Risk Prediction for Early In-Hospital Mortality Following Heart Transplantation in the United States

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Background—Risk factors for early mortality after heart transplant (HT) have not been used for quantitative risk prediction. We sought to develop and validate a risk prediction model for posttransplant in-hospital mortality in HT recipients.

Methods and Results—We derived the model in subjects aged ≥18 years who underwent primary HT in the United States from January 2007 to June 2009 (n=4248) and validated it internally using a bootstrapping technique (200 random samples, n=4248). We then assessed the model's performance in patients receiving an HT from July 2009 to October 2010 (external validation cohort, n=2346). Posttransplant in-hospital mortality was 4.7% in the model derivation cohort. The best-fitting model based on recipient characteristics at transplant had 6 variables: age, diagnosis, type of mechanical support, ventilator support, estimated glomerular filtration rate, and total serum bilirubin. Model discrimination for survivors versus nonsurvivors was acceptable during derivation and internal validation (C statistic, 0.722 and 0.731, respectively) as was model calibration during derivation (Hosmer Lemeshow [HL] $P=0.47$). Model performance was reasonable in the external validation cohort (predicted mortality, 4.9%; actual mortality, 4.3%; $R^2=0.95$; C statistic, 0.68; HL $P=0.48$). Adding the donor-related variables of age and ischemic time to the model improved its performance in both the model derivation (C statistic, 0.742; HL $P=0.70$) and the external validation (C statistic, 0.695; HL $P=0.42$) cohorts.

Conclusions—The proposed model allows risk stratification of HT candidates for early posttransplant mortality and may be useful in counseling patients with regard to their posttransplant prognosis. The model with additional donor-related variables may be useful during donor selection. **(*Circ Heart Fail*. 2012;5:259-266.)**

Key Words: transplantation ■ survival ■ risk factors ■ decision support techniques ■ heart failure

Despite rapid progress in ventricular assist device (VAD) technology during the past decade,[1–3] heart transplantation (HT) remains the definitive therapy for patients in advanced heart failure.[4] The early posttransplant period, in particular the hospitalization associated with HT surgery, is associated with a higher risk of death compared with any other period after HT.[4,5] This risk is heterogeneous and related to several recipient factors, such as age, heart failure severity, and the presence and absence of end-organ dysfunction at transplant.[4,5]

Clinical Perspective on p 266

Risk prediction has been the bedrock of preventive cardiovascular medicine since the publication of the Framingham Risk Score.[6–10] It has allowed individualized medicine based on predicted cardiovascular risk, has formed the scientific basis for health-related guidelines and public policies, and has helped to provide focus for innovation in primary and secondary prevention.[11–15] In recent years, risk prediction has been applied to other cardiovascular settings, such as to predict risk of death in ambulatory patients with heart failure,[16–18] to predict risk of perioperative cardiac complications after noncardiac surgery,[19] and to predict risk of in-hospital mortality in patients undergoing cardiac surgery.[20,21] Although risk factors for early posttransplant mortality after HT have been previously described,[4,5] a quantitative risk prediction model has not been developed and validated. In the present study, we sought to develop and validate a risk prediction model for posttransplant in-hospital mortality in adult recipients of primary HT using data from HT recipients in the United States.

Methods

Study Population

We identified all subjects aged ≥18 years in the Organ Procurement and Transplantation Network (OPTN) database who underwent their first HT in the United States between January 1, 2007, and June 30, 2009. Baseline variables in this model derivation cohort were used to develop a risk prediction model for posttransplant in-hospital mortality. The OPTN database includes demographic and clinical infor-

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mation on all HT recipients in the United States submitted by their transplant centers and is provided to investigators as deidentified data. The Health Resources and Services Administration, US Department of Health and Human Services, provides oversight of the activities of the OPTN contractor, the United Network of Organ Sharing (UNOS). We excluded patients who underwent an HT or a multiorgan transplantation. All study subjects were followed until hospital discharge or death.

For external validation, we assessed the model's performance in an independent prospective cohort of HT recipients comprising all patients who underwent a primary HT in the United States from July 1, 2009, to October 31, 2010 (external validation cohort), using the OPTN data. Vital status was available in all subjects in the study, and discharge date was available in all but 11 subjects.

Study Definitions

All baseline recipient variables were assessed at the time of HT. Cardiac diagnosis was assessed as mutually exclusive categories of dilated cardiomyopathy, ischemic cardiomyopathy, restrictive cardiomyopathy, hypertrophic cardiomyopathy, valvular heart disease, congenital heart disease, and other. Mechanical support at the time of HT was assessed as mutually exclusive categories of extracorporeal membrane oxygenation, total artificial heart, biventricular assist device (BIVAD), pulsatile left ventricular assist device (LVAD), and continuous-flow LVAD. Ventilator support, inotrope support, implantable cardioverter-defibrillator, and intraaortic balloon pump were assessed as dichotomous (yes/no) variables. Inotrope support was defined as use of any intravenous inotrope at the time of HT. Ventilator support was defined as respiratory support using intubation and invasive ventilation. Listing status was defined according to UNOS definitions.[22]

Patient race and ethnicity was recorded as reported by the transplant center and analyzed as white, black, Hispanic, or other. Renal function was analyzed variously as a dichotomous variable (plasma creatinine level >1.5 mg/dL), as a continuous variable (glomerular filtration rate [GFR] estimated using the Modification of Diet in Renal Disease equation,[23,24] and as GFR categories 30–59 mL/min per 1.73 m^2, <30 mL/min per 1.73 m^2, and dialysis versus ≥ 60 mL/min per 1.73 m^2). Total serum bilirubin, a marker of hepatic function in patients with heart failure, was analyzed as a continuous variable and as 3 mutually exclusive categories (>2.5 mg/dL, 1.0–2.5 mg/dL, and <1.0 mg/dL). Missing values of GFR (1% of subjects) and total serum bilirubin (4% of subjects) were imputed using multivariable linear regression analyses. Variables used for imputation were age, sex, diagnosis, patient support at listing (including inotropes, ventilator, intraaortic balloon pump, mechanical support), patient support at transplant, GFR at listing, total serum bilirubin at transplant (to impute GFR at transplant), and GFR at transplant (to impute total serum bilirubin at transplant).

The primary end point was in-hospital mortality (ie, death before discharge after HT surgery). Subjects who died before hospital discharge were considered to have reached the primary end point.

Statistical Analysis

Summary data are presented as median (25th, 75th percentile) or number (percent). Baseline characteristics between patients in the model derivation cohort and in the external validation cohort were compared using the χ^2 test for categorical variables and the Wilcoxon rank sum test for continuous variables.

We used multivariable logistic regression to derive the best-fitting risk prediction model for in-hospital mortality using forward selection. All recipient variables in Table 1 were considered. Variables that were statistically significant at the 0.05 level, improved the ability of the model to discriminate hospital survivors from nonsurvivors, and added to the overall likelihood ratio χ^2 were retained in the final model. The ability of the model to discriminate hospital survivors from nonsurvivors was quantified using the area under the receiver operating characteristic curve (C statistic). Model calibration was assessed using the Hosmer-Lemeshow (HL) goodness-of-fit test. The final model was used to estimate the risk of in-hospital death in patients with specific sets of covariates. The model was internally validated using a bootstrapping technique (200 random samples, 4248 patients in each sample with replacement). Model performance was then assessed in the external validation cohort of HT recipients (July 2009–October 2010), using the C statistic to quantify model discrimination and the HL goodness-of-fit test to assess model calibration.

The data were analyzed using SAS version 9.1 and STATA version 11.0 statistical software. The authors had full access to the data and take responsibility for their integrity. All authors have read and agreed to the manuscript as written.

Results

Study Population

Between January 2007 and June 2009, 4558 subjects aged ≥ 18 years underwent an HT in the United States. Of these, 157 underwent a heart retransplant, and 153 underwent multiorgan transplant. The remaining 4248 subjects formed the model derivation cohort. A second cohort of 2346 subjects who received an HT during July 2009 to October 2010 and had similar inclusion and exclusion criteria to the model derivation cohort served as the external validation cohort. Baseline characteristics at transplant among HT recipients in the model derivation and the external validation cohorts are compared in Table 1.

The median age of the model derivation cohort was 55 years (45–61 years), 14% were aged ≥ 65 years, 76% were men, 48% had dilated cardiomyopathy, 41% had ischemic cardiomyopathy, 69% were white, and 16% had Medicaid. Overall, 27% of subjects in the model derivation cohort were on mechanical support at the time of HT (continuous-flow LVAD, 12%; pulsatile LVAD, 10%; BIVAD, 4%; total artificial heart, 1%; extracorporeal membrane oxygenation, 1%). Estimated GFR at the time of transplant was ≥ 60 mL/min per 1.73 m^2 in 55%, 30 to 59 mL/min per 1.73 m^2 in 39%, and <30 mL/min per 1.73 m^2 in 4%; 2% of HT recipients were on dialysis. Total serum bilirubin was <1.0 mg/dL in 56%, 1.0 to 2.5 mg/dL in 36%, and >2.5 in 8% mg/dL of HT recipients.

The percentage of HT recipients on mechanical support at the time of transplant was higher in the external validation cohort than in the model derivation cohort (37% versus 27%, $P<0.001$). Compared to the model derivation cohort, HT recipients in the external validation cohort were less likely to be supported on inotropes (39% versus 44%, $P<0.001$), less likely to be supported on a pulsatile LVAD (3% versus 10%), and more likely to be supported on a continuous-flow LVAD (29% versus 12%, $P<0.001$ for distribution of mechanical support). Other statistically significant differences between the 2 cohorts appeared to be due to large sample size of groups and did not appear to be clinically important (Table 1).

Model Derivation and Internal Validation

There were 201 posttransplant deaths before hospital discharge (4.7% of HT recipients) in the model derivation cohort. In univariate analysis, posttransplant in-hospital mortality was associated with age, cardiac diagnosis, mean pulmonary artery pressure, pulmonary vascular resistance, type of mechanical support, intraaortic balloon pump, ventilator support, recent treatment with intravenous antibiotics,

Table 1. Baseline Characteristics of Development and Validation Cohorts

Recipient Variable	Model Derivation Cohort	External Validation Cohort	*P*
No. recipients	4248	2346	
Age at transplant, y	55 (45, 61)	56 (46, 62)	0.002
Age at transplant			0.04
18–39 y	691 (16)	372 (16)	
40–54 y	1414 (33)	714 (30)	
55–64 y	1543 (36)	885 (38)	
≥65 y	600 (14)	375 (16)	
Female sex	1013 (24)	550 (23)	0.72
Height, cm	175 (168, 180)	175 (168, 180)	0.45
BMI			0.17
<25 kg/m^2	1567 (37)	826 (35)	
25–29.9 kg/m^2	1590 (37)	918 (39)	
30–34.9 kg/m^2	849 (20)	447 (19)	
≥35 kg/m^2	242 (6)	155 (7)	
Diagnosis			<0.001
Dilated CM	2030 (48)	1084 (46)	
Ischemic CM	1742 (41)	924 (39)	
Hypertrophic CM	93 (2)	40 (2)	
Restrictive CM	89 (2)	70 (3)	
Valvular CM	83 (2)	40 (2)	
Congenital heart disease	90 (2)	64 (3)	
Other	121 (3)	124 (5)	
Diabetes	1120 (26)	593 (25)	0.31
Mean PAP			0.04
>30 mm Hg	1648 (39)	895 (38)	
≤30 mm Hg	2113 (50)	1225 (52)	
Not reported	487 (11)	226 (10)	
PVR			0.003
<3 Wood units	2622 (62)	1528 (65)	
≥3 Wood units	1103 (26)	589 (25)	
Not reported	523 (12)	229 (10)	
Mechanical support			<0.001
ECMO	24 (1)	15 (1)	
Total artificial heart	36 (1)	28 (1)	
BIVAD	183 (4)	61 (3)	
Pulsatile LVAD	408 (10)	81 (3)	
Continuous-flow LVAD	501 (12)	674 (29)	
None	3096 (73)	1487 (63)	
IABP	252 (6)	112 (5)	0.05
ICD	3345 (79)	1911 (81)	0.009
Ventilator	103 (2)	67 (3)	0.29
Inotropes	1865 (44)	920 (39)	<0.001
Listing status[22]			0.004
1A	896 (21)	510 (22)	
1B	1620 (38)	982 (42)	
2	1601 (38)	794 (34)	
Missing	131 (3)	60 (3)	
Dialysis before transplant	97 (2)	47 (2)	0.46
Serum creatinine			0.01
<1.5 mg/dL	3120 (73)	1772 (76)	
≥1.5 mg/dL	1102 (26)	570 (24)	
Missing	26 (1)	4 (<1)	
GFR (MDRD)			0.10
≥60 mL/min per 1.73 m^2	2357 (55)	1356 (58)	
30–59 mL/min per 1.73 m^2	1638 (39)	878 (37)	
<30 mL/min per 1.73 m^2	156 (4)	65 (3)	
Dialysis	97 (2)	47 (2)	
Serum bilirubin			0.002
<1.0 mg/dL	2374 (56)	1397 (60)	
1.0–2.5 mg/dL	1528 (36)	805 (34)	
>2.5 mg/dL	346 (8)	144 (6)	
IV antibiotic treatment <2 wk before transplant	426 (10)	250 (11)	0.03
Race/ethnicity			0.89
White	2946 (69)	1635 (70)	
Black	825 (19)	439 (19)	
Hispanic	320 (8)	184 (8)	
Other	157 (4)	88 (4)	
Medicaid insurance	676 (16)	332 (14)	0.06
Donor age			
<40 y	3089 (73)	1689 (72)	0.76
40–54 y	1018 (24)	581 (25)	
≥55 y	141 (3)	76 (3)	
Donor ischemic time			
<2.5 h	926 (22)	569 (24)	0.07
2.5–3.2 h	1144 (27)	657 (28)	
3.3–3.9 h	1107 (26%)	570 (24%)	
≥4.0 h	946 (22%)	482 (21%)	
Not reported	125 (3%)	68 (3%)	

Data are presented as n (%) or median (25th, 75th percentile).

BMI indicates body mass index; CM, cardiomyopathy; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; ECMO, extracorporeal membrane oxygenation; BIVAD, biventricular assist device; LVAD, left ventricular assist device; IABP, intraaortic balloon pump; ICD, implantable cardioverter-defibrillator; GFR, glomerular filtration rate; MDRD, Modification of Diet in Renal disease; IV, intravenous.

renal function, and total serum bilirubin at the time of transplant (online-only Data Supplement Table I).

The best-fitting risk prediction model based on recipient characteristics comprised the following 6 categorical variables (Table 2): (1) age at transplant (≥65 years [odds ratio (OR), 1.89] versus age <65 years), (2) cardiac diagnosis (ischemic cardiomyopathy/other [OR, 1.44], hypertrophic/restrictive car-

Table 2. Risk Prediction Model of Posttransplant In-Hospital Mortality Using Recipient Variables

Recipient Variable	Coefficient	OR	95% CI	*P*
Age at transplant				0.001
18–64 y	. . .	1.00	. . .	
≥65 y	0.6376	1.89	(1.30–2.75)	
Diagnosis				0.001
Dilated/valvular CM	. . .	1.00	. . .	
Ischemic CM/other	0.3649	1.44	(1.05–1.98)	
Hypertrophic/ restrictive CM	0.7698	2.16	(1.11–4.21)	
Congenital heart disease	1.4295	4.18	(1.93–9.03)	
Mechanical support				<0.001
ECMO	1.7911	6.00	(2.11–17.0)	
Total artificial heart/BIVAD	1.4345	4.20	(2.65–6.66)	
LVAD	0.7036	2.02	(1.42–2.88)	
None	. . .	1.00	. . .	
Ventilator	1.2515	3.50	(1.96–6.22)	<0.001
GFR				<0.001
≥60 mL/min per 1.73 m^2	. . .	1.00	. . .	
30–59 mL/min per 1.73 m^2	0.5554	1.74	(1.27–2.40)	
<30 mL/min per 1.73 m^2	0.8344	2.30	(1.22–4.35)	
Dialysis	1.3323	3.79	(2.01–7.13)	
Total serum bilirubin				0.001
<1.0 mg/dL	. . .	1.00	. . .	
1.0–2.5 mg/dL	0.2866	1.33	(0.96–1.84)	
>2.5	0.9074	2.48	(1.59–3.86)	

The probability of posttransplant in-hospital mortality may be calculated by using the coefficients provided (see Results section for the equation); the intercept is −4.2973.

OR indicates odds ratio; CM, cardiomyopathy; ECMO, extracorporeal membrane oxygenation; BIVAD, biventricular assist device; LVAD, left ventricular assist device; GFR, glomerular filtration rate.

diomyopathy [OR, 2.16], and congenital heart disease [OR, 4.18] versus dilated cardiomyopathy/valvular heart disease), (3) presence and type of mechanical support (extracorporeal membrane oxygenation [OR, 6.0], total artificial heart/BIVAD [OR, 4.20], and LVAD [OR, 2.02] versus none), (4) ventilator support (OR, 3.50) versus none, (5) estimated GFR (30–59 mL/min per 1.73 m^2 [OR, 1.74], <30 mL/min per 1.73 m^2 [OR, 2.30], and dialysis [OR, 3.79] versus >60 mL/min per 1.73 m^2), and (6) total serum bilirubin (>2.5 mg/dL [OR, 2.48], 1.0–2.5 mg/dL [OR, 1.33] versus <1.0 mg/dL). Figure 1 illustrates the incremental contribution of recipient variables to the model receiver operating characteristic curve index (Figure 1A) and to the likelihood ratio χ^2 statistic (Figure 1B). The overall model was highly significant (likelihood ratio χ^2 statistic, 140.5). The model's ability to discriminate HT recipients who died before hospital discharge and those who survived to discharge was

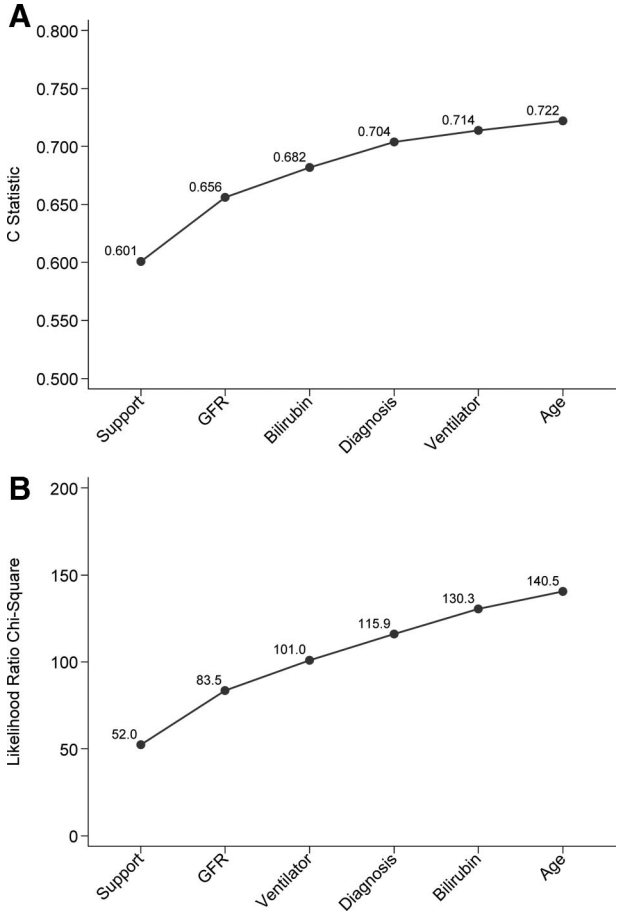

Figure 1. A, Contribution of recipient variables to the model receiver operating characteristic curve. **B**, Contribution of recipient variables to the likelihood ratio χ^2. GFR indicates glomerular filtration rate.

acceptable (C statistic, 0.722), and it calibrated the risk of mortality well (HL goodness-of-fit $P=0.47$) (Figure 2A).

Based on the model, the probability of posttransplant in-hospital mortality in a patient receiving an HT may be calculated as $P=(X/X+1)$, where X is calculated as X=Exp (intercept+coefficient for each of the 6 variables as it applies to the patient in Table 2). Based on the model, the predicted risk of in-hospital mortality varied from 1.3% in the lowest-risk recipient in the model derivation cohort (age 18–64 years, dilated cardiomyopathy, not on mechanical or ventilator support, GFR ≥60 mL/min per 1.73 m^2, bilirubin <1.0 mg/dL) to 70.1% in the highest-risk recipient in the cohort (age ≥65 years, ischemic cardiomyopathy, on BIVAD and ventilator, GFR 30–59 mL/min per 1.73 m^2, bilirubin >2.5 mg/dL). The predicted risk of in-hospital mortality in subjects in the highest-risk decile was 15.5% (Figure 2A). The effect of worsening renal and hepatic function on predicted risk of in-hospital mortality in patients with dilated and ischemic cardiomyopathy on no mechanical support, in patients on LVAD support, and in patients on BIVAD support is illustrated in Figure 3A through 3C, respectively. On internal validation by bootstrapping, the area under the receiver operating characteristic curve in repeated samples ranged from 0.698 to 0.765 (mean, 0.731; 95% CI, 0.729–0.733).

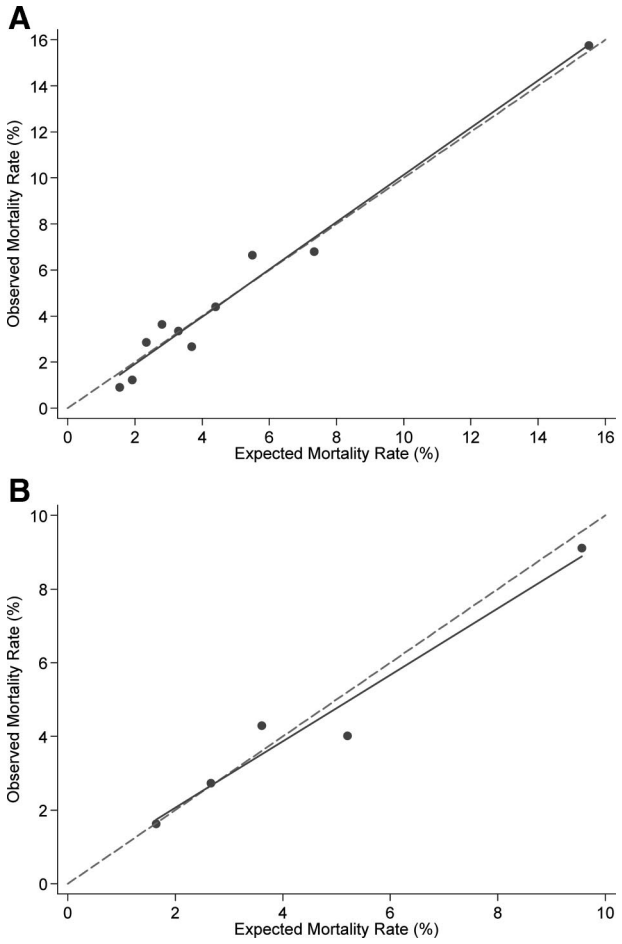

Figure 2. Predicted versus observed posttransplant in-hospital mortality. **A**, Derivation model cohort. **B**, External validation cohort. The dotted line represents the line of identity, and the points represent deciles (**A**) or quintiles (chosen because of fewer events) (**B**) of risk in the corresponding cohorts.

External Validation

Application of the risk prediction model to the external validation cohort predicted a posttransplant in-hospital mortality of 4.9%. Of the 2346 HT recipients in this cohort, 101 (4.3%) died before hospital discharge. Model performance was acceptable in the external validation cohort (R^2=0.95 by quintiles of risk; C statistic, 0.68; HL P=0.48) (Figure 2B).

Risk Prediction With Addition of Donor Variables

The addition of the 2 donor-related variables of age (>55 years [OR, 2.29] and 40–55 years [OR, 1.53] versus <40 years) and donor ischemic time (>4.5 hours [OR 1.91] versus ≤4.5 hours) to the recipient-based model in Table 2 improved model performance in both the model derivation (Table 3) (C statistic, 0.742; HL P=0.70; P value for comparison to C statistic for Table 2 model, 0.02) and the external validation (C statistic, 0.695; HL P=0.42) cohorts.

Discussion

In this study, we developed and validated a model to predict the risk of early in-hospital mortality after HT using easily available variables at the time of transplant. Although the overall hospital mortality after HT surgery is <5% in the United States, the risk of death varies widely. The model allows risk stratification based on the following 6 recipient variables at the time of transplant: age; diagnosis; mechanical support; and the presence and severity of respiratory, renal, and hepatic dysfunction (assessed as mechanical ventilation, estimated GFR, and serum bilirubin levels). The ability of the model to discriminate hospital survivors and nonsurvivors (based on area under the receiver-operating characteristic curve [C statistic, 0.72]) and its predictive accuracy (based on model calibration) appeared acceptable, as was its performance during internal and external validation. The model has potential utility during clinical decision-making and during patient counseling at the time of listing and while awaiting HT. Adding 2 donor-related variables (age and ischemic time) to the model further improved its performance and may be useful during donor selection in conjunction with recipient characteristics.

Weiss et al[25] recently reported a risk score to predict 1-year mortality after HT using 12 recipient variables. The score was developed using 80% of US recipients from 1997 to 2008 (C statistic, 0.65) and cross-validated it in the remaining 20%. The present model differs importantly by its focus on posttransplant in-hospital mortality as the primary end point, use of a more recent US cohort (2007–2009) for model derivation, differentiation of patients on VADs into those on LVAD and BIVAD, and validation of the model internally (using bootstrapping) as well as externally (in a prospective cohort from 2009–2010). Although most of the risk factors in the model have been previously linked with higher post-HT mortality,[4,5] the goal of the present study was to quantify risk for well-defined cohorts of HT candidates. Other published models in heart failure,[16,18] though useful in predicting prognosis on standard medical therapy, do not stratify patients based on their post-HT outcome.

The model presented here aims to complement current models and to improve on the 30-day post-HT mortality model used by the Scientific Registry of Transplant Recipients (SRTR) for risk adjustment when evaluating center performance.[26] In contrast to the SRTR model, the present model does not treat missing values of a variable as a risk factor and has a higher C statistic, despite being more parsimonious than the SRTR model. The SRTR model assigns a uniform relative risk to all HT recipients with cardiomyopathy and to all recipients transplanted from a VAD, findings that are not consistent with clinical observation. We found a higher risk of early hospital mortality in patients with restrictive or hypertrophic cardiomyopathy compared with those with dilated cardiomyopathy. Furthermore, categorizing the type of mechanical support improved risk stratification by perhaps acting as a surrogate for the severity of heart failure and because of differences in morbidity associated with different devices during the waiting and posttransplant periods.[27] We also found that characterizing renal function based on GFR categories led to better risk stratification of transplant recipients than using serum creatinine level, for which interpretation is known to be affected by recipient size, sex, and race.[23,28] Conceptually, the present model is similar to the EuroSCORE (European System for Cardiac Operative Risk Evaluation) model insofar as it focuses on early hospital mortality after major cardiac surgery when the risk of death is the highest.[21] In contrast to other cardiac surgeries, however, the risk of post-HT mortality among the highest-risk candidates awaiting HT may be rather dynamic

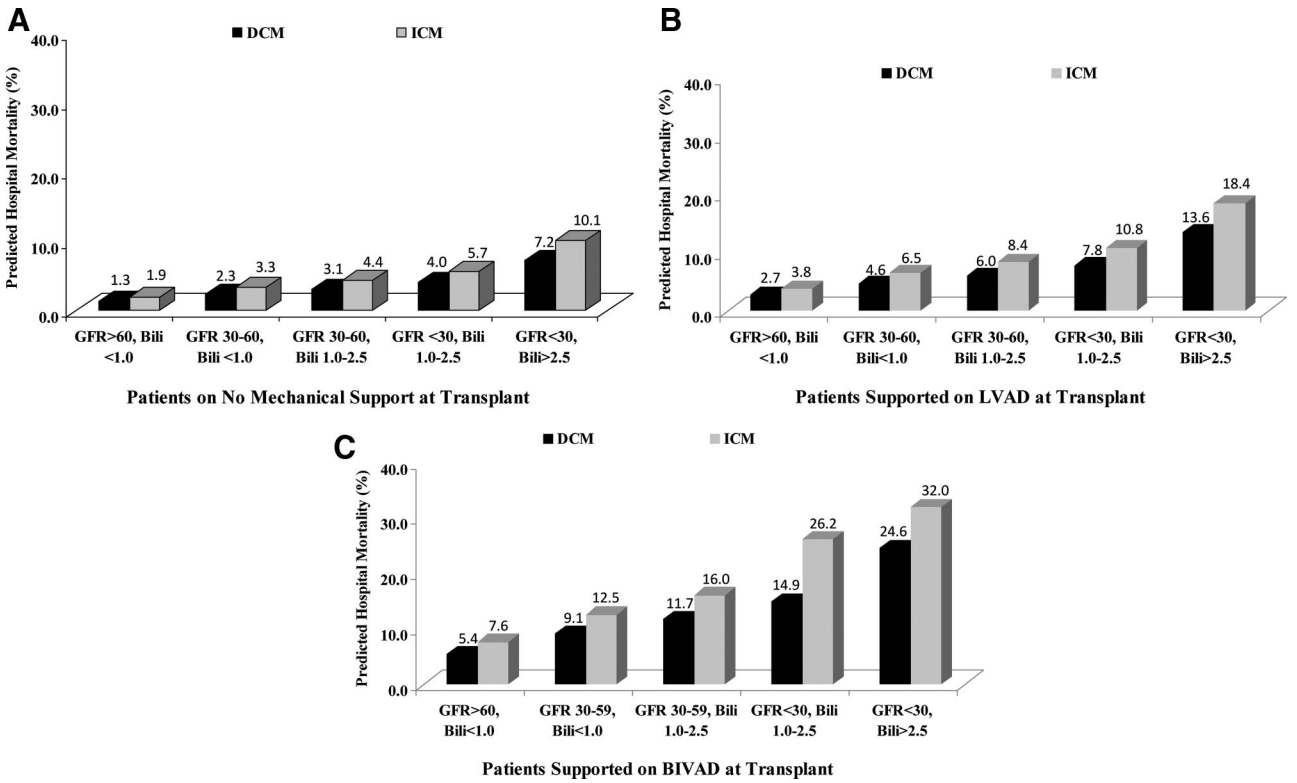

Figure 3. Effect of worsening end-organ dysfunction on predicted posttransplant in-hospital mortality in recipients aged 18 to 64 years with DCM and ICM at the time of transplant. **A**, Recipients on no mechanical support. **B**, Recipients supported on an LVAD. **C**, Recipients supported on a BIVAD. Bili indicates bilirubin; BIVAD, biventricular assist device; DCM, dilated cardiomyopathy; GFR, glomerular filtration rate; ICM, ischemic cardiomyopathy; LVAD, left ventricular assist device.

because they may be especially prone to developing end-organ dysfunction with worsening of heart failure or with complications related to invasive monitoring and management.

We found it interesting that although recent data and clinical practice favor continuous-flow LVADs over pulsatile LVADs in patients with heart failure,[29,30] we could find no difference in early posttransplant mortality for patients transplanted from a continuous-flow LVAD versus a pulsatile LVAD. In fact, we originally developed the model using separate terms for continuous-flow and pulsatile devices, assuming the outcomes might be different, but because of near-identical risks for patients supported on a pulsatile LVAD (OR, 2.00; 95% CI, 1.23–3.25) and those supported on a continuous-flow LVAD (OR, 2.04; 95% CI, 1.33–3.15), we merged these support categories in the final model. Similarly, the decision to merge recipients on BIVAD and total artificial heart into a single category, recipients aged <65 years into a single age category, and some of the diagnostic categories in the final model was based on our analysis that showed a similar risk of posttransplant death in these groups during model development. It should be noted that although patients on LVAD at the time of HT have higher early posttransplant mortality than those on no mechanical support (at similar levels of end-organ dysfunction), the predicted risk of early posttransplant mortality in a patient on LVAD with normal end-organ function at the time of HT is lower than that of a patient who is not on mechanical support but has mild renal and hepatic dysfunction (Figure 3).

The model has several potential applications in clinical practice. For example, risk-stratification based on predicted early posttransplant mortality may be useful when deciding about the candidacy and timing of HT listing in a patient with heart failure. A comparison of predicted posttransplant mortality with predicted survival on standard medical therapy may allow a more objective assessment of HT benefit than is currently feasible. Second, the model may be used to counsel patients regarding their expected posttransplant risk and to illustrate the dynamic nature of this risk with worsening heart failure and with changes in end-organ function. Third, the model with both recipient and donor variables may be useful during donor selection, particularly for high-risk candidates. Fourth, because randomized studies usually follow hypothesis-generating observations, the predicted risk of posttransplant mortality based on baseline variables may allow classification of HT recipients into homogeneous risk strata, which may be useful for comparing treatments using an observational study design. Finally, risk adjustment for severity of heart failure based on predicted post-HT outcomes may be used to assess HT centers for quality of care, resource utilization, and patient outcomes.

This study has several limitations. First, the model was developed using a retrospective analysis of a national database. The quality control of submitted data may be variable among centers and perhaps not as rigorous as for data collected during a controlled clinical trial. However, because these data are collected prospectively at the time of candidate listing and at the time of HT, are used by UNOS for real-time organ allocation

Table 3. Risk Prediction Model of Posttransplant In-Hospital Mortality Using Recipient and Donor Variables

Variable	Coefficient	OR	95% CI	*P*
Age at transplant				0.002
18–64 y	. . .	1.00	. . .	
≥65 y	0.6091	1.84	(1.26–2.68)	
Diagnosis				0.002
Dilated/valvular CM	. . .	1.00	. . .	
Ischemic CM/other	0.3571	1.43	(1.04–1.96)	
Hypertrophic/ restrictive CM	0.7139	2.04	(1.04–4.01)	
Congenital heart disease	1.3968	4.04	(1.86–8.79)	
Mechanical support				<0.001
ECMO	1.6930	5.44	(1.87–15.8)	
Total artificial heart/BIVAD	1.4079	4.09	(2.56–6.52)	
LVAD	0.7208	2.06	(1.44–2.94)	
None	. . .	1.00	. . .	
Ventilator	1.2825	3.61	(2.02–6.44)	<0.001
GFR				<0.001
≥60 mL/min per 1.73 m^2	. . .	1.00	. . .	
30–59 mL/min per 1.73 m^2	0.5174	1.68	(1.22–2.31)	
<30 mL/min per 1.73 m^2	0.7943	2.21	(1.17–4.18)	
Dialysis	1.3332	3.79	(2.01–7.17)	
Total serum bilirubin				0.001
<1.0 mg/dL	. . .	1.00	. . .	
1.0–2.5 mg/dL	0.2783	1.32	(0.96–1.83)	
>2.5	0.8905	2.44	(1.55–3.82)	
Donor age				0.006
<40 y	. . .	1.00	. . .	
40–54 y	0.4221	1.53	(1.10–2.11)	
≥55 y	0.8176	2.27	(1.20–4.27)	
Ischemic time				<0.001
<4.5 h	. . .	1.00	. . .	
≥4.5 h	0.6477	1.91	(1.34–2.72)	

The probability of posttransplant in-hospital mortality may be calculated using the coefficients provided (see Results section for the equation); the intercept is −4.5310.

OR indicates odds ratio; CM, cardiomyopathy; ECMO, extracorporeal membrane oxygenation; BIVAD, biventricular assist device; LVAD, left ventricular assist device; GFR, glomerular filtration rate.

and for subsequent evaluation of center performance, and are subject to periodic audits by UNOS, safeguards to data quality are to be expected. Second, the results of the study may not be applicable to patients undergoing a second HT or a multiorgan transplant because additional risks exist for these patients. We chose not to include these patient groups in the analysis because of their small number. Finally, heart failure management, in particular the field of ventricular mechanical support, continues to advance rapidly. The model may need to be updated periodically as the overall posttransplant outcomes improve with time and risk factors change with advances in clinical practice.

In conclusion, we have described and validated a risk prediction model of early in-hospital posttransplant mortality based on easily available variables at the time of transplant. The model with only recipient variables has potential utility during decision-making for HT candidacy and in counseling patients regarding their posttransplant prognosis. The model with additional donor variables may be useful during donor selection when used in conjunction with recipient variables. Further studies to assess the performance and predictive accuracy of this model in other countries and regions are needed.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The risk of death following heart transplantation is higher during the hospitalization for transplant surgery than at any other time after transplant. The risk is not uniform in all transplant recipients, however, and is related to recipient factors such as age, heart failure severity, and the presence and absence of end-organ dysfunction at the time of transplant. In this study, we derived a model to predict early posttransplant in-hospital mortality using data from 4248 adult patients who underwent their first heart transplant in the United States between January 2007 and June 2009. We used a bootstrapping statistical technique to validate the model internally (in patients from whom the model was developed) and then applied the model to 2346 patients receiving heart transplants between July 2009 and October 2010 to test its predictive performance externally. Overall, hospital mortality after transplant was 4.7% in the model derivation group and 4.3% in the external validation group. The model that best predicted posttransplant mortality was based on 6 variables at the time of transplant: patient age, diagnosis, type of mechanical support, ventilator support, renal function, and serum bilirubin level. Model performance was acceptable during its derivation, internal validation, and external validation. Adding donor age and ischemic time to the model improved its overall performance. The model may be used in counseling patients regarding their posttransplant prognosis. The model with additional donor-related variables may be useful during donor selection.