ORIGINAL ARTICLE

Performance of existing risk scores around heart transplantation: validation study in a 4-year cohort

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SUMMARY

Several risk scores exist to help identify best candidate recipients for heart transplantation (HTx). This study describes the performance of five heart failure risk scores and two post-HTx mortality risk scores in a French single-centre cohort. All patients listed for HTx through a 4-year period were included. Waiting-list risk scores [Heart Failure Survival Score (HFSS), Seattle Heart Failure Model (SHFM), Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC), Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) and Get With The Guidelines-Heart Failure (GWTG-HF)] and post-HTx scores Index for Mortality Prediction After Cardiac Transplantation (IMPACT and CARRS) were computed. Main outcomes were 1-year mortality on waiting list and after HTx. Performance was assessed using receiver operator characteristic (ROC), calibration and goodness-of-fit analyses. The cohort included 414 patients. Waiting-list mortality was 14.0%, and post-HTx mortality was 16.3% at 1-year follow-up. Heart failure risk scores had adequate discrimination regarding waiting-list mortality (ROC AUC for HFSS = 0.68, SHFM = 0.74, OPTIMIZE-HF = 0.72, MAGGIC = 0.70 and GWTG = 0.77; all P-values <0.05). On the contrary, post-HTx risk scores did not discriminate post-HTx mortality (AUC for IMPACT = 0.58, and CARRS = 0.48, both P-values >0.50). Subgroup analysis on patients undergoing HTx after ventricular assistance device (VAD) implantation (i.e. bridge-to-transplantation) (n = 36) showed an IMPACT AUC = 0.72 (P < 0.001). In this single-centre cohort, existing heart failure risk scores were adequate to predict waiting-list mortality. Post-HTx mortality risk scores were not, except in the VAD subgroup.

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Introduction

Heart transplantation (HTx) remains the best therapeutic option in advanced heart failure (AHF). In a context of heart graft shortage [1], with more and more patients presenting with AHF, selection of the ideal recipient has never been so critical. Two periods need to be considered as follows: (i) while the patient is on the waiting list for HTx and (ii) after HTx with short-term postoperative mortality and longer-term mortality.

Risk stratification scores for patients presenting with AHF are plentiful [2]. Although designed more than a

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decade ago, the Heart Failure Survival Score (HFSS) [3] and Seattle Heart Failure Model (SHFM) [4,5] remain the most validated in patients listed for HTx [1,4,6]. Numerous other scores have been developed afterwards, such as the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) [7–9], the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) [10,11] and Get With The Guidelines-Heart Failure (GWTG) [12]. External validity of these risk scores was described in heterogeneous heart failure patients but not specifically in patients listed for HTx [4,6].

Although several risk scores have been developed and validated for patients on a waiting list for HTx, fewer scores predict post-transplantation mortality. One-year survival after transplantation is predicted by the Index for Mortality Prediction After Cardiac Transplantation (IMPACT) score [13]. IMPACT was validated in an external cohort in Europe [14]. The CARRS score, although designed for higher-risk patients, was not validated in a regular cohort of transplanted patients [15].

This study focuses on a contemporary French cohort of patients listed for HTx. It evaluates the performance of existing risk scores to predict mortality around HTx: while on waiting list and after the surgery.

Methods

All heart transplant candidates listed for HTx between January 2011 and December 2014 in a single French HTx centre were included. Retransplantations and combined transplantations were excluded.

Main endpoint was all-cause mortality assessed 1 year after listing for heart failure risk scores (no-HTx scores) and 1 year after HTx for post-HTx risk scores (post-HTx scores). Follow-up was complete for all patients.

Studied heart failure risk scores included HFSS [3], SHFM [5], MAGGIC [7,8], OPTIMIZE-HF [10,11] and GWTG [12]. Among heart failure risk scores, HFSS, SHFM and MAGGIC were considered *chronic* HF scores, and OPTIMIZE-HF and GWTG were considered *acute* HF scores.

Studied post-HTx risk scores included IMPACT [13] and CARRS [15].

The computation of these scores required variables that are listed in Table 1. Data were extracted from the Pitié-Salpétrière University Hospital subset of the Cristal registry, used for clinical investigations by the Agence de Biomedecine (ABM), the national institution in charge of organ transplantation in France. The registry systematically collects data at the time of listing and at the time of transplantation (detail of data collection is available in Appendix).

Retrospective data collection from the hospital electronic and paper archives was performed on all other data needed for the computation of existing scores on the derivation cohort.

During the study period, French heart transplant allocation was based on a priority status, depending on the degree of medical urgency presented by the recipient candidate. High-emergency priority status could be obtained for patients who were under mandatory inotrope support or short-term extracorporeal life support (ECLS) or patients assisted by long-term mechanical circulatory support device but with complications inherent to these devices. High-emergency priority status was requested by the patients' referent HTx specialist (cardiologist or cardiac surgeon) and granted by an independent panel of ABM medical experts. For medically treated patients, its maximum duration was 48 h, renewable once, during which patient was put on top of the waiting list, on a national scale.

Standard care of patients did not change during the course of the study and considered homogeneous regarding pre- and postoperative care.

Statistics

Summary data are presented as median (interquartile range) or number (percentage). Computation of the existing risk scores was performed as described in their original publications, summing the variables of interest with their associated beta-coefficient.

Multiple imputation techniques were used to handle missing values required for the computation of existing scores. Variables for which more than 15% values were missing were only imputed but not used as predictors: VO_2 peak, heart rate, intraventricular conduction delay, total cholesterol and factor V.

Risk scores were assessed using their main characteristics as follow. *Discrimination*, the ability for the score to discriminate between patients who will die and those who will not, was assessed with the area under receiver operator curves (AUROC). The relative goodness-of-fit of the scores, assessing overall *prediction*, was quantified by the Akaike information criterion (AIC). *Calibration*, the correlation between observed and predicted mortality, was assessed by Nam-D'-tino statistics using the Hosmer and Lemeshow test (with a *P*-value >0.05 meaning the observed results are not statistically different from the predicted values). Risk scores were compared on their AUROC using DeLong test.

Multivariable Cox regression analysis was performed to assess independent variables associated with 1-year

Table 1. Variables required for the computation of studied risk scores.

Variable	HFSS	SHFM	MAGGIC	OPTIMIZE-HF	GWTG	IMPACT	CARRS
Male gender		x	x			x	
Age at listing		x	x	x	x	x	
African ethnicity				x	x		
Weight or body mass index		x	x				
Medical history							
Retransplantation							x
History of heart surgery							x
Familial cardiomyopathy						x	
Smoker (former or active)			x				
Diabetes			x				
Ischemic aetiology	x	x				x	
Pulmonary comorbidity or COPD			x	x	x		
History of stroke				x			x
Peripheral arterial disease				x			
History of psychiatric disorder				x			
IVCD	x						
Liver failure				x			
Heart failure severity							
NYHA		x	x	x			
Time since diagnosis			x				
Systolic blood pressure	x	x	x	x	x		
Diastolic blood pressure				x			
Heart rate	x			x	x		
LVEF	x	x	x	x			
VO_2 peak	x						
Laboratory data at listing							
Creatininemia			x	x			
Blood urea nitrogen					x		
Sodium	x	x		x	x		
Haemoglobin		x					
Lymphocytes (%)		x					
Total cholesterol		x		x			
Preoperative state							
Total bilirubin						x	
Albumin							x
eGFR						x	x
Ongoing dialysis						x	
Active sepsis						x	
IABP support						x	
Mechanical ventilation						x	
ECLS support						x	
VAD support						x	
Medications							
ACEI		x	x	x			
ARB		x	x				
Anti-aldosterone		x					
Beta-blockers		x	x	x			
Diuretics		x					
Allopurinol		x					
Statins		x					

Table 1. Continued.

Variable	HFSS	SHFM	MAGGIC	OPTIMIZE-HF	GWTG	IMPACT	CARRS
Medical devices							
Implantable cardioverter device		x					
Cardiac resynchronization therapy		x					

HFSS, Heart Failure Survival Score; SHFM, Seattle Heart Failure Model; MAGGIC, Meta-Analysis Global Group in Chronic Heart Failure; OPTIMIZE-HF, Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure; GWTG-HF, Get With The Guidelines Heart Failure; IMPACT, Index for Mortality Prediction After Cardiac Transplantation; COPD, chronic obstructive pulmonary disease; IVCD, intraventricular conduction delay; ECLS, extracorporeal life support; VAD, ventricular assistance device; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers.

mortality after HTx. SPSS v23.0 (IBM, Armonk, NY, USA) was used for all calculations.

Results

Cohort characteristics at listing

The cohort included 414 patients, listed on the national waiting list for HTx during a 4-year period.

Patients' characteristics at listing are presented in Table 2. At listing, they had a median age of 50.8 years, with a sex ratio of 4:1 male-to-female gender. Ischaemic heart disease was causal in 139 patients (33.6%). Patients presented severe end-stage heart failure with a symptomatic NYHA class of three or more, median LVEF 20.0% and a peak VO_2 uptake of 12.0 ml/min/kg.

At listing, 186 (44.9%) were hospitalized in a critical care unit; 176 (42.5%) patients were under intravenous inotropic support, and 79 (19.1%) were under ECLS. One hundred and fourteen (27.5%) were under high-priority emergency status at listing. Thereafter, during follow-up, emergency HTx was performed in 191 patients (59.7% of patients benefitting from HTx).

Median time to HTx was 6 (3–18) days for medically treated patients who were granted high-emergency status as compared to 68 (19–160) days in other patients ($P < 0.0001$).Regarding procedures, 300 patients (74.5%) were transplanted during the first year after listing. Comparatively, 13 patients (3.1%) were implanted with an LVAD during the first year.

Patients' data on the day of HTx are available in Appendix, Table A1.

Waiting-list mortality

Fifty-eight (14.0%) patients died within 1 year after listing.

Receiver operator characteristic (ROC) curves of the studied risk scores are presented in Fig. 1. All scores showed adequate discriminative performance with significant AUROC. Goodness-of-fit and calibration were adequate (see Table 3).

There was no significant difference in discrimination between risk scores, and between *chronic* and *acute* HF scores (all *P*-values >0.05 in DeLong AUROC comparison).

Post-transplant mortality

One-year mortality after HTx was 16.3% (52 patients over 320 who were transplanted).

Among existing risk scores for post-HTx mortality, ROC analysis showed the IMPACT and CARRS score had an AUROC of 0.58 ($P = 0.09$) and 0.48 ($P = 0.66$) respectively (see Fig. 2). Calibration and predictive power were not assessed, as the discriminative characteristics of these scores were not significant.

Subgroup analysis in patients who underwent HTx while assisted by LVAD (i.e. bridge-to-transplantation) ($n = 36$), showed that IMPACT was adequate in this subgroup with an AUROC of 0.72 ($P < 0.001$). CARRS was not (AUROC = 0.53, $P = 0.55$). In this subgroup, goodness-of-fit and calibration were not assessed due to sample size restrictions.

Variables independently associated with 1-year mortality after HTx were the age [per 1-year increase, adjusted hazard ratio: 1.05 (1.01–1.09), $P = 0.008$] and preoperative total bilirubin [per unit, adjusted hazard ratio: 1.02 (1.01–1.04), $P = 0.011$]. In univariate analysis, other variables that were associated with 1-year mortality were COPD [unadjusted hazard ratio: 2.21 (1.00–4.90), $P = 0.05$] and preoperative blood urea nitrogen [per unit, unadjusted hazard ratio: 1.04 (1.00–1.08), $P = 0.035$]. All other variables that were tested were not associated with 1-year mortality, including

Table 2. Baseline characteristics of patients at listing.

Variables	Missing values	Overall cohort (n = 414)
Male gender	0 (0.0)	335 (80.9)
Age at listing	0 (0.0)	50.8 (43.6; 60.3)
BMI (kg/m^2)	0 (0.0)	24.7 (22.0; 27.1)
Blood type		
AB	0 (0.0)	14 (3.4)
A	0 (0.0)	159 (38.4)
B	0 (0.0)	69 (16.7)
O	0 (0.0)	172 (41.5)
Rhesus positive	19 (4.6)	342 (86.6)
Medical history		
Hypertension	34 (8.2)	129 (33.9)
Smoker (former or active)	0 (0.0)	266 (65.8)
Diabetes	0 (0.0)	88 (21.3)
Ischemic aetiology	0 (0.0)	139 (33.6)
Pulmonary comorbidity	4 (1.0)	25 (6.1)
History of stroke	0 (0.0)	50 (12.1)
Peripheral arterial disease	0 (0.0)	38 (9.2)
History of malignancy	0 (0.0)	33 (8.0)
History of psychiatric disorder	0 (0.0)	5 (1.2)
Cardiac arrhythmia	17 (4.1)	225 (56.7)
IVCD	184 (44.4)	82 (35.7)
History of thromboembolism	15 (3.6)	26 (6.5)
Heart failure severity		
NYHA		
2	0 (0.0)	1 (0.2)
3	0 (0.0)	235 (56.8)
4	0 (0.0)	178 (43.0)
Resting SBP (mmHg)	46 (11.1)	100 (91; 111)
Heart rate (bpm)	123 (29.7)	83 (70; 100)
LVEF (%)	23 (5.6)	20 (15; 25)
VO_2 peak (ml/kg/min)	295 (71.3)	12.0 (10.0; 14.4)
High emergency status at listing	0 (0.0)	114 (27.5)
Critical care setting at listing	0 (0.0)	186 (44.9)
IV inotropic support at listing	0 (0.0)	176 (42.5)
Mechanical ventilation at listing	0 (0.0)	23 (5.6)
ECLS support	0 (0.0)	79 (19.1)
Laboratory data		
Creatininemia (µmol/l)	0 (0.0)	110 (83; 147)
eGFR (Cockroft) (ml /min /kg)	0 (0.0)	69.4 (50.2; 99.0)
Blood urea nitrogen (mmol /l)	0 (0.0)	8.9 (6.3; 12.7)
Sodium (mmol/l)	0 (0.0)	136 (132; 139)
Total bilirubin (µmol/l)	0 (0.0)	18 (10; 28)
AST (µ /l)	0 (0.0)	34 (26; 49)
ALT (µ /l)	0 (0.0)	31 (20; 51)
Protids (g /l)	1 (0.2)	70 (63; 75)
NT Pro-BNP (ng /l)	25 (6.0)	3925 (1812; 7563)
Hematocrit (%)	0 (0.0)	35.9 (30.6; 41)
Haemoglobin (g/dl)	0 (0.0)	12.0 (10.2; 13.7)
Lymphocytes (%)	5 (1.2)	16.2 (9.8; 23.3)
Platelets (10^9/l)	0 (0.0)	202 500 (157 500; 244 250)
Albumin (g /l)	23 (5.6)	39.4 (33.0; 43.0)
Total cholesterol (mmol/l)	174 (42.0)	3.2 (2.6; 4.0)
Uric acid (µmol/l)	36 (8.7)	451.5 (324.0; 578.5)
Factor V (%)	135 (32.6)	83 (68; 100)
Prothrombin ratio (%)	0 (0.0)	64 (40.1; 79.0)
INR	7 (1.7)	1.4 (1.2; 2.0)

Transplant International 2018; 31: 520–530

Table 2. Continued.

Variables	Missing values	Overall cohort (n = 414)
Medications		
VKA	4 (1.0)	151 (36.8)
ACEI	16 (3.9)	172 (43.2)
ARB	16 (3.9)	37 (9.3)
Anti-aldosterone	16 (3.9)	175 (44.0)
Beta-blockers	16 (3.9)	168 (42.2)
Diuretics	18 (4.3)	300 (75.8)
Medical devices		
Implantable cardioverter device	0 (0.0)	245 (59.2)
Cardiac resynchronization therapy	30 (7.2)	130 (33.9)
VAD support	0 (0.0)	28 (6.8)
TAH support	0 (0.0)	3 (0.7)

BMI, body mass index; SBP, systolic blood pressure; ECLS, extracorporeal life support; VAD, ventricular assistance device; TAH, total artificial heart; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; VKA, vitamin K antagonist; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers.

Data are presented as median (interquartile range) for continuous variables and n (%) for categorical variables.

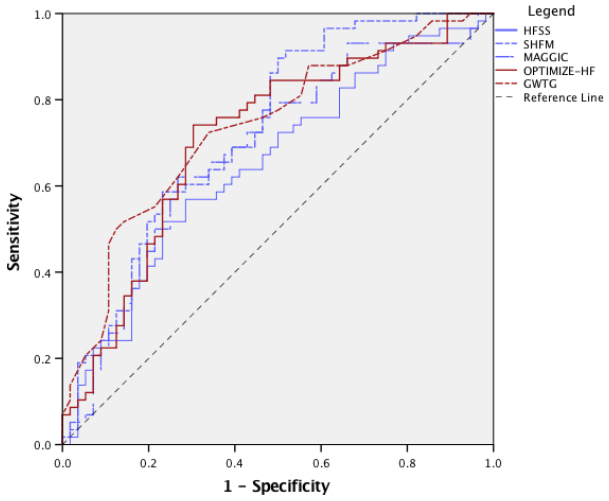

Figure 1 Receiver operator characteristic curves of risk scores for 1-year mortality, on the waiting-list (n = 414). Blue line: chronic heart failure (HF) scores, red line: acute HF scores.

ECLS and inotropic support immediately prior to the HTx procedure (respectively Figs 3 and 4).

Discussion

Main findings were that (i) heart failure risk scores were adequate for predicting mortality in patients waiting for HTx and (ii) post-HTx mortality risk score could not be validated in this single-centre cohort.

The International Society of Heart and Lung Transplantation (ISHLT) recommends with a class IIb, level of evidence C, the use of prognosis risk scores to guide HTx listing [1]. Studied risk scores were so, either because of their external validation in cohorts of candidates for HTx, or because they were recent and showed good discrimination and calibration when published [16].

Waiting-list mortality risk scores

All the risk scores for end-stage heart failure, which were tested, were validated in this cohort with good overall predictive power, accuracy and calibration. AUROC ranging from 0.68 to 0.78, with adequate AIC and goodness-of-fit, showed this cohort was similar to other end-stage heart failure cohorts waiting for heart transplantation previously described [4,6,8,17].

Interestingly, even though these scores were validated in this single-centre cohort, they were originally derived from cohorts of patients suffering from heart failure not necessarily listed for HTx; such as SHFM, which has been described to underestimate mortality in the most severe patients [18]. Notably, apart from SHFM, which was developed and validated in composite cohorts of medically treated and LVAD-supported patients [5,17], the other hereby evaluated heart failure risk scores (HFSS, MAGGIC, OPTIMIZE-HF and GWTG-HF) also proved relevant in this mixed population.

Moreover, it added the notion that these existing heart failure risk score may also be adequate in patients under short-term ECLS, which was the case of 19.1% of patients at listing.

Table 3. Performance comparison of risk scores for 1-year mortality while on the waiting list.

	HFSS	SHFM	MAGGIC	OPTIMIZE-HF	GWTG-HF
Discrimination					
AUROC	0.68*	0.74*	0.70*	0.72*	0.78*
Prediction					
AIC	153.01	143.08	149.58	145.34	62.10
Calibration					
H-L	χ^2: 5.73 (P = 0.68)	χ^2: 9.57 (P = 0.40)	χ^2: 9.23 (P = 0.34)	χ^2: 7.19 (P = 0.50)	χ^2: 7.12 (P = 0.53)

AUROC, area under curve of receiver operator characteristics; AIC, Akaike information criteria; H-L, Hosmer-Lemeshow goodness-of-fit test.

*P-value <0.00001.

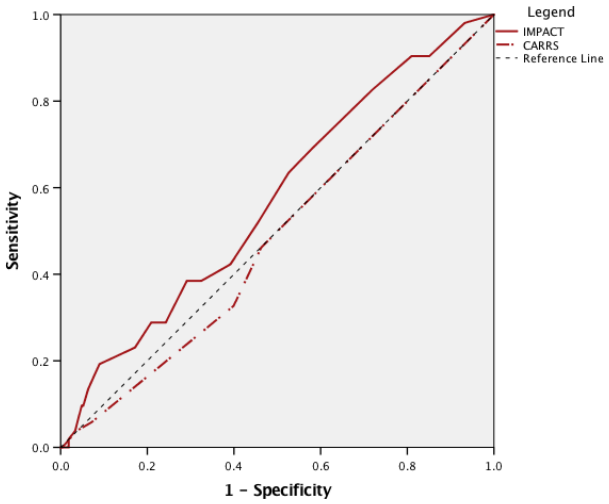

Figure 2 Receiver operator characteristic curves of risk scores for 1-year mortality after heart transplantation (n = 320).

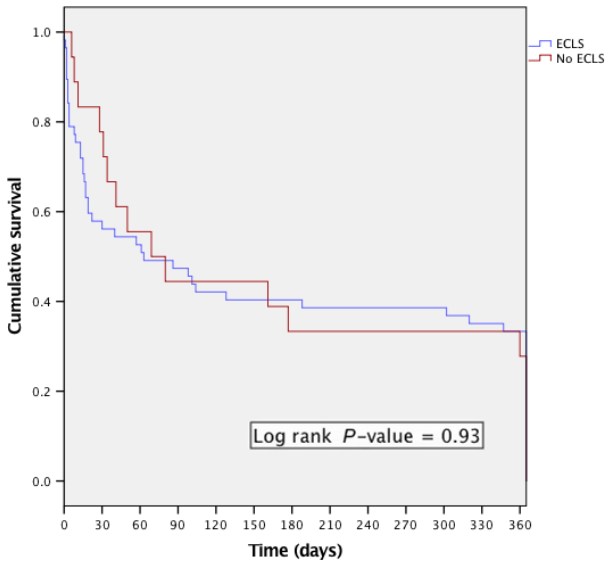

Figure 3 Survival curves comparing post-heart transplantation (HTx) mortality between patients under extracorporeal life support immediately prior to HTx (n = 78) and those without (n = 242).

To close waiting-list mortality risk scores, results also showed that HF patients listed for HTx had similar prognosis regarding mortality as compared to patients hospitalized for acute decompensation. Hence, this allows using acute HF scores in this subset of severe HF patients, instead of scores meant for more chronic patients.

Post-transplantation risk scores

On the other hand, the existing prognostic scores for post-HTx mortality could not be validated in our cohort. Both the IMPACT score and the CARRS score had poor AUROC. IMPACT was validated in a large international cohort [14], and results such as those which were found in the present study may mostly be due to the differences in treatment of post-HTx recipients and allocation system.

As CARRS is based on a few risk factors, one of which was retransplantation, an exclusion criteria in this cohort, the discrimination performance of this post-HTx risk score was not expected to be important. However, with an AUROC of 0.47, CARRS could not be considered adequate in this cohort, even considering the retransplantation risk factor, not to mention its rarity as this procedure is performed in less than 2.5% of paediatric patients, even less in adult patients [19].

Preoperative variables known to be associated with post-HTx mortality in other cohorts were not in ours (i.e. ECLS and preoperative critical state). Indeed, although perioperative care is standardized in most HTx centres, that is such as the one in which this study took place; these protocols are not the same worldwide or even nationwide, which may partly explain discrepancies in transplantation results and

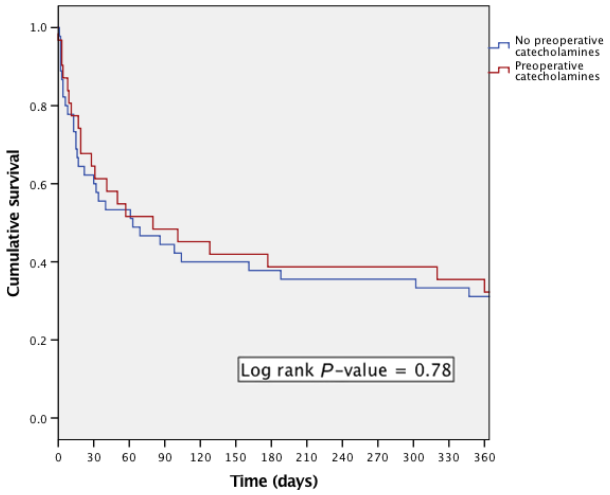

Figure 4 Survival curves comparing post-heart transplantation (HTx) mortality between patients under catecholamines immediately prior to HTx (n = 140) and those without (n = 180).

outcomes across the world. Specifically, IMPACT heavily relies on critical preoperative state immediately prior to HTx to predict post-HTx mortality. Thus, finding there was no association between ECLS nor catecholamine use and mortality explain why IMPACT was not validated in the present cohort. This between-centre difference in mortality in patients under ECLS has been described before and is confirmed in this cohort [20,21].

Moreover, the cohort on which IMPACT was designed included 15.5% of patients transplanted while under long-term VAD support, as compared to the 11.0% bridge-to-transplantation in our cohort [13]. It was later validated in an international cohort of 29 924 patients, including 17.8% supported by VAD [14]. This difference may yet participate to the discrepancy observed in IMPACT performance in the present study, although previous validation studies in European cohort found similar results [17]. Nevertheless, in the present study, the subgroup analysis in patients under VAD, albeit low-powered due to the small sample size, did show the same described discrimination performance of IMPACT in bridge-to-transplantation patients, which may indicate that the difference lies in non-VAD patients.

Finally, more than objecting to the accuracy of existing post-HTx risk scores, these findings emphasize the need of using more local risk scores (i.e. derived from national cohorts) rather than using international risk scores which, even if statistically relevant on a large international scale, would be less relevant when focusing on smaller scale cohorts such as the one presented in this study, because of heterogeneity of practice between countries.

This may further advance the idea of local *tailored* risk scores rather than *one-fit-all* risk score. In this sense, the work started by Jasseron *et al.* [22], on a national risk score, may be the first step towards such change in practices. The next logical step would be the inclusion of centre-specific adjustment factors to account for centre-scale, although this would require more statistical power which heart transplantation does not necessarily allow, yet.

Limitations

We acknowledge several limitations to our study. Inherent to the retrospective nature of the study design, data were extracted from a registry used in clinical routine, with its associated bias (i.e. miscategorization at the time of listing). However, these data are mandatory and used by the ABM for real-time heart allocation. As such, safeguards of data quality are in place with regular audits by ABM staff members.

The study was single-centre; however, results on waiting-list mortality showed that the cohort behaved akin to larger cohorts of HF patients. Indeed, variables associated with mortality in this study were also similar to that of the recent Candidate Risk Score (CRS) assessing 1-year mortality after listing, based on the overall Cristal database registry [22].

The low proportion of patients transplanted while under long-term VAD support (11.9%) was representative of the French standard of care. It was counterbalanced by a higher rate of short-term ECLS implantation rate (24% in this cohort), due to a short expected median waiting time for patients granted higher-priority while medically treated or under short-term ECLS: 6 days. Hence, results have to be somewhat cautiously interpreted in countries in which VAD support has been more generalized, but remain relevant in countries with more restricted access to these devices. In time, France may increase its VAD implantation rate, given that the allocation system was changed on January 2018, from a two-tier prioritization to a more granular allocation score system. For patients for whom waiting would no longer be an option (i.e. former medically treated high-emergency status patients), VAD implantation would be relevant. Even so, the use of postoperative predictive prognosis scores may be helpful in such settings.

Finally, regarding missing values, it has to be noted that even though existing risk scores had a good

predictive value for 1-year mortality, some components had to be imputed. While missing values are unavoidable in a retrospective analysis, in the context of listing for HTx, many parameters can also prove unavailable or inadequate at the time of the listing and even afterwards (i.e. pulmonary artery catheterism or peak VO_2 for a recent cardiogenic shock complicating a myocardial infarction). Reliance upon imputation techniques is then necessary to address missing data [2,7,23,24]. In the present study, imputed data did not impact results as missing data were mostly associated with heart failure scores; which in the end were associated with waiting-list mortality. On the other hand, in post-HTx risk scores, data were exhaustive.

Conclusion

In this 4-year cohort, although existing risk scores were accurate for predicting mortality in patients waiting for HTx, they were not for post-HTx mortality. While these results do not question the validity of existing international risk scores, they may call for the use of more local (i.e. national) risk scores when deploying allocation score systems.

Authorship

LSN: designed the study, collected data, performed statistical analyses and wrote the manuscript. GC: participated in the study design, collected data and provided critical review to the manuscript. SO: collected data and provided critical review to the manuscript. NZ: collected data and provided critical review to the manuscript. NB: collected data and provided critical review to the manuscript. AG: collected data and provided critical review to the manuscript. AB: collected data and provided critical review to the manuscript. GL: collected data and provided critical review to the manuscript. PL: collected data and provided critical review to the manuscript. SV: participated in the study design, collected data and provided critical review to the manuscript.

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Conflicts of interest

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APPENDIX

Systematic data collection in the CRISTAL database

Variables include the following: gender, age (years), body mass index (kg/m^2), blood and rhesus type, ischemic aetiology, cardiovascular risk factors [history of smoking, hypertension, diabetes (any type)], cardiac comorbidities [cardiac arrhythmia, intraventricular conduction disturbances (IVCD)], vascular comorbidities [history of stroke, peripheral artery obstructive disease (PAOD), deep vein thrombosis (DVT), pulmonary embolism (PE)], other comorbidities [history of cancer (any), pulmonary comorbidity (any), chronic obstructive pulmonary disease (COPD), psychiatric disorder history (any), history of alcohol addiction, renal impairment (any history of chronic kidney disease or estimated glomerular filtration rate (eGFR) computed with MDRD formula below 90 ml/min/kg)], other medical or surgery history (cardiac surgery, thoracic surgery, pregnancy, blood transfusion), heart failure severity [New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF) (in %), peak VO_2 (ml/kg/min)] features at the time of listing (systolic and diastolic blood pressure (respectively SBP and DBP in mmHg), heart rate (HR) in beats per minutes (bpm), medical setting (ambulatory or critical care), treatments [intraveinous (IV) inotropic support (any), mechanical ventilator support, extracorporeal life support (ECLS), ventricular assistance device (VAD), total artificial heart support (TAH), vitamin K antagonists (VKA), angiotensin-converting-enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), antialdosterone, beta-blockers, loop diuretics] and biology (creatininemia (µmol/l), eGFR (MDRD formula) (ml/min/kg), sodium (mmol/l), total bilirubin (µmol/l), aspartate aminotransferase (AST) (µ/l), alanine aminotransferase (ALT) (µ/l), factor V (%), prothrombin ratio (%), platelets, hematocrit (%).

Table A1. Preoperative characteristics of patients who underwent HTx.

Variable	Missing values	Patients who underwent HTx (*N* = 320)
Male gender	0.0	195 (60.9)
Age (years)	0.0	52 (43–60)
Weight (kg)	0.0	70 (63–81)
Previous sternotomy	0.0	62 (19.4)
Critical care setting	0.0	172 (53.8)
Sepsis	4.2	26 (8.0)
Creatininemia (μmol/l)	0.0	95 (72–130)
eGFR (ml/min)	0.0	78 (58–107)
Urea (mmol/l)	6.6	7.8 (5.7–11.7)
Sodium (mmol/l)	0.0	132 (135–138)
Total bilirubin (μmol/l)	24.7	20 (14–32)
AST (μ/l)	0.6	33 (26–51)
ALT (μ/l)	3.4	29 (20–48)
Prothrombin ratio	0.0	65 (44–78)
INR	0.3	1.36 (1.2–1.8)
Platelets (10^9/l)	0.0	202 000 (150 000–255 000)
VKA	1.9	98 (31.0)
ECLS	0.3	78 (24.0)
LVAD	0.0	36 (11.0)
Mechanical ventilation	0.0	11 (3.0)
IV inotropic support	0.0	140 (44.0)

ECLS, extracorporeal life support; LVAD, left ventricular assistance device; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase; ALT, alanine aminotransferase; VKA, vitamin K antagonist; INR, index of normalized ratio.

Data are presented as median (interquartile range) for continuous variables or *n* (%) for categorical variables).

REFERENCES

1. Mehra MR, Canter CE, Hannan MM, *et al.* The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. *J Heart Lung Transplant* 2016; **35**: 1.
2. Rahimi K, Bennett D, Conrad N, *et al.* Risk prediction in patients with heart failure: a systematic review and analysis. *JACC Heart Fail* 2014; **2**: 440.
3. Aaronson KD, Schwartz JS, Chen TM, Wong KL, Goin JE, Mancini DM. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. *Circulation* 1997; **95**: 2660.
4. Goda A, Williams P, Mancini D, Lund LH. Selecting patients for heart transplantation: comparison of the Heart Failure Survival Score (HFSS) and the Seattle heart failure model (SHFM). *J Heart Lung Transplant* 2011; **30**: 1236.
5. Levy WC, Mozaffarian D, Linker DT, *et al.* The Seattle Heart Failure Model: prediction of survival in heart failure. *Circulation* 2006; **113**: 1424.
6. Goda A, Lund LH, Mancini D. The Heart Failure Survival Score outperforms the peak oxygen consumption for heart transplantation selection in the era of device therapy. *J Heart Lung Transplant* 2011; **30**: 315.
7. Pocock SJ, Ariti CA, McMurray JJV, *et al.* Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. *Eur Heart J* 2013; **34**: 1404.
8. Sartipy U, Dahlström U, Edner M, Lund LH. Predicting survival in heart failure: validation of the MAGGIC heart failure risk score in 51,043 patients from the Swedish heart failure registry. *Eur J Heart Fail* 2014; **16**: 173.
9. M-aGGiCH F. The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. *Eur Heart J* 2012; **33**: 1750.
10. O'Connor CM, Abraham WT, Albert NM, *et al.* Predictors of mortality after discharge in patients hospitalized with heart failure: an analysis from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). *Am Heart J* 2008; **156**: 662.
11. Abraham WT, Fonarow GC, Albert NM, *et al.* Predictors of in-hospital mortality in patients hospitalized for heart failure: insights from the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF). *J Am Coll Cardiol* 2008; **52**: 347.
12. Peterson PN, Rumsfeld JS, Liang L, *et al.* A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association get with the guidelines program. *Circ Cardiovasc Qual Outcomes* 2010; **3**: 25.

13. Weiss ES, Allen JG, Arnaoutakis GJ, *et al.* Creation of a quantitative recipient risk index for mortality prediction after cardiac transplantation (IMPACT). *Ann Thorac Surg* 2011; **92**: 914; discussion 21–2.
14. Kilic A, Allen JG, Weiss ES. Validation of the United States–derived Index for Mortality Prediction After Cardiac Transplantation (IMPACT) using international registry data. *J Heart Lung Transplant* 2013; **32**: 492.
15. Schulze PC, Jiang J, Yang J, *et al.* Preoperative assessment of high-risk candidates to predict survival after heart transplantation. *Circ Heart Fail* 2013; **6**: 527.
16. Cowger J, Shah P, Stulak J, *et al.* INTERMACS profiles and modifiers: Heterogeneity of patient classification and the impact of modifiers on predicting patient outcome. *J Heart Lung Transplant* 2016; **35**: 440.
17. Smits JM, de Vries E, De Pauw M, *et al.* Is it time for a cardiac allocation score? First results from the Eurotransplant pilot study on a survival benefit-based heart allocation. *J Heart Lung Transplant* 2013; **32**: 873.
18. Gorodeski EZ, Chu EC, Chow CH, Levy WC, Hsich E, Starling RC. Application of the Seattle Heart Failure Model in ambulatory patients presented to an advanced heart failure therapeutics committee. *Circ Heart Fail* 2010; **3**: 706.
19. Benden C, Goldfarb SB, Edwards LB, *et al.* The registry of the International Society for Heart and Lung Transplantation: seventeenth official pediatric lung and heart-lung transplantation report–2014; focus theme: retransplantation. *J Heart Lung Transplant* 2014; **33**: 1025.
20. Barbaro RP, Odetola FO, Kidwell KM, *et al.* Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. *Am J Respir Crit Care Med* 2015; **191**: 894.
21. Combes A, Brodie D, Bartlett R, *et al.* Position paper for the organization of extracorporeal membrane oxygenation programs for acute respiratory failure in adult patients. *Am J Respir Crit Care Med* 2014; **190**: 488.
22. Jasseron C, Legeai C, Jacquelinet C, *et al.* Prediction of waitlist mortality in adult heart transplant candidates: the candidate risk score. *Transplantation* 2017; **101**: 2175.
23. Backholer K, Hirakawa Y, Tonkin A, *et al.* Development of an Australian cardiovascular disease mortality risk score using multiple imputation and recalibration from national statistics. *BMC Cardiovasc Disord* 2017; **17**: 17.
24. Kalogeropoulos A, Psaty BM, Vasan RS, *et al.* Validation of the health ABC heart failure model for incident heart failure risk prediction: the Cardiovascular Health Study. *Circ Heart Fail* 2010; **3**: 495.