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

Running title: Risk scores around heart transplantation

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ABSTRACT (204 words)

Background. Several risk scores exist to help identify best candidate recipients for heart transplantation (HTx). This paper describes the performance of 5 heart failure risk scores and 2 post-HTx mortality risk scores in a French single center cohort.

Methods. All patients listed for HTx through a 4-year period were included. Waiting-list risk scores (HFSS, SHFM, MAGGIC, OPTIMIZE-HF and Get With The Guidelines-Heart Failure (GWTG-HF)) and post-HTx scores (IMPACT and CARRS) were computed. Main outcomes were 1-year mortality on waiting list and after HTx. Performance was assessed using ROC, calibration and goodness-of-fit analyses.

Results. The cohort included 414 patients. Waiting-list mortality was 14.0% and post-HTx mortality was 16.3% at one-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 VAD implantation (i.e. bridge-to-transplantation) (n=36) showed an IMPACT AUC=0.72 (p<0.001).

Conclusion. In this single-center 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.

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: 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 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.[4, 6, 7] Numerous other scores have been developed afterwards, such as the Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC),[8-10] the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF)[11, 12] and Get With The Guidelines-Heart Failure (GWTG).[13] 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.[14] IMPACT was validated in an external cohort in Europe.[15] The CARRS score, although designed for higher-risk patients, was not validated in a regular cohort of transplanted patients.[16]

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 center were included. Retransplantations and combined transplantations were excluded.

Main endpoint was all-cause mortality assessed one year after listing for heart failure risk scores (no-HTx scores) and one 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,[8, 9] OPTIMIZE-HF [11, 12] and GWTG.[13] 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 [14] and CARRS.[16]

The computation of these scores required variables that are listed in **Table 1**. Data were extracted from the Pitié-Salpêtrière 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 transplants 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 hours, 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 (percent). 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 technique was 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: VO2 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'Agostino 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 one-year mortality after HTx. SPSS v23.0 (IBM, Armonk, United States of America) 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. Ischemic heart disease was causal in 139 patients (33.6%). Patients presented severe end-stage heart failure with a symptomatic NYHA class of 3 or more, median LVEF 20.0% and a peak VO₂ 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 extracorporeal life support (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 A**.

Waiting list mortality

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

ROC curves of the studied risk scores are presented in **Figure 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 **Figure 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 one-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 one-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 one-year mortality, including ECLS and inotropic support immediately prior to the HTx procedure (respectively **Figure 3.** and **Figure 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-center 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.[17]

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, 9, 18]

Interestingly, even though these scores were validated in this single-center 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.[19] Notably, apart from SHFM, which was developed and validated in composite cohorts of medically-treated and LVAD-supported patients,[5, 18] 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.

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,[15] 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 pediatric patients, even less in adult patients.[20]

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 centers, i.e. such as the one in which this study took place; these protocols are not the same worldwide or even nation-wide, which may partly explain discrepancies in transplantation results and 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-center difference in mortality in patients under ECLS has been described before and is confirmed in this cohort.[21, 22]

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.[14] It was later validated in an international cohort of 29,924 patients, including 17.8% supported by VAD.[15] 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.[18] 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, on a national risk score, may be the first step towards such change in practices.[23] The next logical step would be the inclusion of center-specific adjustment factors to account for center-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-center, 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.[23]

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, 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 one-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 VO₂ for a recent cardiogenic shock complicating a myocardial infarction). Reliance upon imputation techniques are then necessary to address missing data.[2, 8, 24, 25] 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.

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Author roles

L.S.N. designed the study, collected data, performed statistical analyses and wrote the manuscript.

G.C. participated to the study design, collected data and provided critical review to the manuscript.

S.O. collected data and provided critical review to the manuscript.

N.Z. collected data and provided critical review to the manuscript.

N.B. collected data and provided critical review to the manuscript.

A.G. collected data and provided critical review to the manuscript.

A.B. collected data and provided critical review to the manuscript.

G.L. collected data and provided critical review to the manuscript.

P.L. collected data and provided critical review to the manuscript.

S.V. participated to the study design, collected data and provided critical review to the manuscript.

Figure legends

Figure 1. Receiver operator characteristic (ROC) curves of risk scores for one-year mortality, on the waiting-list (n=414).

Blue line: chronic HF scores, red line: acute HF scores.

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

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

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

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

Variable	HFSS	SHFM	MAGGIC	OPTIMIZE-HF	GWTC	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 etiology	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			
VO2 peak	x						
Laboratory data at listing							
Creatininemia			x	x			
Blood urea nitrogen					x		
Sodium	x	x		x	x		
Hemoglobin		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		
Betablockers	x	x	x
Diuretics	x		
Allopurinol	x		
Statins	x		
Medical devices			
Implantable cardioverter device	x		
Cardiac resynchronization therapy	x		

Abbreviations: 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

Table 2. Baseline characteristics of patients at listing.

Variable	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 etiology	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 (Cockcroft) (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 (u/l)	0 (0.0)	34 (26; 49)
ALT (u/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)
Hemoglobin (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)
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)
Betablockers	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)

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

Abbreviations: 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

Table 3. Performance comparison of risk scores for one-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)

*p-value < 0.00001

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

Figure 1.

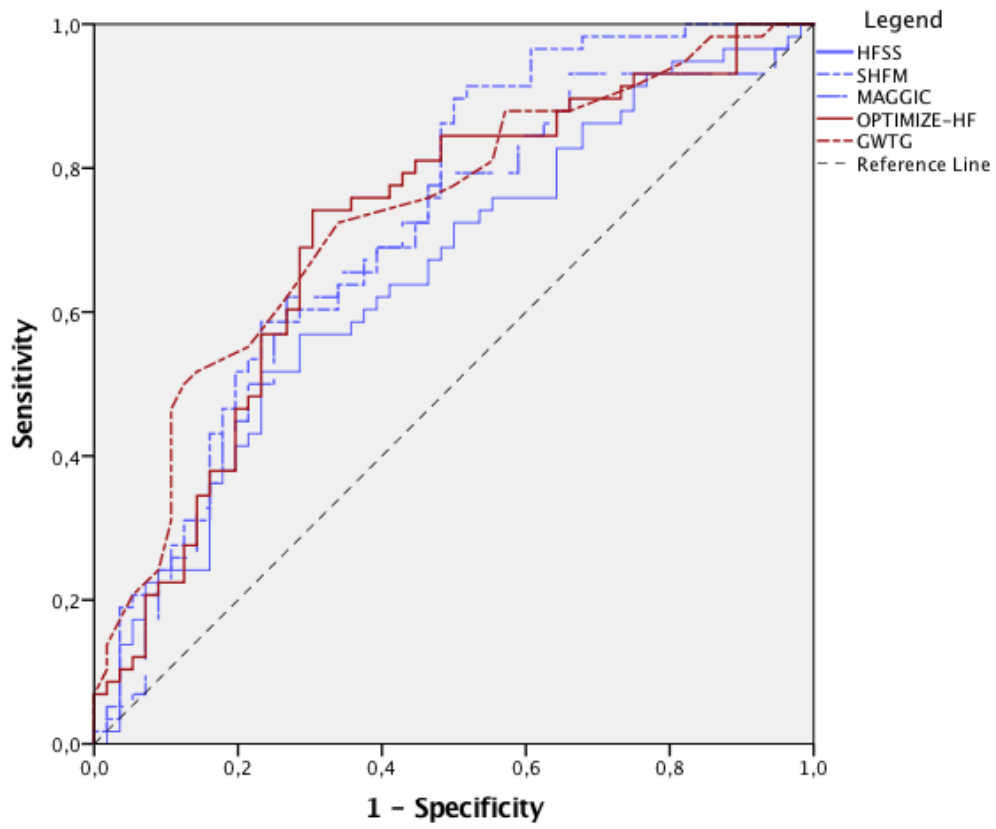


Figure 2.

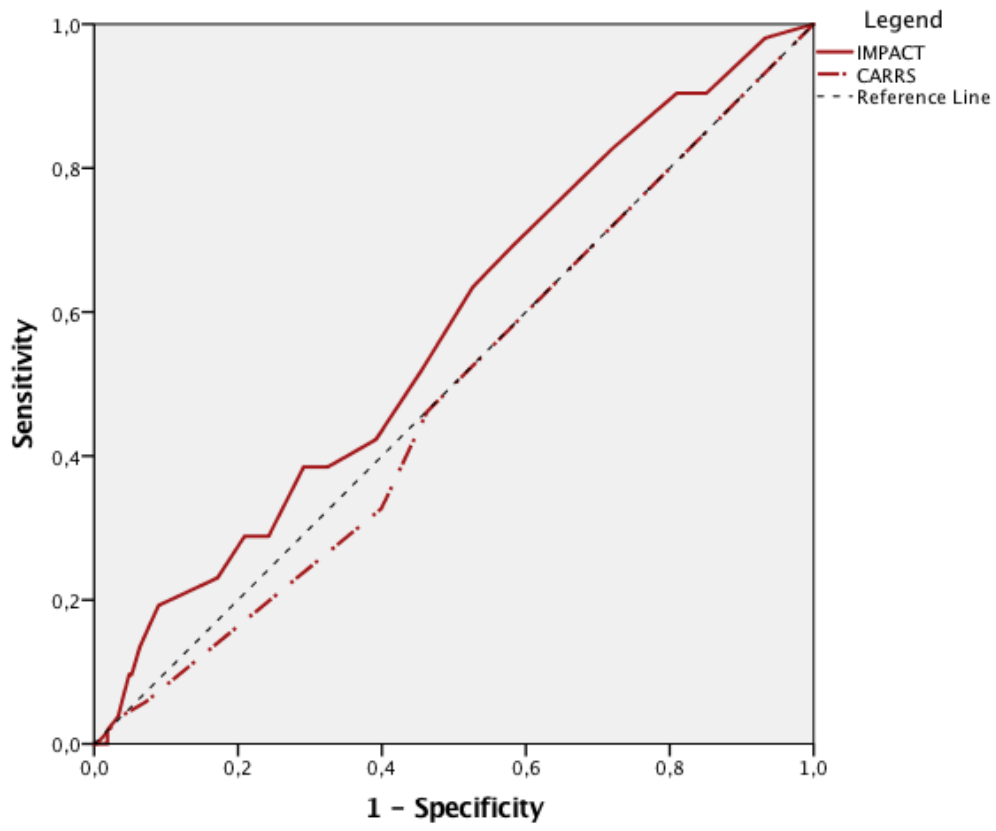


Figure 3.

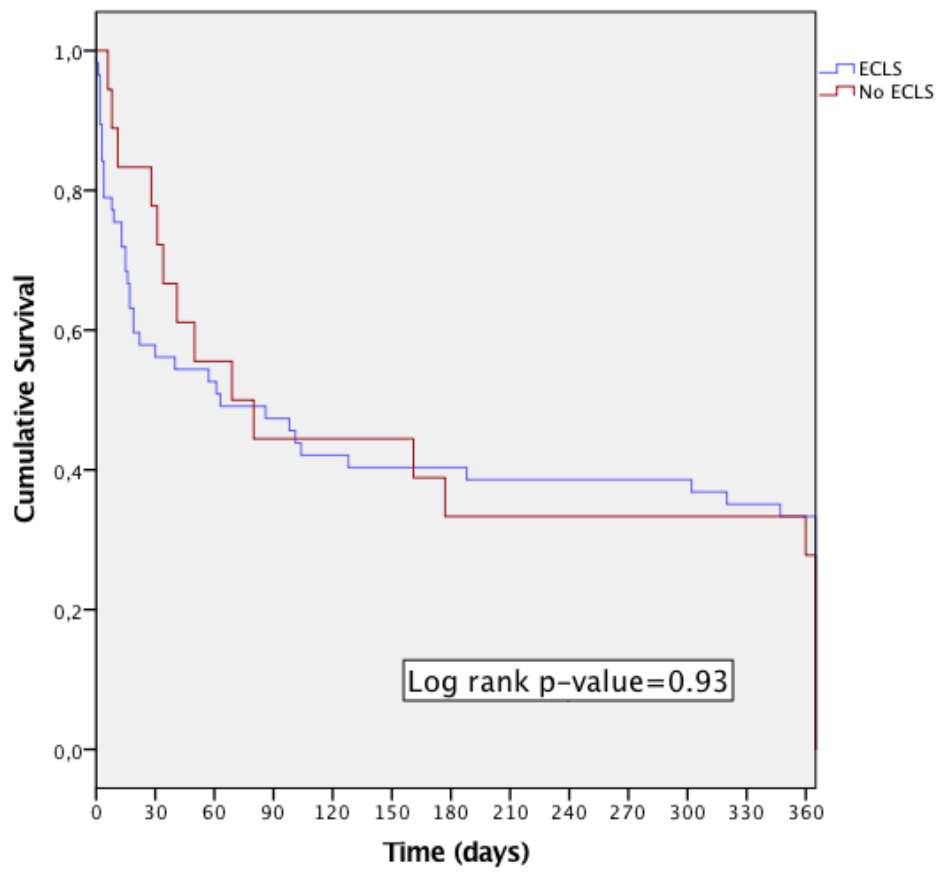


Figure 4.

