI, n (%)	2 (0.16)	4 (0.25)	11 (0.22)	0.882
Emergency CABG, n (%)	1 (0.08)	2 (0.12)	4 (0.08)	0.858
Tamponade, n (%)	8 (0.65)	8 (0.50)	36 (0.73)	0.612
Perforation, n (%)	58 (4.70)	95 (5.89)	248 (5.00)	0.278
Pericardiocentesis, n (%)	14 (1.13)	8 (0.50)	47 (0.95)	0.144
Vascular access complications, n (%)	19 (1.54)	13 (0.81)	57 (1.15)	0.189
Dissection/thrombus of donor artery, n (%)	5 (0.40)	13 (0.81)	39 (0.79)	0.341
Bleeding, n (%)	12 (0.97)	14 (0.87)	24 (0.48)	0.069
Aortocoronary dissection, n (%)	1 (0.08)	5 (0.31)	17 (0.34)	0.312

Abbreviations: CABG, coronary artery bypass graft surgery; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

4 | DISCUSSION

The main findings of our study are that patients with decreased LVEF undergoing CTO PCI have similar technical success, procedural success, and overall risk of MACE as those with higher LVEF, but have a higher in-hospital and post-discharge mortality ([Supplementary Online Material](#)).

CTO PCI is performed frequently in patients with reduced LVEF: 16% of all CTO PCIs in the PROGRESS-CTO registry were performed in patients with LVEF ≤35%, which is higher than a previously published study from Europe (8.6%).⁵

In our study, patients with low LVEF underwent CTO PCI with high technical success rates, similar to those with normal LVEF. Moreover, they had a similar overall risk of in-hospital and follow-up MACE but had higher in-hospital and follow-up mortality even after adjusting for potential confounders.

One of the potential explanations for the higher mortality in patients with low LVEF is higher comorbidity burden. While lower LVEF was associated with death in multivariable analysis, patients with lower LVEF had higher risk characteristics, such as prior MI, chronic kidney disease, and chronic lung disease that may have affected subsequent clinical outcomes. Second, while we did not find any statistically significant associations between low LVEF and complications other than death, complications that resulted in death might have been considered less important and less likely to be recorded since the patient died. Third, the more frequent use of MCS devices and the complications associated with their use might have increased mortality in patients with low LVEF. Fourth, patients with low LVEF would be expected to be less tolerant of ischemia, in case of a complication.

A study by Galassi et al.,⁵ reported findings that are similar to ours, with high overall CTO PCI success rates (93.6%) even in patients with low LVEF. Similar to the findings of Galassi et al., we also found high prevalence of comorbidities in patients with low LVEF. While in the Galassi study the incidence of periprocedural events was not compared between LVEF strata, the incidence of periprocedural complications was 6.52% (36/552) in LVEF ≥50%, 8.83% (19/215) in LVEF 35%–50%, and 4.2% (3/72) in LVEF ≤35% patients.⁵ Similarly, in our study, we did not observe a statistically significant difference in MACE between the LVEF strata.

In line with our findings, a recent study of 75 patients investigating the relationship between baseline LVEF and CTO PCI outcomes demonstrated similar technical success rates between the LVEF strata (<40%, 40%–49%, and ≥50%) despite higher comorbidity burden in patients with low LVEF. Moreover, MACE rates were comparable between the LVEF strata at 6-month follow-up.¹⁰

In contrast to our findings, a preliminary study of 65 patients who underwent CTO PCI showed that patients with low LVEF (<50%) had lower recanalization rates (75% vs. 94%) and higher in-hospital mortality (3% vs. 0%) compared with patients who had LVEF >50%.¹¹

4.1 | Limitations

Our study has important limitations. First, we did not adjust for multiple statistical comparisons of all-cause mortality, which could increase false-positive findings. Second, because absolute numbers for MACE were low, false-negative findings cannot be excluded.

Third, our registry lacks a clinical events adjudication committee. Fourth, follow-up was limited to 35% of all patients.

5 | CONCLUSION

CTO PCI is performed with high technical success rates regardless of baseline LVEF. Lower LVEF is associated with higher in-hospital and postdischarge mortality, but similar incidence of periprocedural and post-discharge MACE.

CONFLICT OF INTERESTS

Dr. Brilakis: consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor *Circulation*), Amgen, Asahi Intecc, Biotronik, Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), ControlRad, CSI, Elsevier, GE Healthcare, IMDS, InfraRedx, Medicare, Medtronic, Opsens, Siemens, and Teleflex; research support: Boston Scientific, GE Healthcare; owner, Hippocrates LLC; shareholder: MHI Ventures, Cleerly Health, Stallion Medical. Dr. Alaswad: consultant and speaker for Boston Scientific, Abbott Cardiovascular, Teleflex, and CSI. Dr. Karpaliotis: Honoraria: Boston Scientific, Abbot Vascular; Equity: Saranas, Soundbite, Traverse Vascular. Dr. Jaffer: Sponsored research: Canon, Siemens, Shockwave, Teleflex, Mercator, Boston Scientific; Consultant: Boston Scientific, Siemens, Magenta Medical, IMDS, Asahi Intecc, Biotronik, Philips, Intravascular Imaging. Equity interest – Intravascular Imaging Inc, DurVena. Massachusetts General Hospital – licensing arrangements: Terumo, Canon, Spectrawave, for which FAJ has the right to receive royalties. Dr. Doshi: speaker's bureau for Abbott Vascular, Boston Scientific, and Medtronic and research support from Biotronik. Dr. Khatri: Personal Honoria for proctoring and speaking: Abbott Vascular, Asahi Intecc, Terumo, Boston Scientific. Dr. Davies: honoraria/consulting from Medtronic, Seimens Healthineers, and Asahi intec. Dr. Patel: Consulting Honoraria from Abbott, Medtronic, Terumo, Cardiovascular Systems, Inc. Dr. ElGuindy: Consulting Honoraria: Medtronic, Boston Scientific, Asahi Intecc, Abbott; Proctorship fees: Medtronic, Boston Scientific, Asahi Intecc, Terumo; Educational grants: Medtronic. Others: None.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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