JACC Vol. 29, No. 3
March 1, 1997:623–9

Relation of Donor Age and Preexisting Coronary Artery Disease on Angiography and Intracoronary Ultrasound to Later Development of Accelerated Allograft Coronary Artery Disease

SHAO-ZHOU GAO, MD, SHARON A. HUNT, MD, FACC, EDWIN L. ALDERMAN, MD, FACC, DAVID LIANG, MD, ALAN C. YEUNG, MD, FACC, JOHN S. SCHROEDER, MD, FACC

Stanford, California

Objectives. **This study assessed the influence of donor age and preexisting donor coronary artery disease on the later development of allograft coronary artery disease, ischemic events and overall survival.**

Background. **The increasing demand for heart donors has led to a tendency to liberalize age criteria for donor acceptability.**

Methods. **A total of 233 consecutive heart transplant recipients who had baseline, early postoperative and follow-up coronary angiograms, as well as a subset of 47 patients with baseline intracoronary ultrasound imaging recordings, were analyzed (mean 3.8 years of follow-up). Patients were subclassified according to the presence of donor coronary artery disease on the baseline angiogram and stratified at age 40 years.**

Results. **Patients without evidence of preexisting coronary artery disease on a baseline angiogram (n = 219) were significantly less likely to develop new disease than the 14 patients with preexisting coronary artery disease (p = 0.002). Although older donors exhibited earlier coronary artery disease than younger donors at 3 years of follow-up, there was no difference by 5 years (p = 0.25). There was no difference in survival or probability of developing ischemic events between the groups. Baseline ultrasound imaging revealed substantial disease in 7 of 9 older donated hearts, and in only 7 of 38 younger donated hearts (p = 0.002). Preexisting coronary artery disease, nonuse of calcium channel blocking agents, older donor age, posttransplantation cytomegalovirus infection, elevated very low density lipoprotein levels and previous ischemic heart disease in the recipient were significant predictors of allograft coronary artery disease.**

Conclusions. **Heart donors with angiographic evidence of preexisting coronary artery disease and older donors are more likely to develop new allograft coronary artery disease by 3 years. However, there is no difference in patient survival or freedom from ischemic events between younger and older donors at a mean follow-up of 3.8 years.**

(J Am Coll Cardiol 1997;29:623–9)

It has been a generally accepted principle that organs used for transplantation should be healthy and normally functioning at the time of "harvesting" and should have a good prognosis for long-term function. With this in mind, selection criteria for donor hearts were established in the early era of clinical heart transplantation and included not only freedom from any overt cardiac disease, but also arbitrary upper age limits, usually in the 35 to 40 year range (1–3). As heart transplantation has come to be regarded as the treatment of choice for end-stage heart failure in appropriate recipients, there has been an ever-increasing demand for heart donors—a demand not met by a seemingly fixed donor pool size (4). In this setting, there has been a general move to expand the donor pool by expanding donor criteria, especially by increasing the upper age limit for acceptability (5–8). Earlier reports with short-term follow-up have suggested no adverse effects on survival or development of accelerated allograft coronary artery disease with the use of older donors (8,9). In this retrospective study, we analyzed the influence of older donor age and either angiographic or intracoronary ultrasound imaging evidence of donor coronary artery disease at early posttransplantation study on the later angiographic incidence of allograft coronary artery disease and overall survival. We also examined other risk factors potentially related to allograft coronary artery disease in this cohort of patients.

Methods

Study patients. A total of 256 consecutive adult patients underwent heart transplantation at Stanford University Medical Center between July 1986 and June 1993. Of these, 237 patients had baseline early posttransplantation coronary angiograms and form the basis of this report. Fourteen patients had angiographic evidence of preexisting coronary artery disease at baseline study and form the donor coronary artery disease group. The other 223 patients had normal angiograms at

From the Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, California. Financial support for this study was provided by the Gottlieb Foundation, Kansas City, Missouri.

Manuscript received November 17, 1995; revised manuscript received October 21, 1996, accepted November 5, 1996.

Address for correspondence: Dr. John S. Schroeder, Division of Cardiovascular Medicine, CVRC-293, Stanford University School of Medicine, Stanford, California 94305.

0735-1097/97/$17.00
PII S0735-1097(96)00521-9

baseline study; 219 of these 223 patients had follow-up records available for review. The other four patients did not have clinical or angiographic follow-up records and were excluded from this study. These 219 patients comprise the no-donor coronary artery disease group. The patients in the no-donor coronary artery disease group were subclassified into those with older versus younger donor hearts. Older donors were defined as those ≥40 years of age. The older donor group consisted of 30 patients (donor age 40 to 54 years, mean 44.8 ± 4.9). The younger donor group received hearts from donors <40 years old (13 to 39 years, mean 23.9 ± 6.6) at the time of brain death, and consisted of 189 patients. A subset of 47 patients with both baseline and follow-up coronary angiograms and baseline intracoronary ultrasound imaging recordings was also reviewed; three of them had angiographic evidence of pre-existing coronary artery disease at baseline study, one with older and two with younger donors.

Follow-up times range from 0.2 to 9.4 years (mean 3.8 ± 2.3). There was no significant difference among mean follow-up times for the subgroups (3.6 years in the donor coronary artery disease group; 3.8 years in the no-donor coronary artery disease group). The mean follow-up time for the subset of 47 patients with both baseline angiograms and intracoronary ultrasound imaging recordings was 2.4 ± 0.9 years, and was equal for those with minimal or no intimal thickening versus those with more advanced disease. All participants gave written informed consent to the protocol, which was approved by the Committee for the Protection of Human Subjects in Research at Stanford University Medical Center.

Study measurements. Clinical and laboratory risk factors—including recipient and donor age and gender; recipient type of cardiac disease; donor ischemic time; number of human leukocyte antigen (HLA) mismatches; cytomegalovirus infection after transplantation; postoperative blood pressure; number of rejection episodes during the first year after transplantation; lipid profile (triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and very low density lipoprotein cholesterol); prednisone, azathioprine and cyclosporine doses; and calcium channel blocker use—were included in the data base. Blood pressure, drug dosage and lipid measurements were computed for each patient as the average of all available annual follow-up visits.

Coronary arteriography. Coronary arteriograms were performed with a femoral approach, using standard angiographic techniques at "baseline" (within 6 weeks postoperative) and subsequently at approximately annual intervals. Multiple projections of both right and left coronary systems were obtained after sublingual nitroglycerin premedication. Identical projections were obtained and compared in serial studies, which were reviewed on the basis of side by side comparisons of projected cineangiograms to detect subtle disease progression. The criteria for diagnosis of angiographic allograft coronary artery disease was the presence of any evidence of coronary lumen narrowing. The criteria for progression of coronary artery disease in patients with preexisting coronary artery disease included either the development of new lesions or the progression of preexisting lesions. Quantitative angiographic measurements were not used. Final interpretation was based on a consensus of two angiographers (S.Z.G., E.L.A.).

Of the 233 patients with baseline angiographic studies, 94% of 1-year survivors, 93% of 2-year survivors and 97% of 3-year survivors completed the angiographic studies. Of the 47 patients with both baseline intracoronary ultrasound imaging studies and angiograms, 95% had 1-year angiograms and 100% of 2-year survivors and 96% of 3-year survivors had follow-up angiograms. All patients who died or were retransplanted because of allograft coronary artery disease had previous angiography.

Intracoronary ultrasound. Imaging of the left anterior descending coronary artery was performed immediately after routine coronary arteriography using a 30-MHz ultrasound transducer enclosed within an acoustic housing on the tip of a 1.7-mm diameter (3.5F), 135-cm long, flexible catheter (CVIS Inc.). A mean of 2.3 segments (range 1 to 4) per patient were recorded. Details of imaging technique and image analysis have been reported elsewhere (10).

Vascular disease severity was classified according to our previously reported categories (11), which take into account both intimal thickness and degree of vessel circumference involved. Patients were classified on the basis of their most severely diseased site as having either minimal or no disease (class 1/2) or moderate or severe disease (class 3/4). The left anterior descending coronary artery was imaged in all 47 patients; the left circumflex coronary artery was also studied in four patients. Only data from the left anterior descending coronary artery were analyzed in this study.

Immunosuppressive protocol. All patients received triple immunosuppression with cyclosporine, azathioprine and prednisone. After September 1986, patients who consented were randomized to receive diltiazem or no calcium blocker shortly after the operation. Nine patients (64%) in the donor coronary artery disease group and 98 patients (44.9%) in the no-donor coronary artery disease group received diltiazem; 18 patients (58.1%) in the older donor group and 80 patients (42.6%) in the younger donor group received diltiazem. All patients received aspirin and dipyridamole. Antihypertensive therapy was generally similar in the subgroups, although angiotensin-converting enzyme inhibitors were used more often in the patients who did not receive diltiazem.

Criteria for diagnosis of cytomegalovirus infection. Cytomegalovirus infection after transplantation was defined for purposes of this study by any of the following: seroconversion of a previously cytomegalovirus-seronegative patient; fourfold rise in a previously positive cytomegalovirus immunoglobulin G titer; positive cultures for cytomegalovirus; demonstration of cytomegalovirus inclusion bodies in tissue specimens; or a clinical illness documented to be due to cytomegalovirus.

Ischemic events. Patients were classified as having ischemic events if they had any of the following during their postoperative period: clinical diagnosis of myocardial infarction; typical electrocardiographic evidence of Q wave myocardial infarction

in the absence of symptoms; appearance of congestive heart failure in a patient with an abnormal angiogram in the presence of a normal heart biopsy; or sudden death with autopsy evidence of allograft coronary artery disease and no rejection.

Statistical analysis. All results are presented as mean value ± SD. The Kaplan-Meier method was used to calculate probability of freedom from allograft coronary artery disease. The Mantel-Haenszel log-rank test was used to compare the equality of survival curves. Differences between the group characteristics were assessed with the chi-square test for categoric variables and two-tailed *t* test for continuous variables.

Analysis of the predictors of time to initial detection of angiographic allograft coronary artery disease was carried out using standard stepwise regression techniques on SPSS programs. One analysis included all data collectable within 3 months of transplantation, including donor features (age, gender, cytomegalovirus serostatus and ischemic time) and recipient features (age, gender, cause of heart failure, number of HLA mismatches, cytomegalovirus serostatus before and after transplantation and calcium channel blocker use). A second analysis included, in addition to the donor and recipient characteristics, additional data that could only be collected in 1-year survivors. This follow-up information included the number of rejection episodes during the first year after transplantation, blood lipid measurements (triglycerides, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and very low density lipoprotein cholesterol), immunosuppressive medication dosage (azathioprine, prednisone and cyclosporine) and blood pressure (systolic and diastolic). There were 195 patients with donor and recipient data collectable within 3 months of transplantation and 144 one-year survivors with one or more years of complete follow-up results available. Significant associations were defined by $p < 0.05$.

Results

Fourteen (6%) of the 233 patients with baseline angiographic studies showed some evidence of coronary artery disease. Of the 47 patients with both baseline angiograms and intracoronary ultrasound imaging studies, 14 patients (28%) had class 3 or 4 intimal thickening. Of these 14 patients, only 3 (21%) had abnormal angiograms. These results confirm the known higher sensitivity of intracoronary ultrasound imaging compared with angiography in detecting intimal thickening.

Of the 14 patients with abnormal baseline angiograms (10% to 40% stenosis), 6 did not show progression at any time during follow-up and eight did show progression. Of the latter group, all eight patients developed new lesions and four of the eight patients also had progression in preexisting lesions. Three of these eight patients showed lesion progression to >50% stenosis—52%, 62% and 80% at 2, 3 and 4 years, respectively—after transplantation. One patient had an acute myocardial infarction at 5 years, and the other two patients underwent retransplantation 5 and 6 years after the operation.

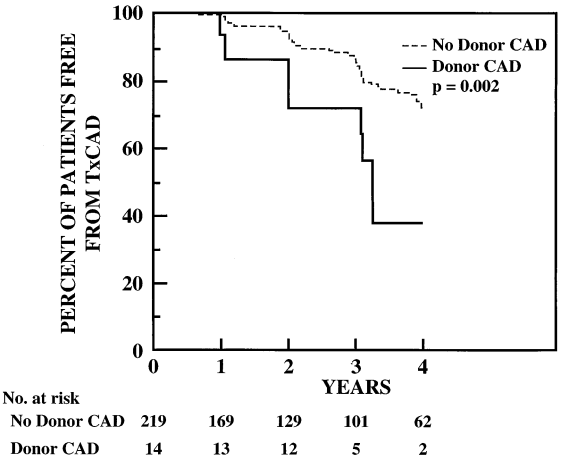

Figure 1. Graph comparing time-related percent freedom from new or progressive allograft coronary artery disease (CAD) in patients with and those without donor coronary artery disease. TxCAD = allograft coronary artery disease.

When patients with and without baseline angiographic abnormalities are compared, it is clear that those with baseline coronary artery disease have an increased probability of developing later progressive allograft coronary artery disease. Figure 1 demonstrates 95%, 89%, 78% and 67% freedom from new allograft coronary artery disease at 1, 2, 3 and 4 years, respectively, in patients with normal baseline angiograms as compared with 86%, 71%, 37% and 37% freedom from progression of coronary artery disease in patients with abnormal baseline angiograms ($p = 0.002$). In a similar analysis, patients with normal baseline angiograms were subclassified into groups with younger versus older donors. Patients with older donor hearts had an increased probability of developing allograft coronary artery disease by 3 years after transplantation ($p = 0.04$), but the disease incidence in younger versus older donor recipients was no longer significantly different in the subsequent 3 years of follow-up (Fig. 2). Ninety-six percent, 81%, 56% and 52% of patients in the younger donor group versus 92%, 64%, 56% and 56% of patients with older donor hearts were free from allograft coronary artery disease at 1, 3, 5 and 6 years, respectively, after transplantation. The results shown in Figure 2 suggest earlier onset of coronary artery disease in older donor hearts, but the convergence of the curves is in accord with the eventual inevitability of the disease.

Table 1 lists the baseline intracoronary ultrasound imaging classes in the subset of 47 patients studied with this modality, subclassified according to donor age, and shows a significantly increased prevalence of more advanced classes of intimal thickening in older donors. Table 2 shows the incidence of later development of progressive angiographic allograft coronary artery disease in the groups subclassified according to the presence and severity of baseline intimal disease. There is no significant difference between the groups ($p = 0.87$).

Multivariate Cox regression analysis was used to identify

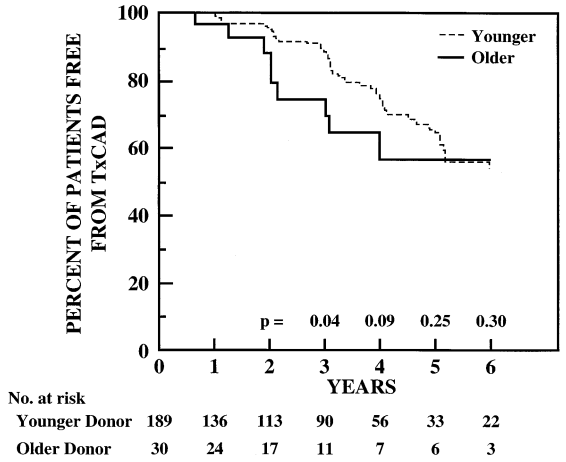

Figure 2. Graph showing comparison of time-related percent freedom from new allograft coronary artery disease (CAD) in patients receiving hearts from younger (<40 years) and older (≥40 years) donors in patients with normal baseline angiograms. TxCAD = allograft coronary artery disease.

potential risk factors associated with development (or progression) of allograft coronary artery disease (Table 3). This analysis showed that donor preexisting coronary artery disease, nonuse of calcium channel blockers, older donor age, previous ischemic heart disease and elevated very low density lipoprotein cholesterol levels were associated with earlier development of allograft coronary artery disease. This multivariate analysis, which included all follow-up data, showed that a positive cytomegalovirus serology in the recipient before transplantation is associated with earlier onset of coronary artery disease. Another multivariate analysis was performed with truncation at 4 years because only 28% of the original cohort remained alive and free of coronary artery disease beyond 4 years. In this truncated analysis, the occurrence of cytomegalovirus infection after transplantation was the highest ranked predictor of a shorter interval to onset of coronary artery disease ($p = 0.007$).

Comparison of actuarial freedom from ischemic events showed no significant differences between the donor coronary artery disease and no-donor coronary artery disease groups ($p = 0.61$), or between the younger and older donor groups ($p = 0.73$). Actuarial survival curves for the two subsets of older versus younger donor hearts also showed no difference, with a mean follow-up of 3.8 years ($p = 0.64$). In addition, there was no significant difference in survival between the donor coronary artery disease and no-donor coronary artery disease groups ($p = 0.26$).

A variety of other potential coronary artery disease risk factors were compared between the groups (Table 4). No significant differences were found between the no-donor coronary artery disease and donor coronary artery disease groups. In comparing of these same factors in older and younger donor groups, there were no significant differences, except a higher level of HLA mismatch in the younger donor group, as listed in Table 4.

Table 1. Comparison of Intimal Thickening Detected by Intracoronary Ultrasound at Baseline in Younger and Older Donor Groups

	Baseline ICUS		
Donor Age Subgroups	Class 1/2	Class 3/4	p Value
Younger pts (n = 38)	31/38 (82%)	7/38 (18%)	0.002
Older pts (n = 9)	2/9 (22%)	7/9 (78%)	

ICUS = intracoronary ultrasound; pts = patients.

Table 2. Development of Angiographically Apparent Coronary Artery Disease in 41 Patients With Baseline Intracoronary Ultrasound Evaluations

	Follow-Up Angiographic Findings		
Baseline ICUS Class	No TxCAD	TxCAD	p Value
1/2 (n = 33)	26/33 (79%)	7/33 (21%)	0.87
3/4 (n = 14)	10/14 (71%)	4/14 (29%)	

ICUS = intracoronary ultrasound; TxCAD = allograft coronary artery disease.

Discussion

This retrospective analysis of 233 consecutive adult heart transplant recipients strongly suggests that the use of donor hearts with preexisting coronary artery disease is associated with a higher incidence of progression and development of allograft coronary artery disease after transplantation, but not with a different probability of survival or ischemic events with a mean follow-up of 3.8 years. Because the number of patients with disease at baseline was small, it is possible that larger numbers or longer follow-up will, in fact, see these curves diverge. The fact that older donor age, at least as defined by our arbitrary cutoff point of age 40 years, was not associated with an increased prevalence of later coronary artery disease on angiography or with a difference in later ischemic events or overall survival, is an important point of this study. Both findings suggest that the use of carefully selected older donor hearts can safely increase the size of the donor pool, confirming earlier reports of short-term good results with older donors (8,9).

Cytomegalovirus infection and allograft coronary artery disease. The significance of recipient cytomegalovirus infection as a risk factor for development of coronary artery disease is of interest because postoperative cytomegalovirus infection was first reported by our group to correlate with later development of coronary artery disease on angiography in heart transplant recipients (12). Our earlier study described patients transplanted between 1980 and 1988, and differs from the current report of patients transplanted between 1986 and 1993, in that this latter group was influenced by the introduction of cytomegalovirus prophylaxis therapy with ganciclovir in 1987,

Table 3. Multivariate Stepwise Regression Analysis of Time to Detection of Angiographic Allograft Coronary Artery Disease in a Consecutive Series of 233 Heart Transplant Recipients

All Transplant Recipients (includes data collectable immediately after transplantation; 195 patients available for analysis)		1-Year Survivors (includes data collectable within 12 months after transplantation; 144 patients available for analysis)	
Donor features: age, CAD, CMV and ischemic time Recipient features: age, gender, CAD, CMV, HLA mismatch and calcium blocker use		Donor features: age, CAD, CMV and ischemic time Recipient features: Age, gender, CAD, CMV, HLA mismatch, calcium blocker use, lipids, rejection episodes, blood pressure and immunosuppressive medications	
Variable	p Value	Variable	p Value
Donor CAD at entry	0.0002	Donor CAD at entry	0.003
Calcium blocker nonuse	0.001	Calcium blocker nonuse	0.0001
Older donor age	0.007	Older donor age	0.002
Recipient heart disease: ischemic	0.03	Recipient pre-Tx CMV serology positive	0.01
		VLDLC	0.004

CAD = coronary artery disease; CMV = cytomegalovirus infection; HLA = human leukocyte antigen; Tx = transplantation; VLDLC = very low density lipoprotein cholesterol.

first as part of a randomized trial (until 1990) and subsequently as routine therapy (13). Despite current use of cytomegalovirus prophylaxis, the overall incidence of cytomegalovirus infection after transplantation in this report is 31% compared with 30.2% for the 1980 to 1988 cohort using the same diagnostic criteria. The results of this study suggest that cytomegalovirus infection after transplantation is still a major factor in early onset of allograft coronary artery disease (14), despite the use

Table 4. Comparison of Risk Factors in Older and Younger Donor Groups

	Older (n = 30)	Younger (n = 189)	p Value
Recipient age (yr)	49 ± 12.9	47.1 ± 11.9	0.26
Donor age (yr)	44.8 ± 4.0*	23.9 ± 6.6*	< 0.001
Recipient gender (% male)	76	85	0.31
Original cardiac disease			
Coronary artery disease	18	82	
Cardiomyopathy	12	91	
Other	0	15	0.11
HLA mismatch (no. of loci)			
A	1.1 ± 0.6†	1.4 ± 0.6†	0.04
B	1.3 ± 0.7	1.4 ± 0.6	0.51
A + B	2.5 ± 1.1	2.9 ± 0.9	0.08
Ischemic time (min)	148 ± 46	158 ± 47	0.27
CMV infection before Tx			
Recipient CMV positive	18	111	0.89
Donor CMV positive	16	89	0.69
CMV infection after Tx			
By serology	11	56	0.55
Symptom	7	31	0.51
No. of rejection episodes (first year after operation)	1.9 ± 1.2	1.9 ± 1.1	0.99
Blood pressure (mm Hg)			
Systolic	136 ± 13	136 ± 14	0.94
Diastolic	89 ± 9	89 ± 9	0.74
Prednisone dose (mg/kg body weight per day)	0.15 ± 0.1	0.16 ± 0.1	0.55
Cyclosporine dose (mg/kg per day)	3.6 ± 1.5	4.1 ± 2.2	0.30
Azathioprine dose (mg/kg per day)	1.6 ± 0.8	1.7 ± 0.8	0.65
Plasma triglyceride (mg/dl)	191 ± 111	202 ± 121	0.70
Total cholesterol (mg/dl)	215 ± 41	231 ± 59	0.21
HDL-C (mg/dl)	45 ± 10	45 ± 16	0.99
LDL-C (mg/dl)	135 ± 36	144 ± 41	0.34
VLDL-C (mg/dl)	39 ± 24	40 ± 28	0.82

Data presented are mean value ± SD or number of patients, unless otherwise indicated. CMV = cytomegalovirus; HDL-C = high density lipoprotein cholesterol; HLA = human leukocyte antigen; LDL-C = low density lipoprotein cholesterol; Tx = transplantation; VLDL-C = very low density lipoprotein cholesterol.

of cytomegalovirus prophylaxis and its clinical success in ameliorating the severity of cytomegalovirus disease. A detailed evaluation of the effect of cytomegalovirus prophylaxis on the incidence of allograft coronary artery disease is currently ongoing.

The observation that the recipient's previous ischemic heart disease and elevated very low density lipoprotein cholesterol level contribute to the risk of earlier onset of coronary artery disease suggests a role for typical atherosclerosis risk factors. Histopathologic study of transplanted hearts shows that older lesions exhibit features typical of ordinary complex atheromas (15). Moreover, a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor has been shown to decrease the incidence of allograft coronary artery disease (16).

Intracoronary ultrasound imaging for detection of allograft coronary artery disease. The intracoronary ultrasound imaging data presented here are preliminary, but add to the growing body of evidence supporting the validity of intracoronary ultrasound measurements as a more sensitive modality for the detection and monitoring of allograft coronary artery disease (11,17). Serial intracoronary ultrasound imaging data reported from our institution suggest that the usual rate of intimal hyperplasia in heart transplant recipients that occurs in disease-free arteries is superimposed on any pre-existing lumen narrowing. The combination of preexisting and incremental hyperplasia may lead more rapidly to angiographically detectable and ultimately clinically important lumen compromise. Therefore, one does not need to invoke acceleration of the usual rate of intimal hyperplasia in older donor hearts to explain earlier angiographic detection of coronary lesions (18).

In our patients, we demonstrated a significantly higher incidence of moderate to severe intracoronary ultrasound imaging class in older donors—a finding similar to observations already reported by Tuzcu et al. (19). However, knowledge of the extent to which advanced intimal thickening in older donor hearts is associated with a higher incidence of later allograft coronary artery disease on angiography, particularly in patients with substantially detectable disease on intracoronary ultrasound imaging, is limited by the small number of patients and short follow-up duration. Fourteen (28%) of the 47 patients in our study group had class 3 or 4 intimal thickening on baseline intracoronary ultrasound examinations, and 33 patients (72%) showed class 1 or 2 intimal changes. Therefore, by extrapolation, about one-third of donor hearts had moderate to severe preexisting intimal thickening. This fact limits the validity of intracoronary ultrasound for the diagnosis of allograft coronary artery disease if patients have not had a baseline study.

Calcium channel blocker use. In this study, the use of calcium channel blockers was correlated with a lower incidence of allograft coronary artery disease—a finding concordant with our previously reported results of a randomized trial of diltiazem, which showed less decline in coronary artery diameter during the first postoperative year (20) and fewer clinical events in later years (21) in diltiazem-treated patients. These results and others (22) suggest an important role for the use of calcium channel blockers after transplantation, perhaps most importantly in high risk patients such as recipients of older donor hearts and those with any evidence of preexisting donor coronary artery disease.

Conclusions. Cardiac donors with angiographic evidence of pre-existing coronary artery disease have a greater tendency to develop new allograft coronary artery disease. Despite the higher incidence of moderate to severe intimal thickening detected by intracoronary ultrasound found in older donors, older donor age was not significantly associated with the development of later allograft coronary artery disease on angiography. There was no difference in patient survival or freedom from ischemic events between patients with younger versus older donor hearts at a mean 3.8 years of follow-up.

We are grateful to Ms. Anne Schwarzkopf for the collection of ICUS imaging results.

References

1. Griepp RB, Stinson EB, Clark DA, Dong E, Shumway NE. The cardiac donor. Surg Gynecol Obstet 1971;133:792–8.
2. DeBakey ME, Deitrich EB, Glick G, et al. Human cardiac transplantation: clinical experience. J Thorac Cardiovasc Surg 1969;58:303–17.
3. English TAH, Spratt P, Wallwork J, Cory-Pearce R, Wheeldon D. Selection and procurement of hearts for transplantation. BMJ 1984;288:1889–91.
4. Hosenpud JD, Novick RJ, Breen TJ, Daily OP. The registry of the International Society for Heart and Lung Transplantation: eleventh annual report—1994. J Heart Lung Transplant 1994;13:561–70.
5. Schüler S, Warnecke H, Loebe M, Fleck E, Hetzer R. Extended donor age in cardiac transplantation. Circulation 1989;80 Suppl III:III-133–9.
6. Menkis AH, Novick RJ, Kostuk WJ, et al. Successful use of the "unacceptable" heart donor. J Heart Lung Transplant 1991;10:28–32.
7. Mulvagh SL, Thornton B, Frazier OH, et al. The older cardiac transplant donor: relation to graft function and recipient survival longer than 6 years. Circulation 1989;80 Suppl III, Pt. 2:III-126–32.
8. Pflugfelder PW, Singh NR, McKenzie FN, Menkis AH, Novick RJ, Kostuk WJ. Extending cardiac allograft ischemic time and donor age: effect on survival and long-term cardiac function. J Heart Lung Transplant 1991;10: 394–400.
9. Schüler S, Matschke K, Loebe M, Hummel M, Fleck E, Hetzer R. Coronary artery disease in patients with hearts from older donors: morphologic features and therapeutic implications. J Heart Lung Transplant 1993;12: 100–9.
10. St.Goar FG, Pinto FJ, Alderman EL, et al. Detection of coronary atherosclerosis in young adult hearts using intravascular ultrasound. Circulation 1992;86:756–63.
11. St.Goar FG, Pinto FJ, Alderman EL, et al. Intracoronary ultrasound in cardiac transplant recipients: in vivo evidence of "angiographically silent" intimal thickening. Circulation 1992;85:979–87.
12. Grattan MT, Moreno-Cabral CE, Starnes VA, Oyer PE, Stinson EB, Shumway NE. Cytomegalovirus infection is associated with cardiac allograft rejection and atherosclerosis. JAMA 1989;261:3561–6.
13. Merigan TC, Renlund DG, Keay S, et al. A controlled trial of ganciclovir to prevent cytomegalovirus disease after heart transplantation. N Engl J Med 1992;326:1182–6.
14. Gao SZ, Hunt SA, Schroeder JS, Alderman EL, Hill IR, Stinson EB. Early development of accelerated graft coronary artery disease: risk factors and course. J Am Coll Cardiol 1996;28:673–9.
15. Johnson DE, Gao SZ, Schroeder JS, DeCampli WM, Billingham ME. The spectrum of coronary artery pathologic findings in human cardiac allografts. J Heart Transplant 1989;8:349–59.
16. Kobashigawa JA, Katznelson S, Laks H, et al. Effect of pravastatin on outcomes after cardiac transplantation. N Engl J Med 1995;333:621–7.
17. Pflugfelder PW, Boughner DR, Rudas L, Kostuk WJ. Enhanced detection of

cardiac allograft arterial disease with intracoronary ultrasonographic imaging. Am Heart J 1993;125:1583–91.

18. Botas J, Pinto FJ, Chenzbraun A, et al. Influence of preexistent donor coronary artery disease on the progression of transplant vasculopathy; an intravascular ultrasound study. Circulation 1995;92:1126–32.
19. Tuzcu EM, Hobbs RE, Rincon G, et al. Occult and frequent transmission of atherosclerotic coronary disease with cardiac transplantation: insights with intravascular ultrasound. Circulation 1995;91:1706–13.
20. Schroeder JS, Gao S-Z, Alderman EL, et al. A preliminary study of diltiazem in the prevention of coronary artery disease in heart transplant recipients. N Engl J Med 1993;328:164–70.
21. Schroeder JS, Gao S-Z, Alderman EL, Hunt SA, Hill I, Stinson EB. Prevention of transplant coronary vascular disease with diltiazem [abstract]. J Am Coll Cardiol 1994;23:231A.
22. Mehra MR, Ventura HD, Smart FW, Collins TJ, Ramee SR, Stapleton DD. An intravascular ultrasound study of the influence of angiotensin-converting enzyme inhibitors and calcium entry blockers on the development of cardiac allograft vasculopathy. Am J Cardiol 1995;75:853–7.