BRIEF COMMUNICATION

Evaluation of Mortality Risk with the IMPACT Scale in Patients with Cardiac Transplantation from a Latin American Population

Evaluación del riesgo de mortalidad de pacientes de trasplante cardíaco a través de la escala IMPACT en una población latinoamericana

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ABSTRACT

Background: Given the importance of optimizing organ allocation due to shortage of donors and high costs, it is essential to assess and improve survival rate in patients undergoing heart transplantation. There is currently no specific, integrated and widely accepted tool to assess mortality risk in these patients.
Objective: To assess the predictive capacity of the IMPACT scale for in-hospital and one-year mortality in patients undergoing heart transplantation at the Colombian Heart Foundation.
Methods: This was a prospective cohort study of 72 patients. Incidences, survival curves, discriminative capacity of the final model, and factors associated with mortality were determined.
Results: The incidence of in-hospital and one-year mortality was 11.11% (95% CI 4.92-20.72) and 23.61% (95% CI 14.37-35.09), respectively. Patients >60 years of age (HR 2.68; 95% CI 1.54-4.66; p=0.000), with creatinine clearance <30 ml/min (HR 5.07; 95% CI 1.11-23.15; p=0.036), and dialysis (HR 1.66; 95% CI 1.15-2.40; p=0.006), had higher risk of in-hospital mortality. The characteristics associated with one-year mortality were age >60 years (HR 1.57; 95% CI 1.11-2.23; p=0.011), dialysis (HR 1.62; 95% CI 1.18-2.23; p=0.003), intra-aortic balloon pump counterpulsation (HR 1.42; 95% CI 1.02-1.98; p=0.040) and ventricular assist device (HR 1.57; 95% CI 1.03-2.3; p=0.034). The area under the ROC curve for in-hospital and one-year mortality after transplantation was 74.22% (95% CI 50.67-97.76) and 59.09% (95% CI 42.20-75.97), respectively.
Conclusions: IMPACT had better performance in predicting in-hospital than one-year mortality at our institution. It should be cautiously interpreted until variables explaining their regional performance are included.

Key words: Heart Transplantation - Mortality - Heart Failure

RESUMEN

Introducción: Dada la importancia de optimizar la asignación de órganos debido a la escasez de donantes y los altos costos, es fundamental evaluar y mejorar la supervivencia en los pacientes sometidos a trasplante cardíaco. Actualmente no contamos con una herramienta unificada, ampliamente aceptada y específica para evaluar el riesgo de mortalidad en estos pacientes.
Objetivo: Evaluar el desempeño de la escala IMPACT para predecir mortalidad hospitalaria y a un año en pacientes sometidos a trasplante cardíaco en la Fundación Cardiovascular de Colombia.
Material y métodos: Estudio de cohorte retrospectivo de 72 pacientes. Se determinaron incidencias, curvas de sobrevida, capacidad discriminativa del modelo final y evaluación de los factores asociados con mortalidad.
Resultados: La incidencia de mortalidad hospitalaria fue del 11,11% (IC 95% 4,92-20,72) y al año fue del 23,61% (IC 95% 14,37-35,09). Los pacientes > 60 años (HR 2,68, IC 95% 1,54-4,66; p = 0,000), con depuración de creatinina < 30 ml/min (HR 5,07, IC 95% 1,11-23,15; p = 0,036) y en diálisis (HR 1,66, IC 95% 1,15-2,40; p = 0,006) tuvieron mayor riesgo de mortalidad hospitalaria. Las características asociadas con mortalidad al año fueron: edad > 60 años (HR 1,57, IC 95% 1,11-2,23; p = 0,011), diálisis (HR 1,62, IC 95% 1,18-2,23; p = 0,003), balón de contrapulsación intraaórtico (HR 1,42 IC 95% 1,02-1,98; p = 0,040) y dispositivo de asistencia ventricular (HR 1,57, IC 95% 1,03-2,39; p = 0,034). El área bajo la curva ROC para mortalidad hospitalaria y a un año postrasplante fue 74,22% (IC 95% 50,67-97,76) y 59,09% (IC 95% 42,20-75,97), respectivamente.
Conclusiones: La escala IMPACT tuvo mejor desempeño en la predicción de mortalidad hospitalaria que a un año. Su interpretación debe ser cautelosa mientras se incorporan variables que expliquen su desempeño regional.

Palabras clave: Trasplante de corazón - Mortalidad - Insuficiencia cardíaca

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INTRODUCTION

Assessing and improving survival rate in patients undergoing heart transplantation is essential, given the importance of optimizing organ allocation due to shortage of donors and high costs. (1) There is currently no specific, integrated and widely accepted tool to assess mortality risk in these patients.

The following scales have been published: RADIAL (Right atrial pressure, recipient Age, Diabetes mellitus, Inotrope dependence, donor Age, Length of ischemic time), focusing on predicting primary graft failure; (2) RSS (Risk Stratification Score), also predicting early and one-year graft loss after heart transplantation, but includes cold ischemia time, which makes the model inappropriate for pretransplant risk stratification; (3) and IMPACT (Index for Mortality Prediction After Cardiac Transplantation), (4) based on the UNOS (United Network for Organ Sharing) data in the American population. It proposes a 50-point quantitative risk index based on 12 pretransplant variables of receptors undergoing their first heart transplantation, and predicts one-year mortality risk. IMPACT was validated using the international population database ISHLT (International Society for Heart and Lung Transplantation), being highly predictive for short- and long-term mortality. (5)

The purpose of this study was to assess the discriminatory capacity of IMPACT to predict in-hospital and one-year mortality in adult patients undergoing heart transplantation at the Colombian Heart Foundation.

METHODS

This was a retrospective cohort study at the Colombian Heart Foundation. All patients aged 18 or older who underwent orthotopic heart transplantation between October 2004 and September 2012 were consecutively included. The sample was selected following a non-probabilistic model.

The information was taken from electronic and paper-based medical records and was incorporated in an Excel™ datasheet by a trained physician. The transplantation program contemplates in-hospital follow up or by telephone contact for all the patients.

Statistical analysis

A descriptive analysis of the population characteristics based on the IMPACT variables was carried out, reporting absolute and relative values. In-hospital and one-year post-transplant cumulative incidence of mortality with their corresponding 95% confidence intervals was established, and survival rate for the cohort was determined with the Kaplan Meier method. Survival curves stratified by sex, age and etiology of heart failure were compared with the log rank test. In-hospital mortality was defined as death during hospital stay and one-year mortality as death one year after transplantation.

Bivariate analysis was performed following the Cox proportional-hazards regression model. Discriminatory capacity of the final model was assessed with the ROC (Receiver Operating Characteristic) curve. A p value <0.05 was considered statistically significant for all comparisons. Statistical analysis was performed using Stata version 12 software package.

Ethical considerations

The study was approved by the institutional Research Ethics Committee.

RESULTS

A total of 72 transplanted patients were analyzed: 87.50% were men, 50% older than 51.5 years of age (youngest, 19 years; oldest, 67 years), 26.39% had hypertension, 11.11% diabetes mellitus, and 5.56% chronic kidney disease. The cause of heart failure was idiopathic in 36.11% of patients, ischemic in 29.17%, chagasic in 27.78%, and due to other causes in 6.94%. Table 1 shows the variables included in the IMPACT scale for the study cohort.

The incidence of in-hospital and one-year mortality was 11.11% (95% CI 4.92-20.72) and 23.61% (95% CI 14.37-35.09), respectively.

Survival rate at one year for the whole cohort was 76.39% (95% CI 64.80-84.60). No statistically significant differences were found when comparing in-hospital survival curves by sex and etiology [chi2 (1) =0.00 (p=0.9967) and chi2 (3) =5.31 (p=0.1503), respectively]. Conversely, statistically significant differences were found by age, survival rate being lower in patients >60 years [chi2 (1) =18.39; p=0.000].

Neither were statistically significant differences found when comparing survival curves by sex or etiology at one year [chi2 (1) =0.73 (p=0.3919) and chi2 (3) =3.65 (p=0.3020), respectively]. Still, the difference remained statistically significant by age [chi2 (1) =7.55; p=0.006] (Figure 1).

The characteristics of the IMPACT scale and its association with in-hospital mortality showed that patients >60 years of age (HR 2.68, 95% CI 1.54-4.66, p=0.000), with creatinine clearance <30ml/min (HR 5.07; 95% CI 1.11-23.15; p=0.036), and dialysis (HR: 1.66; 95% CI 1.15-2.40; p=0.006), had higher risk of in-hospital mortality than the reference group. The characteristics associated with one-year mortality were age >60 years (HR: 1.57; 95% CI 1.11-2.23; p=0.011), dialysis (HR: 1.62; 95% CI 1.18-2.23; p=0.003), intra-aortic balloon pump counterpulsation (HR: 1.42; 95% CI 1.02-1.98; p=0.040) and ventricular assist device implantation (HR: 1.57; 95% CI 1.03-2.3; p=0.034) (Table 2).

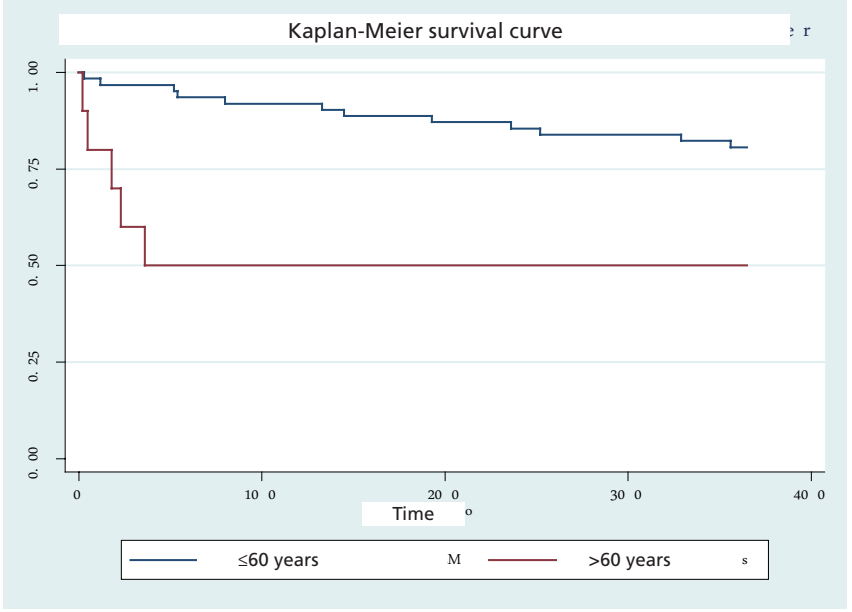
Median IMPACT total score was 3 points, with a minimum value of 0 and a maximum value of 28. Regarding the IMPACT score diagnostic performance, the area under the ROC curve for in-hospital mortality was 74.22% (95% CI 50.67-97.76) (Figure 2), and for one-year mortality 59.09% (95% CI 42.20-75.97).

The highest discriminative cut-off point for in-hospital mortality was a score ≥4 in the IMPACT scale, with 75% sensitivity, 60.94% specificity, and 62.5% correct classification; conversely, for one-year mortality, the highest discriminative cut-off point was a

Table 1. Characteristics included in the IMPACT (Index for Mortality Prediction after Cardiac Transplantation) scale for the study cohort (n=72)

Characteristics	Assigned points	n (%)
Age >60 years	3	10 (13.89)
Serum bilirubin (mg/dl)		
0-0.99	0	52 (72.22)
1-1.99	1	8 (11.11)
2-3.99	3	7 (9.72)
≥4	4	5 (6.94)
Creatinine clearance (ml/min)		
≥50	0	52 (72.22)
30-49	2	13 (18.06)
<30	5	7 (9.72)
Dialysis in the list and transplantation	4	4 (5.56)
Female	3	9 (12.50)
Etiology of heart failure		
Idiopathic	0	26 (36.11)
Ischemic	2	21 (29.17)
Congenital	5	1 (1.39)
Other (chagasic, valvular, peripartum)	1	24 (33.33)
Recent infection	3	11 (15.28)
Intra-aortic balloon pump counterpulsation	3	14 (19.44)
Pretransplant mechanical ventilation	5	13 (18.06)
Race (Hispanic)	0	72 (100.00)
Temporary circulatory support	7	9 (12.50)
Ventricular assist devices	5	1 (1.39)

Fig. 1. Survival curves by age at 1 year of heart transplantation.



score ≥2, with 76.47% sensitivity, 38.18% specificity, and 47.22% correct classification.

DISCUSSION

Our results show that IMPACT is a scale with adequate predictive capacity of in-hospital mortality at our institution, and high-risk variables were age >60 years, creatinine clearance <30 ml/min, and dialysis patients.

Although IMPACT global predictive capacity for one-year mortality was low, the independent variables at higher risk were patients >60 years, those in dialysis, with intra-aortic balloon counterpulsation, and with ventricular assist device. Regarding the higher

Variable	In-hospital mortality		One-year mortality	
	HR	95% CI	HR	95% CI
Age				
≤60 years	REF			
>60 years	2.68	1.54-4.66*	1.57	1.11-2.23*
Serum bilirubin (mg/dl)				
0-0.99	REF			
1-1.99	-	-	-	-
2-3.99	0.89	0.11-7.25	1.86	0.53-6.56
≥4	-	-	0.71	0.09-5.45
Creatinine clearance (ml/min)				
<30	5.07	1.11-23.15*	2.81	0.78-10.10
30-49	0.74	0.08-6.78	1.09	0.30-3.91
≥50	REF			
Dialysis in the list and transplantation				
Yes	1.66	1.15-2.40*	1.62	1.18-2.23*
No	REF			
Sex				
Female	1.00	0.12-8.17	0.75	0.38-1.47
Male	REF			
Etiology of heart failure				
Other	1.99	0.18-22.05	0.45	0.12-1.75
Ischemic	6.46	0.75-55.41	1.43	0.50-4.07
Congenital	2.23	-	-	-
Idiopathic	REF			
Recent infection				
Yes	1.29	0.78-2.11	1.39	0.98-1.97
No	REF			
Intra-aortic balloon pump counterpulsation				
Yes	1.43	0.89-2.32	1.42	1.02-1.98*
No	REF			
Pretransplant mechanical ventilation				
Yes	1.12	0.82-1.51	1.09	0.87-1.36
No	REF			
Temporary circulatory support				
Yes	1.07	0.84-1.36	1.07	0.90-1.28
No	REF			
Ventricular assist devices				
Yes	1.32	0.84-2.06	1.57	1.03-2.39*
No	REF			

Table 2. Factors associated with mortality in the study cohort Factors associated with mortality in the study cohort

* p <0.05

potential risk of in-hospital and one-year mortality in patients older than 60 years, we believe that recommendations of the Colombian Guidelines for Heart Transplantation should be followed, which define the age limit for transplantation in 65 years and state its contraindication in patients over 70 years, stressing that patients aged 65-70 years should be evaluated individually according to their comorbidities. (6)

Cumulative incidence of in-hospital mortality was 11.11%, which was within the ISHLT range, having decreased from 16% to 9% in recent years. ISHLT reported 15% one-year mortality, despite obvious regional differences. Cumulative incidence of one-year mortality in our cohort was 23.61%, similar to that in South America (21%) and Europe (20%), but far from that in North America (9%). Despite the few South American publications, one-year mortality reports for different centers and countries vary in a wide range: Brazil 34%, (7) Argentina 20%, (8) and Chile 12%. (9) These differences in one-year mortality may be

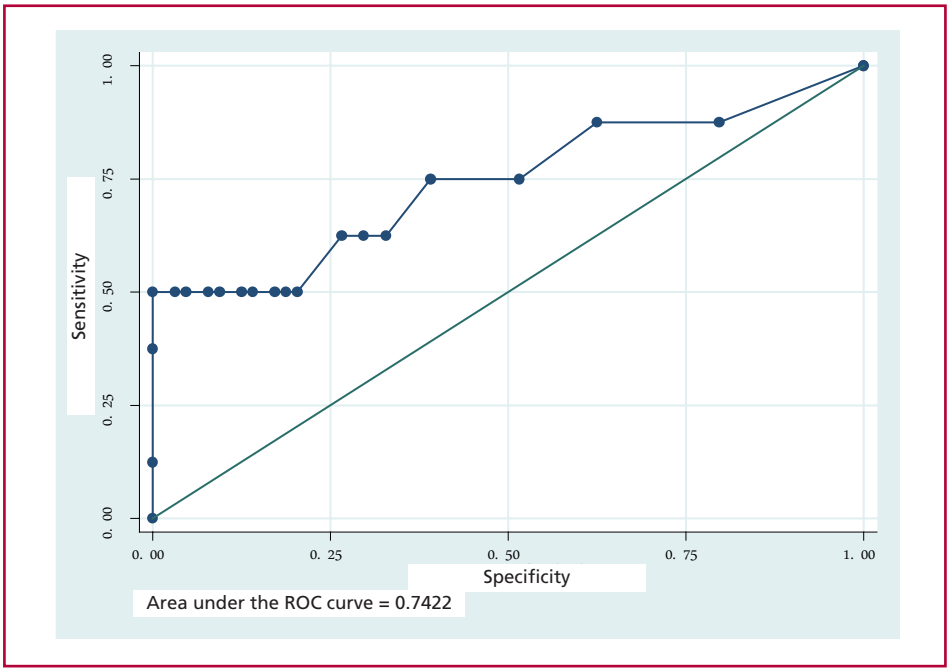


Fig. 2. Area under the ROC curve for in-hospital mortality

due to difficult follow-up by the different health care systems of the region. We believe that the lower one-year predictability of IMPACT can be associated with other influencing variables, such as social insurance and education, (10) preoperative B-type natriuretic peptide levels, (11) panel reactive antibody (PRA) screening, (12) social and economic factors during post-transplant follow-up, adherence to treatment, and influence of institutional volume. (13) According to ISHL, most centers (77%) perform fewer than 20 transplantations per year, as is the case in our center. Fewer centers (23%) perform 20 or more transplantations per year and are responsible for 52% of all transplanted patients. (1) Influence of variables associated with donors but which are not part of IMPACT, may also influence the outcome, such as age, sex, ischemia times (14) and donor to recipient weight ratios (15), among others. Therefore, we believe it is relevant to study all those variables in order to improve IMPACT predictability for in-hospital and long-term mortality in our population.

Our study is limited to a retrospective cohort and to a single Latin American center; therefore, results are not applicable to other centers given the differences in population and resources. Latin America lacks organized databases such as UNOS, and regional data come from centers reporting to ISHLT, where 56% are from North America, 37% from Europe, and 5% from the rest of the centers, including South America. There is an urgent need to consolidate the information of heart transplantation patients in Latin America, and continue searching for new variables to be included in a widely accepted scale of our own (or in an adjusted one), so that it is possible to objectively predict short- and long-term mortality, prospectively evaluate transplant candidates, facilitate clinical discussion with patients and their families, compare transplantation centers, and optimize the limited donors and financial resources available, among others.

CONCLUSIONS

At our center, IMPACT predictability evidenced better performance for in-hospital mortality than for one-year mortality in heart transplantation patients. We believe that validation studies on large Latin American populations are necessary. It is important to adjust the index according to variables that could affect long-term mortality due to the wide technological gap and the socio-cultural diversity of the region. Therefore, it should be cautiously interpreted until variables explaining the regional performance are included.

Conflicts of interest

None declared.
(See authors' conflicts of interest forms in the website/ Supplementary material).

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