HEART TRANSPLANTATION IN PATIENTS SEVENTY YEARS OF AGE AND OLDER: A COMPARATIVE ANALYSIS OF OUTCOME

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Objective: Advanced age has traditionally been considered a contraindication for heart transplantation because of the reported adverse effect of increased age on long-term survival. However, as the field of transplantation continues to evolve, the criteria regarding the recipient's upper age limit have been expanded and older patients are being considered as potential candidates. We analyzed the outcome of heart transplantation in patients 70 years of age and older and compared these results with those in younger patients (<70 years) over a 4-year period.

Method: We retrospectively analyzed the results of 15 patients 70 years of age and older who underwent heart transplantation between November 1994 and May 1999 and compared them with results in 98 younger patients undergoing transplantation during the same period.

Results: The older age group had a higher preoperative left ventricular ejection fraction (P = .02), higher incidence of female donors (P = .02), and longer cardiac allograft ischemic time (P = .01). No differences were found regarding incidence of diabetes mellitus, donor age, donor/recipient weight ratio, and mismatch (<0.80). The 30-day or to-discharge operative mortality was similar in both groups (0% in the older vs 5.1% in younger patients). Actuarial survival at 1 year and 4 years was not statistically different between the older and younger patients (93.3% ± 6.4% vs 88.3% ± 3.3% and 73.5% ± 13.6% vs 69.1% ± 5.8%, respectively). The length of intensive care unit stay and total post-transplantation hospital stay, incidence of rejection, and incidence of cytomegalovirus infection were similar between the groups.

Conclusions: Heart transplantation in selected patients 70 years of age and older can be performed as successfully as in younger patients (<70 years of age) with similar morbidity, mortality, and intermediate-term survival. Advanced age as defined (≥70 years) should not be an exclusion criterion for heart transplantation. The risks and benefits of transplant surgery should be applied individually in a selective fashion. (J Thorac Cardiovasc Surg 2001;121:532-41)

With the increased life expectancy of the American population over the past few decades, elderly persons are becoming the fastest growing segment of the US population. The mean estimated life expectancy was 75.6 years in 1990 and is projected to increase further. The average American who reaches 65 years of age will live into his or her ninth decade.[1] These demographic changes are reflected in the present-day cardiac surgery practice, with an increased number of elderly individuals in need of highly sophisticated and complex cardiac interventions, including transplantation. Heart transplantation has indeed evolved into a highly successful therapeutic modality for patients with end-stage cardiomyopathy, with an actuarial survival of 80% at 1 year and 75% at 3 years for those patients who have undergone transplantation after 1991.[2] However, despite many technologic advances and more refined and specific immunosuppression developed during the past decade, advanced age remains "the last frontier" in heart transplantation and is still considered a con-

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Table I. *Preoperative patient characteristics*

Characteristic	*Patient age group*		P *value*
	<70 y (n = 98)	*≥70 y (n = 15)*	
Age at transplant (y)			
Mean ± SD	55.8 ± 1	72.7 ± 2	
Range	14-69.9	70-77	
Sex			1.0
Male	81 (83%)	13 (88%)	
Female	17 (17%)	2 (12%)	
Cardiomyopathy			.49
Ischemic	52 (53%)	10 (67%)	
Idiopathic	45 (46%)	5 (33%)	
Sarcoid	1 (1%)	— (0%)	
NYHA class			.42
II	7 (7%)	— (0%)	
III	33 (34%)	7 (47%)	
IV	58 (59%)	8 (53%)	
Diabetes mellitus	33 (34%)	2 (13%)	.14
Body surface area (m^2)			
Male	2.0 ± 0.2	1.9 ± 0.1	.46
Female	1.6 ± 0.2	1.8 ± 1.5	.31
Hemodynamic factors			
LVEF	21.8 ± 8.8	24.4 ± 5.0	.02
CO (L/min)	4.3 ± 1.3	3.7 ± 0.8	.15
CI ($L \cdot min^{-1} \cdot m^{-2}$)	2.2 ± 0.7	2.0 ± 0.4	.04
TPG (mm Hg)	10.2 ± 5.6	7.7 ± 5.2	.09
PVR (Wood units)	2.7 ± 1.6	2.3 ± 1.5	.27
Creatinine (mg/dL)	1.3 ± 0.7	1.4 ± 0.5	.64
Range	0.4-6.4	0.9-2.4	
Transplant status (UNOS)			
1	63 (64%)	1 (7%)	
2	35 (36%)	14 (93%)	

CI, Cardiac index; *CO,* cardiac output; *LVEF,* left ventricular ejection fraction; *NYHA,* New York Heart Association; *PVR,* pulmonary vascular resistance; *TPG,* transpulmonary gradient; *SD,* standard deviation; *UNOS,* United Network for Organ Sharing.

traindication in many centers. Data from the Registry of the International Society for Heart and Lung Transplantation (ISHLT) show that advanced age is still a strong factor that adversely affects survival.[2]

Since the inception of our heart transplant program in December 1988, carefully selected patients 70 years of age and older have undergone transplantation for treatment of end-stage heart disease not amenable to further medical therapy or surgical intervention. This cohort of patients represents 6% of our total heart transplant patient population. Our initial experience with this group of patients was reported in 1996.[3] On the basis of satisfactory results from this older population, as well as positive results in younger patients, we now report data on 15 patients 70 years of age and older who have undergone transplantation since 1994. In addition, these patients are compared with 98 patients younger than 70 years of age who underwent transplantation during the same time interval with a similar transplant protocol.

Patients and methods

Between November 1994 and May 1999, 113 patients underwent orthotopic heart transplantation at Cedars-Sinai Medical Center. This group included 15 (13%) patients 70 years of age and older who were retrospectively reviewed and compared with the remaining 98 patients younger than 70 years of age. During the same period, 65 patients 70 years of age and older were referred for transplantation, but only 44 patients were fully evaluated. Twenty-two patients were refused for a variety of medical reasons (acceptance ratio = 0.50) and 4 patients died while awaiting a donor heart (18% mortality in listed patients). The preoperative evaluations performed in these older patient were more extensive than those performed in younger patients, and they included a through assessment of clinical conditions commonly seen in elderly patients, such as colon, bladder, and prostate cancer, as well as gastrointestinal studies to detect diverticular disease or potential sources of blood loss. A vascular evaluation of carotid and peripheral vascular disease was performed, and hepatic, renal, and pulmonary function was thoroughly assessed. An evaluation for osteoporosis was performed, and

Table II. *Previous patient operations*

	Patient age group	
Previous operations	*<70 y*	*≥70 y*
CABG	33	4
AVR	2	0
MVR	2	1
CABG + MVR	1	2
CABG + AVR	0	2
AVR + MVR	2	1
Partial left ventriculectomy	2	0
LV aneurysmectomy	1	0
LVAD	1	0
Heart transplantation	3	0
Total	47 (48%)	10 (73%)
AICD	29 (30%)	4 (29%)

AVR, Aortic valve replacement; *CABG,* coronary artery bypass grafting; *AICD,* automatic implantable cardioverter defibrillator; *MVR,* mitral valve replacement; *LVAD,* left ventricular assist device; *LV,* left ventricle.

the impact of diabetes mellitus, if present, on end-organ function was carefully assessed. Finally, a psychosocial screening was done by a psychiatrist and a social worker to verify compliance and a clear understanding of the diverse implications of transplantation. The presence of strong family support with total and unrestricted commitment to transplantation was mandatory. Patients were considered for transplantation only if they had a positive outlook on life with a high degree of personal and familial satisfaction. A work-related activity was not essential, but because, by age definition, these patients are at high-risk for transplantation, a less-than-optimal evaluation indicated exclusion from consideration.

By comparison, during the same period, 469 patients younger than 70 years of age were referred for transplantation, but only 247 of these were fully evaluated and 129 patients were listed for transplantation (acceptance ratio = 0.52).

The preoperative characteristics of both patient age groups are listed in Table I. The older age group had a higher preoperative left ventricular ejection fraction ($P = .02$) and cardiac index ($P = .04$) than the younger group. The patients' previous operations are listed in Table II. Donor heart characteristics are given in Table III. Patients 70 years of age and older had a higher incidence of female donors than the younger group ($P = .02$). Of note, 4 older patients received allografts from donors older than 50 years (range 52 to 56 years old) and 7 younger patients received allografts from donors between 50 and 55 years old. Waiting time before transplantation is shown in Table IV. As shown in Table V, older patients had a longer cardiac allograft ischemic time than younger patients ($P = .01$). One older patient underwent combined heart-kidney transplantation with allografts from the same donor, and 5 patients in the younger group received such combined transplants. The donor criteria used for the older patients were similar to those used for younger patients, although there was a stated willingness to use "borderline" or "high-risk" donor organs for this group of patients. The organ procurement agencies were alerted that we would evaluate donor hearts that were deemed unsuitable for transplantation by other transplant programs. This included older donors, prolonged ischemic time, prolonged donor "down time," echocardiographic or angiographic abnormalities, high inotropic support, and a high degree of donor/recipient weight mismatch. Moderate to advanced undersizing of donor hearts (eg, donor/recipient weight ratio of 0.8 to 0.5) was undertaken when the recipient had a normal transpulmonary gradient and pulmonary vascular resistance. The exception to this high-risk donor organ criterion being allocated to the elderly patients was applied to those patients who were less than 70 years of age when listed for heart transplantation but were septuagenarians at the time of transplantation, thus receiving a "regular" allograft. In contrast, the use of "high-risk" or "borderline" donors in the younger population is currently very restrictive and highly selective, because those patients can benefit from mechanical assist devices if a donor organ is not available. However, in the early part of our experience, those potentially compromised donor organs were used in younger patients as well.

Endomyocardial biopsies were performed according to our surveillance protocol or when acute rejection was clinically suspected. Rejection episodes were treated if greater than 1B (ISHLT classification).

Surgical technique. Two techniques for orthotopic heart transplantation were used. In most patients (98%), our standard technique was used. This consisted of total excision of the recipient's atria with cardiac allograft implantation performed by means of bicaval and pulmonary vein anastomoses.[4] In a few patients (2%), a modified approach was used, namely, bicaval and single left atrial anastomoses.[5] The intraoperative decision regarding the appropriate technique was based on the safety of dissecting the posterior mediastinal adhesions surrounding the posterior aspect of the left atrium.

Immunosuppressive therapy. Immunosuppressive therapy consisted of OKT3 induction therapy (5 mg intravenously daily) maintained for 7 days, although some patients (those with abnormal renal function with creatinine levels over 2.5 mg/dL or those patients undergoing combined heart-kidney transplantation) received antithymocyte globulin (15 mg/kg) for 7 days. Maintenance immunosuppressive therapy consisted of cyclosporine (INN: ciclosporin) (5 mg/kg per day, for a level of 200 to 400 ng/mL, as measured by monoclonal fluorescence polarization immunoassay, within the first 12 weeks after transplantation, and for a level of 120 to 200 ng/mL thereafter, started postoperatively once the serum creatinine level was <2.0 mg/dL); azathioprine (4 mg/kg preoperatively and 2 mg/kg per day postoperatively, adjusted to the patient's white blood cell count) but switched to mycophenolate mofetil (1000 mg twice daily) for all patients as of January 1997; and steroids (methylprednisolone sodium succinate, 1 g at removal of the aortic crossclamp intraoperatively, and then 125 mg intravenously every 8 hours for 3 doses postoperatively, followed by prednisone, 0.25 mg/kg per day during OKT3 therapy, increased to 0.5 mg/kg per day, and then tapered in the subsequent 3 to 8 months).

Although the same immunosuppressive protocol was used for older and younger patients, the levels of cyclosporine in older patients were generally in the lower end of the intend-

Table III. *Donor heart characteristics*

	Patient age group		
Characteristic	*<70 y (n = 98)*	*≥70 y (n = 15)*	P *value*
Age (y)	28.3 ± 13	34.1 ± 17	.12
Range	11-55	10-56	
Sex			.02
Male	67 (68%)	5 (33%)	
Female	31 (32%)	10 (67%)	
Body surface area (m^2)			
Male	1.9 ± 0.3	1.7 ± 0.4	.55
Female	1.7 ± 0.2	1.7 ± 0.3	.75
Donor/recipient weight ratio	1.0 ± 0.2	0.9 ± 0.3	.22
Donor/recipient weight mismatch (<0.80)	27 (28%)	7 (47%)	.14

Table IV. *Waiting time before transplantation*

	Patient age group		
Waiting time	*<70 y (n = 98)*	*≥70 y (n = 15)*	P *value*
UNOS status 1 (d)	27.7 ± 0.36	19*	
UNOS status 2 (d)	140.6 ± 22.2	105.9 ± 23	.47

*The first (and only) patient underwent transplantation as UNOS status 1, but all subsequent patients (n =14) as UNOS status 2 according to our current protocol.
UNOS, United Network for Organ Sharing.

Table V. *Intraoperative and postoperative characteristics*

	Patient age group		
Characteristic	*<70 y (n = 98)*	*≥70 y (n = 15)*	P *value*
Allograft ischemic time (min)	170 ± 41	201 ± 49	.01
ICU stay (d)	9.4 ± 19.4	7.3 ± 4.2	.5
Range	2-166	4-18	
Post-transplantation hospital stay (d)	16.3 ± 20.9	17.1 ± 14	.56
Range	2-188	9-61	
Follow-up (mo)	59	60	.27
Mean ± SD	27.9 ± 17.1	33.3 ± 18.7	

ICU, Intensive care unit; *SD,* standard deviation.

ed range. In addition, older patients were tapered off steroids faster than younger patients, so most of them had stopped receiving prednisone by the end of the sixth month after transplantation.

Cytomegalovirus prophylaxis. Most patients were given 6 doses of intravenous immunoglobulin (500 mg/kg) within 1 week after transplantation, with 5 doses of intravenous cytomegalovirus (CMV)–specific immune globulin (125 mg/kg) after the first intravenous immunoglobulin dose. Intravenous ganciclovir was also administered (5 mg/kg every 12 hours but adjusted for renal function) for 14 weeks followed by oral ganciclovir (1000 mg twice daily but adjusted for renal function) for an additional 38 weeks for those patients who were donor CMV positive/recipient CMV negative (high risk). For those patients donor CMV positive/recipient CMV positive and for those donor CMV negative/recipient CMV positive (low risk), prophylaxis consisted of 6 doses of intravenous immunoglobulin and intravenous ganciclovir for 2 weeks followed by oral acyclovir (3200 mg daily but adjusted for renal function) for 24 weeks. Prophylaxis for high-risk patients spanned the first post-transplantation year, whereas CMV prophylaxis for low-risk patients lasted the first 6 months after transplantation.

Osteoporosis prophylaxis. Osteoporosis prophylaxis for both groups of patients consisted of calcium carbonate (Smith Kline Beecham Pharmaceutical, Philadelphia, Pa), 1.25 g per day; calcitriol (Roche Pharmaceuticals, Nutley, NJ), 0.25 μg daily, and chelated magnesium (Freeda, New

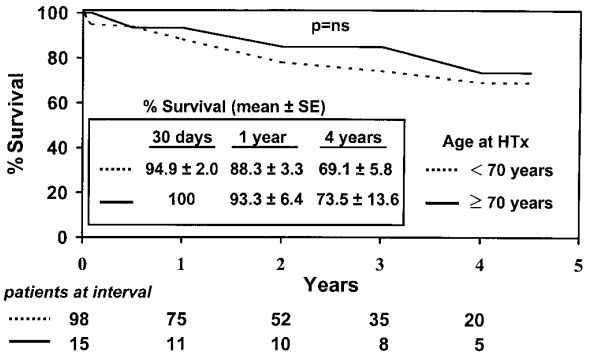

Fig 1. Thirty-day operative survival and actuarial survival up to 4 years for both patient age groups. *ns,* Not significant; *SE,* standard error; *HTx,* heart transplantation.

York, NY), 1 to 2 g per day, adjusted according to the patient's renal function.

Statistical methods. Patients were stratified on the basis of age (<70 years or ≥70 years of age). Data were presented as frequency distributions and simple percentages. Values of continuous variables were expressed as the mean ± standard deviation. Patient preoperative group characteristics were compared by either the 2-sample *t* test for continuous variables or the Fisher exact test for categoric variables. When data were heavily skewed, data transformations were used to normalize data. The *t* test was performed on the transformed scale for these variables. A log-rank test (Mantel-Cox) was used to compare the survival curves of the two age groups. All testing was 2-sided using an alpha of .05. The statistical software packages SAS (Statistical Analysis System 6.12, SAS Institute, Inc, Cary, NC) and BMDP (Berkeley, Calif) were used in all analyses.

Results

The 30-day or to-discharge operative mortality was 0% in the older group and 5.1% (5/98 patients) in the younger group ($P = 1.0$). Actuarial survival at 1, 2, 3, and 4 years was not statistically different between the older and the younger patients (93.3% ± 6.4% vs 88.3% ± 3.3%, 84.9% ± 10.0% vs 77.9% ± 4.5%, 84.9% ± 10.0% vs 74.4% ± 5.0%, and 73.5% ± 13.6% vs 69.1% ± 5.8%, respectively) ($P = .64$) (Fig 1). The post-transplantation intensive care unit stay and total hospital stay were similar in both groups, which translated into similar total hospital costs. Mean follow-up time was the same in both groups (33.3 ± 18.7 months in the older group and 27.9 ± 17.1 months in the younger patients) ($P = .27$). The incidence of rejection episodes was similar in both groups, with a mean number of rejection episodes of 0.13 ± 0.35 per patient in the older group and 0.24 ± 0.5 per patient in the younger group ($P = .77$) (Table VI). Similarly, the incidence of CMV infection was similar in both groups, with a mean number of CMV infection episodes of 0.14 ± 0.36 for the older group and 0.26 ± 0.5 for the younger group ($P = 1.0$) (Table VII). The causes of death in both patient populations are shown in Table VIII. Nonspecific allograft dysfunction without allograft coronary artery vasculopathy was the cause of death in 2 elderly patients at 18 and 42 months after transplantation, and another older patient died of pulmonary embolus 6 months after transplantation.

Discussion

With the increasing number of elderly patients being referred for cardiac interventions, cardiologists and cardiac surgeons are faced with evaluating older patients with end-stage heart disease not amenable to further medical or conventional cardiovascular surgical therapy for heart transplantation. Any intervention in the older population should seek to improve functional independence and quality of life at an acceptable risk. However, despite meeting all criteria, older recipients have been traditionally denied transplantation because of the critical shortage of donor organs and because of the assumption that selection for heart transplantation should be based on patient potential for maximum benefit in terms of functional recovery and length of survival. It has been argued that older patients have a postoperative period characterized by higher infection rate, higher incidence of malignant disease, greater functional impairment, increased postoperative hospital stay and associated costs, and poorer survival.[6-10] However, the definition of advanced age for heart transplantation among those reports is poorly defined, having been reported as more than 55 years,[10] 60 years,[8,9] and 65 years of age.[6] These results are supported by data from the Registry of the ISHLT that show a significant decrease in survival at 1 and 5 years with increasing recipient age, especially in those over 65 years. Age remains a predictor of transplantation mortality in a multivariate analysis even when adjusted for other comorbidity factors. Further, the vast majority of risk factors known to affect the 1-year mortality, advanced age included, persist at the 5-year point.[2] However, the Registry data have to be taken only as a reference point and in the right statistical context, because there is significant variability regarding donor and recipient selection and management among institutions and because differences in the recipient risk factors may not be fully taken in considerations in the variables collected for the multivariate analysis.

On the basis of these data, it is easy to understand the natural reluctance of most heart transplant centers to consider elderly patients as potential candidates.

Table VI. *Incidence of rejection episodes (>1B)**

	Patient age group		
No. of rejection episodes	*< 70 y (n = 98)*	*≥ 70 y (n = 15)*	P *value*
0	76 (78%)	13 (87%)	
1	21 (21%)	2 (13%)	
2	0	0	
3	1 (1%)	0	
Mean ± SD	0.24 ± 0.5	0.13 ± 0.35	.77

SD, Standard deviation.
*According to the International Society of Heart and Lung Transplantation classification.

Table VII. *Incidence of CMV infection episodes*

	Patient age group		
No. of episodes of CMV infection	*< 70 y (n = 98)*	*≥ 70 y (n = 15)*	P *value*
0	77 (79%)	13 (87%)	
1	17 (17%)	2 (13%)	
2	3 (3%)	0	
3	1 (1%)	0	
Mean ± SD	0.26 ± 0.5	0.14 ± 0.36	1.0

CMV, Cytomegalovirus; *SD,* standard deviation.

Table VIII. *Cause of death*

	Patient age group	
Cause of death	*< 70 y (n = 23)*	*≥ 70 y (n = 3)*
Transplant atherosclerosis	7	0
Infection	6	0
Rejection	4	0
Mediastinal hemorrhage	2	0
Nonspecific graft failure	1	2
Cancer	1	0
Renal failure	1	0
Respiratory failure	1	0
Pulmonary embolus	0	1

However, several studies have shown that heart transplantation in older patients (defined as older than 55 to 65 years of age) can be performed successfully with acceptable morbidity and mortality and excellent long-term survival, comparable with those of younger patients. These reports have concluded that the recipient's age is not a significant risk factor for mortality, and advanced age, although its definition is not uniform, should not be considered a major contraindication for heart transplantation.[11-17] Notwithstanding the fact that all of the reports are from single institutions and involve a relatively small number of patients, most transplant centers have advanced the upper age limit of potential recipients within the past few years. In fact, the mean age of heart transplant recipients has increased steadily within the past decade, with the number of patients 65 years of age undergoing transplantation increasing from 1.4% (n = 24) in 1988 to 8.8% (n = 206) in 1998.[18] Currently, the upper age limit for heart transplantation remains undefined, although according to available data, most transplant centers consider 65 years of age a significant risk factor that determines eligibility for transplantation.

In view of this compelling information, is there medical justification to offer transplantation to older recipients? Does an older patient deserve to be considered for transplantation in light of the widely known shortage of donor organs? How old is too old for heart transplantation? Can elderly patients sustain the rigors of transplantation, be rehabilitated, and have a productive life? Do they deserve suboptimal or potentially compromised donor organs? Should they "jump ahead" of younger patients on the transplant list if their condition deteriorates? Is transplantation cost-effective? Most important, do they do as well in the long term as younger patients? The medico-ethical and moral implications in this regard are indeed complex but perhaps can be partially addressed by the fact that liver and kidney transplantation are selectively offered to patients 70 years of age and older. These issues have important implications regarding the provision of expensive medical care achieving cost-effective outcomes in the fastest growing and largest segment of the population with the current trend of managed care.

Our present study, as well as our earlier studies,[3,19] attempts to answer some of these questions, although it could be argued that the profound selection bias for the older patients may invalidate the statistical comparison between the groups. However, the transplant acceptance ratio for older and younger patients was similar (0.50 vs 0.52, respectively), indicating a highly selective criterion in younger patients as well. Despite these potential lim-

itations, a reference point was needed to validate these results. The results of the current study indicate that the 30-day or to-discharge operative mortality, actuarial survival up to 4 years, length of stay in the intensive care unit and total post-transplantation hospital stay, incidence of rejection, and incidence of CMV infection were similar in patients less than 70 years of age and in those 70 years of age or older. Although we have not used objective indicators to measure quality of life in either group in this study, the subjective improvement and indeed quality of life after transplantation for the older patients was substantial and not clinically different from that in younger patients. In addition, an aggressive approach regarding the use of potentially compromised or "suboptimal" allografts has been used in these elderly patients with excellent clinical results, as previously documented.[20,21] The relevant question is then whether we should penalize older patients by placing them in a lower priority status in the transplant list or by giving them a suboptimal or potentially compromised donor heart on the basis of their age. These are complex medical, ethical, and socioeconomic issues that go beyond the scope of this study.

Several lessons were learned from our initial experience, which remain valid over time. First, a highly selective acceptance criterion for potential candidates 70 years of age and older was used to minimize postoperative complications, which may adversely affect survival and quality of life.

Second, these elderly patients are listed for transplantation only as United Network for Organ Sharing (UNOS) status 2 to minimize perioperative morbidity. Our current practice is not to upgrade these patients to UNOS status 1 in the case of hemodynamic deterioration, even if intravenous inotropic support is needed to temporarily stabilize hemodynamics. This practice prevents elderly patients from "jumping ahead" of younger patients waiting for transplantation. The use of intra-aortic balloon pumps or mechanical assist devices as a bridge to transplantation is probably not warranted because older patients may not be able to tolerate related complications.

Third, it is clear to us that carefully selected patients can withstand the rigors of transplantation and related protocols, have a cost-effective outcome, achieve an excellent functional result and quality of life, return to an independent lifestyle, and continue to be productive in society.

Fourth, we have not observed an increased incidence of rejection, CMV, or other infections in this group of patients. In addition, although a purely observed phenomenon without statistical validation, the incidence of malignant tumors has been no greater in older patients than in younger patients. This is perhaps due to the proper tailoring of immunosuppressive protocols to accommodate the decreased immune responsiveness seen in elderly patients. The impact of an individualized approach of the immunosuppressive protocol in the final outcome of older transplant recipients cannot be overemphasized. However, a continuous awareness for the development of malignant disease with the necessary surveillance for early detection is needed.

Fifth, our experience with "borderline" or potentially compromised cardiac allografts indicates that the selective use of marginally acceptable organs is compatible with excellent cardiac function and survival.[20,21] This aggressive approach of liberalizing the criteria of acceptability for donor hearts could alleviate the donor shortage in cardiac transplantation by increasing the number of available organs. However, extending the age limit of potential candidates for heart transplantation into the seventies would certainly increase the demand for organ donors and affect even further the supply-demand donor heart mismatch. This increased demand placed on an already fixed donor pool could increase the waiting time and mortality in younger patients needing a donor heart, which in turn may raise additional moral questions and concerns.

Sixth, as the indications for transplantation constantly evolve and the results in selected septuagenarians undergoing transplantation yield satisfactory results, the reasons to justify the use of marginally acceptable or "borderline" donor organs rather than "regular" allografts in elderly patients are becoming less clear. The use of an "alternate list"[22] seems also to discriminate against these patients solely on the basis of their age. The concept of matching high-risk donors with an elderly patient population that may already be at high risk may serve to expand the donor pool without compromising the lower risk and younger candidates. However, this may artificially produce a lower survival in the older patients, thus perpetuating the idea that advanced age implies less than satisfactory results.

Seventh, special attention should be given to the common problems associated with elderly patients, such as steroid-related osteoporosis, particularly during the early months of transplantation. In addition, intense rehabilitation and nutritional counseling should be provided to hasten functional recovery. In the late follow-up period, close surveillance of renal and hepatic function, as well as a psychological profile, is needed to detect behavioral changes such as depression that may change the ultimate outlook for adequate functional recovery.

Eighth, the presence of strong family support with total and unrestricted commitment to the patient's well-being is essential, perhaps more so than in younger patients. Although most of these elderly patients do not carry an active full-time job, a high degree of personal and familial satisfaction can be obtained with hobby-oriented activities and easy noncompetitive sports, which in turn may produce a more positive outlook in life.

Finally, the issue of retransplantation for chronic graft atherosclerosis in patients 70 years of age and older who had undergone heart transplantation in earlier years, and are otherwise good candidates, remains unclear. This subset of transplant recipients may eventually have to be addressed as more long-term survivors approach and cross the septuagenarian line.

In summary, our preliminary experience with heart transplantation in selected patients 70 years of age and older is encouraging and indicates that advanced age per se (as defined in this report) is not a contraindication to heart transplantation. However, care must be taken not to interpret these data as an endorsement to pursue this treatment modality in all septuagenarians who may be candidates for heart transplantation. Instead, highly selective criteria should be applied, identifying risks and benefits individually. The medical and socioeconomic implications are complex and the decisions involving the use of available resources and technology in a cost-effective fashion can only be made with increased knowledge regarding the unique issues associated with elderly patients. Perhaps more moral and ethical questions have been raised than answered with this study, but with the aging of the American population and the proven efficacy of heart transplantation for end-stage heart disease, these issues have to be addressed.

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Discussion

Dr Robbins. This study is a retrospective analysis of the outcome of cardiac transplantation in patients 70 years of age and older compared with the results achieved in recipients less than 70 years old. Fifteen older and 98 younger patients received cardiac transplantation at Cedars-Sinai from 1994 to 1999. The authors concluded that cardiac transplantation can be performed as successfully in patients over 70 years of age as in younger patients and that advanced age should not be an exclusion criterion for heart transplantation. They also stated that perhaps more moral and ethical questions have been raised than answered with this study, and I would agree with that. Their program's current policy is to list patients 70 years and older on an alternative list so that they do not take donor organs away from younger patients. Furthermore, these patients receive borderline organs deemed unsuitable for use by other transplant centers. This group of potential recipients is only considered in the UNOS status 2 outpatient category. As was pointed out, this presents a dilemma for the authors as to whether older patients should be penalized by placing them in a lower priority status in the transplant list and giving them access only to suboptimal or potentially compromised donor hearts on the basis of their age alone.

I have a few observations and questions about these data. Several studies including the most recent ISHLT Registry report have identified recipient age over 65 as a predictor of decreased survival at 1 and 5 years after cardiac transplantation. Dr Bull and his colleagues from Utah presented a paper at this meeting in 1995 about their results with cardiac transplantation in patients over 60 years old. They observed a 6-year actuarial survival of 54% for the older patients and 72% for those younger than 60 years of age. They pointed out that they did not use any unusual selection criteria but treated the older patients the same as the younger. The outstanding results achieved in this current report are thought to be the result of proper patient selection and tailoring of immunosuppressive protocols toward a reduction in immunosuppression for the older recipients. Sixty-five patients 70 years of age or older were referred for evaluation. Forty-four were fully evaluated and 22 accepted, for an acceptance rate of 33%.

My first question is this: How many patients under the age of 70 were referred and what was the acceptance rate for this cohort of patients?

Dr Blanche. The acceptance ratio for transplantation for those patients older than 70 years of age was 0.50, thus indicating high selective criteria. However, younger patients were also selected carefully, as the acceptance ratio for that group of patients was 0.52 (129 patients listed for transplantation out of 247 patients fully evaluated).

Dr Robbins. In other words, you were being very selective in these patients.

Dr Blanche. That is correct.

Dr Robbins. I think that is one of the main reasons that you get such good results.

Can you provide more specific details concerning the selection criteria for the older patients with regard to peripheral vascular disease, diabetes, cancer history, and renal dysfunction? For instance, would you use any of those comorbidities as a contraindication for transplantation? Can you give some general guidelines for these problems that often arise in this group of patients?

Dr Blanche. Diabetes is not considered a contraindication unless the patient has severe end-organ damage. Severe peripheral vascular disease is a contraindication, especially in the presence of severe carotid artery disease. If renal dysfunction is mild, we do accept patients over the age of 70 for transplantation. However, 1 patient in the older age group underwent combined heart-kidney transplantation. With regard to the other criteria, we screen the patients rigorously for malignancy, particularly prostate and gastrointestinal, more so than younger patients.

Dr Robbins. The patients in the older cohort had a higher mean ejection fraction than the younger patients. Since all the older patients were in the status 2 outpatient category, it would appear that the younger patients were sicker than the older patients. Do you have any objective data such as myocardial oxygen consumption that might help better define the functional status of the older patients?

Dr Blanche. Unfortunately, we do not have myocardial oxygen consumption data on all patients for a meaningful statistical analysis. Obtaining this information has now become routine as part of the preoperative evaluation, but during the period of this study it was not always obtained.

Dr Robbins. Just in your general sense, is it true that the older patients seem to be less debilitated and sick before the operation?

Dr Blanche. Yes, perhaps so, because we know that we will not place them in the transplant list as a status 1. These patients wait an average of 105 days, so at least they have to be fit enough to wait that long to receive a donor heart.

Dr Robbins. There were 2 recipients in the older group who died 18 and 42 months after transplantation from nonspecific allograft function. Did autopsy exclude graft coronary artery disease as a cause of death?

Dr Blanche. Yes. Their autopsies showed they did not have transplant atherosclerosis.

Dr Robbins. Finally, on the basis of the excellent results achieved in the older group, would you use a marginal donor from a younger patient in an older potential recipient if an older potential recipient was not available on your list? How would you prioritize the use of these donor hearts?

Dr Blanche. The use of a marginal donor in transplant patients is well documented. With the availability of assist

devices, perhaps I would place an assist device in a younger patient and wait for a perfect heart. We have no problems using a marginal donor for an older patient because many studies show that marginal donors in the long run perform as well as "regular" donors. We are in the process of revising our protocols. In view of the good results obtained in the older patients, perhaps older recipients should receive the same type of allografts as younger patients. In other words, they should not be discriminated against because of their age.

Dr Robbins. Right. Another possibility is that the younger patients might receive those marginal hearts.

In summary, this group has demonstrated that satisfactory results can be achieved in patients 70 years or older after cardiac transplantation. The statistical comparison between the two groups of patients seems to be invalid because there was such a profound selection bias for the older patients. Adopting the general policy that age should not be a contraindication to cardiac transplantation should await longer-term follow-up in a larger number of patients. The authors ask the question in the manuscript, "How old is too old for heart transplantation?" These data that were presented in this paper do not provide an answer to this question, and the use of highly selective criteria for listing older patients should continue to be customized on an individual basis.