

Results of medium-term survival in patients undergoing cardiac transplantation: institutional experience

Resultados de sobrevida a médio prazo em pacientes submetidos ao transplante cardíaco: experiência de uma instituição

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Abstract

Introduction: The heart transplant became a consecrated therapy for patients with terminal heart failure, increasingly improving the survival.

Objective: To identify the medium-term results in patients undergoing cardiac transplantation.

Methods: This is a descriptive, documentary and retrospective study, using a quantitative approach, developed in a Unit of Transplant and Heart Failure, of a tertiary level public hospital, located in Fortaleza, CE, Brazil. The data were obtained from a sample of 188 patients (154 men and 34 women), submitted to the heart transplant, in the period from October 1997 to March 2011. There were calculated survival rates based on Kaplan-Meier methods.

Results: There were identified information about the patient's gender (male 81.91%), medical diagnosis which determined the heart transplantation (idiopathic cardiomyopathies 23.98%, ischemic 23.4% and Chagasic 17.02%). The median age of patients was 48 years old (interquartile range = 17.25 years) and the median observation period was 877 days. During this period, 78 patients died, resulting in survival ratios of 72%,

59% and 47% after 1, 5 and 9 years of cardiac transplantation, respectively. Younger patients had longer survival ($P=0.0418$).

Conclusion: The medium-term survival of patients undergoing cardiac transplantation is significant, especially for younger patients.

Descriptors: Heart transplantation. Survival rate. Mortality.

Resumo:

Introdução: O transplante cardíaco transformou-se em terapêutica consagrada para os doentes com insuficiência cardíaca em fase terminal, melhorando cada vez mais a sobrevida.

Objetivo: identificar os resultados de sobrevida a médio prazo em pacientes submetidos ao transplante cardíaco.

Métodos: Trata-se de um estudo descritivo, documental e retrospectivo, com abordagem quantitativa, desenvolvido em uma Unidade de Transplante e Insuficiência Cardíaca, de um hospital público de nível terciário, situado em Fortaleza, CE, Brasil. Os dados foram obtidos a partir de uma amostra de 188 pacientes (154 homens e 34 mulheres), submetidos ao transplan-

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Abbreviations, acronyms & symbols
NYHA New York Heart Association

te cardíaco, no período de outubro de 1997 a março de 2011. As taxas de sobrevida foram calculadas com base nos métodos de Kaplan-Meier.

Resultados: Identificaram-se informações sobre o sexo do paciente (81,91% masculino), diagnóstico médico que determinou o transplante cardíaco (miocardiopatias idiopática 23,98%, isquêmica 23,4% e chagásica 17,02%). A mediana da idade dos

pacientes foi 48 anos (Intervalo interquartilico = 17,25 anos) e a mediana do período de observação foi de 877 dias. Nesse período, 78 pacientes morreram, resultando em razões de sobrevida de 72%, 59% e 47% após 1, 5 e 9 anos do transplante cardíaco, respectivamente. Os pacientes mais jovens apresentaram maior tempo de sobrevida ($P=0,0418$).

Conclusão: A sobrevida em médio prazo de pacientes submetidos ao transplante cardíaco é significativa, especialmente para os pacientes mais jovens.

Descritores: Transplante de coração. Taxa de sobrevida. Mortalidade.

INTRODUCTION

Cardiac transplantation between humans began at the University of Cape Town, South Africa, in 1967, with surgery performed by Bernard [1]. In 1968 Zerbini & Decourt [2] performed the first heart transplant in Latin America and the seventeenth in the world, in patients with dilated cardiomyopathy.

Cardiac transplantation remains the treatment of choice for patients with refractory heart failure, despite the great improvement in life expectancy with clinical treatment, and for patients with end-stage heart failure, getting better survival. It is accepted as an effective method for the treatment of patients without hope, pleasure or satisfaction of a healthy and dignified existence, or at risk of death [3].

However, it cannot be considered an isolated event, but a process of continuous thread throughout the patient's life [4].

The International Society for Heart and Lung Transplantation reported holding 76,538 orthotopic heart transplants in 352 centers in the world [5]. Brazil were recorded in 832 heart transplant procedures [6], showing that the country performs a high quantity of surgeries.

Cardiac transplantation in the State of Ceara is only performed when the recipient is enrolled in the Unified Waiting List to receive the body [7]. Such receptors are patients with heart failure functional class III or IV New York Heart Association (NYHA) that are disabling with symptoms or at high risk of death in the first year and have no alternative to medical or surgical treatment [3]. However, there are limitations created by the higher number of receptors on the ongoing shortage of donors [8]. The increase of people placed on the waiting list for heart transplantation, is greater than those who are transplanted [7].

The success of heart transplantation depends on the quality of donor hearts. The evaluation of these hearts is to ensure the maintenance of adequate hemodynamic conditions on the receiver and ensure their survival. Thus, the selection of transplant candidates should be careful with identification of risk factors and coexisting illnesses. The main factors of

poor prognosis for survival are reduced ventricular ejection fraction, NYHA functional class III/IV, elevation of serum catecholamines, hyponatremia, elevated pulmonary capillary wedge pressure, decreased cardiac index, ventricular arrhythmias and maximal oxygen consumption (VO_2 max) reduced during exercise [9].

Increases observed in cardiac transplant, new surgical techniques, immunosuppressive drugs, diagnostic methods and approaches of the multidisciplinary team in the pre-and postoperative early and late push for survival of patients undergoing heart transplantation. These factors besides influencing the survival of patients still improve their quality of life as they recover physical capacity, return to work and even sports. Confirms that, in the first year, the survival rate is around 80% to 90% in five years 60% to 70% and 60% in ten years after the operation [4,10-12].

Given these considerations, the aim of this study is to identify the medium-term outcomes in patients undergoing heart transplantation.

METHODS

This study examined the survival rates of patients undergoing heart transplantation. Data were obtained from the records of patients who were treated as outpatients in a public hospital that is reference to heart transplantation in a state in northeastern Brazil. The study included patients older than 18 years who underwent heart transplantation because of the following medical conditions: cardiomyopathies (dilated, idiopathic, Chagas disease, alcoholic, ischemic, valvular, hypertensive, hypertrophic, peripartum and viral), tachycardiomyopathy and retransplantation. Children were excluded and patients who did not submit complete data in the records of the transplant unit. For data analysis, medical conditions frequently less than 10 were grouped into other heart conditions.

Thus, most of the patients were male (81.9%) and had a median age at the start-up period of 48 years (interquartile range = 17.25 years). The three most common medical

conditions that determine transplantation were idiopathic cardiomyopathy (23.9%), ischemic (23.4%) and chagasic (17.0%). The median follow-up was 877 days (interquartile range = 1802.8 days), and 58.5% of patients were alive when the study was terminated (Table 1).

Statistical differences in age at transplant were identified by sex ($P=0.0075$, men=49, women=43), state ($P=0.0334$, alive=48.36; dead=44.47), and medical conditions ($P<0.0001$). Medical conditions also were related to gender ($P=0.0489$). Moreover, no relation was found between the condition of the patient at the end of analysis and medical conditions ($P=0.3477$) and sex ($P=0.3573$).

No statistical difference in survival times was identified in relation to gender ($P=0.474$) or medical conditions ($P=0.352$). On the other hand, the median survival time of patients who died was lower than that of patients alive at the end of the study period (113.5 vs. 1346.0, $P<0.0001$). No correlation was found between survival rates and age at transplant ($\rho=0.0171$, $P=0.8152$).

A total of 213 patients underwent heart transplantation since the first transplant in the institution. Of these, 24 were minors and one patient had incomplete data on their records and you cannot locate it. Thus, the records of a sample of 188 patients who underwent heart transplantation between October 1997 and March 2011 were assessed.

Table 1. Distribution of patients submitted to cardiac transplantation. Fortaleza, Ceará, Brazil. 2011

Variable	N	%	IC 95% Inf.	IC 95% Sup.				
1. Gender								
Male	154	81.9	75.66	87.14				
Female	34	18.1	12.86	24.34				
2. Etiology of cardiomyopathy								
Idiopathic cardiomyopathy	45	23.9	18.03	30.69				
Ischemic cardiomyopathy	44	23.4	17.55	30.12				
Chagas cardiomyopathy	32	17.0	11.94	23.17				
Dilated cardiomyopathy	20	10.6	6.62	15.95				
Alcoholic cardiomyopathy	17	9.0	5.36	14.08				
Valvular cardiomyopathy	11	5.9	2.96	10.23				
Other cardiac conditions	19	10.2	6.20	15.33				
3. State of the patient								
Alive (censored)	110	58.5	51.11	65.63				
Dead	78	41.5	34.37	48.89				
4. Age (years)								
	Min.	1° Q.	Median	Average	3° Q.	Max.	DP	P Value*
	19.00	38.00	48.00	46.75	55.25	73.00	12.06	0.0309
5. Tracking time (days)								
	0.0	166.2	877	1206	1969	4449	1183.4	<0.0001

* Shapiro-Wilk test; SD – standard deviation

Table 2. Kaplan-Meier Estimators and Nelson-Aalen for the survival time of patients submitted to cardiac transplantation. Fortaleza, Ceará, Brazil. 2011

Time (Years)	N° of patients In risk	N° of deaths	Kaplan-Meier				Nelson-Aalen			
			S(t)	EP*	IC 95% Inf.	IC 95% Sup.	IC 95% Inf.	IC 95% Sup.		
0 1	188	52	0.719	0.03308	0.657	0.787	0.720	0.03300	0.658	0.788
1 2	127	9	0.666	0.03505	0.601	0.739	0.667	0.03498	0.602	0.739
2 3	105	6	0.626	0.03664	0.558	0.702	0.627	0.03656	0.559	0.703
3 4	69	1	0.617	0.03721	0.548	0.694	0.618	0.03713	0.549	0.695
4 5	54	2	0.594	0.03923	0.522	0.676	0.595	0.03912	0.523	0.677
5 6	51	3	0.556	0.04229	0.479	0.646	0.558	0.04214	0.481	0.647
6 7	37	1	0.541	0.04374	0.462	0.634	0.543	0.04356	0.464	0.636
7 8	32	2	0.503	0.04859	0.416	0.608	0.505	0.04829	0.419	0.609
8 9	17	1	0.473	0.05399	0.378	0.592	0.476	0.05346	0.382	0.593
> 9	16	1	0.444	0.05815	0.343	0.573	0.447	0.05748	0.348	0.575

* EP-standard error

The outcome variable was defined as the time between the transplant and the occurrence of death or study closure. The condition of patients who remained alive at the closing date of the study was treated as censored data. Explanatory variables included gender, medical diagnosis that determined the need for transplantation, the patient's age at transplant and patient status (alive or dead) at the time of the study waxing.

Data were assessed with the support of software R version 2.12.1. Absolute frequencies are presented, and the respective confidence intervals of 95% for qualitative variables. Quantitative variables are presented measures of central tendency (mean and median) and dispersion (standard deviation and quartiles). To check for normal distribution of quantitative variables was applied the Shapiro-Wilk test. In the event that the data were normally distributed, the means between groups were compared by Student's t test. Otherwise, we used the Wilcoxon test or the Kruskal-Wallis test when more than two groups were compared.

To assess the association between qualitative variables was applied the chi-square or Fisher's exact test, depending on the expected frequencies calculated. Estimates of survival time were based on the methods of Kaplan-Meier. For comparison of survival rates by sex and by patient status (censored/death) was applied to the Log-rank test.

We conducted a regression analysis according to the model of Cox proportional hazards to determine the influence of sex, medical conditions and age at transplantation on the survival ratio. The model fit was assessed by residual analysis Schoenfeld and Martingale. The level of statistical significance was 5%.

This study was approved by the Research Ethics Committee of the institution, n° 774/10.

RESULTS

Estimates of the proportion of survivors generated using the Kaplan-Meier show that survival rates fall at higher speed until the third year after transplantation (Table 2). Figure 1 depicts

the survival curve of patients according to the Kaplan-Meier. The median survival time estimated by the Kaplan-Meier was 3268 days (approximately 6.6 years).

Ten models were fitted to identify the variables that best explain the survival time of patients undergoing cardiac transplantation. The model that best performance variables included medical diagnosis, sex and age at transplant ($P=0.0421$).

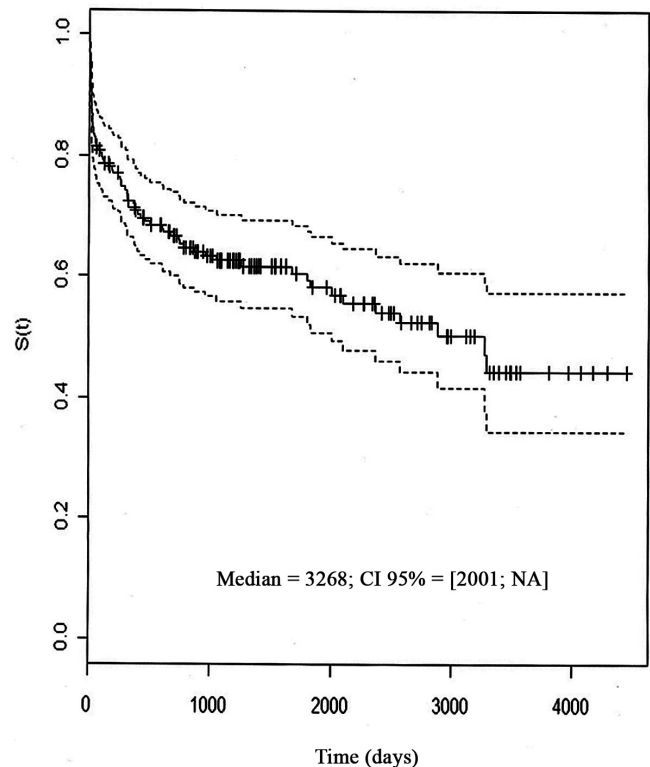


Fig. 1 - Kaplan-Meier curve for the survival time of patients undergoing heart transplant

Table 3. Model from adjusted Cox proportional hazards survival data of patients undergoing heart transplantation. Fortaleza, Ceará, Brazil. 2011

Variables	Coef.	exp(Coef)	Confidence interval		EP (Coef)	P value
			Inferior	Superior		
Idiopathic cardiomyopathy	-0.399	0.670	0.306	1.466	0.399	0.3168
Chagasic cardiomyopathy	-0.716	0.488	0.200	1.189	0.453	0.1147
Ischemic cardiomyopathy	-0.198	0.819	0.357	1.879	0.423	0.6387
Dilated cardiomyopathy	-1.015	0.362	0.121	1.077	0.556	0.0679
Alcoholic cardiomyopathy	-0.581	0.558	0.196	1.593	0.534	0.2766
Valvular cardiomyopathy	0.140	1.151	0.402	3.295	0.536	0.7929
Gender (Female)	0.071	1.074	0.607	1.899	0.291	0.8060
Age	-0.021	0.978	0.958	0.999	0.010	0.0418

$R^2 = 0.055$; (maximum possible = 0.981); Test Likelihood Ratio = 10.6 (GL= 8; $P=0.2252$); Wald test = 10,87 (GL= 8; $P=0.2089$); Logrank test= 11,16 (GL= 8; $P=0.1929$)

The analysis of Schoenfeld residuals showed that the presented model adopted proportionality of errors ($P>0.05$) for all variables and Martingale residual analysis showed that there were no outliers generated by the adjusted model compared to the observed data.

The data model of Cox proportional hazards are presented in Table 3. However, it is observed that the model had a poor fit with only the age variable statistical significance at 5%, showing that younger people have a higher survival rate. Patients with dilated cardiomyopathy showed a reduced survival time significantly only at the level of 7%.

DISCUSSION

In this study, most patients are male (81.9%). Similar results were found in other studies, in which most patients submitted to heart transplantation (81.8%) are male [4,11,13]. In another study with 156 patients enrolled in the Unified Waiting List of Ceará for heart transplantation, concluded that the highest percentage of males (81%), young adults aged between 20-40 years (22.4%) and middle-aged adults 40-64 years (56.4%), with an average of 36 years, had dilated cardiomyopathy (91%), 69% underwent transplantation, 25% died before transplantation and 6% were excluded due to improvement or worsening of symptoms and the average waiting time was 136 days until the day of cardiac transplantation [7].

The average age of patients in this study was 48 years. Found results similar to this study, with a mean age of 44.8 years [4], 44.9 years [13] and 46.9 years [12]. However, other studies showed a higher than average, with the average age of patients after transplantation of 52 [14] years and 54 years [15]. Thus, it was noticed that the majority of patients undergoing transplantation showed age considered productive, i.e., refers to the age at which the person has an occupation.

In relation to etiology of cardiomyopathy frequently determined that heart transplantation were idiopathic cardiomyopathy (23.9%), ischemic (23.4%) and Chagas disease (17%). In similarity with a study that showed predominance in idiopathic dilated cardiomyopathy (39%), chagasic (26.5%), ischemic (24.2%) and other causes (10.3%) [16]. And disagreeing with other studies, which showed that cardiomyopathies motivated the transplantation were dilated (47.4%), Chagas disease (24.7%), ischemic (23.7%), valve (2.1%) and other cardiomyopathies [9,11,14,17].

According to the data of the indication and survival after heart transplantation, it was found in this study percentages of 72%, 59% and 47% after 1, 5 and 9 years, respectively. However, we found some studies demonstrated that survival after heart transplantation is around 72.7% in the first year, 61.5% at five years, 56.4% in seven and 60% in ten years in exercise capacity, return to work and quality of life of patients undergoing the procedure, when compared to conventional treatment of heart failure [3,8,18-20].

Rates of graft survival and patient from the United Network for Organ Sharing October 1987 to December 1994 in the United States ($n=14.665$) showed a graft survival: in one month, 91.4%, one year, 81.8%, 2 years 77.4%, 3 years to five years 73.4%, 65.7%. And patient survival: in one month, 92%, one year, 82.8%; 2 years, 78.6%; 3 years, 75%, and five years, 67.8%. These recipients were predominantly white ($n=12,196$), the others were black ($n=1.429$), Hispanic ($n=610$), Asian ($n=148$), and other unknown ($n=282$). Five-year survival was better in recipients of white (69%) than in other groups (blacks 60%, Hispanics 64%, Asians 63.9%) [21].

The medium-term survival of patients undergoing heart transplantation was significant, particularly for younger patients, and, consistent with results from another study, because despite the impact of age on outcomes of cardiac transplantation continue to be debated, especially regarding adequacy of heart transplantation in patients who are older than 60 or 65 years of age, in general, the worst results are seen in extremes of age, in patients with less than one year of age, and those over 65 years [11]. Research points out that the experience of recipient age greater than 50 years was not a risk factor for early mortality. There was, however, an increased risk for patients over 60 years of age, though the numbers were small, making it difficult statistical inference [22].

Another study shows that the age limit for heart transplantation is relative and difficult decision because biological factors have more influence than the actual chronological age [8]. Some risk factors can help in better selection of donors and recipients and direct new scientific investigations in the field of cardiac transplantation, survival and prognostic factors related to donor age above 40 years, especially in females, and ischemic stroke/hemorrhage as a cause of brain death, and the association of these three factors of poor prognosis. Recipients with cardiac operations have a higher early mortality related to vascular coagulopathy and neurological disorders [4].

It may be noted that 58.51% of patients undergoing heart transplantation were alive when the study was completed, showing the work done by a multidisciplinary team with deep knowledge of the prognosis and management of these patients. The selection of candidates for heart transplantation involves the use of prognostic variables to identify patients with advanced heart failure, combined with the contraindications and comorbidities, which can lead to unfavorable outcomes such as reduced survival after transplantation or high perioperative risk [23].

Limitations of the study

Because the study used existing records in the institution, few variables were studied and registration bias may have influenced the estimates. Thus, other factors may influence survival in patients undergoing heart transplantation were not recorded and therefore were not included in the adjusted

models. The sample size may also have influenced the estimates because some medical conditions that determined the need for transplantation showed small samples. Although it was identified a relationship between longer survival and the age of patients, no inference can be made for children or adolescents from this study. Moreover, few variables were analyzed. There was no way to expand the analysis of the data, because data were available only who were recorded on the forms.

CONCLUSION

To identify the medium-term survival in patients submitted to heart transplantation showed significant results, especially for younger patients. The median survival time was about six and a half years and a little over 40% of patients survive more than nine years after transplantation.

Author's roles & responsibilities	
ILC	Data obtaining, analysis and interpretation, also in the draft and/or critical revision, revision of the final version
FETL	Data obtaining, analysis and interpretation, drafting the outline, critical review and revision of the final version
MVOL	Data obtaining, analysis and interpretation, drafting the outline, critical review and revision of the final version
VMS	Data obtaining, analysis and interpretation, drafting outline, critical review and revision of the final version
JDS	Data obtaining, analysis and interpretation, drafting the outline, critical review and revision of the final version
MPSM	Data obtaining, analysis and interpretation, drafting the outline, critical review and revision of the final version
SCO	Data obtaining, analysis and interpretation, drafting the outline, critical review and revision of the final version

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