EMERGING INVESTIGATORS

Clinical Implications of Respiratory Failure in Patients Receiving Durable Left Ventricular Assist Devices for End-Stage Heart Failure

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BACKGROUND: The impact of respiratory failure on patients undergoing left ventricular assist device (LVAD) implantation is not well understood, especially since these patients were excluded from landmark clinical trials. We sought to evaluate the associations between immediate preimplant and postimplant respiratory failure on outcomes in advanced heart failure patients undergoing LVAD implantation.

METHODS AND RESULTS: We included all patients in the Interagency Registry for Mechanically Assisted Circulatory Support who were implanted with continuous-flow LVADs from 2008 to 2016. Of the 16,362 patients who underwent continuous-flow LVAD placement, 906 (5.5%) required preimplant intubation within 48 hours before implantation, and 1001 (6.1%) patients developed respiratory failure within 1 week after implantation. A higher proportion of patients requiring preimplant intubation were Interagency Registry for Mechanically Assisted Circulatory Support profile 1, required mechanical circulatory support, and presented with cardiac arrest or myocardial infarction (P<0.001, all). At 1 year, 54.3% of patients intubated preimplant were alive without transplant, 20.1% had been transplanted, and 24.2% died before transplant. Patients requiring preimplant intubation had higher rates of postimplant complications, including bleeding, stroke, and right ventricular assist device implantation (P<0.01 for all). Among Interagency Registry for Mechanically Assisted Circulatory Support profile 1 patients, preimplant intubation incurred additional risk of death at 1 year compared with Interagency Registry for Mechanically Assisted Circulatory Support profile 1 patients not intubated (hazard ratio, 1.37 [95% CI, 1.13–1.65]; P=0.001). After multivariable analysis, both preimplant intubation (hazard ratio, 1.20 [95% CI, 1.03–1.41]; P=0.021) and respiratory failure within 1 week (hazard ratio, 2.54 [95% CI, 2.26–2.85]; P<0.001) were associated with higher all-cause 1-year mortality.

CONCLUSIONS: Respiratory failure both before and after LVAD implantation identifies an advanced heart failure population with significantly worse 1-year mortality. This data might be helpful in counseling patients and their families about expectations about life with an LVAD.

Key Words: heart-assist devices ■ heart failure ■ mechanical ventilation ■ respiratory insufficiency

Although survival rates in patients implanted with left ventricular assist devices (LVADs) continue to improve,1 substantial questions remain about proper patient selection and adverse events following LVAD implantation.2 3 4 Notably, very little is known about the effects of peri-implant respiratory failure on clinical outcomes. To date, these patients have either been excluded from or are poorly represented in LVAD clinical trials.4–9 Because of the scarcity of data and the perception that respiratory failure is frequently temporary, currently available guidelines do not mention preimplant intubation for consideration in patient selection.10–12

Early adverse events are common, frequently associated with poorer long-term outcomes, and critical to the
WHAT IS NEW?
• Among 16,362 patients enrolled in the Interagency Registry for Mechanically Assisted Circulatory Support, we found that 906 (5.5%) patients required preimplant intubation, and 1001 (6.1%) patients developed respiratory failure within 1 week.
• We found that preimplant intubation was independently associated with a significantly higher 1-year morbidity and mortality.
• Preimplant intubation identified a group of patients with high clinical acuity.
• Patients that developed postimplant respiratory failure had a 2.5× increased risk of death in the first year.

WHAT ARE THE CLINICAL IMPLICATIONS?
• Patients requiring intubation in the peri-implant period should be identified as particularly high-risk and may require closer monitoring.
• Our results may be used in counseling patients and their families about expectations about life after left ventricular assist device implantation.

Nonstandard Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>INTERMACS</td>
<td>Interagency Registry for Mechanically Assisted Circulatory Support</td>
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<td>LVAD</td>
<td>left ventricular assist device</td>
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care of patients with LVADs. Although respiratory failure has been associated with worse outcomes in patients with heart failure, little is known about respiratory failure in patients with LVADs. Estimates of postimplant respiratory failure from LVAD clinical trials have varied from 14% to 38%. However, associations between respiratory failure soon after LVAD surgery and clinical outcomes are not well described.

Therefore, the aim of our study was to evaluate the clinical impact of both preimplant intubation and early postimplant respiratory failure in patients undergoing LVAD implantation. In addition, we assessed for trends in utilization of mechanical ventilation as well as preimplant predictors of postimplant respiratory failure.

METHODS

Data Source
As previously described, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a prospective registry established in 2005 to study and improve the care of patients with advanced heart failure receiving durable mechanical circulatory support. The registry includes patients who have received a Food and Drug Administration approved device throughout the United States and Canada. We obtained the data via the Biological Specimen and Data Repository Information Coordinating Center where all data and materials have been made publicly available. This study was approved by the Yale University Institutional Review Board.

In addition to preimplant demographic, hemodynamics, and laboratory data, the INTERMACS protocol included patient visits at 1 week, 1 month, 3 months, 6 months, and every 6 months after device implantation. Postimplant follow-up consisted of an interview and physical examination, including an assessment of functional capacity. Per protocol, the interview included quality of life questions, such as an assessment of frailty and the Kansas City Cardiomyopathy Questionnaire-12.

Study Population
We queried the INTERMACS registry for patients receiving durable continuous-flow LVADs between June 2008 and December 2016 and included all adult patients ≥18 years of age receiving their first continuous-flow LVAD (Figure in the Data Supplement). Given their heterogeneity and unique pathophysiology, patients who underwent implant of total artificial hearts, biventricular devices, right ventricular assist devices, or pulsatile devices were excluded.

Outcomes
Our primary objective was to estimate the prognostic implication of preimplant intubation on mortality, adverse events, and patient-centered outcomes (frailty, quality of life, and functional capacity). Our secondary objectives were to estimate the prognostic implication of early postimplant respiratory failure on mortality and to identify predictors of postimplant respiratory failure.

Definitions
Preimplant mechanical ventilation use is recorded in INTERMACS both as a clinical event at any point during the index hospitalization and as an intervention within 48 hours before implant. We presumed that intubation within 48 hours before implantation would be more clinically meaningful and used this variable for our primary preimplant analysis. Postimplant respiratory failure was defined in INTERMACS as impairment of respiratory function requiring intubation or mechanical ventilation, which was collected during routine follow-up. Thus, for our secondary objective, patients were classified as having early postimplant respiratory failure if it occurred in the first week after device implant.

Statistical Analyses
Continuous variables were described as medians and interquartile ranges, and categorical variables were described as frequencies and percentages. For comparison, the Wilcoxon rank-sum test was used for continuous variables and χ² test for categorical variables. Survival analysis by preimplant intubation was performed using Kaplan-Meier estimates at 12 months after implant, using the log-rank test to compare patient groups. We performed unadjusted and multivariable-adjusted Cox proportional-hazards regression models to estimate the association between preimplant intubation and mortality, reporting hazard ratios (HR) with their respective 95% CI. To preserve direct interpretation, the multivariable Cox
models were reported without skewed variable transformation. Consistent with previous INTERMACS analyses,18 our adjusted model contained risk factors identified in the annual report as having the highest risk for early hazard.1 These variables included age, sex, body mass index, INTERMACS profile 1 and 2, presence of implantable cardioverter defibrillator, albumin, blood urea nitrogen, total bilirubin, dialysis, history of previous cardiac surgery, and concomitant surgery at time of implant. In addition, we conducted a sensitivity analysis after transformation of skewed variables (albumin, blood urea nitrogen, total bilirubin, and body mass index), and our primary results remained unchanged (Table I in the Data Supplement).

We then performed a competing risk analysis by estimating the cumulative incidence of death, transplant, and explant using the Aalen-Johansen estimate.19 The survival for patients with a device still in place was estimated by calculating the survival probability for patients censored for explant, transplant, or death events. Finally, consistent with previous INTERMACS studies, we calculated adverse event rates per 100 patient-months of follow-up in the first year.18 To determine the significance of the respiratory outcome trends by year, we used the χ² test and reported the corresponding P value. To assess the impact of preimplant intubation on metrics of quality of life, we constructed a multivariable-adjusted model using the same variables for preimplant and postimplant mortality and reported estimated coefficients as odds ratios for categorical outcomes and linear coefficients for continuous outcomes. To assess for the additional risk of preimplant intubation on INTERMACS profiles, we compared INTERMACS profiles 3–7, 2, and 1 with preimplant intubation compared with the corresponding INTERMACS profile without preimplant intubation.

For our postimplant respiratory failure outcome, patients were included in survival analyses if they developed respiratory failure within the first week and were alive with their device. We then performed Kaplan-Meier survival probability estimates curves from 1-week to 12-month postimplant. We also conducted unadjusted and adjusted Cox proportional hazards regression models using the same variables used in the preimplant analysis.

To assess the preimplant variables associated with early postimplant respiratory failure, we performed univariate unadjusted and adjusted Cox proportional hazard regression analysis using variables with a P<0.05 from the unadjusted analysis. Statistical significance was considered at P<0.05. All analyses were performed on Stata 14.2 (Stata Corp, College Station, TX) except the competing risks analysis, which was performed on R software version 3.5.3, using the survival package.20

RESULTS

From 2008 to 2016, we identified 16362 patients who underwent their first continuous-flow LVAD. In total, 906 patients (5.5%) required preimplant intubation within 48 hours before device implant, which included 215 (23.7%) deaths at 1 year. Baseline patient characteristics stratified by preimplant intubation are depicted in Table 1. Patients requiring preimplant intubation were statistically more likely to be younger, white, and to have a slightly higher body mass index (28.7 versus 27.8 kg/m², respectively; P<0.001, all), which was statistically different but likely not clinically significant. Preimplant intubation recipients were statistically more likely to have a history of ischemic heart disease, to be an active smoker, but less likely to have pulmonary hypertension (P<0.001 for all). Rates of chronic lung disease, diabetes mellitus, previous cardiac surgery, and chronic kidney disease were not statistically different (P>0.05, all).

At 1 year, 54.3% of patients requiring preimplant intubation were alive with continued LVAD support, 20.1% were transplanted, 1.4% recovered and had their LVAD removed, and 24.2% died without transplantation (Figure 1). Comparatively, among patients not requiring preimplant intubation, 62.5% were alive with continued LVAD support, 19.8% were transplanted, 0.6% recovered and had their LVAD removed, and 17.1% died without transplantation. All comparisons (eg, alive preimplant intubation versus alive without intubation) were statistically significant with the exception of transplantation (P=0.82).

Acuity of Illness

Patients requiring preimplant intubation were more critically ill according to both INTERMACS profiles and New York Heart Association functional classes. Over 62% (n=562) of patients in the preimplant intubation group were designated as INTERMACS profile 1 (critical cardiogenic shock) compared with 11.7% (n=1806) of patients not requiring respiratory support (P<0.001). Similarly, patients intubated before implantation were statistically more likely to require temporary mechanical support, such as extracorporeal membrane oxygenation and intraaortic balloon pump, intravenous inotropes, and dialysis before implantation (P<0.001, all). In addition, a higher proportion of patients intubated before implantation presented with cardiac arrest (26.3% versus 3.0%, P<0.001) and/or a major myocardial infarction (18.7% versus 2.0%, P<0.001).

Table 2 summarizes the preimplant laboratory and hemodynamic values. Although clinically very similar, patients intubated before implant had statistically higher median sodium, blood urea nitrogen level, total bilirubin, brain natriuretic peptide, and liver enzymes but lower albumin and platelets levels (P<0.05). Similarly, hemodynamic variables were clinically similar between the groups.

Survival After Preimplant Intubation

Patients requiring preimplant intubation within 48 hours before device implantation had a significantly worse survival compared with those who were not intubated (log-rank test: P<0.001; unadjusted HR, 1.53 [95% CI, 1.33–1.76]; Figure 2A). This association remained significant after multivariable adjustment (HR, 1.20 [95% CI, 1.03–1.41]; P=0.021). Next, we assessed for the independent risk of preimplant intubation in addition
to INTERMACS profile (Figure 2B). Compared with INTERMACS profile 1 patients without preimplant intubation, INTERMACS profile 1 patients with preimplant intubation conferred a greater risk of death (HR, 1.37 [95% CI, 1.13–1.65]; \( P = 0.001 \)). After multivariable adjustment, this relationship was no longer statistically significant (HR, 1.11 [95% CI, 0.90–1.37]; \( P = 0.325 \)).

Comparing INTERMACS profiles 2 and 3–7, we did not...
find a statistically significant increased risk in unadjusted or adjusted analysis ($P>0.05$ for all). However, sample sizes were substantially smaller for these groups and may limit power for this analysis. In addition, we did not find an interaction (coefficient=0.21, $P=0.16$) between preimplant intubation and INTERMACS profile 1.

**Impact of Preimplant Intubation on Adverse Events and Quality of Life**

Compared with patients not requiring preimplant intubation, patients requiring preimplant intubation had higher rates of postimplant bleeding, arrhythmia, stroke, right ventricular assist device implant, renal dysfunction, respiratory failure, and nondevice related infections in the first year ($P<0.01$ for all; Table 3) but less likely to be rehospitalized ($P=0.013$). There was no statistically significant difference in device-related infections ($P=0.36$).

At 3 months postimplant, patients intubated before implantation were more likely to be assessed as frail (4.6% versus 7.4%, $P<0.001$) and have a lower median Kansas City Cardiomyopathy Questionnaire-12 score (66.7 versus 61.5, $P=0.01$; Table 4). Similarly, preimplant intubation was associated with a higher proportion of patients considered New York Heart Association class III at follow-up ($P=0.004$). There was no difference in the 6-minute walk test or gait speed in either group. After multivariable adjustment, patients requiring preimplant intubation were still statistically more likely to be deemed frail, have a lower Kansas City Cardiomyopathy Questionnaire-12 score, and be New York Heart Association class III at 3-month follow-up ($P<0.05$ for all; Table II in the Data Supplement).

**Postimplant Respiratory Failure**

Over the study period, we found that 1001 (6.1%) patients developed respiratory failure within the first week of device implantation, which included 387 (39.8%) deaths at 1 year and 188 patients who were also intubated preimplant. At 1 week, 972 patients were alive with their device and included in the 1-year survival analysis. Compared with those that did not develop respiratory failure, the unadjusted HR for death was 2.93 (95% CI, 2.63–3.26; $P<0.001$; Figure 3). After multivariable adjustment, patients developing respiratory failure within 1 week continued to have a $>2.5\times$ increased risk of death in the first year (HR, 2.54 [95% CI, 2.26–2.85]; $P<0.001$).

**Predictors of Postimplant Respiratory Failure**

After multivariable analysis, patient characteristics associated with respiratory failure in the first week included being INTERMACS profile 1 (HR, 2.05 [95% CI, 1.38–3.05]) or 2 (HR, 1.53 [95% CI, 1.10–2.14]) at the time of implantation, having a history of previous cardiac surgery (HR, 1.36 [95% CI, 1.10–1.67]), atrial arrhythmia (HR, 1.46 [95% CI, 1.17–1.82]), chronic lung disease (HR, 1.88 [95% CI, 1.45–2.45]), and chronic kidney disease (HR, 1.32 [95% CI, 1.05–1.66]; Table III in the Data Supplement). Events during the index admission associated with respiratory failure in the first week included major infection (HR, 1.88 [95% CI, 1.39–2.53]). A higher creatinine (HR, 1.15 [95% CI, 1.01–1.31]) was associated with a higher risk of postimplant respiratory failure while higher albumin (HR, 0.82 [95% CI, 0.70–0.95]) was associated with lower risk.

**Trends Over Time**

From 2008 to 2016, the proportion of patients intubated before device implantation decreased from 8.7% to 5.4% ($P_{\text{trend}}<0.001$; Figure 4). Over the study period, the incidence of postimplant respiratory failure at 1 week has remained largely unchanged at $\approx6.0\%$ ($P_{\text{trend}}=0.14$). Alternatively, there has been a decrease in both the incidence of respiratory failure within 1 month and 1 year ($P_{\text{trend}}<0.01$ for both). Respiratory failure at 1 month decreased from 16.1% in 2008 to 2009 to 11.0% in 2016. Similarly, the incidence of respiratory failure in the first year decreased from 19.3% to 13.5% over the same time period.

**DISCUSSION**

In this analysis of the INTERMACS registry, we describe the incidence and clinical outcomes associated with preimplant intubation and postimplant respiratory failure in patients undergoing LVAD implantation. We found that 5.5% of patients required preimplant intubation within 48 hours before device implantation, and
6.1% developed respiratory failure within the first week. Patients requiring intubation before device implantation were more critically ill than those that did not require intubation. After multivariable analysis, both intubation before and respiratory failure following LVAD implantation were independently associated with a significantly
higher 1-year mortality and were additive to other markers of clinical acuity. Our findings suggest that respiratory failure in the peri-implant period identifies a particularly sick patient population with a worse 1-year survival.

Our study examines the clinical impact of respiratory failure both before and immediately after LVAD implantation, which is especially important given the scarcity of data on this topic. To date, patients requiring preimplant intubation have either been excluded or poorly represented in clinical trials of continuous-flow LVADs. In the landmark trial comparing continuous-flow versus pulsatile-flow LVADs, Slaughter et al included a total of 15 patients (7.5%) with preimplant intubation. The remaining large-scale clinical trials have either excluded patients with or have not reported rates of preimplant intubation.

Table 3. Incidence Rates and Ratios for Adverse Events Within 1 Year of Follow-Up Stratified by Preimplant Intubation

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>No Preimplant Intubation, N=15456 (per 100 Patient-Months)</th>
<th>Preimplant Intubation, N=906 (per 100 Patient-Months)</th>
<th>Incidence Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>4.4</td>
<td>5.3</td>
<td>1.22 (1.07–1.37)</td>
<td>0.002</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>13.7</td>
<td>12.3</td>
<td>0.90 (0.82–0.98)</td>
<td>0.013</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>3.2</td>
<td>3.9</td>
<td>1.23 (1.08–1.41)</td>
<td>0.002</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.5</td>
<td>0.9</td>
<td>1.77 (1.35–2.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVAD implant</td>
<td>0.15</td>
<td>0.34</td>
<td>2.24 (1.43–3.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>1.1</td>
<td>1.8</td>
<td>1.59 (1.31–1.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>1.8</td>
<td>4.3</td>
<td>2.41 (2.11–2.74)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Infection (any)</td>
<td>5.7</td>
<td>7.5</td>
<td>1.35 (1.20–1.47)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Device related</td>
<td>1.3</td>
<td>1.1</td>
<td>0.89 (0.67–1.15)</td>
<td>0.36</td>
</tr>
<tr>
<td>Non-device related</td>
<td>4.4</td>
<td>6.4</td>
<td>1.45 (1.30–1.63)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

RVAD indicates right ventricular assist device.

The association between preimplant intubation and mortality has been reported previously. Two previous INTERMACS annual reports have briefly mentioned the early (<30 days) increased risk of death associated with preimplant intubation, but specific details are absent. Our study builds on these prior reports by including a larger cohort, as well as expanding on the associated risk of death to include adverse events, competing risks, and markers of quality of life. We also describe the prognostic importance of preimplant intubation in addition to other markers of clinical acuity.

Those requiring preimplant intubulation included a group of patients with high clinical acuity, which is a critical finding. Consistent with a higher frequently of INTERMACS profile 1, the preimplant intubation group were more likely to require mechanical circulatory support, such as intraaortic balloon pump or extracorporeal membrane oxygenation. They were also more likely to have a cardiac arrest, myocardial infarction, and a major infection during the index hospitalization. Other indicators of high clinical acuity, such as intravenous inotropes, dialysis, and ultrafiltration, were more likely in the intubated group as well. As opposed to a simple consequence of overall clinical acuity, such as the patient presenting with cardiac arrest, our results suggest that the need for mechanical ventilation identifies a patient population with additional risk.

At 3-month follow-up, we found that patients intubated before device implantation were more likely to be deemed frail and to have lower Kansas City Cardiomyopathy Questionnaire-12 scores. The INTERMACS database includes a subjective provider assessment as opposed to a validated measure of frailty. Previous INTERMACS studies have shown an association between this assessment and mortality. Although agreed on definitions of frailty for patients with LVADs are lacking, several single-center studies, using varying methods and definitions, have shown a link between preimplant frailty and an increased risk of death. In addition, there was a higher proportion of patients New York.

Table 4. Frailty, Exercise Capacity, and Quality of Life Postoperatively for Patients With Preimplant Intubation

<table>
<thead>
<tr>
<th>Three Months of Follow-Up</th>
<th>Overall, N=14351</th>
<th>No Preimplant Intubation, N=13620</th>
<th>Preimplant Intubation, N=731</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frailty</td>
<td>681 (4.7%)</td>
<td>627 (4.6%)</td>
<td>54 (7.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>KCCQ score</td>
<td>66.1 (50–79.2)</td>
<td>66.7 (50.5–79.7)</td>
<td>61.5 (47.6–71.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>6-minute walk, feet</td>
<td>1060 (800–1282)</td>
<td>1060 (800–1282)</td>
<td>1060 (712–1290)</td>
<td>0.75</td>
</tr>
<tr>
<td>Gait speed, m/s</td>
<td>0.99 (0.76–1.23)</td>
<td>0.994 (0.76–1.22)</td>
<td>1.016 (0.75–1.28)</td>
<td>0.86</td>
</tr>
<tr>
<td>NYHA</td>
<td></td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>I</td>
<td>2478 (18.2%)</td>
<td>2377 (18.4%)</td>
<td>101 (14.6%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>5463 (40.1%)</td>
<td>5208 (40.3%)</td>
<td>255 (36.7%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>2225 (16.3%)</td>
<td>2084 (16.1%)</td>
<td>141 (20.3%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>594 (4.4%)</td>
<td>560 (4.3%)</td>
<td>34 (4.9%)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) for continuous measures and n (%) for categorical measures. KCCQ indicates Kansas City Cardiomyopathy Questionnaire; and NYHA, New York Heart Association.
Heart Association functional class III in the preimplant intubated group, which identifies an LVAD group less likely to be living well.26

In addition to including a sicker population, the association between preimplant intubation and worse outcomes is likely multifactorial. Although often lifesaving, invasive mechanical ventilation is also associated with several deleterious effects, including ventilator associated infections, immobilization and resulting muscle weakness, interruptions in nutrition, and unique interactions with both left and right ventricular dysfunction.27–31 Furthermore, intubated patients may have delayed implantation to properly obtain informed consent. All of these complications could potentially slow recovery following LVAD implantation and possibly influence transplantation decisions. These consequences, including potential deconditioning and poorer nutrition, may have also accounted for the higher rates of adverse events we found in the preimplant intubation group.

Perhaps because of the paucity of data from clinical trials, currently available societal guidelines offer limited guidance on how to manage patients intubated at the time of implantation.10–12 Briefly mentioned in one scientific statement, prolonged intubation (time not specified) was reported as a relative contraindication to LVAD implantation.10 Although specific to intubation 48 hours before implant, our findings suggest that these patients are indeed more critically ill but should not independently preclude a patient from undergoing device implantation. In addition, our competing risks analysis, we found that a similar proportion of patients who were intubated versus not intubated at implantation underwent cardiac transplantation at 1 year.

Clinical trials have offered a wide range of postimplant respiratory failure estimates, which have been reported between 14% and 38%.4–9 We found that postimplant respiratory failure occurred in 6.1% of patients in the first week, ≈13% in the first month, and nearly 17% in the first year. Over the study period, the proportion of patients developing respiratory failure in the first week remained largely unchanged while rates of respiratory failure in the first month and year declined. In addition to describing the real-world incidence and trends of postimplant respiratory failure, we found that developing respiratory failure in the first week was independently associated with over a 2.5× increased risk of death in the first year.

There are limited data describing the associated risks and management of postimplant respiratory failure, which is integral to the immediate postimplant care of these patients. One retrospective, single-center study (n=139) evaluated the risks of prolonged postimplant mechanical ventilation (defined as >7 days). In their cohort, 43% of the patients required prolonged mechanical ventilation, which was associated with a significant increase in 180-day mortality.32 In a much larger, multicenter cohort, we corroborate the association between postimplant respiratory failure and an increased risk of death. In addition to identifying a
particularly sick population that may need closer monitoring or follow-up, these results may be helpful in counseling families of patients who develop this early complication.

Study Limitations

In addition to the known limitations of retrospective analyses from registry data, our study has several limitations. We are not able to describe the etiology that required preimplant intubation, which is likely multifactorial, including primary respiratory failure, airway protection, and for another surgical procedure. However, our results did not change after multivariable adjustment for concomitant surgery. Patients intubated before implant were more critically ill than those not intubated. Although we tried to address this issue by performing multivariable adjustment, it is likely that residual confounding remains. Because of limitations of the database, we were unable to describe how long patients were intubated before implant but only that they required intubation within 48 hours before implant. We lack data on the use of noninvasive ventilation, which is often used to treat cardiogenic pulmonary edema and may prevent intubation. The INTERMACS registry is known to have areas of missingness, notably in the quality of life data. Finally, the INTERMACS registry only includes patients that actually received a durable device, which may have incorporated unmeasured bias into our patient population. In particular, sicker patients, such as INTERMACS profiles 1 and 2, may not have been enrolled if consent was not obtained.

CONCLUSIONS

Both preimplant intubation and postimplant respiratory failure occur commonly in patients implanted with continuous-flow LVADs. Over 5% of patients required respiratory support within 48 hours before implant and 6.1% of patients developed respiratory failure within the first week after implant. More importantly, both intubation before and respiratory failure after LVAD implantation are independently associated with a significantly increased risk of adverse clinical outcomes, including mortality at 1 year.

ARTICLE INFORMATION

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REFERENCES


