Catheterization and Cardiovascular Interventions

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Mechanical Circulatory Support With Impella in High-Risk Patients With Chronic Total Occlusion and Complex Multivessel Disease

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ABSTRACT

Background: The therapeutic management of patients with multivessel disease and severe left ventricular dysfunction is complex and controversial.

Aims: The aim of this study was to analyze the clinical outcomes and the changes in left ventricular ejection fraction (LVEF) in patients with severe left ventricular dysfunction and at least one chronic total occlusion (CTO) undergoing percutaneous coronary intervention (PCI) with hemodynamic support provided by Impella.

Methods: Retrospective, multicenter study enrolling patients with severe left ventricular dysfunction and severe coronary artery disease with at least one CTO who required percutaneous mechanical circulatory support with Impella, from January 2019 to December 2023. The primary endpoints were the incidence of MACE (composite of cardiovascular death, acute myocardial infarct, and target lesion revascularization) at 90 days. The secondary endpoint was changes in LVEF and functional class during the same period.

Results: A total of 27 patients (34 CTOs) were included in the study. The mean SYNTAX score was 35 ± 11. The median J-CTO score of 2 (1–3). At 90 day of follow-up, there were three MACE (11%), two cardiovascular deaths and one TLR; three vascular complications were related to access for the Impella device (only one required invasive treatment); and LVEF improved significantly after revascularization (delta LVEF: 10% [CI 95% 6, 15]). A total of 81% of patients improved their angina or dyspnea status at 90 days.

Conclusions: In high-risk patients with severe left ventricular dysfunction with complex coronary disease including CTO, PCI with mechanical circulatory support using the Impella device is associated with favorable safety and efficacy outcomes at short-term follow-up.

Soledad Ojeda and Manuel Pan contributed equally to this study as senior authors.

1 | Introduction

Coronary artery disease is currently the most frequent cause of heart failure and left ventricular dysfunction [1]. Coronary artery bypass grafting (CABG) is the revascularization technique of choice for patients with complex coronary anatomy and left ventricular ejection fraction (LVEF) < 35% [2, 3]. However, percutaneous revascularization may be considered in selected patients with angina and high risk for CABG or in those patients who refuse surgery [4]. The presence of a CTO in the context of multivessel disease and poor LVEF complicates the percutaneous procedure due to lower success rates and higher incidence of complications [5]. The manipulation of the contralateral donor vessel for lesion treatment or retrograde access to the chronically occluded vessel may induce prolonged ischemia and hemodynamic deterioration, sometimes with catastrophic consequences [6]. The development of ventricular assist devices may improve the safety of percutaneous revascularization in these patients providing certain protection toward hemodynamic compromise and severe complications during the procedure [7]. The aim of this study was to analyze the clinical outcomes and the changes in LVEF in patients with poor left ventricular function and at least a CTO who underwent percutaneously revascularization with mechanical circulatory support (MCS) with Impella (Abiomed, Danvers, MA).

2 | Materials and Methods

2.1 | Study Design and Population

We performed a retrospective, multicenter study enrolling patients with severe left ventricular dysfunction and severe coronary artery disease with at least one CTO who required percutaneous MCS with Impella CP. The study protocol was approved by the Local Clinical Research Ethics Committee according to institutional and Good Clinical Practice guidelines of the 1975 Declaration of Helsinki. Participants were recruited between January 2019 and December 2023 at three centers from Spain and the United States. We included all the patients who multivessel diseases with received percutaneous MCS with Impella during PCI of at least a CTO that presented dyspnea or angina in functional class III–IV and LVEF ≤ 35%. The use of percutaneous hemodynamic support for high-risk percutaneous coronary intervention (PCI) was due to likely prolonged ischemia (retrograde approach or revascularization of more than two territories) and severe LVEF. All patients included had been rejected for CABG by the Heart Team.

2.2 | Endpoints and Definitions

The primary endpoint was the incidence of MACE (composite of cardiovascular death, acute myocardial infarct, and target lesion revascularization) at 90 days, as well as changes in LVEF and functional class during the same period. Death before LVEF assessment at follow-up was considered as an intercurrent event and no change in LVEF was assumed in those patients. Secondary endpoints were changes in left ventricular volumes and the individual components of MACE at follow-up. Other in-hospital complications were also analyzed: death, stroke, tamponade, mayor bleeding, vascular complications, and acute kidney injury.

Periprocedural myocardial infarction was defined by an elevation of cTn values > 5 times of the ninth percentile upper reference limit in patients with normal baseline values; if cTn level are stable (≤ 20% variation) must meet the criteria for a > 5 fold increase and manifest a change from the baseline value of > 20%; these criteria must be accompanied by electrocardiographic changes according to the fourth universal definition of myocardial infarction [8]. Major bleeding was defined according to type 3 or 5 of the BARC criteria (Bleeding Academic Research Consortium) [9]. Technical success was defined as residual stenosis < 30% with TIMI 2–3 flow in the CTO vessel and all its ≥ 2.5 mm branches. Procedural success was defined as technical success and the absence of in-hospital major adverse cardiovascular events (death, MI, or target vessel revascularization [TVR]) [10]. Post-PCI acute kidney injury was defined as an absolute increase in serum creatinine of 0.3 mg/dL or more (≥ 26.4 μmol/L) or a ≥ 50% increase in serum creatinine (1.5-fold from baseline) within 48 h; or a reduction in urine output (documented oliguria of < 0.5 mL/kg/h for > 6 h) [11]. The cut-off points to define chronic kidney disease (CKD) was a glomerular filtration rate (GFR) < 60 mL/min/1.73 m for more than 6 months or due to the presence of a structural or functional renal alteration (sediment, image, histology). Heart failure and angina severity were determined according to the New York Heart Association (NYHA) classification and the Canadian Cardiovascular Society (CCS) angina grade, respectively. LVEF and left ventricular volumes were quantified by the Simpson technique [12]. Surgical risk was calculated using the Euroscore II scale [13]. Extensive coronary disease was calculated with the SYNTAX score [14]. The anatomic complexity of CTO was assessed using the J-CTO score and the PROGRESS-CTO anatomic score [15–17]. The risk of complications was estimated using the PROGRESS-CTO complications risk scores. Complete revascularization was defined as the revascularization of any lesion with > 70% stenosis in vessels > 2 mm, 50% for left main lesions or intermediate lesions demonstrating ischemia as assessed by intracoronary physiology (FFR or resting indices).

2.3 | Data Collection at Follow Up

The collection of clinical follow-up variables at the end of the 90 days postprocedure was carried out by reviewing electronic medical records and/or phone calls. An echocardiography study was obtained at baseline conditions and after the revascularization procedures within this period.

2.4 | Statistical Analysis

Categorical data are presented as counts (percentages) and continuous data as mean ± standard deviation or median (interquartile range). Between groups comparisons were made using the Student's *t* test for continuous variables and Wilcoxon test for ordinal variables. All tests were 2-tailed and were

TABLE 1 | Baseline characteristics.

	N: 27
Age (years) (mean, SD)	63 (±9)
Male	25 (93%)
Hypercholesterolemia	19 (70%)
Diabetes	11 (41%)
Hypercholesterolemia	18 (67%)
Smoker history	16 (59%)
Prior heart failure	19 (70%)
Prior ischemic heart disease	8 (30%)
Prior PCI	7 (26%)
Prior CABG	1 (4%)
Prior stroke	2 (7%)
Peripheral artery disease	9 (33%)
Prior atrial fibrillation	3 (11%)
COPD	5 (19%)
Chronic kidney disease	7 (26%)
Euroscore II (mean, SD)	5.07 (±3.8)
Hemoglobin (mg/dl) (mean, SD)	14 (±1.95)
Glomerular filtration rate (mL/min) (mean, SD)	59 (±21)
Hs-cTnI (ng/l) (median, IQR)	174 (49–1116)
NT-proBNP (pg/mL) (median, IQR)	5881 (3938–7439)

Abbreviations: CABG, Coronary artery bypass grafting; COPD, Chronic obstructive pulmonary disease; Hs-cTnI, High sensitivity cardiac troponin I; IQR, Interquartile range; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCI, Percutaneous coronary intervention; SD, Standard deviation.

considered significant when $p < 0.05$. Statistical analyses were performed using SPSS software (version 24; IBM Corp., Armonk, NY, USA).

3 | Results

3.1 | Baseline Clinical Characteristics

A total of 27 patients were included. The baseline characteristics of the patients are shown in Table 1. Twenty-five patients were men (93%), and the mean age of 63 ± 9 years The majority of patients had the main cardiovascular risk factors. Seventy percent of the patients had prior heart failure. Surgical risk was moderate to high (median EuroScore II 5.1 ± 3.8). Thirteen patients (48%) had CCS 3–4 angina and 20 (74%) had NYHA 3–4 dyspnea (Figure 1).

3.2 | Angiographic and Procedural Data

The main angiographic and procedural variables are shown in Table 2. Eleven patients (41%) had two-vessel coronary disease and 14 patients (52%) had three-vessel disease. Seven patients (26%) presented left main coronary artery disease. The mean SYNTAX score was 35 ± 11. A total of 34 occlusions were included, and the most frequent target vessel was the right coronary artery (*n*: 16, 47%). In 13 cases the CTO involved a bifurcation (38%), and in eight cases, the CTO was branch ostial (24%). Most CTOs were at least of intermediate difficulty ($n = 30$, 88%) with a median J-CTO score of 2 [1–3]. The median of the PROGRESS-CTO score was 1 [1, 2]. In 85% of the cases,

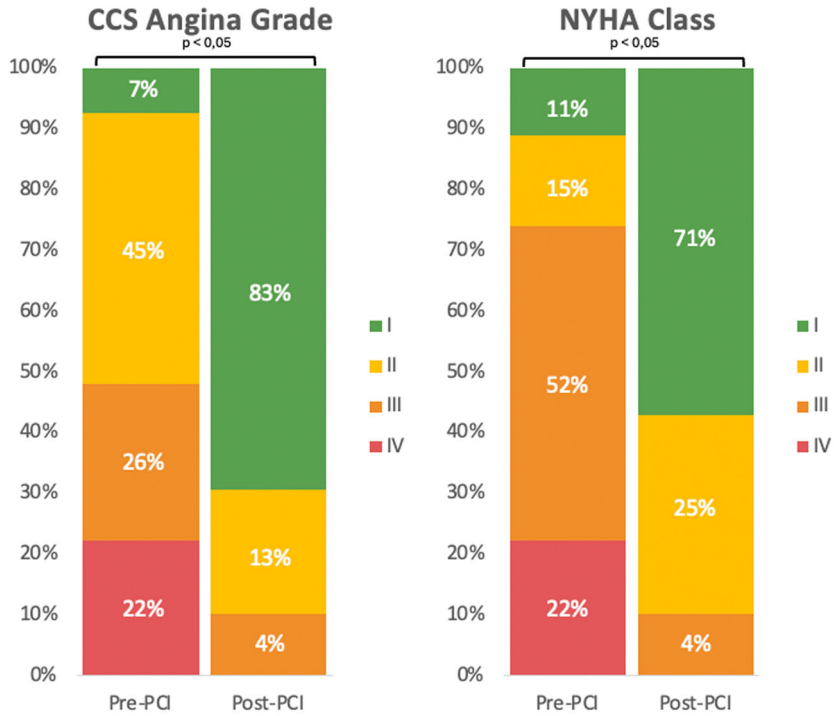

FIGURE 1 | Baseline clinical status and at 90 days. CCS: Canadian Cardiovascular Society. NYHA: New York Heart Association. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 | Angiographic and procedural characteristics.

	***N*: 27 PATIENTS; *N*: 34 CTOS**
Severity of coronary artery disease	
Left main coronary artery	7 (26%)
Two-vessel coronary artery disease	11 (41%)
Three-vessel coronary artery disease	14 (52%)
SYNTAX score (mean, SD)	35 (±11)
Residual SYNTAX score (mean, SD)	10.8 (±14)
Target vessel CTO	
Left anterior descending	13 (38%)
Circumflex	5 (15%)
Right coronary artery	16 (47%)
Distal cap at bifurcation	13 (38%)
Ostial CTO	8 (24%)
Aorto ostial CTO	4 (12%)
Blunt stump	21 (62%)
Length of occlusion > 20 mm	29 (85%)
Bending > 45°	11 (32%)
Calcification moderate-severe	18 (53%)
Reattempt	2 (6%)
Proximal cap ambiguity	19 (56%)
Proximal vessel tortuosity	10 (29%)
Interventional collaterals	29 (85%)
CTO length (mean, SD)	49 (±29)
Lesion length (mean, SD)	62 (±31)
J-CTO SCORE (median, IQR)	2 (1–3)
PROGRESS CTO Score (median, IQR)	1 (1–2)
PROGRESS CTO Complication (median, IQR)	
MACE Risk	2.5 (1–4)
Mortality Risk	1.4 (0.2–3)
Perforation Risk	3.0 (1–6)
Pericardiocentesis Risk	2.0 (0.5–3)
Acute Myocardial Infarction Risk	0.5 (0.2–1)
Wires (mean, DS)	4 (±3)
Vascular access for CTO PCI	
Radial	1 (4%)
Femoral	4 (14%)
Radial + femoral	13 (48%)
Femoral + femoral	8 (30%)
Radial + Axilar	1 (4%)
Impella access	
Transfemoral	23 (85%)
Transaxillar	3 (11%)
Transcarotid	1 (4%)
Support device taken out in cath lab at procedure end	20 (74%)
Successful crossing technique	
AW	16 (47%)
ADR	3 (9%)
RW	3 (9%)
RDR	9 (26%)
Laser atherectomy	1 (3%)
Rotational atherectomy	5 (15%)
Lithotripsy	1 (3%)
Intravascular ultrasound	23 (68%)
Contrast volume (mL) (median, IQR)	218 (±106)
Fluoroscopy time (min) (median, IQR)	67 (±23)
Radiation dose (mGy) (median, IQR)	1,296 (632–2686)
Complete revascularization	15 (56%)
Technical success	31 (91%)
Procedural success	31 (91%)

Abbreviations: ADR, Anterograde dissection and re-entry; AW, Anterograde wiring; CTO, Chronic total occlusion; IQR, Interquartile range; RDR, Retrograde dissection and re-entry; RW, Retrograde wiring; SD, Standard deviation.

the vascular access for MCS with the Impella device was transfemoral (n: 23), three cases were performed through transaxillary access (11%) and one case through transcarotid access (4%) [18]. Technical and procedural success was observed in 31 patients (91%). The most common successful crossing technique was antegrade wiring (*n*: 16, 47%), followed by retrograde dissection and re-entry (*n*: 9, 26%). Advanced plaque modification techniques were only used in seven CTO recanalization attempts (21%). In 23 CTOs (68%), revascularization was guided by intravascular ultrasound.

3.3 | Changes in Echocardiographic Parameters

The mean baseline LVEF was 23 ± 7%. At 90 days follow-up, left ventricular function improved significantly after revascularization (delta LVEF: 10% [CI 95% 6, 15]). Similarly, left ventricle end-diastolic (LVEDV) and end-systolic volumes (LVESV) also presented a statistically significant improvement (delta LVEDV: −35 mL [CI 95% −58, −11] and delta LVESV: −59 mL [CI 95% −80, −38]) (Table 3; Figure 2; and Supporting Information S2: Video 1).

TABLE 3 | Echocardiographic parameters.

	Pre-PCI	Post-PCI	Delta (CI)	*p* value
LVEF (%)	23 (±7)	33 (±12)	10% (CI 95% 6, 15)	< 0.005
LVEDV (mL) (mean, DS)	198 (±45)	164 (±46)	35 mL (CI 95% −58, −11)	< 0.005
LVESV (mL) (mean, DS)	175 (±55)	116 (±48)	59 mL (CI 95% −80, −38)	< 0.005

Abbreviations: LVEDV, Left ventricular end-diastolic volume; LVEF, Left ventricular ejection fraction; LVESV, Left ventricular end systolic volume; PCI, Percutaneous coronary intervention; SD, Standard deviation.

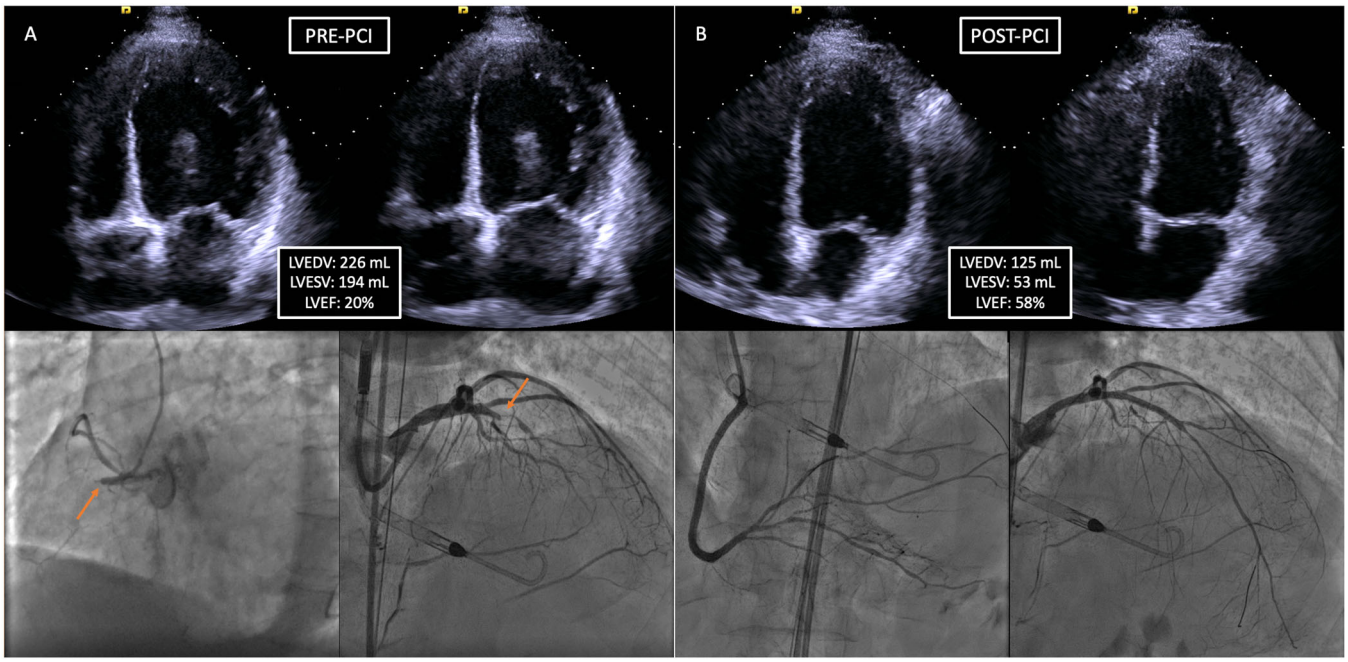

FIGURE 2 | Results of a registry case. (A) Echocardiogram and baseline coronary angiography. (B) Echocardiogram and coronary angiography after percutaneous revascularization. LVEDV, Left ventricular end-diastolic volume; LVEF, Left ventricular ejection fraction; LVESF, Left ventricular end-systolic volume; PCI, Percutaneous coronary intervention. [Color figure can be viewed at wileyonlinelibrary.com]

3.4 | In-Hospital Events

During the hospital admission, the following events occurred: an intraprocedural myocardial infarction (4%) and a cardiac tamponade (4%) that caused the death of the patient. Additionally, four vascular complications were observed (15%): three local hematomas with spontaneous resolution and one complete occlusion of the femoral artery that required recanalization with a stent. Three of these complications were related to access for the Impella device and one with the contralateral femoral access. Three patients (12%) presented acute kidney injury post-PCI that resolved with intravenous hydration (Table 4).

3.5 | Clinical Results at Follow Up

At 90 days of follow-up, there were 3 MACE (11%), two cardiovascular deaths and one TLR (both deaths were due to sudden death). Twenty-two (81%) patients improved their angina or dyspnea status at 90 days, all, except the two patients whose revascularization was not successful (Figure 1).

4 | Discussion

The main findings of our study were (1) High-risk PCI with Impella support in patients with CTO was safe and effective, with a reasonable rate of major complications during the procedure and adverse events at short-term follow-up; (2) The majority of presented significant clinical improvement after the procedure; (3) LVEF improved significantly after revascularization on 90-day follow-up (Figure 3). The significant technological progress witnessed by interventional cardiology and the presence of an aging population with a higher comorbidity burden and a high surgical risk have led to an increase in the use of percutaneous revascularization in many scenarios such as complex coronary interventions (like revascularization of left main disease, bifurcated or calcified lesions, or total chronic occlusions). In particular, CTO PCI has received intense scrutiny, and there is compelling evidence that it is associated with significant improvement in angina status, quality of life, and functional capacity [6, 19]. However, this high complexity is associated with higher risk of complications and technical challenges, particularly in cases with severe left ventricular dysfunction. In this context, the use of MCS such as the Impella device makes it possible

to minimize the risk of hemodynamic compromise during the procedure and increase its safety [20]. Recently published studies have reported favorable data regarding Impella protected-percutaneous revascularization in patients with extensive coronary disease and severe ventricular dysfunction [7, 21]. To date, the PROTECT III [21] study is the largest trial published in patients undergoing PCI with severely depressed LVEF function and percutaneous MCS with Impella and included 13.6% of patients with CTO. They report a low percentage of in-hospital events with a percentage similar to our series in terms of events at 90 days. Compared to this trial, our series presents a slightly higher percentage of vascular complications requiring intervention and acute kidney injury, probably related to longer and more complex procedures. However, they report a similar percentage of in-hospital death.

TABLE 4 | Clinical outcomes.

In-hospital	
Death	1 (4%)
Periprocedural MI	1 (4%)
Stroke	0
Tamponade	1 (4%)
Mayor bleeding	0
Vascular complication requiring intervention	1 (4%)
Acute kidney injury	3 (11%)
At 90 days	
MACE	3 (11%)
Cardiovascular death	2 (7%)
AMI	0
TLR	1 (4%)

Abbreviations: AMI, acute myocardial infarction; MACE, Major adverse cardiac events; TLR, Target lesion revascularization.

Although the benefit of coronary revascularization has been demonstrated in different scenarios, the implication in patients with heart failure with reduced ejection fraction (HFrEF) and extensive coronary artery disease has recently been discussed. Recently, this benefit is under debate as a result of the publication of the REVIVED-BCSI2 trial [22]. This study has concluded the absence of prognostic benefit of revascularization and improvement of LVEF by PCI compared to optimal medical treatment. Data very different from those reported by numerous studies and from those obtained in our registry, as already indicated [21–24].

Despite the importance of improved prognosis and ventricular function in these patients, one aspect to highlight is the benefit of revascularization from a symptomatic perspective. The indication for revascularization in symptomatic patients with optimal medical treatment is established [4]. In this sense, in these important studies, PCI has shown improvement in quality of life and functional class [22]. Specifically, the RESTORE EF study, a retrospective registry that included 406 patients Impella protected-percutaneous revascularization, reported a significant improvement in dyspnea and angina [23]. Curiously, only one of these trials included patients with CTOs [21]. In our series, patients present a very significant improvement in functional class in line with the improvement reported in the evidence regarding recanalization of CTOs [25].

In recent years, several multicenter registries have been published that evaluate the use of percutaneous MCS in CTO PCI [26–28]. These registries demonstrate that the use of MCS in these procedures is increasing with a percentage that is around 4% of all CTO-PCI. In turn, they reported that the use of elective percutaneous MCS in PCI-CTO was used in patients with complex clinical and angiographic characteristics with a success

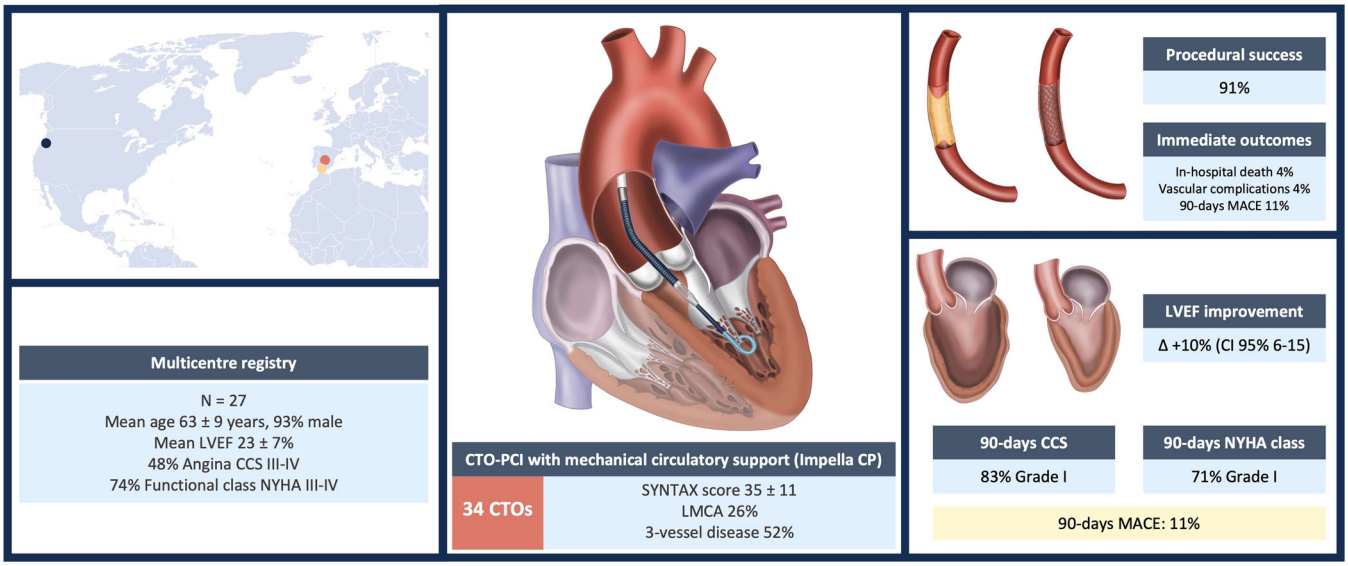

FIGURE 3 | Central illustration. Main findings of the study. CCS, Canadian Cardiovascular Society; CTO, Chronic total occlusion; LVEF, Left ventricular ejection fraction; MACE, Major adverse cardiac events; NYHA, New York Heart Association; PCI, Percutaneous coronary intervention. [Color figure can be viewed at wileyonlinelibrary.com]

rate similar to patients who did not receive elective percutaneous MCS, at the cost of an increased risk of bleeding and vascular complications. To date, only one study focused on PCI-CTO with MCS with Impella has been published [29]. Riley et al. published a series of 57 patients with hospital complications similar to those in our study. In contrast, they do not evaluate clinical results, symptomatic or echocardiographic improvement during follow-up.

5 | Limitations

The present study has several limitations, including the small sample size, the inherent limitations of retrospective designs and selective reporting, lack of angiogram and clinical event adjudication by core laboratory and clinical event committee, and the fact that the operators who participated in this study are very experienced in this type of procedures, which can limit the external validity of our findings. On the other hand, only those patients who underwent Impella-assisted PCI were included, excluding those whose Impella was not or could not be used.

6 | Conclusions

In patients with severe left ventricular dysfunction with complex coronary disease who present CTO, advanced symptoms and a high surgical risk, percutaneous revascularization with MCS using the Impella device is associated with a good safety and efficacy profile on short-term follow-up.

Conflicts of Interest

L. Azzalini received consulting fees from Teleflex, Abiomed, GE Healthcare, Reflow Medical, and Cardiovascular Systems Inc; serves on the advisory board of GE Healthcare; and owns equity in Reflow Medical. A. Jurado-Román received speaker and consulting fees, and served as a proctor for Shockwave, Philips, Boston Scientific and Abbott. F. Hidalgo received speaker fees from Philips Volcano. S. Ojeda received consulting fees from Medtronic and Edwards, speaker fees from Philips, World Medical and Boston Scientific and holes a research grant (PI21/00949) from the Spanish Ministry of Science and Innovation (Instituto de Salud Carlos III). M. Pan received speaker fees from Abbott, Boston Scientific, World Medical and Philips and holds a research grant (PI21/00949) from the Spanish Ministry of Science and Innovation (Instituto de Salud Carlos III). The other authors have no disclosures.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.