

SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics for males versus females in the Derivation and Validation Cohorts

| | Derivation Cohort (n=9,113) | | | Validation Cohort (n=6,074) | | | P-Value for Difference between DC and VC |
|--|-----------------------------|-------------------|---------|-----------------------------|-------------------|---------|--|
| | Male (n=7,230) | Female (n=1,883) | P-Value | Male (n=4,810) | Female (n=1,264) | P-Value | |
| Age at implant, years | 59 (49, 66) | 57 (45, 64) | <0.001 | 59 (50, 66) | 56 (46, 64) | <0.001 | 0.45 |
| BMI, kg/m ² | 27.2 (23.6, 31.7) | 27.2 (22.7, 32.4) | 0.54 | 27.2 (23.7, 31.6) | 27.3 (22.9, 33.1) | 0.78 | 0.50 |
| Ischemic Cardiomyopathy | 2,934 (40.6%) | 434 (23.0%) | <0.001 | 1,962 (40.8%) | 275 (21.8%) | <0.001 | 0.86 |
| Cardiogenic Shock (INTERMACS 1 and 2) | 1,073 (14.8%) | 303 (16.1%) | 0.04 | 731 (15.2%) | 216 (17.1%) | 0.04 | 0.42 |
| Dialysis, pre-implant | 210 (2.9%) | 49 (2.6%) | 0.54 | 143 (3.0%) | 38 (3.0%) | 1.00 | 0.62 |
| Major infection during index hospitalization pre-implant | 398 (5.5%) | 119 (6.3%) | 0.07 | 270 (5.6%) | 83 (6.6%) | 0.07 | 0.73 |
| BUN, mg/dL | 26 (18, 39) | 22 (15, 32) | <0.001 | 26 (18, 38) | 22 (15, 32) | <0.001 | 0.86 |
| Total Bilirubin, mg/dL | 1.0 (0.7, 1.6) | 0.8 (0.6, 1.4) | <0.001 | 1.0 (0.7, 1.7) | 0.8 (0.5, 1.3) | <0.001 | 0.88 |
| ALT, U/L | 29 (19, 49) | 25 (17, 43) | <0.001 | 28 (19, 49) | 25 (17, 42) | <0.001 | 0.33 |
| Serum Sodium, meq/L | 136 (132, 138) | 136 (133, 138) | <0.001 | 135 (132, 138) | 136 (133, 139) | <0.001 | 0.84 |
| INR | 1.2 (1.1, 1.4) | 1.2 (1.1, 1.4) | <0.001 | 1.2 (1.1, 1.4) | 1.2 (1.1, 1.4) | <0.001 | 0.24 |
| Hemoglobin, gm/dL | 11.5 (9.9, 13) | 10.6 (9.4, 12) | <0.001 | 11.5 (9.9, 13) | 10.6 (9.3, 11.9) | <0.001 | 0.14 |
| Platelet count | 183 (137, 236) | 199 (143, 257) | <0.001 | 185 (140, 236) | 197 (143, 261) | <0.001 | 0.31 |
| Albumin, gm/dL | 3.5 (3.1, 3.9) | 3.5 (3.0, 3.9) | 0.58 | 3.4 (3.0, 3.9) | 3.4 (3.0, 3.8) | 0.47 | 0.09 |

| | | | | | | | |
|--|----------------|----------------|--------|----------------|----------------|--------|------|
| PA Diastolic Pressure, mmHg | 25 (19, 31) | 24 (18, 30) | 0.007 | 25 (19, 31) | 24 (18, 29) | <0.001 | 0.81 |
| RA Pressure, mmHg | 11 (7, 16) | 11 (7, 16) | 0.98 | 11 (7, 16) | 11 (7, 16) | 0.12 | 0.33 |
| Echocardiographic Characteristics | | | | | | | |
| • Moderate to Severe TR | 2,616 (36.2%) | 851 (45.2%) | <0.001 | 1,741 (36.2%) | 569 (45.0%) | <0.001 | 0.98 |
| • LVEDD, cm | 6.9 (6.2, 7.6) | 6.5 (5.8, 7.2) | <0.001 | 6.9 (6.2, 7.6) | 6.4 (5.8, 7.1) | <0.001 | 0.23 |
| Working for income | 1,254 (17.3%) | 253 (13.4%) | <0.001 | 814 (16.9%) | 171 (13.5%) | <0.001 | 0.41 |
| Major depression or other psychiatric disorder | 223 (3.1%) | 107 (5.7%) | <0.001 | 135 (2.8%) | 67 (5.3%) | <0.001 | 0.30 |
| Single, Divorced, or Widowed | 2,100 (29.0%) | 820 (43.5%) | <0.001 | 1,444 (30.0%) | 537 (42.5%) | <0.001 | 0.53 |

ALT: Alanine Aminotransferase; BMI: Body Mass Index; BUN: Blood Urea Nitrogen; INR: International Normalized Ratio; INTERMACS Profile: Interagency Registry for Mechanical Circulatory Support Profile; LVEDD: Left Ventricular End Diastolic Diameter; PA Diastolic Pressure: Pulmonary Artery Diastolic Pressure; RA Pressure: Right Atrial Pressure; TR: Tricuspid Regurgitation

Table S2. Risk discrimination of IMACS-RS versus MELD in the Derivation and Validation Cohorts

| | Female | | | Male | | |
|-----------------------------|--------------------|-----------------------------|---------|--------------------|-----------------------------|---------|
| | MELD | IMACS-RS | P-value | MELD | IMACS-RS | P-value |
| Derivation cohort (n=9,113) | | | | | | |
| AUC | 0.63 [0.59 - 0.67] | 0.73 [0.70 - 0.77] | <0.0001 | 0.60 [0.57 - 0.62] | 0.71 [0.69 - 0.73] | <0.0001 |
| NRI | | 59.65% [47.02% - 72.29%] | <0.0001 | | 52.51% [44.79% - 60.24%] | <0.0001 |
| IDI | | 0.068 [0.051 - 0.085] | <0.0001 | | 0.049 [0.042 - 0.056] | <0.0001 |
| Validation cohort (n=6,074) | | | | | | |
| AUC | 0.60 [0.54 - 0.65] | 0.71 [0.66 - 0.76] | <0.0001 | 0.60 [0.57 - 0.63] | 0.69 [0.66 - 0.72] | <0.0001 |
| NRI | | 33.84% [20.90% - 46.78%] | <0.0001 | | 45.29% [35.82% - 54.75%] | <0.0001 |

| | | | | | | |
|-----|--|--------------------------|---------|--|--------------------------|---------|
| IDI | | 0.076 [0.052 – 0.099] | <0.0001 | | 0.037 [0.029 – 0.045] | <0.0001 |
|-----|--|--------------------------|---------|--|--------------------------|---------|

AUC: Area Under the Receiver Operating Characteristic curve; MELD: Model for End-Stage Liver Disease score; IDI: Integrated Discrimination Improvement index; IMACS-RS: ISHLT Mechanical Assisted Circulatory Support Registry- Risk Score; NRI: Net Reclassification Index

Table S3. Summary of LVAD mortality risk scores

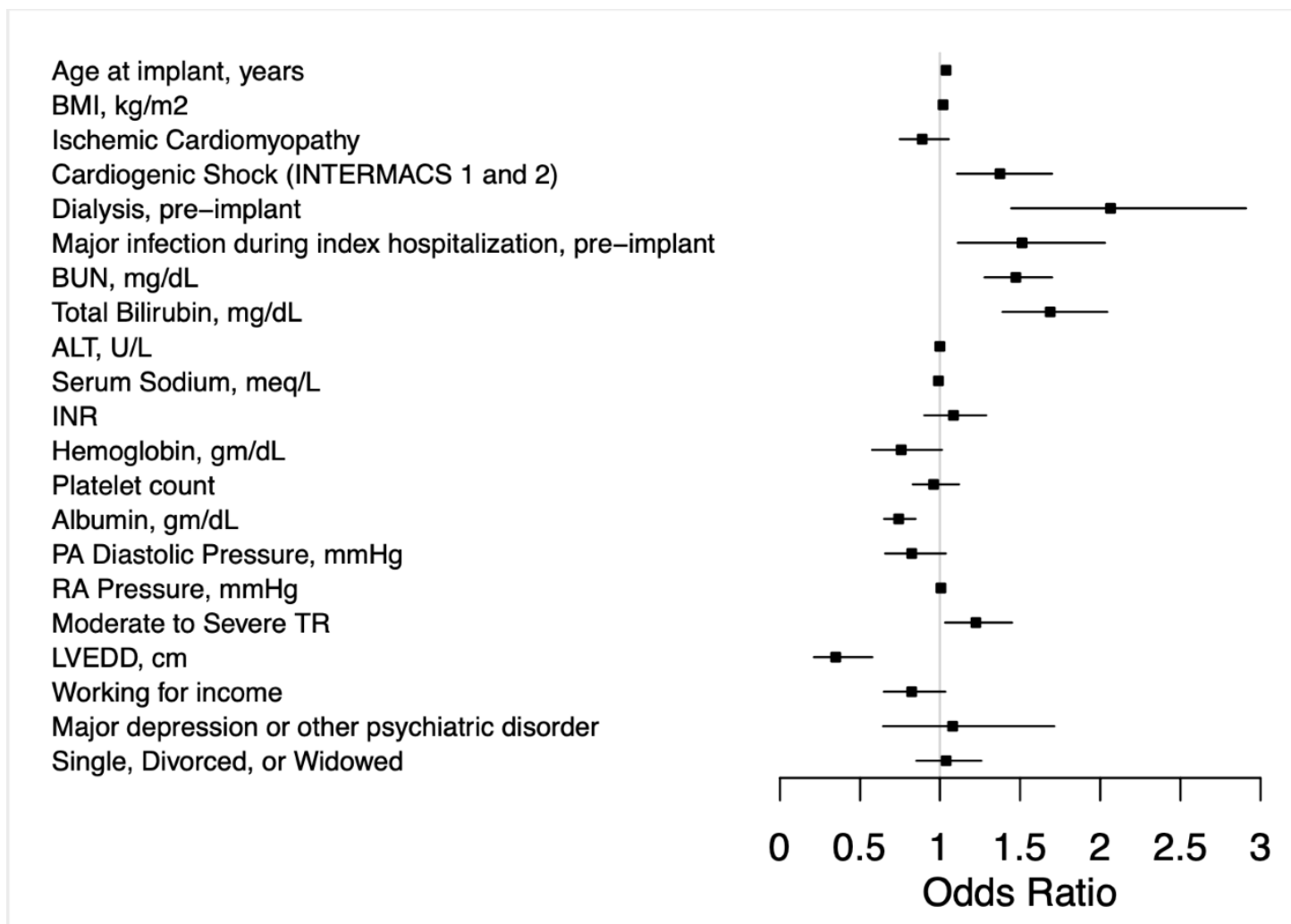
| Risk Score | % Females in Derivation Cohort | Predictors | Advantages | Limitations |
|-------------|--------------------------------|---|--|--|
| MELD | 20% | <ul style="list-style-type: none"> • Creatinine • Bilirubin • INR | <ul style="list-style-type: none"> • Easy calculation based on 3 variables • Incorporates markers of multisystem dysfunction and coagulopathy • Predicts 90-day mortality | <ul style="list-style-type: none"> • No inclusion of sex-specific interaction effects • No sex-specific data on score performance provided • Derived from cohort with multifactorial liver disease • No documented cardiac dysfunction in derivation cohort • Poor performance in external validation studies |
| DTRS | 18% | <ul style="list-style-type: none"> • Platelet count • Albumin • INR • Vasodilator therapy • Mean pulmonary artery pressure • AST • Hematocrit • BUN • Lack of IV inotropic support | <ul style="list-style-type: none"> • Stratifies patients into four risk categories • Predicts 90-day and 1-year mortality | <ul style="list-style-type: none"> • No inclusion of sex-specific interaction effects • No sex-specific data on score performance provided • Developed in a pulsatile device cohort • Exclusion of BTT candidates • Requires pulmonary catheter measurement to calculate score • Poor performance in external validation studies |
| HMRS | 23% | <ul style="list-style-type: none"> • Age • Albumin • Creatinine • INR • Center volume <15 | <ul style="list-style-type: none"> • Easy calculation based on 5 variables • Stratifies patients into 3 risk categories • Predicts 90-day and 1-year mortality | <ul style="list-style-type: none"> • No inclusion of sex-specific interaction effects • No sex-specific data on score performance provided • Score derived in a clinical trial population with only 1 pump type |

- Better risk discrimination than DTRS and MELD
- Modest performance in external validation studies

AST: Aspartate Aminotransferase; BTT: Bridge to Transplant; BUN: Blood Urea Nitrogen; DTRS: Destination Therapy Risk Score;

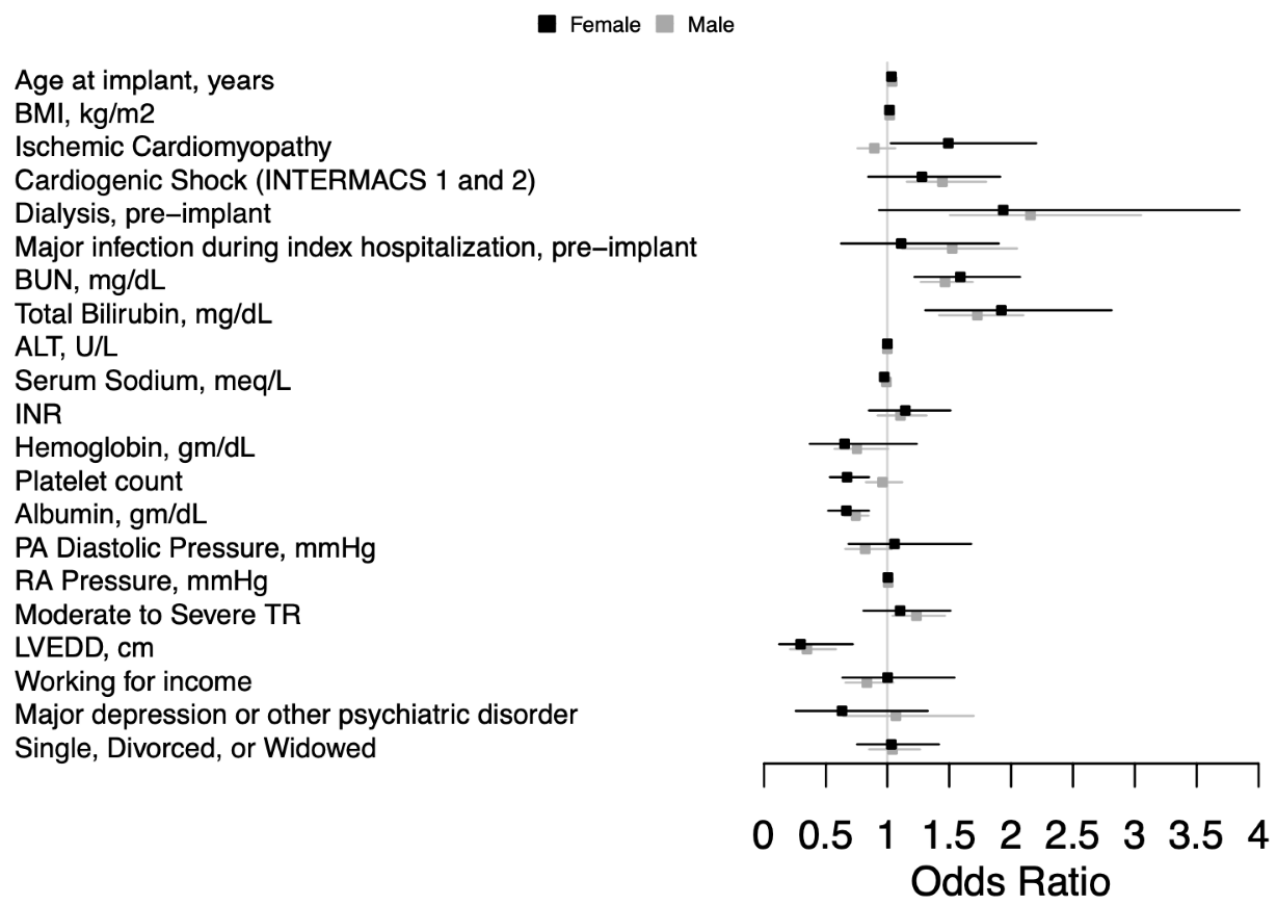
HMRS: HeartMate II Risk Score; INR: International Normalized Ratio; MELD: Model for End-Stage Liver Disease score

Figure S1. Odds Ratios for candidate predictor variable association with 3-month mortality in multivariable models in the Derivation Cohort.



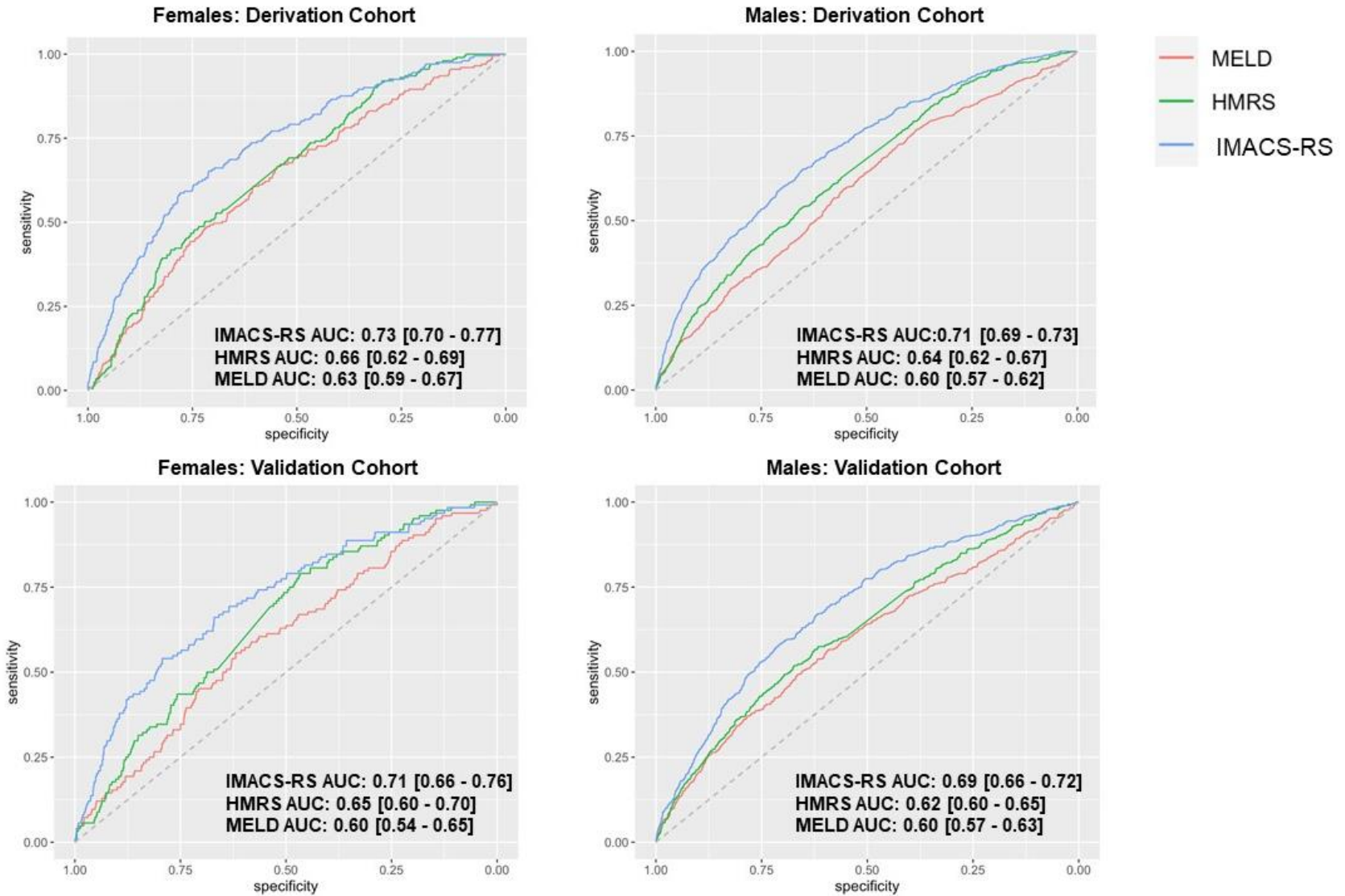
ALT: Alanine Aminotransferase; BMI: Body Mass Index; BUN: Blood Urea Nitrogen; INR: International Normalized Ratio;
INTERMACS Profile: Interagency Registry for Mechanical Circulatory Support Profile; LVEDD: Left Ventricular End Diastolic
Diameter; PA Diastolic Pressure: Pulmonary Artery Diastolic Pressure; RA Pressure: Right Atrial Pressure; TR: Tricuspid
Regurgitation

Figure S2. Sex-Stratified Odds Ratios for candidate predictor variable association with 3-month mortality in multivariable models in the Derivation Cohort.



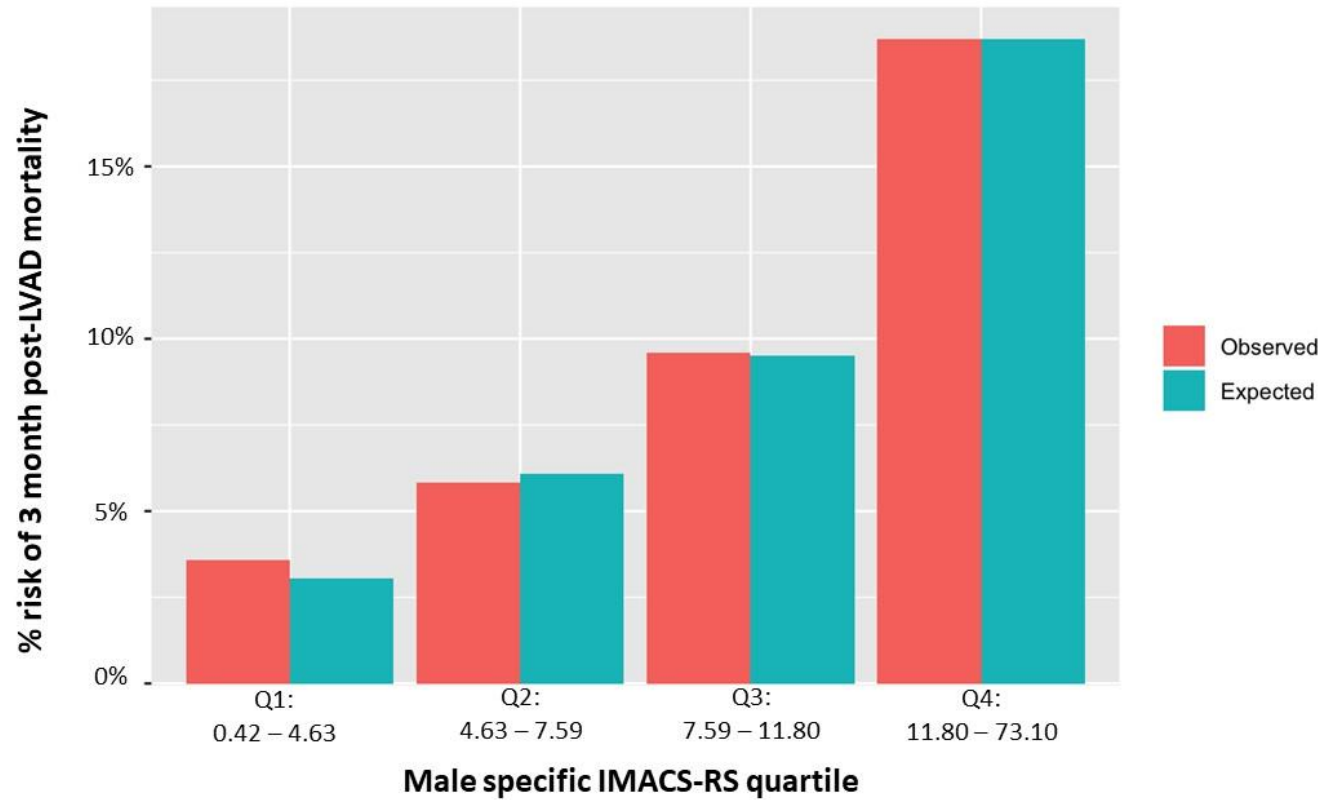
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Diameter; PA Diastolic Pressure: Pulmonary Artery Diastolic Pressure; RA Pressure: Right Atrial Pressure; TR: Tricuspid
Regurgitation

Figure S3. Receiver Operating Characteristic (ROC) curves for IMACS-RS, HMRS and MELD, for prediction of 3-month mortality



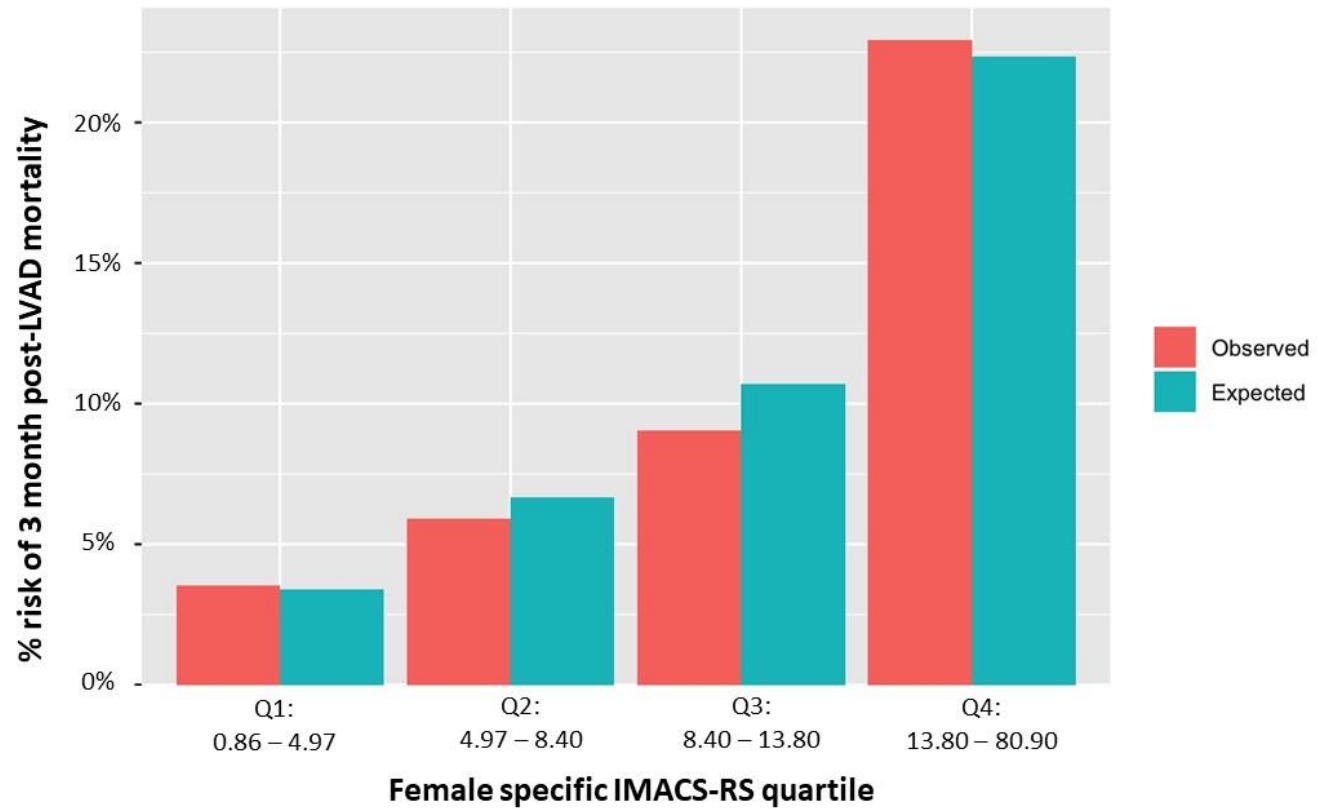
HMRS: HeartMate II Risk Score; IMACS-RS: ISHLT Mechanical Assisted Circulatory Support Registry- Risk Score; MELD: Model for End-Stage Liver Disease score

Figure S4. Calibration charts of predicted versus observed risk in Males according to sex-specific IMACS-RS quartile.



IMACS-RS: ISHLT Mechanical Assisted Circulatory Support Registry- Risk Score; LVAD: Left Ventricular Assist Device

Figure S5. Calibration charts of predicted versus observed risk in Females according to sex-specific IMACS-RS quartile.



IMACS-RS: ISHLT Mechanical Assisted Circulatory Support Registry- Risk Score; LVAD: Left Ventricular Assist Device