ORIGINAL ARTICLE

Demographic and Epidemiological Profile of Aging and Elderly Patients Receiving Heart Transplant During the Period from 2009 to 2018

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Abstract

Background: The aging process may be associated with the accumulation of a wide variety of health damages, such as cardiovascular diseases. HF is the final common path of the majority of these diseases, and, in its refractory form, heart transplantation continues to be the best treatment choice.

Objective: To describe the demographic and epidemiological profile of aging and elderly patients receiving heart transplant from 2009 to 2018.

Methods: Retrospective, descriptive longitudinal study on heart transplantation in aging and elderly patients using data from medical records and institutional documents.

Results: From a total of 234 transplant recipients, 127 were 45 years or older. For the demographic profile, the variables used were sex, age, marital status, home state, and profession. For the epidemiological profile, the variables used were previous diagnosis, comorbidities before and after transplantation, and survival. Age varied from 45 to 74 years, with a mean of 57 years. The male sex accounted for 58.27% of recipients, and 59.84% were from the Federal District. Chagas, dilated, and ischemic cardiomyopathy accounted for 66.14%, 18.9%, and 14.17% of transplants, respectively. The main comorbidities were Chagas disease (66.14%), malignant arrhythmia requiring cardioverter-defibrillator implantation (28.35%), arterial hypertension (27.56%), and dyslipidemia (15.75%). Mean survival was 3 years and 4 months.

Conclusion: The demographic profile showed that the majority of patients were aging, male, married, and from the Federal District. The epidemiological profile showed that Chagas cardiomyopathy was the main cause of HF, followed by dilated cardiomyopathy.

Keywords: Heart Transplantation; Immunology; Thoracic,Surgery/complications; Postoperative Complications; Aged; Aging; Epidemiology

Introduction

The Brazilian population is aging rapidly and intensely. According to the Brazilian Institute of Geography and Statistics, the elderly population is composed of approximately 30 million people, accounting for 14.3% of the country's total population. In 2016, life expectancy for both sexes increased to 75 years, 79 years for women and 72 years for men. This represents an important social achievement, resulting from the improvement of the population's living conditions.[1] People aged 65 years or older in developed countries and people aged 60 years or older in developing countries are considered elderly.[2]

This process of aging is associated with the accumulation of a wide variety of molecular and cellular damage. As the years pass, this damage leads to gradual loss of physiological reserves, increasing the risk of contracting various diseases, keeping in mind that these changes are not linear or consistent, and they occur throughout life.[3] Thus, the perception of physiological changes in the organism begins in adulthood, in the aging age range (45 to 60 years).[4]

In Brazil, for the age group between 40 and 59 years old, ischemic heart disease is the main cause of death, for both sexes. From the age of 60 years onwards, the main causes of mortality in both sexes are predominantly chronic non-communicable diseases (cardiovascular diseases, cancer, chronic respiratory diseases, and diabetes mellitus). [5] The older a population is, the higher the prevalence of these conditions will be. Cardiovascular diseases are the main cause of mortality in this age group.[6]

Cardiovascular diseases can cause changes in the structure and function of the heart, which can lead to heart failure (HF). When HF is refractory to treatment, heart transplantation is an important therapeutic alternative to improve survival in appropriately selected patients.[7]

HF can manifest slowly and progressively or even in a short timeframe. With the limitations of elderly people's daily living activities, they tend to be diagnosed late, when the disease may have already reached a more advanced stage, possibly with a greater risk of decompensation.[8]

The main indication for heart transplantation in Brazil and worldwide is dilated cardiomyopathy, which is a common cause of heart failure, involving different etiologies (idiopathic, infectious, genetic). Ischemic cardiomyopathy is in second place. Chagas cardiomyopathy plays a prominent role, and it is the third leading cause of transplantation in Brazil, presenting the best results.[9]

In this manner, it is possible to observe that HF is the final consequence of a wide variety of cardiovascular diseases. When patients do not respond to optimal clinical treatment of HF, heart transplantation currently continues to be the best choice.

The objective of this study was to describe the demographic and epidemiological profile of aging and elderly heart transplant recipients, retrospectively, in a transplant center and, thus, compare the results with similar studies.

Methods

A retrospective, descriptive longitudinal study was carried out on heart transplantation in aging and elderly patients of both sexes during the period from 2009 to 2018.

The center where the study was carried out is considered a Brazilian reference in high complexity and heart, liver, kidney, cornea, and bone marrow transplants. The structure has more than 106 beds, 4 operating rooms, and 2 hemodynamic, outpatient, and emergency rooms.

The center performs an average of 84 surgeries per month. The heart transplant program at the hospital was implemented in 2009.

The sample was by convenience, quantifying all heart transplant recipients who were aging (between 45 and 59 years of age[4]) and elderly (60 years of age or older).

Demographic and epidemiological information was obtained from medical records and data stored in the hospital's transplant department. A spreadsheet containing the following variables was generated: identification, transplant date, age, sex, marital status, residence, profession/occupation, diagnosis, diseases before transplantation, listing date, comorbidities after transplantation, waiting time, and survival.

Statistical Analysis

Descriptive analyses of each of the variables were performed by means of graphs, frequency tables, and tables with summary measures. Categorical variables were presented as percentages. Continuous variables were expressed as median, mean, interquartile range, and standard deviation.

For data analysis, R Software version 3.5.3 was used.

Results

During the period from 2009 to December 2018, 234 heart transplants were performed, 127 of which were in patients age 45 years or older.

Corresponding to the study objectives, the results are ordered as follows: profile of heart transplant patients age 45 years or older, comorbidities before transplantation, diagnoses that led to transplantation, waiting time for transplantation, complications after transplantation, and survival time.

The profile of heart transplant recipients age 45 years and older is displayed in Table 1.

The main comorbidities with which the patients were diagnosed before heart transplantation are displayed in Table 2.

Table 3 displays the diagnoses that led to heart transplantation. The highest frequency was among patients with Chagas cardiomyopathy, which was observed in 84 of the 127 patients, that is, 66.14%. The second most common diagnosis was dilated cardiomyopathy, accounting for 18.9% of patients, including dilation due to non-compacted and idiopathic myocardium. Ischemic cardiomyopathy

Table 1 – Demographic profile of the heart transplant population age 45 years and older, from 2009 to 2018			
Variable	**Category**	**Frequency (n=127)**	**%**
Age range (years)	45 to 49	27	21.26
	50 to 54	24	18.9
	55 to 59	37	29.13
	60 to 64	25	19.68
	65 to 69	13	10.24
	70 to 74	1	0.79
Age group	Aging	88	69.29
	Elderly	39	30.71
Sex	Female	53	41.73
	Male	74	58.27
Marital status	Married	73	57.48
	Single	29	22.83
	Divorced	18	14.17
	Widow	4	3.15
	Civil union	3	2.36
Home state	DF	76	59.84
	GO	34	26.77
	MG	9	7.09
	BA	3	2.36
	AM	2	1.57
	SP	2	1.57
	RO	1	0.79
Profession	Unspecified	68	53.54
	Others	21	16.54
	Home	14	11.02
	Rural producer	6	4.72
	Driver	4	3.15
	Construction worker	4	3.15
	Unemployed	3	2.36
	Salesperson	3	2.36
	Mechanic	2	1.57
	Professor	2	1.57
Retired	No	80	62.99
	Yes	47	37.01

AM: Amazonas; BA: Bahia; DF: Federal District; GO: Goiás; MG: Minas Gerais; RO: Rondônia; SP: São Paulo. Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Table 2 – Frequency of types of pathological antecedents in the sample		
Antecedents	**N**	**%**
Chagas	84	66.14
CDI	36	28.35
SAH	35	27.56
Others	20	15.75
Dyslipidemia	17	13.39
Stroke	15	11.81
Pacemaker	13	10.24
Diabetes mellitus	12	9.45
CKD	11	8.66
AMI	9	7.09
Hypothyroidism	7	5.51
Denied antecedents	5	3.94
CAD	5	3.94
COPD	4	3.15
Diabetes mellitus 2	4	3.15
Megaesophagus	3	2.36
MRS	3	2.36
Thrombosis	2	1.57
Megacolon	2	1.57
AF	2	1.57

┼ *AF: atrial fibrillation; AMI: acute myocardial infarction; CAD: coronary artery disease; CDI: cardioverter-defibrillator implantation; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; MRS: myocardial revascularization surgery; SAH: systemic arterial hypertension.*
Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Table 3 – Frequency distribution of diagnoses in the sample		
Diagnosis	**N**	**%**
Chagas cardiomyopathy	84	66.14
Dilated cardiomyopathy	24	18.9
Ischemic cardiomyopathy	18	14.17
Peripartum cardiomyopathy	1	0.79
Total	127	100

‡ *Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.*

followed, with 14.17% of cases. In the sample, only 1 patient was diagnosed with peripartum cardiomyopathy.

The observed frequencies among diagnoses and the patients' antecedents were also recorded. In Chagas cardiomyopathy, the most frequent antecedents were cardioverter-defibrillator implantation, systemic arterial hypertension, and pacemaker implantation. In dilated cardiomyopathy, the most frequent was "others", meaning that the antecedents observed only once were grouped together in this category. In ischemic cardiomyopathy, the most frequent were systemic arterial hypertension, dyslipidemia, acute myocardial infarction, and coronary artery disease. Two out of three cases of myocardial revascularization surgery observed were in patients who were diagnosed with ischemic cardiomyopathy.

In Table 4, waiting times are divided into classes of the same range (60 days). It was possible to observe that almost half of the sample (47.24%) had a waiting time of up to 2 months (or 60 days). In following, 19.68% of cases occurred between 60 and 120 days. In this manner, the intervals follow in a decreasing fashion almost continuously, to the final class.

Mean waiting time was 110 days, whereas the median was 71 days. The latter statistic best describes the data, given that the mean is affected by the most extreme values. The standard deviation of 124.50 shows considerable data dispersion, as it has a value above the mean (110), that is, a coefficient of variation greater than 100% (Table 5).

This section analyzes the complications that affected patients after transplantation (Table 6).

In relation to survival after transplantation (days between the date of transplantation and death), it was possible to observe that a large portion of patients (30.71%) had a survival time of up to 1 year. Between 1 and 2 years, there was also an expressive number, namely, 25.20%. In following, 16.54% of the total sample was between 2 and 3 years. In general, median survival was 2 years.

Patients who did not die as of July 31, 2019 (date for calculating survival) had a maximum survival time of approximately 10 years and 6 months. Mean survival was 3 years and 4 months (1233.8 days), in contrast to the sample median, which was 1006 days (2 years and 9 months). This difference between mean and median indicates that the survival of these patients is not homogenously distributed in the sample. This result can also be interpreted by means of calculation of the standard deviation of this variable, as displayed in Table 7.

The results obtained when analyzing survival time and cause of death are displayed in Table 8.

It was not possible to ascertain whether the cases of death occurred in or out of the hospital during data collection.

Table 4 – Frequency of classes of waiting time		
Time (days)	f_i	f_r
1 to 61	60	47.24%
61 to 121	25	19.68%
121 to 181	16	12.60%
181 to 241	11	8.66%
241 to 301	5	3.94%
301 to 361	4	3.15%
361 to 421	1	0.79%
421 to 481	2	1.57%
481 to 541	1	0.79%
541 to 601	0	0.0%
601 to 661	2	1.57%
Total	127	100%

§ Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Table 5 – Summary measures of waiting time (in days)

Measures	Values
Minimum	1
First quartile	22
Median	71
Third quartile	150
Maximum	647
Mean	110
Standard deviation	124.50

// Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Table 6 – List of the 13 most reported complications following heart transplantation

Complications	N	%
Death	42	33.07
Rejection	33	25.98
CMV	23	18.11
Chagas reactivation	22	17.32
ECMO	17	13.39
Pneumonia	16	12.60
AKF	14	11.02
CKD	9	7.09
Septic shock	6	4.72
Sepsis	6	4.72
Ischemic stroke	5	3.94
Pacemaker	5	3.94
No comorbidities	5	3.94

§ AKF: acute kidney failure; CKD: chronic kidney disease; CMV: cytomegalovirus; ECMO: extracorporeal membrane oxygenation. Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Discussion

The part of the population that most undergoes heart transplantation is between 40 and 60 years of age.[10] According to a study carried out in the South Region of Brazil, the mean age of heart transplant recipients was 52 years.[11] This is due to the increase in the prevalence of heart failure in the age group between 55 and 64 years, explaining the higher rate of transplantation in this population.[12] The international report published this year indicates that recipients' mean age is 55 years.[13]

Also in relation to age, 30.71% of the sample was 60 years or older, demonstrating that heart transplantation is significantly performed in this age range. The number of elderly patients with advanced HF has increased over the years, generating a greater demand for heart surgery in this age range,[14] making

Table 7 – Summary measures of survival time (in days) of patients who did not die

Measures	Values
Minimum	224
Median	1006
Mean	1233.8
Maximum	3836
Standard deviation	798.22

¶Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

Table 8 – Mean survival time of patients who died after transplantation according to the respective cause of death

Cause of death	Number of patients	Mean (days)
Infectious	15	245.5
Cardiovascular	14	167.8
Multiple organ failure	4	126.25
Hemorrhagic stroke	2	59
Cardiogenic shock	2	127
Septic shock	2	377.5
Rejection	1	13
Bronchoaspiration	2	404
Hemorrhagic shock	1	10
Hepatic cirrhosis	1	38
Extensive intestinal ischemia	1	5
Brain death	1	108
Neoplasia	1	1167
Total	47	-

 # Source: Ribeiro, J.S. Oliveira, M.L.C. Transplante cardíaco de envelhecentes e idosos no período de 2009 a 2018.

heart transplantation in elderly recipients without adverse comorbidities an option to reduce suffering and improve quality of life.[15]

It was possible to observe that the majority of patients were men, as they have a higher prevalence of HF in relation to women.[16-17]

In relation to marital status, the majority of patients (57.48%) were married. This finding is of the utmost importance for the transplant process, because it may mean that these patients have family support and companionship.[18]

Patients who receive transplants need to follow several guidelines to maintain health and prevent complications, and all of these changes involve family and social adaptations.[19]

The majority of heart transplant recipients came from the Federal District and the state of Goiás, accounting for 86% of the sample. However, this finding is contradictory in comparison with the epidemiological factor of the sample, which states that the majority of patients had Chagas cardiomyopathy, and the Federal District is not included in the list of cities at risk for Chagas disease.[17] This may be explained by the migration of patients who were already

affected by the disease moving from endemic states to the Federal District.[20]

In relation to profession/occupation, for the majority of the sample, there was no information regarding profession in the medical records. The term retired was reported in 37.01% of the cases. Work activity in patients with HF may be limited or contraindicated. Nevertheless, according to the symptoms presented, it is possible to return to work with the implementation of therapeutic interventions and increased functional capacity.[11]

With respect to comorbidities before heart transplantation, 66% of cases had Chagas disease. It is an endemic disease that is more frequent in South America, and it can cause damage to the cardiovascular system, leading to cardiomyopathy and resulting in HF.[21] Even after several national and international governmental efforts, transmission is only partially controlled, and the disease continues to appear through other transmission mechanisms, such as the oral route.[22]

Chagas cardiomyopathy represents a major cause of mortality and morbidity in Latin America, where early diagnosis and treatment can alter the clinical course of the disease. However, when reaching the terminal stage, heart transplantation is the best treatment choice.[23]

The second most frequent comorbidity was malignant arrhythmia requiring cardioverter-defibrillator implantation, which was present in 36 patients, 25 of whom had Chagas cardiomyopathy. Cardioverter-defibrillator implantation is used to treat severe arrhythmias caused by Chagas disease, preventing sudden death.[11,21] The third most frequent was systemic arterial hypertension, which is considered a risk factor for the development of cardiovascular system diseases.[5]

Among the indications for heart transplantation, the most frequent was Chagas cardiomyopathy, accounting for 66.14% of the total. A study carried out in the Brazilian state of Minas Gerais reached a similar result, Chagas cardiomyopathy being the most frequent disease.[9] In contrast, in 2015, a review was conducted, indicating dilated cardiomyopathy as the most frequent.[9] In our study, dilated cardiomyopathy came next, and ischemic cardiomyopathy was third most frequent. The international report, on the other hand, indicated the following as the main indications for transplantation on a global scale: non-ischemic dilated cardiomyopathy (51%) and ischemic cardiomyopathy (32%), with no subdivision for Chagas disease, which, in this context, was integrated into non-ischemic dilated cardiomyopathy.[12]

By relating the antecedents that led to these diagnoses, it was possible to observe the prevalence of coronary artery disease and acute myocardial infarction as causes of ischemic cardiomyopathy. These diseases cause an imbalance between the supply and consumption of oxygen by the heart muscle, and they are directly related to risk factors such as tobacco use, arterial hypertension, diabetes mellitus, dyslipidemia, obesity, and sedentary lifestyle.[24,25]

In this study, the median waiting time for transplantation was 1 month and 11 days, the longest time being 20 months. This is relatively quick compared to another study where the median waiting time was 6 months, and there were patients who waited up to 5 years for a heart.[26]

After transplantation, patients may suffer different types of complications; the main one was death, in 48 patients out of a total of 127, and the most frequent causes were infectious and cardiovascular, which are considered common during the first year after transplantation.[12] Death due to infectious complications is highest during the first year after transplantation.[13]

Even with advances in immunosuppression and antimicrobial prophylaxis over the past years leading to considerable improvements in outcome after heart transplantation [30], infectious complications continue to be one of the leading causes of mortality.[13]

Next, the following complications occurred: rejection, cytomegalovirus, Chagas reactivation, and the use of extracorporeal membrane oxygenation. The most common complications during the first year after heart transplantation are graft failure, rejection, and infection.[28] According to the International Society for Heart and Lung Transplantation, in patients who received transplants between 2010 and 2016, 12.6% were treated for rejection between discharge and 1 year after transplantation.[12] Cytomegalovirus is an important infectious agent in transplant recipients, and it is very frequent. The presence of this infection predisposes to immune rejection; for this reason, screening and early treatment are necessary, due to its pathogenicity.[7]

In relation to reactivation of Chagas disease, it is a frequent clinical problem, due to immunosuppression performed after transplantation.[9] The incidence of reactivation varies from 21% to 45% after heart transplantation.[29]

Another complication can be acute graft failure and consequent need for extracorporeal membrane oxygenation during the post-transplant period, but survival is lower in patients who undergo this procedure.[12]

In this study, 30.71% of the patients survived up to 1 year after the procedure. Post-transplant survival has improved over time. However, the older the recipient, the shorter the long-term survival.[13]

Maximum survival time in this study was 10 years and 6 months, and mean survival in the study period was 3 years and 4 months. With heart transplantation, patients can prolong survival by approximately 10 years after surgery. Approximately 85% survive the first year after heart transplantation.[26,28]

Mean survival after transplantation can reach 12.5 years according to an international report that analyzed data from countries in North America, Europe, and others. [13]

Study Limitations

This study had limitations related to access to the heart transplantation database at the research center, in addition to difficulties in finding similar studies in the context of Brazil.

Conclusion

In relation to the demographic and epidemiological profile, it was possible to observe that the majority of patients were male, and the mean age of the study participants was 57 years. The most frequent state of origin was the Federal District. The most common antecedent before transplantation was Chagas disease. In relation to the diagnosis that preceded transplantation, Chagas cardiomyopathy accounted for the majority of cases. In relation to survival, the maximum time observed was 10 years and 6 months.

Understanding the profile of patients who receive heart transplants is fundamental to decision making, in order both to prevent comorbidities associated with cardiovascular diseases as well as their complications and to treat the complications inherent to transplantation, with the objective of early recognition and adequate follow-up, thus maintaining patients' quality of life and consequently increasing survival after heart transplantation.

Author contributions

Conception and design of the research: Ribeiro JS, Oliveira MLC; Acquisition of data: Ribeiro JS; Analysis and interpretation of the data: Ribeiro JS, Oliveira MLC; Statistical analysis: Ribeiro JS, Oliveira MLC; Writing of the manuscript: Ribeiro JS; Critical revision of the manuscript for intellectual content: Ribeiro JS, Oliveira MLC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Study Association

This article is part of the thesis of master submitted by Joseane de Souza Ribeiro, from Universidade Católica de Brasília.

Ethics approval and consent to participate

This study was approved by the Ethics Committee on Animal Experiments of the Instituto de Cardiologia do DF-ICDF under the protocol number 01030818.8.0000.00.26 Parecer nº: 3.171.339.

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