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Research Article

Predictive Factors for Mortality in Adult Patients Undergoing Heart Transplantation

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ABSTRACT:

Objective: To evaluate the predictive factors for mortality in adult patients undergoing heart transplantation.

Method: a retrospective cohort study in a tertiary hospital, which is reference in cardiology and pneumology in Latin America. It was included 70 patients older than 18 years who underwent heart transplantation and excluded patients under 18 years as well as those diagnosed with congenital heart disease.

Results: No differences were observed between the groups in relation to male gender (67.2% vs. 66.7%, p=0.969) and age (44 ± 12 vs. 52 ± 13, p=0.086). Regarding comorbidities the groups were not different, however, when comparing the score values of the Cleveland Clinic we observed a significant difference (5 [4 – 7] vs. 7 [5.25 – 8.75], p=0.010), being higher in the non-survivors group. In the multivariate analysis we observed that the Cleveland Clinic Score (OR: 1.573, p=0.007), baseline creatinine greater than 1.5 mg / dL (OR: 3.426, p=0.007), previous cardiac surgery (OR: 5.200, p = 0.032) and need for dialysis (OR: 6.750, p = 0.017) were the main predictive factors for death.

Conclusion: The main predictive factors for death in this population were Cleveland Clinic Score increased, baseline creatinine greater than 1.5 mg / dL, having undergone heart surgery in advance and requiring dialysis.

Descriptors: Heart Transplantation; Mortality; Thoracic Surgery; Postoperative Complications.

Introduction

Heart failure (HF) is a clinical syndrome that affects 23 million people worldwide. The prevalence of HF in the American population aged over 20 years is approximately 2,6% [(1)]. The cardiac transplantation is considered the definitive treatment for advanced heart failure [(2)]. The results after transplantation have improved considerably in recent years due to better selection of donors, improvement of surgical techniques, improved postoperative management in intensive care units and new immunosuppression regimens enabling longer survival of these patients [(3,4)]. Despite advances in the short-term outcomes of patients undergoing heart transplantation, some complications are associated with worse long-term prognosis. The most common complications in patients after heart transplantation are acute kidney injury (AKI), infection, cardiac allograft dysfunction, gastrointestinal disorders, bleeding, arrhythmias, shock, sepsis, tamponade, seizures and encephalopathy [(5,6)]. In the last decade, the mortality of patients awaiting transplantation was approximately 17%, these numbers declined continuously over the years to 13.7%, probably due to the improvement in medical therapy for patients with HF in the terminal phase and the increase in use of an implantable cardioverter-defibrillator, as well as resynchronization therapy [(7)]. Thus, the objective of this article was to evaluate the predictive factors of mortality in adult patients undergoing heart transplantation.

Method

This is a retrospective cohort study performed at the Heart Institute (InCor) do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. The research project was approved with the number 1.191.055, by the Institutional Board Review.

To collect data, we evaluated the records of all patients over 18 years, who underwent heart transplantation at InCor from January 2011 to January 2015. Patients with congenital heart defects were excluded from the study because they had an abnormality in the heart structure present even before birth and that could interfere with the results of this research.

The search of the records of patients submitted to heart

transplantation was performed at Heart Institute (InCor) do Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo. From this search, all records of transplanted patients were used to acquire physical records and to collect information in the electronic medical record. Eighty nine patient records were selected from the search, of which 19 were excluded, as shown in figure 1.

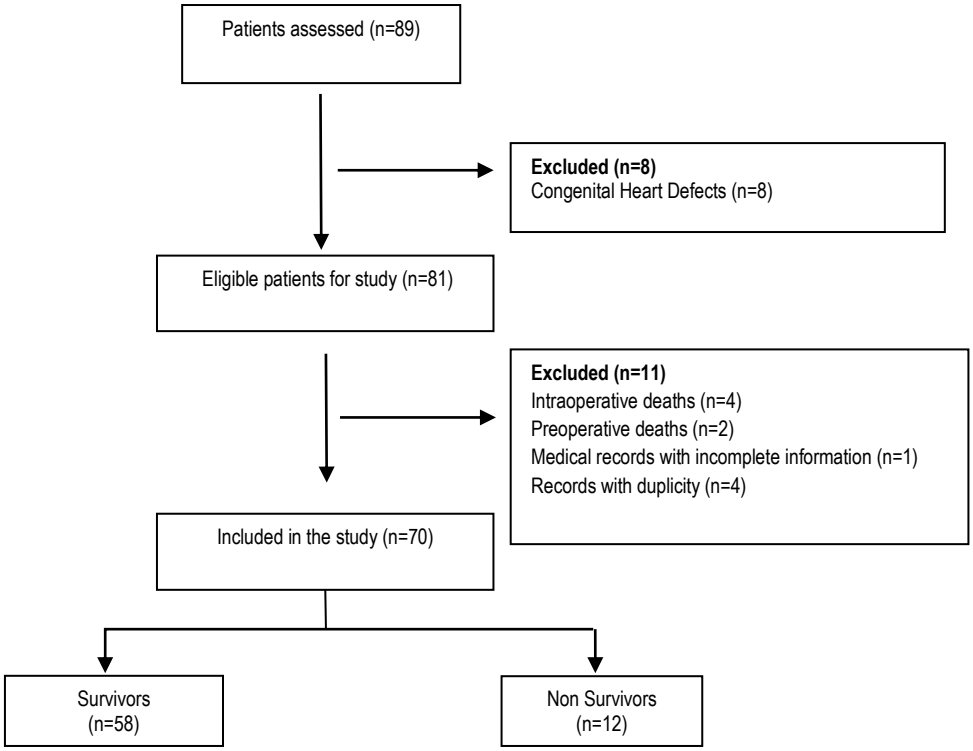

Figure 1. Flowchart of study

A specific instrument was designed with information about patient identification for the data collection, demographic data, clinical characteristics, procedure data, clinical assessment, outcomes and implementation scores for evaluation of surgical risk (EuroSCORE), prognosis assessment (SAPS 3), prediction of AKI in the postoperative period of cardiac surgery (Cleveland Clinic Score) and for the comorbidities evaluation and mortality prediction in 10 years (Charlson Score) [8-11].

The medical records evaluation occurred until discharge where the outcomes were analised (discharge or death). Hemoglobin, creatinine, central venous oxygen saturation, use of blood products, administered medications, need for mechanical ventilation, isolated microorganisms in cultures, neurological or cardiovascular complications, and need for dialysis and surgical re-intervention were recorded daily. Laboratory tests were measured in routine Surgical ICU and available in medical records.

Qualitative variables were described using absolute and relative frequencies. The average, standard deviation, median and interquartile range were calculated for quantitative variables. The Kolmogorov-Smirnov test was used to verify the normal distribution of continuous variables. The difference between the groups was performed using the two-tailed t test, Mann-Whitney U test, Chi-square test and Fisher's exact test, when it was appropriate. Variables in the multivariate analysis were included when demonstrated significant results in the univariate analysis with a p value <0.10. A p value <0.05 in the multivariate analysis was considered significant. The statistical software SPSS (version 20.0; IBM, Armonk, USA) was used for data analysis.

Results

This study included 70 patients, of whom 58 survived during hospitalization and 12 died. For the analysis of the data groups were divided into survivors and non-survivors. Table 1 shows the clinical and demographic characteristics and perioperative survivors and non-survivors patients undergoing heart transplantation from 2010 to 2015.

There was no difference between the groups in relation to males (67.2% vs. 66.7%, p = 0.969), age (44 $\pm$ 12 $\pm$ 13 vs. 52, p = 0.086) and white (75, 4% vs. 90.9%, p = 0.341). Regarding comorbidities groups were similar, however, when comparing the values of the Cleveland Clinic Score we found significant differences (5 [4-7] vs. 7 [5.25 to 8.75]) between survivors and non-survivors groups, respectively. More patients from non-survivors had undergone some cardiac surgery prior to transplantation and had a worse renal function compared to those who survived, baseline serum creatinine values were higher, while the glomerular filtration rate and volume of urine output were lower in those.

Table 1 - Clinical-demographic and perioperative characteristics of survivors and non-survivors undergoing heart transplantation.

Variable	Survivors (n=58)	Non-survivors (n=12)	p (value)
Preoperative period			
Male	39 (67.2)	8 (66.7)	0.969
Age	44 ± 12	52 ± 13	0.086
White	43 (75.4)	10 (90.9)	0.341
BMI, kg/m^2	22.1 ± 4.0	23.4 ± 3.4	0.254
LVEF , %	24 ± 9	24 ± 6	0.907
EuroSCORE	7.3 ± 2.1	8.3 ± 2.1	0.155
Chalrson Score	2.4 ± 1.6	3.2 ± 1.9	0.240
Cleveland Clinic Score	5 [4 – 7]	7 [5.25 – 8.75]	0.010
Previous Cardiac surgery	5 (8.8)	4 (33.3)	0.039
Arterial Hypertension	14 (24.1)	5(41.7)	0.229
Acute myocardial infarction	10 (17.2)	4 (33.3)	0.228
Diabetes	12 (20.7)	1 (8.3)	0.279
Dyslipidemia	10 (17.2)	1 (8.3)	0.410
Previous smoking	17 (29.3)	5 (41.7)	0.410
Atrial defibrillation	27 (46.6)	6 (50)	0.828
Pre-transplant Diagnosis			
Dilated Cardiomyopathy	46 (79.3)	8 (66.7)	0.695
Ischemic Cardiomyopathy	8 (13.8)	3 (25)	
Restrictive Cardiomyopathy	3 (5.2)	1 (8.3)	
Valvar Cardiomyopathy	1 (1.7)	0	
Pre-transplant Clinical Condition			
Baseline Creatinine	1.38 [1.12 – 1.73]	1.94 [1.25 – 2.98]	0.013
Glomerular Filtration Rate	49.4 ± 11.9	38.3 ± 17.5	0.030
Inotropic use	50 (87.7)	10 (83.3)	0.690
Inotropic dose, mcg/kg/min	14.6 ± 6	15.1 ± 5.7	0.462
Intra-aortic Balloon	30 (52.8)	6 (50)	0.868
Intraoperative period			
Organ Ischemia Time, min	161 ± 46	171 ± 49	0.539
Pre-transplantation Hospitalization, days	9 [1 – 41]	13 [2.25 – 104.75]	0.243
Pre-transplantation ICU Admission, days	22 [12 – 65]	45 [1 – 94]	0.274
Surgery time, min	437.5 ± 77.1	494.3 ± 91.8	0.077
EC time, min	94.2 ± 25.5	92.8 ± 35.2	0.902
Hydric Balance, ml/kg	26.7 ± 19.2	32.4 ± 23.8	0.452
Diuresis, ml/kg/min	0.42 [0.33 – 0.69]	0.28 [0.08 – 0.47]	0.022
Transfusion of Hemocomponents	48 (82.8)	10 (83.3)	0.962
Hemocytes Concentrate, units	2.11 ± 0.8	2.44 ± 1.6	0.550
Platelets, units	5.38 ± 3.5	5.25 ± 3.7	0.951
Postoperative period			
SAPS 3 (ICU admission)	36.5 ± 11.4	39.5 ± 14.6	0.508
Nitric Oxide, ppm	51 (89.5)	11 (91.7)	0.815

Data expressed in absolute and relative frequency n (%); Mean ± standard deviation, median and [interquartile range]. BMI: body mass index; LVEF: left ventricular ejection fraction; EC: extracorporeal circulation; SAPS: Simplified Acute Physiology Score.

Table 2 shows the association of six variables with mortality. The variables Cleveland Clinic Score, baseline creatinine, diuresis and dialysis were considered for the analysis. Gender and age were part of the analysis because of the potential to influence outcomes. We note that the Cleveland Clinic Score (OR: 1.573, p = 0.007), baseline creatinine (OR: 3.426, p = 0.007), previous cardiac surgery (OR: 5.200, p = 0.032) and need for dialysis (OR: 6.750, p = 0.017) were associated with mortality. The presence of heart surgery, high baseline serum creatinine values, increased Cleveland Clinic score and need for dialysis elevated the death risk. These influences were exercised independently.

Table 2 - Multivariate analysis of predictive factors of death.

Variable	OR	CI (95%)	p (value)
Male	1.026	0.274 – 3.840	0.969
Age	1.057	0.999 – 1.120	0.056
Cleveland Clinic Score	1.573	1.130 – 2.191	0.007
Baseline Creatinine	3.426	1.406 – 8.345	0.007
Previous Cardiac surgery	5.200	1.148 – 23.559	0.032
Dialysis	6.750	1.401 – 32.519	0.017

OR: odds ratio; CI: confidence interval

Table 3 shows the clinical course and outcomes of the study patients. We found a significant difference between the survivors and non-survivors group on the need for dialysis (6.9% vs. 33.3%, p = 0.021), the development of cardiogenic shock (10.3% vs. 66.7, p <0.001) and septic shock (1.7% vs. 72.7%, p <0.001) and length of hospital stay (71 [48.5 to 116.5] vs. 127 [77.5 to 169 75], p = 0.031), respectively.

Table 3 – Clinical course and outcomes of survivors and non-survivors adult patients in the postoperative period of Heart Transplantation.

Outcomes	Survivors (n=58)	Non-survivors (n=12)	p (value)
Acute Kidney Injury			
KDIGO 1	36 (75)	6 (50)	0.057
KDIGO 2	10 (20.8)	4 (33.3)	
KDIGO 3	2 (4.2)	2 (16.7)	
Dialysis	4 (6.9)	4 (33.3)	0.021
Need for Reoperation	18 (31)	7 (58.3)	0.078
Bleeding	11 (19)	3 (25)	0.642
Cardiac Tamponade	8 (13.8)	2 (16.7)	0.799
Cerebrovascular Accident	4 (6.9)	3 (25)	0.088
Mechanical Ventilation (>48 hours)	7 (12.1)	4 (33.3)	0.089
Infection	6 (10.3)	3 (25)	0.201
Cardiogenic Shock	6 (10.3)	8 (66.7)	<0.001
Septic Shock	1 (1.7)	8 (72.7)	<0.001
ICU length of stay	25 [13 – 47]	30.5 [14.75 – 92]	0.307
Length of Hospital Stay	71 [48.5 – 116.5]	127 [77.5 – 169.75]	0.031

Data expressed in absolute and relative frequency n (%); Mean ± standard deviation, median and [interquartile range]. KDIGO: kidney disease Improving Global Outcomes; ICU: Intensive Care Unit.

Discussion

In this retrospective cohort study conducted at a specialized cardiology and pneumology center of high complexity we demonstrated that mortality of adult patients undergoing heart transplantation was 17.1% during the admission time. In a 21-year cohort study (12), which evaluated more than 36,000 patients who underwent heart transplantation in the United States, the mortality rate at six months was almost three times higher (46.3%) than that found in our institution.

Exposure to a previous cardiac surgery was another factor associated with mortality in the postoperative transplant. In the sample, 33.3% of patients had undergone prior surgical procedures. A study that evaluated the post heart transplant mortality factors showed correlation between exposure to previous cardiac surgery and mortality, which corroborates this study[1].

The Cleveland Clinic Score, an instrument that assesses the risk of patients developing postoperative AKI was associated with mortality, higher values of the score were observed among non-survivors. Risk stratification in cardiac surgery is a relevant issue. Many risk assessment models are currently available to physicians and institutions. They are used to assign a specific risk of post-operative mortality for individuals [(14).]

One study compared the Cleveland score and EuroSCORE, both are risk scores, both the Cleveland Clinic and the EuroSCORE were effective in predicting mortality of patients undergoing elective coronary artery bypass surgery, however, the Cleveland score was more sensitive in predicting mortality [(6.15)]

Creatinine was another factor related to mortality after heart transplantation. Loef et. al. [(16)] shown from the analysis of 843

patients undergoing coronary artery bypass surgery, an increase of 25% or more in creatinine from baseline was associated with a 15-fold increase in hospital mortality after cardiac surgery. AKI occurs in up to 30% of patients undergoing cardiac surgery, requiring dialysis in about 1% of these patients. The pathogenesis of AKI involves multiple pathways, hemodynamic factors, inflammatory and nephrotoxic are involved and overlap each other, which leads to kidney damage [17]. Numerous studies have demonstrated that short-term AKI is associated with increased hospital admission, increased risk of infection, increased hospital costs, and increased mortality [18].

The observed outcomes in heart transplantation postoperative period associated with mortality were the presence of septic shock and cardiogenic shock. Septic shock is a major problem in the intensive care unit, and it is a challenge for its high incidence, high mortality and high costs [19]. In our study, septic shock, occurred in 70% of patients who died. In a study evaluating the need for readmission to the ICU after lung transplantation showed that the main cause of readmission to the ICU was the presence of septic shock [20]. The literature shows that sepsis is common in transplantation, and infectious complications occur in 19.5% of patients. It is known that infectious processes distributions accompany the rejection curve, they are more frequent and severe in the first few months after transplantation because in this phase the immunosuppression is more intense. In turn, cardiogenic shock was also a mortality predictor in this study, affecting 66.6% of patients who progressed to death. What is known is that the cardiogenic shock is a clinical condition of inadequate tissue perfusion due to cardiac dysfunction, and remains frequent and severe, with almost 50% of hospital mortality, despite the progress in the currently established therapy which corroborates this study that the presence of heart failure was responsible for a poor prognosis after heart transplantation [21].

Cardiac surgery is a complex procedure that has important repercussions organic, changing in many ways the physiological mechanisms of patients. In our study, there was an association between length of stay and mortality. Studies show that intensive care unit has mortality rates between 5.4% and 33%. The length of stay in the ICU in our study was not significant for mortality, however, studies show that complications in the postoperative period are responsible for a longer length of stay in the ICU and a high mortality. Postoperative infections of heart surgery, as well as the AKI and dialysis use, as seen above, contribute to the high morbidity and mortality, length of stay and hospital costs [22-23].

Even though the institution where the study was conducted is the seventh largest transplant center in the heart of the world and the largest in Brazil, we recognize some limitations. We used a relatively small sample and a single center, which limits the generalization of our results and the retrospective nature of the study makes it difficult to monitor the information related to patients in real time.

Conclusion

The main predictive factors for death of the studied population were increased Cleveland Clinic Score, baseline creatinine values above 1.5 mg / dL, having undergone previous heart surgery and requiring dialysis postoperative period. The knowledge of complications that occur in heart transplant postoperative will subsidize the care planning, in order to establish measures for prevention and control of post-operative complications.

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