A NEW PREDICTION MODEL FOR QUANTIFYING MORTALITY RISK IN CHD PATIENTS AFTER HEART TRANSPLANT

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INTRODUCTION

Mortality after heart transplant (HTx) in congenital heart disease (CHD) patients remains high. Accurate assessment of mortality risk is crucial to ensure optimal outcomes in CHD patients being considered for HTx .

The objectives of this study were:

1 - Develop and validate a short-term mortality risk score for adolescent and adult CHD (ACHD) patients following primary HTx.

2 - Compare the newly developed risk score with the Index for Mortality Prediction After Cardiac Transplantation (IMPACT), a non-CHD HTx risk score[1].

METHODS

Data was obtained from registrations from the International Society for Heart and Lung Transplantation (ISHLT) with CHD who received primary heart transplants between 2005 – 2013 at age > 10 years with follow-up through 2015.

For prognostic model development, CHD HTx recipients were randomly divided into training (n=966, 70%) and validation samples (n=415, 30%). Survival random forest models in the derivation cohort identified the 5 most important clinical variables for post HTx survival: gender mismatch, bilirubin, creatinine clearance, recipient age and recipient/donor age ratio. A CHD risk score (CRS) was created based upon the association of each clinical variable with mortality.

The CRS was validated in terms of discriminatory power and calibration on the validation sample. Survival among low (score <10%), medium and high risk (>20%) patients was compared using the Kaplan-Meier (KM) method. After re-calibration in the validation cohort the CRS was compared to IMPACT evaluating discrimination (c-statistic), calibration (observed vs predicted survival) and risk reclassification (net absolute reclassification index -NARI). Discriminatory power assesses if patients with higher risk scores are at higher mortality risk than those with lower risk scores. Calibration assesses if the predicted mortality is aligned with the observed mortality.

Figure 1 – Risk of death after cardiac transplant associated with the recipient's bilirubin and creatinine levels, age ratio and age

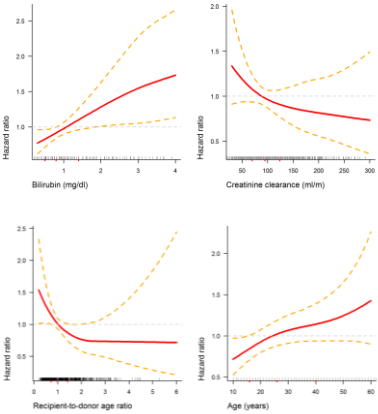
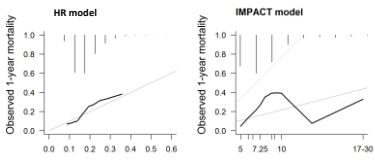


Figure 2C – Calibration plot for 1-yr mortality from CHD risk score (left) and IMPACT (right)

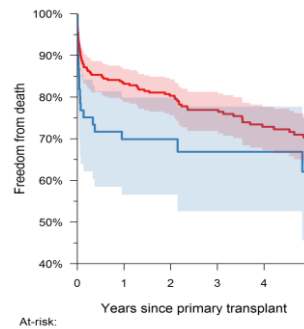


RESULTS

The sample consisted of 1381 mostly male (n=850, 61.5%) recipients with CHD aged 10 to 74 yrs. with a mean (median) recipient age of 28.9 (26) yrs. Donor age ranged from 1 to 67 yrs. with a mean (median) of 28.1 (25). Female to male gender mismatch occurred in 265 HTx (19.2%) whereas male to female gender mismatch occurred in 221 HTx (16%). The mortality association of the 4 remaining variables is shown.

377 (27.3%) CHD HTx recipients died over a mean follow up of 2.79 years. Whereas IMPACT classified all patients as medium and high risk (Figure 2A) the CRS classified a small proportion (4%) of CHD recipients as low risk. In the validation cohort, CRS showed better discrimination than IMPACT [Figure 2B, c-statistic 0.65 (0.59-0.70) vs 0.62 (CI 0.56-0.68) for IMPACT]. The CRS showed adequate calibration while IMPACT's calibration was poor (Fig 2C). The CRS better classified 18 (16%) patients with events but misclassified 18 (6%) patients with events leading to a similar net risk reclassification to IMPACT [NARI 0.04 [-0.06, 0.12], p = 0.98].

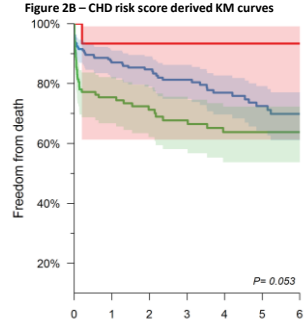
Figure 2A – IMPACT derived KM curves



At-risk:

5-10:	354	260	205	168	133	96
11+:	61	36	26	20	18	13

Figure 2B – CHD risk score derived KM curves



At-risk:

< 10:	15	12	9	9	7	4	4
10-19:	214	170	134	104	80	59	41
20+:	125	79	64	57	48	35	25

CONCLUSION

A new prediction model that incorporates 5 simple variables with adequate discrimination, excellent calibration and better identification of low risk CHD HTx recipients is presented.

References: Weiss, E.S. et al., 2011. Creation of a quantitative recipient risk index for mortality prediction after cardiac transplantation (IMPACT). The Annals of thoracic surgery, 92(3), pp.914–922.