

# Biventricular Function after Myocardial Revascularization in Humans: Deterioration and Recovery Patterns during the First 24 Hours

Dennis T. Mangano, Ph.D., M.D.\*

Critical changes in left and right ventricular function immediately after myocardial revascularization may affect the success of the procedure, morbidity, and mortality. To delineate these changes and identify vulnerable patient populations and times of highest risk, ventricular function was studied for 24 h in 22 patients undergoing myocardial revascularization. Preoperative ejection fractions ranged from 0.26 to 0.81. For each patient, eight left and eight right ventricular function curves (LVFC and RVFC) were generated by altering preload during the 24-h perioperative period. Central venous pressure ranged from 0 to 19 mmHg and pulmonary capillary wedge pressure from 0 to 31 mmHg. In all patients, significant ( $P < 0.05$ ) left and right ventricular dysfunction occurred at 15 min following bypass, LVFCs and RVFCs being depressed 35-75% of control. The degree of depression and the pattern of recovery could be predicted best (stepwise logistic regression) by two preoperative indices: the ejection fraction and degree of dyssynergy. Patients with ejection fractions greater than 0.55 and no significant dyssynergy ( $n = 11$ ) had postbypass LVFCs and RVFCs that were 75% and 60% of control, respectively. However, these depressions were transient, and recovery to 90% of control occurred within 4 h of revascularization. In contrast, patients having preoperative ejection fractions less than 0.45 or dyssynergy ( $n = 11$ ) had more severely depressed ventricular function (LVFC = 40% and RVFC = 30% of control) that persisted for 24 h after revascularization, resulting in only 60% recovery of ventricular function. In conclusion, the preoperative indices—ejection fraction and degree of dyssynergy—best identified patients most likely to have significant and prolonged biventricular dysfunction after revascularization. (Key words: Anesthetics, intravenous: morphine. Heart: ischemia; ventricles. Surgery: cardiac.)

THE SUCCESS of coronary artery bypass surgery usually is measured by the long-term adequacy of revascularization.<sup>1-3</sup> However, short-term perioperative concerns such as the adequacy of surgical revascularization, the effectiveness of myocardial preservation, and the maintenance of ventricular function can be critical to this success. A heart that is manipulated, cannulated, fibrillated, made hypothermic, and deprived of normal coronary blood flow can develop perioperative left ventricular dysfunction,

which may worsen the prognosis significantly.<sup>4-8</sup> The right ventricle may play a significant role as well.<sup>9</sup> Thus, to improve the success of this procedure, attention should be drawn to right and left ventricular function immediately following revascularization.

Unfortunately, few studies have characterized the sequential changes in biventricular function following revascularization in diverse groups of patients. Therefore, in patients with and without preoperative ventricular dysfunction, sequential changes in both left and right ventricular function were investigated following cardiopulmonary bypass and for 24 h after myocardial revascularization.

## Methods

The study was approved by the Committee on Human Research. Informed consent was obtained from 22 men (41-72 years of age) scheduled for coronary artery surgery because of unstable (eight patients) or stable progressive (14 patients) angina pectoris. Patients with valvular heart disease or ventricular aneurysms were excluded. Eighteen patients had electrocardiographic evidence (Q waves) of previous myocardial infarction. All patients had stenosis (90% or greater) of one or more coronary arteries. Five had a history of left ventricular failure; no patient had evidence of left or right ventricular failure at the time of surgery. Preoperatively, left ventriculography was performed in the single plane, 30 degree right anterior oblique projection. The left ventriculograms quantitatively were analyzed in longitudinal, transverse, and hemiaxial segments according to the method of Herman and Gorlin.<sup>10</sup> If two or more segments had less than 20% of normal contraction, dyssynergy was said to exist. Left ventricular dyssynergy existed in eight patients.

Ejection fractions were determined using end-systolic and end-diastolic volumes obtained by the area-length method of Kennedy *et al.*<sup>11</sup> The range of ejection fractions was from 0.26 to 0.81 (normal  $0.66 \pm 0.06$ ), left ventricular end-diastolic volume indices from 42 to 131 ml/m<sup>2</sup> (normal  $70 \pm 20$  ml/m<sup>2</sup>), pulmonary capillary wedge pressures (PCWP) from 2 to 18 mmHg, and

\* Associate Professor of Anesthesia.

Received from the Department of Anesthesia, University of California, San Francisco, and the Veterans Administration Medical Center, San Francisco. Accepted for publication November 8, 1984.

Address reprint requests to Dr. Mangano: Department of Anesthesia (129), Veterans Administration Medical Center, Room 3C-14, Building 203, 4150 Clement Street, San Francisco, California 94121.

central venous pressures (CVP) from 1 to 12 mmHg. All patients were cigarette smokers, but none had elevated pulmonary vascular resistance, pulmonary hypertension, or cor pulmonale. Medications included isosorbide and nitroglycerin for all patients and propranolol (40–160 mg po qid) for 21 patients. Medications were continued until surgery.

All patients were premedicated with morphine sulfate (10 mg im) and diazepam (10 mg po). Anesthesia consisted of morphine sulfate (1.5–3 mg/kg iv) and diazepam (0.25–0.50 mg/kg iv). Pancuronium (0.1 mg/kg iv) provided muscle relaxation, and ventilation (with 100% oxygen) was controlled. Hemodynamic variables were monitored via radial-artery and triple-lumen thermodilution pulmonary arterial catheters. All pressure measurements were recorded on a Gilson® polygraph from equisensitive Bell and Howell transducers calibrated with a mercury manometer. Before each set of measurements was made, zero reference point was located 5 cm posterior to the sternal angle and perpendicular to the frontal plane of the chest.

After pericardiotomy,<sup>12</sup> surgery was stopped and a 2-min period of hemodynamic equilibrium was established (*i.e.*, systolic blood pressure varied less than 10 mmHg and heart rate less than 5 beats/min). With the patient horizontal (0 degrees), the following variables were recorded at end-expiration: systolic and diastolic pressures of the radial and pulmonary arteries, heart rate, CVP, PCWP, and two thermodilution cardiac outputs (that were within 10% of each other). Filling pressure then was altered by changing body position from horizontal to 30 degrees Trendelenburg and to 30 degrees reverse-Trendelenburg. Pressure transducers were referenced continually 5 cm posterior to the sternal angle and perpendicular to the frontal plane of the chest. Three sets of measurements (one for each body position) were made at the following eight times: before bypass—after pericardiotomy (control); at 15 min and 1 h after revascularization (in the operating room); and at 2, 4, 8, 18, and 24 h after revascularization (in the intensive care unit). No pharmacologic agent was given, or respiratory adjustment made before (15 min) or during the measurement period.

During cardiopulmonary bypass, cold cardioplegia was used for myocardial protection. Ischemic arrest time averaged  $54 \pm 4$  min (range 32–81 min), and an average of 3.2 vessels per patient were bypassed.

For all patients, anesthesia was maintained with morphine sulfate (30–75 mg) and diazepam (10–25 mg) until 12 h after surgery. Ventilation was controlled to maintain the  $P_{CO_2}$  between 35 and 45 mmHg ( $P_{O_2} > 70$  mmHg) until 18–22 h after surgery. Tidal volumes ranged from 12 to 15 ml/kg, and positive end-expiratory pressure was not used. All measurements were made at

end-expiration. The final set of measurements (24 h) was made after resumption of spontaneous respiration. Temperature (rectal) was monitored hourly. Upon arrival in the ICU, the temperature averaged  $34.7^\circ\text{C}$ ; at 4 h,  $36.7^\circ\text{C}$ ; at 8 h,  $37.7^\circ\text{C}$ ; and at 24 h  $37.1^\circ\text{C}$ .

All values are expressed as means  $\pm$  SEM, with significance taken at  $P < 0.05$  unless corrections (Bonferroni) are included. Statistical analyses involving comparisons of control with other time periods, or between the time period results themselves, were performed with analysis of variance with repeated measures; the Bonferroni correction was used for multiple comparisons. Statistical analyses involving comparison of Group 1 with Group 2 at any one time period were performed using unpaired *t* testing.<sup>13</sup>

In addition to the above statistical comparisons, a nonlinear stepwise logistic regression analysis (BMDPLR Health Services Computing Facility, University of California, Los Angeles) was used to determine the statistical value of preoperative patient characteristics in predicting perioperative ventricular dysfunction. (Ventricular dysfunction is defined here as the following: 1) a decrease of stroke work [and stroke volume] to less than 50% of control at 15 min following bypass, and 2) a continued decrease to less than 75% of control at 4 h following bypass.) In the initial step (0) of this statistical model, no predictor terms are entered into the model, and the variables are evaluated independently. After step zero, the highest predictor, if significant ( $P < 0.05$ ), then is incorporated into the model, and the stepwise process is repeated until no terms provide additional significance. The predictor terms considered are as follows: 1) age, 2) number of anginal episodes per week, 3) use of  $\beta$ -blockers, 4) number of previous myocardial infarctions, 5) Q waves on ECG; cardiac catheterization information: 6) ejection fraction, 7) dyssynergy, 8) end-systolic volume, 9) end-diastolic volume, 10) stroke work, 11) stroke volume, 12) cardiac output, and 13) end-diastolic pressure. Also considered were intraoperative predictor terms: 14) duration of bypass, 15) duration of aortic cross-clamp, and 16) use of inotropes.

## Results

### GENERAL CHARACTERISTICS

Although patients manifested many changes in ventricular function after bypass, certain characteristics were common: 1) immediately after bypass (15 min), both left and right ventricular function were moderately to severely depressed (35 to 75% of control;  $P < 0.05$ ); 2) partial recovery of ventricular function occurred 1–2 h after bypass; 3) recovery patterns over the following 24 h varied; and 4) right ventricular function significantly improved with resumption of spontaneous ventilation.

DYSFUNCTION-RECOVERY PATTERNS

Two patterns of dysfunction-recovery occurred. In the first (Group 1 patients), 1) the degree of immediate (15 min) biventricular dysfunction was "moderate" but statistically significant (60-75% of control;  $P < 0.05$ ); and 2) almost complete recovery of ventricular function

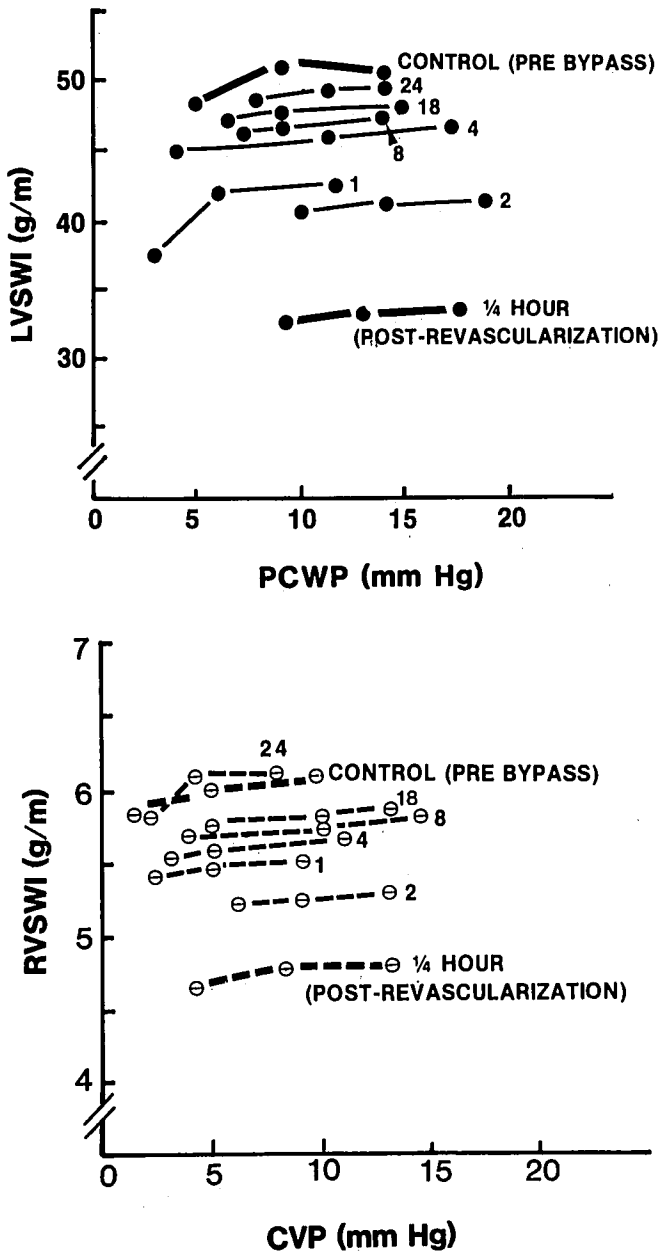


FIG. 1. Left (A, upper) and right (B, lower) ventricular function curves for a patient with a preoperative ejection fraction of 0.61 and no dyssynergy (Group 1; see text). The curves measured before (control) and 15 min, 1, 2, 4, 8, 18, and 24 h after revascularization are shown. LVSWI = left ventricular stroke work index; RVSWI = right ventricular stroke work index; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure.

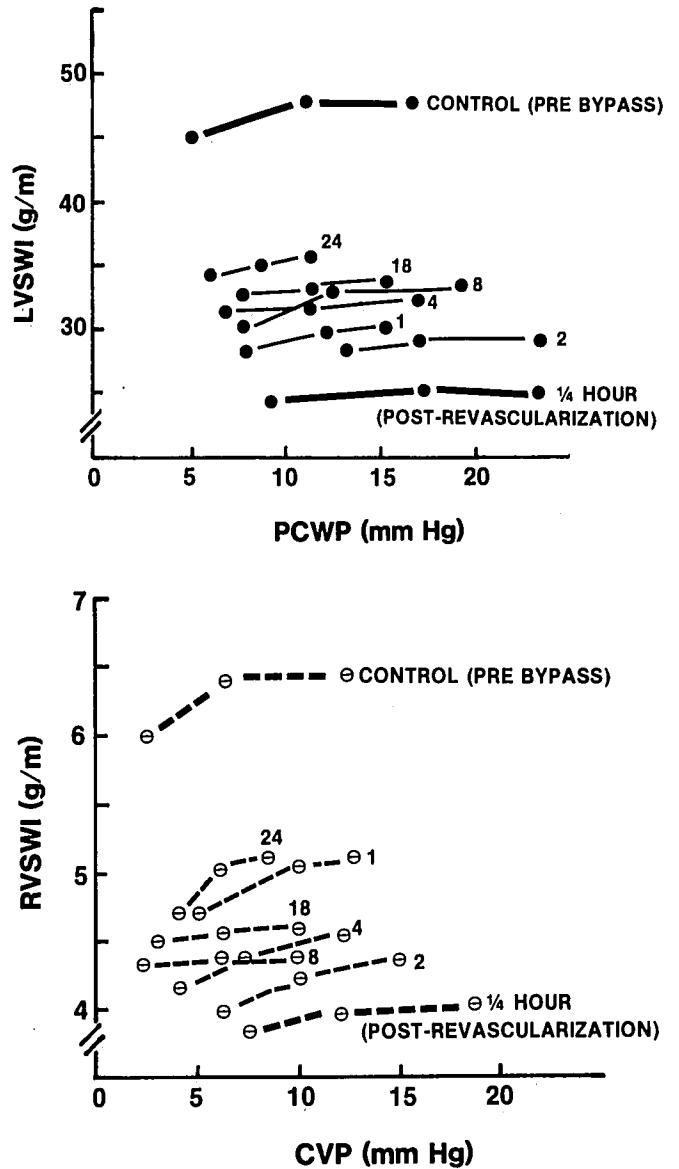


FIG. 2. Left (A, upper) and right (B, lower) ventricular function curves for a patient who had a preoperative ejection fraction of 0.39 and anterior wall hypokinesis (Group 2; see text). The curves measured before (control) and 15 min, 1, 2, 4, 8, 18, and 24 h after revascularization are shown.

( $\geq 90\%$  of control) occurred within 4 h of bypass. (No statistically significant difference between control and 4 h, 8 h, 18 h, and 24 h was found.) Figures 1A and B show the eight ventricular function curves for a Group 1 patient during the 24-h period. Compared with prebypass curves, the curves 15 min after bypass are depressed for both the left (1A) and right (1B) ventricles. Recovery of ventricular function commences within the first hour of bypass and progresses over the next 24 h. Also noteworthy is the relative flatness of these ventricular function curves over their filling pressure ranges throughout the 24-h perioperative period.

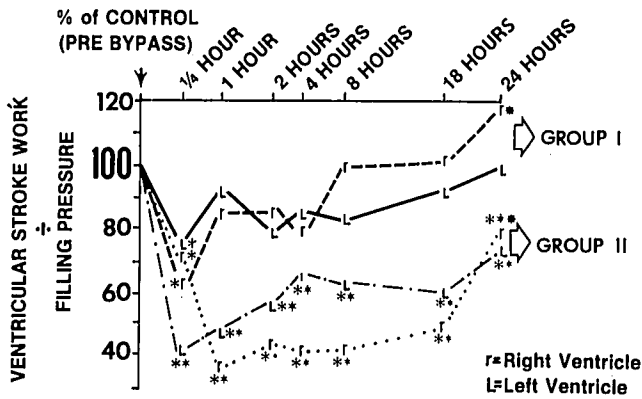


FIG. 3. Mean values for LVSWI/PCWP and RVSWI/CVP for Group 1 and 2 patients for each measurement period are compared with control values (100%). \* Indicates a significant difference from control,  $P < 0.05$ . ★ Indicates a significant difference from Group 1,  $P < 0.05$ . ✱ Indicates a significant difference from the 18 h data,  $P < 0.02$ .

In the second pattern (Group 2 patients), 1) biventricular function at 15 min following bypass was 35–40% of control ( $P < 0.05$ ) and significantly lower than that of Group 1 ( $P < 0.05$ ); and 2) recovery did not occur ( $\leq 60\%$  of control) within 24 h of bypass. (Both left and right ventricular function remained significantly lower than control throughout the entire 24-h postbypass period.) An example is shown in figures 2A and B. This Group 2 patient has greater left and right ventricular dysfunction immediately after bypass than does the Group 1 patient in figures 1A and B. Also, complete

recovery does not occur, even 24 h after bypass. Left and right ventricular function curves are also relatively flat over their filling pressure ranges throughout the 24-h period.

The ventricular function characteristics shown for these individual patients were typical for all patients in their respective groups. In order to quantitate the ventricular function curves for all Group 1 and 2 patients, the ratio of ventricular stroke work to filling pressure (normalized stroke work: LVSWI/PCWP, RVSWI/CVP) was calculated and averaged over all patients for each time period. The results are shown in figure 3 and are consistent with the previous results (figs. 1 and 2). The results demonstrate the following: 1) immediate left and right ventricular dysfunction in both groups—the normalized stroke work is significantly lower than control, and Group 2 is significantly lower than Group 1 ( $P < 0.05$ ); 2) early ( $\leq 4$  h) recovery for Group 1—the normalized stroke work (left or right) is not statistically significant from control at 4–24 h; 3) incomplete recovery for Group 2, even at 24 h—the normalized stroke work is statistically significant from control throughout the 24-h postbypass period; 4) right ventricular dysfunction is as severe as left—the degree of right ventricular dysfunction (per cent change from control) is statistically the same as the degree of the left; and 5) significant improvement of right ventricular function when ventilation changed from controlled (18 h) to spontaneous (24 h)—for both groups the normalized right stroke work was significantly greater at 24 h (compared with 18 h).

#### GROUP 1 VERSUS GROUP 2 CHARACTERISTICS

Given these marked differences in dysfunction–recovery patterns, what characteristics or conditions distinguish Group 1 from Group 2? Of the 16 perioperative predictor terms considered (see “Methods”), logistic regression analysis revealed that only the preoperative left ventricular ejection fraction ( $P = 0.02$ ) and dyssynergy ( $P = 0.04$ ) were significant. After redistribution of these terms in the regression model, no other terms were significant ( $P < 0.05$ ). Separation of patients into Group 1 and Group 2 further revealed that Group 1 consisted of 11 patients having ejection fractions greater than 0.55 and no areas of dyssynergy. Group 2 consisted of 11 patients having ejection fractions less than 0.45 or left ventricular dyssynergy. Also, all those having a history of left ventricular failure (two patients), taking digoxin (three patients), or requiring perioperative inotropic support (two patients) belonged to Group 2. No patient in either group had a perioperative myocardial infarction as assessed by ECG, CPK-M bands, and pyrophosphate scan.

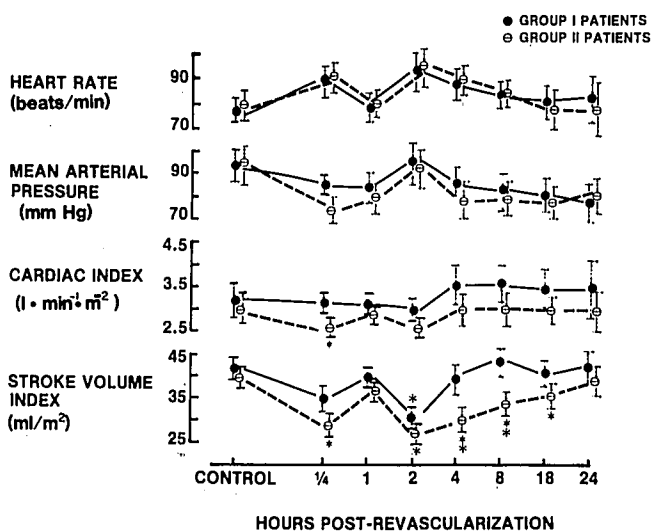


FIG. 4. Values for general hemodynamic variables for Group 1 and Group 2 patients (mean and standard deviation are shown). \* Indicates a significant difference from control,  $P < 0.05$ . ★ Indicates a significant difference from Group 1,  $P < 0.05$ .

GENERAL HEMODYNAMIC VARIABLES

Average values for hemodynamic variables for both groups are shown in figures 4-6. Statistically significant differences between Groups 1 and 2 were found for the following: cardiac index (at 15 min); stroke volume index (at 15 min, 4, 8, 18 h); pulmonary wedge pressure (at 15 min, 1, 2 h); left ventricular stroke work index (at 1, 2, 4 h); and right ventricular stroke work index (at 15 min, 2, 4 h).

Discussion

Three results are particularly noteworthy. First, even when anesthesia and surgery are uncomplicated, biventricular dysfunction occurs immediately after myocardial revascularization, right ventricular function being at least as depressed as left. Second, although a variety of dysfunction-recovery sequences exist, two general patterns emerge (fig. 3): 1) moderate biventricular dysfunction immediately after bypass with almost complete recovery within 4 h; and 2) more severe dysfunction with no recovery even after 24 h. Third, of all the patient and operative characteristics, two best predict the dysfunction-recovery pattern: the preoperative ejection fraction and the degree of dyssynergy. Pattern 1 was associated with an ejection fraction greater than 0.55 and no dyssynergy; and pattern 2, with an ejection fraction less than 0.45 or dyssynergy. Each of these results now will be discussed.

IMMEDIATE BIVENTRICULAR DYSFUNCTION

The immediate changes in left ventricular function (*i.e.*, decreased LVSWI despite increased PCWP and decreased SVR) indicate that left ventricular contractility is depressed following revascularization, especially in Group 2 patients. Mechanisms that have been suspected are as follows: direct damage to the myocardial cells (cannulation, manipulation); alteration of cell function, cellular constituents, or membrane potential (hypothermia, potassium infusion, fibrillation); and alteration of coronary flow. Definitive data are lacking. What is known is that the anesthetic morphine sulfate plus oxygen does not depress contractility in patients with valvular or coronary disease at the dose levels used in this study.<sup>14,15</sup>

Not only was left ventricular dysfunction significant after revascularization, but right ventricular dysfunction was significant as well (fig. 3). Despite no preoperative evidence of right ventricular failure in any patient, 16 of 22 patients had 90% or greater occlusion of the right coronary artery. However, no relationship could be established between this distribution of coronary disease and the degree of right ventricular dysfunction. The

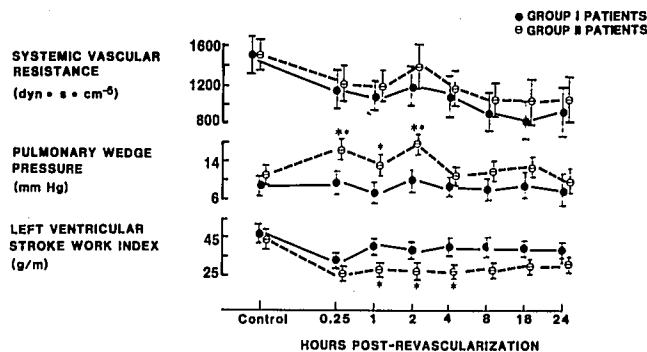


FIG. 5. Values for left ventricular hemodynamic variables for Group 1 and Group 2 patients (mean and standard deviation are shown). \* Indicates a significant difference from control,  $P < 0.05$ . ★ Indicates a significant difference from Group 1,  $P < 0.05$ .

possible mechanisms for left ventricular dysfunction apply here as well. Of note are the unknown, but possibly significant, effects of right atrial cannulation and myocardial preservation on right ventricular function. Also, for both groups, pulmonary vascular resistance was higher than control immediately after revascularization, probably because of loss of lung volume, hypothermia, and elevated catecholamine levels.<sup>16</sup> Thus, increased PVR also may have contributed to right ventricular dysfunction by elevating right ventricular afterload. Finally, it is possible that ventricular interference (septal shift) could have occurred with closure of the chest, further exacerbating left (or right) ventricular dysfunction. However, this effect is probably not significant when filling pressures are normal or only moderately elevated.<sup>12</sup>

DYSFUNCTION-RECOVERY PATTERNS

For the first hour after revascularization, both left and right ventricular function improved for all patients. The mechanism is uncertain but may be associated with

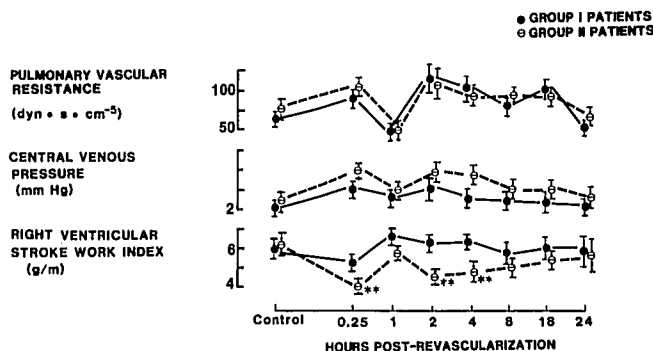


FIG. 6. Values for right ventricular hemodynamic variables for Group 1 and Group 2 patients (mean and standard deviation are shown). \* Indicates a significant difference from control,  $P < 0.05$ . ★ Indicates a significant difference from Group 1,  $P < 0.05$ .

improved coronary perfusion, normalization of myocardial temperature and conduction, and restoration of potassium and calcium balances. Ventricular function continued to improve over 24 h (albeit slowly for Group 2 patients), with the exception of the second hour in the intensive care unit. At this time, external stimulation of the patient (movement of the patient from the operating table to the bed, transportation to the ICU, and chest tube manipulation) was greatest. Heart rate and systemic vascular resistance increased (although not significantly).<sup>17</sup> These increases in myocardial oxygen demand could have altered ventricular systolic and diastolic function, resulting in the decreased stroke work at elevated PCWP and CVP. It is not surprising that Group 2 patients appeared to be more sensitive to these stresses.<sup>18</sup>

With resumption of spontaneous ventilation, PVR decreased significantly, possibly resulting in improved performance (increased RSVWI/CVP). Pulmonary vascular resistance varies with lung volume and is highest at residual volume and at total lung volume, and lowest between these limits.<sup>19</sup> Thus, following revascularization, the tidal volumes commonly employed (approximately 10 ml/kg) may increase PVR and therefore right ventricular afterload. Since right ventricular dysfunction occurs and may be marked (Group 2 patients), the effects of mechanical ventilation on right ventricular function may be substantial immediately after revascularization.

It should be noted that the control measurements and the postbypass measurements (15 min, 1 h) were made with the chest open. However, the ICU measurements were made with the chest closed. Thus, the effects of intrapleural pressure and cardiac constriction by closure of the chest wall may affect the comparison of ICU data with the intraoperative data. The effect of the intrapleural pressure has been minimized by recording all measurements at end-expiration. The effect of cardiac compression by chest closure should be minimal, since the filling pressures (CVP, PCWP) were not excessive. Finally, the effect of pericardiotomy on these results is insignificant over the filling pressure ranges used in this study.<sup>12</sup>

The ventricular function curves generated within the 24 h of revascularization have one common characteristic: they appear to be flat over a considerable range of filling pressures. These results are similar to those in our previous study conducted 30 min after revascularization, in which Starling curves were flat when end-diastolic volumes exceeded 70 ml/m<sup>2</sup> or PCWP exceeded 7 mmHg.<sup>20</sup> The present study extends these results to immediately before bypass and 24 h after and calls into question the effectiveness of the Frank-Starling mechanism (augmentation of ventricular output by volume loading) for this period.

It should be noted here that the measure of ventricular performance chosen in this study was the stroke work *versus* filling pressure (CVP or PCWP) curves measured over varying filling pressures. Although these Starling curves have been used in multiple previous studies and offer distinct advantages, their use can be criticized as well. Stroke work (LVSWI, RVSWI) was chosen instead of stroke volume or cardiac output because it reflects both of the mechanical functions of the ventricle: volume production and pressure generation. Also, since the majority of oxygen consumed is used for (internal) pressure generation, use of stroke work rather than stroke volume is advantageous when considering mechanical efficiency. It should be noted, however, that stroke work (as opposed to stroke volume) has a more direct relationship with afterload (left ventricular wall tension at aortic valve opening). Although both stroke volume and stroke work reflect inotropic and afterload (as well as preload) effects, stroke volume may be less dependent on afterload and therefore easier to interpret. This is addressed in this study by inclusion of afterload effects in the discussion of stroke work changes.

The independent variables of the ventricular function curves are CVP and PCWP. It is known that filling pressure may be an inaccurate estimator of filling volume or preload.<sup>21</sup> As such, the curves using end-diastolic volume may appear quite different from those using end-diastolic pressure. However, it should be noted that in this study the ventricular function curves (figs. 1 and 2) are relatively flat; thus, conclusions regarding changes of stroke work over time should be the same, regardless of the end-diastolic volume change. For example, the stroke work at 24 h is significantly larger than that at 15 min postbypass over the range of filling pressures measured and over the corresponding range of filling volumes (unmeasured), regardless of their magnitude.

#### PREDICTIVE INDICES: EJECTION FRACTION AND DYSSYNERGY

The predictive value of preoperative ejection fraction and degree of dyssynergy in our study is consistent with the general literature on ischemic heart disease and long-term surgical mortality.<sup>22-27</sup> In patients with ischemic heart disease, a decrease in the left ventricular ejection fraction is one of the earliest changes seen in global "pump" function.<sup>25</sup> A decrease in ejection fraction usually occurs before abnormalities of general hemodynamics (blood pressure, heart rate), specific hemodynamics (cardiac output, stroke work, end-diastolic pressure or volume), or findings from a history and physical examination (shortness of breath, rales, cardiomegaly). Also, long-term (1 month to 10 years) postbypass mortality is best related to the preoperative ejection fraction (in addition to the degree and nature of coronary artery

obstruction).<sup>26,27</sup> Our results complement these observations. Ejection fraction is useful in predicting not only long-term surgical and nonsurgical mortality but also intraoperative and postoperative alterations in left and right ventricular function. Finally, it has been shown that the preoperative ejection fraction is also a useful guideline for deciding whether to monitor central venous pressure or pulmonary artery pressure during coronary artery surgery.<sup>28</sup>

It is also not surprising that our second most useful preoperative index was the degree of left ventricular dyssynergy. In patients with ischemic heart disease, with or without prior myocardial infarction, a highly significant correlation exists between the relative size of a dyskinetic segment and the ejection fraction.<sup>25,29,30</sup> In addition, the most sensitive global indicators of fiber shortening are ejection fraction, stroke work, and contractile pattern.<sup>30</sup> Thus, the contractile pattern or degree of dyssynergy also warrants special attention in the preoperative assessment of these patients.

The author thanks the Departments of Anesthesia, Cardiac Surgery, and Cardiology of the University of California, San Francisco, for their cooperation during this study.

### References

1. McIntosh HD, Garcia JA: The first decade of aortocoronary bypass grafting, 1967-1977; A review. *Circulation* 57:405-431, 1978
2. Rahimtoola SH: Coronary bypass surgery for chronic angina—1981: A perspective. *Circulation* 65:225-241, 1982
3. National Institutes of Health Consensus—Development Conference statement: Coronary-artery bypass surgery: Scientific and clinical aspects. *N Engl J Med* 304:680-684, 1981
4. CASS Principal Investigators and Their Associates: Myocardial infarction and mortality in the coronary artery surgery study (CASS) randomized trial. *N Engl J Med* 310:750-758, 1984
5. Berger RL, Davis KB, Kaiser GC, Foster ED, Hammond GL, Tong TGL, Kennedy JW, Sheffield T, Ringqvist I, Wiens RD, Chaitman BR, Mock M: Preservation of the myocardium during coronary artery bypass grafting. *Circulation* 64(Suppl II):II-61-II-66, 1981
6. Kouchoukos NT, Oberman A, Kirklin JW, Russel RO, Karp RB, Pacifico AD, Zorn GL: Coronary bypass surgery: Analysis of factors affecting hospital mortality. *Circulation* 62(Suppl I):I-84-I-89, 1980
7. Davis KB: Operative mortality in the CASS registry, *Coronary Bypass Surgery*. Edited by Hammermeister KE. New York, Praeger, 1983, pp 99-128
8. Cannon DS, Miller DC, Shumway NE, Fogarty TJ, Daily PO, Hu M, Brown B, Harrison DC: The long term follow-up of patients undergoing saphenous vein bypass surgery. *Circulation* 49:77-85, 1974
9. Ferlinz J, Gorlin R, Cohn PF, Herman MV: Right ventricular performance in patients with coronary artery disease. *Circulation* 52:608-615, 1975
10. Herman MV, Gorlin R: Implications of left ventricular asynergy. *Am J Cardiol* 23:538-547, 1969
11. Kennedy JW, Trenholme SE, Kasser IS: Left ventricular volume and mass from single-plane cineangiocardioqram: A comparison of anteroposterior and right anterior oblique methods. *Am Heart J* 80:343-352, 1970
12. Mangano DT: The effect of the pericardium on ventricular systolic function in man. *Circulation* 61:352-357, 1980
13. Wallenstein S, Zucker CL, Fleiss JL: Some statistical methods useful in circulation research. *Circ Res* 47:1-9, 1980
14. Lowenstein E, Hallowell P, Levine FH, Daggett WM, Austen WG, Laver MB: Cardiovascular response to large doses of intravenous morphine in man. *N Engl J Med* 281:1389-1392, 1969
15. Stoelting RK, Gibbs PS: Hemodynamic effects of morphine and morphine-nitrous oxide in valvular heart disease and coronary artery disease. *ANESTHESIOLOGY* 38:45-52, 1973
16. Bergofsky EH: Mechanisms underlying vasomotor regulation of regional pulmonary blood flow in normal and disease states. *Am J Med* 57:378-391, 1974
17. Boudoulas H, Lewis RP, Vasko JS, Karayannacos PE, Beaver BM: Left ventricular function and adrenergic hyperactivity before and after saphenous vein bypass. *Circulation* 53:802-806, 1972
18. Ross J Jr, Braunwald E: The study of left ventricular function in man by increasing resistance to ventricular ejection with angiotensin. *Circulation* 29:739-749, 1964
19. Whittenberger JL, McGregor M, Burglund E, Borst HG: Influence of state of inflation of the lung on pulmonary vascular resistance. *J Appl Physiol* 15:878-882, 1960
20. Mangano DT, Van Dyke DC, Ellis RJ: The effect of increasing preload on ventricular output and ejection in man. *Circulation* 62:535-541, 1980
21. Ellis RJ, Mangano DT, Van Dyke DC: Relationship of wedge pressure to end diastolic volume in patients undergoing myocardial revascularization. *J Thorac Cardiovasc Surg* 78: 605-613, 1979
22. Mock MB, Ringqvist I, Fisher LD, Davis KB, Chaitman BR, Kouchoukos NT, Kaiser GC, Alderman E, Ryan TJ, Russell RO Jr, Mullin S, Fray D, Killip T III: Survival of medically treated patients in the Coronary Artery Surgery Study (CASS) registry. *Circulation* 66:562-568, 1982
23. Nelson GR, Cohn PF, Gorlin R: Prognosis in medically treated coronary artery disease. Influence of ejection fraction compared to other parameters. *Circulation* 52:408-412, 1975
24. Cohn PF, Gorlin R, Cohn LH, Collins JJ Jr: Left ventricular ejection fraction as a prognostic guide in surgical treatment of coronary and valvular heart disease. *Am J Cardiol* 34: 136-141, 1974
25. Moraski RE, Russell RO Jr, Smith M, Rackley CE: Left ventricular function in patients with and without myocardial infarction and one, two or three vessel coronary artery disease. *Am J Cardiol* 35:1-10, 1975
26. Kennedy JW, Kaiser GC, Fisher LD, Fritz JK, Myers W, Mudd JG, Ryan TJ: Clinical and angiographic predictors of operative mortality from the Collaborative Study in Coronary Artery Surgery (CASS). *Circulation* 63:793-802, 1981
27. Hammermeister KE, DeRouen TA, Dodge HT: Comparison of survival of medically and surgically treated coronary disease patients in Seattle Heart Watch: A nonrandomized study. *Circulation* 65(Suppl II):II-53-II-59, 1982
28. Mangano DT: Monitoring pulmonary arterial pressure in coronary-artery disease. *ANESTHESIOLOGY* 53:364-370, 1980
29. Feild BJ, Russell RO Jr, Dowling JT, Rackley CE: Regional left ventricular performance in the year following myocardial infarction. *Circulation* 46:679-689, 1972
30. Hamilton GW, Murray JA, Kennedy JW: Quantitative angiocardio-graphy in ischemic heart disease: The spectrum of abnormal ventricular function and the role of abnormally contracting segments. *Circulation* 45:1065-1080, 1972