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# Effects of Age and Comorbidities on Intensive Care and 1-Year Mortality after HeartMate 3 Implantation

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## ABSTRACT

**Background:** The use of left ventricular assist devices (LVAD) has been rapidly increasing in older people over the past two decades due to their availability as destination therapy. This study aimed to assess the effect of age and comorbidities on the intensive care unit (ICU) and 1-year mortality after HeartMate 3 LVAD implantation.

**Methods:** From 2016 to 2023, all consecutive adult patients implanted with HeartMate 3 LVAD in our tertiary referral center were enrolled in the study. Patients were stratified according to their age at implantation into Group-1 (<45 years), Group-2 (46–64 years), and Group-3 (>65 years). The effect of age and comorbidities on ICU and 1-year mortality were assessed.

**Results:** In total, 135 patients were included (mean age 54±13 years, 79% males). Baseline vital signs, comorbidities, and hemodynamic support were not different between age groups. The older population had significantly lower eGFR (p=0.025), ischemic cardiac diseases as the underlying heart problem (p<0.001), and LVAD as destination therapy (p<0.001). The mortality rate at the ICU and at one year were 90% and 83%, respectively. The median age of the patients who died in the ICU was significantly higher than 63 [56–65] years versus 57 years [49–62, p=0.034). However, age lost its significance with logistic regression analysis. Having a recent major myocardial infarct, high preoperative leukocyte count, and cardiopulmonary bypass time were independent risk factors for ICU mortality. On the other hand, age was an independent risk factor for one-year mortality.

**Conclusion:** Older age predicts increased one-year but not ICU mortality after HeartMate 3 LVAD implantation, while recent major myocardial infarction, high preoperative leukocyte count, and longer cardiopulmonary bypass time were independent risk factors for ICU mortality. Careful patient selection is critical to optimize outcomes after HeartMate 3 LVAD implantation.

**Keywords:** age, comorbidities, mortality, HeartMate 3, LVAD, intensive care unit

## Introduction

Advanced heart failure (AHF) is increasingly common and is estimated to affect more than 30 million patients worldwide (1–3). The main treatment goal of these patients is to improve their quality of life, longevity and preventing hospitalizations. However, despite recent advances in the treatment of AHF, it remains one of the leading causes of hospitalization and one-year mortality, notably in older populations (4,5).

Heart transplantation is the gold standard of AHF refractory to medical treatment; however, the limited availability of donor organs and long waiting lists make it impossible for significant amounts of patients (6). Therefore, strict criteria for the indications and contraindications have been determined for careful patient selection to get optimum benefit from the available donor hearts. According to the International Society for Heart and Lung Transplantation (ISHLT) guidelines, heart transplantation is relatively contraindicated for patients aged >70 years, considering their comorbidities and complications of immunosuppressive therapy (7). So, durable left ventricular assist device (LVAD) implantation has become an alternative as a destination therapy in carefully chosen patients (6). However, LVAD implantation is yet

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very expensive, needs high-risk heart surgery, and is associated with significant short and long-term complications such as acute kidney injury, right-sided heart failure bleedings, stroke, device thrombosis, and driveline exit infections (8,9). Improvements in perioperative care, medical treatment options, and innovations in bioengineering have improved clinical outcomes in contemporary LVAD patients (10). However, several studies have reported that age is a limiting factor for LVAD implantation and is associated with worse 1-year outcomes (11,12).

The HeartMate 3 (HM3) (Abbott Laboratories, Chicago, IL) is the latest generation of continuous flow LVAD technology with a fully magnetically levitated rotor that eliminates bearings and allows for lower shear stress (3,13). As a result, this technology is associated with less pump thrombosis, strokes, and better survival. Whether older age is still a risk factor for early and long-term patient survival after HM 3 LVAD implantation is unknown. The current study aimed to assess age-related demographics and clinical characteristics and intensive care unit (ICU) and 1-year mortality after HM 3 LVAD implantation.

## Methods

Data of all consecutive patients for whom a HeartMate 3 LVAD (Abbott Laboratories, Chicago, IL) was implanted between 2016 and 2023 in the Erasmus Medical Center, Rotterdam (Netherlands), have been prospectively collected. Patients were excluded if their age was <16 years at the time of LVAD implantation or patient died within 24 hours of ICU follow-up. Data were recorded from patient files and computerized databases. Patients were followed from LVAD implantation to the end of 1 year and were categorized into three groups as ≤45 years (Group-1), 46 to 64 years (Group-2), and ≥65 years (Group-3) during LVAD implantation. Clinical and demographic data of LVAD implantation and procedural characteristics were collected from the local input of the European Registry for Patients with Mechanical Circulatory Support (EUROMACS) registry. A general approval was obtained from the institutional medical ethical committee to conduct retrospective chart studies for potential LVAD complications and outcomes (MEC-2017–1013).

The study's primary aims are to examine the characteristic features of HM3 LVAD patients according to age groups and the risk factors of ICU mortality. The secondary aim was 1-year mortality after HM3 LVAD implantation. Demographic features, underlying cardiac disease (ischemic vs. nonischemic), comorbidities, hemodynamic and respiratory support before LVAD surgery (inotrope therapy (norepinephrine, epinephrine, dobutamine, levosimendan, and milrinone), extracorporeal membrane oxygenation (ECMO), other ventricular assist devices, intra-aortic balloon pump (IABP), mechanical ventilation), Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile, indication for LVAD implantation, cardiac rhythm, vital signs, baseline serum creatinine, laboratory findings, and complications were recorded. The patients were followed for at least one year after LVAD implantation.

Baseline creatinine was recorded, and the Modification of Diet in Renal Disease (MDRD) formula was used to calculate eGFR (14). Patients were classified into four groups: eGFR >60 mL/min/1.73 m2, 45–60 mL/min/1.73 $m^2$, 30–45 mL/min/1.73 $m^2$, and <30 mL/min/1.73 $m^2$. Primary cardiac disease was recorded as non-ischemic if the underlying causes were dilated myopathy, hypertrophic cardiomyopathy, restrictive myopathy, valvular heart disease, and congenital heart disease.

### Statistics

All continuous variables were shown as median (interquartile range, IQR) or mean (standard deviation) depending on the data distribution. The Kolmogorov–Smirnov test was used to examine

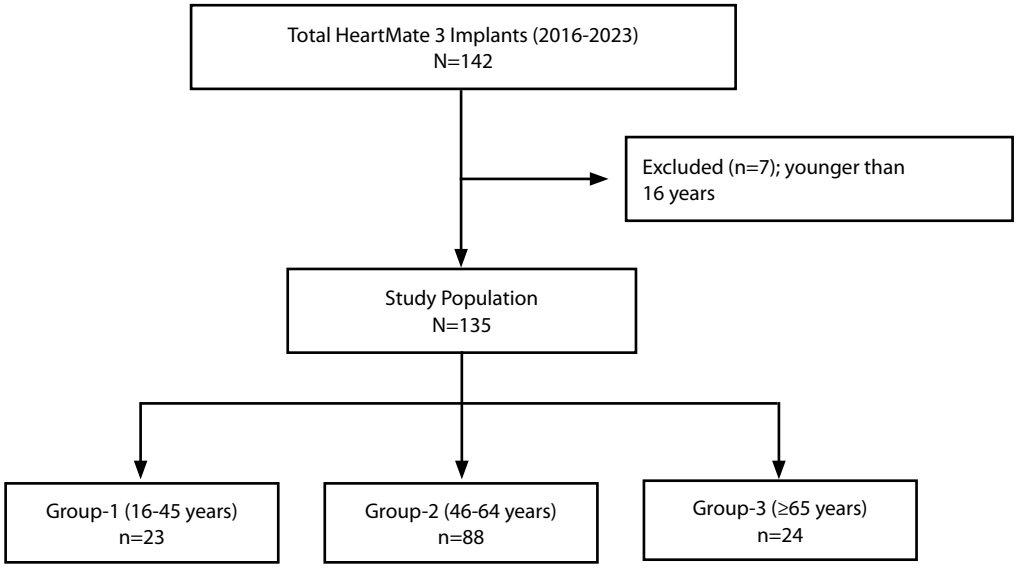


**Figure 1.** Flowchart of study population according to age groups
LVAD, left ventricular assist device

continuous variables for normality. Kruskal-Wallis test, Student's t-test, or ANOVA were used to compare the groups, where appropriate. Categorical variables were shown as numbers and percentages, and tested by the $X^2$ test, Fisher's exact test, or linear-by-linear association. The possible factors with p<0.10 in the univariate analysis were further examined with logistic regression analysis to identify independent predictors for ICU mortality. The model fit was assessed with Hosmer-Lemeshow goodness of fit statistics. For 1-year survival, the log-rank test was performed and estimated event-time distributions using the Kaplan–Meier method. Patients were censored at the time of LVAD removal or heart transplantation. All tests were two-tailed, and p<0.05 was considered statistically significant. All analyses were performed using IBM Statistical Package for Social Sciences (SPSS) program version 29.0 (IBM Corp., Armonk, NY, USA) software.

## Results

From March 2016 to April 2023, 142 patients underwent HM 3 implantation at Erasmus Medical Center (Rotterdam, The Netherlands), of which 135 were included in the study. The demographic and baseline characteristics between age groups are shown in Table 1. Seven patients were under the age of 16 years and excluded from the study. The mean age was 54±13 years. Stratified by age, there were 23 (17%) patients in Group 1, 88 (65.2%) in Group 2, and 24 (17.8%) in Group-3 (Figure-1). The majority of the patients were male (79.3%, n=107), and there was no difference in terms of gender within age groups (p=0.863). The majority of the patients were of Caucasian origin (91.9%), with only five Africans (3.7%) and two Asians (1.5%). One patient (0.7%) had primary education, 77 (57%) had lower or upper secondary education, 21(16%) had post-secondary but non-tertiary education, and 4 (3.0%) had tertiary level education. Group-2 had a significantly higher BMI than younger and older patients (p=0.006).

Considering the underlying etiology, older patients more often had ischemic heart disease as the primary cardiac disease (p<0.001). However, all age groups were not different in terms of comorbidities (diabetes mellitus, hepatitis, chronic obstructive pulmonary disease, malignancy, and stoke). The indication for LVAD implantation was mostly destination therapy in the older population; however, younger patients had it primarily for bridge-to-heart transplantation (p<0.001). Before implantation, all age groups did not show statistical significant differences in requiring hemodynamic support, such as ECMO (p=0.623), IABP (p=0.232), and other VADs (p=0.074). There was a trend for using inotrope support towards the younger population, but it did not reach a significant level (p=0.074). In parallel, all groups were not different for baseline vital signs before LVAD implantation. The older population showed a less severe INTERMACS profile than Group-2 and Group-1 (p=0.018). Within all age groups, the renal dysfunction was predominantly moderate with eGFR between 30–59 mL/min/1.73 $m^2$.

Of all patients, 14 (10.4%) deaths occurred during their stay in ICU. The median age was 63 [56–65] years in the mortality group, in the survival group 57 [49–62] years (p=0.034). The length of stay in ICU was longer in the mortality group (18[12–38] days), whereas it was 8[5–17] days in the survival group (p=0.003). The patients did not show statistical differences in terms of baseline heart rate, systolic-diastolic-mean arterial blood pressures, kidney and liver biochemistry, lactate, pH, and bicarbonate, and the need for hemodynamic support before LVAD implantation for ICU mortality. However, preoperative lactate dehydrogenase (LDH) (p=0.047), white blood cell (WBC) (p=0.023), and C-reactive protein (p=0.003) were higher in the mortality group (Table 2). Logistic regression analysis showed that only recent major myocardial infarction before LVAD implantation, high WBC, and cardiopulmonary bypass time and duration in ICU were risk factors for ICU mortality (Table 3).

**Table 1.** Baseline and perioperative characteristics of patients undergoing LVAD implantation

| | 16–45 years (n=23) | 46–64 years (n=88) | ≥65 years (n=24) | p |
|---|---|---|---|---|
| **Age (years)** | 28 [19–42] | 57 [53–61] | 67 [65–69] | **<0.001** |
| Gender, Male, n (%) | 18 (78.3%) | 69 (78.4%) | 20 (83.3%) | **0.863** |
| Caucasian, n (%) | 20 (87%) | 80 (90.9%) | 24 (100%) | **0.446** |
| **Body mass index, (kg/m²)** | 23.0±4.9 | 26.3±3.6 | 24.3±3.3 | **0.006** |
| **Primary cardiac disease, n (%)** | | | | **<0.001** |
| Non-Ischemic | 21 (91.3%) | 36 (40.9%) | 9 (37.5%) | |
| Ischemic | 2 (8.7%) | 51 (58%) | 15 (62.5%) | |
| **Comorbidities, n (%)** | | | | |
| Diabetes mellitus | 3 (13%) | 20 (22.7%) | 6 (25%) | 0.772 |
| COPD | 0 (0%) | 5 (5.7%) | 2 (8.3%) | 0.674 |
| Malignancy | 2 (8.7%) | 6 (6.8%) | 1 (4.2%) | 0.829 |
| Stroke | 0 (0%) | 11 (12.5%) | 2 (8.3%) | 0.337 |
| **eGFR at baseline (mL/min/1.73 m²)** | | | | **0.025** |
| ≥90 | 5 (21.7%) | 5 (5.9%) | 0 (0.0%) | |
| 60–89 | 5 (21.7%) | 18 (20.5%) | 3 (12.5%) | |
| 30–59 | 9 (39.1%) | 44 (51.8%) | 19 (79.2%) | |
| <30 | 4 (17.4%) | 18 (21.2%) | 2 (8.3%) | |
| **Hemodynamic support, n (%)** | | | | |
| On inotropes | 21 (91.3%) | 59 (67%) | 13 (54.2%) | 0.074 |
| Intra-aortic balloon pump | 6 (26.1%) | 27 (30.7%) | 2 (8.3%) | 0.232 |
| Extracorporeal membrane oxygenation | 4 (17.4%) | 11 (12.5%) | 1 (4.2) | 0.623 |
| Invasive mechanical ventilation | 2 (8.7%) | 11 (12.5%) | 2 (8.3%) | 0.900 |
| **INTERMACS, n (%)** | | | | 0.018 |
| I | 5 (21.7%) | 25 (28.7%) | 2 (8.3%) | |
| II | 6 (26.1%) | 16 (18.4%) | 1 (4.2%) | |
| III | 9 (39.1%) | 21 (24.1%) | 8 (33.3%) | |
| ≥ IV | 3 (13.0%) | 25 (28.7%) | 13 (54.2%) | |
| **LVAD indication, n (%)** | | | | **<0.001** |
| Bridge-to-transplant | 20 (87%) | 67 (76.1%) | 1 (4.2%) | |
| Destination Therapy | 3 (13%) | 21 (23.9%) | 23 (95.8%) | |
| **Cardiac Rhythm, n (%)** | | | | **0.036** |
| Sinus | 17 (77.3%) | 55 (63.2%) | 9 (37.5%) | |
| Atrial Fibrillation/Flutter | 1 (4.5%) | 20 (23.0%) | 8 (33.3%) | |
| Pace rhythm | 4 (18.2%) | 12 (13.8%) | 7 (29.2%) | |
| **Vital Signs** | | | | |
| Systolic Blood Pressure, mmHg | 98±12 | 10114 | 98±12 | 0.405 |
| Diastolic Blood Pressure, mmHg | 61±7 | 60±12 | 59±9 | 0.833 |
| Mean Blood Pressure, mmHg | 73±8 | 74±9 | 72±9 | 0.598 |
| Heart rate, beats/min | 81[69–103] | 77[66–85] | 73[65–82] | 0.095 |

**COPD:** chronic obstructive pulmonary disease; **CVA:** cerebrovascular accident; **eGFR:** estimated glomerular filtration rate; **INTERMACS:** Interagency Registry for Mechanically Assisted Circulatory Support; **LVAD:** left ventricular assist device; **TIA:** transient ischemic attack.

**Table 2.** Baseline characteristics and laboratory findings of patients with or without ICU mortality

| | Survivors (n=121) | Non-survivors (n=14) | p |
|---|---|---|---|
| **Age, years** | **57 [49–62]** | **63 [56–65]** | **0.034** |
| Gender (Male) | 97 (80.2%) | 10 (71.4%) | 0.488 |
| Body mass index, (kg/m$^2$) | 25.3±4.0 | 25.6±3.7 | 0.745 |
| **Preoperative Vital Signs** | | | |
| Heart Rate, mmHg | 57 [49–62] | 63 [56–65] | 0.303 |
| Systolic Blood Pressure, mmHg | 100±14 | 101±10 | 0.834 |
| Diastolic Blood Pressure, mmHg | 60±10 | 6112 | 0.790 |
| Mean Blood Pressure, mmHg | 73±9 | 74±9 | 0.760 |
| **Preoperative Laboratory Parameters** | | | |
| Sodium, mmol/L | 137.7±5.9 | 139.6±11.1 | 0.525 |
| Potassium, mmol/L | 4.1±0.4 | 4.00.5 | 0.321 |
| Creatinine, mg/dl | 143.6±50.4 | 129.3±38.2 | 0.308 |
| eGFR, mL/min/1.73 m$^2$ | 43.0 [32.9–62.4] | 46.6 [41.4–63.7] | 0.502 |
| ALT, U/L | 41 [21–68] | 57 [22–88] | 0.667 |
| AST, U/L | 37 [27–51] | 52 [27–55] | 0.272 |
| **LDH, U/L** | **297 [235–377]** | **450 [283–583]** | **0.047** |
| Total bilirubin, mg/dl | 0.9 [0.7–1.6] | 0.9 [0.6–1.8] | 0.882 |
| **WBC, x10$^9$/L** | 8.5 [6.6–9.8] | 12.7 [7.7–18.0] | 0.023 |
| Platelet, x10$^9$/L | 205±81 | 204±105 | 0.966 |
| INR | 1.5 [1.2–1.8] | 1.6 [1.4–2.2] | 0.101 |
| aPTT, seconds | 16.5 [14.1–20.3] | 17.8 [16.3–23.7] | 0.118 |
| pH | 7.46±0.6 | 7.47±0.6 | 0.877 |
| Lactate, mg/dl | 1.1 [0.9–1.5] | 1.1 [0.9–1.3] | 0.979 |
| HCO3, meq/L | 25.6 [23.3–28.5] | 24.9 [24.5–28.7] | 0.967 |
| **C-Reactive Protein, mg/L** | **88.5 [42–335]** | **460 [240–830]** | **0.003** |
| **Surgical factors** | | | |
| Cardiopulmonary bypass time, minutes | 91[79–111] | 120[85–181] | 0.063 |
| **Surgery time#, minutes** | **319 [277–405]** | **419 [360–505]** | **0.006** |
| **Intensive care stay, days** | **8 [5–17]** | **18[12–38]** | **0.003** |
| **Ventilation time, hours** | **50[28–128]** | **334[168–560]** | **<0.001** |
| **Comorbidities, n (%)** | | | |
| Diabetes | 25 (20.7%) | 4 (28.6%) | 0.755 |
| COPD | 7 (5.8%) | 0 (0%) | 0.611 |
| History of stroke | 12 (9.9%) | 1 (7.1%) | 0.836 |
| **Recent acute myocardial infarction*** | **11 (9.1%)** | **5 (35.7%)** | **0.014** |
| Major infection* | 7 (5.8%) | 1 (7.1%) | 0.873 |
| **Preoperative Hemodynamic Support, n (%)** | | | |
| IV inotropic therapy | 81 (66.9%) | 12 (85.7%) | 0.352 |
| ECMO | 12 (9.9%) | 4 (28.6%) | 0.119 |
| IABP | 31 (25.6%) | 4 (28.6%) | 0.921 |
| OtherVAD | 1 (0.8%) | 0 (0%) | 0.889 |
| **Invasive mechanical ventilation** | **10 (8.3%)** | **5 (35.7%)** | **0.008** |
| **INTERMACS** | | | 0.108 |
| I | 25 (20.8%) | 7 (50%) | |
| II | 21 (17.5%) | 2 (14.3%) | |
| III | 36 (30.0%) | 2 (14.3%) | |
| ≥IV | 38 (31.7%) | 3 (21.4%) | |

**aPTT:** activated partial thromboplastin time; **ALT,** alanine transaminase; **AST,** aspartate transaminase; **COPD:** chronic obstructive pulmonary disease; **ECMO:** extracorporeal membrane **oxygenation;** HCO3, bicarbonate; **IABP:** intraaortic balloon pump; **ICU,** intensive care unit; **INR,** international normalized ratio; **IV:** intravenous; **LDH,** lactate dehydrogenase; **MI:** myocardial infarction; **WBC:** White blood cell, **#**indicates duration of whole surgery period, *indicates a recent event

**Table 3.** Multivariable logistic regression model of characteristics for the association with ICU mortality

| | Univariable model | | Multivariable model | |
|---|---|---|---|---|
| | OR (95% CI) | p | OR (95% CI) | p |
| Age | 1.06(0.99–1.13) | 0.11 | 1.09 (0.98–1.21) | 0.123 |
| **LDH** | **1.01(1.0–1.01)** | **0.033** | | |
| **WBC** | **1.21(1.07–1.36)** | **0.002** | **1.46 (1.15–1.87)** | **0.002** |
| **C-Reactive Protein** | **1.01(1.0–1.01)** | **0.031** | | |
| ECMO | 0.278 (0.08–1.02) | 0.054 | | |
| **Preoperative ventilator support** | **0.164 (0.05–0.58)** | **0.005** | | |
| **Recent myocardial infarction*** | **0.182 (0.05–0.64)** | **0.008** | **9.54 (1.1–82.5)** | **0.040** |
| CPB time | **1.01 (1.0–1.02)** | **0.034** | **1.03 (1.01–1.05)** | **0.015** |
| **Surgery time** | **1.01 (1.0–1.01)** | **0.012** | | |

**CBP:** cardiopulmonary bypass; **CI:** confidence interval; **ECMO:** extracorporeal membrane oxygenation; **ICU:** intensive care unit; **WBC:** White blood cell; **LDH:** Lactate dehydrogenase; **OR:** odds ratio; *indicates a recent event.

Mortality within different age groups in the third and sixth months is shown in (Table 4). During the first year following LVAD implantation, 23 patients (17.0%) died, with the highest cumulative mortality in older patients (log-rank test, p = 0.002) (Figure 2).

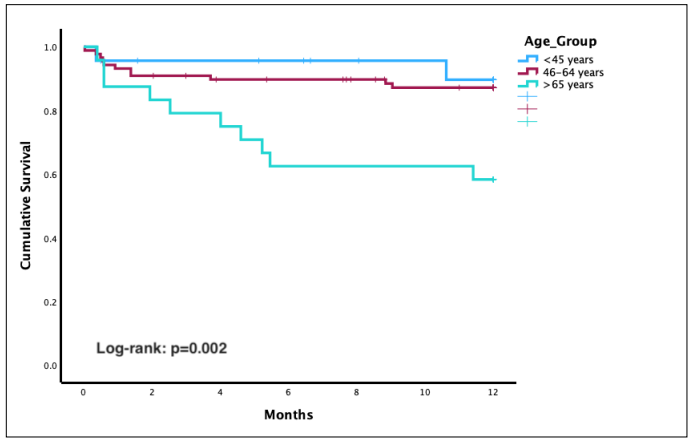


**Figure 2.** Kaplan-Meier curve for the survival rate during the first year after HeartMate 3 implantation stratified by age groups.

**Table 4.** Mortality rates after LVAD implantation within different time points and demonstrations based on age groups.

| | 16–45 years (n=23) | 46–64 years (n=88) | >65 years (n=24) | p |
|---|---|---|---|---|
| ICU mortality | 1 (4.3%) | 8 (9.1%) | 5 (20.8%) | 0.144 |
| Mortality within 1 months | 1 (4.3%) | 6 (6.8%) | 3 (12.5) | 0.133 |
| Mortality within 3 months | 1 (5.3%) | 9 (10.8%) | 8 (33.3%) | **0.010** |
| Mortality within 6 months | 1 (5.9%) | 10 (12.2%) | 9 (37.5%) | **0.006** |
| Mortality within 1 year | 2 (12.5%) | 11 (14.1%) | 10 (41.7%) | **0.009** |

**ICU:** intensive care unit; **LVAD:** left ventricular assist device

## Discussion

In the current study, we assessed the effect of age and comorbidities on ICU mortality in HeartMate3 LVAD patients. We found that the patients who died in the ICU were older; however, in the multivariate analysis, age was not an independent risk factor for ICU mortality. On the other hand, older age was a risk factor for 1-year mortality. Preoperative high WBC levels, recent myocardial infarction, and longer CPB time were independently associated with a higher risk of ICU mortality post HeartMate 3 LVAD implantation. Since patients with advanced heart failure have increasingly been referred to HeartMate 3 LVAD implantation due to ineligibility for heart transplantation, age should not solely affect the selection of the patient who will receive optimum benefit.

The current study is, to our best knowledge, the first study that evaluated age as a risk factor for ICU mortality after HeartMate 3 LVAD implantation. Interestingly, despite being a risk factor for 1-year mortality, age was not an independent risk factor for ICU mortality after LVAD implantation. Besides, the one-month mortality was not different within age groups. In parallel to our study, Caraballo and colleagues also reported a similar finding in a study that used the INTERMACS database. Although they showed a higher rate of early-term mortality within older LVAD patients, age lost its significance with multivariable analysis (15). In another study on non-HM3 LVAD patients, age failed to predict 1-month mortality after LVAD implantation (16). These findings differ from our group's previous study, where older age was reported as a significant risk factor for early mortality (9). However, in that study, the early-term mortality included the deaths of the first ninety-day, not one month, after LVAD implantation.

The second annual report from the ISHLT Mechanically Assisted Circulatory Support Registry showed that 12% of LVAD implants were older than 70 years and had unadjusted survival rates of 90% and 69.4% at one month and one year after LVAD implantation, respectively (8). In the current study, >65 years were used as the cut-off to define older patients. Of all the population, 17.7% were >65 years, of which four (3%) were older than 70. Similar to the ISHLT report, our older population's 1-month and 1-year survival rates were 88% and 68%, respectively. Similar to the current study, Muslem et al reported, mainly with the older generation HeartMate II LVAD devices, a one-month survival ratio of 88% and found age as a determinant of one-year mortality (11). Several studies, including different types of LVAD devices, have also shown that age is a significant risk factor for 1-year and late-term mortality (5,12,15–18). Considering the survival of patients, the impact of age starts to appear after the first month of LVAD implantation and should be taken into account in candidate selection and shared care decisions. Interestingly, despite a trend for having a lower INTERMACS profile in the younger ages, there was not a mortality difference between age groups. This is important because even if the younger population were more critically ill, the mortality did not significantly change. In the current study, the older and the younger patients did not differ for comorbidities such as diabetes, COPD, malignancy, and stroke; however, attention should be paid to patient selection considering the previous research.

Older patients had LVAD implantation primarily as the destination therapy, while the younger population had mostly implanted as a bridge-to-transplantation. This is unsurprising because there is no strict age limit for LVAD implantation compared to heart transplantation. Therefore, older patients were directed to destination therapy instead of heart transplantation.

High BMI is not a contraindication for LVAD implantation, and no cut-off has been suggested to be a candidate for LVAD surgery. However, obese patients have a higher risk for LVAD thrombosis and neurological complications (19,20). In the current study, the patients aged between 46–64 years had higher BMI than younger and older patients, but the higher BMI was not found to be a predictor of ICU mortality. We did not report the association of the presence of complications since the data was not available.

Prolonged time of cardiopulmonary bypass and LVAD surgery were found to be risk factors for early ICU mortality. This finding confirmed the results of two previous studies by our group (9,21). Prolonged LVAD surgery time was associated with the development of right-sided heart failure in the early term of the ICU course. Independent of the type of surgery, increased operation time is a risk factor for early-term mortality and morbidity in other open major heart surgeries due to exposure to prolonged ischemia time (22). Besides, a long stay in ICU is a risk factor for severe ICU-related infections and complications that undesirably decrease early-term patient survival. On the other hand, it should be emphasized that the more severely ill patients have the risk of a long ICU stay.

White blood cell count, C-reactive protein, and lactate dehydrogenase are the markers of inflammation and hemolysis. Higher levels of these parameters could be related to the patients' level of inflammation, i. e. sickness before LVAD surgery (9,23–26). Besides, these patients had the probability of having an ongoing infection before undergoing implantation. Unfortunately, we do not have specific data in these except for the presence of a major infection, which also did not differ between ICU mortality and survival group.

Several limitations to our study should be regarded in interpreting the results. First, this was a single-center study and may differ from other centers regarding clinical management and treatment options. However, our center is a national reference center for advanced heart failure, including LVAD implantation and heart transplantation in the Netherlands, and patient selection procedures were performed based on national and international criteria. Second, it was designed in retrospective nature, precluding assessment of additional perioperative parameters such as detailed hemodynamic variables and ventilation-associated parameters. Third, the age group ≥65 years and ICU mortality group had a relatively small number of patients, which may have influenced our study's outcome. Fourth, due to the retrospective nature of this research, we could not add detailed information regarding hemodynamic variables and certain medications, such as echocardiography values of the right and left ventricular function and the use of nitric oxide ventilation.

In conclusion, older age is a risk factor for 1-year mortality after HeartMate 3 LVAD implantation but not for ICU mortality, while recent major myocardial infarct, high preoperative leukocyte count, and longer cardiopulmonary bypass time were independent risk factors for ICU mortality. Careful patient selection is critical to optimize outcomes after LVAD implantation. Our study requires validation with an extensive, preferably multicenter cohort study with more granular perioperative patient data.

AUTHOR CONTRIBUTIONS:

**Concept: GG, KC; Design:** GG, KC; **Supervision:** GG, KC; **Materials:** GG, KC; **Data Collection and/or Processing:** GG, KC; **Analysis and/or Interpretation:** GG, KC; **Literature Search:** GG, KC; **Writing Manuscript:** GG, KC; **Critical Review:** GG, KC

**Ethics Committee Approval:** The manuscript was approved by the Clinical Researches Ethics Boards of Erasmus Medical Center with number 'MEC-2017-1013'. (Year: 2017)

**Informed Consent:** Retrospective study

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