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Is it time for a cardiac allocation score? First results from the Eurotransplant pilot study on a survival benefit–based heart allocation

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BACKGROUND: Patients awaiting heart transplantation in Eurotransplant are prioritized by waiting time and medical urgency. To reduce mortality, the introduction of post-transplant survival in an allocation model based on the concept of survival benefit might be more appropriate. The aim of this study was to assess the prognostic accuracy of the Heart Failure Survival Score (HFSS), the Seattle Heart Failure Model (SHFM), the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) model, and the Index for Mortality Prediction After Cardiac Transplantation (IMPACT) score for predicting mortality.

METHODS: The HFSS, SHFM, the adapted SHFM, and the INTERMACS model were evaluated for predicting waiting list mortality among heart transplant candidates, and the IMPACT score was tested for predicting post-transplant mortality in separate Cox regression models. Included were the 448 adult heart transplant candidates listed for an urgent status between October 2010 and June 2011 in Eurotransplant. A Cardiac Allocation Score (CAS) was calculated based on the estimated survival times as predicted by the scores. All analyses were performed for the total cohort and separately for ventricular assist device (VAD) and non-VAD patients.

RESULTS: Mortality on the waiting list could significantly be predicted in the non-VAD cohort by HFSS ($p = 0.005$) and SHFM ($p < 0.0001$) and after transplant by IMPACT ($p < 0.0001$). None of the tested scores could predict mortality among VAD-supported patients.

CONCLUSIONS: In non-VAD patients, the HFSS, SHFM, and IMPACT provide accurate risk stratification. Further studies will reveal whether these models should be considered as the basis for a new heart allocation policy in Eurotransplant.
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The current heart allocation policy in Eurotransplant (ET) is ruled by medical urgency and waiting time.[1] Patients with a high urgent status are prioritized over urgent and elective patients, and within the same urgency tier, are sorted by waiting time. While in Germany in recent years, the number

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of available donor hearts decreased by 25%, while the size of the waiting list doubled. The average waiting time on the high urgency list currently is 6 months, and 90% of all heart transplants in Germany are performed in high-urgency patients.[2]

As a consequence, donor hearts are assigned to very sick patients who are inherently more likely to have a low expected post-transplant outcome, which practice could be considered a non-optimal use of donor organs. Designing and achieving a fair and just allocation scheme that upholds all professional ethical standards is hence a moral necessity.

The aim of this study was to design a scheme that would balance waiting list and post-transplant mortality, similar to the Lung Allocation Score (LAS) system, for lung transplantation.[3] Existing risk scores created on external data sets were selected and tested on the ET cohort by assessing their potential for predicting waiting list and post-transplant mortality.

Methods

Study population

Included were all heart-only transplant candidates, aged ≥16 years, for whom a first high urgency or urgent request was submitted to ET in the period October 6, 2010, until June 5, 2011. All patients were monitored from the time of the request until transplantation, death on the waiting list, or closure date (September 6, 2011), resulting in a minimum of follow-up of 3 months. To have a complete 3-month follow-up after transplantation, patients were monitored until December 6, 2011.

Waiting list mortality models

Several models for predicting mortality among an advanced heart failure (AHF) population have been published.[4,5] We validated 4 different models on our cohort. The Heart Failure Survival Score (HFSS) has repeatedly been shown to be a significant predictor of waiting list mortality in ET.[6–8] The Seattle Heart Failure Model (SHFM) includes data on medication and mechanical support device use.[9] A single-center study showed both scores provided accurate and comparable risk stratification in patients referred for heart transplantation.[10] The adapted SHFM, with the addition of inotrope use and intra-aortic balloon pump and/or ventilator, was the best predictor of mortality in a single-center cohort of patients receiving continuous-flow left ventricular assist device (LVAD) support.[11] Finally, the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) score was validated on our sub-set of VAD patients.[12]

Post-transplant mortality models

There is a striking shortage in well-designed studies on prognostic risk indices for mortality after heart transplantation. At the time this study was undertaken, only 3 studies on clinical risk scores were identified. The study by Segovia et al[13] focused only on predicting primary graft failure. Hong et al[14] created a preoperative risk stratification score predicting graft loss at 1 year but incorporated information on cold ischemia time, which renders the model unsuitable for risk stratification in the phase before the transplantation. In our search for a model that could be used for risk stratification at the time of organ allocation, we decided to validate the Index for Mortality Prediction After Cardiac Transplantation (IMPACT) model.[15]

Statistics

The relationships among the HFSS, the SHFM, the adapted SHFM, and the INTERMACS models and the actual waiting list mortality were analyzed in a Cox model for the total cohort and separately for VAD and non-VAD transplant candidates. The IMPACT model was tested for predicting post-transplant mortality in the total study population and separately in the VAD and non-VAD cohorts. The discriminative capacities of the models were assessed by the C-index.[16]

Waiting list time was counted from the date of the first high-urgent/urgent request. To allow comparisons and validations, our patients were grouped into similar classes, as previously defined by several of the models. The probability of waiting list mortality was calculated using competing risk estimation.[17]

Two scores were calculated for each patient: the SHFM score, reflecting the patient's risk of dying on the waiting list, and the IMPACT score, reflecting the risk of dying after transplantation. The number of days a patient was expected to remain alive on the waiting list was calculated by weighing a baseline population risk with the patient's risk as determined by the SHFM score. The number of expected survival days after transplantation was calculated by weighing a baseline risk with the patient's risk as determined by the IMPACT score. Then, the Cardiac Allocation Score (CAS) was obtained by subtracting twice the number of expected days on the waiting list from the number of expected days after transplantation. Hence, CAS is a combination of the 2 scores, such that patients with a high risk of dying without a transplant are prioritized, but only if they have a good chance of survival after the allograft is transplanted.

Results

Study cohort

A request for a first high-urgent or urgent heart transplant status was submitted to ET for 494 patients in the study period. The study excluded 7 patients receiving total artificial heart support, 2 listed for a combined heart and liver transplant, and 37 children, yielding a study cohort of 448 patients. Of these, 49 patients (11%) died on the waiting list, 189 (42%) received a heart allograft, 1 (0.2%) was delisted, and 209 (47%) were still waiting. Notably, 26% ($n = 115$) of the candidates were being supported by a VAD at time of listing, and 15% were receiving extracorporeal support (Table 1).

Demographic statistics

Compared with the patients who received a transplant, those who died on the waiting list had a higher serum creatinine ($p = 0.036$), were more in need of extracorporal support ($p = 0.002$), were more likely to have a VAD ($p = 0.005$), and had a higher SHFM value ($p = 0.03$; Table 1).