Heart Transplantation in Patients Older than 65 Years: Worthwhile or Wastage of Organs?

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Abstract

Background Patients older than 65 years have traditionally not been considered candidates for heart transplantation. However, recent studies have shown similar survival. We evaluated immediate and medium-term results in patients older than 65 years compared with younger patients.

Methods From November 2003 to December 2013, 258 patients underwent transplantation. Children and patients with other organ transplantations were excluded from this study. Recipients were divided into two groups: 45 patients (18%) aged 65 years and older (Group A) and 203 patients (81%) younger than 65 years (Group B).

Results Patients differed in age (67.0 ± 2.2 vs. 51.5 ± 9.7 years), but gender (male 77.8 vs. 77.3%; $p = 0.949$) was similar. Patients in Group A had more cardiovascular risk factors and ischemic cardiomyopathy (60 vs. 33.5%; $p < 0.001$). Donors to Group A were older (38.5 ± 11.3 vs. 34.0 ± 11.0 years; $p = 0.014$). Hospital mortality was 0 vs. 5.9% ($p = 0.095$) and 1- and 5-year survival were 88.8 ± 4.7 versus 86.8 ± 2.4% and 81.5 ± 5.9 versus 77.2 ± 3.2%, respectively. Mean follow-up was 3.8 ± 2.7 versus 4.5 ± 3.1 years. Incidence of cellular/humoral rejection was similar, but incidence of cardiac allograft vasculopathy was higher (15.6 vs. 7.4%; $p = 0.081$). Incidence of diabetes de novo was similar ($p = 0.632$), but older patients had more serious infections in the 1st year ($p = 0.018$).

Conclusion Heart transplantation in selected older patients can be performed with survival similar to younger patients, hence should not be restricted arbitrarily. Incidence of infections, graft vascular disease, and malignancies can be reduced with a more personalized approach to immunosuppression. Allocation of donors to these patients does not appear to reduce the possibility of transplanting younger patients.

Keywords
- transplantation
- heart
- heart failure
- surgery
- complications

Introduction

Despite major advances in medical and surgical treatment of heart failure, heart transplantation is still the elective treatment for patients refractory to other medical therapies or conventional cardiac procedures.[1] Due to improved results, the criteria for selection of candidates for transplantation have been gradually extended and the age has been one of the criteria more exposed.[2] However, the upper age limit remains poorly defined, partly due to the high demand for transplantation and the scarcity of organs. Still, advanced age has traditionally been viewed as a contraindication for heart transplantation, despite the improved outcomes recently reported.[3]

Older candidates often have multiple cardiovascular risk factors and deficient physical and psychological conditions

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and it is known that the immediate results of transplantation are very sensitive not only to the quality of the donor organ but also to the clinical status of the candidate to transplantation. Adequate selection of recipients is essential to the success of a transplantation program.

In this article, we analyzed our own experience and compared the early and late results of cardiac transplantation in two groups of patients, younger and older than 65 years.

Methods

Definition, Origin, and Collection of Data

In the period from November 2003 to December 2013, 258 patients were consecutively submitted to heart transplantation at this center. Exclusion criteria for this study included patients previously transplanted with other organs ($n = 2$) and patients younger than 18 years ($n = 8$). In this way, the study population comprised 248 patients, of whom 72 (29%) were in the intensive care unit, under inotropic support and/or mechanical assistance, while 176 (71%) were awaiting transplantation at home.

The data for this patient population were obtained from a national database specifically designed for the prospective registration (*online* platform) of data of recipient, donor, surgery, immunosuppression protocol, and follow-up of patients undergoing cardiac transplantation.

All surviving patients were followed by regular consultation at the surgical center by a dedicated medical/surgical team, for 1 to 10 years, and none was lost to follow-up. The mean follow-up period in this study was 4.4 ± 3.1 years (1,091 patient-years).

Recipients and Donors

►**Table 1** shows the preoperative data of the recipients of the two groups and respective donors, as well as the results of the comparative analysis. When compared with the population of Group B, patients in Group A had a higher rate of cardiovascular risk factors, such as hypertension (53.3 vs. 35.5%; $p = 0.026$), dyslipidemia (71.1 vs. 43.3%; $p = 0.001$), prior cardiac surgery (44.4 vs. 26.1%; $p = 0.015$), prior coronary artery bypass grafting (CABG) (24.4 vs. 12.3%; $p = 0.037$), ischemic cardiomyopathy (60 vs. 33.5%; $p = 0.001$), and carotid disease (57.8 vs. 34.5%; $p = 0.004$). They also had decreased glomerular filtration rate (49.2 ± 15.4 vs. 63 ± 23.2 mL/min; $p < 0.001$), and higher serum creatinine (1.6 ± 0.8 vs. 1.4 ± 0.5 mg/dL; $p = 0.099$). Finally, there were fewer patients in high urgency for transplantation (equivalent to United Network for Organ Sharing (UNOS) status 1A and 1B) in Group A than in Group B (22.2 and 29.5%, respectively; $p = 0.174$), and the time on the waiting list was 48.8 ± 50.0 vs. 42.3 ± 44.6 days, respectively ($p = 0.384$).

There were no major differences in any of the variables between the two groups, with regard to donors. Male donors were most common (66.7 vs. 76.8%) and the cause of death was mostly traumatic (51.1 vs. 57.6%). However, there was a significant number of older donors for patients in group A (38.5 ± 11.3 vs. 34.0 ± 11.0% years; $p = 0.014$), who also had a tendency for prolonged inotropic (8.9 vs. 3%; $p = 0.067$) or ventilator support (20 vs.10.3%; $p = 0.072$). In total, there were 53 donors older than 45 years (21.4%), 16 in group A (35.6%) and 37 in group B (18.2%; $p = 0.014$). The distribution of donor age versus recipient age is shown in ►**Fig. 1**.

Due to the fact that our region counts with a high donation rate (37.8 donors/million population), 41% of the donors were local and 59% distant (mean = 168 ± 78 km).

Surgical Technique

All transplantations were performed using the bicaval method, under cardiopulmonary bypass (CPB) and moderate systemic hypothermia (28°C). To decrease ischemic times, priority is given to the left side heart anastomoses after which the aortic cross-clamp is removed and the anastomoses of the right side are done under perfusion. Typical ischemic time was 40 to 45 minutes for local donation and 90 to 120 minutes for distant harvesting. All patients received an infusion of dobutamine (5 µg/kg/min) after all the anastomoses were completed, for its chronotropic effect. Need for further inotropic support or posttransplantation mechanical assistance was determined after a period of adequate reperfusion and this decision was based on intraoperative direct visualization of the heart, hemodynamic signs, and transesophageal echocardiogram.

Of notice, as another method to expand the numbers of donors, and based on the large experience of the center with this procedure, concomitant mitral valvuloplasty was performed in 12 donor hearts previously known to have moderate mitral valve disease, 4 in Group A and 8 in Group B. On most occasions, this was done in the form of a suture posterior annuloplasty, but other procedures were performed.[4]

Immunosuppression Therapy and Rejection Monitoring

Routine induction therapy consisted of mycophenolate mofetil (1 g oral), methylprednisolone sodium succinate (500 mg i.v.) and basiliximab (20 mg i.v.) administered pre- and during transplantation. After transplantation, patients entered a protocol consisting of a calcineurin inhibitor (mostly cyclosporin, dose-adjusted to blood levels assessed by monoclonal fluorescence polarization immunoassay), mycophenolate mofetil (1 g twice daily), and steroids (125 mg of methylprednisolone intravenously every 8 hours for three doses postoperatively, followed by prednisone, 0.8 mg/kg/day during the 1st week and then tapered off in the subsequent 4 weeks to 0.2 mg/kg/day).

Right ventricular endomyocardial biopsies were performed by a routine protocol or when it was considered to be clinically necessary, and acute cardiac rejection was diagnosed and treated if ≥ 2R according to the International Society for Heart and Lung Transplantation (ISHLT) classification.[4]

Coronary angiograms were performed at yearly intervals. Cardiac allograft vasculopathy followed the definitions proposed by the ISHLT.[5,6]

Table 1 Characterization of the recipient and donor populations

Recipient group	A	B	p
N	45	203	
Age (y, mean ± SD); range (minimum–maximum)	67.0 ± 2.2 (65–72)	51.5 ± 9.7 (20–64)	< **0.001**
Gender (male)	35 (77.8%)	157 (77.3%)	0.949
Follow-up (y)	3.8 ± 2.7	4.5 ± 3.1	0.146
Wait-list time (d)	48.8 ± 50.0	42.3 ± 44.6	0.384
BMI mean (kg/m^2)	23.8 ± 3.0	23.8 ± 3.4	0.996
Diabetes	15 (33.3%)	56 (27.6%)	0.440
Hypertension	24 (53.3%)	72 (35.5%)	**0.026**
Dyslipidemia	32 (71.1%)	88 (43.3%)	**0.001**
Prior cardiac surgery	20 (44.4%)	53 (26.1%)	**0.015**
Ischemic cardiomyopathy	27 (60.0%)	68 (33.5%)	**0.001**
Dilated cardiomyopathy	9 (20.0%)	66 (32.5%)	0.098
Peripheral vascular disease	19 (42.2%)	64 (31.5%)	0.169
Cardiac index (L/min/m^2)	1.9 ± 0.4	2.0 ± 0.5	0.229
Transpulmonary gradient (mm Hg)	9.9 ± 3.5	9.4 ± 4.8	0.444
Pulmonary vascular resistance (WU)	3.6 ± 2.8	3.3 ± 2.1	0.399
VO2 max (mL/kg/min)	13.9 ± 2.5	13.2 ± 2.8	0.141
Glomerular filtration rate (mL/min)	49.2 ± 15.4	63.0 ± 23.2	< **0.001**
Creatinine level (mg/dL)	1.6 ± 0.8	1.4 ± 0.5	0.099
Urgency/emergency	10 (22.2%)	62 (30.6%)	0.174
Donor			
Age (y)	38.5 ± 11.3	34.0 ± 11.0	**0.014**
Gender, male	30 (66.7%)	156 (76.8%)	0.154
Inotropic dependence > 1 wk	4 (8.9%)	6 (3.0%)	0.067
Ventilatory assistance > 1 wk	9 (20.0%)	21 (10.3%)	0.072
Donor female/recipient male	10 (22.2%)	33 (16.3%)	0.339
Death by cerebral vascular accident	15 (33.3%)	71 (34.8%)	0.933
Death by brain trauma	23 (51.1%)	117 (57.6%)	0.425
Local procurement	14 (31.0%)	88 (43.3%)	0.180
Distant procurement	31 (69.0%)	115 (56.7%)	0.180

Abbreviations: BMI, body mass index; SD, standard deviation. P values in bold are those considered significant
Note: Univariate comparative analysis of preoperative data of Groups A and B.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and evaluated using the independent Student *t*-test for normally distributed continuous variables and Mann–Whitney *U* test for nonnormally distributed continuous variables. Normality was accessed by the Kolmogorov–Smirnov and Shapiro–Wilk tests. Categorical variables are reported as frequency and percentage, and compared using the chi-square test or the Fisher exact test when appropriate. Survival and event-free survival were calculated by the Kaplan–Meier method and comparison between groups obtained by log-rank test. Statistical significance was defined as *p* value < 0.05 (two-tailed). Data were analyzed using the IBM Corp. program (released 2011; IBM SPSS Statistics for

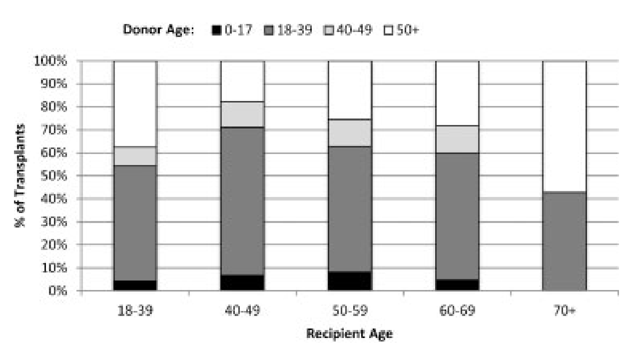

Fig. 1 Adult heart transplantation: donor and recipient age.

Table 2 Peri- and postoperative data

Recipient group	A	B	*p*
N	45	203	
Total ischemic time (min)	96.3 ± 35.2	88.8 ± 36.4	0.213
CPB time mean (min)	97.3 ± 22.8	101.9 ± 49.2	0.543
Time to extubation (h)	17.1 ± 8.9	20.9 ± 26.4	0.347
Inotropic requirement	8 (17.8%)	26 (12.8%)	0.381
Mechanical assistance	3 (6.7%)	10 (4.9%)	0.636
Hemorrhage	5 (11.1%)	9 (4.4%)	0.079
Mitral valvuloplasty	4 (8.9%)	8 (3.9%)	0.162
Length of hospital stay (d)	17.4 ± 14.4	15.3 ± 15.8	0,454

Note: Univariate analysis of comparative data of Groups A and B.

Windows, Version 20.0; IBM Corp., Armonk, New York, United States).

Results

Surgery

The surgical data, as well as the results of the comparative analysis of the two groups, are shown in ►**Table 2**. No statistically significant differences were observed relatively to times of ischemia (96.3 ± 35.2 vs. 88.8 ± 36.4 minutes; $p = 0.213$), CPB (97.3 ± 22.8 vs. 101.9 ± 49.2 minutes; $p = 0.543$), and mechanical ventilation (17.1 ± 8.9 vs. 20.9 ± 26.4 hours; $p = 0.347$). There were also no significant differences in the need for inotropic (17.8 vs. 12.8%; $p = 0.381$) or mechanical circulatory (6.7 vs. 4.9%; $p = 0.636$) support.

There was no hospital mortality in Group A and there were 12 early deaths (5.9%) in Group B ($p = 0.095$). The length of hospital stay was similar in both groups (17.4 ± 14.4 vs. 15.3 ± 15.8 days; $p = 0.454$).

After a mean follow-up of 4.4 ± 3.1 years (1–10 years; 1,091 patient-years), the overall mortality did not show significant differences between the two groups of patients (28.9vs. 22.7%; $p = 0.375$) and the same goes for comparison of in-hospital mortality and death at 6 months, 1 year, and late follow-up between both groups (►**Table 3**). The most frequent causes of death in both groups were infections (11.1 vs. 5.9%; $p = 0.212$) and peripheral vascular disease (4.4 vs. 5.4%; $p = 0.791$).

Overall survival up to 8 years after transplantation did not differ between the older age group and the younger group, as shown in the respective survival curves (►**Fig. 2**, $p = 0.289$). Survival rates at 1, 5, and 8 years were 88.8 ± 4.7, 81.5 ± 5.9, and 52.3 ± 12.7%, respectively, and median survival was 6.7 ± 0.6 years for older patients; equivalent rates were 86.8 ± 2.4, 77.2 ± 3.2, and 72.0 ± 3.9%, respectively, and median survival was 7.9 ± 0.3 years for the younger age group.

Cellular and/or Humoral Rejection, and Graft Vascular Disease

The data on acute cellular rejection, humoral rejection, and vascular disease of the graft in Groups A and B are shown in ►**Table 4**. One hundred and four patients (42%) had no

Table 3 Mortality and causes of death

Recipient group	A	B	*p*
N	45	203	
Hospital mortality	0 (0.0%)	12 (5.9%)	0.095
Total mortality	13 (28.9%)	46 (22.7%)	0.375
Mortality < 6 mo	5 (11.1%)	21 (10.3%)	0.879
Mortality < 1 y	5 (11.1%)	26 (12.8%)	0.756
Causes of death			
Cardiac	1 (2.2%)	8 (3.9%)	0.577
Vascular	2 (4.4%)	11 (5.4%)	0.791
Malignant tumor	2 (4.4%)	6 (3.0%)	0.609
Neuropsychiatric	0 (0.0%)	4 (2.0%)	0.342
Infectious	5 (11.1%)	12 (5.9%)	0.212

Note: Univariate analysis of comparative data in Groups A and B.

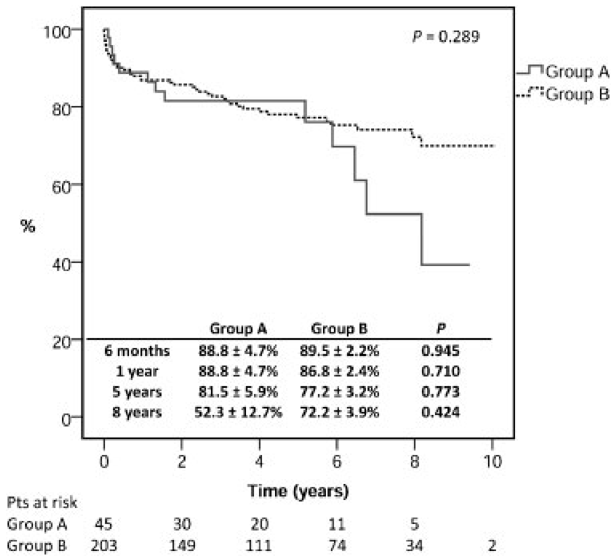

Fig. 2 Overall survival in Groups A and B.

episodes of acute cellular rejection (grade 0R of the ISHLT). The remaining patients ($n = 144$, 58%) had at least one episode of rejection, but it was only mild (1R), requiring no treatment, in 99 of these. The comparative analysis of the two groups showed no statistically significant difference in any of the cellular rejection grades. Forty-five patients (18.1%), 7 (15.5%) in Group A and 38 (18.7%) in Group B, had at least one episode of cellular rejection grade $\geq$ 2R, the majority (39 cases, 86.7%) occurring during the 1st year. No statistically significant difference ($p = 0.652$) was observed in the survival free from cellular rejection grade $\geq$ 2R between Groups A and B (►**Fig. 3A**).

Humoral rejection was diagnosed in six patients (2.4%), with no significant difference between the study groups ($p = 0.924$). Graft vascular disease (GVD) was diagnosed in 22 patients (8.8%), with some difference in the incidence between the study groups (15.6 vs. 7.4%; $p = 0.081$). Survival free from GVD was significantly different between the two groups ($p = 0.001$, ►**Fig. 3B**).

New Onset Diabetes and Severe Infections

The incidence of diabetes de novo in the 1st year after transplantation was 13.3%, with no difference between the two groups (11.1 vs. 13.8%; $p = 0.632$).

The incidence of serious infections requiring hospitalization and i.v. antibiotics during the 1st year posttransplantation was significantly higher in Group A (28.9 vs. 14.3%; $p = 0.018$). In fact, the incidence of pneumonia in the first 6 months was significantly higher in Group A (37.8 vs. 22.7%; $p = 0.035$). Survival free from serious infections was significantly lower in Group A throughout follow-up ($p = 0.028$), as shown in ►**Fig. 3C**.

Renal Function after Transplantation

At the time of transplantation, patients in Group A showed a tendency to a lower value of the glomerular filtration rate (GFR), as compared with Group B patients (49.2 ± 15.4 vs. 63 ± 23.2 mL/min; $p < 0.001$) and creatinine (1.6 ± 0.8 vs. 1.4 ± 0.5 mg/dL; $p = 0.099$). At 1 month posttransplantation, a tendency toward recovery of the renal function was observed in both groups, although this was not statistically significant. However, this was followed by progressive deterioration of the GFR, so that from the 1st to the 6th months posttransplantation values dropped significantly in both groups and continued to decline in Group A (45.2 ± 15.5 mL/min) and, although at a slower pace, in Group B (58.9 ± 24.0 mL/min) up to 12 months. The progression of chronic renal failure to end-stage renal disease required dialysis in four patients. Two of these underwent kidney transplantation.

Malignancies

Older patients had an increased risk of development of malignancies after transplantation (26.7 vs. 13.3%; $p = 0.026$), clearly demonstrated in the 5-year free survival of 67.7 ± 9.1 and 87.0 ± 3.0%, respectively ($p = 0.002$) (►**Fig. 3D**).

Discussion

There is still some controversy and even reluctance to offer cardiac transplantation to older patients, especially above

Table 4 Data on rejection and other complications

Recipient group	A	B	*p*
N	45	203	
No rejection (0R)	17 (37.8%)	87 (42.9%)	0.532
Acute cellular rejection 2R	5 (11.1%)	31 (15.3%)	0.474
Acute cellular rejection 3R	2 (4.4%)	7 (3.4%)	0.746
Humoral rejection	1 (2.2%)	5 (2.5%)	0.924
Graft vascular disease	7 (15.6%)	15 (7.4%)	0.081
New onset diabetes	5 (11.1%)	28 (13.8%)	0.632
Cancer	12 (26.7%)	27 (13.3%)	**0.026**
Pneumonia $\leq$ 6 mo	17 (37.8%)	46 (22.7%)	**0.035**
Infections $\leq$ 12 mo	13 (28.9%)	29 (14.3%)	**0.018**

Note: Univariate analysis of comparative data in Groups A and B.

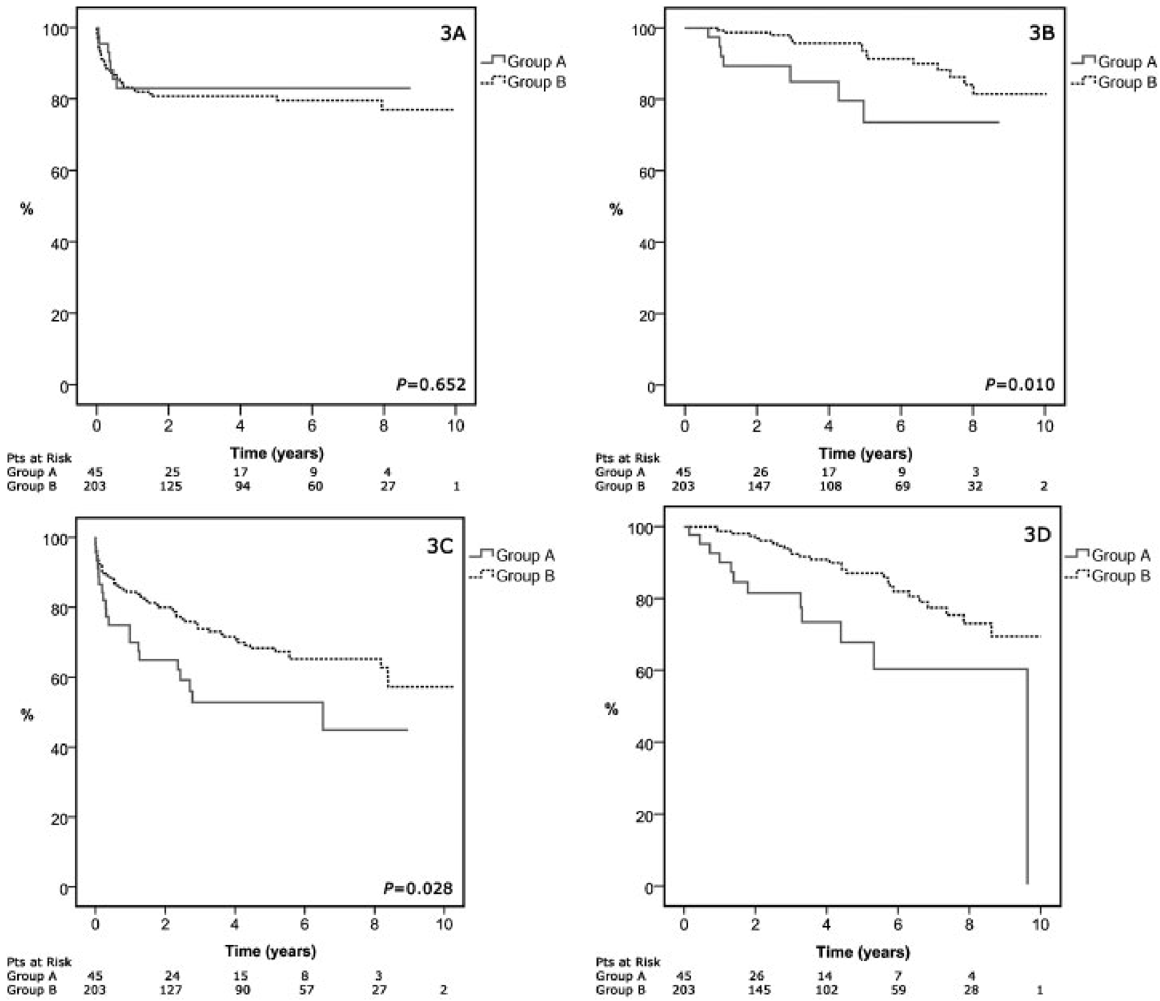

Fig. 3 Survival free from complications related to immunosuppression in Groups A and B. (A) Cellular rejection grade ≥ 2R (ISHLT). (B) Graft vascular disease. (C) Infection. (D) Malignancy. ISHLT, International Society for Heart and Lung Transplantation.

70 years of age, resulting from consideration that they most often have associated comorbidities that influence life expectancy, thus significantly reducing the potential benefit of the procedure.[7] In addition, there is the presumption of greater difficulties to withstand the rigors of surgery and associated complications, notably those related to immunosuppression.[8] This limitation is now being questioned, due to the satisfactory results reported in septuagenarians.[9] In fact, the advances in heart transplantation during the recent decades have considerably changed the clinical practice and outcome in most centers. Yet, the percentage of patients older than 65 years currently being transplanted is 17% in North America, and in Europe (Eurotransplant) is only 6.7%.[10,11]

The main argument against cardiac transplantation in old people is their short life expectancy, to which one has to add the scarcity of organs for transplantation. In choosing a donor one is looking for the best result, hence patients with a higher potential of functional recovery, low morbidity, and long survival will naturally have priority. How can we, then, justify transplantation of an old person when the donors are scarce for the young? Which should be the age limit to transplant? These questions are being asked almost daily, as the population older than 65 years now accounts for approximately 20% of the total, and greater in some settings. In 2011, UNOS highlighted the significant increase in the percentage of transplanted patients older than 65 years compared with 2001 (17 vs. 10.8%) and demonstrated a 5-year survival of 74% for those undergoing heart transplantation in 2005 to 2006.[10]

On the contrary, when one extrapolates the results of the older population (even octogenarians) submitted to conventional cardiac surgery, we find low rates of morbidity and mortality and improved clinical, functional autonomy, and quality of life.[12,13] In both situations, the decisive factor is the careful selection of the patient. Evidently, in this setting of refractory chronic cardiac failure, often resulting in poor physical and psychological condition, not every older patient can be a candidate for transplantation.

In our experience, there was a natural and undeniably selective inclusion process for older patients in the waiting list for transplantation, which is difficult to characterize and quantify. Transplanted patients older than 65 years were mostly male, with predominantly ischemic heart disease (60%), a high incidence of carotid and peripheral vascular disease (42 and 57%), diabetes (33%), hypertension and dyslipidemia, and 44% of them had previous cardiac surgery (CABG, 25%). As expected, the renal function was more impaired in these patients than in the younger group. All of these are known important risk factors of morbidity and mortality after transplantation, thus significantly limiting benefit. In the experience of Goldstein et al with heart transplantation in septuagenarians, there was a similar incidence of ischemic heart disease (59%), yet there were a smaller number of diabetic patients (19%), fewer patients with peripheral vascular disease (4.5%), and the serum creatinine levels were slightly lower.[14]

The priority and selection of the donors for these patients is another topic of discussion. In our case, the typical donor assigned to older patients (Group A) was older and 35.6% of these donors were older than 45 years and had longer mechanical ventilation or inotropic support, thus often considered as suboptimal. Yet, this has not had a negative impact on perioperative and hospital mortality, although a higher incidence of early transient graft dysfunction was apparent (17.8 vs. 12.8%; $p = 0.381$). In fact, there was no early mortality in Group A, but mortality at the end of 1st year was similar in the two groups.

However, the number of infectious episodes who required hospitalization and intravenous antibiotic treatment during the first posttransplant year was higher in Group A (28.9 vs. 14.3%; $p = 0.018$), a circumstance that may have had relevant impact in the overall mortality. The greatest risk of developing serious infections in this group of patients should alert us to the need for taking more forceful prevention measures. Also, relevant was the incidence of malignant pathology in Group A, reflected by a significant difference in free survival at 5 years (67.7 ± 9.1 vs. 87.0 ± 3.0%; $p = 0.002$). Finally, a higher incidence of GVD (15.6 vs. 7.4%) was observed in Group A, with a trend toward statistical significance ($p = 0.081$), a fact that is reinforced when we look at the free-survival curve (73.4 ± 9.4 vs. 93.6 ± 2.2%, at 5 years; $p = 0.010$). This disease is a multifactorial entity, which is more aggressive in individuals with risk factors or predicted cardiovascular disease, more present in older patients.

By contrast, the incidence of acute cell rejection that required treatment ($\geq$ 2R) was similar in both groups throughout the follow-up. This appears to be a common occurrence in many studies in this age group.[15,16] The decline in immune competence that occurs with aging is associated with a progressive reduction in the generation of new T and B lymphocytes, with the consequent loss of diversity and functional competence.[17] It establishes a dramatic reduction in responsiveness as well as disruption of the function. Both facts contribute to lower rejection rates but to the increased incidence in morbidity and mortality from infectious diseases and cancer.[18,19]

The understanding of this immunosenescence thus requires a different attitude in the handling of the immunosuppression in this age group. Therefore, it has been suggested by others that the immunosuppression load be reduced so as to minimize its side effects without increasing the risk of rejection, especially in the 1st year posttransplant, when it could be expected to diminish the number of infectious episodes and its impact on mortality. Similarly, it could also reduce the incidence of malignancies and GVD.[20] We were aware of this phenomenon early in this experience and the results reported herein may already incorporate the benefits thereof.

Also analyzed in this study was the evolution of the renal function, measured by the serum creatinine level and creatinine clearance, during the 1st year, as it would be at this time that one would expect greater divergence. In both groups, there was a stabilization or improvement of the renal function immediately after transplantation, but this was followed by a gradual deterioration of the GFR over the 1st year, greater in Group A (42.2 ± 15.5 vs. 58.9 ± 24.0 mL/min; $p = 0.002$). An eventual reduction of the immunosuppression doses may also have an impact here.[21,22]

Despite these complications, the survival curve in the medium term is similar in older and younger transplant patients, although we appear to witness a decrease in the long-term survival, which has to be naturally expected in this population. Increased and differentiated care, not only in the selection of candidates for transplantation but also in postoperative care and follow-up (medium and long term), conditions we can only find in units with high volume and experience, will almost certainly improve outcomes.[23,24]

A last comment, paradoxically, the simple existence of these older candidates in the waiting list, parallel to better donor procurement, appears to facilitate the use of better donors in younger candidates, perhaps raising questions of ethical order, although the use of marginal donors has been demonstrated to have an acceptable outcome also in younger individuals.[25]

Conclusion

The number of patients awaiting heart transplantation has been increasing, unlike the supply of donors. This panorama requires strengthening of the borders of donation and the need to consider responsibly and pragmatically the allocation of available organs. This situation becomes more complex when there is an increase in the number of older patients who are potential candidates for transplantation. In our experience, the results obtained in older patients were similar to those in younger recipients, at least in the medium-term survival, but with significantly higher rates of important morbidity. The results could perhaps be improved by reducing the intensity of immunosuppression in this population.

The allocation of donors to this older group does not seem to reduce the overall success of transplantation, but it is difficult to assess the impact on the younger population awaiting transplantation. The key will be a more rigorous, responsible, and pragmatic selection of both patients and donors.

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Invited Commentary

Age Over 65: To Transplant or Not to Transplant?

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Orthotopic heart transplantation (OHT) is still the only curative treatment for patients with terminal heart failure. However, widespread use of heart transplantation has been increasingly limited by the growing discrepancy between the number of patients on the waiting list and the number of available organs. On the contrary, as population of people older than 65 years is increasing these days, the prevalence of heart failure is increasing, leading to more patients with terminal heart failure. The recent article[1] shows similar outcomes in heart transplant recipients older than 65 years compared with younger patients. Previous publications on survival outcomes of OHT in older patients showed conflicting results.[2–10]

Some large-cohort registry analyses—for example, the International Society for Heart & Lung Transplantation (ISHLT) registry—have identified older age as a risk factor for both early and late mortality after OHT.[2,3,6–8] In older recipients, death from graft failure together with cardiac allograft vasculopathy and acute rejection becomes less common, whereas death from nonlymphoma malignancy, renal failure, organ failure, and infection increases.[6] Other single-institutional experiences have demonstrated that with careful patient selection, OHT can be performed in elderly patients with mortality and morbidity equivalent to younger recipients as reported in other publications.[1,5,9] Furthermore, multicenter data have demonstrated acceptable long-term outcomes in selected older recipients.[10] However, despite the overall similar results in selected older transplant recipients compared with younger patients, the conflict of transplanting in older patients still remains.[11] The waiting time and urgency for a patient on the waiting list has risen over the last years. The increasing organ shortage, which entails longer waiting time and the fact that sicker patients are transplanted, is considered to be an important factor for the declining results over the last years. The criteria that account for the high-urgency status are almost the same as the risk factors for 1-year mortality.[6] As a consequence, the expected outcome after transplantation has gained increasing attention both in the transplant community and in the general public.[12]

In fact, next to the urgency of the transplantation the chances of success are explicitly named as the second important allocation principle in the German transplant law. Recently, allocation based on urgency and outcome has already been realized for lung transplantation by the introduction of the lung allocation scores (LAS) in 2011. The initial experiences with the LAS are promising; therefore, a cardiac allocation score has currently been developed.[13] The consequence will be that a younger patient with a higher probability of long-term survival will have a higher chance of getting a transplant than a patient of advanced age, for example, older than 65 years. Older recipients will not be excluded from heart transplantation in general, but the rare organs will primarily be allocated to younger patients. For older patients, an "old-for-old" program could be introduced. Then, hearts from younger donors would be reserved for younger recipients with a higher probability of favorable long-term outcome. Alternatively, older patients could receive a left ventricular assist device, either as destination therapy or as bridge-to-transplantation. A recent UNOS analysis demonstrated that OHT recipients aged 70 years and older who were bridged with ventricular assist device had outcomes equivalent to patients younger than 70 years.[3]

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