

ORIGINAL ARTICLE - BASIC SCIENCE

Mechanical Circulatory Support Use in Chronic Total Occlusion Percutaneous Coronary Intervention: A Systematic Review

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ABSTRACT

Background: Mechanical circulatory support (MCS) during percutaneous coronary intervention (PCI) remains controversial, particularly in high-risk procedures such as chronic total occlusion PCI (CTO-PCI), and real-world data on its frequency, patient selection, and outcomes are limited.

Aims: To assess the frequency of MCS use during CTO-PCI, to describe the clinical and procedural characteristics of supported patients, and to synthesize the available outcome data.

Methods: A systematic review was conducted according to PRISMA guidelines and registered in PROSPERO (CRD420251044868). PubMed, Scopus, and the Cochrane Library were systematically searched.

Results: Nine studies were included in the qualitative synthesis. Reported rates of MCS use during CTO-PCI ranged from 0.7% to 6.4%. MCS was used more frequently in elderly patients and those with diabetes mellitus, chronic kidney disease, impaired left ventricular systolic function, greater anatomical complexity, and in procedures employing a retrograde approach. Across studies, procedural and clinical outcomes were consistently more favorable when MCS was implanted prophylactically rather than used as urgent rescue therapy.

Conclusions: Overall, MCS use during CTO-PCI is infrequent and largely reserved for selected high-risk cases. In patients with a meaningful anticipated risk of hemodynamic instability, prophylactic implantation should be considered. Prospective multicenter studies are needed to refine indications and assess cost-effectiveness.

Abbreviations: ACS, acute coronary syndrome; AKI, acute kidney injury; CTO, chronic total occlusion; IABP, intra-aortic balloon pump; MACE, major adverse cardiovascular events; MCS, mechanical circulatory support; MI, myocardial infarction; PCI, percutaneous coronary intervention; PSM, propensity score matching; pVAD, percutaneous ventricular assist device; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

1 | Introduction

Chronic total occlusion (CTO) percutaneous coronary intervention (PCI) is among the most technically challenging procedures in interventional cardiology, with procedural success heavily reliant on operator expertise, patient selection, and lesion complexity [1–6]. Despite substantial advances in devices and techniques have significantly improved outcomes, CTO-PCI remains associated with a risk of hemodynamic instability, particularly in high-risk subsets [7].

Mechanical circulatory support (MCS) devices, including intra-aortic balloon pump (IABP), percutaneous ventricular assist device (pVAD) such as Impella (Abiomed, Danvers, MA), and veno-arterial extracorporeal membrane oxygenation (VA-ECMO), may be deployed either prophylactically or as rescue therapy during CTO-PCI to manage hemodynamic compromise [8]. However, the real-world frequency of MCS use, the clinical characteristics of patients requiring support, and their associated outcomes remain poorly defined across real-world practice. Current guidelines do not provide specific recommendations regarding the routine use of MCS during CTO-PCI, reflecting the limited and heterogeneous evidence base [9, 10].

Accordingly, this systematic review aims to synthesize contemporary evidence on MCS use during CTO-PCI, with three specific objectives to: (a) explore the frequency of MCS use during CTO-PCI, (b) characterize clinical and procedural profiles associated with MCS usage, and (c) evaluate procedural and clinical outcomes of patients requiring support.

2 | Methods

This systematic review was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions [11] and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12]. The study protocol was registered on PROSPERO (ID: CRD420251044868). The literature search strategy was developed based on the PICO framework: patients (P), individuals undergoing CTO-PCI; intervention (I), use of MCS during CTO-PCI; comparator (C), no use of MCS; outcome (O), frequency of MCS use, type of MCS device used, clinical and procedural characteristics, and clinical outcomes. A systematic search was performed in PubMed, Scopus, and the Cochrane Library databases, covering studies published up to October 2025. The detailed search strategy is available in Supporting Information S1: Table S1. Two reviewers (M.B. and J.Z.) independently screened titles and abstracts for eligibility and extracted data using a standardized form. Discrepancies were resolved by consulting a third reviewer (A.J.-R.). Extracted data included study design, year, population, and procedural characteristics, number of CTO-PCI procedures, number of MCS uses, type of MCS device, MCS timing (prophylactic vs. bailout), and reported clinical outcomes. Due to substantial heterogeneity in study design, patient populations, and outcome definitions, a qualitative synthesis was performed without formal quantitative pooling. Given that all included studies were observational registries, the Newcastle–Ottawa Scale was used to assess the methodological quality and risk of bias [13].

3 | Results

The PRISMA flowchart is shown in Figure 1 and Supporting Information S1: Table S2. A total of 237 articles were initially identified through the systematic literature search. After automatic removal of duplicates and screening of both titles and abstracts, 26 full-text papers were assessed for eligibility. A total of nine studies met the eligibility criteria and were included in the qualitative synthesis [14–22]. Study characteristics are detailed in Supporting Information S1: Table S3. The risk of bias assessment is presented in Supporting Information S1: Tables S4.

3.1 | Frequency and Type of MCS Use

Across studies, the use of MCS during CTO-PCI was infrequent and varied markedly, reflecting geographic and temporal differences (Figure 2). In the European registry, the reported incidence of MCS use was 0.7% [14], whereas North American series showed higher rates ranging from 3% to 4.3% [15, 16]. In contrast, a large recent prospective cohort from China reported a 6.4% incidence of MCS use among high-risk elective CTO-PCI procedures [22].

3.2 | MCS Device Selection Among Registries

The choice of MCS device during CTO-PCI varied substantially across the included studies (Figure 3). As illustrated in Table 1, IABP and pVAD were the most used devices, although their relative use varied considerably between studies. In registries reporting multiple MCS types, earlier studies more commonly reported the use of IABP, whereas more recent registries showed increasing use of pVAD, suggesting a temporal shift in device preference [14–17]. Less commonly, other support strategies such as VA-ECMO and TandemHeart were employed. Notably, Karacsonyi et al. highlighted the differential use of MCS devices depending on whether support was prophylactic or urgent. Across both contexts, pVAD remained the most frequently used device (employed in 76.9% of prophylactic cases and 50% of urgent ones). VA-ECMO use was more than twice as common in urgent settings (8.1%) compared to prophylactic ones (2.6%). Similarly, IABP was used more frequently in urgent scenarios (48.4%) than in prophylactic contexts (6.1%) [16]. In the prospective Chinese cohort by Yu et al., all MCS were prophylactic and limited to IABP and/or VA-ECMO; among 137 supported procedures, device use was IABP alone in 66.4% of cases, ECMO + IABP in 26.3%, and ECMO alone in 7.3% [22].

3.3 | Clinical and Procedural Characteristics of Patients Requiring MCS

Clinical and procedural characteristics of patients undergoing CTO-PCI with MCS are summarized in Table 1. Across studies, the mean age of patients requiring MCS ranged from 62 to 71 years, and the majority were male (ranging from 74% to 92%). The prevalence of diabetes mellitus ranged between 34% and 57%, and a considerable proportion of patients had chronic kidney disease (approximately 21%–32%). Impaired left ventricular ejection fraction (LVEF) was common, with mean values ranging from 20% to 32% across studies. Baseline coronary anatomy demonstrated substantial lesion complexity, with a

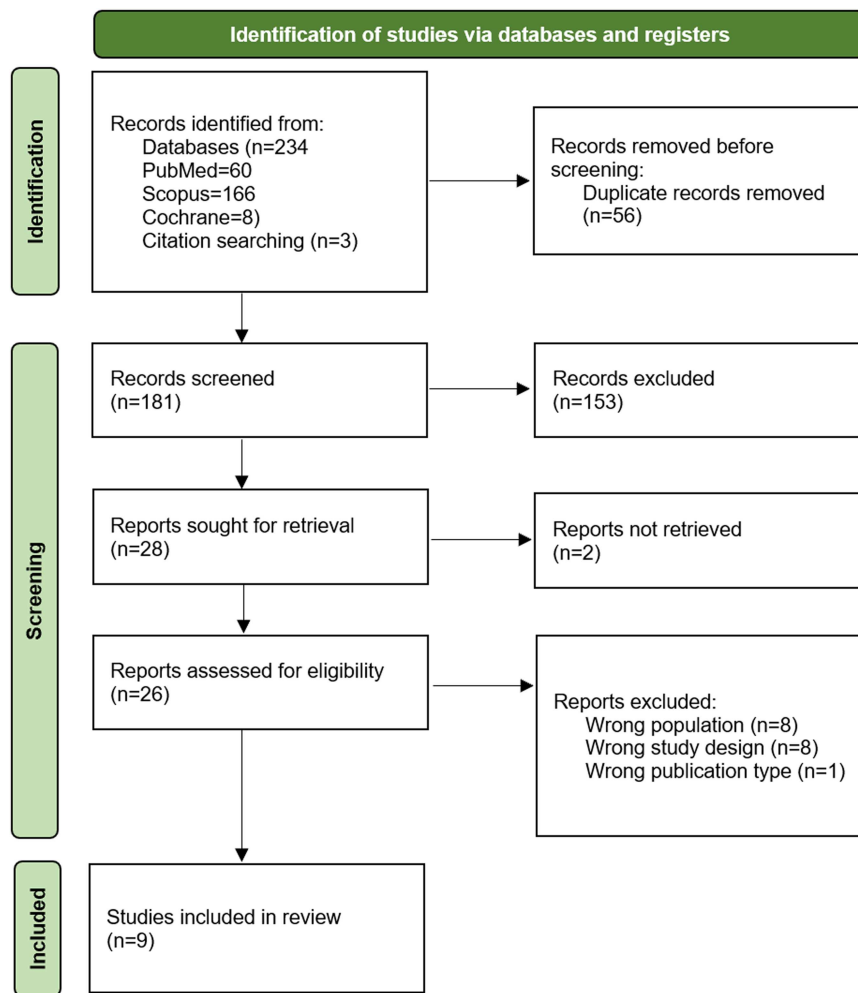


FIGURE 1 | Flow diagram of the search for studies included in the meta-analysis according to the Preferred Reporting Items for Systematic Reviews. [Color figure can be viewed at wileyonlinelibrary.com]

high portion of CTOs located in the right coronary artery (32%–47%) and the left anterior descending artery (29%–51.8%). Mean J-CTO scores ranged from 2 to 2.8, while PROGRESS CTO score from 1 to 1.4. Retrograde crossing was used in 39% to 49% of cases where reported, underscoring the procedural complexity. The use of MCS devices varied substantially across the included studies. Overall, IABP was the most frequently employed device, accounting for 15% to 85% of MCS use depending on the registry. The use of pVAD ranged from 0% to 100% of cases and often represented the preferred option for prophylactic support in high-risk patients, in non-Asian cohorts. The use of VA-ECMO was very limited, ranging from 0.5% to 7.3% of cases [14, 16, 22] and typically reserved for urgent bailout situations [16]. The use of TandemHeart (LivaNova) was reported in a single-center study, where it accounted for 25% of supported CTO-PCI procedures [18]. Among CTO-PCI procedures involving MCS, prophylactic support predominated across studies (53%–100%), while urgent MCS deployment was observed in 0%–47% of cases. Al-Khadra et al. observed a marked increase in overall MCS use between 2014 and 2019, driven primarily driven by expanding pVAD adoption, while the use of IABP declined sharply over the same period [15].

Patients undergoing CTO-PCI with MCS consistently exhibited more complex clinical and anatomical profiles compared with

those treated without MCS. In the study by Karacsonyi et al., prophylactic MCS use was associated with higher lesion complexity, including more frequent moderate-to-severe calcification (71% vs. 44%, $p < 0.001$), proximal cap ambiguity (42% vs. 34%, $p = 0.013$), and greater anatomical difficulty as reflected by higher mean J-CTO (2.80 ± 1.22 vs. 2.39 ± 1.27 , $p < 0.001$) and PROGRESS-CTO scores (1.39 ± 1.03 vs. 1.18 ± 1.00 , $p = 0.002$). The use of the retrograde approach (45% vs. 30%, $p < 0.001$) and rotational atherectomy (7.4% vs. 4.2%) was also more common in the MCS group [16]. Importantly, patients who received MCS had significantly lower LVEF ($31.5 \pm 15\%$ vs. $51 \pm 12\%$, $p < 0.001$). Interestingly, they compared the characteristics of patients requiring urgent MCS with those receiving prophylactic support. Patients requiring urgent MCS were older, had higher baseline LVEF, and more frequently had prior coronary artery bypass grafting or peripheral artery disease. Procedurally, urgent MCS cases more often involved right coronary artery CTOs, and presented greater lesion complexity, with higher J-CTO and PROGRESS-CTO scores, and more frequent use of the retrograde approach [16]. Similarly, in the National Inpatient Sample analysis by Al-Khadra et al., patients receiving MCS during CTO-PCI were older (mean age 67.4 vs. 66.4 years), more likely to be male (76% vs. 73.6%), and had a higher burden of comorbidities, including coronary artery disease, congestive heart failure, and

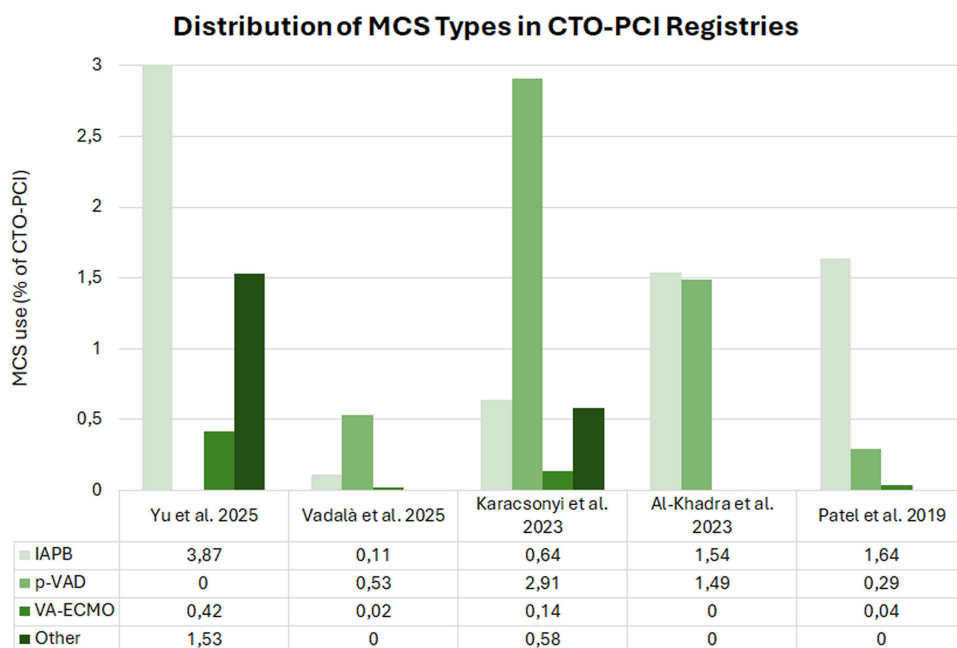


FIGURE 2 | Distribution of MCS types in CTO-PCI registries. Overall use of MCS devices expressed as a percentage of total CTO-PCI procedures in each registry included in the quantitative synthesis. In the study by Yu et al., “other MCS type” refers to the combined use of IABP + VA-ECMO. CTO, chronic total occlusion; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; pVAD, percutaneous ventricular assist device; VA-ECMO, veno-arterial extracorporeal membrane oxygenation. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

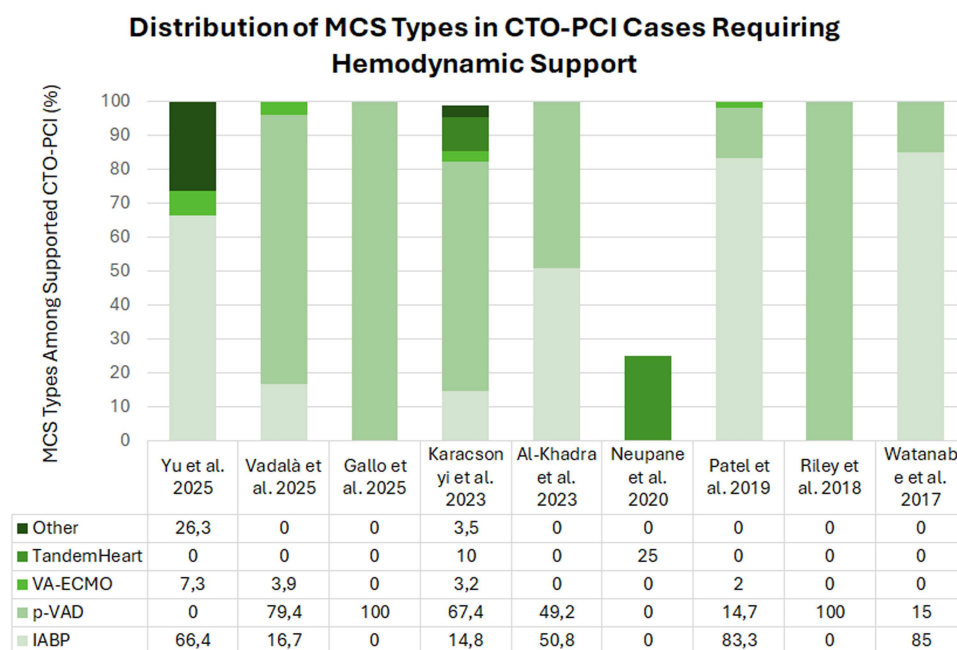


FIGURE 3 | Distribution of MCS types in CTO-PCI cases requiring hemodynamic support. Distribution of MCS types among CTO-PCI cases requiring hemodynamic support, highlighting inter-study variability in device selection. In the study by Yu et al., “other MCS type” refers to the combined use of IABP + VA-ECMO. In the study by Neupane et al., only the percentage of TandemHeart use among all CTO-PCIs is reported, with no information provided on the use of other MCS types. CTO, chronic total occlusion; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; pVAD, percutaneous ventricular assist device; VA-ECMO, veno-arterial extracorporeal membrane oxygenation. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

atrial fibrillation (all $p < 0.001$) [15]. In the cohort reported by Yu et al., patients selected for prophylactic MCS had a markedly higher risk profile before matching: lower LVEF ($41.62 \pm 10.42\%$ vs. $50.41 \pm 7.97\%$; $p < 0.001$), greater anatomic complexity with higher J-CTO scores (2.59 ± 1.34 vs. 2.02 ± 1.17 ; $p < 0.001$),

higher incidence of long-segment occlusions (> 20 mm length: 39.42% vs. 29.84% , $p = 0.01$), more frequent multivessel CTO involvement (two-vessel 30.5% vs. 18.7% ; three-vessel 5.3% vs. 1.36% ; both $p < 0.001$), and a higher prevalence of diabetes (35.8% vs. 25.6% ; $p = 0.006$) [22].

TABLE 1 | Baseline clinical and procedural characteristics of CTO-PCI patients who received MCS.

Study	Yu et al. 2025^d	Vadalá et al. 2025	Gallo et al. 2025	Karacsonyi et al. 2023	Al-Khadra et al. 2023	Neupane et al. 2020^b	Patel et al. 2019	Riley et al. 2018	Watanabe et al. 2017
CTO-PCI patients	2349	15,329	27	7171	208,123	395	93,109	57	383
MCS (%)	151	102 (0.67)	27 (100)	310 (4.3)	6319 (3)	52 (13)	1832 (2)	57 (100)	181 (47)
Age (years)	65.7	NA	63	62.6	67.5	71	65	62	NA
Male (%)	119 (86.9)	NA	25 (93)	245 (79)	4802 (76)	10 (83)	1367 (74.6)	50 (87.8)	NA
Hypertension (%)	57 (41.6)	NA	19 (70)	250 (81)	134,864 (64.8)	9 (75)	1163 (63.5)	50 (87.8)	NA
Diabetes mellitus (%)	46 (33.6)	NA	11 (41)	146 (47.1)	118,006 (56.7)	5 (42)	623 (34)	30 (52.6)	NA
Dyslipidemia (%)	NA	NA	18 (67)	270 (87.1)	141,316 (67.9)	NA	NA	NA	NA
CKD (%)	NA	NA	7 (26)	NA	66,391 (31.9)	3 (25)	385 (21)	NA	NA
ACS (%)	0 (0)	NA	0 (0)	131 (42.2)	0 (0)	1 (8)	0 (0)	0 (0)	383 (100)
Prior PCI (%)	40 (29.2)	NA	7 (26)	NA	NA	NA	NA	25 (43.9)	NA
Prior CABG (%)	2 (1.5)	NA	1 (4)	103 (33.2)	NA	NA	NA	21 (36.8)	NA
Prior heart failure (%)	110 (80.3)	NA	19 (70)	174 (56.1)	NA	11 (92)	147 (8)	NA	NA
LVEF (%) (mean ± SD)	42.9 ± 9	NA	23 ± 7	31.9 ± 14	NA	NA ^c	NA	20 ± 11	NA
Number of CTO vessels	NA	NA	34	NA	NA	13	NA	57	NA
CTO target vessel (%)									
LAD	71 (51.8)	NA	13 (38)	89 (28.7)	NA	4 (31)	NA	19 (33.3)	NA
RCA	46 (33.6)	NA	16 (47)	113 (36.4)	NA	5 (38)	NA	18 (31.6)	NA
LCX	58 (42.3)	NA	5 (15)	66 (21.3)	NA	4 (31)	NA	20 (35.1)	NA
LM	4 (2.9)	NA	0 (0)	6 (1.9)	NA	0 (0)	NA	0 (0)	NA
Others	NA	NA	0 (0)	6 (1.9)	NA	0 (0)	NA	0 (0)	NA
SYNTAX score (mean ± SD)	NA	NA	35 ± 11	NA	NA	NA	NA	NA	NA
Retrograde crossing strategy (%)	NA	NA	12 (44)	151 (48.7)	NA	6 (46)	NA	22 (38.6)	NA
J-CTO score (mean ± SD)	2.46 ± 1.3	NA	2 ± 1	2.8 ± 1.2	NA	3 ± 1	NA	NA	NA
Progress CTO score (mean ± SD)	NA	NA	1 ± 1	1.4 ± 1.1	NA	2 ± 1	NA	NA	NA
Atherectomy ^a (%)	NA	NA	6 (22)	36 (12)	NA	1 (8)	NA	10 (17.5)	NA
Unprotected LM or last remaining conduit	NA	NA	NA	NA	NA	NA	NA	20 (35.1)	NA
Type of MCS used (%)									
IABP	91 (66.4)	17 (16.7)	0 (0)	46 (14.8)	3209 (50.8)	NA	1525 (83.3)	0 (0)	154 (85)
pVAD	0 (0)	81 (79.4)	27 (100)	209 (67.4)	3110 (49.2)	NA	270 (14.7)	57 (100)	27 (15)
VA-ECMO	10 (7.3)	4 (3.9)	0 (0)	10 (3.2)	0 (0)	NA	37 (2)	0 (0)	0 (0)

(Continues)

TABLE 1 | (Continued)

Study	Yu et al. 2025 ^d	Vadalà et al. 2025	Gallo et al. 2025	Karacsonyi et al. 2023	Al-Khadra et al. 2023	Neupane et al. 2020 ^b	Patel et al. 2019	Riley et al. 2018	Watanabe et al. 2017
TandemHeart	0 (0)	0 (0)	0 (0)	31 (10)	0 (0)	13 (25)	0 (0)	0 (0)	0 (0)
Others	36 (26.3) ^e	0 (0)	0 (0)	11 (3.5)	0 (0)	NA	0 (0)	0 (0)	0 (0)
Prophylactic MCS (%)	137 (100)	NA	NA	229 (78.7)	NA	13 (100)	969 (52.9)	57 (100)	0 (0)
Urgent MCS (%)	0 (0)	NA	NA	62 (21.3)	NA	0 (0)	863 (47.1)	0 (0)	181 (100)

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CKD, chronic kidney disease; CTO, chronic total occlusion; IABP, intra-aortic balloon pump; LAD, left anterior descending artery; LCM, left circumflex artery; LM, left main stem; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; NA, not available; PCI, percutaneous coronary intervention; pVAD, percutaneous ventricular assist device; RCA, right coronary artery; SD, standard deviation; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

^aAtherectomy was defined as the use of rotational and orbital laser atherectomy.

^bThe baseline and procedural characteristics of Neupane et al. are referred to the 13 CTO-PCIs (12 patients) receiving TandemHeart.

^cIn the study by Neupane et al., the mean LVEF was not specified, although six patients had a LVEF <30% (67%).

^dIn the study by Yu et al., the total number of patients receiving MCS was 151; however, baseline and procedural characteristics were reported for 137 patients—the cohort after propensity score matching—so percentages were calculated using 137 as the denominator.

^eIn the study by Yu et al., “other MCS type” refers to the combined use of IABP + VA-ECMO.

3.4 | MCS Use in CTO-PCI Performed During Acute Coronary Syndromes (ACS)

Most of the included studies primarily focused on patients undergoing elective or stable CTO-PCI, with minimal representation of ACS. Karacsonyi et al. reported a mixed cohort, with 42.2% of patients presenting with ACS [16]. In contrast, Watanabe et al., in the CREDO-Kyoto AMI Registry, analyzed only CTO-PCI procedures performed within 24 h after symptom onset in the context of ST-segment elevation MI (STEMI) [20]. In this cohort, the frequency of MCS use was substantially higher, reaching 47% (95% CI, 42%–52%), a figure markedly above the rates reported in stable CTO-PCI populations, reflecting the greater hemodynamic vulnerability associated with acute presentations. Among patients requiring support, IABP was used in 85% of cases, whereas pVAD devices were used in 15%.

3.5 | Procedural and Clinical Outcomes

Procedural success rates and clinical outcomes among patients undergoing CTO-PCI with MCS were heterogeneously reported across the included studies. Despite variability in study design and outcome, several consistent findings emerged. In-hospital mortality among patients requiring MCS ranged from 3.6% to 25.9%, markedly higher than the rates observed in patients without MCS (ranging from 0.3% to 1.6%). In the study by Patel et al., in-hospital mortality was 25.9% among patients treated with MCS compared to 1.6% in the non-MCS group. Among patients with cardiogenic shock, mortality reached 33.3%, and was higher in those treated with MCS (38.6%) compared to those without (29.1%) [17]. Al-Khadra et al. reported a mortality rate of 9.2% in the MCS cohort compared to 0.7% in those without [15]. Karacsonyi et al. similarly reported higher in-hospital mortality in MCS patients (5.8%) compared to controls (0.3%) [16]. AKI was another common complication associated with MCS, with incidence rates ranging from 20.4% to 31.3% in the MCS group, compared to 9.8%–10% in the control group [15, 17]. In Gallo et al., 12% of patients experienced AKI following PCI, although the small sample size and absence of a comparison group limit interpretation [19]. Procedural metrics, including fluoroscopy time, radiation dose, and procedural duration, were significantly higher in patients treated with MCS [16]. Technical and procedural success ranged from 86% to 95.6% and 75.4% to 91%, respectively [16, 18, 19, 21, 22]. Interestingly, Yu et al., after propensity score matching (PSM) with a non-MCS group, found significantly higher technical success (95.6 vs. 87.6; $p = 0.027$) and complete revascularization rate (89% vs. 66.4%; $p < 0.001$) in the MCS cohort compared to the non-MCS group, while no differences were found in procedural success. They reported higher in-hospital MACE (10.9% vs. 4.4%; $p = 0.041$) in the MCS group, while no significant differences were observed in terms of procedural complications and 1-year MACE rates [22]. Karacsonyi et al. described a periprocedural MACE incidence of 6.5% [16]. In the series by Gallo et al. documented a 4% incidence of periprocedural MI and a fatal cardiac tamponade in one case. At 90-day follow-up, 11% of patients experienced MACE, while 81% reported symptomatic improvement [19]. In the TandemHeart case series by Neupane et al., the 6-month mortality rate was 25%, with no reported cases of major bleeding [18]. Major bleeding was reported in 3%–3.5% of cases [15, 21]. Yu et al. reported a

limb ischemia rate of 10.2% in their MCS cohort, driven by higher rates in IABP + VA-ECMO (22.2%) versus IABP alone (6.6%) [22]. Procedural and clinical outcomes are fully displayed in Table 2.

3.6 | Outcomes According to Timing of MCS Use

The timing of MCS placement, whether planned prophylactically or used urgently as a bailout, has a substantial impact on procedural and clinical outcomes [23, 24]. However, among the studies included in this review, only Karacsonyi et al. provided a detailed stratification of outcomes according to MCS timing [16]. This distinction is clinically relevant, as it reflects different hemodynamic conditions and procedural complexity at the time of device deployment. Notably, rates of MACE, mortality, and acute myocardial infarction were markedly higher in the bailout group (32.3%, 14.5%, and 11.3%, respectively) compared to the prophylactic group (6.5%, 3.1%, and 0.9%). Procedural complications also occurred more frequently in the urgent MCS cohort: coronary perforation (37.1% vs. 5.7%), pericardiocentesis (11.3% vs. 2.2%), donor artery dissection or thrombosis (12.9% vs. 1.3%), and vascular access site complications (6.4% vs. 2.6%). As a result, both technical and procedural success rates were significantly lower in patients receiving urgent MCS (67.7% and 38.7%, respectively) compared to those managed with prophylactic support (85.6% and 80.4%). These findings highlight that bailout MCS use is associated with substantially higher procedural risk and an adverse event burden compared with prophylactic use, likely reflecting the unstable and emergent context in which support is initiated.

4 | Discussion

This systematic review provides a contemporary synthesis of the frequency, clinical characteristics, procedural, and clinical outcomes of MCS use during CTO-PCI (Central Illustration 1). The overall frequency of MCS use during CTO-PCI was relatively low, a finding that likely reflects not only careful patient selection and improvements in contemporary CTO techniques, but also the limited indication for revascularizing an occluded vessel in patients with severely reduced LVEF, who often presented with extensive myocardial necrosis. In such cases, the absence of viable myocardium markedly reduces the expected benefit of CTO recanalization, and these patients are therefore less frequently considered for complex PCI procedures that might otherwise require hemodynamic support. The heterogeneity observed across studies further reflects the multifactorial nature of MCS use—shaped by anatomical complexity, operator judgment, institutional protocols, and individual patient risk profiles.

Moreover, practice patterns vary significantly between regions: while American registries reported a frequency of MCS use of approximately 3%–4.3%, the European registry documented a rate of 0.67% [22], and a Chinese cohort reported 6.4%, suggesting geographic differences in thresholds for support deployment. This variability is further supported by descriptive data showing that MCS use is more common in patients with advanced age, male sex, reduced LVEF, diabetes, chronic kidney disease, and prior heart failure. Prior studies have consistently shown that reduced LVEF is associated with increased

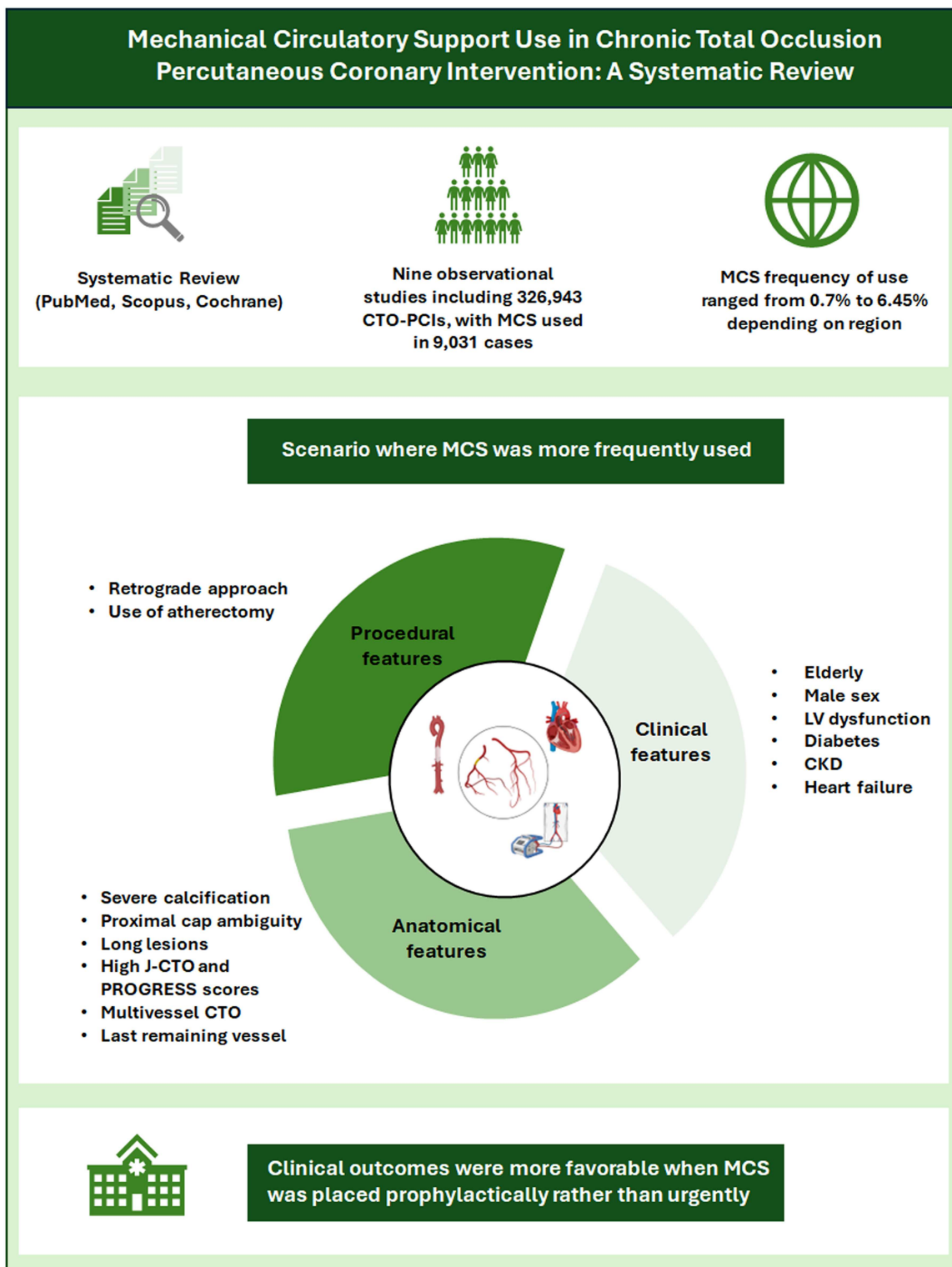
TABLE 2 | Procedural and in-hospital clinical outcomes of CTO-PCI patients treated with MCS.

Study	Yu et al. 2025	Gallo et al. 2025	Al-Khadra et al. 2023	Karacsonyi et al. 2023	Neupane et al. 2020 ^a	Patel et al. 2019	Riley et al. 2018	Watanabe et al. 2017
Supported CTO-PCI	137	27	6319	310	13	1832	57	383
Technical success	131 (95.6)	31 (91)	NA	253 (81.6)	12 (92)	NA	50 (87.7)	NA
Procedural success	118 (86.1)	31 (91)	NA	221 (71.3)	10 (77)	NA	43 (75.4)	NA
Coronary perforation	6 (4.3)	NA	NA	(11.6)	1 (8)	NA	1 (1.8)	NA
In-hospital mortality	5 (3.6)	1 (4)	581 (9.2)	81 (25.9)	1 (8)	474 (25.9)	3 (5.3)	NA
Periprocedural MI	4 (2.9)	1 (4)	NA	(3.5)	NA	NA	NA	NA
AKI	NA	3 (11)	1289 (20.4)	NA	NA	573 (31.3)	NA	NA
MACE	15 (10.9) ^a	3 (11) ^b	NA	39 (12.6)	NA	NA	NA	NA
MACCE	NA	NA	NA	NA	2 (15)	NA	NA	NA
Bleeding	21 (15.3)	0 (0)	765 (12.1)	NA	0 (0)	NA	2 (3.5)	NA
Limb artery ischemia	14 (10.2)	NA	NA	NA	NA	NA	NA	NA

Abbreviations: AKI, acute kidney injury; CTO, chronic total occlusion; MACCE, major adverse cardiovascular and cerebrovascular events; MACE, major adverse cardiovascular events; MCS, mechanical circulatory support; MI, myocardial infarction; NA, not available; PCI, percutaneous coronary intervention.

^aIn-hospital MACE.

^bReported MACE at 90 days.



CENTRAL ILLUSTRATION 1 | In this systematic review of nine observational studies including 3,26,943 CTO-PCI procedures, MCS was used in 9031 cases. MCS use was overall infrequent, but more common in patients with high-risk clinical, anatomical, and procedural features. Outcomes appeared more favorable when support was planned prophylactically rather than deployed urgently. CKD, chronic kidney disease; CTO, chronic total occlusion; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

peri-procedural and long-term morbidity and mortality in patients undergoing CTO PCI, especially in anatomically complex cases or when collateral circulation from donor arteries is jeopardized. In these settings, MCS devices such as Impella or VA-ECMO may enhance procedural safety by maintaining

systemic perfusion and unloading the left ventricle during the procedure [15, 25]. Anatomically, MCS cases were characterized by higher lesion complexity, more severe calcification, proximal cap ambiguity, higher J-CTO and PROGRESS CTO scores, and multivessel CTO. These observations indicate that operators

often reserve MCS for patients with particularly high-risk clinical and anatomical profiles. The proportion of retrograde crossing among MCS patients requiring MCS was markedly higher than that reported in international CTO registries, further emphasizing the procedural complexity of this subset [26, 27]. Furthermore, the use of rotational atherectomy was more frequent when MCS was used [16]. These findings could help explain the less favorable outcomes often observed in MCS recipients, which are more likely attributable to their higher baseline risk than to the device itself. This reflects a classic example of confounding by indication, where the indication for MCS inherently predisposes to worse outcomes, independently of the treatment administered [28]. This interpretation is supported by contemporary data showing that periprocedural mortality during CTO-PCI, while overall rare, is markedly higher among patients requiring MCS, further emphasizing the advanced risk profile of this subgroup [29]. Importantly, PSM evidence from an Asian cohort (all prophylactic IABP and/or VA-ECMO) showed that, once baseline characteristics were balanced, long-term outcomes were comparable between MCS and non-MCS patients [22].

MCS use varied across studies, with prophylactic use predominating. When employed preemptively in stable but high-risk cases, MCS was associated with moderate rates of complications and relatively high procedural success. In contrast, when MCS was initiated emergently (typically in response to hemodynamic deterioration), outcomes were markedly worse, with significantly lower technical and procedural success rates and substantially higher rates of major adverse events [16]. This dichotomy highlights the potential value of early risk stratification in identifying patients who may benefit from planned hemodynamic support. To this end, the PROGRESS CTO MCS score was recently developed as a dedicated tool to predict the need for urgent MCS during CTO-PCI. The score incorporates key clinical and angiographic variables, including retrograde crossing strategy, impaired LVEF, and long lesion length. These factors were independently associated with hemodynamic collapse requiring urgent support [30]. This score could serve as a pragmatic aid in procedural planning, potentially enabling more selective and effective use of prophylactic MCS in complex CTO interventions. Nevertheless, these findings derive exclusively from observational registries, and no randomized evidence is available; therefore, no firm conclusions can be drawn, and this concept should be considered hypothesis-generating.

MCS use was considerably higher in ACS patients, particularly after STEMI. In the CREDO-Kyoto AMI Registry, nearly 47% required MCS. In these cases, MCS was often used urgently in response to procedural or hemodynamic deterioration, underscoring the impact of the acute clinical context on support needs [20]. However, routine CTO revascularization during STEMI is not indicated in most cases, and an early CTO revascularization strategy is not associated with improved outcomes [31]. Non-culprit CTO-PCI should be considered only after careful assessment of myocardial viability, post-culprit ventricular function, and persistent symptoms despite optimal medical therapy. Early CTO-PCI should thus be reserved for highly selected patients, given the elevated procedural risk and greater likelihood of requiring MCS in unstable settings [2].

Beyond clinical outcomes, the implementation of MCS raises important considerations in terms of cost, resource allocation, and institutional logistics. Patel et al. reported that both median

length of hospital stay (6 vs. 3 days, $p \leq 0.001$) and median hospitalization cost (\$45,654 vs. \$16,707, $p \leq 0.001$) were significantly higher in patients treated with MCS compared to those without [17]. These findings highlight that, in addition to clinical complexity, the use of MCS is associated with a substantial increase in healthcare resource utilization. However, formal cost-effectiveness analyses in the specific setting of CTO-PCI are currently lacking, and the economic impact of MCS is likely to vary substantially according to device type.

Despite its increasing use, MCS during CTO-PCI remains an area of clinical uncertainty. Current European and American guidelines do not provide specific recommendations, leaving decisions to operator discretion [9, 10]. Moreover, the available evidence is derived exclusively from observational studies; therefore, residual confounding and selection bias cannot be excluded. Similarly, recent expert consensus statements acknowledge the potential benefit of MCS in selected high-risk cases but offer limited guidance on optimal patient selection, device choice, or timing [32, 33]. This reflects the paucity of prospective evidence in the field and reinforces the need for robust data to support standardized strategies. Future research, including well-designed registries and randomized trials, should aim to define the role of MCS in improving procedural safety, myocardial preservation, and long-term outcomes. Solid evidence is also essential to guide resource allocation and inform cost-effectiveness in this technically demanding setting. In the meantime, MCS use should remain individualized, based on anatomical and hemodynamic risk, ventricular function, and lesion complexity; because outcomes are consistently worse when support is placed urgently, whenever there is a reasonable possibility that MCS will be needed, it should be planned prophylactically. When appropriate, a multidisciplinary Heart Team discussion may help refine the treatment strategy in borderline or high-risk scenarios [2].

4.1 | Practical Guidance: When to Consider Prophylactic MCS in Elective CTO-PCI

In elective CTO-PCI, we favor prophylactic MCS when several factors converge to define a truly high-risk profile, as this cluster essentially reflects the anticipated risk of hemodynamic collapse. Outcomes are consistently worse when support is instituted urgently, and patients who ultimately require bailout MCS are often those in whom this risk was underestimated during pre-procedural evaluation. Risk accumulates across three domains: clinical (advanced age, chronic kidney disease, diabetes, prior heart failure, and especially reduced LVEF), anatomic (severe calcification requiring atherectomy, proximal cap ambiguity, long occlusion length, high J-CTO or PROGRESS scores, multivessel CTO, or a last-remaining-vessel scenario), and procedural (planned retrograde approach, collateral channel crossing, or atherectomy). These factors must be carefully weighed against the potential risks of vascular complications and integrated with the experience of the center and operator in performing complex, supported CTO-PCI.

5 | Conclusions

In conclusion, this systematic review offers the first contemporary synthesis of MCS use during CTO-PCI, integrating frequency data with clinical and procedural profiles, as well as

insights on clinical outcomes. Although overall use is low, MCS is more often employed in anatomically complex, high-risk patients, potentially explaining poorer outcomes. The wide variability in MCS use and the predominance of urgent deployment underscore the need for careful patient selection and procedural planning. Prospective studies and randomized trials are urgently needed to define the clinical value of MCS. Until then, its use should remain individualized, based on multidisciplinary evaluation and thorough risk stratification.

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Conflicts of Interest

Dr Alfonso Jurado-Román is a proctor for Abbott, Boston Scientific, World Medica, and Philips; has received consulting fees from Boston Scientific and Philips; and has received speaker fees from Abbott, Boston Scientific, Shockwave Medical, Philips, and World Medica. Dr Alfredo R. Galassi has received consulting and speaker honoraria from Asahi Intecc and iVascular. Dr Roberto Garbo has received proctorship and consulting fees from Boston Scientific, Asahi Intecc, Philips, Terumo, Teleflex, and IMDS. Dr Kambis Mashayekhi has received consulting, speaker, and proctoring honoraria from Abbott, Abiomed, Asahi Intecc, Astra-Zeneca, Biotronik, Boston Scientific, Cardinal Health, Daiichi-Sankyo, Medtronic, Orbus Neich, Shockwave Medical, Teleflex, and Terumo. Prof Mohaned Egred is a proctor for ELCA, Rotablation, and IVUS and has received honoraria, speaker and proctor fees from Philips, Abbott Vascular, Boston Scientific, Vascular Perspectives, Biosensors, Biotronik, Abiomed, and AstraZeneca. Dr Emmanouil S. Brilakis has received consulting/speaker honoraria from Abbott Vascular, American Heart Association (associate editor Circulation), Biotronik, Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), Cordis, CSI, Elsevier, GE Healthcare, Haemonetics, IMDS, Medtronic, SIS Medical, Teleflex, and Orbus Neich; research support: Boston Scientific, GE Healthcare; owner, Hippocrates LLC; shareholder: Cleerly Health, LifeLens Technologies, Inc, MHI Ventures, Stallion Medical, TrueVue Inc. The other authors declare no conflicts of interest.

References

1. G. Vadalà, A. R. Galassi, G. S. Werner, et al., “Contemporary Outcomes of Chronic Total Occlusion Percutaneous Coronary Intervention in Europe: The ERCTO Registry,” *EuroIntervention* 20, no. 3 (2024): e185–e197, <https://doi.org/10.4244/EIJ-D-23-00490>.
2. A. R. Galassi, G. Vadalà, G. S. Werner, et al., “Evaluation and Management of Patients With Coronary Chronic Total Occlusions Considered for Revascularisation. A Clinical Consensus Statement of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the ESC, the European Association of Cardiovascular Imaging (EACVI) of the ESC, and the ESC Working Group on Cardiovascular Surgery,” *EuroIntervention: Journal of EuroPCR in Collaboration With the Working Group on Interventional Cardiology of the European Society of Cardiology* 20, no. 3 (2024): 174, <https://doi.org/10.4244/EIJ-D-23-00749>.
3. C. Di Mario, K. M. Mashayekhi, R. Garbo, S. P. Pyxaras, N. Ciardetti, and G. W. Werner, “Recanalisation of Coronary Chronic Total Occlusions,” *EuroIntervention* 18, no. 7 (2022): 535–561, <https://doi.org/10.4244/EIJ-D-21-01117>.
4. A. Avran, A. Zuffi, C. Gobbi, et al., “Gender Differences in Percutaneous Coronary Intervention for Chronic Total Occlusions From the ERCTO Study,” *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions* 101, no. 5 (2023): 918–931, <https://doi.org/10.1002/ccd.30616>.
5. T. Lefèvre, M. Pan, G. Stankovic, et al., “CTO and Bifurcation Lesions,” *JACC: Cardiovascular Interventions* 16, no. 17 (2023): 2065–2082, <https://doi.org/10.1016/j.jcin.2023.06.042>.
6. A. R. Galassi, G. Vadalà, G. Testa, et al., “Dual Guidewire Balloon Antegrade Fenestration and Re-Entry Technique for Coronary Chronic Total Occlusions Percutaneous Coronary Interventions,” *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions* 100, no. 4 (2022): 492–501, <https://doi.org/10.1002/ccd.30324>.
7. L. Azzalini, D. Karpaliotis, R. Santiago, et al., “Contemporary Issues in Chronic Total Occlusion Percutaneous Coronary Intervention,” *JACC: Cardiovascular Interventions* 15, no. 1 (2022): 1–21, <https://doi.org/10.1016/j.jcin.2021.09.027>.
8. E. G. Ferro, J. M. Kim, C. Lalani, D. J. Abbott, and R. W. Yeh, “Mechanical Circulatory Support for Complex, High-Risk Percutaneous Coronary Intervention,” *EuroIntervention* 21, no. 3 (2025): e149–e160, <https://doi.org/10.4244/EIJ-D-24-00386>.
9. C. Vrints, F. Andreotti, K. C. Koskinas, et al., “2024 ESC Guidelines for the Management of Chronic Coronary Syndromes,” *European Heart Journal* 45, no. 36 (2024): 3415–3537, <https://doi.org/10.1093/eurheartj/ehae177>.
10. S. S. Virani, L. K. Newby, S. V. Arnold, et al., “2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines,” *Circulation* 148, no. 9 (2023): E9–E119, <https://doi.org/10.1161/cir.0000000000001168>.
11. J. Higgins, J. Thomas, J. Chandler, et al., *Cochrane Handbook for Systematic Reviews of Interventions. Version 6.5 (2024)* (Cochrane, 2024), <https://training.cochrane.org/handbook>.
12. M. J. Page, J. E. McKenzie, P. M. Bossuyt, et al., “The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews,” *Systematic Reviews* 10, no. 1 (2021): 89, <https://doi.org/10.1186/s13643-021-01626-4>.
13. A. Stang, “Critical Evaluation of the Newcastle-Ottawa Scale for the Assessment of the Quality of Nonrandomized Studies in Meta-Analyses,” *European Journal of Epidemiology* 25, no. 9 (2010): 603–605, <https://doi.org/10.1007/s10654-010-9491-z>.
14. G. Vadalà, K. Mashayekhi, M. Behnes, et al., “Procedural Impact of Advanced Calcific Plaque Modification Devices Within Percutaneous Revascularization of Chronic Total Occlusions,” *JACC: Cardiovascular Interventions* 18, no. 11 (2025): 1376–1390, <https://doi.org/10.1016/j.jcin.2025.04.035>.
15. Y. Al-Khadra, M. Salih, M. Al-Akchar, K. Sawalha, T. DeMartini, and A. M. Hafiz, “National Trends of Percutaneous Mechanical Support Utilization During Percutaneous Coronary Interventions in Chronic Total Occlusion,” *American Journal of Cardiology* 200 (2023): 215–222, <https://doi.org/10.1016/j.amjcard.2023.05.029>.
16. J. Karacsonyi, K. Deffenbacher, K. H. Benzuly, et al., “Use of Mechanical Circulatory Support in Chronic Total Occlusion Percutaneous Coronary Intervention,” *American Journal of Cardiology* 189 (2023): 76–85, <https://doi.org/10.1016/j.amjcard.2022.10.049>.
17. K. Patel, R. Doshi, D. Decter, J. Shah, and P. Meraj, “Trends in the Utilization and In-Hospital Outcomes When Using Mechanical Circulatory Support Devices for Stable Chronic Total Occlusion Treated With Percutaneous Coronary Intervention,” *European Journal of Internal Medicine* 59 (2019): e11–e13, <https://doi.org/10.1016/j.ejim.2018.09.008>.
18. S. Neupane, M. Basir, M. Alqarqaz, W. O’Neill, and K. Alaswad, “High-Risk Chronic Total Occlusion Percutaneous Coronary Interventions Assisted With TandemHeart,” *Journal of Invasive Cardiology* 32, no. 3 (2020): 94–97, <https://doi.org/10.25270/jic/19.00333>.
19. I. Gallo, L. Azzalini, R. González-Manzanares, et al., “Mechanical Circulatory Support With Impella in High-Risk Patients With Chronic

- Total Occlusion and Complex Multivessel Disease,” *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions* 105, no. 4 (2025): 883–890, <https://doi.org/10.1002/ccd.31392>.
20. H. Watanabe, T. Morimoto, H. Shiomi, et al., “Chronic Total Occlusion in a Non-Infarct-Related Artery Is Closely Associated With Increased Five-Year Mortality in Patients With ST-Segment Elevation Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention (From the CREDO-Kyoto AMI Registry),” *EuroIntervention: Journal of EuroPCR in Collaboration With the Working Group on Interventional Cardiology of the European Society of Cardiology* 12, no. 15 (2017): 1874, <https://doi.org/10.4244/EIJ-D-15-00421>.
21. R. F. Riley, J. M. McCabe, S. Kalra, et al., “Impella-Assisted Chronic Total Occlusion Percutaneous Coronary Interventions: A Multicenter Retrospective Analysis,” *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions* 92, no. 7 (2018): 1261–1267, <https://doi.org/10.1002/ccd.27679>.
22. T. Yu, S. Zhao, B. Zhang, et al., “Mid-Term Efficacy and Safety of Mechanical Circulatory Support in High-Risk Elective Chronic Total Occlusion Percutaneous Coronary Intervention: A Prospective Propensity-Matched Cohort Study,” *Catheterization and Cardiovascular Interventions* 106, no. 6 (2025): 3160–3170, <https://doi.org/10.1002/ccd.70137>.
23. F. Archilletti, L. Giuliani, G. D. Dangas, et al., “Timing of Mechanical Circulatory Support During Primary Angioplasty in Acute Myocardial Infarction and Cardiogenic Shock: Systematic Review and Meta-Analysis,” *Catheterization and Cardiovascular Interventions: Official Journal of the Society for Cardiac Angiography & Interventions* 99, no. 4 (2022): 998–1005, <https://doi.org/10.1002/ccd.30137>.
24. B. P. O’Neill, C. Grines, J. W. Moses, et al., “Outcomes of Bailout Percutaneous Ventricular Assist Device Versus Prophylactic Strategy in Patients Undergoing Nonemergent Percutaneous Coronary Intervention,” *Catheterization and Cardiovascular Interventions* 98, no. 4 (2021): E501–E512, <https://doi.org/10.1002/ccd.29758>.
25. M. Vaez, M. Dalén, Ö. Friberg, et al., “Regional Differences in Coronary Revascularization Procedures and Outcomes: A Nationwide 11-Year Observational Study,” *European Heart Journal-Quality of Care and Clinical Outcomes* 3, no. 3 (2017): 243–248, <https://doi.org/10.1093/ehjcco/qcx007>.
26. G. Vadalà, K. Mashayekhi, M. Boukhris, et al., “Reclassification of CTO Crossing Strategies in the ERCTO Registry According to the CTO-ARC Consensus Recommendations,” *JACC: Cardiovascular Interventions* 17, no. 20 (2024): 2425–2437, <https://doi.org/10.1016/j.jcin.2024.09.002>.
27. S. S. Allana, S. Kostantinis, A. Rempakos, et al., “The Retrograde Approach to Chronic Total Occlusion Percutaneous Coronary Interventions,” *JACC: Cardiovascular Interventions* 16, no. 22 (2023): 2748–2762, <https://doi.org/10.1016/j.jcin.2023.08.031>.
28. D. N. Kyriacou and R. J. Lewis, “Confounding by Indication in Clinical Research,” *Journal of the American Medical Association* 316, no. 17 (2016): 1818–1819, <https://doi.org/10.1001/jama.2016.16435>.
29. B. Simsek, A. Rempakos, S. Kostantinis, et al., “Periprocedural Mortality in Chronic Total Occlusion Percutaneous Coronary Intervention: Insights From the PROGRESS-CTO Registry,” *Circulation: Cardiovascular Interventions* 16, no. 6 (2023): e012977, <https://doi.org/10.1161/CIRCINTERVENTIONS.123.012977>.
30. J. Karacsonyi, L. Stanberry, B. Simsek, et al., “Development of a Novel Score to Predict Urgent Mechanical Circulatory Support in Chronic Total Occlusion Percutaneous Coronary Intervention,” *American Journal of Cardiology* 202 (2023): 111–118, <https://doi.org/10.1016/j.amjcard.2023.06.051>.
31. L. Paolucci, A. Diego-Nieto, A. Jurado-Román, et al., “Timing of Chronic Total Occlusion Percutaneous Coronary Intervention in Acute Coronary Syndromes: Early Versus Late Complete Revascularization and Clinical Outcomes,” *Cardiovascular Revascularization Medicine: Including Molecular Interventions* 83 (2025): 1–7, <https://doi.org/10.1016/j.carrev.2025.05.019>.
32. A. R. Galassi, G. S. Werner, M. Boukhris, et al., “Percutaneous Recanalisation of Chronic Total Occlusions: 2019 Consensus Document From the EuroCTO Club,” *EuroIntervention* 15, no. 2 (2019): 198–208, <https://doi.org/10.4244/eij-d-18-00826>.
33. E. B. Wu, A. Kalyanasundaram, E. S. Brilakis, et al., “Global Consensus Recommendations on Improving the Safety of Chronic Total Occlusion Interventions,” *Heart, Lung and Circulation* 33, no. 7 (2024): 915–931, <https://doi.org/10.1016/j.hlc.2023.11.030>.

Supporting Information

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

Supplementary Table S1: Full electronic search strategy through October 2025. **Supplementary Table S2:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist for reporting a systematic review involving a meta-analysis. **Supplementary Table S3:** Study characteristics. **Supplementary Table S4:** Assessment of observational studies quality using the Newcastle-Ottawa scale.