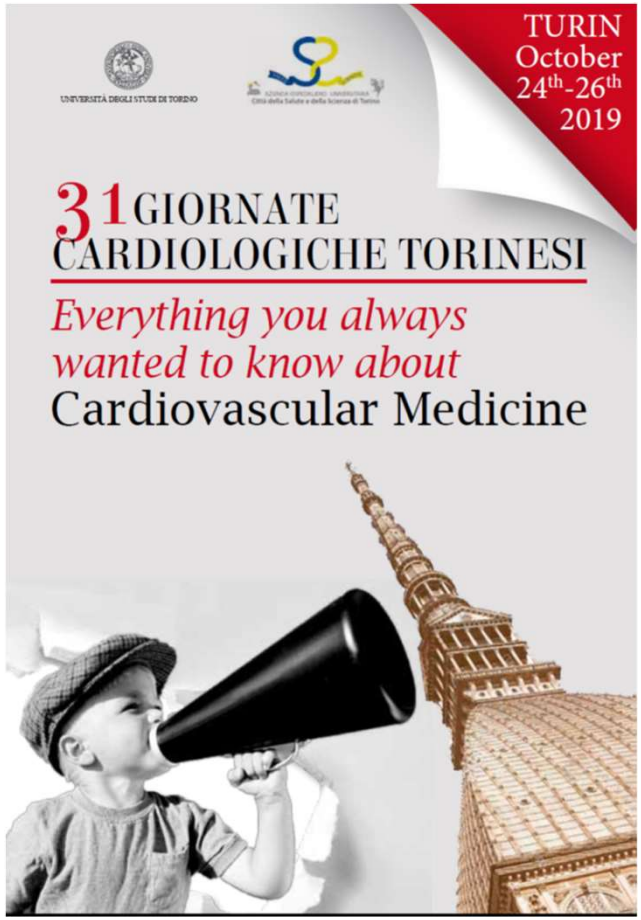
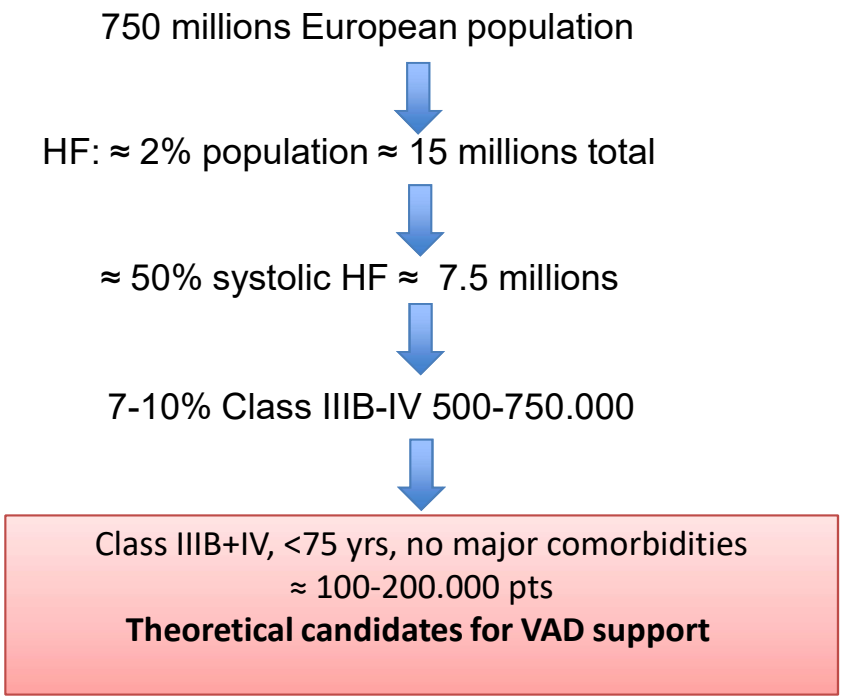


Advanced and acute heart failure management. The role of ECMO and LVAD

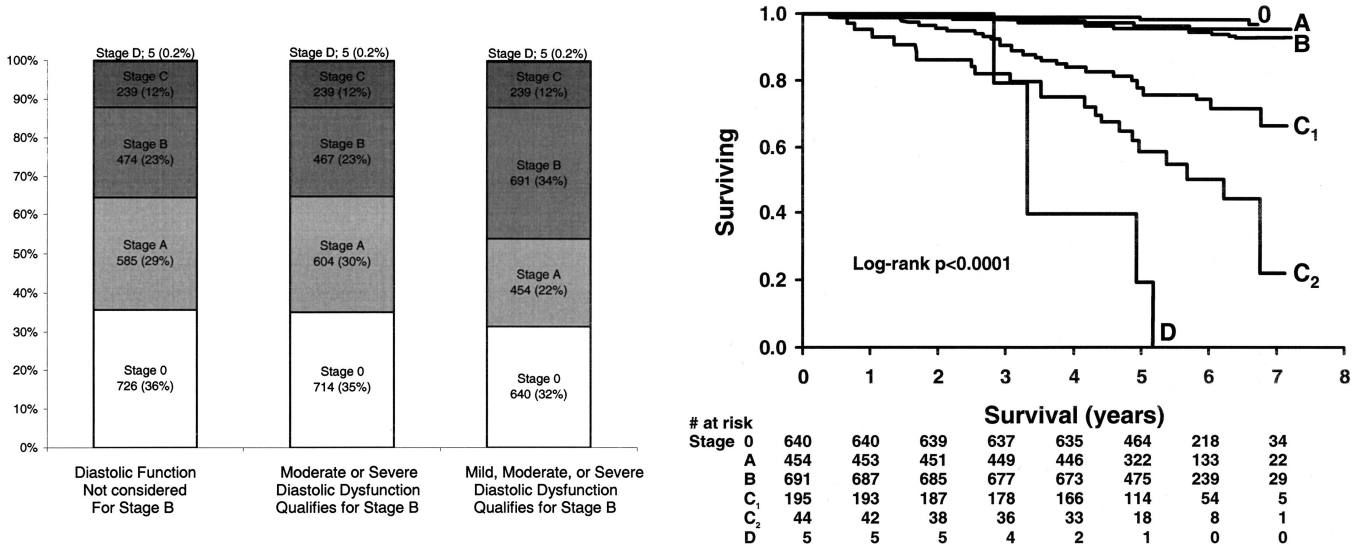
Marco Metra, MD
Brescia. Italy

Number of patients with Advanced HF and potential permanent LVAD candidates in Europe



Based on Miller LW, Guglin M. J Am Coll Cardiol 2013; 61: 1209–1221
and Ponikowski et al. ESC Heart Fail. 2014 Sep;1(1):4-25.

Prevalence and survival curves of subjects at different stages of HF



Khawaja Afzal Ammar et al. Circulation. 2007;115:1563-1570

Advanced Heart Failure

- Progressive and persistent severe signs and symptoms of heart failure
- Frequent episodes of decompensation
- Lack of efficacy of conventional medical, surgical, and device (CRT/ ICD) therapy.
- Need of advanced therapies
  - Cardiac transplantation
  - Mechanical circulatory assistance
  - Palliative therapies, e.g. inotropic infusions, ultrafiltration, peritoneal dialysis, others

ELSEVIER

European Journal of Heart Failure 9 (2007) 684–694

The European Journal of Heart Failure

www.elsevier.com/locate/ejheart

Review

Advanced chronic heart failure: A position statement from the Study Group on Advanced Heart Failure of the Heart Failure Association of the European Society of Cardiology

Marco Metra [a,*], Piotr Ponikowski [b], Kenneth Dickstein [c], John J.V. McMurray [d], Antonello Gavazzi [e], Claes-Hakan Bergh [f], Alan G. Fraser [g], Tiny Jaarsma [h], Antonis Pitsis [i], Paul Mohacsi [j], Michael Böhm [k], Stefan Anker [l,m], Henry Dargie [n], Dirk Brutsaert [o], Michel Komajda [p]
on behalf of the Heart Failure Association of the European Society of Cardiology

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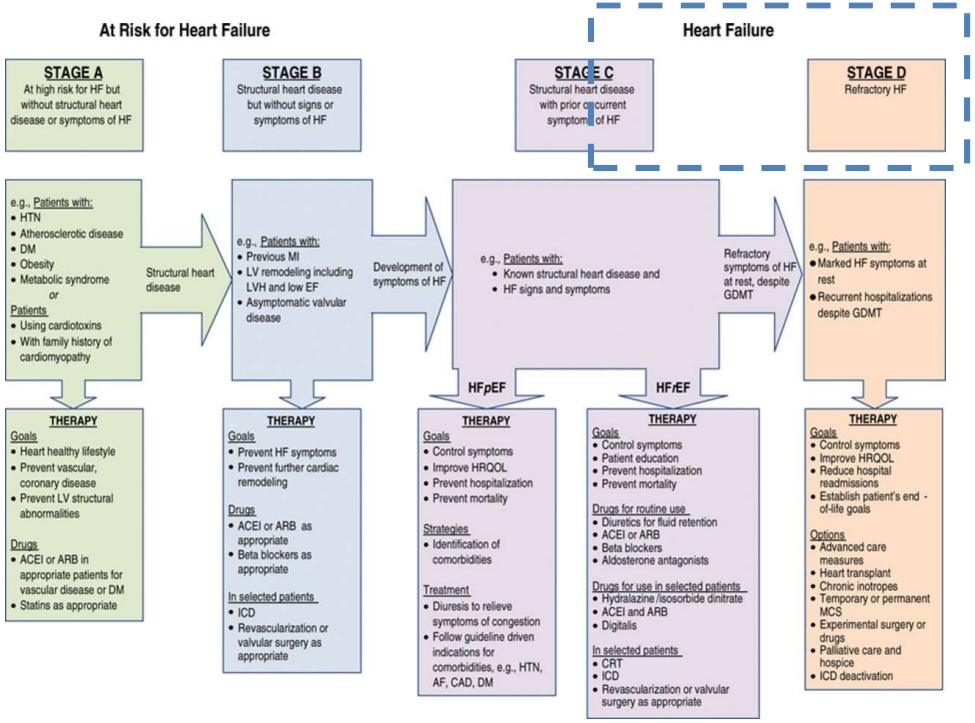
Received 28 December 2006; received in revised form 5 March 2007; accepted 18 April 2007

HFA criteria for Advanced chronic HF: 2007 position statement

1.	Severe symptoms of HF (NYHA class III or IV) with
2.	Episodes of fluid retention and/or peripheral hypoperfusion
3.	History of ≥1 HF hospitalization in the past 6 months
4.	Severe cardiac dysfunction (EF<30%, high PWP/ BNP)
5.	Severe impairment of functional capacity (inability to exercise, 6MWTD≤300, pVO_2 ≤12-14)
6.	All the previous features despite “attempts to optimise” therapy, including β-blockers and ACE inhibitors

Metra, Ponikowski, Dickstein et al. EJHF 2007; 9:684-694

Stages in the development of heart failure: ACCF/AHA Guidelines



Circulation. 2013; 128, 16: 1810-1852, DOI: (10.1161/CIR.0b013e31829e8807)

INTERMACS Profiles

Stage	Definition	Description
1	Critical cardiogenic shock	“Crash and burn”
2	Progressive decline	“Sliding fast” on inotropes
3	Stable but inotrope dependent	Stable on inotropes
4	Recurrent advanced HF	“Frequent flyer”
5	Exertion intolerant	“housebound”
6	Exertion limited	“walking wounded”
7	Advanced NYHA class III	

Stevenson et al. J Heart Lung Transplant 2009; 28:535

INTERMACS profiles

- Developed to classify patients undergoing long-term mechanical circulatory support (MCS) implantation
  - based on the symptoms present at the time of implantation
  - specific for HFrEF, whereas the term of advanced HF should be applied to all the patients with HF, independently from their LVEF

Current limitations of the 2007 position statement on advanced HF

- The treatment armamentarium for HFrEF has improved: CRT, ivabradine, ARNI
- Outpatient visits with i.v. loop diuretics and/or other vasoactive medications are often replacing HF hospitalizations
- Recurrent malignant arrhythmias are now well recognized contributors to and can be consequences of advanced HF
- Co-morbidities can complicate the clinical course and evaluation of patients with advanced HF, and influence candidacy for MCS or heart transplantation
- LVAD technology has had major improvements

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1236

HFA POSITION STATEMENT

Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology

Maria G. Crespo-Leiro[1]*, Marco Metra[2], Lars H. Lund[3], Davor Milicic[4], Maria Rosa Costanzo[5], Gerasimos Filippatos[6], Finn Gustafsson[7], Steven Tsui[8], Eduardo Barge-Caballero[1], Nicolaas De Jonge[9], Maria Frigerio[10], Righab Hamdan[11], Tal Hasin[12], Martin Hülsmann[13], Sanem Nalbantgil[14], Luciano Potena[15], Johann Bauersachs[16], Aggeliki Gkouziouta[17], Arjang Ruhparwar[18], Arsen D. Ristic[19], Ewa Straburzynska-Migaj[20], Theresa McDonagh[21], Petar Seferovic[22], and Frank Ruschitzka[23]

ESC European Society of Cardiology

European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1313

EDITORIAL COMMENT

Advanced heart failure: Trans-Atlantic perspectives on the Heart Failure Association of the European Society of Cardiology position statement

Barry Greenberg[1]*, James Fang[2], Mandeep Mehra[3], and Lynne Warner Stevenson[4]

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This article refers to 'Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology' by M.G. Crespo-Leiro *et al.*, published in this issue on pages xxx.

The treatment of heart failure has changed dramatically over the past several decades. With the availability of an increasing number of safe and effective therapies, heart failure patients survive longer and experience a far superior quality of life than in the past. An unanticipated consequence of this otherwise favourable turn of events, however, has been the emergence of a population of heart failure patients who have progressed to an advanced stage of their disease. This paradox is due to the fact none of the drugs and devices currently available for treating heart failure cure the underlying disease. Thus, while therapies afford patients the opportunity to lead fairly normal and productive lives for extended periods, they remain at risk for progressive deterioration in their condition over time. The reasons for this include persistent activation of disease pathways that are not fully silenced by (or which circumvent) existing heart failure therapies, occurrence of further episodes of myocardial damage, development of right heart failure and cardiorenal syndrome as well as the cumulative deleterious effects of environmental factors and co-morbid conditions.

Although it is difficult to quantitate the prevalence of advanced heart failure (also termed refractory or Stage D heart failure in the American College of Cardiology/American Heart Association classification scheme), it is estimated that approximately 5% of Stage C patients progress to Stage D each year[1] and that between 5–10% of the heart failure population falls into this category.[2] In Europe alone, the population currently suffering from advanced heart failure would then range from 500 000 to 750 000 patients. For these patients, entry into this stage of their disease marks a turning point, as the clinical course now takes a sharp and irreversible turn downwards. Symptoms that were controlled in the past become more refractory to therapy, quality of life deteriorates, and hospitalizations occur with increasing frequency. Most importantly, patients with advanced heart failure experience a marked reduction in their survival.

Coincident with (and stimulated by) the rise in numbers of advanced heart failure patients, there have been important advances in therapeutic strategies for their management. Survival rates and quality of life following cardiac transplantation are far superior to those seen with medical therapy alone.[3] Recent improvements in durable mechanical circulatory support (MCS) systems also greatly ameliorate the clinical course in selected cases.[4] While these therapies are appropriate for only a minority of patients, their ability to dramatically alter the clinical course emphasizes the importance of early identification of potential candidates and referral to centres with specialized expertise in guiding their management. For the remaining vast majority of patients who are not candidates for transplantation or durable MCS support, recognition of their advanced disease remains vitally important as there still is much that can be done to improve their clinical course. Despite the fact that advanced heart failure patients often experience difficulty in tolerating drugs that are the mainstay of treatment for earlier stages of their disease, careful titration (both up and down) of the dose of neurohormonal agents and diuretics can still result in substantial clinical benefits. More information is needed in advanced heart failure patients who experience hypotension or worsening renal function or who are repeatedly hospitalized for episodes of decompensation to determine how to best utilize neurohormonal agents, when to substitute direct acting vasodilators

 doi: 10.1002/ejhf.1236
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Updated HFA-ESC criteria for defining advanced HF

All the following criteria must be present despite optimal guideline-directed treatment:

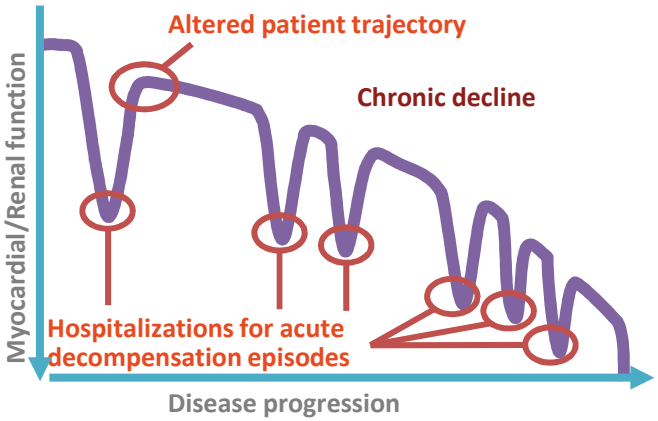
1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by a reduced LVEF ≤30%, isolated RV failure (e.g. ARVC) or non-operable severe valve abnormalities or congenital abnormalities or persistently high (or increasing) BNP or NT-proBNP values and data of severe diastolic dysfunction or LV structural abnormalities according to the ESC definition of HFpEF and HFmrEF.[9]
3. Episodes of pulmonary or systemic congestion requiring high-dose intravenous diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.
4. Severe impairment of exercise capacity with inability to exercise or low 6MWTD (<300 m) or pVO_2 (<12–14 mL/kg/min), estimated to be of cardiac origin.

In addition to the above, extra-cardiac organ dysfunction due to heart failure (e.g. cardiac cachexia, liver, or kidney dysfunction) or type 2 pulmonary hypertension may be present, but are not required.

Criteria 1 and 4 can be met in patients who have cardiac dysfunction (as described in criterion #2), but who also have substantial limitation due to other conditions (e.g. severe pulmonary disease, non-cardiac cirrhosis, or most commonly by renal disease with mixed aetiology). These patients still have limited quality of life and survival due to advanced disease and warrant the same intensity of evaluation as someone in whom the only disease is cardiac, but the therapeutic options for these patients are usually more limited.

Acute HF leads to and is a frequent presentation of advanced HF

- Over 1 million **hospitalizations** annually in Europe or US
- **Poor patient survival**: the mortality rate at 1 year up to 17–37%
- High rehospitalization rates, up to 40-50%
- 5–42% of patients may experience **in-hospital worsening heart failure (WHF)**
- **Limited evidence** for many commonly used AHF treatments with **no proven long-term benefits**



Adapted from Gheorghiade M, et al. 2005

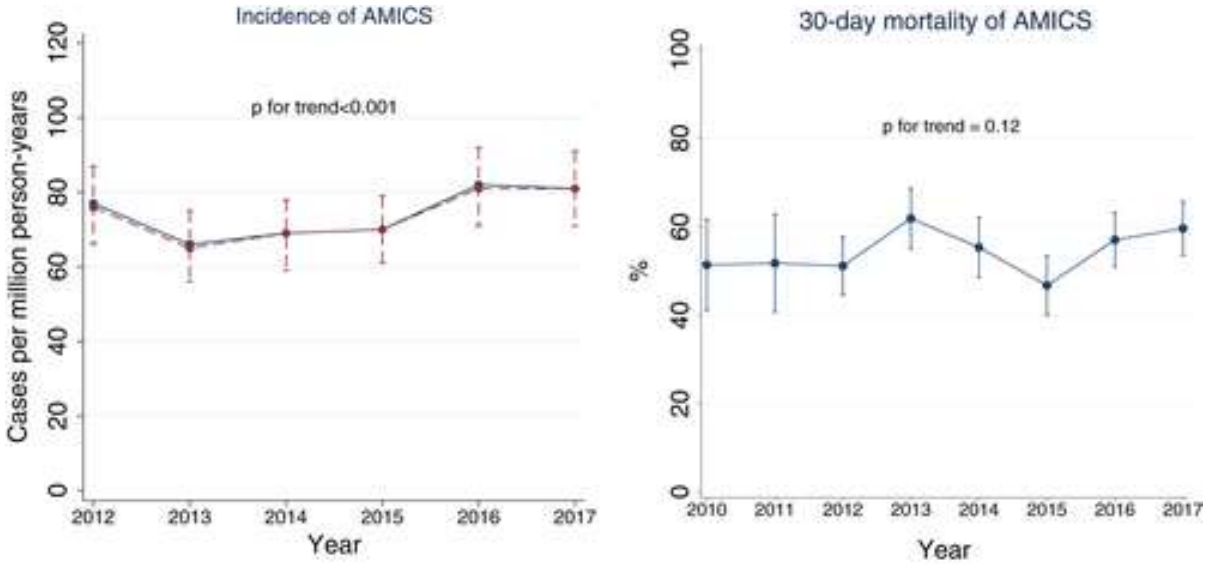
Benjamin EJ, *et al. Circulation* 2017;135(10):e146-e603; Cowie MR, *et al. ESC Heart Failure* 2014;1:110-45 Gheorghiade M, *et al. J Am Coll Cardiol* 2013;61(4):391-403; Butler J, *et al. Eur J Heart Fail* 2015;17(11):1104-13; Gheorghiade M, *et al. Am J Cardiol* 2005;96(6A):11G-17G5.

ESC European Society of Cardiology
European Journal of Heart Failure (2019)
doi:10.1002/ejhf.1566

RESEARCH ARTICLE

Temporal trends in incidence and patient characteristics in cardiogenic shock following acute myocardial infarction from 2010 to 2017: a Danish cohort study

Ole K.L. Helgestad[1,2*], Jakob Josiassen[3], Christian Hassager[3,4], Lisette O. Jensen[1], Lene Holmvang[3,4], Anne Sørensen[1], Martin Frydland[3,4], Annmarie T. Lassen[5], Nanna L.J. Udesen[1], Henrik Schmidt[6], Hanne B. Ravn[4,7], and Jacob E. Møller[1,2]



Eur J Heart Fail, First published: 24 July 2019, DOI: 10.1002/ejhf.1566

Indications to short-term MCS

- Cardiogenic shock
  - ACS / Mechanical complications
  - Acute myocarditis
  - Advanced HF
- Post-cardiotomy
  - Fail wean cardiompulmonary bypass / Post cardiopulmonary bypass
  - Post-Tx allograft failure or RV failure
  - Post-LVAD RV failure
- Cardiac arrest / refractory arrhythmia
- Prophylactic
  - High risk PCI or high risk EP procedures
  - Prophylactic temporary RVAD at LVAD implantation

ESC HF Guidelines EHJ 2016
Rihal, SCAI/ACC/HFSA/STS Statement, JACC 2015
ISHLT Guidelines for MCS, JHLT 2013

Types of short-term MCS

IABP
Low cost
Percutaneous, easy to insert and remove
Duration: days

↑ DBP
↓ Afterload
↓ Myocardial O2 consumption
↑ Coronary perfusion
↑ CO by 0.5 L/min

Rihal et al. SCAI/ACC/HFSA/STS Statement, JACC 2015

ESTABLISHED IN 1812 OCTOBER 4, 2012 VOL. 367 NO. 14

Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock

Holger Thiele, M.D., Uwe Zeymer, M.D., Franz-Josef Neumann, M.D., Miroslaw Ferenc, M.D., Hans-Georg Olbrich, M.D., Jörg Hausleiter, M.D., Gert Richardt, M.D., Marcus Hennersdorf, M.D., Klaus Empen, M.D., Georg Fuernau, M.D., Steffen Desch, M.D., Ingo Eitel, M.D., Rainer Hambrecht, M.D., Jörg Fuhrmann, M.D., Michael Böhm, M.D., Henning Ebelt, M.D., Steffen Schneider, Ph.D., Gerhard Schuler, M.D., and Karl Werdan, M.D., for the IABP-SHOCK II Trial Investigators*

ABSTRACT

BACKGROUND

In current international guidelines, intraaortic balloon counterpulsation is considered to be a class I treatment for cardiogenic shock complicating acute myocardial infarction. However, evidence is based mainly on registry data, and there is a paucity of randomized clinical trials.

METHODS

In this randomized, prospective, open-label, multicenter trial, we randomly assigned 600 patients with cardiogenic shock complicating acute myocardial infarction to intraaortic balloon counterpulsation (IABP group, 301 patients) or no intraaortic balloon counterpulsation (control group, 299 patients). All patients were expected to undergo early revascularization (by means of percutaneous coronary intervention or bypass surgery) and to receive the best available medical therapy. The primary efficacy end point was 30-day all-cause mortality. Safety assessments included major bleeding, peripheral ischemic complications, sepsis, and stroke.

RESULTS

A total of 300 patients in the IABP group and 298 in the control group were included in the analysis of the primary end point. At 30 days, 119 patients in the IABP group (39.7%) and 123 patients in the control group (41.3%) had died (relative risk with IABP, 0.96; 95% confidence interval, 0.79 to 1.17; P=0.69). There were no significant differences in secondary end points or in process-of-care measures, including the time to hemodynamic stabilization, the length of stay in the intensive care unit, serum lactate levels, the dose and duration of catecholamine therapy, and renal function. The IABP group and the control group did not differ significantly with respect to the rates of major bleeding (3.3% and 4.4%, respectively; P=0.51), peripheral ischemic complications (4.3% and 3.4%, P=0.53), sepsis (15.7% and 20.5%, P=0.15), and stroke (0.7% and 1.7%, P=0.28).

CONCLUSIONS

The use of intraaortic balloon counterpulsation did not significantly reduce 30-day mortality in patients with cardiogenic shock complicating acute myocardial infarction for whom an early revascularization strategy was planned. (Funded by the German Research Foundation and others; IABP-SHOCK II ClinicalTrials.gov number, NCT00491036.)

From the University of Leipzig–Heart Center, Leipzig (H.T., G.F., S.D., I.E., G.S.), Klinikum Ludwigshafen and Institut für Herzinfarktforschung, Ludwigshafen (U.Z., S.S.), Heart Center Bad Krozingen, Bad Krozingen (F.-J.N., M.F.), Asklepios Clinic Langen-Seligenstadt, Langen (H.-G.O.), German Heart Center Munich, Munich (J.H.), Heart Center–Segeberger Kliniken, Bad Segeberg (G.R.), SLK Kliniken Heilbronn, Heilbronn (M.H.), Ernst-Moritz-Arndt University Greifswald, Greifswald (K.E.), Klinikum Links der Weser, Bremen (R.H.), Zentralklinik Bad Berka, Bad Berka (J.F.), University Clinic of Saarland, Homburg/Saar (M.B.), and Martin-Luther University Halle-Wittenberg, Halle (H.E., K.W.) — all in Germany. Address reprint requests to Dr. Thiele at the University of Leipzig–Heart Center, Department of Internal Medicine/Cardiology, Strümpellstr. 39, 04289 Leipzig, Germany, or at thielh@medizin.uni-leipzig.de.

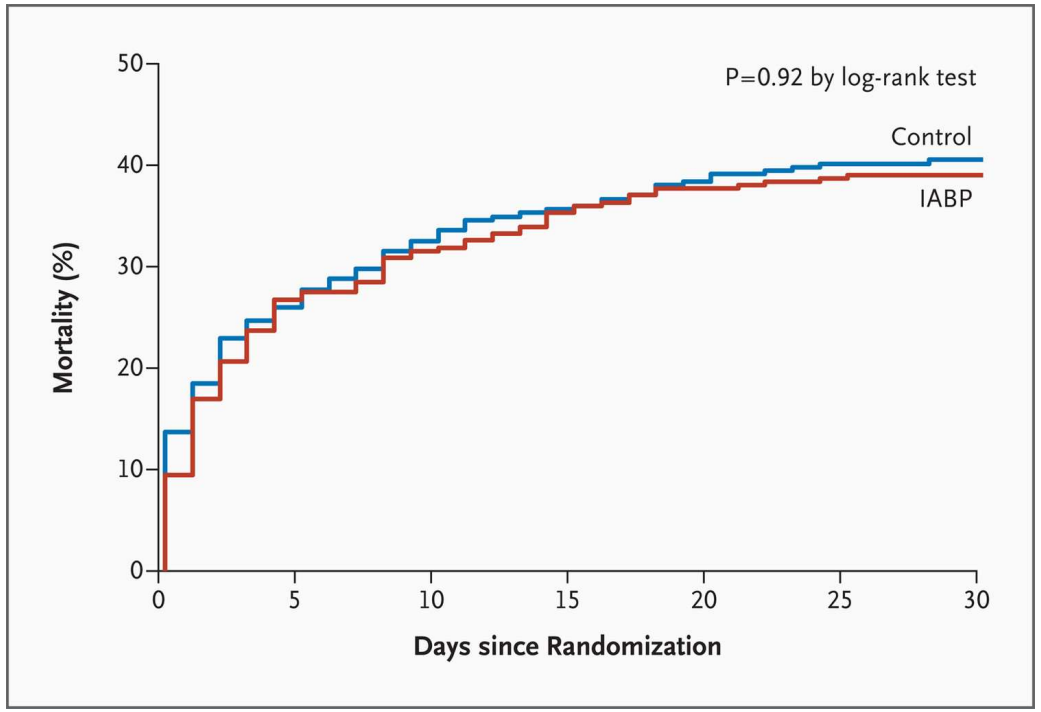
Drs. Schuler and Werdan contributed equally to this article.

*Investigators in the Intraaortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) trial are listed in the Supplementary Appendix, available at NEJM.org.

This article was published on August 27, 2012, at NEJM.org.

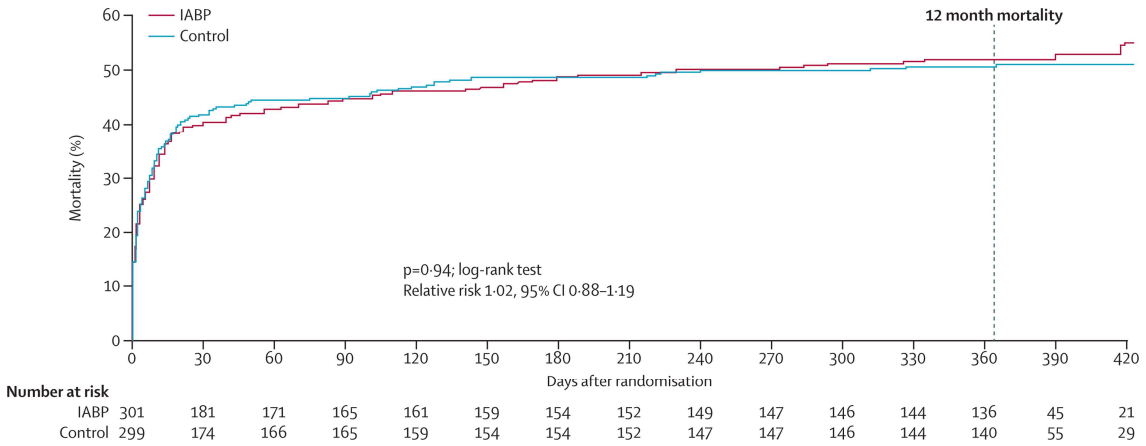
N Engl J Med 2012;367:1287-96.
DOI: 10.1056/NEJMoa1208410

IABP-SHOCK-II trial: Time-to-Event Curves for the Primary End Point (all-cause mortality)



Thiele H et al. N Engl J Med 2012;367:1287-1296.

Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results



Thiele et al. The Lancet 2013 382, 1638-1645DOI: (10.1016/S0140-6736(13)61783-3)

Indications to MCS in 2016 ESC Heart Failure Guidelines

Recommendations	Class	level
IABP is not routinely recommended in cardiogenic shock	III	B
Short-term mechanical circulatory support may be considered in refractory cardiogenic shock depending on patient age, comorbidities and neurologic function	IIb	C

Ponikowski et al, Eur J Heart Fail 2016; 18: 891-975.

Types of short-term MCS

IABP

Low cost
Percutaneous, easy to insert and remove
Duration: days

↑ DBP
↓ Afterload
↓ Myocardial O2 consumption
↑ Coronary perfusion
↑ CO by 0.5 L/min

LV to aorta: Impella

Percutaneous
Anticoagulation
Duration: days

↓ Filling pressure
↓ LV wall stress
↓ LV work
↓ Myocardial O2 consumption
Provides 2.5-3.5 L/min

LA to aorta: TandemHeart

Percutaneous
Anticoagulation
Duration: days-weeks

↓ Preload and filling pressure
↑ Afterload
↓ LV wall stress
↓ LV work
↓ Myocardial O2 consumption
Provides 5 L/min

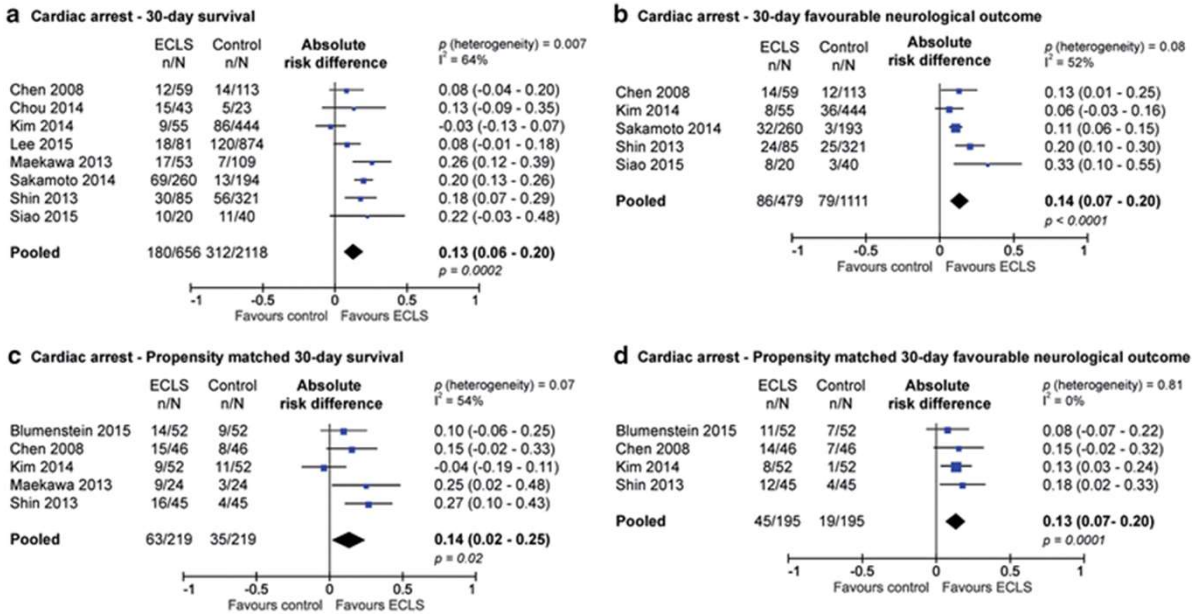
RA to membrane to aorta: VA ECMO

Percutaneous
Anticoagulation
Duration: weeks-months

↓ RV preload
↑ coronary, cerebral, peripheral perfusion;
↑ blood oxygen
↑ LV Afterload
↑ LV wall stress
Provides 6-8 L/min

Modified from Rihal et al. SCAI/ACC/HFSA/STS Statement, JACC 2015

ECMO during cardiac arrest and cardiogenic shock: a systematic review and meta-analysis



Ouweneel et al. Intensive Care Med 2016;42:1922–1934.

European Journal of Heart Failure (2017) 19, 404–412
doi:10.1002/ejhf.668

RESEARCH ARTICLE

Concomitant implantation of Impella® on top of veno-arterial extracorporeal membrane oxygenation may improve survival of patients with cardiogenic shock

Federico Pappalardo[1†*], Christian Schulte[2†], Marina Pieri[1], Benedikt Schrage[2], Rachele Contri[3], Gerold Soeffker[4], Teresa Greco[1], Rosalba Lembo[1], Kai Müllerleile[2], Antonio Colombo[3], Karsten Sydow[2], Michele De Bonis[5], Florian Wagner[6], Hermann Reichenspurner[6], Stefan Blankenberg[2,7], Alberto Zangrillo[1], and Dirk Westermann[2,7*]

Aims Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) support stabilizes patients with cardiogenic shock. Despite improved oxygenation and peripheral circulation, LV unloading may be impeded due to the increased afterload, resulting in a failing static left ventricle and in high mortality.

Methods and results We describe for the first time a large series of patients treated with the combination of VA-ECMO and Impella® compared with patients with VA-ECMO only. We retrospectively collected data on patients from two tertiary critical care referral centres. We enrolled 157 patients treated with VA-ECMO from January 2013 to April 2015: 123 received VA-ECMO support and 34 had concomitant treatment with VA-ECMO and Impella. A propensity-matching analysis was performed in a 2:1 ratio, resulting in 42 patients undergoing VA-ECMO alone (control group) compared with 21 patients treated with VA-ECMO and Impella. Patients in the VA-ECMO and Impella group had a significantly lower hospital mortality (47% vs. 80%, $P < 0.001$) and a higher rate of successful bridging to either recovery or further therapy (68% vs. 28%, $P < 0.001$) compared with VA-ECMO patients. A higher need for continuous veno-venous haemofiltration (48% vs. 19%, $P = 0.02$) and increased haemolysis (76% vs. 33%, $P = 0.004$) were reported in the study group due to higher survival. There was no difference in major bleeding rates between the two groups (VA-ECMO and Impella 38% vs. VA-ECMO 29%, $P = 0.6$).

Conclusions Concomitant treatment with VA-ECMO and Impella may improve outcome in patients with cardiogenic shock compared with VA-ECMO only. Nevertheless, randomized studies are needed to validate these promising results further.

European Journal of Heart Failure (2017) 19, 413–415
doi:10.1002/ejhf.695

EDITORIAL COMMENT

Are two crutches better than one? The ongoing dilemma on the effects and need for left ventricular unloading during veno-arterial extracorporeal membrane oxygenation

Roberto Lorusso*

Cardio-Thoracic Surgery Department, Heart & Vascular Centre, Maastricht University Medical Centre, Maastricht, The Netherlands

European Journal of Heart Failure Supplements (2017) 19 (Suppl. 2) 84–91
doi:10.1002/ejhf.850

Modalities and Effects of Left Ventricle Unloading on Extracorporeal Life support: a Review of the Current Literature

Paolo Meani[1†], Sandro Gelsomino[2†], Eshan Natour[2], Daniel M Johnson[2], Hans-Peter Brunner La Rocca[1], Federico Pappalardo[3], Elham Bidar[2], Maged Makhoul[2], Giuseppe Raffa[5], Samuel Heuts[2], Pieter Lozekoot[2], Suzanne Kats[2], Niels Sluijpers[2], Rick Schreurs[2], Thijs Delnoij[1,4], Alice Montalti[4], Jan Willem Sels[1,4], Marcel van de Poll[4], Paul Roekaerts[4], Thomas Poels[2], Eric Korver[2], Zaheer Babar[2], Jos Maessen[2], and Roberto Lorusso[2*]

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 87–165
doi:10.1093/eurheartj/ehy394

ESC/EACTS GUIDELINES

2018 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)

Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)

Authors/Task Force Members: Franz-Josef Neumann* (ESC Chairperson) (Germany), Miguel Sousa-Uva*[1] (EACTS Chairperson) (Portugal), Anders Ahlsson[1] (Sweden), Fernando Alfonso (Spain), Adrian P. Banning (UK), Umberto Benedetto[1] (UK), Robert A. Byrne (Germany), Jean-Philippe Collet (France), Volkmar Falk[1] (Germany), Stuart J. Head[1] (The Netherlands), Peter Jüni (Canada), Adnan Kastrati (Germany), Akos Koller (Hungary), Steen D. Kristensen (Denmark), Josef Niebauer (Austria), Dimitrios J. Richter (Greece), Petar M. Seferović (Serbia), Dirk Sibbing (Germany), Giulio G. Stefanini (Italy), Stephan Windecker (Switzerland), Rashmi Yadav[1] (UK), Michael O. Zembala[1] (Poland)

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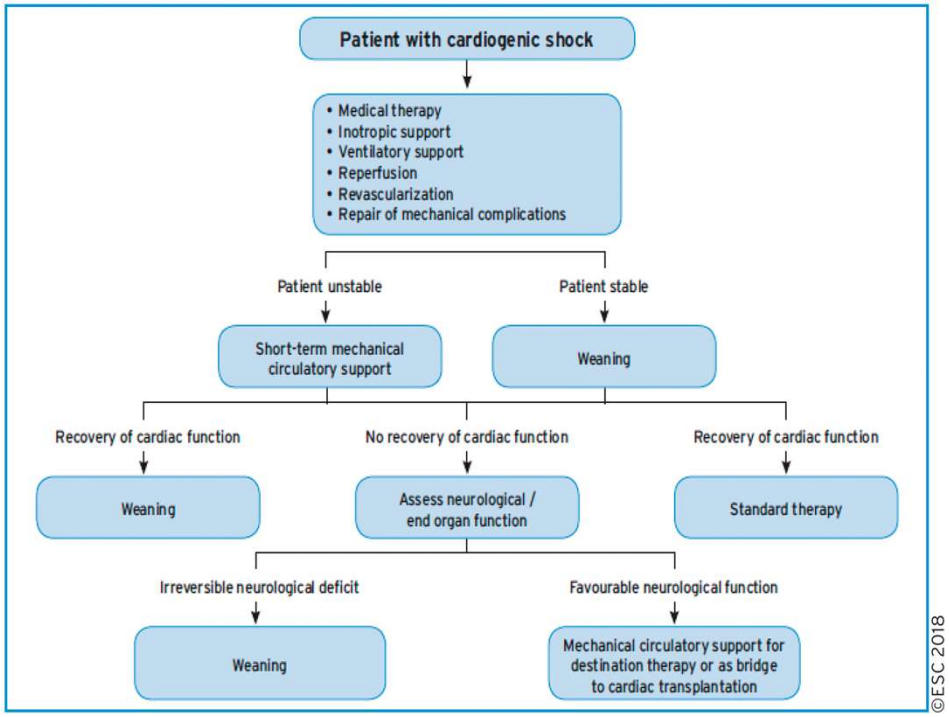
Indications to MCS in 2018 ESC Revascularization Guidelines

Recommendations	Class	level
Routine use of IABPs in patients with cardiogenic shock due to ACS is not recommended	III	B
In selected patients with ACS and cardiogenic shock, short-term mechanical circulatory support may be considered, depending on patient age, comorbidities, neurological function, and the prospects for long-term survival and predicted quality of life.	IIb	C

Ponikowski et al, Eur J Heart Fail 2016; 18: 891-975.

2018 ESC Revascularization Guidelines: Algorithm for the management of patients with cardiogenic shock.



Neumann F et al. European Heart Journal, Volume 40, Issue 2, 07 January 2019, Pages 87–165, https://doi.org/10.1093/eurheartj/ehy394

Indications to percutaneous mechanical support in 2016 ESC HF GLs

- **Bridge to recovery**
  - to support patients with left or biventricular failure until cardiac and other organ function have recovered. Typically a few days to weeks.
- **Bridge to decision**
  - to stabilize haemodynamics, recover end-organ function and allow for a full clinical evaluation for the possibility of either heart transplant or a more durable MCS device in patients with acute and rap-idly deteriorating HF or cardiogenic shock

Ponikowski et al, Eur J Heart Fail 2016; 18: 891-975.

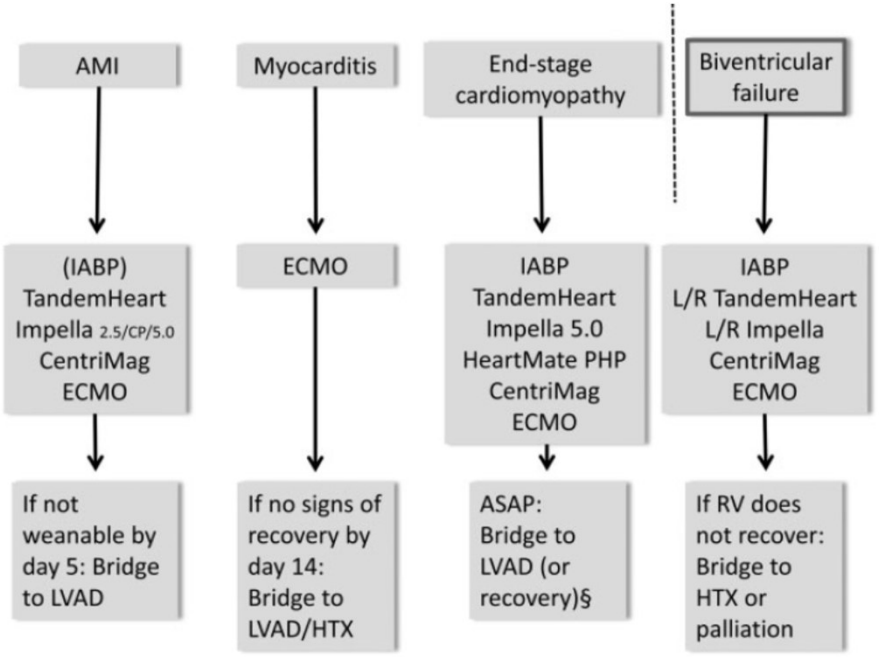
European Journal of Cardio-Thoracic Surgery 52 (2017) 14–25
doi:10.1093/ejcts/ezx088 Advance Access publication 3 May 2017

REVIEW

Cite this article as: den Uil CA, Akin S, Jewbali LS, dos Reis Miranda D, Brugts JJ, Constantinescu AA *et al.* 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. Eur J Cardiothorac Surg 2017;52:14–25.

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

Corstiaan A. den Uil[a,b,*], Sakir Akin[a,b], Lucia S. Jewbali[a,b], Dinis dos Reis Miranda[b], Jasper J. Brugts[a], Alina A. Constantinescu[a], Arie Pieter Kappetein[c] and Kadir Caliskan[a]



European Journal of Heart Failure (2018) 20, 178–186
doi:10.1002/ejhf.956

RESEARCH ARTICLE

Clinical outcomes of temporary mechanical circulatory support as a direct bridge to heart transplantation: a nationwide Spanish registry

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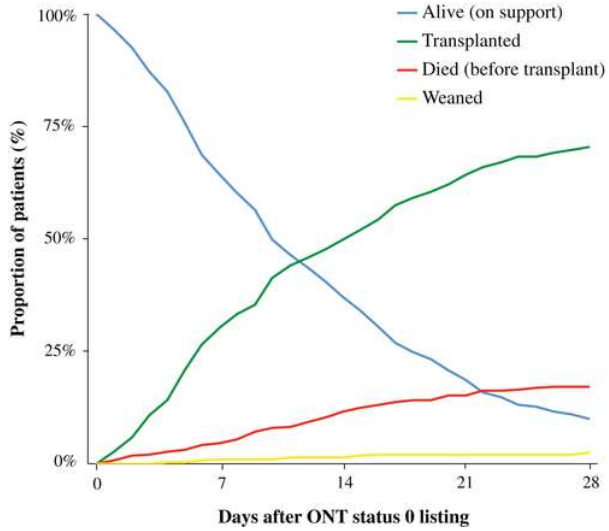
Background In Spain, listing for high-urgent heart transplantation is allowed for critically ill candidates not weanable from temporary mechanical circulatory support (T-MCS). We sought to analyse the clinical outcomes of this strategy.

Methods and results We conducted a case-by-case, retrospective review of clinical records of 291 adult patients listed for high-urgent heart transplantation under temporary devices from 2010 to 2015 in 16 Spanish institutions. Survival after listing and adverse clinical events were studied. At the time of listing, 169 (58%) patients were supported on veno-arterial extracorporeal membrane oxygenation (VA-ECMO), 70 (24%) on temporary left ventricular assist devices (T-LVAD) and 52 (18%) on temporary biventricular assist devices (T-BiVAD). Seven patients transitioned from VA-ECMO to temporary ventricular assist devices while on the waiting list. Mean time on T-MCS was 13.1 ± 12.6 days. Mean time from listing to transplantation was 7.6 ± 8.5 days. Overall, 230 (79%) patients were transplanted and 54 (18.6%) died during MCS. In-hospital postoperative mortality after transplantation was 33.3%, 11.9% and 26.2% for patients bridged on VA-ECMO, T-LVAD and T-BiVAD, respectively ($P = 0.008$). Overall survival from listing to hospital discharge was 54.4%, 78.6% and 55.8%, respectively ($P = 0.002$). T-LVAD support was independently associated with a lower risk of death over the first year after listing (hazard ratio 0.52, 95% confidence interval 0.30–0.92). Patients treated with VA-ECMO showed the highest incidence rate of adverse clinical events associated with T-MCS.

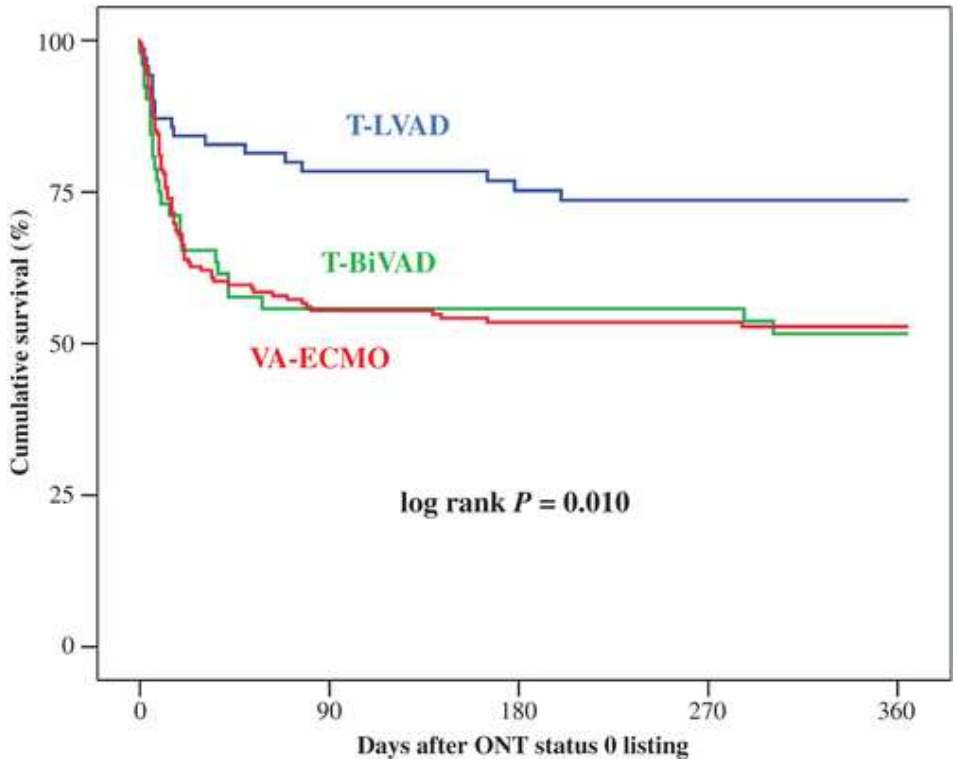
Conclusion Temporary devices may be used to bridge critically ill candidates directly to heart transplantation in a setting of short waiting list times, as is the case of Spain. In our series, bridging with T-LVAD was associated with more favourable outcomes than bridging with T-BiVAD or VA-ECMO.

Competing outcomes of temporary MCS as a direct bridge to heart transplantation: a nationwide Spanish registry



Crspo-Leiro et al. European Journal of Heart Failure, Volume: 20, Issue: 1, Pages: 178-186, First published: 26 September 2017, DOI: (10.1002/ejhf.956)

One year survival with temporary MCS as a direct bridge to heart transplantation: a nationwide Spanish registry



Crspo-Leiro et al. European Journal of Heart Failure, Volume: 20, Issue: 1, Pages: 178-186, First published: 26 September 2017, DOI: (10.1002/ejhf.956)

ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Post-transplant outcome in patients bridged to transplant with temporary mechanical circulatory support devices

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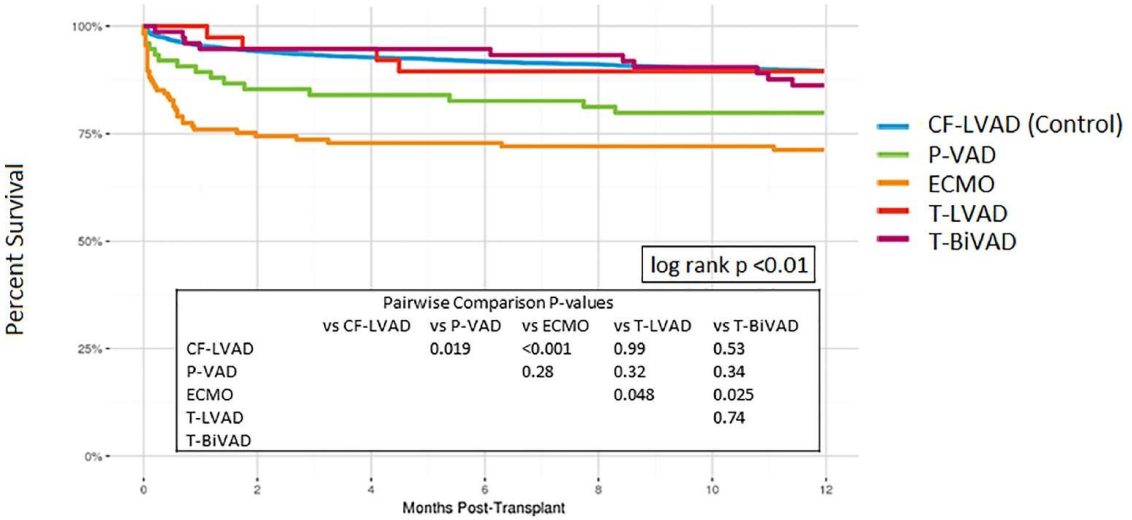
risk prediction;
survival

METHODS: Using data from the International Society for Heart and Lung Transplantation Thoracic Transplant Registry, we included subjects who underwent transplantation between 2005 and 2016 with known use of mechanical circulatory support. Pre-transplant recipient, donor, and transplant-specific variables were abstracted. The primary outcome was patient survival at 1-year post-transplant. Outcomes of patients bridged to transplant with TMCS were compared with those of patients bridged with CF-LVADs. Cox regression analyses were performed to identify clinical variables associated with the outcomes.

RESULTS: There were 6,528 patients bridged to transplant with the following types of mechanical circulatory support: durable CF-LVADs ($n = 6{,}206$), extracorporeal membrane oxygenation (ECMO, $n = 134$), percutaneous temporary CF-LVADs ($n = 75$), surgically implanted temporary CF-LVADs ($n = 38$) or surgically implanted temporary BiVAD ($n = 75$). Bridging with ECMO (hazard ratio 3.79, 95% confidence interval [CI] 2.69−5.34, $p < 0.001$) or percutaneous temporary CF-LVADs (hazard ratio 1.83, 95% CI 1.09−3.08, $p = 0.02$) was independently associated with higher risk of mortality. Additional risk factors included older donor age, female/male donor-recipient match, older recipient age, higher recipient body mass index, higher recipient creatinine, and prolonged ischemic time.

Kaplan–Meier estimates for patient survival within 1 year



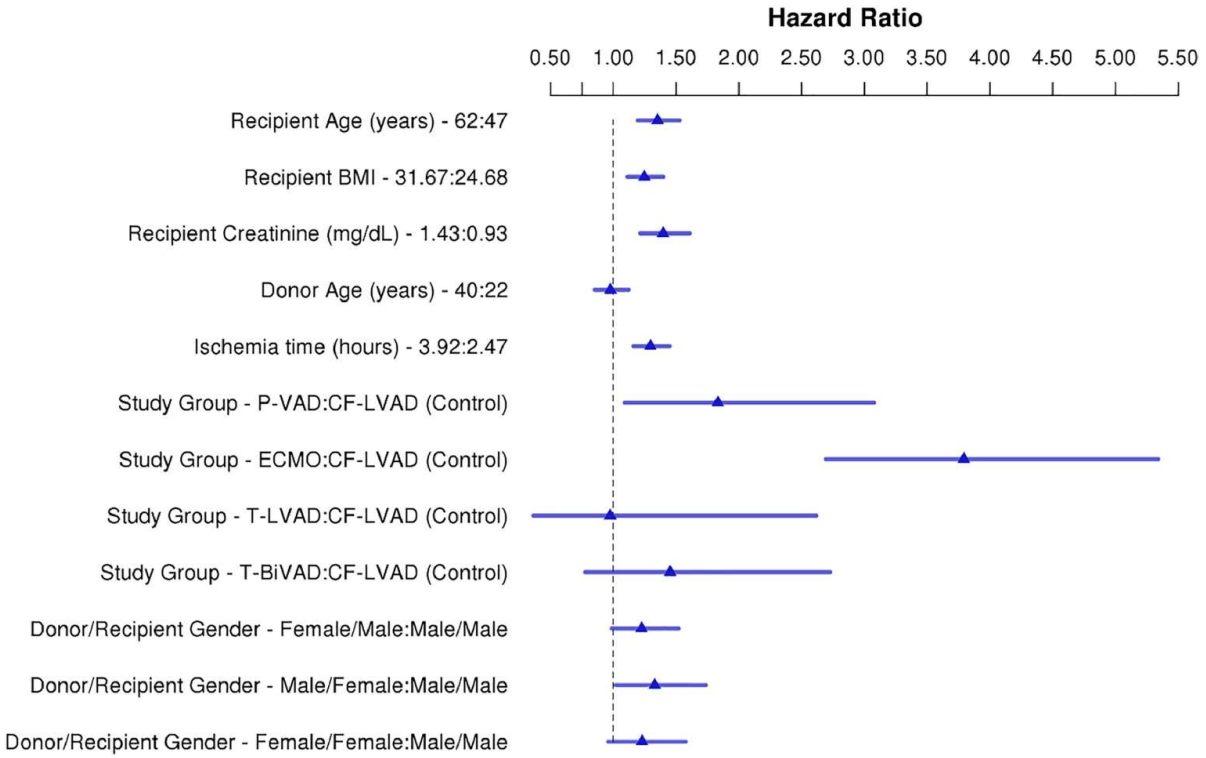
Pairwise Comparison P-values

	vs CF-LVAD	vs P-VAD	vs ECMO	vs T-LVAD	vs T-BiVAD
CF-LVAD		0.019	<0.001	0.99	0.53
P-VAD			0.28	0.32	0.34
ECMO				0.048	0.025
T-LVAD					0.74
T-BiVAD					

Months Post-Transplant					
1 month		6 months		12 months	
Number at Risk	Survival (95% CI) (%)	Number at Risk	Survival (95% CI) (%)	Number at Risk	Survival (95% CI) (%)
5902	95.5 (95.0, 96.0)	5644	91.8 (91.1, 92.5)	5314	89.6 (88.8, 90.3)
68	89.3 (82.6, 96.6)	61	82.6 (74.4, 91.7)	55	79.9 (71.2, 89.5)
99	76.0 (69.0, 83.6)	94	72.8 (65.6, 80.8)	86	71.2 (63.9, 79.4)
38	100.0 (100.0, 100.0)	35	89.5 (80.2, 99.8)	31	89.5 (80.2, 99.8)
72	94.7 (89.7, 100.0)	69	94.7 (89.7, 100.0)	60	86.2 (78.6, 94.5)

The Journal of Heart and Lung Transplantation 2019 38, 858-869DOI: (10.1016/j.healun.2019.04.003)

Risk factors for death at 1 year after Tx
(3rd quartile vs 1st quartile for continuous variables)



The Journal of Heart and Lung Transplantation 2019 38, 858-869DOI: (10.1016/j.healun.2019.04.003)

1 Year Heart Mortality Calculator

Recipient Age (years)

18 — 69 — 80

Recipient BMI (kg/m2)

16 — 30 — 40

Recipient Creatinine (mg/dL)

0.5 — 1.5 — 4

Donor Age (years)

15 — 36 — 80

Donor/Recipient Gender

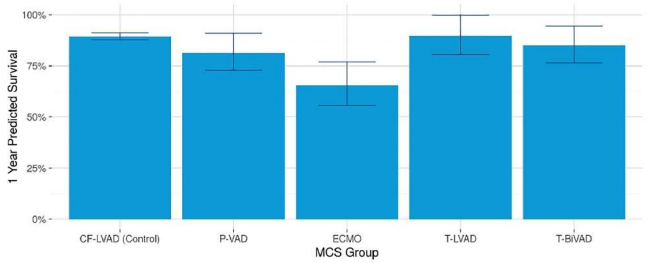
- (•) Male/Male
- ( ) Female/Male
- ( ) Male/Female
- ( ) Female/Female

Ischemia Time (hours)

1 — 3.3 — 8

Reset

MCS Group	Survival	95% CI
CF-LVAD (Control)	89.4%	(87.8%, 91.1%)
P-VAD	81.5%	(72.9%, 91.0%)
ECMO	65.4%	(55.6%, 76.9%)
T-LVAD	89.7%	(80.4%, 99.9%)
T-BiVAD	85.0%	(76.5%, 94.4%)



The calculator was developed using ISHLT International Thoracic Organ Transplant Registry data for adult heart alone transplants performed during 1/1/2005 - 6/30/2016.

Study groups are defined as follows

- **CF-LVAD (Control):** Patients bridged with durable continuous flow LVAD support (HeartMateII, HeartMate3, HeartWare HVAD, Jarvik 2000)
- **P-VAD:** Percutaneous ventricular assist devices (Impella 2.5, Impella CP, Impella 5.0, TandemHeart)
- **ECMO:** Extracorporeal membrane oxygenation (ECMO) and no VAD device
- **T-LVAD:** Centrally implanted temporary LVAD (CentriMag LVAD)
- **T-BIVAD:** Centrally implanted temporary Bi-VAD (CentriMag Bi-VAD)

Nine contemporary therapeutic directions in heart failure

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ABSTRACT

The global burden of heart failure has continued to increase dramatically with 26 million people affected and an estimated health expenditure of $31 billion worldwide. Several practice-influencing studies were reported recently, bringing advances along many frontiers in heart failure, particularly heart failure with reduced ejection fraction. In this article, we discuss nine distinct therapeutic areas that were significantly influenced by this scientific progress. These distinct areas include the emergence of sodium-glucose cotransporter-2 inhibitors, broadening the application of angiotensin-neprilysin inhibition, clinical considerations in therapy withdrawal in those patients with heart failure that 'recover' myocardial function, benefits of low-dose direct oral anticoagulants in sinus rhythm, targeted therapy for treating cardiac amyloidosis, usefulness of mitral valve repair in heart failure, the advent of newer left ventricular assist devices for advanced heart failure, the role of ablation in atrial fibrillation in heart failure, and finally the use of wearable defibrillators to address sudden death.

Food and Drug Administration (FDA) and the European Medicines Agency began requiring comprehensive evaluation of the cardiovascular safety of all new antidiabetic agents.[6 7] Drug classes tested under these new requirements include dipeptidyl peptidase-4 inhibitors, glucagon-like peptide 1 receptor agonists and sodium-glucose cotransporter-2 inhibitors (SGLT2i), all of which exert their glucose-lowering effect through distinct mechanisms. SGLT2 inhibition in the proximal tubule of the nephron leads to glucosuria, diuresis, weight loss and blood pressure lowering.[8] While all subsequently tested medications for type 2 diabetes mellitus have reached the formal non-inferiority criteria, that is, demonstrated safety for a composite cardiovascular endpoint most often comprising cardiovascular death, MI or stroke, the class of SGLT2i also signalled a reduction in composite cardiovascular risk and in the risk of heart failure.[9–13]

Results from the cardiovascular outcome trial of the third SGLT2i, DECLARE-TIMI 58 (Dapagliflozin Effect on Cardiovascular Events-Thrombol-

European Journal of Heart Failure (2017) 19, 595–602
doi:10.1002/ejhf.779

REVIEW

Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes

Finn Gustafsson[1]* and Joseph G. Rogers[2]

HeartMate II

HeartMate III

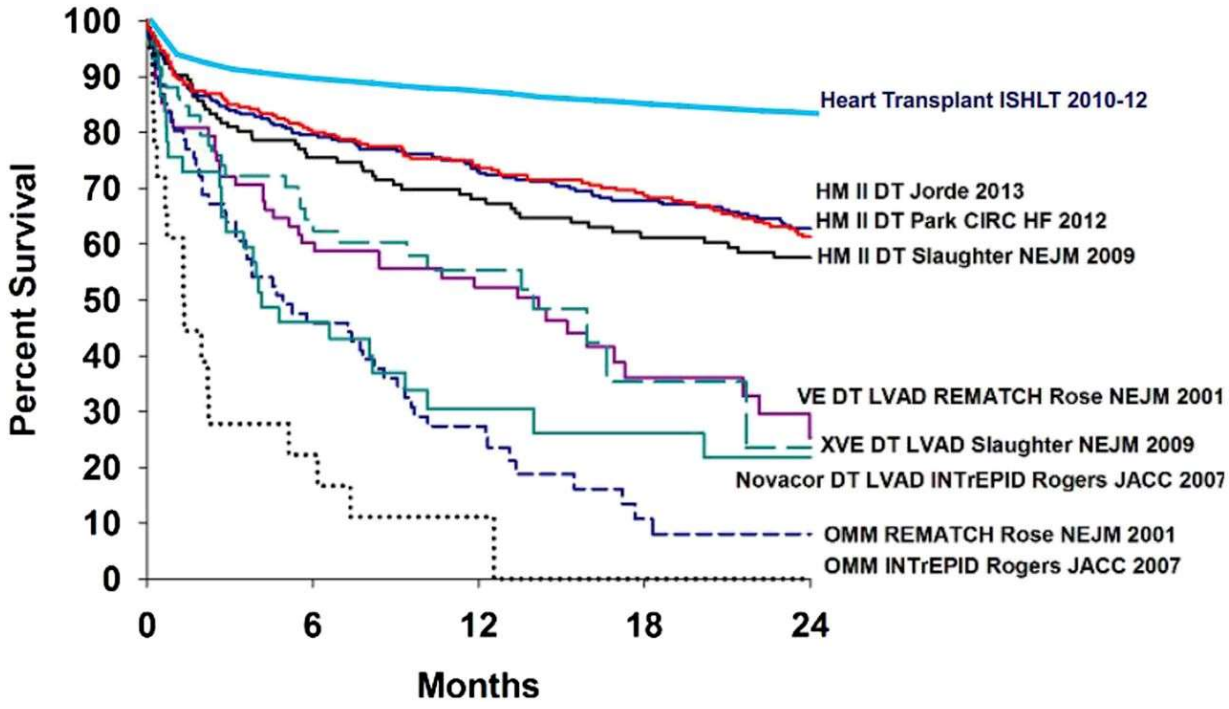
HeartWare

Recommendations for LVAD implantation

Recommendations	Class [a]	Level [b]	Ref [c]
An LVAD should be considered in patients who have end- stage HFrEF despite optimal medical and device therapy and who are eligible for heart transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (Bridge to transplant indication).	IIa	C	
An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are not eligible for heart transplantation to, reduce the risk of premature death.	IIa	B	605, 612, 613

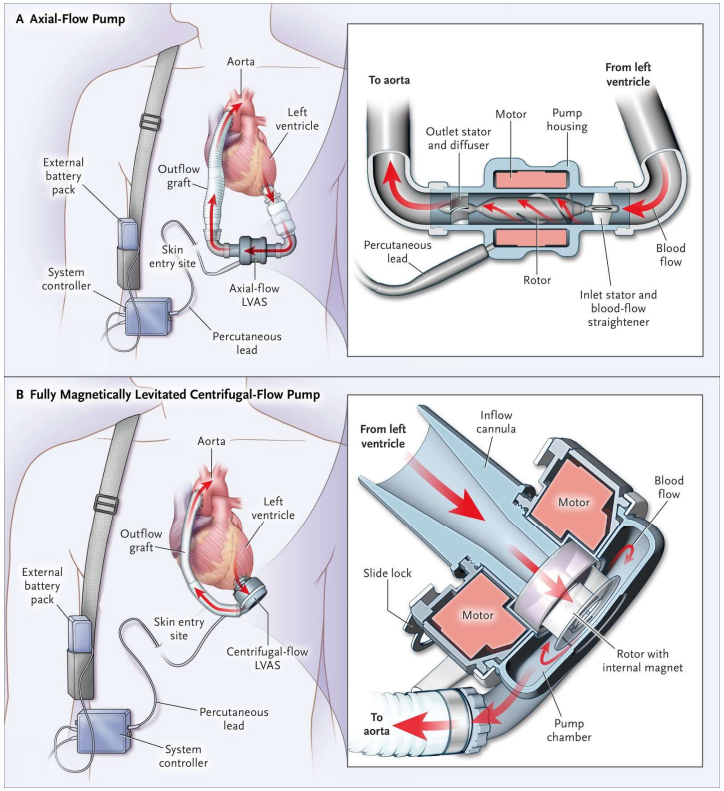
Rose et al. N Engl J Med 2001; 345: 1435-43; Slaughter et al. N Engl J Med 2009; 361:2241-51; Estep et al. J Am Coll Cardiol 2015; 66:1747-61
Ponikowski et al. Eur J Heart Fail 2016; 18 891-975

Survival rates in trials and registry reports of Heart Tx and chronic MCS as destination therapy (DT)



Stavros G. Drakos JACC 2014;63:1758-1760

Diagrams of the Axial-Flow Pump and the Centrifugal-Flow Pump.



Mehra MR et al. N Engl J Med ;376:440-450

ORIGINAL ARTICLE

A Fully Magl Pump fo

Mandeep R. Mehr
Daniel J. Goldstein, M.D.,
Mary N. Walsh, M.D
Ulrich P. Jorde, M.D.,
David A. Dean, M
Gregory A. Ewald, M.D.,
and Christopher Sal

BACKGROUND

Continuous-flow left ventr
patients with advanced h
pump thrombosis. We inv
trifugal continuous-flow p

METHODS

We randomly assigned pat
centrifugal continuous-flo
pump. Patients could be e
(bridge to transplantation
posite of survival free of
modified Rankin score >3
more severe disability) or s
at 6 months after implant
the primary end point (no

RESULTS

Of 294 patients, 152 were
the axial-flow pump grou
point occurred in 131 pati
109 (76.8%) in the axial-flo
95% lower confidence bo
0.55; 95% confidence inter
There were no significant
abling stroke, but reoperat
trifugal-flow pump group
hazard ratio, 0.08; 95%
pump thrombosis occurr
and in 14 patients (10.1%

CONCLUSIONS

Among patients with advan
tated centrifugal-flow pun
was implantation of an a
reoperation for pump ma
ClinicalTrials.gov number

the Brigham and Women's Hospital
t and Vascular Center and Harvard
cal School, Boston (M.R.M.); Colum-
University College of Physicians and
ons and New York Presbyterian Hos-
(Y.N., P.C.C.) and Montefiore Ein-
Center for Heart and Vascular Care
., U.P.J.) — all in New York; Univer-
of Chicago School of Medicine and
cal Center, Chicago (N.U.); University
olorado School of Medicine, Denver
.); St. Vincent Heart Center, India-
lis (M.N.W., C.S.); Duke Heart Cen-
uke University, Durham, NC (C.A.M.,
); University of Michigan Health Sys-
Ann Arbor (F.D.P., K.D.A.); Piedmont
ital, Atlanta (D.A.D., K.M.); Washing-
University School of Medicine, St.
(A.I., G.A.E.); and Integris Baptist
cal Center, Oklahoma City (D.H.,
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Heart and Vascular Center, Center for
nced Heart Disease, 75 Francis St.,
on, MA 02115, or at mmehra@bwh
ard.edu.

omplete list of the Multicenter Study
agLev Technology in Patients Under-
g Mechanical Circulatory Support
rapy with HeartMate 3 (MOMENTUM
vestigators is provided in the Supple-
tary Appendix, available at NEJM.org.

Mehra and Naka contributed equally
s article.

rticle was published on November 16,
at NEJM.org.

gl J Med 2017;376:440-50.
10.1056/NEJMoa1610426

ORIGINAL ARTICLE

Two-Year Outcomes with a M Levitated Cardiac Pump in H

M.R. Mehra, D.J. Goldstein, N. Uriel, J.C. Cleveland, J
C. Salerno, M.N. Walsh, C.A. Milano, C.B. Patel, G.A. E
A. Krishnamoorthy, W.G. Cotts, A.J. Tatooles, U.P. Jo
J.D. Estep, V. Jeevanandam, G. Sayer, D. Horstmansho
E.R. Skipper, J.B. O'Connell, G. Heatley, P. Sooc
for the MOMENTUM 3 Investigator

ABSTRACT

BACKGROUND

In an early analysis of this trial, use of a magnetically levitate
flow circulatory pump was found to improve clinical outc
a mechanical-bearing axial continuous-flow pump, at 6
advanced heart failure.

METHODS

In a randomized noninferiority and superiority trial, we c
flow pump with the axial-flow pump in patients with ac
respective of the intended goal of support (bridge to trans
therapy). The composite primary end point was survival at
stroke (with disabling stroke indicated by a modified Ra
range from 0 to 6, with higher scores indicating more sev
free of reoperation to replace or remove a malfunctioning
ity margin for the risk difference (centrifugal-flow pump
pump group) was −10 percentage points.

RESULTS

Of 366 patients, 190 were assigned to the centrifugal-flo
to the axial-flow pump group. In the intention-to-treat
end point occurred in 151 patients (79.5%) in the centrifu
compared with 106 (60.2%) in the axial-flow pump gro
19.2 percentage points; 95% lower confidence boundary
[P<0.001 for noninferiority]; hazard ratio, 0.46; 95% confid
0.69 [P<0.001 for superiority]). Reoperation for pump malfi
in the centrifugal-flow pump group than in the axial-flow
[1.6%] vs. 30 patients [17.0%]; hazard ratio, 0.08; 95% C
The rates of death and disabling stroke were similar in
overall rate of stroke was lower in the centrifugal-flow pump
flow pump group (10.1% vs. 19.2%; hazard ratio, 0.47; 95%

CONCLUSIONS

In patients with advanced heart failure, a fully magnetically
pump was superior to a mechanical-bearing axial-flow pum
free of disabling stroke or reoperation to replace or remo
vice. (Funded by Abbott; MOMENTUM 3 ClinicalTrials.gov

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Mehra at the Brigham and Women's Hospital Heart and Vascular Center, Center for Advanced Heart Disease, 75 Francis St., Boston, MA 02115 or at mmehra@bwh.harvard.edu.

*A complete list of the investigators in the MOMENTUM 3 trial is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Mehra and Goldstein contributed equally to this article.

This article was published on March 17, 2019, at NEJM.org.

N Engl J Med 2019;380:1618-27.
DOI: 10.1056/NEJMoa1900486

ORIGINAL ARTICLE

A Fully Magnetically Levitated Left Ventricular Assist Device — Final Report

M.R. Mehra, N. Uriel, Y. Naka, J.C. Cleveland, Jr., M. Yuzefpolskaya, C.T. Salerno, M.N. Walsh, C.A. Milano, C.B. Patel, S.W. Hutchins, J. Ransom, G.A. Ewald, A. Itoh, N.Y. Raval, S.C. Silvestry, R. Cogswell, R. John, A. Bhimaraj, B.A. Bruckner, B.D. Lowes, J.Y. Um, V. Jeevanandam, G. Sayer, A.A. Mangi, E.J. Molina, F. Sheikh, K. Aaronson, F.D. Pagani, W.G. Cotts, A.J. Tatooles, A. Babu, D. Chomsky, J.N. Katz, P.B. Tessmann, D. Dean, A. Krishnamoorthy, J. Chuang, I. Topuria, P. Sood, and D.J. Goldstein, for the MOMENTUM 3 Investigators*

ABSTRACT

BACKGROUND

In two interim analyses of this trial, patients with advanced heart failure who were treated with a fully magnetically levitated centrifugal-flow left ventricular assist device were less likely to have pump thrombosis or nondisabling stroke than were patients treated with a mechanical-bearing axial-flow left ventricular assist device.

METHODS

We randomly assigned patients with advanced heart failure to receive either the centrifugal-flow pump or the axial-flow pump irrespective of the intended goal of use (bridge to transplantation or destination therapy). The composite primary end point was survival at 2 years free of disabling stroke or reoperation to replace or remove a malfunctioning device. The principal secondary end point was pump replacement at 2 years.

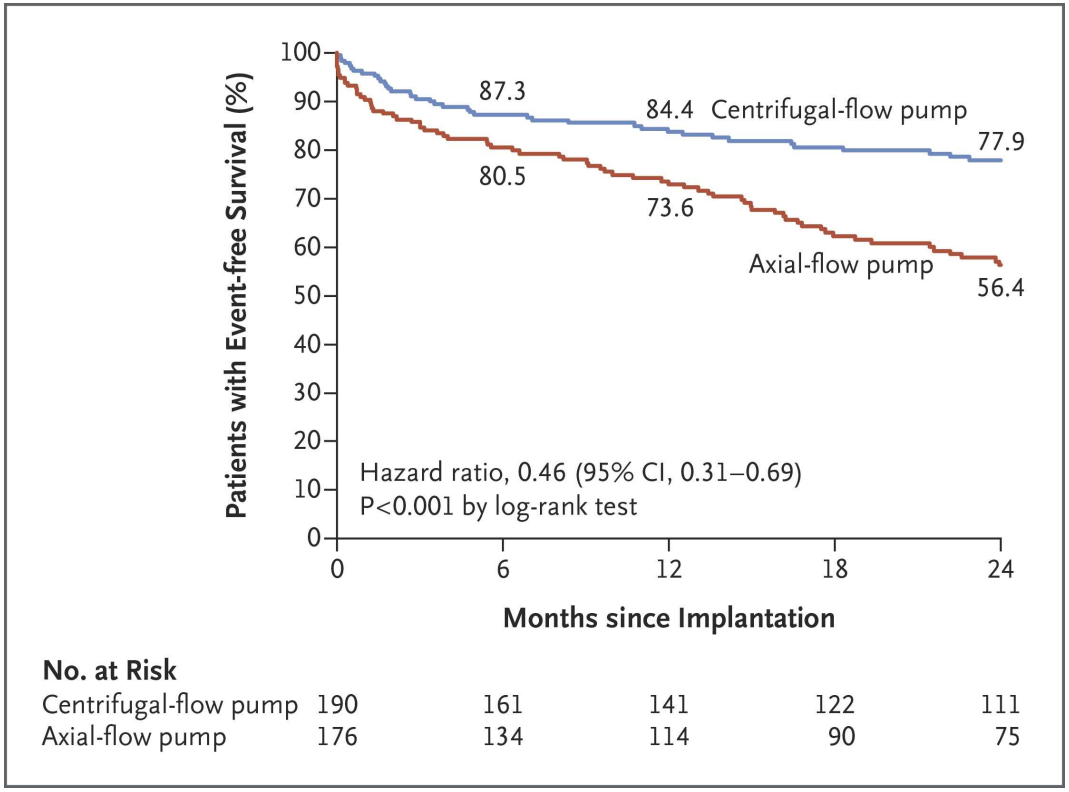
RESULTS

This final analysis included 1028 enrolled patients: 516 in the centrifugal-flow pump group and 512 in the axial-flow pump group. In the analysis of the primary end point, 397 patients (76.9%) in the centrifugal-flow pump group, as compared with 332 (64.8%) in the axial-flow pump group, remained alive and free of disabling stroke or reoperation to replace or remove a malfunctioning device at 2 years (relative risk, 0.84; 95% confidence interval [CI], 0.78 to 0.91; P<0.001 for superiority). Pump replacement was less common in the centrifugal-flow pump group than in the axial-flow pump group (12 patients [2.3%] vs. 57 patients [11.3%]; relative risk, 0.21; 95% CI, 0.11 to 0.38; P<0.001). The numbers of events per patient-year for stroke of any severity, major bleeding, and gastrointestinal hemorrhage were lower in the centrifugal-flow pump group than in the axial-flow pump group.

CONCLUSIONS

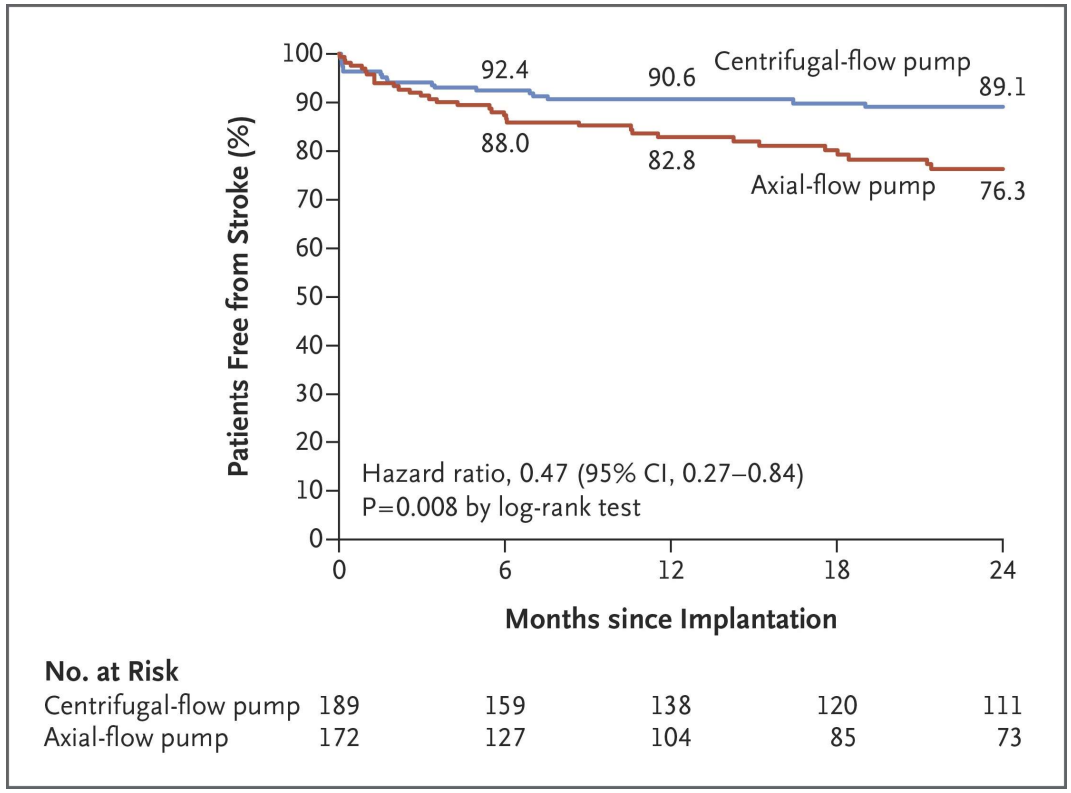
Among patients with advanced heart failure, a fully magnetically levitated centrifugal-flow left ventricular assist device was associated with less frequent need for pump replacement than an axial-flow device and was superior with respect to survival free of disabling stroke or reoperation to replace or remove a malfunctioning device. (Funded by Abbott; MOMENTUM 3 ClinicalTrials.gov number, NCT02224755.)

Kaplan–Meier Estimates of the Primary End Point in the Intention-to-Treat Population.



Mehra MR et al. N Engl J Med 2018;378:1386-1395

Actuarial Freedom from Stroke of Any Severity in the Per-Protocol Population.



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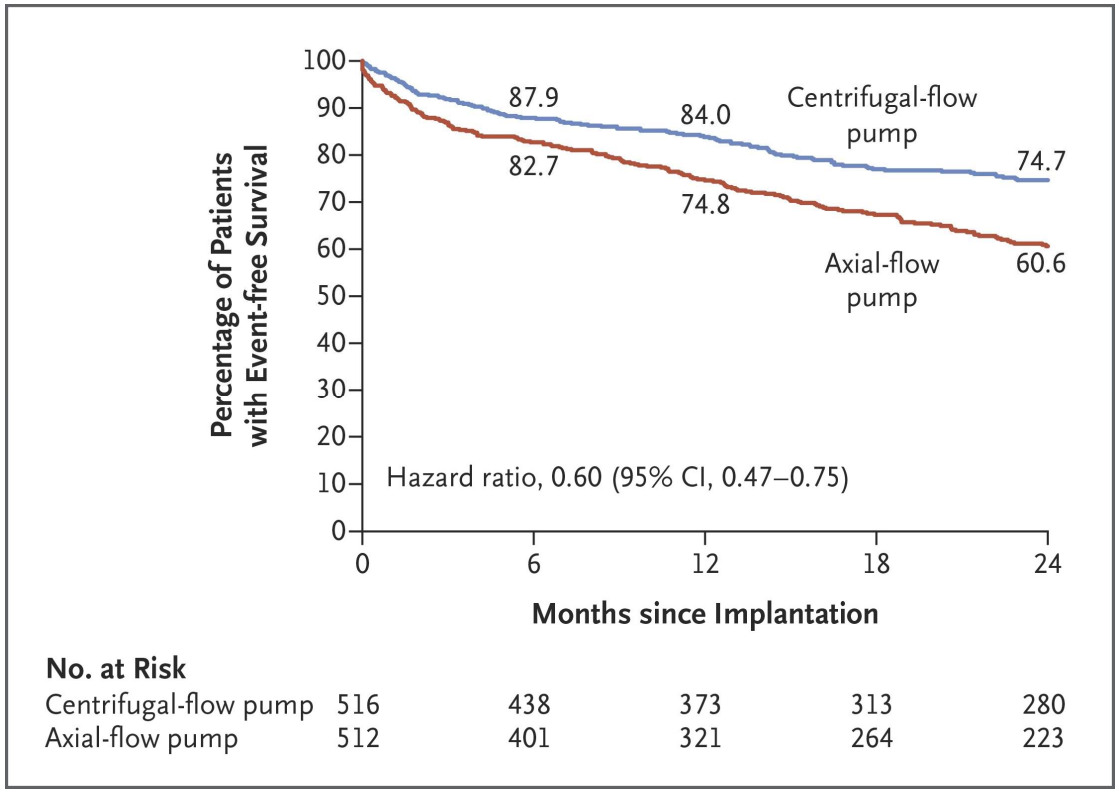
Kaplan–Meier Estimates of the Primary End Point in the Intention-to-Treat Population.



No. at Risk

Centrifugal-flow pump	516	438	373	313	280
Axial-flow pump	512	401	321	264	223

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Principal Safety Outcomes in the Per-Protocol Population.

Adverse Event	Centrifugal-Flow Pump	Axial-Flow Pump	Centrifugal-Flow Pump	Axial-Flow Pump	Relative Risk (95% CI)	P Value
	no. of patients with events (%)		*events per patient-yr*			
Suspected or confirmed pump thrombosis	7 (1.4)	70 (13.9)	0.01	0.12	0.08 (0.04–0.16)	<0.001
Any stroke	51 (9.9)	98 (19.4)	0.08	0.18	0.42 (0.30–0.57)	<0.001
Disabling stroke	26 (5.0)	38 (7.5)	0.04	0.07	0.54 (0.34–0.85)	0.008
Any bleeding	225 (43.7)	278 (55.0)	0.61	0.95	0.64 (0.57–0.72)	<0.001
Gastrointestinal bleeding	126 (24.5)	156 (30.9)	0.31	0.49	0.64 (0.54–0.75)	<0.001
Other neurologic event	59 (11.5)	47 (9.3)	0.09	0.08	1.25 (0.88–1.79)	0.21
Any major infection	300 (58.3)	285 (56.4)	0.82	0.82	1.00 (0.89–1.12)	0.96
Right heart failure	176 (34.2)	143 (28.3)	0.27	0.23	1.15 (0.94–1.42)	0.18
Cardiac arrhythmia	185 (35.9)	207 (41.0)	0.37	0.45	0.82 (0.70–0.97)	0.02
Respiratory failure	111 (21.6)	98 (19.4)	0.19	0.17	1.10 (0.86–1.40)	0.44
Renal dysfunction	73 (14.2)	56 (11.1)	0.11	0.08	1.36 (0.98–1.89)	0.07
Hepatic dysfunction	25 (4.9)	27 (5.3)	0.03	0.04	0.78 (0.46–1.34)	0.38

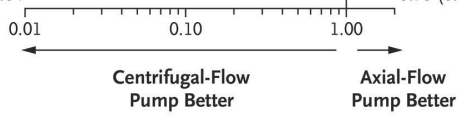

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Table 1. Baseline Characteristics of Patients in the Intention-to-Treat Population.*

Characteristic	Centrifugal-Flow Pump Group (N = 516)	Axial-Flow Pump Group (N = 512)
Age — yr		
Mean	59±12	60±12
Median (range)	62 (18–83)	63 (21–84)
Male sex — no. (%)	411 (79.7)	419 (81.8)
Race or ethnic group — no. (%)†		
White	342 (66.3)	367 (71.7)
Black	145 (28.1)	120 (23.4)
Asian	8 (1.6)	3 (0.6)
Native Hawaiian or Pacific Islander	0	4 (0.8)
Other	21 (4.1)	18 (3.5)
Body-surface area — m^2	2.1±0.3	2.1±0.3
Ischemic cause of heart failure — no. (%)	216 (41.9)	240 (46.9)
History of atrial fibrillation — no. (%)	215 (41.7)	238 (46.5)
History of stroke — no. (%)	50 (9.7)	56 (10.9)
Previous cardiac surgical procedures — no. (%)		
Coronary-artery bypass	102 (19.8)	114 (22.3)
Valve replacement or repair	36 (7.0)	31 (6.1)
Left ventricular ejection fraction — %	17.3±5.1	17.2±5.0
Arterial blood pressure — mm Hg		
Systolic	108.4±14.7	106.5±14.5
Diastolic	66.8±10.6	65.7±10.2
Mean arterial pressure — mm Hg	79.2±10.4	79.2±10.1
Pulmonary-capillary wedge pressure — mm Hg	23.1±8.6	22.9±9.2
Cardiac index — liters/min/m^2	2.0±0.5	2.0±0.6
Pulmonary vascular resistance — Wood units	3.1±1.7	3.0±1.7
Right atrial pressure — mm Hg	10.8±6.5	10.7±6.8
Serum sodium level — mmol/liter	135.4±4.1	135.5±4.2
Serum creatinine level — mg/dl	1.4±0.4	1.4±0.4
Estimated glomerular filtration rate — ml/min/1.73 m^2	61.3±23.7	59.5±22.0
Intended goal of pump support — no. (%)		
Bridge to transplantation	113 (21.9)	121 (23.6)
Bridge to candidacy for transplantation	86 (16.7)	81 (15.8)
Destination therapy	317 (61.4)	310 (60.5)

* Plus–minus values are means ±SD. There were no significant differences between the groups in any characteristic except for race ($P=0.04$) and systolic blood pressure ($P=0.03$). The intention-to-treat population included all patients who underwent randomization. Data on Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles and concomitant medications and cardiac interventions are provided in Table S1 in the Supplementary Appendix. Percentages may not total 100 because of rounding. To convert the serum creatinine level to micromoles per liter, multiply by 88.4.
† Race or ethnic group was reported by the patient.

Primary and Principal Secondary End Points.

Table 2. Primary and Principal Secondary End Points.*

End Point	Centrifugal-Flow Pump Group (N=516)		Axial-Flow Pump Group (N=512)		Absolute Difference	Relative Risk (95% CI)	P Value
	no. of patients	*% (95% CI)*	*no. of patients*	*% (95% CI)*	*percentage points (95% LCB)*		
Primary end point†							
Noninferiority analysis	397	76.9 (73.1–80.5)	332	64.8 (60.5–69.0)	12.1 (6.0)		<0.001‡
Superiority analysis	397	76.9 (73.1–80.5)	332	64.8 (60.5–69.0)		0.84 (0.78–0.91)	<0.001‡
First event that resulted in treatment failure with respect to the primary end point§							
Withdrew before implantation	1	0.2 (0.0–1.1)	7	1.4 (0.6–2.8)		0.14 (0.02–1.15)	
Withdrew after implantation	4	0.8 (0.2–2.0)	3	0.6 (0.1–1.7)		1.32 (0.30–5.88)	
Underwent reoperation to replace or remove pump¶	14	2.7 (1.5–4.5)	73	14.3 (11.4–17.6)		0.19 (0.11–0.33)	
Had disabling stroke‖	20	3.9 (2.4–5.9)	30	5.9 (4.0–8.3)		0.66 (0.38–1.15)	
Died within 24 months after implant**	80	15.5 (12.5–18.9)	67	13.1 (10.3–16.3)		1.18 (0.88–1.60)	
Principal secondary end point††							
Pump replacement within 24 months after implantation	12	2.3 (1.2–4.0)	57	11.3 (8.7–14.4)		0.21 (0.11–0.38)	<0.001‡‡

* The 95% confidence intervals have not been adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible. LCB denotes lower confidence boundary.

† The primary end point was a composite of survival free of disabling stroke or reoperation to replace or remove a malfunctioning device at 24 months after implantation. Disabling stroke was defined by a modified Rankin score of greater than 3 (scores range from 0 to 6, with higher scores indicating more severe disability). The intention-to-treat population included all patients who underwent randomization.

‡ P values for the primary end-point analyses are from Farrington–Manning risk difference (in the noninferiority analysis) or the z test of proportions with normal approximation to the binomial distribution (in the superiority analysis).

§ The event that occurred first was noted as the treatment-failure event in this component analysis. Patients could have multiple events after the first event leading to treatment failure with regard to the primary end point (e.g., disabling stroke after a pump exchange), which are not accounted for in the primary analysis. Table S2 in the Supplementary Appendix shows this in the context of disabling strokes and deaths as first events or recurrent events.

¶ For the component analysis, this category includes pump replacement (12 patients in the centrifugal-flow pump group and 56 in the axial-flow pump group), urgent heart transplantation for device malfunction (2 patients in the centrifugal-flow pump group and 15 in the axial-flow pump group), or explantation or permanent deactivation of the device for a reason other than myocardial recovery (2 patients in the axial-flow pump group). There were 57 patients in the axial-flow pump group who underwent pump replacement; 56 pump replacements in the axial-flow pump group were first events that led to treatment failure in a patient with regard to the primary end point.

‖ There were 26 patients in the centrifugal-flow pump group and 38 patients in the axial-flow pump group who had a disabling stroke; the corresponding rates of disabling stroke for the treatment groups were 0.04 events per patient-year and 0.07 events per patient-year. Among all the disabling stroke events, 20 in the centrifugal-flow pump group and 30 in the axial-flow pump group were first events that led to treatment failure in a patient with regard to the primary end point.

** A total of 98 patients in the centrifugal-flow pump group and 103 patients in the axial-flow pump group had died at 2 years; 80 deaths in the centrifugal-flow pump group and 67 deaths in the axial-flow pump group were first events that led to treatment failure in a patient with regard to the primary end point.

†† The secondary end point was evaluated in the per-protocol population (515 patients in the centrifugal-flow pump group and 505 patients in the axial-flow pump group) for the first event of pump replacement.

‡‡ The P value for the principal secondary end point was calculated with Fisher's exact test.

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Table 3. Postdischarge End Points among Patients Discharged while Receiving Left Ventricular Assist Device Support (Per-Protocol Population).*

End Point	Centrifugal-Flow Pump Group (N=485)	Axial-Flow Pump Group (N=471)	Difference or Hazard Ratio (95% CI)
Median duration of rehospitalization (interquartile range) — days	13 (4 to 37)	18 (6 to 40)	−5 (−8.7 to −1.3)
Median duration receiving left ventricular assist device support outside hospital (interquartile range) — days	653 (333 to 696)	605 (259 to 690)	48 (−0.8 to 96.8)
Rate of rehospitalization for any cause — events per patient-yr	2.26	2.47	0.92 (0.86 to 0.99)†

* The per-protocol population included all patients who underwent randomization and received the assigned device. The 95% confidence intervals have not been adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible.
† The hazard ratio was derived from the Andersen–Gill model for the comparison of all-cause readmissions between the groups.

ESC European Society of Cardiology

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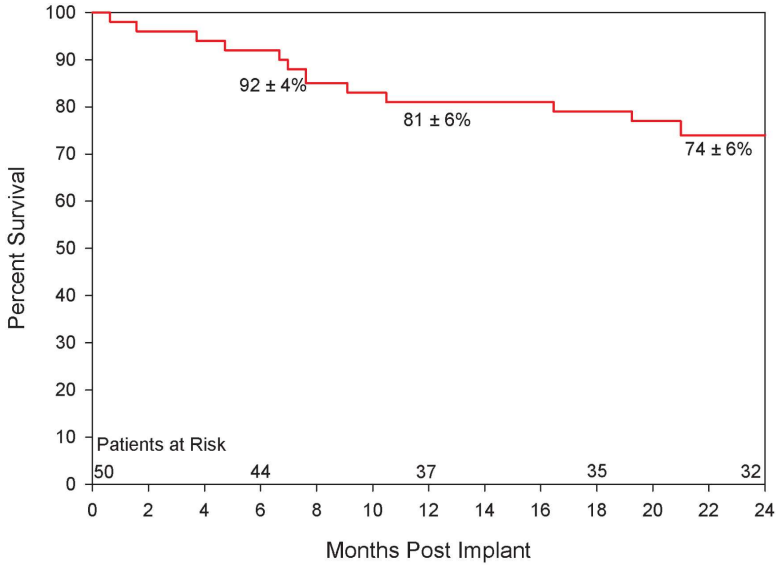

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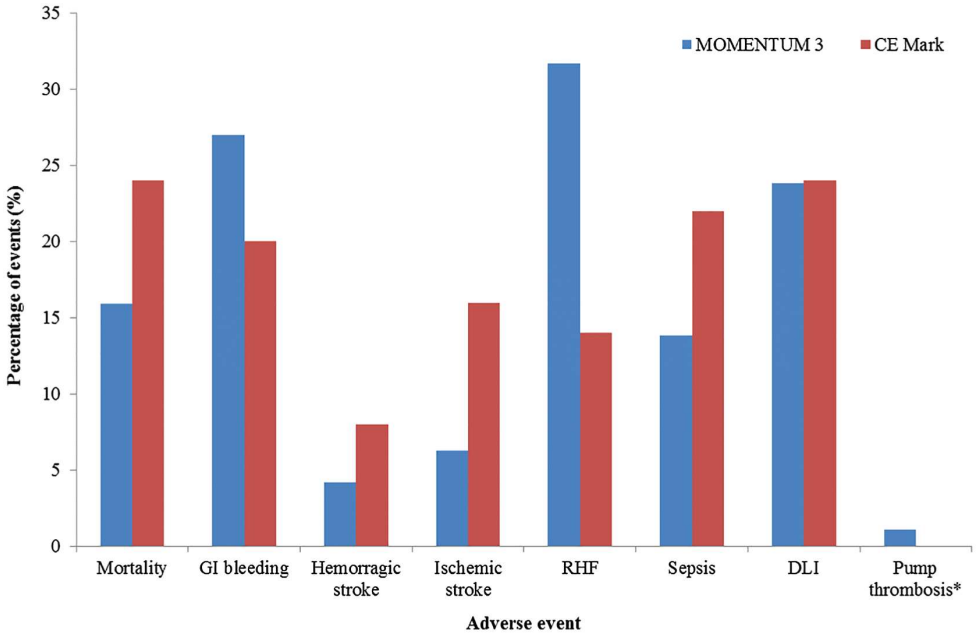

INTERMACS stages for patients with advanced heart failure

INTERMACS level	NYHA Class	Description	Device	1y survival with LVAD therapy
1. Cardiogenic shock "Crash and burn"	IV	Haemodynamic instability in spite of increasing doses of catecholamines and/or mechanical circulatory support with critical hypoperfusion of target organs (severe cardiogenic shock).	ECLS, ECMO, percutaneous support devices	52.6±5.6%
2. Progressive decline despite inotropic support "Sliding on inotropes"	IV	Intravenous inotropic support with acceptable blood pressure but rapid deterioration of renal function, nutritional state, or signs of congestion.	ECLS, ECMO, LVAD	63.1±3.1%
3. Stable but inotrope dependent "Dependent stability"	IV	Haemodynamic stability with low or intermediate doses of inotropics, but necessary due to hypotension, worsening of symptoms, or progressive renal failure.	LVAD	78.4±2.5%
4. Resting symptoms "Frequent flyer"	IV ambulatory	Temporary cessation of inotropic treatment is possible, but patient presents with frequent symptom recurrences and typically with fluid overload.	LVAD	78.7±3.0%
5. Exertion intolerant "Housebound"	IV ambulatory	Complete cessation of physical activity, stable at rest, but frequently with moderate fluid retention and some level of renal dysfunction.	LVAD	93.0±3.9%[a]
6. Exertion limited "Walking wounded"	III	Minor limitation on physical activity and absence of congestion while at rest. Easily fatigued by light activity.	LVAD / Discuss LVAD as option	-
7. "Placeholder"	III	Patient in NYHA Class III with no current or recent unstable fluid balance.	Discuss LVAD as option	-

Ponikowski et al. Eur J Heart Fail 2016; 18 891-975

Take home messages

- ECMO is among the best options for short-term MCS in patients with acute HF
- ECMO is associated with worse post-TX mortality
- LVAD is the best option as a bridge to Tx
- MOMENTUM 3 has shown improved survival free of survival free of disabling stroke or reoperation to replace or remove a malfunctioning device