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REVIEW

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Short-term mechanical circulatory support as a bridge to durable left ventricular assist device implantation in refractory cardiogenic shock: a systematic review and meta-analysis

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Summary

Short-term mechanical circulatory support (MCS) is increasingly used as a bridge to decision in patients with refractory cardiogenic shock. Subsequently, these patients might be bridged to durable MCS either as a bridge to candidacy/transplantation, or as destination therapy. The aim of this study was to review support duration and clinical outcome of short-term MCS in cardiogenic shock, and to analyse application of this technology as a bridge to long-term cardiac support (left ventricular assist device, LVAD) from 2006 till June 2016. Using Cochrane Register of Trials, Embase and Medline, a systematic review was performed on patients with cardiogenic shock from acute myocardial infarction, end-stage cardiomyopathy, or acute myocarditis, receiving short-term MCS. Studies on periprocedural, post-cardiotomy and cardiopulmonary resuscitation support were excluded. Thirty-nine studies, mainly registries of heterogeneous patient populations ($n = 4151$ patients), were identified. Depending on the device used (intra-aortic balloon pump, TandemHeart, Impella 2.5, Impella 5.0, CentriMag and peripheral veno-arterial extracorporeal membrane oxygenation), mean support duration was (range) 1.6–25 days and the mean proportion of short-term MCS patients discharged was (range) 45–66%. The mean proportion of bridge to durable LVAD was (range) 3–30%. Bridge to durable LVAD was most frequently performed in patients with end-stage cardiomyopathy (22 [12–35]%). We conclude that temporary MCS can be used to bridge patients with cardiogenic shock towards durable LVAD. Clinicians are encouraged to share their results in a large multicentre registry in order to investigate optimal device selection and best duration of support.

Keywords: Mechanical circulatory support • Left ventricular assist device • Cardiogenic shock • Heart failure

INTRODUCTION

Refractory cardiogenic shock is a deadly complication of acute myocardial infarction (AMI), fulminant myocarditis, and end-stage cardiomyopathy (CMP). Short-term mechanical circulatory support (MCS) using different techniques (Supplementary Material, Table S1) has become a realistic and cost-effective option to reverse shock [1]. In this way, time can be taken to assess and ameliorate secondary organ failures and to predict the chance of cardiac recovery ('bridge to recovery and decision') [2]. When recovery cannot be expected, a multidisciplinary decision has to be made to subsequently bridge the patient either to urgent heart transplantation (HTX), or to durable MCS (mainly left ventricular assist device (LVAD) implantation as 'bridge to bridge' or 'bridge to destination') or to withdrawal of support ('bridge to palliative care') [3]. Due to extremely limited suitable donor hearts and good long-term function of second generation LVADs, selected severe heart failure patients around the world are increasingly being bridged to durable MCS, either as destination therapy or as a bridge to candidacy or transplantation [4]. However, the extent and optimal timing of bridging towards recovery or long-term MCS in patients with cardiogenic shock being supported with short-term MCS is currently unclear. We aimed at reviewing (i) support duration, (ii) outcome including feasibility of bridging towards durable LVAD stratified to device and diagnosis, and (iii) providing a real-life algorithm on the selection of patients receiving short-term support who can be bridged successfully to long-term support using optimal timing for changing the device.

METHODS

We created this manuscript according to the PRISMA guidelines (see Supplementary Material, data for checklist) [5].

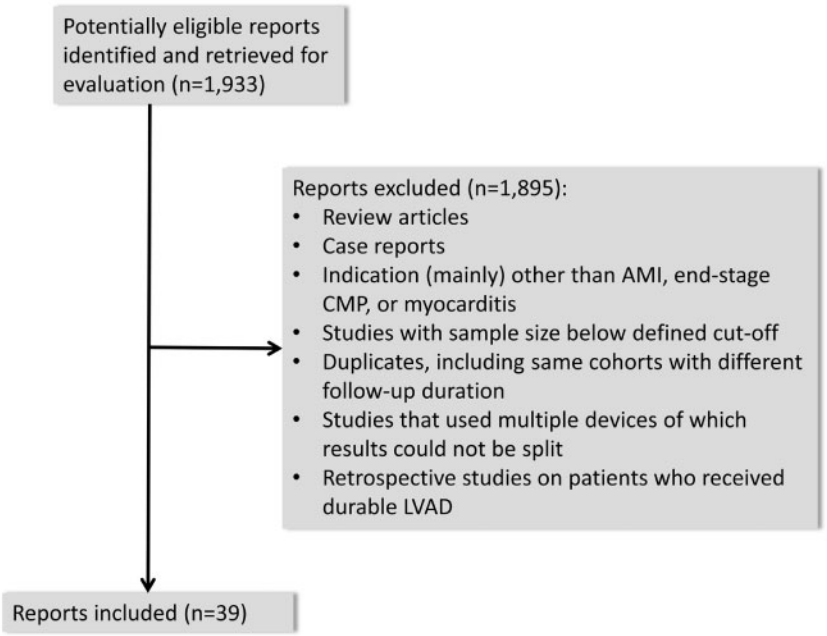

Figure 1: Identification of studies.

Using Cochrane Central Register of Controlled Trials, Embase and Medline, we performed a literature search in June 2016 using the following search terms: (i) 'heart-assist devices' [MeSH Terms] AND ('heart failure' [MeSH Terms] OR 'shock, cardiogenic' [MeSH Terms]) AND 'bridge' [text word]; and (ii) extracorporeal membrane oxygenation [MeSH Terms] OR mechanical circulatory support [text word]. Two investigators (C.A.U. and S.A.) then independently retrieved potentially eligible reports for evaluation. Both investigators independently examined design, patient population and interventions in the reports. A methodological filter was used to limit the results to adult humans, published in the last 10 years (back to the year 2006), in English. We restricted results to the last 10 years given the introduction of durable, truly long-term LVADs in the year 2006. In addition, we performed hand searching of reference lists of obtained (review) articles, www.clinicaltrials.gov was searched, and conference proceedings were checked. We had contact with several expert colleagues to ensure that no potentially eligible studies were missed.

We selected all retrospective and prospective cohort studies on adult cardiogenic shock patients receiving short-term (hours to weeks) MCS for pump failure (i.e. severe left or biventricular (Biv) cardiac dysfunction). We excluded reports on patients (primarily) undergoing high risk (coronary) intervention, with post-cardiotomy heart failure, cardiac allograft failure or refractory cardiac arrest and case reports. To exclude severely underpowered, low quality studies, we made (arbitrary) cut-offs for study size (intra-aortic balloon pump (IABP) in cardiogenic shock from AMI: at least 100 patients; IABP in end-stage CMP, TandemHeart, Impella and central extracorporeal membrane oxygenation (ECMO): at least 10 patients; peripheral veno-arterial (VA)-ECMO: at least 50 patients). Studies that included a lower number of patients than these cut-offs were excluded.

We evaluated the mode and duration of MCS, the proportion of patients bridged to the next therapy or condition (bridge to transplant versus bridge to durable MCS versus bridge to recovery versus bridge to palliation), and hospital discharge. Outcomes were stratified according to the device that was used. Additional meta-analysis was performed of studies stratified to diagnosis in which only studies investigating isolated patients with AMI, acute myocarditis, or end-stage CMP/heart failure (ESHF) were included.

Statistical analysis

All data were analysed with SPSS 22.0 (SPSS Inc., Chicago, IL, USA), and MedCalc (MedCalc Software, Ostend, Belgium) software. Categorical variables were presented in numbers and in percentages. Continuous variables were presented as mean ± standard deviation (SD). For continuous variables reported as median and interquartile range (IQR), the mean and SD were estimated. The mean was estimated by the formula $x = (a + 2m + b)/4$ using the values of the median (m), P25 and P75 (a and b, respectively) [6]. The estimator SD = interquartile range/1.35 was used to estimate SD from the interquartile range [7]. For continuous variables reported as median and range, we calculated mean ± SD by using the appropriate formulas according to the size of the sample as proposed by Hozo *et al.* [6].

The final results were presented as mean ± SD or as proportions with the associated 95% confidence interval (CI). Heterogeneity between trials, defined as variation among the results of individual trials beyond that expected from chance, was assessed with Cochran's Q-statistic (P_{hetero}) and I^2 statistic. As a result of general heterogeneity of patient populations, a random effects model was consistently used to calculate averages. Differences between groups concerning a binary outcome were tested with a chi-square test. Differences between groups concerning a continuous outcome were tested with a *t*-test (2 groups) or analysis of variance (ANOVA, more than 2 groups).

RESULTS

Thirty-nine studies ($n = 4151$ patients) met our inclusion criteria (Fig. 1). Patients were supported with IABP ($n = 2527$), TandemHeart ($n = 272$), Impella 2.5 ($n = 343$), Impella 5.0 ($n = 123$), CentriMag ($n = 128$) or VA-ECMO ($n = 758$).

Table 1: Intra-aortic balloon pump

Reference	N	Patients	Design	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Culprit vessel LM or LAD (%)	Mean duration of support (days)	Bridge to transplant (%)	Bridge to durable MCS (%)	Bridge to recovery (%)	Bridge to palliation (%)	Hospital discharge (%)
AMI:															
[8]	225	AMI	Registry	66 ± 14	NA	NA	NA	NA	73	NA	NA	NA	NA	NA	62
[9]	128	AMI	Registry	65 ± 12	1.2 ± 0.4	NA	NA	63	52	NA	NA	NA	NA	NA	54
[10]	487	AMI	Registry	68 ± NA	NA	NA	NA	NA	72	NA	NA	NA	NA	NA	57
[15]	300	AMI	RCT	70 ± 15	1.3 ± 0.5	3.6 ± 3.8	42	80	54	3.0 ± 1.5	0	4	NA	NA	60
[11]	199	AMI	Registry	65 ± 13	1.2 ± 0.7	6.0 ± 4.3	NA	NA	60	NA	NA	NA	NA	NA	53
[12]	466	AMI	Registry	64 ± 14	NA	NA	NA	NA	NA	5.9 ± 6.1	NA	NA	NA	NA	59
[13]	162	AMI	Registry	65 ± 12	NA	NA	47	36	70	NA	NA	NA	NA	NA	52
[14]	300	AMI	Registry	61 ± 11	NA	NA	33	56	57	3.0 ± 4.3	NA	NA	NA	30	58
Mean ± SD or proportion (95% CI)	2.267			65 ± 14	1.2 ± 0.6	4.6 ± 4.2	40 [33–48] I^2 = 80% P_{hetero} <0.01	59 [40–77] I^2 = 97% P_{hetero} <0.001	63 [56–69] I^2 = 89% P_{hetero} <0.001	4.3 ± 4.9					57 [55–60] I^2 = 12% P_{hetero} = NS
ESHF:															
[18]	107	ESHF = 69% AMI = 15% Biv failure = 44%	Registry	58 ± 16	1.9 ± 0.9	NA	NA	25	NA	NA	10	30	40	20	NA
[16]	88	ESHF Biv failure = 3%	Registry	57 ± 13	1.9 ± 1.3	NA	0	0	NA	21 ± 22	66	24	3	7	NA
[19]	15	ESHF IM1 = 53% IM2 = 47% Contra-indication HTX/LVAD Biv failure=100%	Registry	50 ± 12	2.1 ± 1.3	NA	0	0	NA	78 ± 41	NA	40	20	40	60
[17]	50	ESHF, BTT strategy, relative or absolute contra-indication for LVAD Biv failure=NA	Registry	56 ± 11	1.7 ± 0.9	NA	0	0	NA	18 ± 37	86	6	0	8	NA
Mean ± SD or proportion (95% CI)	260			57 ± 14	1.9 ± 1.1	NA	0 [0–2] I^2 = 0% P_{hetero} = NS	4 [1–21] I^2 = 95% P_{hetero} <0.001	NA	25 ± 33	53 [10–94] I^2 = 98% P_{hetero} <0.001	23 [12–37] I^2 = 82% P_{hetero} <0.001	12 [0–39] I^2 = 96% $P_{hetero} \leq$ 0.001	16 [7–27] I^2 = 79% P_{hetero} <0.01	NA

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; LM: left main (coronary artery); LAD: left anterior descending (coronary artery); ESHF: end-stage heart failure; AMI: acute myocardial infarction; Biv: biventricular; IM: INTERMACS profile; HTX: heart transplantation; NA: not applicable; NS: not significant.

Table 2: TandemHeart

Reference	*N*	Patients	Design	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Culprit vessel LM or LAD (%)	Mean duration of support (days)	Bridge to transplant (%)	Bridge to durable MCS (%)	Bridge to recovery (%)	Bridge to palliation (%)	Hospital discharge (%)
[20]	65 Left = 79% Right = 8% BiVAD = 13%	ESHF Biv failure = 13%	Registry	54 ± 15	1.8 ± 1.1	3.6 ± 4.2	25	NA	NA	5.8 ± 2.9	0	14	35	51	49
[21]	49 Tandem Heart = 86% Impella = 14%	AMI = 88% Biv failure = NA	Registry	59 ± 14	NA	NA	65	NA	NA	2.9 ± 3.3	0	12	41	47	45
[22]	117	AMI = 68% ESHF = 32% Biv failure = NA	Registry	55 ± 16	1.5 ± 1.0	2.7 ± 8.2	48	46	NA	5.8 ± 4.8	4	27	NA	NA	60
[23]	22	AMI = 23% ESHF = 64% Myocarditis = 9% Refractory VF = 4% Biv failure = NA	Registry	48 ± 14	2.0 ± NA	NA	4	NA	NA	6.8 ± 9.4	27	23	14	36	46
[24]	19	Mainly AMI Biv failure = NA	RCT	66 ± 14	1.8 ± 0.8	0.5 ± 0.5	NA	NA	NA	2.5 ± 1.9	0	16	53	32	53
Mean ± SD or proportion (95% CI)	272			56 ± 16	1.6 ± 1.0	2.8 ± 6.7	35 [15–58] I^2 = 92% P_{hetero} <0.001	NA	NA	5.1 ± 4.8	4 [0–11] I^2 = 80% P_{hetero} <0.001	19 [13–27] I^2 = 45% P_{hetero} = NS	36 [23–49] I^2 = 64% P_{hetero} = 0.04	45 [38–53] I^2 = 41% P_{hetero} = NS	53 [46–59] I^2 = 8% P_{hetero} = NS

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; LM: left main (coronary artery); LAD: left anterior descending (coronary artery); VF: ventricular fibrillation; AMI: acute myocardial infarction; NA: not applicable; RCT: randomized controlled trial; NS: not significant; SD: standard deviation; ESHF: end-stage heart failure; MCS: mechanical circulatory support.

Table 3: Impella

Reference	*N*	Patients	Design	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Culprit vessel LM or LAD (%)	Mean duration of support (days)	Bridge to transplant (%)	Bridge to durable MCS (%)	Bridge to recovery (%)	Bridge to palliation (%)	Hospital discharge (%)
Impella 2.5:															
[30]	22	AMI	Registry	58 ± 12	1.2 ± 0.3	6.4 ± 5.3	55	55	68	1.5 ± 1.1	0	5	72	23	59
[26]	154	AMI	Registry	64 ± 13	1.4 ± 0.7	4.1 ± 3.6	49	66	69	1.2 ± 1.9	NA	NA	NA	NA	50.7
[25]	120	AMI	Registry	64 ± 12	NA	5.8 ± 4.9	41	69	NA	1.8 ± 2.1	0	2	44	42	36
[29]	10	AMI = 70% Post CPR = 30%	Registry	70 ± 9	NA	NA	30	NA	70	2.2 ± 2.6	0	10	80	10	80
[28]	25	AMI	Registry	58 ± 10	NA	5.7 ± 3.4	56	92	96	3.5 ± 6.9	0	0	28	40	24
[27]	12	AMI	RCT	65 ± 10	NA	6.5 ± 1.5	85	92	54	0.9 ± 0.8	0	0	75	25	50
Mean ± SD or proportion (95% CI)	343			63 ± 12	1.4 ± 0.7	5.0 ± 4.3	50 [41–60] I^2 = 55% P_{hetero} <0.05	73 [62–83] I^2 = 71% P_{hetero} <0.01	72 [57–85] I^2 = 72% P_{hetero} <0.01	1.6 ± 2.7	0 [0–2] I^2 = 0% P_{hetero} = NS	3 [1–5] I^2 = 0% P_{hetero} = NS	57 [39–74] I^2 = 78% P_{hetero} <0.01	32 [22–43] I^2 = 45% P_{hetero} = NS	47 [35–59] I^2 = 72% P_{hetero} <0.01
Impella 5.0:															
[31]	40	ESHF IM1 = 32% IM2 = 66% IM3 = 3% Biv failure = 65%	Registry	55 ± 13	2.0 ± 0.8	NA	0	0	NA	7.0 ± 5.0	33	38	5	25	68
[32]	14	AMI = 50% PCS = 43% CMP = 7% Biv failure = NA	Registry	64 ± 15	NA	4.7 ± 1.2	NA	71	NA	8.5 ± 4.7	0	29	43	29	64
[33]	40 Primary Impella = 62.5% Primary ECMO = 37.5%	AMI = 43% DCM = 30% PCS = 18% Others = 10% Biv failure = NA	Registry	57 ± 11	NA	3.8 ± 3.1	23	73	NA	7.3 ± 3.7	8	23	40	30	65
[34]	29 Impella RD = 17%	AMI = 38% ESHF = 24% Myocarditis = 10% PCS = 14% Other = 14% Biv failure = 0%	Registry	54 ± 13	NA	NA	48	97	NA	3.2 ± 3.1	0	28	41	31	59
Mean ± SD or proportion (95% CI)	123			56 ± 13	2.0 ± 0.8	4.0 ± 2.8	19 [0–55] I^2 = 94% P_{hetero} <0.001	57 [7–98] I^2 = 98% P_{hetero} <0.001	NA	6.1 ± 3.9	19 [2–48] I^2 = 88% P_{hetero} <0.01	30 [22–38] I^2 = 0% P_{hetero} = NS	30 [11–54] I^2 = 87% P_{hetero} <0.001	29 [22–37] I^2 = 0% P_{hetero} = NS	64 [55–72] I^2 = 0% P_{hetero} = NS

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; LM: left main (coronary artery); LAD: left anterior descending (coronary artery); AMI: acute myocardial infarction; DCM: dilated cardiomyopahty; NA: not applicable; NS: not significant; SD: standard deviation; ESHF: end-stage heart failure; IM: INTERMACS profile; MCS: mechanical circulatory support; Biv: biventricular; BiVAD: biventricular assist device.

We identified 8 studies of patients with AMI complicated by shock (Table 1): 7 were registries [8–14] and 1 was a randomized controlled trial (RCT) (IABP-SHOCK II trial: IABP versus conventional care) [15]. Most patients had anterior myocardial infarction, where the rate of Biv failure was not reported in any study. Support time was reported in only 3 studies [12, 14, 15]; means ranged from 3.0 to 5.9 days. One study found an association of support time and long-term survival: patients being assisted for 6 days or more had worse outcome [14]. Patients were bridged to either recovery or palliative care (30%, reported in 1 study [14]). Most studies presented cohorts from the pre-LVAD era. Thiele *et al.* reported that 3.7% of patients who received an IABP were bridged to durable MCS with good long-term outcome [15]. More than 55% of patients could be discharged from the hospital. Four studies investigated INTERMACS profile type I-II patients receiving prolonged IABP support via surgical subclavian (through a graft) [16], percutaneous axillary [17], or femoral access [18, 19] (Table 1). Tanaka *et al.* [16] and Estep *et al.* [17] succeeded to bridge most patients to transplantation. Ntalianis *et al.* [19] were able to reverse right ventricular dysfunction in some patients who had a former contra-indication for LVAD implantation. Bridge to LVAD was possible in 23 [12–37]% (I^2 = 82%, *P* for heterogeneity <0.001) with 30-day survival greater than 80%. Survival rate at discharge was not reported in most studies.

The TandemHeart was investigated in 5 studies: 4 cohort studies [20–23] and 1 RCT (Table 2) [24]. Occurrence of prior IABP/Impella support was 44–82% [20, 22, 24]. Median support time was 5.1 ± 4.8 days. One study provided the protocol for weaning [22]. Bridging to durable MCS was performed in 19 [13–27]%. Thirty-day survival in patients bridged to LVAD was 60–100%. About half of the patients survived until discharge.

Six studies reported Impella 2.5 support, predominantly in patients with cardiogenic shock from AMI (Table 3) [25–30]. Most patients had anterior myocardial infarction, the rate of Biv failure was not reported in any study. Occurrence of prior IABP support was 29–49% [25, 26]. Support time was short, 1.6 ± 2.7 days. Bridging to LVAD was performed in few patients. Forty-seven [35–59]% of patients were discharged alive (*P* for heterogeneity <0.01). Four studies evaluated the use of Impella 5.0 in mixed populations of cardiogenic shock (Table 3) [31–34]. Occurrence of prior IABP support was 0–52%. Mean support time was 6.1 ± 3.9 days. Thirty [22–38]% of patients could be bridged to durable MCS with good 30-day survival (63–100%). Two studies provided weaning protocols [32, 33]. A relative high proportion of patients were discharged alive (64 [55–72]%).

Four studies investigated central ECMO, mainly in Biv support mode (Table 4) [35–38]. Occurrence of prior IABP support was 59–85%. Based on our inclusion criteria we excluded cases from two studies and performed the analysis on the remaining patients [35, 36]. Support times were relatively long (20 ± 20 days). The weaning protocol was described in 1 study [35]. Several patients (25 [18–33]%) were bridged towards implantable VAD and 83–100% of them were discharged. Survival until discharge was relatively good: 66 [58–74]%.

We identified 5 cohorts of patients who received peripheral ECMO in cardiogenic shock of mixed etiology (Table 5) [39–43]. Prior IABP/Impella support occurred in 31–55% of the cases. Support time was longer in patients who survived at least until the next therapy than in patients who died [7.1 ± 6.1 vs 5.0 ± 6.9 days, standardized mean difference 0.4 [0.2–0.6], *P* < 0.001, I^2 = 0%, P_{hetero} = not significant (NS)]. Cannulation was changed to the subclavian or directly central position in 4–18%. Weaning protocols were provided by the groups from Padua and Paris [40, 42, 43]. A minority of patients was bridged to transplantation or LVAD. Carroll *et al.* reported that 24% of patients were bridged from ECMO to another form of MCS: 53% received durable LVAD, 23% received right ventricle assist device, 13% needed short-term biventricular assist device, 7% had right ventricle assist device + durable LVAD, and 3% received IABP. Fifty-nine percent of the patients who were bridged to any type of VAD survived to discharge, whereas 67% who were bridged to durable LVAD survived to discharge [41]. Tarzia *et al.* [40] demonstrated that recovery of cardiac function was achieved only in patients with *de novo* heart failure. Forty-five [39–51]% of patients survived until hospital discharge (*P* for heterogeneity NS). Three registries were found on peripheral VA-ECMO in isolated myocarditis (Table 5) [44–46]. Prior IABP support occurred in 31–65%. Support time was 7.0 ± 9.1 days. Hsu *et al.* [46] provided the protocol for weaning. Most patients (69 [64–75]%) were weaned and a minority (7 [3–11]%) was bridged towards durable mechanical support. Survival until hospital discharge was 64 [58–70]% (*P* for heterogeneity NS).

Additional analysis was performed of studies on isolated AMI, myocarditis or end-stage CMP/heart failure (Table 6). AMI (*n* = 2752): Patients receiving Impella or (central/peripheral) ECMO were younger than patients receiving IABP support (*P* = 0.04, *P* < 0.001, respectively). Patients receiving ECMO had higher creatinine levels than IABP or Impella patients (both *P* < 0.001). Lactate levels were lower in ECMO patients than in Impella patients (*P* < 0.05). Impella patients underwent cardiopulmonary resuscitation more frequently than IABP patients (*P* < 0.001). Impella and ECMO patients were more frequently mechanically ventilated than IABP patients (both *P* < 0.001). Support time was highest in ECMO patients and lowest in Impella patients (*P* < 0.001). Bridge to LVAD occurred most frequently in ECMO patients. Hospital discharge was greatest in IABP patients and lowest in Impella patients (*P* < 0.001). Myocarditis (*n* = 279): Isolated myocarditis was only investigated in peripheral ECMO studies. End-stage CMP/heart failure (*n* = 258): Preoperative cardiopulmonary resuscitation was more likely in combined TandemHeart/Impella 5.0 patients than in IABP assisted patients (*P* < 0.001). Support times were greater in patients treated with IABP than in patients who received TandemHeart or Impella 5.0 (*P* < 0.001). TandemHeart/Impella 5.0 patients were more frequently bridged towards LVAD (*P* < 0.01) but heterogeneity among studies was high.

DISCUSSION

We provide an overview of recent reports on short-term MCS (IABP, TandemHeart, Impella and ECMO) in cardiogenic shock from AMI, end-stage CMP, and myocarditis. Mortality was high in all studies. Bridge to durable MCS occurred in all device groups, but was more frequently performed in patients with end-stage CMP than in patients with AMI or myocarditis.

We present a variety of MCS techniques. Pros and cons of these techniques are presented in the Supplementary Material, Table S1. For years, the IABP has been first-line mechanical support in patients with severe heart failure and cardiogenic shock. However, IABP-SHOCK II reported no general benefit in patients with cardiogenic shock from AMI [15]. In this trial, the median time needed until haemodynamic stabilization was 3.0 days [15]. The IABP is still widely used in clinical practice with hospital

Table 4: Central extracorporeal membrane oxygenation (CentriMag)

Reference	*N*	Patients	Design	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Culprit vessel LM or LAD (%)	Mean duration of support (days)	Bridge to transplant (%)	Bridge to durable MCS (%)	Bridge to recovery (%)	Bridge to palliation (%)	Hospital discharge (%)
[35]	71 BiVAD = 67%	AMI = 45% ESHF = 42% Other = 13% Biv failure = 67%	Registry	50 ± 18	2.1 ± 3.6	3.4 ± 2.6	NA	70	NA	16 ± 13	25	23	24	28	66
[38]	27 BiVAD = 96%	AMI = 48% ESHF = 52% IM1 = 67% Biv failure = 96%	Registry	47 ± 16	NA	NA	NA	74	NA	16 ± 12	30	22	37	11	74
[36]	14 BiVAD = 93%	AMI Biv failure = 93%	Registry	60 ± 11	NA	NA	NA	100	NA	22 ± 18	0	21	29	50	50
[37]	16 BiVAD = 63%	ESHF = 75% Myocarditis = 25% Biv failure = 63%	Registry	33 ± 15	2.2 ± 0.9	NA	NA	56	NA	47 ± 32	19	38	19	25	69
Mean ± SD or proportion (95% CI)	128			48 ± 18	2.1 ± 3.3	3.4 ± 2.6	NA	76 [58–91] I^2 = 77% P_{hetero} <0.01	NA	20 ± 20	19 [8–34] I^2 = 68% P_{hetero} = 0.03	25 [18–33] I^2 = 0% P_{hetero} = NS	27 [20–35] I^2 = 0% P_{hetero} = NS	27 [15–41] I^2 = 59% P_{hetero} = NS	66 [58–74] I^2 = 0% P_{hetero} = NS

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; LM: left main (coronary artery); LAD: left anterior descending (coronary artery); MCS: mechanical circulatory support; BiVAD: biventricular assist device; AMI: acute myocardial infarction; NA: not applicable; NS: not significant; SD: standard deviation; Biv: biventricular; CI: confidence interval.

Table 5: Peripheral extracorporeal membrane oxygenation

Reference	*N*	Patients	Design	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Culprit vessel LM or LAD (%)	Mean duration of support (days)	Bridge to transplant (%)	Bridge to durable MCS (%)	Bridge to recovery (%)	Bridge to palliation (%)	Hospital discharge (%)
Mixed etiology:															
[39]	138	AMI Biv failure = NA	Registry	55 ± 13	1.7 ± 0.7	4.1 ± 4.5	57	100	67	7.0 ± 4.4	9	13	36	43	47
[40]	64	AMI = 41% Myocarditis = 6% ESHF = 42% Biv failure = NA	Registry	50 ± 16	NA	NA	50	72	NA	7.0 ± 7.0	19	36	31	14	58
[41]	123	AMI = 28% PE = 14% Acute CMP = 11% ESHF = 12% PCS = 21% Other = 14% Biv failure = NA	Registry	56 ± 18	NA	7.5 ± 6.2	46	NA	NA	3.9 ± 4.0	2	15	40	44	39
[42]	75	AMI = 46% ESHF = 54% Myocarditis = 16% Other = 14% Biv failure = NA	Registry	46 ± 15	1.9 ± 1.2	9 ± 7	41	100	NA	NA	4	7	41	48	43
[43]	81	AMI = 20% ESHF = 22% Myocarditis = 20% PCS = 32% Other = 6% Biv failure = NA	Registry	46 ± 16	2.1 ± 1.0	6.3 ± 7.8	75	100	NA	NA	10	7	36	47	42
Mean ± SD or proportion (95% CI)	479			52 ± 16	1.9 ± 0.9	6.4 ± 6.5	54 [43–65] I^2 = 84% P_{hetero} <0.001	92 [70–100] I^2 = 96% P_{hetero} <0.001	NA	5.8 ± 5.1	8 [3–14] I^2 = 80% P_{hetero} <0.001	15 [8–23] I^2 = 84% P_{hetero} <0.001	37.1 [33–42] I^2 = 0% P_{hetero} = NS	39 [28–51] I^2 = 85% P_{hetero} <0.001	45 [39–51] I^2 = 40% P_{hetero} = NS
Isolated myocarditis:															
[44]	57 Biv failure = 100%	Myocarditis	Registry	38 ± 12	NA	12.0 ± 4.6	21	100	NA	9.9 ± 19	5	4	75	16	72
[45]	147 Biv failure = 100%	Myocarditis	Registry	31 ± 19	NA	NA	37	100	NA	5.8 ± 5.8	6	NA	69	25	61
[46]	75 Biv failure = 100%	Myocarditis	Registry	30 ± 19	1.3 ± 0.7	8.1 ± 5.3	47	100	NA	7.1 ± 5.0	4	8	67	21	64
Mean ± SD or proportion (95% CI)	279			32 ± 18	1.3 ± 0.7	9.8 ± 5.4	35 [23–48] I^2 = 79% P_{hetero} <0.01	100 [98–100] I^2 = 0% P_{hetero} = NS	NA	7.0 ± 9.1	6 [3–9] I^2 = 0.0% P_{hetero} = NS	7 [3–11] I^2 = 2.9% P_{hetero} = NS	69 [64–75] I^2 = 0.0% P_{hetero} = NS	22 [18–28] I^2 = 3.9% P_{hetero} = NS	64 [58–70] I^2 = 1.7% P_{hetero} = NS

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; AMI: acute myocardial infarction; NA: not applicable; NS: not significant; SD: standard deviation; ESHF: end-stage heart failure; MCS: mechanical circulatory support.

Table 6: Meta-analysis of studies according to diagnosis

AMI (Ref)	N	Device	Heart failure, predominant side	Age (years)	Creatinine (mg/dl)	Lactate (mmol/l)	CPR (%)	MV (%)	Support time	Bridge to durable MCS (%)	Hospital discharge (%)
[8]	225	IABP	Left	66 ± 14							62
[9]	128	IABP	Left	65 ± 12	1.2 ± 0.4			63			54
[10]	487	IABP	Left	68 ± NA							57
[11]	199	IABP	Left	65 ± 13	1.2 ± 0.7	6.0 ± 4.3					53
[12]	466	IABP	Left	64 ± 14					5.9 ± 6.1		59
[13]	162	IABP	Left	65 ± 12			47	36			52
[14]	300	IABP	Left	61 ± 11			33	56	3.0 ± 4.3		58
[15]	300	IABP	Left	70 ± 15	1.3 ± 0.5	3.6 ± 3.8	42	80	3.0 ± 1.5	4	60
Subtotal:	2267			65 ± 14	1.2 ± 0.6	4.6 ± 4.2	40 [33–48] I^2 = 80% P_{hetero} <0.01	59 [40–77] I^2 = 97% P_{hetero} <0.001	4.3 ± 4.9	4	57 [55–60] I^2 = 12% P_{hetero} = NS
[25]	120	Impella 2.5	Left	64 ± 12		5.8 ± 4.9	41	69	1.8 ± 2.1	2	36
[26]	154	Impella 2.5	Left	64 ± 13	1.4 ± 0.7	4.1 ± 3.6	49	66	1.2 ± 1.9		51
[27]	12	Impella 2.5	Left	65 ± 10		6.5 ± 1.5	85	92	0.9 ± 0.8	0	50
[28]	25	Impella 2.5	Left	58 ± 10		5.7 ± 3.4	56	92	3.5 ± 6.9	0	24
[30]	22	Impella 2.5	Left	58 ± 12	1.2 ± 0.3	6.4 ± 5.3	55	55	1.5 ± 1.1	5	59
Subtotal:	333			63 ± 12	1.4 ± 0.7	5.1 ± 4.3	52 [42–62] I^2 = 60% P = 0.04	73 [62–83] I^2 = 71% P_{hetero} <0.001	1.6 ± 2.7	3 [1–5] I^2 = 0% P_{hetero} = NS	43 [32–55] I^2 = 69% P_{hetero} = 0.01
[36]	14	CentriMag	Biventricular	60 ± 11				100	22 ± 18	21	50
[39]	138	Peripheral ECMO	Left	55 ± 13	1.7 ± 0.7	4.1 ± 4.5	57	100	7.0 ± 4.4	13	47
Subtotal:	152			55 ± 13	1.7 ± 0.7	4.1 ± 4.5	57	100 [98–100]	8.4 ± 8.0	14 [9–20]	47 [40–55]
Cumulative AMI: Mean ± SD or proportion [95% CI]	2752			64 ± 14	1.3 ± 0.6	4.7 ± 4.3	48 [41–54] I^2 = 79% P_{hetero} <0.001	76 [61–88] I^2 = 97% P_{hetero} <0.001	4.1 ± 5.2	6 [2–11] I^2 = 72% P_{hetero} <0.01	53 [49–57] I^2 = 70% P_{hetero} <0.001
Myocarditis (ref)											
[44]	57	Peripheral ECMO	Biventricular	38 ± 12		12.0 ± 4.6	21	100	9.9 ± 19	3.5	72
[45]	147	Peripheral ECMO	Biventricular	31 ± 19		NA	37	100	5.8 ± 5.8		61
[46]	75	Peripheral ECMO	Biventricular	30 ± 19	1.3 ± 0.7	8.1 ± 5.3	47	100	7.1 ± 5.0	8	64
Cumulative myocarditis: Mean ± SD or proportion (95% CI)	279			32 ± 18	1.3 ± 0.7	9.8 ± 5.3	35 [23–48] I^2 = 79% P_{hetero} <0.001	100 [99–100] I^2 = 0% P_{hetero} = NS	7.0 ± 10.0	7 [3–11] I^2 = 3% P_{hetero} = NS	64 [58–70] I^2 = 2% P_{hetero}=NS
End-stage heart failure (ref)											
[16]	88	IABP	Left	57 ± 13	1.9 ± 1.3		0	0	21 ± 22	24	
[17]	50	IABP	Left	56 ± 11	1.7 ± 0.9		0	0	18 ± 37	6	
[19]	15	IABP	Biventricular	50 ± 12	2.1 ± 1.3		0	0	78 ± 41	40	60
Subtotal:	153			56 ± 12	1.9 ± 1.5		0 [0–2] I^2 = 0% P_{hetero}=NS	0 [0–2] I^2 = 0% P_{hetero} = NS	26 ± 34	21 [6–40] I^2 = 84% P_{hetero} <0.001	
[20]	65	TandemHeart	Left	54 ± 15	1.8 ± 1.1	3.6 ± 4.2	25		5.8 ± 2.9	14	49
[31]	40	Impella 5.0	Biventricular	55 ± 13	2.0 ± 0.8		0	0	7.0 ± 5	38	68
Subtotal:	105			54 ± 14	1.9 ± 1.0	3.6 ± 4.2	9 [2–45]		6.3 ± 3.9	25 [6–50]	58 [40–74]
Cumulative ESHF: Mean ± SD or proportion (95% CI)	258			55 ± 13	1.9 ± 1.3	3.6 ± 4.2	3 [0–13] I^2 = 90% P_{hetero} <0.001	0 [0–2] I^2 = 0% P_{hetero} = NS	18 ± 28	22 [12–35] I^2 = 80% P_{hetero} <0.001	58 [45–69] I^2 = 41% P_{hetero} = NS

Numbers in rows called 'subtotal' and 'total' represent mean ± SD or proportion [95% CI].

CPR: cardiopulmonary resuscitation; MV: mechanical ventilation; AMI: acute myocardial infarction; NA: not applicable; NS: not significant; SD: standard deviation; ESHF: end-stage heart failure; CI: confidence interval; MCS: mechanical circulatory support.

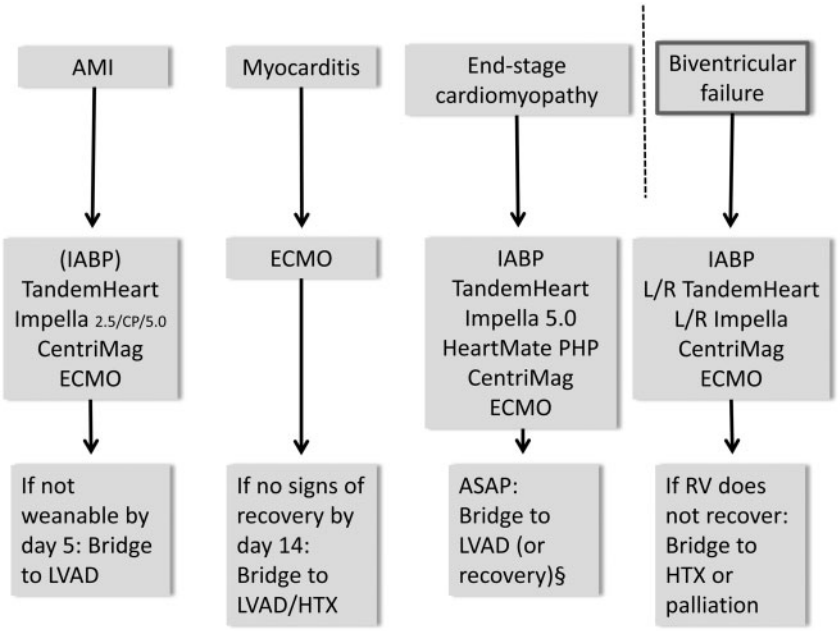

Figure 2: Current application of short-term mechanical circulatory support and possible timing towards durable left ventricular assist device in patients with refractory cardiogenic shock. § Bridge to recovery is only realistic in case of *de novo* heart failure or in acute on chronic heart failure when a clear cause for exacerbation exists.

discharge rates >50% [47]. However, registries did not include patients who did not survive before IABP placement. IABP-SHOCK II excluded patients without an intrinsic heart action [15], but these patients were included in TandemHeart and ECMO registries. Therefore, the reported outcomes in IABP studies might well be biased as a result of not selecting the sickest or dying patients. The majority of IABP studies did not bridge patients towards long-term MCS. Only recently have studies been done in patients with end-stage CMP demonstrating promising rates of bridge to transplant or long-term MCS. However, most investigators did not report survival rate until discharge (Table 1). Patients treated with TandemHeart, Impella 5.0 and peripheral ECMO had median support times of 5–6 days. This time was used to stabilize the patient, to reverse other organ failure, and to bridge them towards the next therapy. Using these 3 devices, a bridge to recovery or successful weaning was possible in at least one quarter of the patients. A minority of these patients finally did not survive until hospital discharge. Patients supported with TandemHeart or Impella 5.0 could be bridged to long-term MCS in >25% of the cases, with good long-term outcome. Only a minority of patients treated with a peripheral ECMO were bridged to long-term MCS, possibly because more ECMO patients were bridged to recovery. Impella 2.5 supported patients had a median support duration <2 days, that might be too limited to bridge patients until haemodynamic stabilization. Bridging until durable MCS only occurred in few patients in these AMI studies. Most patients supported with central ECMO (CentriMag) had Biv failure and long support times and could be bridged to implantable VAD in a quarter of patients.

Complication rates of the IABP are very low and were in fact not different from controls in IABP-SHOCK II [15]. All larger bore percutaneous and surgical MCS carry a relatively high risk of bleeding [35, 48]. ECMO by femoral approach requires placement of a cannula in the superficial femoral artery to ensure antegrade leg perfusion. Mortality was high in all studies. Survival until hospital discharge was heterogeneous, however, this was probably primarily caused by the fact that the studies included different patient populations (Table 6).

Although baseline characteristics were lacking in several studies, clear differences across device groups were present. In general, patients receiving low-level support (IABP) were less sick as compared to patients receiving higher level support. We believe these differences may, at least in part, explain the observed differences in outcome.

Timing and the possibility of durable LVAD implantation depends primarily on the severity of other organ failure as well as on possible recovery of ventricular function, and consequently determined by the underlying diagnosis of cardiogenic shock (Table 6). Due to heterogeneous patient populations, the use of different devices, and the lack of controlled studies, it is currently impossible to provide evidence-based recommendations on best timing to durable LVAD. We therefore present a broad overview of current application of short-term MCS and suggest possible timing (Fig. 2) but individualized decisions taken by a dedicated multidisciplinary MCS-team are important.

Limitations

Limitations of our study include the fact that 95% of the studies were uncontrolled registries resembling heterogeneous patient populations, treatments and outcomes, as also reflected by the multiple significant tests for heterogeneity.

CONCLUSION

We conclude that temporary MCS, with differential support duration according to diagnosis and device, can be used to bridge patients towards durable LVAD. To investigate this more thoroughly, clinicians are encouraged to share their results in a large multicentre registry where at least patient characteristics,

diagnosis, the nature of cardiac failure and device and timing aspects should be well recorded.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

Conflict of interest: none declared.

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