Usefulness of the INTERMACS Scale to Predict Outcomes After Mechanical Assist Device Implantation

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Background: The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) scale classifies advanced heart failure patients according to hemodynamic status. This study assessed the usefulness of the INTERMACS scale to predict outcomes in advanced heart failure patients undergoing mechanical circulatory support (MCS).

Methods: Fifty-four patients underwent MCS implantation from 2001 to 2007. Group A included 27 patients at INTERMACS level 1 and 2. Group B included 27 at INTERMACS level 3 and 4. Patient characteristics pre-MCS implant, incidence of complications during support, and survival between groups were compared.

Results: Before MCS implantation, Group A had significantly lower cardiac index, mean arterial blood pressure, systolic pulmonary pressure, higher central venous pressure, and lower urine output (p < .05). After MCS, Group A had a lower incidence of infections (17% vs 46%; odds ratio [OR], 0.25, 95% confidence interval [CI], 0.06–0.6) and a higher incidence of liver injury (39% vs 11%; OR 5, 95% CI, 1.15–25). Mortality at 30 days was higher in Group A (38% vs 11%; OR, 4.8; 95% CI, 1.1–21); however, the mortality after 30 days post-MCS support was significantly higher in Group B (0% vs 18%, p < .05). Cox model showed overall survival was poorer in Group A (hazard ratio, 2.7; 95% CI, 1.1–7).

Conclusion: INTERMACS levels identified patients at risk for developing complications after MCS support. INTERMACS is a valid score system that should be considered as a tool to assess patient profile and predict complications and mortality after MCS implantation. J Heart Lung Transplant 2009;28: 827–33. Crown Copyright © 2009 Published by Elsevier Inc. on behalf of the International Society for Heart and Lung Transplantation. All rights reserved.

The heart failure patient profile ranges from an asymptomatic individual with no functional limitations to a critically decompensated patient with a life expectancy measured in hours or days. At the extreme end of this continuum are patients with advanced heart failure. The numbers of these patients are increasing and their prognosis remains poor. Heart transplantation is the best option for selected patients with refractory heart failure. Given the limited supply of hearts available for transplantation, the use of mechanical circulatory support (MCS) has evolved to become a standard therapeutic option in many cardiac programs. MCS has been shown to improve the functional status, quality of life, and survival of patients with end-stage heart disease.1–7 The effect of this therapy within the pool of eligible patients differs, however, due to the heterogeneity of baseline characteristics and prognosis before device implantation.

The spectrum of advanced heart failure patients who are considered for MCS is wide and varied. It includes patients with life-threatening hypotension despite the use of inotropic support and even intra-aortic balloon pump (IABP), as well as those who are at home, mildly symptomatic but have experienced multiple and frequent decompensations.

The National Institutes of Health-sponsored Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) scale has focused on advancing the field of MCS through extensive and disciplined data collection. It has developed a classification that divides these patients into 7 levels according to their hemodynamic status before ventricular assist device (VAD) implant (Table 1). The scale facilitates communication between colleagues and refines patient selection for optimizing outcomes.8 Therefore, the objective of our study was to assess the usefulness of the INTERMACS scale to define patient profiles and predict outcomes in advanced heart failure patients undergoing MCS.
therefore patients were categorized into two groups.

Group A comprised 27 (50%) patients at INTERMACS level 1 and 2, including 6 patients with post-cardiotomy shock requiring MCS. Group B comprised 27 patients at INTERMACS level 3 and 4.

Variables

Several clinical, laboratory, and hemodynamic parameters measured before, during, and after MCS implantation were evaluated. Pre-MCS implantation factors evaluated were age, sex, race, body mass index (BMI), body surface area, blood type, diabetes, arterial hypertension, peripheral vascular disease, chronic renal failure (defined as glomerular filtration rate < 60 mL/min for more than 3 months), New York Heart Association (NYHA) class IV at 1 month before admission, implantable cardioverter defibrillator (ICD)-cardiac resynchronization therapy (CRT) implantation, cause of cardiomyopathy, previous sternotomy, and treatment, including inotropes, mechanical ventilation, and intra-aortic balloon pump (IABP). Pre-VAD laboratory and hemodynamic values were recorded. The pre-operative Columbia University VAD score for each patient was calculated using 5 clinical variables: post-cardiotomy shock, use of mechanical ventilation, previous use of left ventricular assist device (LVAD), central venous pressure > 16 mm Hg, and prothrombin time > 16 seconds. Intraoperative data and the development of complications during the implantation were also recorded.

Complications after MCS placement recorded within the index hospital stay included:

- infection, defined as systemic, pneumonia, pocket or driveline;
- bleeding > 1 liter during the first 6 hours after operation;
- reoperation;
- RV failure as defined by clinical parameters of low LVAD output, and high central venous pressure (> 15 mm Hg), and the use of inhaled nitric oxide > 48 hours, inotropic support > 14 days, or need for RVAD after LVAD implantation;
- need for RVAD;
- ventricular arrhythmias;
- stroke;
- acute renal dysfunction, defined as at least 2-fold increase in the serum creatinine or glomerular filtration rate decrease >50%, compared with the preoperative level, or urine output < 0.5 ml/kg/h for 12 hours; and
- liver injury, defined as 2-fold increase in the transaminases vs the value before VAD.

The outcomes of interest included duration of VAD support, total length of stay (LOS) in the hospital and intensive care unit, days on inotropes, days on mechan-
ical ventilation, rate of bridge to transplantation (patients transplanted/total patients × 100), and survival.

Statistical Analysis

Data were analyzed with SAS 8.2 software (SAS Institute, Cary, NC). Qualitative data were recorded in a categoric fashion, and quantitative covariates were measured as continuous variables. Categoric variables were represented as proportions with their correspondent odds ratio (OR), hazard ratio (HR), and 95% confidence interval (95% CI). Continuous variables were represented as mean ± standard deviation. Mann-Whitney/Wilcoxon 2-sample test was used for continuous variables. Fisher’s exact test or chi-square analysis, according to the number of events, was used for categoric variables. Univariate logistic regression analysis was performed to evaluate the relationship between various peri-operative and intraoperative factors and the level of INTERMACS. This type of analysis was also used to evaluate the association between complications and INTERMACS scale. Kaplan-Meier, the long-rank test, and Cox regression analysis were performed to evaluate the survival data. A value of \( p \leq 0.05 \) was considered to be statistically significant.

RESULTS

Baseline Characteristics

Pre-operative characteristics are summarized in Table 2. The groups had similar baseline characteristics. At the time of VAD placement, Group A consisted of 27 patients (18 men, 9 women) with a mean age of 45 ± 13 years (range, 21–62 years) and Group B consisted of 27 patients (23 men, 4 women) with a mean age of 47 ± 13 years (range, 24–69 years). However, the prevalence 1 month before admission of NYHA class IV was 78% in Group B vs 52% in Group A (\( p < 0.05 \)). Group B had a 44% incidence of chronic renal failure before VAD implantation vs 8% in Group A (OR, 10.7; 95% CI, 2–54; \( p < 0.01 \)), 30% use of CRT vs 8% in Group A (OR 5; 95% CI, 1–27; \( p < 0.05 \)), and showed a trend toward higher use of ICD. The use of mechanical ventilation and IABP before VAD-implantation were significantly higher in Group A (\( p < 0.001 \)). Group A had a 54% incidence of Columbia University VAD score > 5 vs 4% in Group B (95% CI, 33–237; \( p < 0.001 \)), with a mean VAD score of 5 ± 2.7 vs 1 ± 1.5 (\( p < 0.001 \)).

Pre-operative hemodynamic profiles are summarized in Table 3. Although LV ejection fraction before VAD implant was < 20% in both groups, the hemodynamic differences were substantial. Group A had significantly lower cardiac index (\( p = 0.05 \)), lower mean arterial blood pressure (\( p = 0.03 \)), lower systolic pulmonary pressure (\( p < 0.05 \)), higher central venous pressure (\( p = 0.05 \)) and lower right ventricular work index (\( p = 0.01 \)). Group A also had a lower urinary output pre-VAD implantation (\( p = 0.01 \)).

Pre-operative laboratory profiles of patients are listed in Table 4. Serum creatinine (SCr) levels, creatinine clearance, and glomerular filtration rate were comparable in both groups; however, SCr 7 days before implant was significantly lower in Group A (\( p < 0.01 \)). Group A had higher alanine transerase levels (\( p < 0.01 \)), longer prothrombin time (\( p < 0.001 \)), and lower levels of albumin (\( p = 0.01 \)).

Intraoperative Data

Intraoperative details are outlined in Table 5. Group A had a higher emergency indication for MCS (defined as time between decision of VAD implantation and implantation within 24 hours). The most frequent indication was bridge to transplant in Group A (37%), whereas it was bridge to candidacy (BTC) in Group B (59%; Figure 1). The principal reason of BTC were the presence of pulmonary hypertension in Group B (\( n = 16 \)) and possible ventricular recovery at the time of implant in Group A. None of the patients in Group A received a VAD as a destination therapy. Abiomed BVS50000 (48% vs 4%, \( p < 0.001 \)) and biventricular support (48% vs 0%, \( p < 0.001 \)) were used more frequently in Group A.
Mean arterial BP, mmHg 68/110
Cardiac index, liters/min/m² 2.3
Low urine output b 30
Urine output, ml/hour 74
RVSWI, mm Hg ml/m² 380
Implantation time; RVSWI, right ventricular stroke work index.

Hemodynamic Values Before Ventricular Assist Device Implantation

<table>
<thead>
<tr>
<th>Variable</th>
<th>INTERMACS, mean ± SD or %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Level 1–2</td>
</tr>
<tr>
<td>Cardiac output, liters/min²</td>
<td>4.2 ± 1.1</td>
</tr>
<tr>
<td>Cardiac index, liters/min/m²</td>
<td>2.3 ± 0.6</td>
</tr>
<tr>
<td>Mean arterial BP, mmHg</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>CVP, mm Hg</td>
<td>14 ± 6</td>
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<tr>
<td>SVR, dynes·sec/cm²</td>
<td>1052 ± 241</td>
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<tr>
<td>LVEF, %</td>
<td>17 ± 6</td>
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<tr>
<td>Systolic PAP, mm Hg</td>
<td>43 ± 12</td>
</tr>
<tr>
<td>Mean PAP, mm Hg</td>
<td>28 ± 8</td>
</tr>
<tr>
<td>PCWP, mm Hg</td>
<td>22 ± 7</td>
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<tr>
<td>PVR, dynes·sec/cm²</td>
<td>147 ± 52</td>
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<tr>
<td>RVSWI, mm Hg ml/m²</td>
<td>380 ± 310</td>
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<tr>
<td>Urine output, ml/hour</td>
<td>74 ± 51</td>
</tr>
<tr>
<td>Low urine output</td>
<td>30</td>
</tr>
</tbody>
</table>

BP, blood pressure; CVP, central venous pressure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; SVR, systemic vascular resistance; LVEF, left ventricular ejection fraction; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; PVR, pulmonary vascular resistance; RVSWI, right ventricular stroke work index; SD, standard deviation.  

Patients in Group A had longer cardiopulmonary bypass time (121 ± 58 vs 83 ± 20 minutes in Group B, p < 0.01). The need for other procedures, including repair of patent foramen ovale, aortic valve repair, and coronary artery bypass graft, was significantly higher in Group A. Although the incidence of intraoperative bleeding (≥ 1 liter) was similar between the groups, Group A had a trend to greater blood loss during surgery (1.9 ± 1.9 vs 1.4 ± 1.7 liters in Group B, p < 0.05).

Post-operative Complications and Clinical Outcomes

The incidence of complications during VAD support is shown in Figure 2. Group A had a 39% incidence of liver injury vs 11% in Group B (OR, 5; 95% CI, 1.15–25; p < 0.05). Group B showed higher overall occurrence of infections of 46% vs 17% in Group A (OR, 4.3; 95% CI, 1.1–16; p < 0.05), including driveline infection (1 patient in Group B), pneumonia (6 patients in Group B and 1 in Group A) and systemic infection (6 patients in the Group B and 3 in Group A). No pocket infections were detected. The incidence of bleeding (≥ 1 liter in the first 6 hours after implantation), renal dysfunction, and RV failure after VAD implantation was not different between groups.

![Figure 1](image-url)  

**Figure 1.** Distribution of Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) levels according to the intention of treatment. BTT, bridge to transplantation; BTR, bridge to recovery; BTC, bridge to candidacy; DT, destination therapy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>INTERMACS, mean ± SD or %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Level 1–2</td>
</tr>
<tr>
<td>Pre-7-day creatinine, mg/dl</td>
<td>1.4 ± 0.8</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.5 ± 0.76</td>
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<tr>
<td>Creatinine clearance, ml/min</td>
<td>74 ± 36</td>
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<tr>
<td>GFR, ml/min</td>
<td>62 ± 31</td>
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<tr>
<td>Total bilirubin, mg/dl</td>
<td>1.45 ± 1.10</td>
</tr>
<tr>
<td>AST, U/liter</td>
<td>149 ± 225</td>
</tr>
<tr>
<td>ALT, U/liter</td>
<td>169 ± 242</td>
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<tr>
<td>Albumin, g/dl</td>
<td>3.1 ± 0.5</td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>11 ± 1.6</td>
</tr>
<tr>
<td>Platelet count, ×10⁹/liter</td>
<td>217 ± 76</td>
</tr>
<tr>
<td>PT, seconds</td>
<td>18 ± 2.7</td>
</tr>
<tr>
<td>MVOS, %</td>
<td>61 ± 12</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate transferase; GFR, glomerular filtration rate; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVEF, left ventricular ejection fraction; MVOS, mixed venous oxygen saturation; PCWP, pulmonary capillary wedge pressure; PT, prothrombin time; RVSWI, right ventricular stroke work index.
The LOS in the hospital and ICU were longer in Group B (45 ± 38 and 22 ± 28 days vs 27 ± 36 and 9 ± 7 in Group A, *p* < 0.05). The mean duration of VAD support was also longer in Group B (151 ± 225 days vs 35 ± 52 in Group A, *p* < 0.001); however, the days of use of mechanical ventilation and inotropes were similar between both groups.

Heart transplantation was performed in 11 patients (41%) in Group A and in 16 patients (59%) in Group B (*p* = 0.14). LV recovery occurred in 4 patients (15%) in Group A and in 1 patient (4%) in Group B (*p* = 0.17).

**Mortality Rates and Survival**

Mortality rates are shown in Figure 4. The rate of total mortality (total number of deaths/total number of patients during VAD support × 100) was not significantly different between the groups. However, mortality at 30 days (early mortality) was 44% higher in Group A vs 11% in Group B (OR 4.8; 95% CI, 1.1–21; *p* < 0.01), whereas the mortality rate > 30 days after MCS support (late mortality) was 18% in Group B vs 0% in Group A (*p* < 0.05). The main causes of death were infections in Group B (53%) and multiorgan failure in Group A (25%).

Despite this non-significantly different total mortality rate, the overall survival (Figure 3), analyzed by the Cox model, was significantly lower in Group A vs Group B: 55% vs 80% at 30 days after implant, 46% vs 75% at 75 days, and 35% vs 68% at 120 days. The mortality risk, obtained by Cox proportional model, was 2.7 (95% CI, 1.1–7; *p* < 0.05).

**DISCUSSION**

The INTERMACS scale is a useful classification to categorize advanced heart failure patients and predict outcomes before MCS implantation. We stratified patients in 2 groups: Group A included hemodynamically unstable patients despite optimized intensive medical therapy (INTERMACS level 1 and 2), and Group B included patients who were hemodynamically stable and inotrope-dependent (INTERMACS level 3 and 4). Among the significant baseline differences, Group A had a lower incidence of NYHA class IV symptoms 1-month before admission and less frequent use of CRT. Patients in Group A had a higher incidence of acute decompen-sated heart failure requiring VAD support, which explains the less frequent use of CRT in this group. This group was more hemodynamically unstable, requiring more mechanical ventilation and IABP before implantation and a greater need for emergency device implantation.

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**Figure 2.** Incidence of complications during ventricular assist device (VAD) support according to Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) levels. RVF, right ventricular failure; Ventr Arrhyth, ventricular arrhythmias; TE, thromboembolism.

*Only considering the 14 patients in Group A (INTERMACS level I–II) and 27 in Group B (INTERMACS level III–IV) who received a left VAD.*

**Figure 3.** Mortality rates according to Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) level.

**Figure 4.** Cox model analysis of survival according to Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) level. VAD, ventricular assist device.
During MCS, Group A had a higher incidence of liver injury. This is probably related to liver hypoxic injury due to lower cardiac output and liver hypoperfusion before VAD placement and not as a consequence of the development of RV failure, because the incidence of this complication was similar between both groups. It was also associated with higher rate of mortality within 30 days after implantation and less overall survival. However, the lower late mortality rate implies that if patients overcome the acute injury (acute heart failure decompensation and surgery), they may have a relatively good outcome thereafter. These findings suggest an acute development of heart failure or a sudden profound decompensation of previous advanced heart failure.

Conversely, Group B patients were more likely to be at NYHA class IV and had a greater use of CRT. The main indication of VAD implantation was bridge to decision, which indicates that this population had a higher incidence of comorbidities, including renal dysfunction and high pulmonary arterial pressure. Elective VAD implantation was more frequent in Group B. The major complication during support was infection, which may explain the longer ICU LOS in this group. Although the overall survival was better in Group B, there was a higher mortality after 30 days post-implantation. These features may be related to the chronicity of heart failure and associated comorbidities.

Some features present in Group B may explain the differences in patient’s profiles and outcomes between both groups. For example, Group B was associated with more non-urgent device implants, which was due to the relatively less severe hemodynamics compared with Group A. Group B was also associated with higher use of long-term support devices (Novacor, HeartMate and HeartMate II) and to the presence of some relative contraindications for heart transplantation at the time of VAD-implant plausible to be reverted during VAD support. In addition, the higher incidence of NYHA class IV in Group B demonstrates the chronicity of the underlying heart failure. This characteristic may explain the higher incidence of infections due to the presence of several predisposing factors in advanced heart failure patients, including malnutrition, pulmonary hypertension, renal dysfunction, and older age.

Although our study included patients who received short-term and long-term devices, our results are comparable with those reported by the INTERMACS registry that only included patients who received a device for long-term support. They reported a 1-year survival of 67% in patients that received an LVAD, which is comparable to the survival of patients in Group B (62% at 1 year) that only included patients with LVAD support. Only 1 patient with an LVAD died in Group A. Similarly to our results, they observed that in patients at INTERMACS level 1 and 2, the use of destination therapy device was less frequent. In contrast, BTC was the most frequent indication in these patients. This is not in agreement with our findings, in which BTC was more frequent with patients in INTERMACS levels 3 and 4 due to the presence of plausibly reversible transplant contraindications at the time of the device placement.

The design of our study suggests that INTERMACS levels 1 and 2 may be considered as a single group of patients because they share important characteristics such as the impossibility of reaching hemodynamic stability with aggressive medical therapy. Similarly, INTERMACS levels 3 and 4 may be considered as a second group of patients who are able to gain hemodynamic stability but are dependent on permanent (INTERMACS level 3) or recurrent (INTERMACS level 4) inotropic support. However, this study is underpowered to detect differences in outcomes in each INTERMACS stratum due to the small number of patients included in each group.

Many different classifications and scores have been used to assess risk in patients undergoing VAD insertion, all with strengths and weakness. Rao et al proposed the use of a VAD score using the 5 variables of post-cardiomyotomy shock, ventilation, pre-LVAD, central venous pressure, and prothrombin time. They evaluated a group of 130 patients who received a HeartMate XVE as a bridge to transplantation and found that a VAD score > 5 was associated with higher operative mortality (46% vs 12%, p < 0.001). Our study demonstrated a strong association between the Columbia University score and INTERMACS level, showing that low INTERMACS levels are associated with higher VAD scores, a higher mortality rate, and poorer survival. However, the Columbia University score is not accurate to discriminate risk in relatively stable heart failure patients (INTERMACS levels ≥ 3) due to the variables in consideration.

More recently, the modified Sequential Organ Failure Assessment (SOFA) score has been applied peri-operatively in patients undergoing VAD insertion. Qedra et al found that a SOFA ≥ 11 points is a strong predictor of mortality related to multiple organ failure after VAD implantation (p < 0.05), with a specificity of 96.7% and a sensitivity of 92.9%. Nonetheless, the performance of the SOFA score is complex and mainly limited to academic purposes. This and other emerging scores need prospective evaluation using the INTERMACS profiles to identify the risk and outcomes in a wide variety of potential MCS patients.

Another important advantage of INTERMACS is to generate objective performance criteria to compare results across and within future studies. The unified information obtained from published and future studies will assist physicians to refine patient management and
improve outcomes. In addition, this scale will facilitate a better assessment of the cost-benefit relation of patients undergoing a VAD implantation. This point constitutes an important issue, especially in critically ill patients (INTERMACS levels 1 and 2).

The main limitations of this study are that it is retrospective and is limited to a single institution. To minimize this, all data were collected into the database prospectively as a part of routine patient management by a single investigator. In addition, the number of patients in the study is not large enough to demonstrate some differences, such as total mortality, between the groups (β error or type II error). This scale will need to be validated in larger multicenter studies. Owing to the heterogeneity of patients and devices the results of single-center studies should be interpreted cautiously.

In conclusion, because of the increasing use of MCS assistance for the treatment of acute and chronic heart failure, a greater proportion of patients will likely undergo device implantation. However, clinical variables, hemodynamic status, and outcomes of this pool of patients vary considerably. Therefore, the INTERMACS patient profile is a useful tool to accurately assess patients before MCS implant, facilitate communication among professionals, improve management and outcomes, and unify criteria for future clinical trials and devices. The INTERMACS levels 1 and 2 were associated with more profound decompensated heart failure, higher mortality rate, and poorer overall survival, whereas INTERMACS levels 3 and 4 were associated with better outcomes. Hence, MCS implantation should be considered early in advanced heart failure patients undergoing an episode of heart failure decompensation, before a critical deterioration.

REFERENCES