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ORIGINAL RESEARCH

Temporary mechanical circulatory support as a bridge to transplant in peripartum cardiomyopathy

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KEYWORDS:
temporary mechanical circulatory support;
peripartum cardiomyopathy;
intra-aortic balloon pump;
heart failure;
heart transplant

BACKGROUND: Use of temporary mechanical circulatory support (tMCS) for peripartum cardiomyopathy (PPCM) shock has been described in small cohorts, but not on a national scale. This study compares tMCS, durable MCS (dMCS), and no MCS as bridge to transplant strategies for PPCM.
METHODS: Female patients ≥14 years, listed for first-time isolated heart transplant (HT) between January 1, 2000 and June 30, 2021, were identified in the United Network for Organ Sharing database. Patients were stratified by receipt of MCS at any point during the waitlist period. Patients on multiple devices were excluded.
RESULTS: A total of 1,043 PPCM patients were listed for HT, including 575 bridged on no MCS, 177 on tMCS, and 291 on dMCS. The tMCS cohort included 10 patients on extracorporeal membrane oxygenation, 113 on intra-aortic balloon pump, and 54 on nondischargeable ventricular assist device (VAD) or percutaneous device. The dMCS group primarily received durable VADs. Compared to dMCS, tMCS recipients were more likely to require inotropes, mechanical ventilation, and longer hospitalizations pre-transplant (all $p < 0.001$). tMCS patients were more likely to be transplanted after 6 months than those on no device (adjusted subhazard ratio 1.57 [1.24-2.01]). Six hundred and eighty-one patients underwent HT. tMCS support was associated with similar 3-year graft survival compared to no MCS and dMCS (both $p > 0.05$). After multivariable risk adjustment, neither tMCS (adjusted hazard ratio 0.56 [0.06-5.43]) nor dMCS (adjusted hazard ratio 0.36 [0.05-2.82]) significantly predicted 3-year graft survival.
CONCLUSIONS: Compared to patients bridged to HT on dMCS or no MCS, PPCM patients receiving tMCS are higher acuity candidates but have equivalent post-transplant graft survival.
JHLT Open 2024;6:100126

Background

Peripartum cardiomyopathy (PPCM) is a syndrome of systolic heart failure that presents either late in pregnancy or during the months following delivery.[1] Although the pathophysiology remains incompletely understood, hormone-induced vasculopathy

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https://doi.org/10.1016/j.jhlto.2024.100126

and underlying genetic predisposition may play a role.[1] Incidence of PPCM in the United States (US) varies by race and geography, ranging from 1:1,000 to 1:4,000 live births, and is rising over time, possibly reflecting higher awareness and recognition of the disease, as well as increasing maternal age and frequency of multigestational pregnancies.[1]

Although recovery is common, typically occurring in over 50% of patients and within 6 months of diagnosis, a significant portion of PPCM patients will suffer complications including cardiogenic shock, cardiac arrest, and death.[1,2] Those with heart failure refractory to medical management may require mechanical circulatory support (MCS) and even transplantation—PPCM accounts for about 5% of orthotopic heart transplants (OHT) in US females.[3] In most cases, aggressive treatment, including employment of MCS as appropriate, should be pursued, in light of the often young age of and great potential for recovery in PPCM patients.

Temporary mechanical circulatory support (tMCS) devices, including intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), and temporary ventricular assist devices (VADs) such as Impella (Abiomed), have been successfully used to manage PPCM-associated cardiogenic shock but are described in the literature only in small cohorts.[4-7] PPCM patients often also have unique manifestations, including smaller left ventricular cavities, that may impact the utilization of temporary devices in this cohort. This study compares tMCS to durable MCS (dMCS) and no MCS as a bridge to transplant strategies for PPCM in a large national sample.

Materials and methods

We performed a retrospective cohort study of female patients ≥14 years listed for a first-time isolated heart transplant (HT) from January 1, 2000 to June 30, 2021 using data recorded in the United Network for Organ Sharing (UNOS) database. The UNOS database was queried for patient demographics, preoperative characteristics, and postoperative outcomes, as well as donor and transplant characteristics. The need for written informed consent was waived by the University of Pennsylvania institutional review board (protocol #: 850952, approval date: March 10, 2022). This study was performed in compliance with the International Society for Heart and Lung Transplantation Ethics statement.

To explore patterns of MCS use, PPCM patients were propensity matched to non-PPCM controls based on age, race, body mass index (BMI), blood type, listing year, cardiomyopathy type, diabetes and smoking history, and inotrope or ventilator dependence. Propensity scores were matched using a 1:1, nearest-neighbor strategy without replacement. Standardized mean differences were calculated to assess covariate balance between propensity-matched cohorts (Table S1).

The remaining analysis focused only on those patients with a primary diagnosis of PPCM. These patients were stratified by use of MCS at any point during the waitlist period, resulting in 3 distinct cohorts: tMCS, dMCS, and no device. tMCS was defined as ECMO, IABP, nondischargeable VAD, or percutaneous device. dMCS included durable VADs and total artificial hearts. Patients were excluded if they received multiple types of MCS throughout their waitlist period.

Descriptive statistics were presented as medians with interquartile ranges for continuous data or counts with frequencies for categorical data. Groups were compared using Kruskal-Wallis tests for continuous variables, and either chi-square or Fisher's exact tests for categorical variables, where appropriate. Missingness of all but 3 variables was < 15%. All variables with nonzero missingness are reported in Table S2.

Waitlist outcomes were categorized as transplantation, death, delisting due to recovery, or delisting due to sickness, and censored at 6 months from time of listing. Competing-risks regression was performed according to the method of Fine and Gray.[8] Models were adjusted for age, race, BMI, blood type, allocation era, cardiomyopathy type, diabetes and smoking history, and inotrope or ventilator dependence.

For transplanted patients, the primary outcome was 3-year graft failure, defined as death or cardiac retransplantation. Time-to-event analyses were performed using Kaplan-Meier estimation. Log-rank tests were used to determine statistical significance between groups. Cox proportional-hazards models for 3-year graft failure were developed. Candidate variables included preoperative recipient, donor, and transplant characteristics selected based on clinical expertise. Variables with univariable $p < 0.4$ for 3-year graft failure and missingness < 5% were included in the development of the final multivariable model, which was created using backward elimination with an exclusion criterion of $p < 0.2$. Univariable Cox regressions for all predictor variables can be found in Table S3. Analyses were performed using Stata/BE 18.0 (StataCorp, College Station, TX).

Results

Patient population

During the study period, 1,043 patients with a primary diagnosis of PPCM were listed for OHT. Of these, 575 (56%) were bridged on no MCS, 177 (17%) on tMCS, and 291 (28%) on dMCS (Figure S1). The tMCS group included 113 (64%) on IABP, 54 (31%) on nondischargeable VAD or percutaneous device, and 10 (6%) patients on ECMO. The dMCS group primarily received dischargeable VADs (n = 284, 98%), with the remainder receiving total artificial hearts (n = 7, 2%).

Patterns of tMCS use

Propensity matching resulted in 1,027 pairs of matched PPCM patients and non-PPCM controls. Baseline differences between groups were minimal (Table S1) and greater than 97% of patients in both groups were classified as dilated cardiomyopathy. Compared to controls, PPCM patients were more frequently supported with tMCS (17% vs 13%, p = 0.036), and, in particular, IABPs (11% vs 7%,

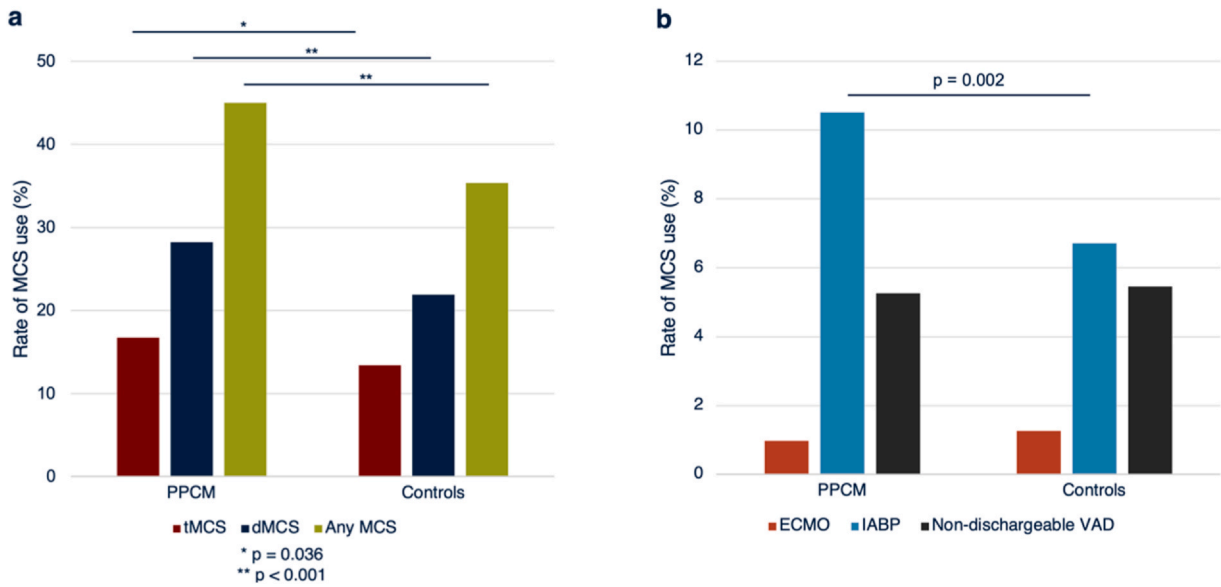

Figure 1 Rates of MCS use in PPCM patients and propensity-matched controls listed for heart transplant. (a) Rates of MCS use, including tMCS, dMCS, and any MCS use, in PPCM patients and controls. (b) Rates of tMCS use, including ECMO, IABP, and non-dischargeable VAD use, in PPCM patients and controls. PPCM and control groups were propensity matched based on age, race, body mass index (BMI), blood type, listing year, cardiomyopathy type, diabetes and smoking history, and inotrope or ventilator dependence. Smoking history was positive if ≥10 pack-year history. dMCS, durable mechanical circulatory support; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support; VAD, ventricular assist device.

p = 0.002) (Figure 1). The proportion receiving tMCS increased over the 21-year study period from 6% to 53%, with a notable rise from 13% to 31% between 2018 and 2019 (Figure 2a and b). Similar temporal trends in tMCS use were observed in the propensity-matched controls (Figure 2c and d).

Baseline characteristics

Table 1 describes baseline characteristics of the 1,043 PPCM patients listed for HT. Patients bridged with tMCS were younger than non-tMCS recipients (median age 31 vs 34 years, $p = 0.001$). Incidence of Black race was 50.6% overall and was similar across the 3 cohorts ($p > 0.05$). tMCS recipients were more likely to require inotropes (71% vs 23%, $p < 0.001$) and ventilation (11% vs 3%, $p = 0.001$), compared to dMCS.

Waitlist outcomes

PPCM patients bridged on tMCS were more likely to be transplanted after 6 months on the waitlist compared to those on no device (adjusted SHR 1.57 [1.24-2.01], $p < 0.001$) or dMCS (adjusted SHR 2.43 [1.79-3.30], $p < 0.001$) (Figure 3). Six-month cumulative incidence of waitlist mortality and recovery were similar in tMCS recipients compared to dMCS or no device ($p > 0.05$, Figure 3). Delisting due to sickness was most common in the tMCS group, compared to no device (adjusted SHR 2.75 [1.08-7.01], $p = 0.035$) or dMCS (adjusted SHR 18.47 [1.93-176.77], $p = 0.011$) (Figure 3). A complete table of subhazard ratios for competing waitlist outcomes can be found in Table S4. Within the tMCS cohort, 6-month cumulative incidence of transplant did not differ by type of tMCS received, but ECMO patients were more likely than those on IABP to be delisted due to sickness (adjusted SHR 11.74 [1.04-133.12], $p = 0.047$) (Figure S2). Eighty-one of the 1,043 patients (8%) were ultimately delisted due to clinical improvement; of these, patients on tMCS were less likely to recover than those on no device (3% vs 11%, $p = 0.002$) but not dMCS (3% vs 3%, $p = 0.979$). Notably, tMCS recipients did have the shortest waitlist times (median 21 days, Table 2), and patients with waitlist intervals longer than the cohort median (109 days) were much more likely to recover (15% vs 1%, $p < 0.001$).

Transplant characteristics

Of the 1,043 PPCM patients listed for HT, 681 (65%) ultimately underwent HT. Transplant and donor characteristics are described in Table 2. Waitlist time varied significantly by bridging strategy ($p < 0.001$)—tMCS recipients spent a median of 21 days waiting, compared to 190 days for dMCS patients. The tMCS cohort had the longest pretransplant hospitalizations (tMCS vs dMCS vs no device, 23 vs 1 vs 3 days, $p < 0.001$). Donor characteristics were largely similar between the 3 groups.

Post-transplant outcomes

Post-transplant outcomes are detailed in Table 3. PPCM patients bridged with any MCS had longer postoperative hospitalizations compared to those who received no MCS (17 vs 12 days, $p < 0.001$). Rates of acute rejection, dialysis, and

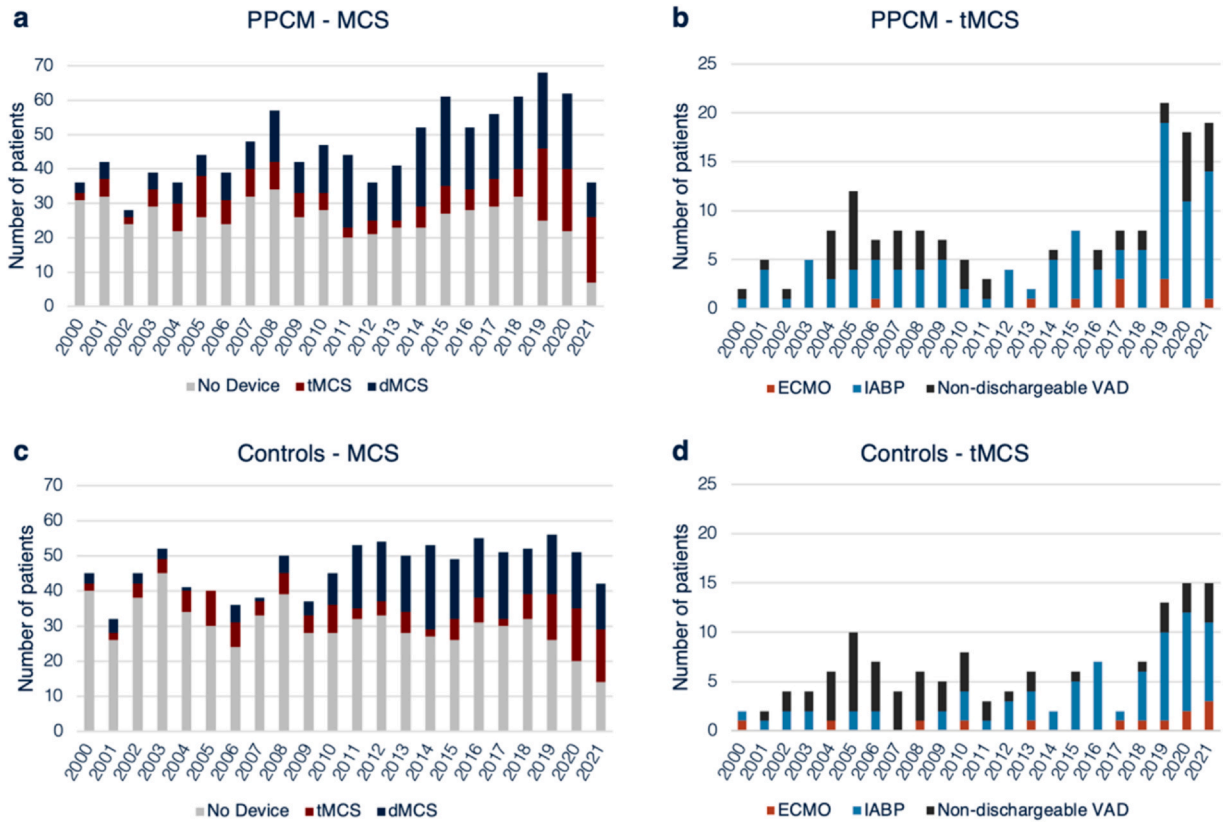

Figure 2 Patterns of (a) MCS and (b) tMCS use in PPCM patients listed for heart transplant. Patterns of (c) MCS and (d) tMCS use in propensity-matched controls. Because study period ended on June 30, 2021, number of patients is incomplete for 2021. dMCS, durable mechanical circulatory support; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support; VAD, ventricular assist device.

stroke before discharge were similar across all 3 groups ($p > 0.05$). Rates of rejection within 1 year were nondifferent between the tMCS and dMCS cohorts (44% vs 35%, $p > 0.05$). Twenty-four patients underwent repeat transplantation, the majority (17/24, 71%) of whom had not received any MCS. Kaplan-Meier survival analysis revealed no significant difference in unadjusted 3-year post-transplant graft survival between PPCM patients bridged with tMCS (77%) compared to dMCS (84%) and no device (73%) (both log-rank $p > 0.05$) (Figure 4). Among the tMCS cohort, bridging with IABP, nondischargeable VAD, or ECMO did not result in significantly different 3-year post-transplant graft survival (log-rank $p > 0.05$) (Figure S3), although lack of difference may be related to insufficient sample size. After multivariable risk adjustment, bridging with neither tMCS (AHR 0.56 [0.06-5.43], $p = 0.620$) nor dMCS (AHR 0.36 [0.05-2.82], $p = 0.332$) significantly predicted 3-year graft failure (Table 4).

Discussion

PPCM is a leading cause of cardiovascular maternal mortality in the US.[9] Although many patients recover, some present with severe disease requiring temporizing measures to stabilize cardiogenic shock. Our analysis of tMCS in PPCM is the first to do so in a large national cohort. We showed that tMCS use in PPCM patients listed for HT trended upward over the 2-decade study period, with a particular increase from 2018-2019 corresponding with the start of the new heart allocation era. tMCS was employed more frequently as a bridging strategy in PPCM patients compared to propensity-matched female controls, with this difference primarily driven by high rates of IABP use in PPCM. Crucially, although PPCM patients supported on tMCS often have higher acuity pretransplant, post-transplant outcomes are equivalent to those of patients bridged on dMCS or no MCS.

tMCS use on the waitlist has risen dramatically since the October 2018 change in the US heart allocation system, which confers higher status for patients on tMCS.[10-13] In our PPCM cohort, we observed an increase in tMCS usage over the 20-year study period, with a remarkable surge in use after 2018 (Figure 2), mirroring trends reported in the general population.[11-13] Transplant teams may be tempted to select tMCS devices with the hope of increasing a patient's chances of receiving a heart by raising their listing status. Indeed, we found that PPCM patients bridged with tMCS were more likely to be transplanted after 6 months of waiting compared to dMCS or no device (Figure 3). tMCS recipients also had the shortest waitlist duration of the 3 cohorts (Table 2), suggesting that tMCS support expedites transplantation in PPCM under the current US allocation system. Among the 3 groups in our analysis, patients on tMCS were most likely to have adverse waitlist outcomes,

Table 1 Baseline Characteristics at Time of Listing of PPCM Patients Listed for Heart Transplant, by MCS Bridging Strategy

Variable	Total ($n = 1,043$)	No device ($n = 575$)	tMCS ($n = 177$)	dMCS ($n = 291$)	p value
Demographics					
Age, years	33 (27-42)	34 (27-43)	31 (25-38)	34 (28-42)	**0.005**
Black race	528 (50.62%)	302 (52.52%)	83 (46.89%)	143 (49.14%)	0.355
BMI, kg/m^2	27.37 (23.04-31.63)	26.63 (22.62-31.20)	25.13 (22.13-29.90)	29.30 (25.24-32.96)	**< 0.001**
Comorbidities					
Diabetes	130 (12.46%)	81 (14.14%)	14 (8.00%)	35 (12.03%)	0.095
Dialysis	16 (1.53%)	8 (1.40%)	6 (3.39%)	2 (0.69%)	0.070
Cerebrovascular disease	55 (5.27%)	29 (5.09%)	7 (4.14%)	19 (6.60%)	0.485
Smoking history	282 (27.04%)	135 (23.81%)	48 (27.59%)	99 (34.02%)	**0.006**
Severe functional impairment	327 (31.35%)	134 (23.30%)	107 (60.45%)	86 (29.55%)	**< 0.001**
Status—before October 18, 2018					**< 0.001**
1A	236 (27.35%)	95 (18.41%)	68 (58.12%)	73 (31.74%)	
1B	355 (41.14%)	218 (42.25%)	29 (24.79%)	108 (46.96%)	
2	251 (29.08%)	192 (37.21%)	19 (16.24%)	40 (17.39%)	
Status—after October 18, 2018					**< 0.001**
1	4 (2.23%)	0 (0.00%)	3 (5.00%)	1 (1.64%)	
2	49 (27.37%)	6 (10.34%)	36 (60.00%)	7 (11.48%)	
3	22 (12.29%)	8 (13.79%)	4 (6.67%)	10 (16.39%)	
4	67 (37.43%)	17 (29.31%)	10 (16.67%)	40 (65.57%)	
5	2 (1.12%)	2 (3.45%)	0 (0.00%)	0 (0.00%)	
6	33 (18.44%)	25 (43.10%)	6 (10.00%)	2 (3.28%)	
Listing year	2012 (2006-2017)	2010 (2004-2016)	2015 (2006-2019)	2014 (2010-2018)	**< 0.001**
On MCS at listing	323 (30.97%)	0 (0.00%)	115 (64.97%)	208 (71.48%)	**< 0.001**
Inotrope-dependent	510 (48.90%)	317 (55.13%)	125 (70.62%)	68 (23.37%)	**< 0.001**
Ventilator-dependent	41 (3.93%)	11 (1.91%)	20 (11.30%)	10 (3.44%)	**< 0.001**
Hemodynamic data					
Cardiac index, liter/min m^2	2.06 (1.64-2.49)	2.02 (1.64-2.48)	1.98 (1.59-2.41)	2.17 (1.67-2.60)	**0.037**
Mean PAP, mm Hg	29 (23-35)	29 (23-35)	31 (26-38)	28 (20-35)	**< 0.001**
PCWP, mm Hg	20 (13-25)	20 (14-25)	22.5 (16-28)	18 (10-25)	**< 0.001**
PVR, WU	2.44 (1.67-3.61)	2.5 (1.67-3.68)	2.90 (1.74-4.05)	2.19 (1.62-3.21)	**0.026**

Abbreviations: BMI, body mass index; dMCS, durable mechanical circulatory support; MCS, mechanical circulatory support; PAP, pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; PPCM, peripartum cardiomyopathy; PVR, pulmonary vascular resistance; tMCS, temporary mechanical circulatory support.

Number (frequency) or median (interquartile range). Bold type denotes $p < 0.05$.

that is, death or delisting due to sickness (significantly more so than dMCS patients; difference was not significant in comparison to patients on no MCS, Figure 3e). In fact, 6-month incidence of delisting due to illness in the tMCS population was higher than 6-month waitlist mortality (Figure 3). These findings highlight the high acuity of PPCM patients requiring tMCS support while waiting for HT.

Although PPCM is a relatively infrequent cause of end-stage heart failure requiring transplantation, accounting for 5% of HTs in US females, PPCM patients are a particularly vulnerable group of patients undergoing OHT.[3] A large registry study of over 800 PPCM patients transplanted from 1987-2020 reported higher post-transplant mortality in PPCM patients compared to other female OHT recipients.[14] This disparity was present in the early postoperative period and persisted to 15 years post-transplant.[14] PPCM patients are particularly at risk for post-transplant rejection (which occurs more frequently in young female patients) and allosensitization.[3] Allosensitization is associated with poor peritransplant outcomes, including longer waitlist outcomes due to reduced donor pools, increased incidence and severity of rejection, and higher post-transplant mortality.[15] PPCM patients may develop allosensitization from antigenic exposure during pregnancy (particularly if multiparous) and also are 4 times as likely to be of Black race, which is a novel risk factor for allosensitization.[1,2,15] Notably, VAD support is a known risk factor for allosensitization—35% to 66% of patients bridged to OHT with VADs have been reported to be allosensitized.[15] This phenomenon is thought to be due to perioperative blood transfusions and immunologic reaction to the device's prosthetic material.[15] Although these mechanisms of sensitization could theoretically also occur with tMCS devices, allosensitization appears to occur more rarely in tMCS recipients and is described only in case reports.[16, 17] In our study, PPCM patients were more likely than propensity-matched female controls to receive any type of MCS (Figure 1), reflecting higher pretransplant acuity. Reassuringly, use of tMCS or dMCS did not translate to increased risk for post-transplant graft rejection or failure (Tables 3 and 4).

Given the increasing use of tMCS in the new allocation era for patients with PPCM, we wanted to evaluate the

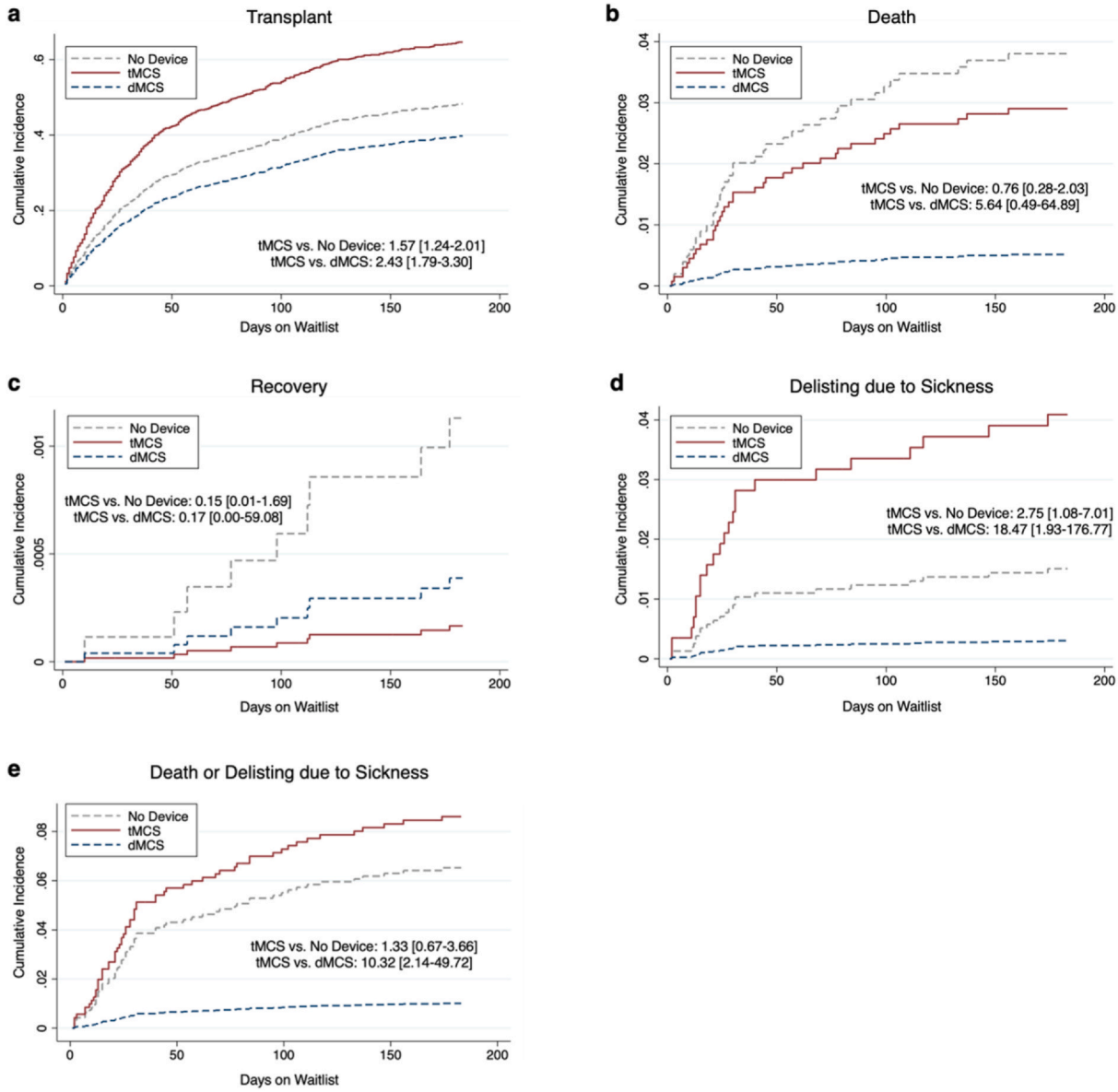

Figure 3 Six-month waitlist outcomes, including (a) transplant, (b) death, (c) recovery, (d) delisting due to sickness, and (e) composite of death and delisting due to sickness, in PPCM patients listed for heart transplant, by MCS bridging strategy. Adjusted cumulative incidence and subhazard ratios for specified waitlist outcomes with 95% confidence interval are shown. dMCS, durable mechanical circulatory support; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support.

outcomes of tMCS as a bridging strategy in this vulnerable population with many inherent risk factors for poor cardiac graft outcomes. Existing studies describe the successful employment of IABP, ECMO, and Impella devices, with acceptable risk profiles, in PPCM-associated cardiogenic shock, primarily with the intention of bridge to recovery (and sometimes VAD), but only in case reports and small cohorts.[4-7,18,19] Based on these reports, the Heart Failure Association of the European Society of Cardiology Study Group's statement on PPCM recommends considering initiation of MCS in severe PPCM.[20] The majority (64%) of patients supported with tMCS in our cohort received IABPs (Table 1). IABP use primarily drove the difference in tMCS usage between patients with and without PPCM (Figure 1). For peripartum patients experiencing the hemodynamic changes of pregnancy, the afterload reduction and coronary perfusion support provided by IABPs, which can be easily placed percutaneously at the bedside, may provide additional benefit beyond inotropes.[7, 19] In our cohort, tMCS patients were higher acuity on the waitlist than even their dMCS counterparts, as demonstrated by higher listing status, inotrope and ventilator dependency, and longer pretransplant hospitalizations (Tables 1 and 2). The ability of tMCS to support sicker patients, yet achieve equivalent

Table 2 Transplant and Donor Characteristics of PPCM Patients Undergoing Heart Transplant, by MCS Bridging Strategy

Variable	Total ($n = 681$)	No device ($n = 329$)	tMCS ($n = 137$)	dMCS ($n = 215$)	p value
Recipient characteristics at time of transplant					
Status—before October 18, 2018					**< 0.001**
1A	320 (57.35%)	125 (41.95%)	75 (91.46%)	120 (67.42%)	
1B	202 (36.20%)	138 (46.31%)	6 (7.32%)	58 (32.58%)	
2	36 (6.45%)	35 (11.74%)	1 (1.22%)	0 (0.00%)	
Status—after October 18, 2018					**< 0.001**
1	10 (8.13%)	0 (0.00%)	8 (14.55%)	2 (5.41%)	
2	62 (50.41%)	6 (19.35%)	46 (83.64%)	10 (27.03%)	
3	21 (17.07%)	7 (22.58%)	1 (1.82%)	13 (35.14%)	
4	23 (18.70%)	11 (35.48%)	0 (0.00%)	12 (32.43%)	
6	7 (5.69%)	7 (22.58%)	0 (0.00%)	0 (0.00%)	
MCS support at time of transplant	328 (48.16%)	0 (0.00%)	122 (89.05%)	206 (95.81%)	**< 0.001**
Waitlist time, days	53 (16-189)	40 (14-106)	21 (9-54)	190 (68-478)	**< 0.001**
Transplant year	2012 (2006-2017)	2009 (2005-2015)	2016 (2007-2019)	2014 (2010-2017)	**< 0.001**
Days admitted before transplant	3 (1-27)	3 (0-27)	23 (9-42)	1 (0-1)	**< 0.001**
ICU before transplant	266 (39.47%)	133 (40.80%)	116 (84.67%)	17 (8.06%)	**< 0.001**
Hemodynamic data					
Cardiac index, liter/min m^2	2.15 (1.71-2.55)	2.11 (1.67-2.56)	1.90 (1.59-2.38)	2.25 (1.85-2.63)	**< 0.001**
Mean PAP, mm Hg	28 (21-35)	28 (22-35)	31 (24-36)	24 (18-32)	**< 0.001**
PCWP, mm Hg	18 (12-25)	19 (13-25)	21.5 (16-27)	15 (10-23)	**< 0.001**
PVR, WU	2.27 (1.52-3.21)	2.39 (1.54-3.26)	2.64 (1.70-3.74)	2.03 (1.43-2.80)	**0.003**
Donor and transplant characteristics					
Age, years	29 (21-38)	28 (20-38)	31 (23-40)	30 (22-38)	0.403
Sex mismatch	342 (50.22%)	176 (53.50%)	72 (52.55%)	94 (43.72%)	0.069
Size mismatch	282 (41.41%)	123 (37.39%)	65 (47.45%)	94 (43.72%)	**< 0.001**
Cause of death					
Cardiovascular	8 (1.17%)	8 (2.43%)	0 (0.00%)	0 (0.00%)	**0.014**
Stroke	181 (26.58%)	92 (27.96%)	32 (23.36%)	57 (26.51%)	0.591
Trauma	292 (42.88%)	143 (43.47%)	51 (37.23%)	98 (45.58%)	0.290
Organ ischemic time, hours	3.19 (2.53-3.85)	3.08 (2.45-3.80)	3.43 (2.87-3.97)	3.27 (2.42-3.75)	**0.015**
Donor distance, miles	136 (19-334)	119 (14-333)	184 (51-369)	126 (12-310)	**0.032**

Abbreviations: dMCS, durable mechanical circulatory support; MCS, mechanical circulatory support; ICU, intensive care unit; PAP, pulmonary artery pressure; PPCM, peripartum cardiomyopathy; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; tMCS, temporary mechanical circulatory support.

Number (frequency) or median (interquartile range). Bold type denotes $p < 0.05$.

post-transplant graft survival as patients requiring no MCS support or stable enough for dMCS (Figure 4, Table 4), suggests that tMCS is a safe and effective bridging strategy in PPCM, providing strong corroborating evidence for the European Society of Cardiology Heart Failure Association's recommendation.[20]

In comparison to tMCS, durable VADs have been more widely studied in PPCM. In a registry study of 99 PPCM patients who received VADs, survival was better in PPCM patients than non-PPCM female patients, attributed to younger age and fewer comorbidities in the PPCM population.[21] However, rates of recovery were low (6%) overall, and less than half of PPCM patients underwent OHT after 3 years.[21] Similarly, we observed strikingly longer waitlist time in our dMCS cohort (median 190 days) compared to the tMCS (21 days) and no device (40 days) groups (Table 2). Although dMCS is a known risk factor for allosensitization, we found 3-year graft survival to be similar in patients bridged with dMCS and no MCS (Table 4). dMCS support was also protective against waitlist death at 6 months, compared to no MCS (Table S4). VADs are evidently a safe option for long-term support in PPCM. However, given low rates of recovery and explantation, quality of life in PPCM patients living with VADs vs those who have undergone OHT should be investigated.

Limitations of our study include all those inherent to its retrospective design. Analysis was restricted to variables recorded in the UNOS Thoracic database. Notably, clinically relevant information on PPCM course (i.e., parity, allosensitization) and MCS duration and complications were either not available or very sparse and therefore excluded. Additionally, we focused on patients supported on

Table 3 Post-Transplant Outcomes of PPCM Patients, by MCS Bridging Strategy

Variable	Total ($n = 681$)	No device ($n = 329$)	tMCS ($n = 137$)	dMCS ($n = 215$)	p value
Post-op length of stay, days	15 (10-22)	12 (9-20)	17 (12-24)	16.5 (12-24)	**< 0.001**
Events before discharge					
Acute rejection	133 (22.93%)	56 (21.88%)	32 (25.81%)	45 (22.50%)	0.683
Dialysis	53 (7.91%)	24 (7.38%)	12 (8.76%)	17 (8.17%)	0.870
Stroke	11 (1.65%)	6 (1.86%)	2 (1.47%)	3 (1.44%)	0.917
Permanent pacemaker	12 (1.79%)	2 (0.62%)	2 (1.46%)	8 (3.81%)	**0.025**
30-day mortality	17 (2.52%)	8 (2.45%)	4 (2.92%)	5 (2.37%)	0.900
Rejection within 1 year	236 (42.60%)	128 (47.58%)	45 (43.69%)	63 (34.62%)	**0.023**
Follow-up time, years	3.9 (1.1-8.1)	4.8 (1.5-9.0)	2.0 (0.6-6.1)	4.0 (2.0-7.8)	**< 0.001**
Cause of death					0.365
Graft failure	62 (29.81%)	42 (33.60%)	8 (25.00%)	12 (23.53%)	
Cardiovascular	66 (31.73%)	43 (34.40%)	9 (28.12%)	14 (27.45%)	
Infection	14 (6.73%)	5 (4.00%)	4 (12.50%)	5 (9.80%)	
Pulmonary	11 (5.29%)	7 (5.60%)	0 (0.00%)	4 (7.84%)	
Cerebrovascular	6 (2.88%)	3 (2.40%)	2 (6.25%)	1 (1.96%)	
Hemorrhage	4 (1.92%)	3 (2.40%)	0 (0.00%)	1 (1.96%)	
Malignancy	4 (1.92%)	3 (2.40%)	1 (3.12%)	0 (0.00%)	
Other	41 (19.71%)	19 (15.20%)	8 (25.00%)	14 (27.45%)	
Retransplant	24 (3.68%)	17 (5.50%)	4 (2.94%)	3 (1.44%)	**0.049**
Time to retransplant, years	4.6 (2.0-8.9)	4.7 (2.6-9.4)	3.9 (1.5-5.8)	4.5 (1.8-15.0)	0.754

Abbreviations: dMCS, durable mechanical circulatory support; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support.

Number (frequency) or median (interquartile range). Bold type denotes $p < 0.05$.

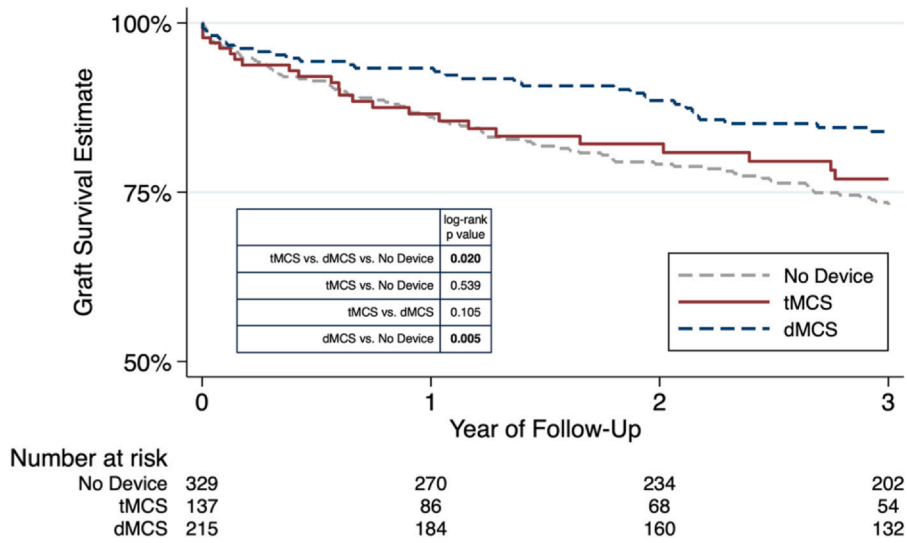

Figure 4 Three-year unadjusted Kaplan-Meier post-transplant graft survival estimates in PPCM patients, by MCS bridging strategy. dMCS, durable mechanical circulatory support; MCS, mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support.

only 1 type of MCS throughout their waitlist period, resulting in the exclusion of 12 PPCM patients who were initially on tMCS and transitioned to VAD. Interpretation of cumulative incidence of waitlist outcomes is limited by the inclusion of patients supported on MCS at any time point during their waitlist period, not necessarily for the entire duration of their listing, particularly for those supported on tMCS devices.

In conclusion, our analysis demonstrates a trend toward increasing use of tMCS in PPCM patients on the HT waitlist and confirms that these devices are a safe and effective bridging strategy in PPCM. To our knowledge, this is the first and largest study to investigate tMCS as a bridge to transplant in the PPCM population. More investigation into ideal timing and candidates, as well as immunologic profile, for different tMCS devices would

Table 4 Cox Proportional-hazards Model for 3-Year Graft Failure After Heart Transplant in PPCM Patients

	Univariable analysis		Multivariable analysis	
Variable	Hazard ratio [95% CI]	*p* value	Adjusted hazard ratio [95% CI]	*p* value
tMCS vs no device	0.87 [0.55-1.37]	0.545	0.56 [0.06-5.43]	0.620
dMCS vs no device	0.56 [0.37-0.84]	**0.006**	0.36 [0.05-2.82]	0.332
Inotrope dependence	1.20 [0.85-1.69]	0.293	0.41 [0.12-1.44]	0.165
Mechanical ventilation	0.51 [0.16-1.59]	0.243	5.56 [0.56-54.82]	0.141
Sex mismatch	1.23 [0.88-1.73]	0.221	2.93 [1.08-7.97]	**0.035**
Pulmonary vascular resistance > 3 at listing	1.02 [0.73-1.43]	0.903	0.40 [0.11-1.39]	0.147
Donor death due to stroke	1.08 [0.75-1.57]	0.669	3.50 [1.22-10.05]	**0.020**

Abbreviations: CI, confidence interval; dMCS, durable mechanical circulatory support; PPCM, peripartum cardiomyopathy; tMCS, temporary mechanical circulatory support.

Bold type denotes $p < 0.05$.

help to continue improving outcomes in this vulnerable patient population.

Author contributions

C.S., A.I., and P.A. conceived the study design. C.S. performed the data analysis and wrote the manuscript with support from S.K., D.R., and A.I. N.W., M.S., J.J., M.A., and M.C. provided critical guidance on data interpretation and statistical plan. All authors discussed the results and contributed to the final manuscript.

Disclosure statement

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.

The authors thank UNOS for the data used in this analysis.

None of the authors of this paper report any financial conflicts of interest or sources of funding relevant to this research.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhlto.2024.100126.

References

1. Arany Z, Elkayam U. Peripartum cardiomyopathy. Circulation 2016;133:1397-409.
2. Arany Z. Peripartum cardiomyopathy. N Engl J Med 2024;390:154-64.
3. Rasmusson K, Brunisholz K, Budge D, et al. Peripartum cardiomyopathy: post-transplant outcomes from the United Network for Organ Sharing Database. J Heart Lung Transplant 2012;31:180-6.
4. Bouabdallaoui N, Demondion P, Leprince P, Lebreton G. Short-term mechanical circulatory support for cardiogenic shock in severe peripartum cardiomyopathy: La Pitie-Salpetriere experience. Interact Cardiovasc Thorac Surg 2017;25:52-6.
5. Olson TL, O'Neil ER, Ramanathan K, Lorusso R, MacLaren G, Anders MM. Extracorporeal membrane oxygenation in peripartum cardiomyopathy: a review of the ELSO Registry. Int J Cardiol 2020;311:71-6.
6. Elkayam U, Schafer A, Chieffo A, et al. Use of Impella heart pump for management of women with peripartum cardiogenic shock. Clin Cardiol 2019;42:974-81.
7. Gevaert S, Van Belleghem Y, Bouchez S, et al. Acute and critically ill peripartum cardiomyopathy and 'bridge to' therapeutic options: a single center experience with intra-aortic balloon pump, extra corporeal membrane oxygenation and continuous-flow left ventricular assist devices. Crit Care 2011;15:R93.
8. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 1999;94:496-509.
9. Hameed AB, Lawton ES, McCain CL, et al. Pregnancy-related cardiovascular deaths in California: beyond peripartum cardiomyopathy. Am J Obstet Gynecol 2015;213:379.e1-379.e10.
10. Shore S, Golbus JR, Aaronson KD, Nallamothu BK. Changes in the United States adult heart allocation policy: challenges and opportunities. Circ Cardiovasc Qual Outcomes 2020;13:e005795.
11. Cogswell R, John R, Estep JD, et al. An early investigation of outcomes with the new 2018 donor heart allocation system in the United States. J Heart Lung Transplant 2020;39:1-4.
12. Hill MA, Kwon JH, Shorbaji K, Kilic A. Waitlist and transplant outcomes for patients bridged to heart transplantation with Impella 5.0 and 5.5 devices. J Card Surg 2022;37:5081-9.
13. Seese L, Hickey G, Keebler ME, et al. Direct bridging to cardiac transplantation with the surgically implanted Impella 5.0 device. Clin Transplant 2020;34:e13818.
14. Kwon JH, Tedford RJ, Ramu B, et al. Heart transplantation for peripartum cardiomyopathy: outcomes over 3 decades. Ann Thorac Surg 2022;114:650-8.
15. Al-Mohaissen MA, Virani SA. Allosensitization in heart transplantation: an overview. Can J Cardiol 2014;30:161-72.
16. Shakoor H, Abdelrehim A, Maliakkal N, et al. Alert! Does prolonged temporary support induce an immunological response? JACC Case Rep 2023;16:101877.
17. Goetz RL, Kaleekal TS, Wille KM, et al. HLA sensitization in patients bridged to lung transplantation with extracorporeal membrane oxygenation. Transplant Direct 2023;9:e1497.
18. Kiriyama Y, Kinishi Y, Hiramatu D, et al. Outcomes of severe peripartum cardiomyopathy and mechanical circulatory support: a case series. JA Clin Rep 2021;7:80.

19. Samalavicius RS, Puodziukaite L, Radaviciute I, et al. Prophylactic use of an intra-aortic balloon pump in a high-risk patient with peripartum cardiomyopathy requiring cesarean delivery. Int J Obstet Anesth 2018;33:67-71.
20. Bauersachs J, Konig T, van der Meer P, et al. Pathophysiology, diagnosis and management of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Study Group on peripartum cardiomyopathy. Eur J Heart Fail 2019;21:827-43.
21. Loyaga-Rendon RY, Pamboukian SV, Tallaj JA, et al. Outcomes of patients with peripartum cardiomyopathy who received mechanical circulatory support. Data from the Interagency Registry for Mechanically Assisted Circulatory Support. Circ Heart Fail 2014;7:300-9.