Influence of Preoperative Pulmonary Artery Pressure on Mortality After Heart Transplantation: Testing of Potential Reversibility of Pulmonary Hypertension With Nitroprusside Is Useful in Defining a High Risk Group

ANGELIKA COSTARD-JÄCKLE, MD, MICHAEL B. FOWLER, MB, MRCP, FACC

Stanford, California

Patients with pulmonary hypertension are at risk of developing fatal right heart failure after heart transplantation. To evaluate this risk potential, candidates for heart transplantation are screened by measuring rest right heart pressures and the response to nitroprusside. To test the validity of this approach, the influence of pretransplantation right heart catheterization data on outcome after transplantation was analyzed in 293 of 301 consecutive patients.

Patients with a pulmonary vascular resistance >2.5 Wood units measured at baseline study had a 3-month mortality rate of 17.9% compared with 6.9% in patients with resistance ≤2.5 units (p < 0.02). Patients with a pulmonary vascular resistance >2.5 units at baseline study could be differentiated further according to their hemodynamic response to nitroprusside: those whose resistance could be reduced to ≤2.5 units with a stable systemic systolic

pressure ≥85 mm Hg had a 3-month mortality rate of only 3.8%. In contrast, patients whose pulmonary vascular resistance could not be reduced to <2.5 units, and those whose resistance could be reduced to ≤2.5 units but only at the expense of systemic hypotension (systolic pressure <85 mm Hg) had a 3-month mortality rate of 40.6% and 27.5%, respectively. Furthermore, all 10 patients who died of right heart failure belonged to the latter two groups.

These findings confirm the value of right heart hemodynamic measurements and the response to nitroprusside in predicting early mortality after heart transplantation and, in particular, mortality due to right heart failure. Valid risk stratification based on the hemodynamic response to nitroprusside requires consideration of the concomitant change in systemic pressure.

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Most patients with advanced heart failure under consideration for heart transplantation have at least moderately elevated pulmonary artery pressure. Severe pulmonary hypertension is considered a contraindication to orthotopic transplantation because of the risk of acute right ventricular failure when the right ventricle of the grafted heart is unable to adapt to significant pulmonary hypertension in the immediate postoperative period (1–3). Recently, several studies (4–6) have confirmed that elevated pulmonary vascular resistance is an independent risk factor for mortality both early and late after transplantation.

However, some patients with moderate to severe pulmonary hypertension have successfully undergone transplantation. In these patients, serial hemodynamic measurements after transplantation demonstrated a progressive decrease in pulmonary artery pressure, illustrating the potential reversibility of pulmonary hypertension (7–12). Hemodynamic measurement of the potential reversibility of pulmonary

hypertension by administration of 100% oxygen, nitroglycerin or nitroprusside is frequently performed in evaluating candidates for heart transplantation (6,13–15). However, no systematic study has been performed of whether these maneuvers aid in assessing the risk of acute right heart failure and the attendant early mortality after transplantation.

At Stanford, candidates for heart transplantation undergo right heart catheterization and, for those with elevated pulmonary vascular resistance or systolic pulmonary pressure, or both, an attempt is made to evaluate the reversibility of pulmonary hypertension with a graded nitroprusside infusion. The data obtained have been reviewed and retrospectively analyzed in 293 of 301 consecutive transplant recipients to evaluate the relation between right heart hemodynamics, response to nitroprusside and outcome after heart transplantation.

Methods

Study patients. Between December 1980 (when cyclosporine was introduced as the immunosuppressive regimen) and July 1988, 301 New York Heart Association functional class IV patients underwent heart transplantation at Stanford University Medical Center. The patients (231 men and

70 women) ranged in age from 9 months to 60 years (mean 39 ± 4 years). The primary diagnosis was cardiomyopathy in 154 patients, end-stage left ventricular failure from coronary artery disease in 112, congenital heart disease in 13, postpartum cardiomyopathy in 6, valvular heart disease in 4, adriamycin-induced cardiomyopathy in 3, restrictive heart disease in 3, sarcoidosis in 2, acute myocarditis in 3 and amyloidosis in 1.

Right heart catheterization. Two hundred ninety-three of the 301 patients underwent right heart catheterization in the catheterization laboratory at Stanford University Hospital; under fluoroscopic guidance, a 7F balloon flotation pulmonary artery catheter was advanced to the pulmonary occlusive position (usually by way of the jugular vein). A cannula inserted into a brachial or radial artery was used for systemic pressure recordings and for repeated arterial blood sampling. Micron transducers were used to record on a Hewlett Packard recorder these pressures (in mm Hg): mean right atrial; pulmonary artery systolic, diastolic and mean (PAP mean); pulmonary capillary wedge (PCWP); and systemic arterial systolic, diastolic and mean pressures. Cardiac output (CO) was measured by the Fick method and normalized for body surface area (cardiac index, CI).

Pulmonary vascular resistance (PVR, Wood units) is calculated as

$$ PVR = \frac{(PAP\ mean\ -\ PCWP)}{CO}. $$

Pulmonary vascular resistance index (PVRI, units × m²) is calculated as

$$ PVRI = \frac{(PAP\ mean\ -\ PCWP)}{CI}. $$

Transpulmonary gradient (TPG, mm Hg) is calculated as

$$ TPG = PAP\ mean\ -\ PCWP. $$

Patients with pulmonary vascular resistance >2.5 units or systolic pulmonary artery pressure >40 mm Hg, or both, received a graded nitroprusside infusion to evaluate reversibility of pulmonary hypertension.

Nitroprusside infusion. An intravenous nitroprusside infusion was started at a dose of 25 to 50 μg/min. The dose was increased rapidly and hemodynamic measurements were obtained during the 5th min after every dose increase, until there was a clinically significant reduction in mean arterial pressure or a reduction of pulmonary vascular resistance to ≤2.5 units and a reduction of systolic pulmonary artery pressure to ≤40 mm Hg. For repeated determinations of cardiac output, only arterial and mixed venous blood samples were collected serially; oxygen consumption was routinely calculated from results of an expired gas collection at baseline study.

Evaluation of catheterization data and correlation with clinical course. Catheterization data obtained before transplantation, including hemodynamic response to nitroprus-
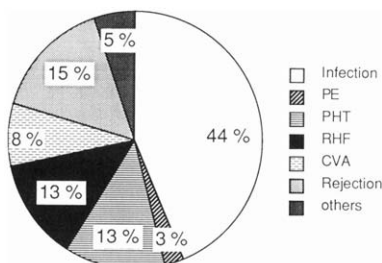

Figure 1. Cause of death in the 1st 3 months after heart transplantation in 301 consecutive patients. CVA = cerebrovascular accident; PE = pulmonary embolism; PHT = pulmonary hypertension; RHF = right heart failure.

side infusion, were reviewed and correlated with the patient's clinical course after transplantation. Analysis included incidence of early postoperative mortality (defined as death ≤90 days after transplantation) and presence or absence of significant right heart failure. Postoperative right heart failure was defined as significant when pulmonary vasodilators were required in conjunction with clinical evidence of right ventricular dysfunction and failure. A cause of death was assigned to each patient who died after transplantation. Whenever possible, the assigned cause of death was based on autopsy findings; when these were not available, it was based on all available clinical and laboratory data.

Results

Survival rates and causes of death (Fig. 1). Of the 301 patients, 39 died within 90 days, 7 died within 3 to 6 months and 12 died within 6 to 12 months after heart transplantation, corresponding to a survival rate of 86.7%, 84.4% and 80.4% at 3, 6 and 12 months, respectively, after transplantation. The most common cause of early (≤90 days) postoperative death was infection, accounting for 43.6% of deaths, followed by acute rejection (15.4% of deaths). Twenty-six percent of the deaths were due to pulmonary hypertension or right heart failure, corresponding to an overall mortality rate due to pulmonary hypertension or right heart failure of 3.3% (10 of 301 patients).

Clinical right heart failure. In addition to the patients who died of irreversible right heart failure or pulmonary hypertension, 10 patients had a postoperative course complicated by clinical signs of right heart failure, necessitating prolonged inotropic and vasodilator support given intravenously. Four of these patients were successfully treated with prostaglandin E_1; another four died ≤90 days after transplantation because of infection.

Table 1. Baseline Hemodynamic Variables in 288 Patients

	Mean	Range
CI (liters/min per m²)	2 ± 0.8	0.4 to 5
SAP$_{syst}$ (mm Hg)	97 ± 13	65 to 135
SAP$_{mean}$ (mm Hg)	76 ± 10	55 to 110
RA$_{mean}$ (mm Hg)	11 ± 4	0 to 31
RVEDP (mm Hg)	13 ± 7	0 to 43
PAP$_{syst}$ (mm Hg)	49 ± 13	14 to 88
PAP$_{mean}$ (mm Hg)	36 ± 9	9 to 58
PVR (Wood units)	3.2 ± 2.1	0.2 to 13.4
PVRI (Wood units × m²)	5.7 ± 3.8	0 to 28.8
TPG (mm Hg)	10 ± 6	0 to 37

CI = cardiac index; PAP$_{mean}$ = mean pulmonary artery pressure; PAP$_{syst}$ = systolic pulmonary artery pressure; PVR = pulmonary vascular resistance; PVRI = pulmonary vascular resistance index; RA$_{mean}$ = mean right atrial pressure; RVEDP = right ventricular end-diastolic pressure; SAP$_{mean}$ = mean systemic artery pressure; SAP$_{syst}$ = systolic systemic artery pressure; TPG = transpulmonary gradient.

Table 2. Pulmonary Vascular Resistance, Systolic Pulmonary Artery Pressure and Transpulmonary Gradient According to Different Threshold Values

	No. of Pts.	Deaths Within 90 Days			Deaths Due to RHF/PHT (no.)	Survived (RHF) (no.)
		No.	%	p Value		
PVR ≤2.5	143	10	6.9	<0.02	0	0
PVR >2.5	145	26	17.9		9	10
PVR ≤5	241	25	10.4	NS	8	2
PVR >5	48	11	22.9		3	8
PVR <8	280	34	12.1	NS	9	7
PVR >8	9	2	22.2		0	3
PAP$_{syst}$ ≤50	67	7	10.4	NS	0	1
PAP$_{syst}$ >50	225	29	12.9		9	9
PAP$_{syst}$ ≤50	157	13	8.3	<0.05	1	3
PAP$_{syst}$ >50	135	23	17		8	7
PAP$_{syst}$ ≤60	235	22	9.4	<0.001	6	5
PAP$_{syst}$ >60	57	14	24.6		3	5
TPG ≤10	168	17	9.4	NS	4	1
TPG >10	117	19	24.6		5	8
TPG ≤15	240	27	11.3	<0.02	5	5
TPG >15	45	9	20		4	4
PVRI ≤5	151	13	8.6	<0.05	2	0
PVRI >5	130	23	17.7		7	9
PVRI ≤8	225	26	11.6	NS	7	3
PVRI >8	56	10	17.9		2	6

p values compare deaths in patients whose hemodynamic variables were at or below the threshold value with those whose variables were higher than this value. PHT = pulmonary hypertension; Pts. = patients; RHF = right heart failure. Other abbreviations and units as in Table 1.

Preoperative right heart hemodynamics at baseline study (Table 1). Right heart catheterization was performed in 293 patients. Five of these patients (including one who died early after transplantation because of right heart failure) were dependent on intravenous inotropic support at the time of preoperative evaluation, so that no true baseline data for nitroprusside were available. The baseline hemodynamic data in the remaining 288 patients are summarized in Table 1. Cardiac index ranged from 0.4 to 5 liters/min per m² (mean 2 ± 0.8).

Pulmonary vascular resistance (Table 2). The pulmonary vascular resistance, calculated in Wood units, ranged from 0.2 to 13.4 (mean 3.2 ± 2.1). Figure 2 shows the distribution of baseline values for pulmonary vascular resistance in relation to 3-month mortality. Table 2 summarizes the outcome for transplant patients according to different threshold values. A total of 145 (50.4%) of 288 patients had a baseline pulmonary vascular resistance value >2.5 units. Of these patients, 26 (17.9%) died ≤90 days after transplantation, compared with 10 (6.9%) who died early postoperatively among 143 patients with a baseline pulmonary vascular resistance ≤2.5 units (p < 0.02). All 9 patients who died early after transplantation of pulmonary hypertension or right heart failure, as well as all 10 patients who developed right heart failure postoperatively but survived, had a baseline pulmonary vascular resistance >2.5 units. A higher pulmonary vascular resistance threshold (≤5 vs. >5 resistance units and ≤8 vs. ≥8 units) revealed a higher percent of early postoperative deaths in the groups with higher values (11 deaths [22.9%] in 48 patients with a resistance level >5 units and 2 deaths [22.2%] in 9 patients with a resistance level >8 units). However, among the nine patients who died of right heart failure, six had a pulmonary vascular resistance ≤5 units and all nine had a level ≤8 units, demonstrating loss of sensitivity if the pulmonary vascular resistance threshold was set higher than 2.5 units.

Pulmonary vascular resistance index. This index ranged from 0 to 28.8 resistance index units (mean 5.7 ± 3.8).

Among 130 patients with a pulmonary vascular resistance index >5 index units, 23 died ≤90 days after transplantation. The mortality rate of 17.7% is significantly higher (p < 0.05) than that of the 8.6% (13 deaths) in the 151 patients with a pulmonary vascular resistance index ≤5 index units. Two of the nine patients who died ≤90 days after transplantation as a result of pulmonary hypertension or right heart failure had a pulmonary vascular resistance index ≤5 index units and all nine patients with clinical right heart failure belonged to the group with a resistance index ≤5 index units. Data for patients with an index ≤8 versus >8 index units were also examined. The mortality rate in the group with the higher index (10 deaths among 56 patients, 17.9%) was similar to that obtained in the group with the higher index as defined by a pulmonary vascular resistance index of >5 or ≤5 index units. However, the upper threshold of 8 resistance units failed to include seven of nine patients who died of pulmonary hypertension or right heart failure and three of nine patients with postoperative right heart failure, all of whom had a pulmonary vascular resistance index ≤8 units.

Systolic pulmonary artery pressure ranged from 14 to 88 mm Hg (mean 49 ± 13). Of 293 patients, 135 (46%) had a systolic pulmonary artery pressure >50 mm Hg. Of these
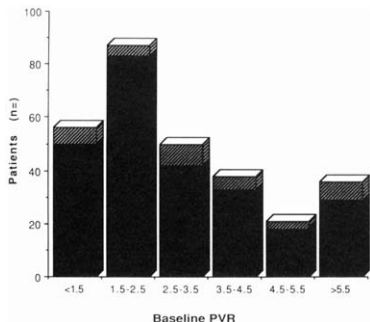
Figure 2. Influence of baseline pulmonary vascular resistance (PVR) values on 3-month mortality after heart transplantation. **Hatched bars** = patients who died within 3 months after transplantation; **solid bars** = patients who survived >3 months.

patients. 23 died ≤90 days after transplantation, which is a significantly higher mortality rate (17%) than that in the group with a systolic pulmonary artery pressure ≤50 mm Hg (8.3%, p < 0.05). Among the 9 patients who died of pulmonary hypertension or right heart failure. 1 patient had a systolic pulmonary artery pressure ≤50 mm Hg, as did 3 of 10 patients with postoperative right heart failure. A higher threshold of 60 mm Hg revealed a higher early postoperative mortality rate in patients with an elevated pressure (24.6%); however, 6 of 9 patients who died of pulmonary hypertension or right heart failure and 5 of 10 patients with postoperative right heart failure had a systolic pulmonary artery pressure ≤60 mm Hg.

The transpulmonary gradient ranged from 0 to 37 mm Hg (mean 10 ± 6). A threshold of 15 mm Hg separates the groups at low and high risk for early postoperative mortality (transpulmonary gradient ≤15 mm Hg; 3-month mortality rate 11.3% vs. transpulmonary gradient >15 mm Hg, 3-month mortality rate 20%; p < 0.02). However, measurement of the transpulmonary gradient did not differentiate between patients at risk of death from pulmonary hypertension or right heart failure early after transplantation; there

were five early postoperative deaths from these causes in patients with a transpulmonary gradient ≤15 compared with four deaths in patients with a transpulmonary gradient >15 mm Hg.

Hemodynamic response to nitroprusside (Table 3). A total of 150 patients received nitroprusside infusion; 135 had a pulmonary vascular resistance >2.5 units and systolic pulmonary artery pressure >40 mm Hg, 10 had systolic pulmonary artery pressure >40 mm Hg and a pulmonary vascular resistance ≤2.5 and 5 patients were dependent on a low dose of nitroprusside given intravenously at preoperative catheterization and therefore no baseline data were available. Patients were divided into three groups according to their hemodynamic response to nitroprusside (Table 3). Group A consisted of 32 patients whose pulmonary vascular resistance could not be decreased to <2.5 units; Group B consisted of 40 patients whose pulmonary vascular resistance could be lowered to ≤2.5, but only at the expense of severe systemic hypotension (systolic arterial pressure ≤85 mm Hg) and Group C consisted of 78 patients whose pulmonary vascular resistance could be lowered to ≤2.5 without concomitant severe systemic hypotension, maintaining a systolic arterial pressure ≥85 mm Hg. Among the 78 Group C patients who showed reactivity of pulmonary hypertension, only 3 (3.8%) died ≤ 90 days after transplantation. In contrast, 11 patients (27.5%) in Group B and 13 patients (40.5%) in Group A died. Moreover, all patients who died of right heart failure or pulmonary hypertension belonged to Group A (3 of 32) or Group B (7 of 40). In addition, all patients who developed but survived postoperative right heart failure were in Group A (n = 8) or B (n = 2).

If hemodynamic data at baseline study and the data after nitroprusside infusion are summarized, the combined data can be used to define two groups (Fig. 3): patients at high and patients at considerably lower risk of death early after transplantation. Patients at high risk included those whose pulmonary vascular resistance could not be decreased to <2.5 units with nitroprusside (Group A) and those in whom such a decrease was achieved only at the expense of severe systemic hypotension (Group B). Patients at lower risk were those who showed a significant reduction in pulmonary vascular resistance but maintained stable systemic pressure after nitroprusside infusion (Group C) and those whose baseline pulmonary vascular resistance was <2.5 units and

Table 3. Cumulative Data From Baseline Hemodynamic Data and the Response to Nitroprusside

Group	Baseline PVR	Response to Nitroprusside		No. of Pts.	Deaths Within 90 Days (no.:%)	Deaths Due to RHF/PHT (no.:%)	Survived RHF* (no.)
		PVR	SAP$_{syst}$				
A	>2.5	>2.5	—	32	13:40.6	3:9.4	8
B	>2.5	≤2.5	≤85	40	11:27.5	7:17.5	2
C	>2.5	≥2.5	≥85	78	3:3.8	0	0
D	<2.5	—	—	140	10:6.9	0	0

*Early postoperative course complicated by clinical right heart failure. Abbreviations and units as in Tables 1 and 2.
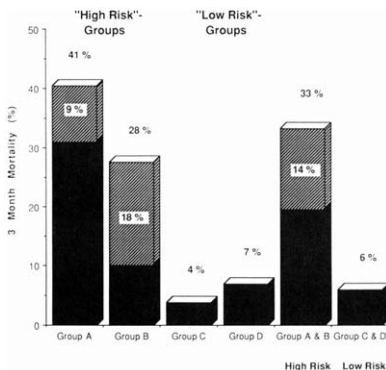
Figure 3. Three-month mortality after transplantation: differentiation of low and high risk groups according to preoperative pulmonary hypertension. Group A = patients whose pulmonary vascular resistance could not be decreased to <2.5 Wood units (n = 32); Group B = patients whose pulmonary vascular resistance could be reduced to ≤2.5 Wood units at the expense of severe systemic hypotension (n = 40); Group C = patients whose pulmonary vascular resistance could (n = 78) be lowered to ≤2.5 units without severe systemic hypotension; Group D = patients whose pulmonary vascular resistance was <2.5 units at baseline. Other abbreviations as in Figure 1. Hatched bars = deaths due to right heart failure and pulmonary hypertension; solid bars = deaths due to other causes.

did not receive nitroprusside (Group D). The high risk group had a five to six times higher early postoperative mortality rate (33.3 vs. 6%; p < 0.0001). Forty-two percent of deaths in the high risk group (10 of 24) were due to pulmonary hypertension or right heart failure resulting in an mortality rate due to right heart failure or pulmonary hypertension of 13.9% in this group. Moreover, an additional 15% of these high risk patients developed, but survived, postoperative right heart failure.

Table 4 compares clinical data and hemodynamic variables in these two groups of patients. There were no statistically significant differences between the high and low risk groups in recipient or donor age and gender, ischemic time, waiting time for transplantation, donor-recipient weight mismatch and diagnosis. A statistically significant higher percent of patients at high versus low risk were dependent on intravenous inotropic support before transplantation, reflecting the overall poorer preoperative condition of patients in the high risk group. Patients in the high risk group had statistically significant higher values for systolic and mean pulmonary artery pressure, pulmonary vascular resistance and index, transpulmonary gradient and systemic arterial systolic pressure. However, there was significant overlap in values between the high and low risk groups. Therefore, differentiation between patients at high and low risk based on the hemodynamic response to nitroprusside infusion cannot be predicted from baseline hemodynamics alone. Some patients in the low risk group had a baseline pulmonary vascular resistance as high as 13.4 units that could be lowered to <2.5 units while stable systemic pressure was

Table 4. Demographic and Hemodynamic Data of Patients in the High and Low Risk Groups

	High Risk (n = 72)		Low Risk (n = 218)		
	Mean	Range	Mean	Range	p Value
Demographic data					
Recipient age (years)	39 ± 16	9 to 60	39 ± 13	2 to 60	
Waiting time (days)	43 ± 56	0 to 247	45 ± 55	0 to 291	
Ischemic time (min)	127 ± 50	38 to 233	140 ± 54	38 to 322	
Donor age (years)	23 ± 8	3 to 44	23 ± 8	2 to 48	
Weight mismatch (kg)	−6 ± 12	−32 to 23	−2 ± 11	−34 to 27	
Recipient gender (M/F) (%)	72/28		79/21		
Donor gender (M/F) (%)	81/19		82/18		
Precondition* (%)	68/31/1		82/13/5		<0.005
Diagnosis†	39/49/4/8		38/51/5/6		
Hemodynamic data					
Cardiac index (liters/min per m²)	1.9 ± 1.1	0.4 to 3.8	2 ± 0.7	0.7 to 5	
SAP_{syst} (mm Hg)	93 ± 10	75 to 130	99 ± 14	65 to 135	<0.002
SAP_{mean} (mm Hg)	75 ± 9	55 to 110	76 ± 10	55 to 111	
PAP_{syst} (mm Hg)	56 ± 11	36 to 82	47 ± 13	14 to 88	<0.001
PAP_{mean} (mm Hg)	40 ± 7	26 to 56	34 ± 9	9 to 58	<0.001
PVR (units)	4.9 ± 2.1	2.6 to 11.4	2.7 ± 1.7	0.2 to 13.4	<0.001
PVRI (units × m²)	8.1 ± 3.6	1.5 to 19.5	4.9 ± 3.6	0 to 28.8	<0.001
TPG (mm Hg)	14 ± 6	3 to 37	9 ± 5	0 to 25	<0.001

*No support/intravenous support/intraaortic balloon pump or left ventricular assist device. †Coronary artery disease/idiopathic dilative cardiomyopathy/congenital heart disease/other. For differentiation between high and low risk groups, see Figure 3. Abbreviations as in Table 1.

maintained, whereas some patients had a baseline pulmonary vascular resistance as low as 2.7 units that could not be decreased without systemic pressure compromise.

Discussion

Elevated pulmonary vascular resistance and posttransplantation mortality. Resistant pulmonary hypertension has long been identified as a major cause of early mortality (1–3), although this concept has only recently been systematically evaluated. Kirklin et al. (5) analyzed the outcome in 63 patients who underwent heart transplantation and found an elevated pulmonary vascular resistance to be the most important risk factor for both early and late mortality. Our data confirm the importance of assessing baseline hemodynamics: patients with a baseline pulmonary vascular resistance >2.5 units have an approximately twofold greater risk of dying ≤90 days postoperatively, compared with patients with a pulmonary vascular resistance ≤2.5 units at baseline study. Furthermore, all patients who died of pulmonary hypertension or right heart failure early after transplantation, as well as all surviving patients whose early postoperative course was complicated by right heart failure, had a pulmonary vascular resistance >2.5 units. However, an elevated baseline pulmonary vascular resistance does not preclude a successful outcome after transplantation. Of 145 patients with pulmonary vascular resistance >2.5 units. 119 survived the early postoperative period. The accuracy of baseline pulmonary vascular resistance in differentiating between low and high risk patients could not be improved by changing the critical resistance threshold. Thresholds >2.5 units revealed a higher percent of patients with an elevated pulmonary vascular resistance who died early after operation (that is, the higher thresholds yielded greater specificity in detecting patients at risk of premature death) but sensitivity was reduced. Several patients who died early after transplantation of right heart failure or pulmonary hypertension or developed clinical right heart failure postoperatively had a baseline pulmonary vascular resistance below a threshold of 5 or 8 units.

Elevated pulmonary vascular resistance versus pulmonary hypertension. It was recently suggested that use of a pulmonary vascular resistance *index*, which corrects for individual variations in size, as a measure of pulmonary hypertension or use of the transpulmonary gradient might be superior in identifying patients at risk of premature death after transplantation (6,15). These findings could not be confirmed by our data; we did find that a pulmonary vascular resistance index with a threshold of 5 index units, a transpulmonary gradient with a threshold of 15 mm Hg or a systolic pulmonary artery pressure with a threshold of 50 mm Hg also allowed identification of a group of patients with significantly increased risk of early mortality, but with a specificity no higher than that of pulmonary vascular resistance. Moreover, a pulmonary vascular resistance with a threshold of 2.5 units identified all 9 patients who died of right heart failure

and *all* 10 patients who developed clinical right heart failure postoperatively, whereas use of a pulmonary vascular resistance index (threshold 5 units), the transpulmonary gradient (threshold 15 mm Hg) or the systolic pulmonary artery pressure (threshold 50 mm Hg) did not identify some patients who had values below the threshold but who died of or developed right heart failure early postoperatively. Thus, our data indicate that pulmonary vascular resistance with a threshold of 2.5 units identifies patients at high risk of early postoperative death with an accuracy similar to that of the alternative baseline measures of pulmonary hypertension, but is superior in specifically identifying those at risk of death from right heart failure postoperatively and therefore should be used preferentially for this assessment.

Role of hemodynamic response to nitroprusside in estimating risk of transplantation. The potential of nitroprusside to reduce pulmonary hypertension has long been known (16–18). As early as 1971 it was suggested (1) that the hemodynamic response to nitroprusside could be used to differentiate between fixed and reversible pulmonary hypertension, selecting patients with pulmonary hypertension for transplantation, and since then, vasodilator studies (3,13) have been recommended as a potentially useful tool in selecting candidates for transplantation. Our analysis confirmed the utility of the hemodynamic response to nitroprusside in estimating the risk of transplantation in patients with elevated baseline pulmonary vascular resistance. We found that the hemodynamic response to nitroprusside identified patients at high risk of 1) dying early after transplantation (3-month mortality rate, 33.3%); 2) dying early after operation of right heart failure (13.9%); and 3) developing right heart failure after operation (15%). Patients at high risk include those whose pulmonary vascular resistance could not be reduced to <2.5 units and also those whose pulmonary vascular resistance could be reduced to <2.5 units only at the expense of severe systemic hypotension (systolic pressure <85 mm Hg). These findings highlight the importance of considering the concomitant change in systemic pressure when interpreting the hemodynamic response to nitroprusside.

Conversely, the hemodynamic response to nitroprusside could also be useful in identifying a low risk group. Patients whose pulmonary vascular resistance was reduced with nitroprusside to <2.5 units while a stable systolic pressure ≥85 mm Hg was maintained had an overall early postoperative mortality rate of only 3.8%, and can therefore be classified as having a risk of early postoperative death as low as that of patients with normal pulmonary vascular resistance at baseline study.

Some patients with a baseline pulmonary vascular resistance as high as 13.4 units responded fully to nitroprusside, whereas the only mildly elevated pulmonary vascular resistance in others did not change. These data demonstrate that response to nitroprusside, and thus potential reversibility of pulmonary hypertension, cannot be predicted from baseline data.

The cause of the higher rate among patients with pulmonary hypertension of early postoperative death caused by factors other than right heart failure or pulmonary hypertension is not clear. Many of these patients' general failure to thrive may increase the susceptibility to fatal infection. Preoperative pulmonary hypertension was recently been reported (12,16) to be a risk factor for posttransplantation pulmonary infection. In our study, 4 of the 10 patients who developed significant right heart failure postoperatively died of infection ≤90 days after transplantation.

Prophylactic treatment. Our study did not include any patients who had heterotopic heart transplantation. The benefit of such treatment to patients with pulmonary hypertension was recently questioned (12), and overall survival rates reported in the registry of the International Society for Cardiac Transplantation are generally worse than those for orthotopic transplantation. Prostaglandin E_1 has been used successfully to treat life-threatening postoperative pulmonary hypertension in patients unresponsive to standard therapy (19,20), and its value in reducing perioperative and postoperative mortality is now being studied. If these results are promising, prophylactic treatment of patients at high risk of developing right heart failure in the perioperative and early postoperative periods might be beneficial.

Conclusions. Our data confirm the utility of measurement of right heart hemodynamic variables in the evaluation of risk in candidates for heart transplantation. Our data do not indicate how many patients rejected for cardiac transplantation on the basis of more severe pulmonary hypertension might have fared had they undergone cardiac transplantation. But they show that even among patients whose pulmonary hypertension and responsiveness to nitroprusside were considered acceptable for treatment with heart transplantation, there was a clear relation between preoperative hemodynamic data and subsequent early morbidity or mortality.

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