ESC HEART FAILURE
ESC Heart Failure 2023; **10**: 2754–2756
Published online 2 July 2023 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.14444

Survival after HeartMate 3 left ventricular assist device implantation: real-world data from Europe

Survival of end-stage heart failure patients on left ventricular assist device (LVAD) support continuously increases.[1] Nowadays, the HeartMate 3 (HM3, Abbott, Chicago, IL, USA) LVAD is most commonly implanted. Mehra *et al*. showed a 5 year survival of 58.4% in HM3 patients included in the extended-phase analysis of the MOMENTUM 3 trial. Patients included in this trial were treated in the United States.[2] LVAD patient selection and donor heart availability differ between United States and Europe.[3] In addition, outcomes in clinical trials may differ from those in common practice due to patient selection criteria and intensity of follow-up.

The aim of this study was to present the real world long term survival data of HM3 patients implanted in three large centres in Europe.

A cohort study was performed that was approved by the local ethics committee of the University Medical Centre Utrecht (UMCU), the Netherlands (METC: 20-195). The need for informed consent was waived. The study was conducted in accordance with Good Clinical Practice and the 2002 Declarations of Helsinki. Patients primarily implanted with HM3 between December 2015 and December 2019 in three European participating centres were included for analysis. Participating centres were University Medical Centre Utrecht (UMCU, the Netherlands), Heart and Diabetes Centre North Rhine-Westphalia (HDZ NRW, Bad Oeynhausen, Germany) and the Medical University of Vienna (MedUni Vienna, Austria).[4] Baseline characteristics and survival data were retrieved from the electronic health record and local databases. Patients were followed-up until September 2022. The primary and secondary endpoints were survival and survival free from stroke and pump replacement, respectively. Kaplan–Meier analysis was used to evaluate the endpoints, censoring for LVAD explantation, heart transplantation or ongoing support at the end of the follow-up. Stroke (including both haemorrhagic and ischemic stroke) was defined using the definition of the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).[5] Baseline characteristics were presented as mean and standard deviation or median and interquartile range (IQR). All statistical analyses were done using R software version 4.0.3.

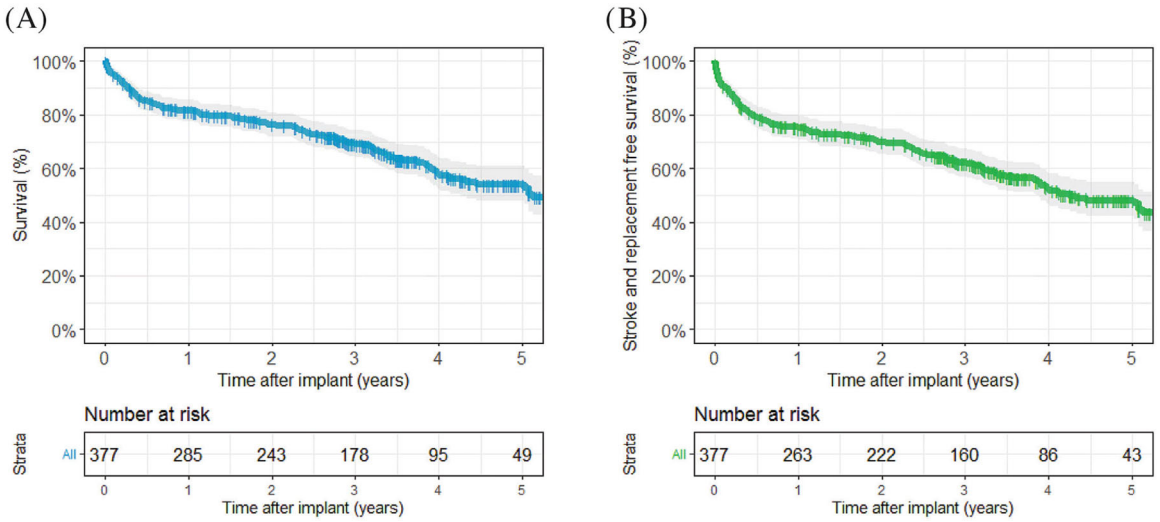
In total, 377 patients were included for analysis. The median time from primary implantation to the end of the follow-up was 4.4 years (IQR 2.2 years). Patients had a median age of 60 at implantation and 83.6% were male (*Table 1*). Baseline characteristics were complete for all patients except for diabetes, stroke in medical history

Table 1 Baseline demographics of all primary HeartMate 3 implantations in all three included centres compared to MOMENTUM characteristics

Variable	Total (n = 377)	UMCU (n = 80)	HDZ NRW (n = 194)	MedUni Vienna (n = 103)	MOMENTUM 3 (n = 515)
Age, median (IQR), years	60 (52–66)	56 (47–61)	60 (53–66)	64 (56–68)	62 (52–68)
Sex (% male)	315 (83.6)	52 (65.0)	171 (88.1)	92 (89.3)	410 (79.6)
BSA, mean (SD), m^2	2.03 (0.21)	1.98 (0.23)	2.05 (0.20)	2.03 (0.20)	2.07 (0.27)
BMI, median (IQR), kg/m^2	25.7 (23.1–29.4)	24.7 (21.6–27.8)	25.7 (23.6–29.6)	27.2 (24.2–31.2)	28.4 (24.6–33.0)
Ischemic CMP (%)	185 (49.1)	19 (23.8)	98 (50.5)	68 (66.0)	216 (41.9)
Diabetes (%)	109 (30.0)	12 (15.0)	63 (35.0)	34 (33.0)	233 (45.2)
Stroke (%)	32 (8.8)	3 (3.8)	21 (11.7)	8 (7.8)	50 (9.7)
eGFR ($mL/min/1.73\ m^2$)	51 (36–70)	61 (43–83)	53 (36–78)	41 (32–53)	58 (43–75)
INTERMACS (%)					
1–2	198 (52.5)	41 (51.2)	114 (58.8)	43 (41.7)	167 (32.5)
3	98 (26.0)	21 (26.2)	56 (28.9)	21 (20.4)	272 (52.9)
4–7	81 (21.5)	18 (22.5)	24 (12.4)	39 (37.9)	75 (14.6)
IABP (%)	8 (2.1)	1 (1.2)	6 (3.1)	1 (1.0)	64 (12.4)

BMI, body mass index; BSA, body surface area; CMP, cardiomyopathy; eGFR, estimated glomerular filtration rate; HDZ NRW, Heart and Diabetes Centre North Rhine-Westphalia; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; MedUni Vienna, Medical University of Vienna; UMCU, University Medical Centre Utrecht.

Figure 1 (A) Long-term survival of patients on HeartMate 3 left ventricular assist device support. (B) Survival free from stroke and pump replacement.



(i.e. before LVAD) and eGFR, with 3.7%, 3.7% and 8.2% missing data, respectively. One hundred forty-four patients (38%) died, 7 patients (2%) were explanted and 75 patients (20%) were transplanted during follow-up. Eight patients underwent replacement surgery after a median of 419 days (IQR: 892 days). Sixty-two patients suffered from a stroke after a median of 159 days (IQR: 436 days). *Figure 1* shows survival of all HM3 patients, with a 5 year survival of 54%. Survival free from stroke and pump replacement was 48% at 5 years.

HM3 is increasingly used in end-stage heart failure patients with a 5 year survival of 54.0% in three large centres across Europe. To put this in perspective, patients included in the extended phase of the MOMENTUM 3 trial had a survival of 58.4% at 5 years.[6] Moreover, they showed a survival free of debilitating stroke or pump replacement of 54.0% at 5 years, which is in line with our results. Although we used a slightly stricter definition in our database(s) and included all haemorrhagic stroke and ischemic stroke, whereas the extended Momentum 3 study used 'disabling stroke'. Nevertheless the results are similar, compatible with the very low rate of disabling stroke seen in both studies. Patients in the MOMENTUM cohort and our cohort differ in baseline characteristics, due to a different patient selection in the United States and Europe. Our cohort included patients with a lower BMI and lower prevalence of diabetes, a higher number of patients with ischemic cardiomyopathy, and more kidney dysfunction. In addition, patients more often were classified as INTERMACS 1 or 2 cLassification before implantation compared to patients included in the MOMENTUM 3 trial. LVAD patients awaiting a donor heart in the United States have a shorter median duration of LVAD support and a higher frequency of comorbid conditions when compared to patients in Europe.[3] Despite differences in patient selection and donor heart availability, long-term survival after HM3 implantation is comparable. In addition, the ELEVATE registry showed similarly beneficial outcomes in a cohort of 463 patients from 26 centres in Europe and the Middle East, although the cohort was slightly different in some baseline characteristics.[7,8] For example, they included more male patients, less patients classified as INTERMACS 1 or 2 and patients were slightly younger when compared to our cohort, including 377 implanted in three large volume centres.

In conclusion, real-world data from patients on HM3 support implanted in Europe confirm the promising findings of the MOMENTUM 3 trial, demonstrating the vital role of LVAD therapy in contemporary treatment of advanced heart failure.

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DOI: 10.1002/ehf2.14444

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References

1. Shah P, Yuzefpolskaya M, Hickey GW, Breathett K, Wever-Pinzon O, Ton VK, Hiesinger W, Koehl D, Kirklin JK, Cantor RS, Jacobs JP, Habib RH, Pagani FD, Goldstein DJ. Twelfth Interagency Registry for Mechanically Assisted Circulatory Support Report: readmissions after left ventricular assist device. *Ann Thorac Surg*. 2022; **113**: 722–737.
2. Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, Ransom J, Ewald GA, Itoh A, Raval NY, Silvestry SC, Cogswell R, John R, Bhimaraj A, Bruckner BA, Lowes BD, Um JY, Jeevanandam V, Sayer G, Mangi AA, Molina EJ, Sheikh F, Aaronson K, Pagani FD, Cotts WG, Tatooles AJ, Babu A, Chomsky D, Katz JN, Tessmann PB, Dean D, Krishnamoorthy A, Chuang J, Topuria I, Sood P, Goldstein DJ. A fully magnetically levitated left ventricular assist device — final report. *N Engl J Med*. 2019; **380**: 1618–1627.
3. Ammirati E, Cipriani M, Moro C, Raineri C, Pini D, Sormani P, Mantovani R, Varrenti M, Pedrotti P, Conca C, Mafrici A, Grosu A, Briguglia D, Guglielmetto S, Perego GB, Colombo S, Caico SI, Giannattasio C, Maestroni A, Carubelli V, Metra M, Lombardi C, Campodonico J, Agostoni P, Peretto G, Scelsi L, Turco A, Di Tano G, Campana C, Belloni A, Morandi F, Mortara A, Cirò A, Senni M, Gavazzi A, Frigerio M, Oliva F, Camici PG, On behalf of the Registro Lombardo delle Miocarditi. Outcome of patients on heart transplant list treated with a continuous-flow left ventricular assist device: insights from the TRans-Atlantic registry on VAd and TrAnsplant (TRAViATA). *Int J Cardiol*. 2021; **324**: 122–130.
4. Numan L, Zimpfer D, Zadok OIB, Aarts E, Morshuis M, Guenther SPW, Riebandt J, Wiedemann D, Ramjankhan FZ, Oppelaar AM, Ben-Gal T, Ben-Avraham B, Asselbergs FW, Schramm R, van Laake LW. Identifying patients at risk: multi-centre comparison of HeartMate 3 and HeartWare left ventricular assist devices. *ESC Heart Fail*. 2023; **10**: 1656–1665.
5. Kormos RL, Antonides CFJ, Goldstein DJ, Cowger JA, Starling RC, Kirklin JK, Rame JE, Rosenthal D, Mooney ML, Caliskan K, Messe SR, Teuteberg JJ, Mohacsi P, Slaughter MS, Potapov EV, Rao V, Schima H, Stehlik J, Joseph S, Koenig SC, Pagani FD. Updated definitions of adverse events for trials and registries of mechanical circulatory support: a consensus statement of the mechanical circulatory support academic research consortium. *J Heart Lung Transplant*. 2020; **39**: 735–750.
6. Mehra MR, Goldstein DJ, Cleveland JC, Cowger JA, Hall S, Salerno CT, Naka Y, Horstmanshof D, Chuang J, Wang AJ, Uriel N. Five-year outcomes in patients with fully magnetically levitated vs axial-flow left ventricular assist devices in the MOMENTUM 3 randomized trial. *JAMA*. 2022; **328**: 1233–1242.
7. Zimpfer D, Gustafsson F, Potapov E, Pya Y, Schmitto J, Berchtold-Herz M, Morshuis M, Shaw SM, Saeed D, Lavee J, Heatley G, Gazzola C, Garbade J. Two-year outcome after implantation of a full magnetically levitated left ventricular assist device: results from the ELEVATE registry. *Eur Heart J*. 2020; **41**: 3801–3809.
8. Schmitto JD, Shaw S, Garbade J. Long-term results in real world patients treated with HeartMate 3 LVAD for advanced heart failure: data frm the ELEVATE registry. Presented at: European Association for Cardio-Thoracic Surgery (EACTS) Annual Meeting; 2022; Milan, Italy.