



ORIGINAL CLINICAL SCIENCE

First Annual IMACS Report: A global International Society for Heart and Lung Transplantation Registry for Mechanical Circulatory Support

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The first annual report of the International Society for Heart and Lung Transplantation (ISHLT) Mechanically Assisted Circulatory Support (IMACS) registry provides global data on 5,942 patients from 31 countries. This initial report focuses on patient demographics, survival, device types, adverse events, competing outcomes, and a risk factor analysis.

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The International Society for Heart and Lung Transplantation (ISHLT) Mechanically Assisted Circulatory Support (IMACS) registry is a global registry to enroll and monitor patients receiving durable mechanical circulatory (MCS) support devices in all countries and hospitals wishing to participate. The specific mission of IMACS is the advancement of patient care through scientific investigations, presentations, and publications based on analyses of

this multinational database, with the collaboration of an international array of authors.

The international precursor to IMACS was a mechanical circulatory device registry established during the ISHLT Presidency of Dr Robert Kormos in 1999. In the Fall of 1999, a motion from the ISHLT Board of Directors was passed to establish a scientific council on ventricular assist devices (VADs) and total artificial hearts, with an initial charge to establish an MCS registry. That initial registry, under the direction of Dr Mario Deng, continued to collect international clinical data for about 5 years. Eventually, with the creation of Interagency Registry for Mechanically Assisted Circulatory Support (IMTERMACS), the National

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Table 1 International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS): Goals of the Registry

- To capture worldwide data related to the implantation and outcome of patients receiving cardiac assist devices designed for and capable of use for 30 or more days
- To identify risk factors for complications
- To improve patient selection and management before and after device implantation
- To generate predictive models of outcome for given patient profiles
- To generate statistical analyses of the data that can be used as the underlying evidence/justification for government agency funded studies and clinical trials
- To identify overall and best practices with the aim of improving current outcomes

Heart, Lung, and Blood Institute–sponsored US MCS Registry, in 2006, the ISHLT MCS Registry discontinued further data collection.

Thereafter, a major international void in the organized collection of multinational MCS data existed until the creation of the European Registry for Patients with

Table 2 International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS): Device List

Durable devices	Temporary devices
Abiomed TAH	Abiomed AB5000
Berlin Heart EXCOR Adult	Adult Abiomed BVS 5000
Berlin Heart EXCOR Pediatric	Pediatric Abiomed Impella 5.0
Berlin Heart INCOR	Impella Recover
Circulite Synergy	Maquet CardioHelp
EvaHeart LVAS	Maquet Rotaflow
DuraHeart LVAS	Medtronic Biomedicus
HeartMate II LVAS	Maquet CardioHelp
HeartMate III	Sorin Revolution
HeartMate IP	Tandem Heart
HeartMate VE	Thoratec (Levitronix) CentriMag
HeartMate XVE	
HeartWare HVAD	
HeartWare MVAD	
Jarvik 2000	
Levacor LVAD	
Medos VAD	
Micromed DeBakey VAD Child	
Micromed HeartAssist 5	
Novacor PC	
Novacor PCq	
SynCardia CardioWest	
Terumo DuraHeart	
Thoratec IVAD	
Thoratec PVAD	
Toyobo/Nipro Heparin Coating LVAS	
Toyobo/Nipro LVAS	

Table 3 Patient Demographics and Pre-Implant Characteristics (IMACS: January 2013–December 2014)

IMACS patient characteristics	No. (%) (N = 5,942)
Age, years	
19-39	733 (12)
40-59	2,508 (42)
60-79	2,662 (45)
≥80	39 (0.6)
Gender	
Female	1,250 (21)
Male	4,633 (78)
Unspecified/missing	59 (1)
INTERMACS patient profile	
1. Critical cardiogenic shock	917 (15)
2. Progressive decline	1,990 (33)
3. Stable but inotrope dependent	1,845 (31)
4. Resting symptoms	870 (15)
5. Exertion intolerant	160 (3)
6. Exertion limited	36 (0.6)
7. Advanced NYHA Class III	29 (0.4)
Unknown	95 (2)

IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; NYHA, New York Heart Association.

Mechanical Circulatory Support¹ in 2009 and of IMACS. The ISHLT Board of Directors approved the concept of the IMACS project in April 2011. Contracts were subsequently executed between ISHLT and the University of Alabama at Birmingham as the Data Coordinating and Analysis Center. Programming for the database was completed in the Fall of 2012, and the Web-based data entry system was opened for patient enrollment on January 1, 2013. The stated goals of this global initiative are listed in [Table 1](#).

Table 4 Implant Characteristics (IMACS: January 2013–December 2014)

Implant characteristics	No (%) (N = 5,942)
Device type	
LVAD	5,537 (93)
RVAD	4 (0)
BiVAD	257 (4)
TAH	133 (2)
Unknown	11 (0.1)
Device strategy	
Bridge to transplant, listed	1,719 (29)
Bridge to candidacy	1,762 (30)
Destination therapy	2,364 (40)
Other (bridge to recovery, rescue, etc.)	97 (1)

BiVAD, Biventricular assist device; IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; RVAD, right ventricular assist device; TAH, total artificial heart.

Table 5 Pre-implant Patient Profile and Device Strategy (IMACS: January 2013–December 2014)

Patient profile	Device strategy (N = 5,942)					
	Bridge to transplant No. (%)	Bridge to candidacy No. (%)	Destination therapy No. (%)	Bridge to recovery No. (%)	Rescue therapy No. (%)	Unknown No. (%)
1. Critical cardiogenic shock	215 (12.5)	343 (19.4)	308 (13.0)	10 (45.4)	33 (62.2)	8 (36.3)
2. Progressive decline	640 (37.2)	574 (32.5)	750 (31.7)	7 (31.8)	8 (15.0)	11 (50.0)
3. Stable but inotrope dependent	555 (32.2)	507 (28.7)	776 (32.8)	2 (9.0)	4 (7.5)	1 (4.5)
4. Resting symptoms	197 (11.4)	270 (15.3)	397 (16.7)	0 (0)	6 (11.3)	0 (0)
5. Exertion intolerant	56 (3.2)	30 (1.7)	72 (3.0)	0 (0)	0 (0)	2 (9.0)
6. Exertion limited	6 (0.3)	14 (0.7)	15 (0.6)	1 (4.5)	0 (0)	0 (0)
7. Advanced NYHA Class III	9 (0.5)	9 (0.5)	11 (0.4)	0 (0)	0 (0)	0 (0)
Unknown	41 (2.3)	15 (0.8)	35 (1.4)	2 (9.0)	2 (3.7)	0 (0)
Total	1,719 (100.0)	1,762 (100.0)	2,364 (100.0)	22 (100.0)	53 (100.0)	22 (100)

IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support; NYHA, New York Heart Association.

Data sources

This Registry receives data from two general sources: multi-center collectives and individual hospitals, with data entry through the IMACS Web site. The collectives include INTERMACS, enrolling patients from the United States; EUROMACS, entering patients from Europe; the UK Registry, entering patients from the United Kingdom; and the Japanese Mechanically Assisted Circulatory Support (JMACS) Registry, enrolling patients from Japan. Including all sources, 31 countries have contributed patient data to the registry. This report covers implants and events within the following ranges:

- IMACS individual hospitals: January 9, 2013, to November 30, 2014 ($n = 85$)
- EUROMACS: January 2013 to June 2014 ($n = 467$)
- INTERMACS: January 2013 to September 30, 2014 ($n = 5,240$)
- JMACS: July 7, 2013, to May 30, 2014 ($n = 91$)
- UK Registry: October 5, 2013, to July 10, 2014 ($n = 59$)

The individual hospitals that have entered data are listed in Appendix 1 (available on the jhltonline.org Web site).

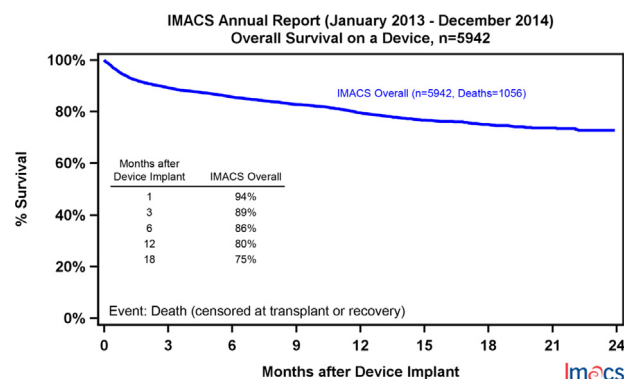


Figure 1 Actuarial (Kaplan-Meier) survival for all patients receiving durable mechanical circulatory support in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry.

This first global IMACS report will focus on patient demographics and survival, device types, adverse events, competing outcomes, and a risk factor analysis. The timeline and list of types of data collected are indicated in Appendix 2 (available on the jhltonline.org Web site.).

Statistical methods

Patient survival is presented using the Kaplan-Meier method. Patients are censored at transplant or device explant for recovery. All “point estimates” for survival are presented as simple percentages for ease of presentation.

Competing outcomes depictions display 4 mutually exclusive outcomes: alive with device in place, transplant, death before transplantation, and device removal for recovery. At any point in time, the sum of each probability

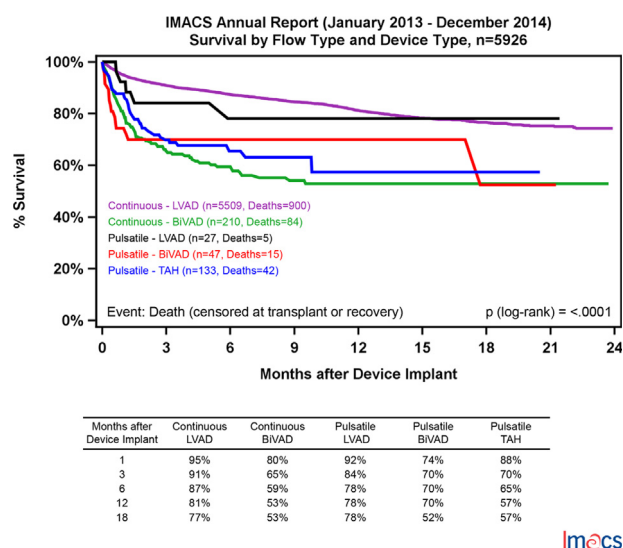


Figure 2 Actuarial survival for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry stratified by type of device. BiVAD, biventricular assist device; LVAD, left ventricular assist device; TAH, total artificial heart.

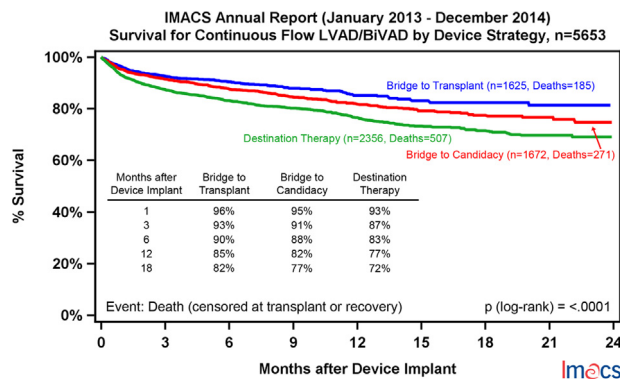


Figure 3 Actuarial survival for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving continuous-flow pumps, stratified by strategy at implant. BiVAD, biventricular assist device; LVAD, left ventricular assist device.

estimate for the 4 mutually exclusive events totals 100%. Probability estimates are presented as percentages for ease of presentation.

Risk factors for death were examined using multivariable analysis in the hazard function domain.² Variables entered into the risk factor model are listed in Appendix 3 (available on the jhltonline.org Web site).

The analysis includes patients who received devices during 2013 and 2014. However, the exact period of data collection varies by collective. The interval for each collective is indicated above. The data entry period for individual hospitals is indicated in Appendix 1 (available on the jhltonline.org Web site).

Patient demographics and device types

The devices implanted and entered into this registry are listed in Table 2. Patients receiving a durable MCS device are included

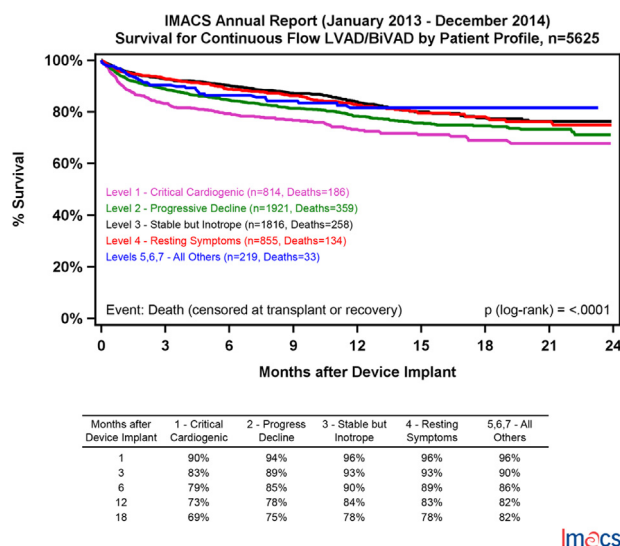


Figure 4 Actuarial survival for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving continuous-flow pumps, stratified by patient profile at implant. BiVAD, biventricular assist device; LVAD, left ventricular assist device.

Table 6 Cause and Mode of Death

IMACS primary cause of death	No. (%) (N = 1,043)
Multisystem organ failure	264 (25.31)
Cardiovascular causes	215 (21)
Neurologic event	190 (18.22)
Withdrawal of support	123 (11.79)
Other	79 (7.57)
Respiratory failure	67 (6.42)
Infection	66 (6.33)
Device malfunction	23 (1.82)
Gastrointestinal disorder	11 (1.05)
Suicide	3 (0.29)
Renal dysfunction	2 (0.19)

IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support.

in the database. Additional temporary devices used in patients who received a durable device are also recorded. Gender and age group information is included in Table 3. Ages 40 to 79 years accounted for 87% of patients. The patient profiles at implant followed the definitions established in INTERMACS.^{3,4} At the time of device implant, nearly 65% of patients were in patient profile 2 or 3 and less than 20% of patients were in the ambulatory heart failure profiles (levels 4–7).

Among patients receiving device implants, 29% were listed for transplantation, and 40% were deemed destination therapy (DT; Table 4). Greater than 90% of patients received an isolated left ventricular assist device, of which 99% were continuous-flow devices. A higher proportion of patients in the bridge-to-transplant category were classified as patient profile 1 or 2 (49.7%) than for patients in the DT category (44.7%; Table 5).

Patient survival

Among all patients in the IMACS Registry, the 12-month survival estimate was 80%, with 75% survival at 18 months

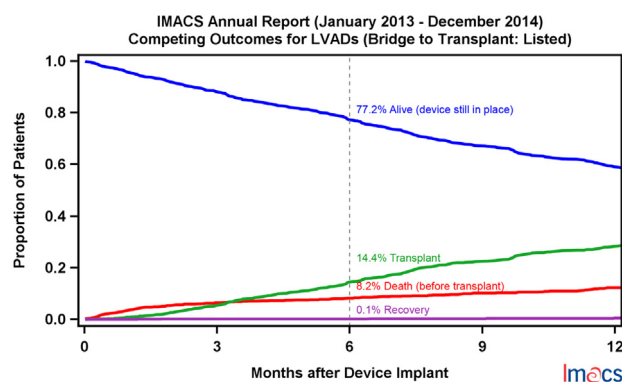


Figure 5 Competing outcomes depiction for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving continuous-flow left ventricular assist devices (LVADs) who are listed for cardiac transplantation. At any given time point, the sum of the proportion of patients experiencing each outcome event equals 1.0.

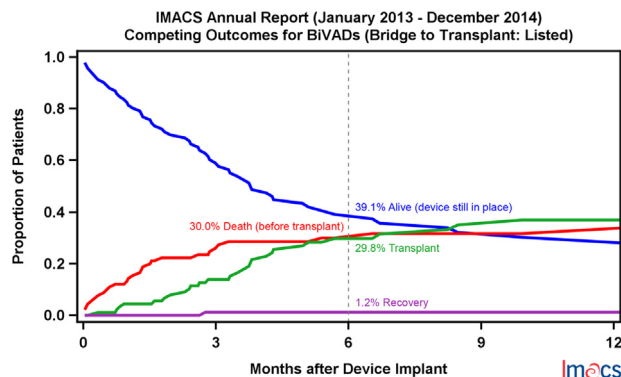


Figure 6 Competing outcomes depiction for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving mechanical circulatory support with a biventricular assist device (BiVAD) who are listed for transplant. The depiction is as in Figure 5.

(Figure 1). Survival by pump type is depicted in Figure 2. Note that survival with continuous-flow LVADS was 81% at 12 months and 77% at 18 months. Among patients requiring BiVAD support, 12-month survival fell to 53%. Actuarial survival with DT was slightly less than with bridge-to-transplant or bridge-to-candidacy strategies (Figure 3). Survival with DT was 77% at 12 months and 72% at 18 months. Patients in cardiogenic shock (Level 1) had a 1-year survival of 73% compared with 84% for patients who were stable but dependent on inotropes (Level 3; Figure 4). Note that these survival estimates are not adjusted for other risk factors that influence patient survival. The two most common causes/modes of death were multisystem organ failure and cardiovascular causes (Table 6).

Competing outcomes

The likelihood of receiving a heart transplant within 6 months was estimated to be 14% among patients actively listed for transplant at the time of LVAD implant (Figure 5).

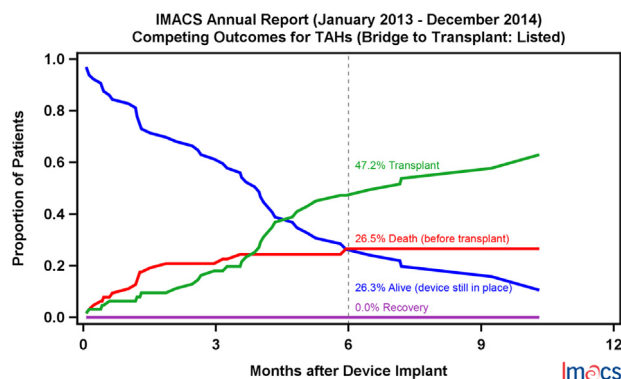


Figure 7 Competing outcomes depiction for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving a total artificial heart (TAH) who are listed for transplant. The depiction is as in Figure 5.

Table 7 Adverse Events (IMACS: January 2013–December 2014)

Adverse events	Patients with event (N = 5,942) No. (%)
Infection	1,972 (33)
Bleeding	1,920 (32)
Respiratory failure	972 (16)
Neurological dysfunction	911 (15)
Device malfunction	625 (11)
Arterial non-CNS thromboembolism	66 (1)

CNS, central nervous system; IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support.

With biventricular support, 30% of patients received a heart transplant within 6 months, but the mortality while waiting increased from 8% with an isolated LVAD to 30% with biventricular support (Figure 6). The likelihood of receiving a heart transplant for patients listed on total artificial heart

Table 8 Adult Patients Receiving Primary Implants from IMACS Hospitals and Collectives from January 2013 to December 2014 (N = 5942)

Risk factors for death	Early hazard		Constant hazard	
	HR	p-value	HR	p-value
Demographics				
Age (older)	1.44	<0.0001		
Female	1.27	0.0106		
Clinical status				
INTERMACS Profile 1	1.34	0.0031		
Non-continuous-flow device	2.00	<0.0001		
LVEDD (lower)	0.81	<0.0001		
Cardiac output			1.24	0.0004
INR			1.39	0.0108
Surgical complexities				
History of CABG	1.35	0.0008		
Concomitant surgery	1.47	<0.0001		
Non-cardiac systems				
Albumin (lower)	0.83	0.0004		
Stroke			2.76	0.0017
Dialysis	2.63	<0.0001		
Blood urea nitrogen (higher)	1.01	<0.0001	1.01	0.0003
Right heart dysfunction				
Right atrial pressure (higher)			1.05	<0.0001
RVAD in same operation	2.67	<0.0001		
Bilirubin (higher)	1.04	<0.0001		
Severe RVEF impairment			1.88	0.018

CABG, coronary artery bypass grafting; HR, hazard ratio; IMACS, International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support; INR, international normalized ratio; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEDD, left ventricular end diastolic dimension; RVAD, right ventricular assist device; RVEF, right ventricular ejection fraction.

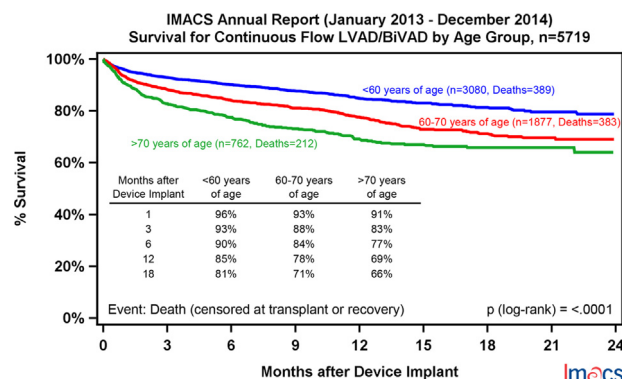


Figure 8 Actuarial survival for patients in the International Society for Heart and Lung Transplantation Mechanically Assisted Circulatory Support (IMACS) registry receiving a continuous-flow pump, stratified by age at implant. BiVAD, biventricular assist device; LVAD, left ventricular assist device.

support was considerably higher, at 47% by 6 months (Figure 7).

Adverse events

The frequency of the 6 major adverse events is listed in Table 7. During the follow-up period, one or more of these adverse events occurred in 59% of patients.

Risk factors for death

Demographic, clinical, surgical, and cardiac risk factors for death are listed in Table 8. The need for biventricular support, dialysis at implant, and the use of a non-continuous flow-device were the strongest predictors of death during the early phase; whereas prior stroke was the major predictor of late death. The incremental risk of advanced age is depicted in Figure 8.

Summary

1. This analysis of more than 5,000 patients from 31 countries represents an extensive analysis of

international mechanical circulatory support in the current era.

2. Current 1-year survival for patients with continuous flow technology is approximately 80%.
3. Patients in cardiogenic shock have an estimated 73% survival at 1 year compared with 84% among patients who are stable on inotropic support.
4. Among listed patients with isolated LVAD support, the likelihood of transplantation within 6 months is currently less than 15%.
5. Severe right ventricular failure, renal failure, and prior stroke are the major predictors of death after implant.

Disclosure statement

None of the authors has a financial relationship with a commercial entity that has an interest in the subject of the presented manuscript or other conflicts of interest to disclose.

Appendix

The appendix associated with this article can be found in the online version at www.jhltonline.org.

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