

# Intracoronary Ultrasound in Cardiac Transplant Recipients

## In Vivo Evidence of "Angiographically Silent" Intimal Thickening

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**Background.** Accelerated coronary atherosclerosis is a major factor limiting allograft longevity in cardiac transplant recipients. Histopathology studies have demonstrated the insensitivity of coronary angiography for detecting early atheromatous disease in this patient population. Intracoronary ultrasound is a new imaging technique that provides characterization of vessel wall morphology. The purpose of this study was to compare in vivo intracoronary ultrasound with angiography in cardiac transplant recipients.

**Methods and Results.** The left anterior descending coronary artery was studied with intracoronary ultrasound in 80 cardiac transplant recipients at the time of routine screening coronary angiography 2 weeks to 13 years after transplantation. A mean and index of intimal thickening were obtained at four coronary sites. Intimal proliferation was classified as minimal, mild, moderate, or severe according to thickness and degree of vessel circumference involved. Twenty patients were studied within 1 month of transplantation and had no angiographic evidence of coronary disease. An intimal layer was visualized by ultrasound in only 13 of these 20 presumably normal hearts. The 60 patients studied 1 year or more after transplantation all had at least minimal intimal thickening. Twenty-one patients (35%) showed minimal or mild, 17 (28%) moderate, and 21 (35%) severe thickening. Forty-two of these 60 patients had angiographically normal coronary arteries, 21 (50%) of whom had either moderate or severe thickening. All 18 patients with angiographic evidence of coronary disease had moderate or severe intimal thickening, but there was no statistically significant difference in intimal thickness or index when compared with the patients with moderate or severe proliferation and normal angiograms (thickness,  $0.53 \pm 0.35$  mm versus  $0.64 \pm 0.30$  mm,  $p=NS$ ; index,  $0.28 \pm 0.10$  versus  $0.34 \pm 0.10$ ,  $p=NS$ ).

**Conclusions.** The majority of patients 1 or more years after cardiac transplantation have ultrasound evidence of intimal thickening not apparent by angiography. Intracoronary ultrasound offers early detection and quantitation of transplant coronary disease and provides characterization of vessel wall morphology, which may prove to be a prognostic marker of disease. (*Circulation* 1992;85:979-987)

**KEY WORDS** • intracoronary ultrasound • heart transplantation • intimal thickening

Accelerated coronary atherosclerosis has emerged as a major cause of morbidity and mortality in cardiac transplant recipients.<sup>1,2</sup> Coronary artery disease accounts for 36% of deaths in patients who survive 1 year beyond transplantation<sup>3</sup> and for 60% of the retransplantation procedures<sup>4</sup> performed at our institution (Stanford University School of Medicine, Stanford, Calif.). Because cardiac allografts are functionally denervated, major clinical sequelae secondary to advanced coronary atherosclerosis, including myocardial infarction, congestive heart failure, and sudden death, can occur without prodromal angina.<sup>3</sup> Therefore,

annual surveillance coronary arteriograms have been performed as a matter of policy at Stanford on all cardiac recipients since shortly after the transplant program was started.<sup>5</sup>

The pathology of transplant coronary artery disease is unique in that it initially is a concentric intimal proliferation throughout the coronary tree that often progresses to diffuse obliterative lesions. These lesions angiographically are characterized by longitudinal narrowing of the arteries with pruning of distal vessels.<sup>6-8</sup> The ability of

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standard coronary arteriography to accurately measure severity of transplant coronary artery disease is limited unless detailed quantitative techniques are applied.<sup>9</sup> Recent angiography-pathology correlation studies have highlighted the insensitivity of angiography for detecting evidence of early transplant coronary atherosclerosis.<sup>10</sup>

Intravascular ultrasound is a new in vivo imaging modality with the ability to study vascular wall morphol-

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TABLE 1. Ultrasound Classification of Coronary Artery Disease in Cardiac Transplant Recipients

	Class			
	I	II	III	IV
Severity	Minimal	Mild	Moderate	Severe
Intimal thickness	<0.3 mm or <180°	>0.3 mm or >180°	0.3–0.5 mm or >0.5 mm, <180°	>1.0 mm or >0.5 mm, >180°

ogy.<sup>11–13</sup> It has been used to measure vessel dimensions, coronary vasomotion, and the efficacy of interventional procedures.<sup>14–17</sup> The purpose of this study was to determine the ultrasound characteristics of coronary arteries in cardiac transplant recipients and to compare the ultrasound findings with coronary angiography.

### Methods

#### Patient Population

The study population consisted of 83 cardiac transplant recipients undergoing routine surveillance coronary angiography. Three patients were excluded because the ultrasound image quality was inadequate for precise measurements. Therefore, our study population consisted of 80 patients: 63 men and 17 women with a mean age of  $46 \pm 11$  years. Patients were studied an average of 3 years after transplantation (range, 2 weeks to 13 years). Twenty of these patients were studied within 1 month of their operation and served as a baseline population. All participants gave informed consent to the protocol approved by the Committee for the Protection of Human Subjects in Research at Stanford University Medical Center.

#### Ultrasound Imaging Procedure

Intracoronary imaging was provided by a 30-MHz ultrasound transducer enclosed within an acoustic housing on the tip of a 1.7-mm diameter, flexible, 135-cm-long catheter (CVIS Inc., Sunnyvale, Calif.). The ultrasound beam is reflected against an angulated mirror rotating at 1,800 rpm, creating a 360° imaging plane perpendicular to the catheter. A flexible drive cable through the length of the catheter is connected to a motor at the distal end that drives the mirror. At a focal depth between 1.5 and 4.5 mm, axial resolution of the image is 150  $\mu$ m and lateral resolution is 200  $\mu$ m. The radius of penetration is approximately 5 mm. Images are acquired at 30 frames per second and recorded on 1/2-in. videotape for subsequent off-line analysis. The imaging catheter has a lumen that accommodates a 0.014-in. coronary guide wire that exits the catheter centrally, distal to the transducer via a flexible, tapered tip. This allows manipulation of the ultrasound catheter in coronary arteries similar to large-diameter coronary balloon angioplasty systems. An 8F high-flow coronary guiding catheter was used for all studies (internal diameter, 0.082 in.).

After anticoagulation with 10,000 units of intravenous heparin, coronary vessels were continuously scanned with the ultrasound catheter from the ostium of the left main coronary artery to the midportion of the left anterior descending artery (LAD), avoiding vessel segments smaller than 2 mm in diameter. Four distinct LAD locations per patient were selected for precise ultrasound measurements. These sites were determined

angiographically and were separated by at least 1 cm but less than 2 cm. Measurement sites were selected where the lumen was circular. Areas of vessel bifurcations and side branches were not used. Image quality was consistent in vessels larger than 2 mm in diameter; therefore, this was not a factor in site selection.

#### Ultrasound Analysis

Ultrasound images were examined on line and later digitized onto a 512×512×8-bit matrix in 34 frame sequences obtained at 30 frames per second by an image-processing computer (Dextra Medical Inc., Lake-wood, Calif.) dedicated to echocardiographic analysis. All patients had resting heart rates above 60 beats per minute (mean,  $86 \pm 14$ ); thus, at least one cardiac cycle was digitized. The largest lumen from the digitized cardiac cycle was obtained for analysis. The lumen-vessel wall interface was traced by planimetry, and when visible, the external border of the intimal layer (i.e., intimal-media interface) was planimtered. This allowed for calculation of mean intimal thickness and a fractional intimal area defined as the ratio of intimal area to the sum of the intimal and lumen areas referred to as the intima index (Figure 1).

Vascular disease severity was classified according to intimal thickness and degree of vessel circumference involved: class 0, no measurable intimal layer by ultrasound; class I (minimal), an intimal layer less than 0.3 mm thick measurable in less than 180° of the vessel circumference; class II (mild), an intimal layer less than 0.3 mm but measurable in greater than 180° of the vessel circumference; class III (moderate), an intimal layer 0.3–0.5 mm thick or an intimal layer greater than 0.5 mm thick involving less than 180° of the vessel circumference; and class IV (severe), greater than 0.5 mm intimal thickening involving greater than 180° of the vessel circumference or an intimal layer greater than 1.0 mm in any one area of the vessel circumference (Table 1). Patients were classified according to their most severe site. Real-time images were also reviewed for discrete echodense areas of calcium sufficient to produce acoustic shadowing.

#### Coronary Arteriography

Multiple projections of both right and left coronary systems were obtained after nitroglycerin premedication. Arteriograms performed in patients 1 year or more after transplantation were compared with identical projections in serial studies. Arteriograms were reviewed on the basis of side-by-side comparisons of projected cineangiograms to detect subtle disease progression. Direct angiographic measurement techniques were not used. Final interpre-

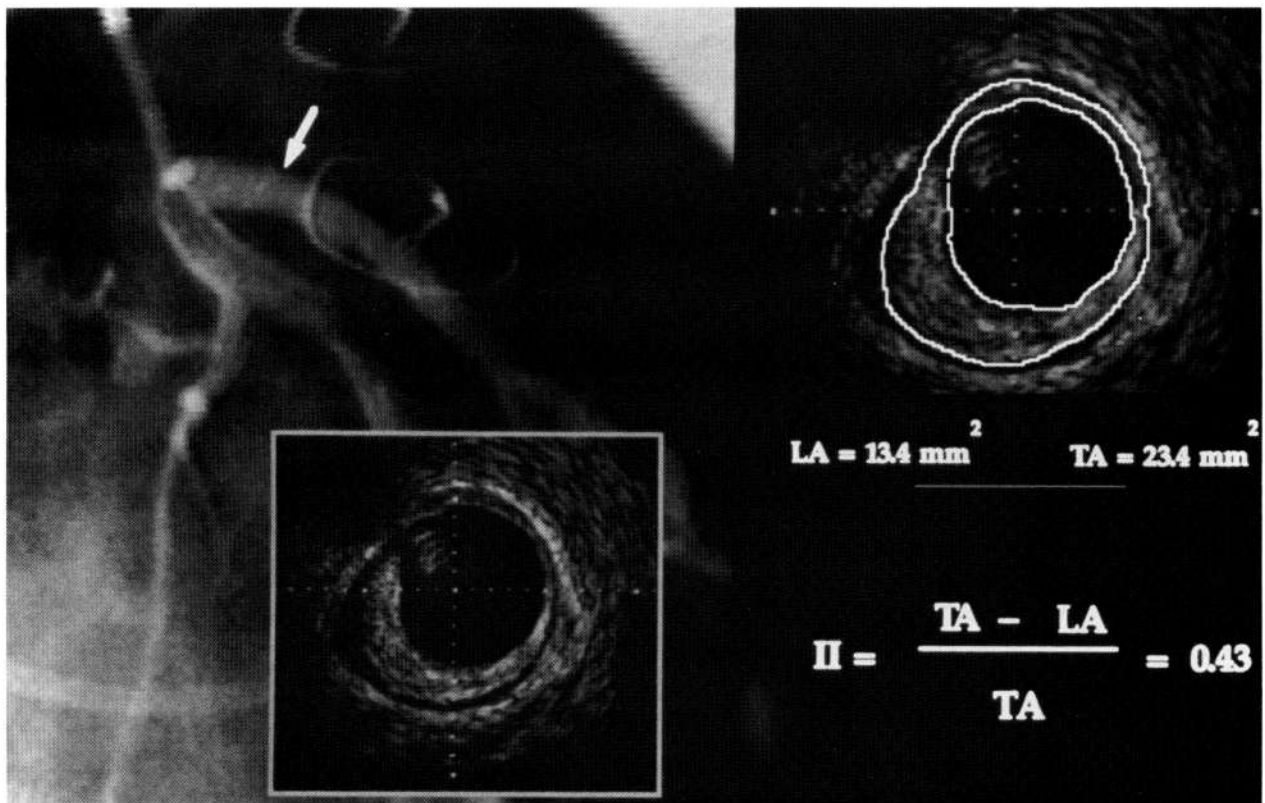


FIGURE 1. Angiogram and intracoronary ultrasound image from a site in the proximal left anterior descending coronary artery of a patient 7 years after transplantation. Ultrasound image shows the catheter, which is the black circle in the center of the picture, the dark vessel lumen, and the three-layered appearance of the vessel wall representing the intima, media, and adventitia. Echodensity at the 11 o'clock position in the lumen is an artifact produced by the coronary guide wire and a mechanical strut. The angiogram is normal and the ultrasound image demonstrates markedly eccentric intimal proliferation. Upper right image shows the same vessel with the measuring system. Inner white circle indicates planimetry of the lumen area (LA) and the outer circle planimetry of the exterior edge of the intimal layer, generating a measurement of lumen plus intima area, or total area (TA). These measurements allow for calculation of the intimal index (II) as shown. Vertical and horizontal grid marks indicate 0.5 mm.

tation was based on consensus reached by two angiographers blinded to the ultrasound data. Evidence of angiographic disease anywhere within the coronary artery system was noted, and abnormalities were coded by the previously described system.<sup>8-10</sup> Interpretations were shown as 1) normal: absolutely no angiographic evidence of luminal narrowings or irregularities; 2) type A lesions: discrete or short tubular stenoses present in proximal, mid, or distal major coronary segments; and 3) type B lesions: diffuse concentric mid or distal luminal narrowings and minor luminal irregularities that did not qualify as type A lesions (i.e., discrete or tubular).

#### Data Analysis

Mean intimal thickness and index of four sequential coronary sites was obtained for each patient. Mean values  $\pm 1$  SD were calculated for each ultrasound-defined disease severity group. Unpaired *t* test was used to compare patients with normal angiograms and moderate or severe disease classification by ultrasound with patients who had abnormal angiograms and moderate or severe disease by ultrasound. A level of statistical significance was set at  $p < 0.05$ .

#### Interobserver Variability

Three ultrasound sites from each of 10 patients ( $n=30$ ) were randomly selected and measured at separate times

by two observers (F.S.G. and F.J.P.). These data were used for evaluating interobserver variability in measuring the thickness and index of the intimal layer. These were expressed as a linear regression between the two observations and as a percent error derived as the absolute difference between observations.<sup>18</sup>

## Results

### Studies Performed Early After Transplantation

Twenty patients were examined with intracoronary ultrasound within 1 month of transplantation. Mean donor age of these hearts was 28 years (range, 15–43 years). In seven patients, a distinct intimal layer separated by a hypoechoic band was entirely absent in all locations examined. Representative ultrasound cross-sectional images from this group are shown in Figure 2. In the 13 other patients, one or more vessel locations had a three-layered appearance on the ultrasound image corresponding to intima, hypoechoic media, and hyper-echoic adventitia involving part or all of the vessel circumference. This is similar to the previously described appearance of coronary arteries in older, nontransplant patients.<sup>12</sup> Three patients studied within 1 month of transplantation had ultrasound evidence of discrete focal, moderate, intimal thickening greater than

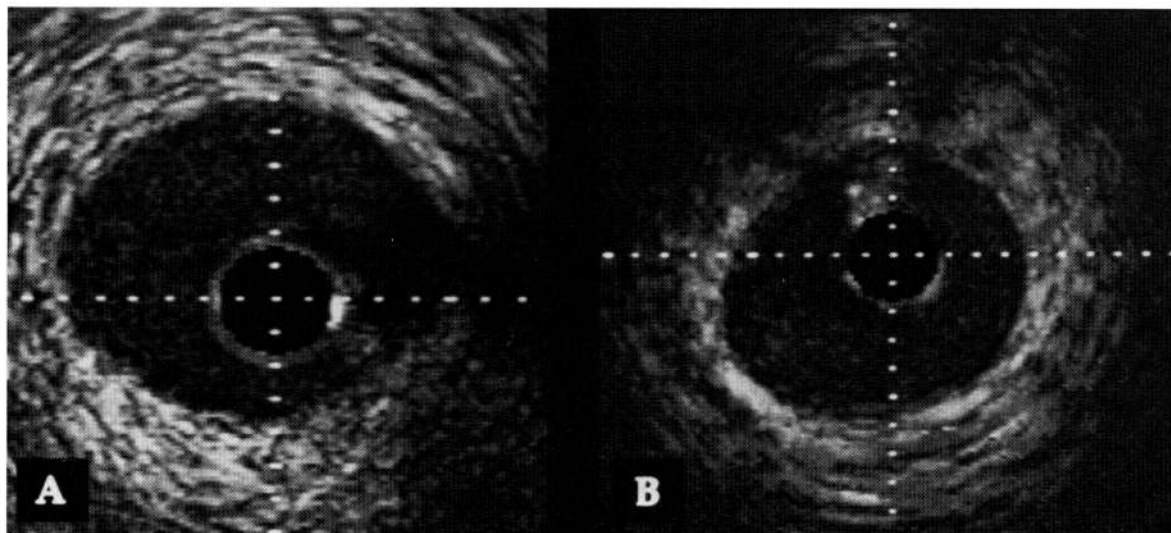


FIGURE 2. Intracoronary ultrasound images from the left anterior descending coronary artery. Panel A: A 17-year-old donor heart 2 weeks after transplantation; vessel wall has a homogeneous appearance without layering. Panel B: A 34-year-old woman 3 years after transplantation without any evidence of intimal thickening.

0.5 mm. The donors for all three of these patients had risk factors associated with coronary artery disease, including male sex in all, heavy tobacco usage in two, and hypertension in one. The remaining 10 patients in whom a distinct intima was visible had a mean intimal thickness measured from four locations of  $0.12 \pm 0.09$  mm and an index of  $0.08 \pm 0.04$ . All 20 patients studied early after transplantation had angiographically normal coronary arteries. The ultrasound findings in this group are presented in detail in a separate report (in preparation).

#### *Studies Performed 1 or More Years After Transplantation*

Sixty patients were studied 1 year or more after transplantation. Forty-two of these patients had no visual evidence of coronary disease by angiography. Examination with ultrasound demonstrated a minimal, measurable intimal layer in at least one coronary site in all 60 patients. The mean intimal thickness in patients with normal coronary angiograms was  $0.38 \pm 0.30$  mm and the mean index was  $0.21 \pm 0.11$ . This group thus demonstrated a wide range of intimal proliferation. At their most severely diseased vessel location, 10 of these patients showed minimal, 11 mild, 12 moderate, and nine severe intimal thickening. The measurements for each of these classification groups are shown in Table 2. The most common ultrasound appearance of the vessel wall consisted of varying amounts of homogeneous concentric intimal thickening. A representative example is shown in Figure 3. No patient with a completely normal angiogram had ultrasound evidence of calcification. Nine patients had at least one site in the left anterior descending coronary artery with ultrasound evidence of calcium; all of these had abnormal angiograms, but calcium was visible on only two.

Five of the 18 patients with abnormal angiograms showed only type A lesions, two of which were in the LAD. The coronary systems of the other 13 patients were characterized by both type A and type B lesions. All patients with abnormal angiograms had either moderate or severe disease by the ultrasound severity clas-

sification system. A representative example is shown in Figure 4. Mean intimal thickening for these patients was 0.72 mm, with a standard deviation of 0.32 mm. Unpaired *t* test analysis of intimal thickness and intimal index of patients with abnormal angiograms compared with those with normal angiograms with a moderate or severe disease severity classification demonstrated no statistically significant difference (thickness,  $0.53 \pm 0.35$  mm versus  $0.64 \pm 0.30$  mm,  $p = \text{NS}$ ; index,  $0.28 \pm 0.10$  versus  $0.34 \pm 0.10$ ,  $p = \text{NS}$ ).

The reproducibility of intravascular ultrasound imaging for measuring coronary lumen dimensions has been previously reported and is excellent.<sup>15,16</sup> In this study, interobserver variability for measuring the intimal layer was examined, and good reproducibility was demonstrated. The interobserver variability for the mean intimal thickness, expressed as percent error, was 5.6% with a correlation coefficient of 0.98 and for ratio of intimal thickness was 4.9% with a correlation coefficient of 0.99.

No significant complications were involved with the ultrasound imaging studies. Four patients demonstrated mild focal coronary spasm induced by the catheter and guide wire, which resolved with the administration of nitroglycerin.

#### **Discussion**

Serial angiographic studies in cardiac transplant recipients have demonstrated increasing prevalence of coronary abnormalities accompanying longer graft survival.<sup>8</sup> By 5 years after transplantation, 40–50% of patients have angiographic evidence of disease.<sup>8,19</sup> Angiographic identification of coronary disease in this population predicts a fivefold greater relative risk of cardiac events such as myocardial infarction, terminal heart failure, and sudden death.<sup>3</sup> A recent study in this population from our institution demonstrated that acute myocardial infarction is characterized by a lack of chest pain and has a high associated mortality risk.<sup>20</sup> The pathology of the patients in this study showed

TABLE 2. Ultrasound Measurements

Patients	Classification	No. of parts	Mean intimal thickness (mm)	Intimal index
$\leq 1$ Mo after transplant				
	0	7	...	...
	I	10	0.12	0.08
	II	0	...	...
	III	3	0.43	0.22
	Total	20	0.19	0.11
$\geq 1$ Yr after transplant				
Normal coronary angiogram				
	0	0	...	...
	I	10	0.17	0.10
	II	11	0.27	0.16
	III	12	0.33	0.22
	IV	9	0.78	0.35
	Total	42	0.38	0.20
Abnormal coronary angiogram				
	0-II	0	...	...
	III	5	0.44	0.25
	IV	9	0.72	0.40
	Total	18	0.64	0.34

diffuse coronary artery disease and a high incidence of multiple foci of nontransmural infarctions.

Comprehensive pathology examinations of coronary arteries from transplant recipients have demonstrated a broad spectrum of abnormalities.<sup>7</sup> The early stages are characterized by a diffuse, homogeneous, and concentric intimal proliferation of smooth muscle and collagen. Focal, complex atherosclerotic plaques that bear a close resemblance to native atherosclerosis occur in more advanced stages of the disease.<sup>7</sup>

Contrast angiography is currently the standard for *in vivo* quantitation and morphological evaluation of coronary atherosclerosis.<sup>21,22</sup> The precision of a system limited to a luminal silhouette has been questioned by pathology-angiography correlation studies demonstrating marked angiographic underestimation of atheromatous plaques.<sup>23-25</sup> This is especially true in the early stages of intimal thickening and atheromatous growth, when vessels initially enlarge to accommodate the proliferative process without a change in lumen size.<sup>26</sup>

Given the concentric and diffuse nature of transplant coronary disease, angiography is especially insensitive in detecting early changes in this population. This was recently highlighted by a pathology study from our institution of 10 transplant recipients who died or underwent retransplantation within 2 months of coronary angiography.<sup>10</sup> In that study of patients, at a mean of 52 months after transplantation, 19 of 26 (73%) angiographically normal coronary segments had mild to moderate fibrous intimal thickening. The remaining 27% exhibited intermediate lesions or atheromatous plaques similar to those seen in non-transplant atherosclerosis.<sup>10</sup> As has been shown in clinical and pathological studies, it is common in transplant patients to find a mixture of typical atheromatous lesions and unique transplant-related, concentric, progressive obliterative disease, with both lesion types causing significant clinical complications.<sup>8,9</sup>

Although transplant coronary artery disease is a rapidly proliferative process, a measurable amount of intimal proliferation is unlikely to occur within the first month after transplantation. The studies performed early after transplantation thus reflect the baseline coronary morphology of the donor heart and provide an opportunity to examine the ultrasound appearance of young adult coronary arteries. As has been shown in pathology studies performed in young, nontransplanted hearts, there is a wide range of intimal thickness.<sup>27</sup> The mean value for thickness of the intimal layer obtained in the present study using ultrasound, 0.12 mm, compares favorably to postmortem measurements in similar age-matched subjects who died accidentally.<sup>28</sup> In seven patients studied early after transplantation, the classic three-layered appearance was not detected. This was most probably due to a thickness of the vessel layers below the resolution of the ultrasound system throughout the circumference and length of the examined vessel. This theory is supported by preliminary *in vitro* data showing that the three-layered appearance becomes apparent only when the intima exceeds 148  $\mu$ m in thickness.<sup>29</sup> The lack of layering of the vessel walls, or minimal amount of measurable intima, is thus the reference ultrasound appearance of a young, morphologically normal coronary artery.

Extensive work has been performed comparing the ultrasonic appearance of vessel wall morphology with *in vitro* pathology.<sup>30,31</sup> These studies have shown that characteristics of the echo image of atherosclerotic lesions relate closely to histological composition. Intravascular ultrasound thus provides detailed characterization of plaque morphology, including distinguishing fibrous tissue, calcification, and lipid or necrotic material within atheromatous plaque, as well as assessment of the extent of disease. A recent *in vivo* study with *in vitro* confirmation suggested that intravascular ultrasound is more sensitive than angiography for demon-



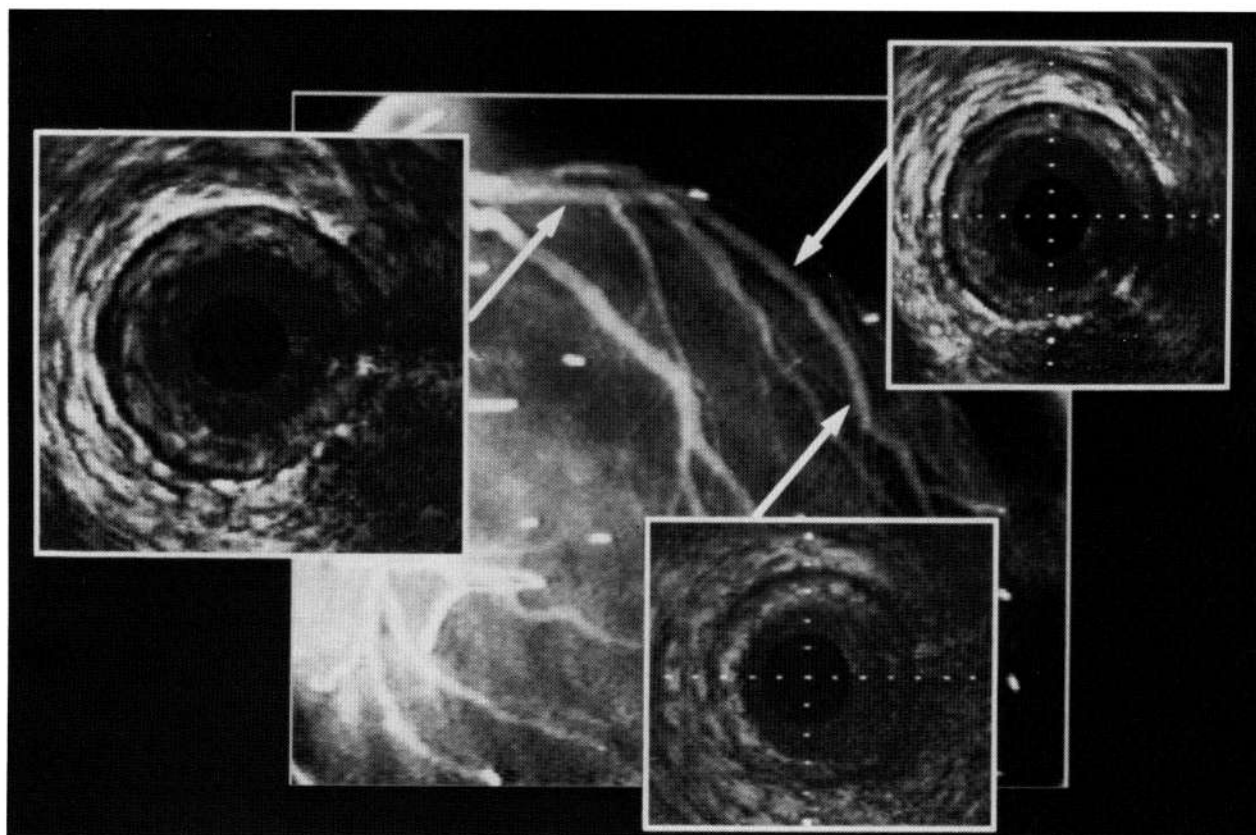


FIGURE 3. Angiogram with ultrasound images from three representative sites in the left anterior descending coronary artery (LAD) of a 37-year-old man 3 years after transplantation. Although the angiogram is without evidence of coronary disease, the ultrasound images demonstrate severe concentric intimal thickening throughout the proximal and mid LAD. Echodensity in the vessel wall in the left ultrasound image at the 3 o'clock position and in the upper right image at the 4 o'clock position are examples of acoustic artifact produced by the coronary guide wire and mechanical support strut.

strating the presence and extent of atherosclerosis and arterial calcification.<sup>32</sup>

The cohort of patients studied 1 year or more after transplantation demonstrated a wide range of intimal proliferation. Planimetry of the lumen and intimal area offers an objective, quantifiable means of evaluating the early intimal proliferative process. Previously, by using angiographic definitions, these patients would have been considered to have normal vessels without evidence of coronary disease. The demonstration of class III and IV intimal thickening in a group of patients with normal angiograms and that is not significantly different from those patients with abnormal angiograms may have significant prognostic implications.

Eighteen patients had abnormal coronary angiograms. In nine of these, the intracoronary ultrasound study demonstrated calcium not visible on seven of the corresponding angiographic studies (Figure 5). All 18 patients with abnormal angiograms had ultrasound evidence of coronary fibrosis (Figures 4 and 5). This supports the concept that ultrasound is a more sensitive method for detecting intracoronary calcium and detailing vessel wall morphology than is angiography, which demonstrates abnormalities only at more advanced stages of the disease.

The ultrasound morphology of the patient 1 year after transplantation shown in Figure 5 (with dense calcium and eccentric intimal plaque) is significantly

different from the concentric intimal proliferation seen in the majority of the transplant ultrasound studies. The arteriogram demonstrates a type A intraluminal filling defect in the corresponding site of the LAD. Ultrasound images from other areas of the same artery in this patient did not show marked concentric intimal proliferation. The angiogram performed 2 weeks after this patient's transplantation had demonstrated "donor" coronary artery disease. This implies that ultrasound evaluations may be able to discriminate between donor coronary disease and the process specifically associated with transplantation; however, serial intracoronary ultrasound studies are needed for confirmation.

Patients at Stanford are candidates for retransplantation when advanced coronary disease (>70% luminal obstruction) occurs in more than one main vessel.<sup>4</sup> Survival after retransplantation is significantly worse than that after the initial graft, with a high rate of redevelopment of coronary disease.<sup>4</sup> Percutaneous balloon angioplasty serves a palliative role in the rare, suitable localized lesion but is only a temporizing measure primarily for patients awaiting retransplantation.<sup>33-35</sup> Given the limited success of transplant coronary balloon angioplasty and the inferior results of retransplantation, early recognition of patients at risk and studies of prophylactic interventions should have a high priority. Intracoronary ultrasound, with its ability to detect and quantify with good reproducibility intimal

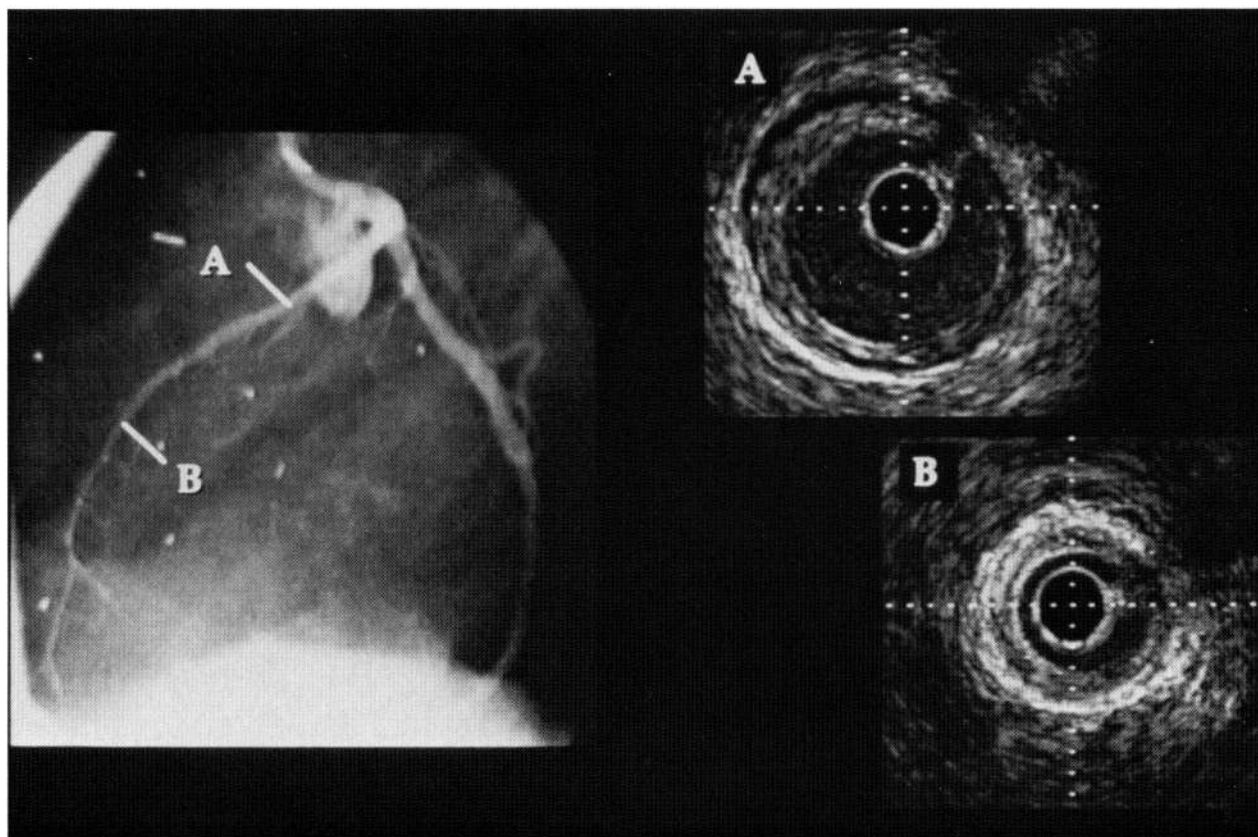


FIGURE 4. Angiogram and two representative ultrasound images from a patient 9 years after transplantation. Angiogram demonstrates both type A and type B lesions.<sup>10</sup> Ultrasound image at the site marked A shows marked concentric soft intimal thickening with increased brightness suggestive of fibrosis in the media at the 7 o'clock position. Site B shows a lesion where the intima has developed a fibrous cap.

proliferation before angiographic evidence of disease, is a powerful imaging technique to aid this study. Its clinical utility goes beyond simple diagnostic capability. It offers significant potential for monitoring therapeutic interventions and improving our understanding of the pathophysiology of transplant coronary disease. The prognostic implications of the 50% of patients 1 year or more after transplantation with normal angiograms but moderate or severe ultrasound disease severity classification and an intimal thickness and index similar to patients with angiographic evidence of disease remain to be determined by longitudinal follow-up studies.

#### Study Limitations

Patients in this study only had the proximal two thirds of their LAD examined by intracoronary ultrasound, and measurements were performed on a selected number of sites; thus, there is incomplete ultrasound evaluation of the extent of coronary artery disease in the study group, and the measurements of intimal thickness and index reflect the disease process only in a limited number of coronary sites in each patient. Transplant coronary disease, however, is a diffuse process,<sup>6,7</sup> and presumably the study of the LAD gives a reasonable indication of the extent and severity of the disease throughout the rest of the coronary tree in this patient population. The one possible group of patients who could be suboptimally evaluated by the limited exami-

nation are those with preexisting focal donor coronary disease not located in the LAD.

Classification of coronary disease severity provides the possibility of grouping patients according to the degree of vessel wall involvement but does not take into account that the disease process is a continuum. A major pitfall of any scaled classification system is determining the cutoff between different grades. Because there are no ultrasound studies to reference the thickness of a normal intima, the value used in the present study was based on previous pathology studies. The choice of 0.3 mm as the upper limit of normal comes from work by Velican and Velican.<sup>28</sup> In 216 unselected male and female patients between the ages of 21 and 40 years, they found the range of intimal thickness in the LAD to be 0.066–0.301 mm. In our study, the ultrasound-obtained value of 0.12 mm for the mean intimal thickness in the baseline, “normal” population is skewed because it does not include the seven patients whose intimal layer was below the resolution of the ultrasound imaging system and is thus unmeasurable by ultrasound. It is also less than the reported resolution of the ultrasound system, 0.148 mm,<sup>29</sup> because it is a mean value and there were areas of vessel wall without a measurable intimal layer. In addition, three patients had significant intimal proliferation suggestive of atheromatous plaques, thus increasing both mean and standard deviations. The use of a classification system, however, has the advantage of providing a working definition that

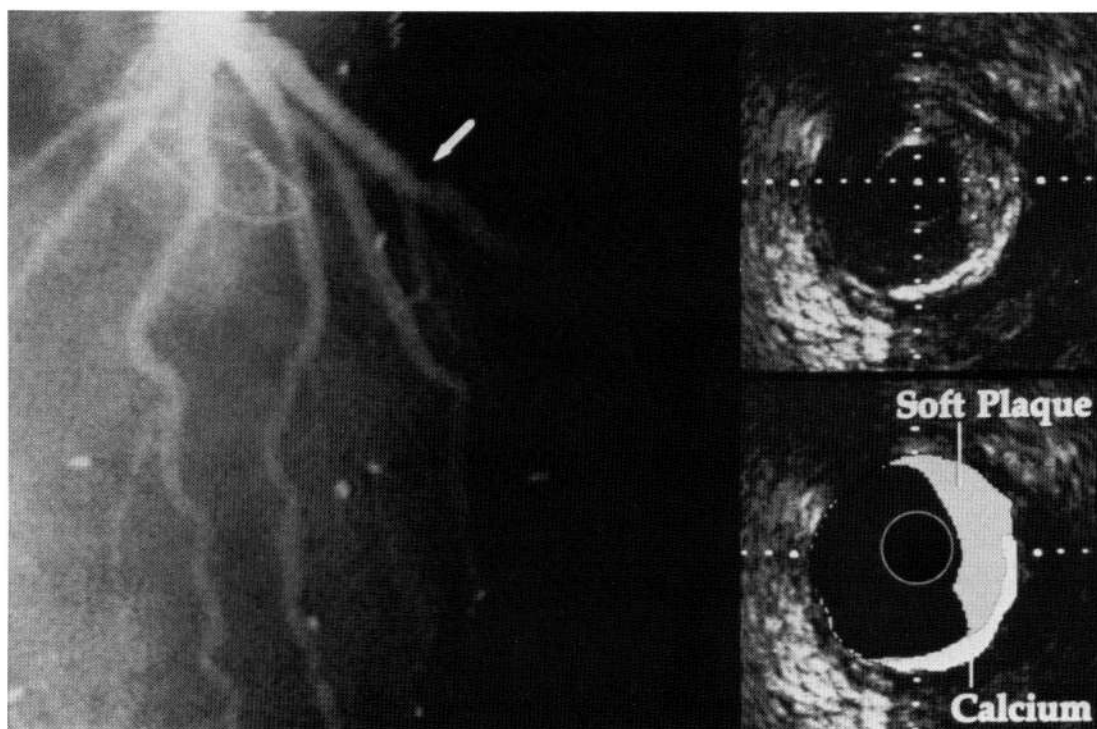


FIGURE 5. Angiogram from a 35-year-old man 1 year after transplantation with a type A lesion in the proximal left anterior descending coronary artery. This patient had evidence of donor coronary artery disease on the angiogram performed immediately after transplantation. Corresponding ultrasound image in upper right corner with schematic in lower right corner indicates soft plaque and calcium. Calcium is suggested by acoustic shadowing beyond the bright echoes within the wall.

may have clinical utility, along with quantitative measurements, for serial studies in patient prognosis assessment. Further studies should address this problem and assess the utility of such a classification system.

### Conclusions

Intracoronary ultrasound is an effective and reproducible method of measuring intimal proliferation in cardiac transplant recipients. The studies performed in patients early after transplantation serve as a reference for the ultrasound appearance of young, morphologically normal coronary arteries. A portion of these patients have ultrasound evidence of early, probably donor-related, atherosclerotic changes. The ultrasound images obtained in patients 1 year or more after transplantation show a broad spectrum of morphological abnormalities and a high incidence of angiographically silent intimal thickening. Longitudinal studies comparing the sensitivity of intravascular ultrasound with coronary angiography for detecting and monitoring progression of atherosclerotic disease will help to determine the value of this new imaging technique. Intravascular ultrasound may serve as a standard for in vivo quantification of atherosclerosis in cardiac allograft recipients and offers significant potential for enhancing our understanding of the pathophysiology of transplant coronary artery disease.

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