Hemodynamic Effects of Preload and Sodium Nitroprusside in Patients Subjected to Coronary Bypass Surgery

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SUMMARY  To differentiate between the hemodynamic effects of afterload reduction produced by sodium nitroprusside (NP) and the effects of preload, left ventricular function curves were constructed during and without NP infusion at the same, normal left ventricular filling pressure (LVFP) levels for 20 patients 8 hours after coronary bypass grafting and for 10 of these patients preoperatively.

Preoperatively, when the patients had normal myocardial performance, NP, in reducing both preload and afterload, decreased the stroke index (SI) (P < 0.05). However, SI and the cardiac index (CI) were 14% and 25% higher, respectively, with than without NP at identical LVFPs (P < 0.02). NP did not displace the left ventricular stroke work index (LVSWI) from a single function curve, nor did it affect myocardial oxygen consumption (MVO2, described as rate-pressure-product) if the cardiac work index (CWI) was unchanged.

Postoperatively, when the patients’ myocardial performance was generally moderately or severely reduced, NP as such did not change SI or CI. However, at constant LVFP level, SI was 29% and CI was 31% greater during NP infusion (P < 0.001); the more horizontal the control ventricular function curve, the more LVSWI was augmented by NP. Postoperatively, NP increased CWI significantly without affecting MVO2 at constant LVFP.

Thus, NP is beneficial even at low preload levels, but the greatest enhancement in blood flow and the smallest diminution in systemic or pulmonary arterial pressures are achieved if LVFP is unchanged or increased while the NP infusion rate is accelerated stepwise to its optimum. At a constant filling pressure, NP produces an enhancement of myocardial pumping performance equal to that caused by a 7 mm Hg increase in the wedge pressure, but during NP infusion, changes in arterial pressures and MVO2 are minimal.

SINCE FRANCIOSA et al.1 first reported the use of sodium nitroprusside (NP) in patients suffering from acute myocardial infarction, several studies have demonstrated the effectiveness of NP in the treatment of acute or chronic left ventricular failure, secondary to various etiologies.2-14 NP directly relaxes the smooth muscles of the vascular walls but has no effect on myocardial contractility or on α- or β-adrenoceptors.15, 16 It may be a calcium antagonist of vascular smooth muscle.16, 17 While reducing the tone in resistance vessels and lowering the impedance to ventricular ejection, NP makes the left ventricle empty more effectively with each ejection, and thus also decreases the left ventricular end-diastolic pressure. The reductive effect on preload is still more marked, because even if NP acts manifestly on the resistance vessels it also directly dilates capacitance vessels and thus causes venous pooling.5, 18 For this reason the reduction of afterload with NP has always been followed by marked diminution of left ventricular filling pressure (LVFP), so the hemodynamic changes produced by NP have been due not only to reduction of impedance to left ventricular ejection but also to reduction of preload.

There is also evidence that NP may exert a direct relaxant effect on ventricular muscle.19 If LVFP is elevated beyond the optimal point of the ventricular function curve (to the descending limb of the Frank-Starling curve), the reduction of filling pressure itself may augment myocardial performance. In such patients the afterload reduction is especially beneficial, and several investigators have seen dramatic enhancement of myocardial performance when NP is used in patients with high filling pressures.9, 10, 12, 14 In very few studies have the hemodynamic effects of preload restoration after vasodilator therapy been investigated.5, 11, 16, 17

The aim of the present study was to differentiate between the hemodynamic effects of preload and afterload alterations by constructing left ventricular function curves with and without NP at the same, normal therapeutic filling pressure levels, and to find the best possible circumstances for myocardial function.

Materials and Methods

Patients and Operation

Twenty male patients coming for coronary bypass surgery were randomly chosen for the study. The mean age of the patients was 56 years (range 28–61 years). Nine patients had had myocardial infarction; eight of these showed hypokinetic areas of the left ventricular wall during angiography. Three patients had diseases other than coronary sclerosis: one had medically compensated congestive heart failure, one had aortic valve insufficiency and one had chronic mesangioproliferative glomerulonephritis. One patient had symptomless slight obstructive ventilatory insufficiency with normal blood gases. During the week before the operation none of the patients took any medicine other than sublingual nitroglycerin. Preoperatively, the functional class of 16 patients was New York Heart Association (NYHA) III, and of four patients, NYHA II.

Four saphenous vein or internal mammary artery
bypasses were performed on two patients, three bypasses on 13 patients and two bypasses on five patients. One patient also underwent aortic valve replacement. Balanced anesthesia, with pancuronium and neuroleptics, N₂O and O₂ was generally used. All patients were given methylprednisolone 30 mg/kg. The mean time for extracorporeal perfusion and the total time for intermittent aortic closures was 142 and 70 minutes, respectively. Patients' hearts were protected during the operation with systemic hypothermia (30°C) and during the periods of aortic cross clamping with topical cold arrest (4°C). After operation patients were kept connected to a volume preset respirator until the next morning (on 17 patients PEEP, cmH₂O was used). Blood losses were balanced with whole blood. Seven of the patients had continuous steady dopamine infusion at an average rate of 3 
μg/kg/min from the end of extracorporeal perfusion throughout the postoperative investigation period. Blood gases and plasma potassium were normal before initial postoperative measurements were started. The average overall time for the investigation of one patient was 3 hours. During this period patients were given no medicine other than NP or the steady dopamine infusion.

The purpose and the possible risks of the study were carefully explained to each patient by the investigator.

Hemodynamic Measurements

Right atrial (RA), pulmonary arterial (PA) and pulmonary capillary wedge (PCW) pressures were measured with a triple lumen balloon tip thermodilution catheter (model 93-118, 7F, Edwards Laboratory, Santa Ana, California), which was introduced percutaneously through the subclavian, external jugular or basilic vein. Arterial blood pressure (AP or BP) was followed continuously by means of a 16 gauge cannula inserted into the radial artery. All the dynamic pressures were amplified and monitored with an Olli-tuote amplifier and oscilloscope (models 295 and 332, Olli-tuote, Kivenlahti, Finland) using Ackers transducers (model AE 840, Ackers Co, Oslo, Norway) and were recorded together with ECG by a Mingograf four-channel recorder (Elema-Schönander, Stockholm, Sweden). Heart rate (HR) was calculated from the recorded ECG. The mean systemic arterial pressures (MAP) were analyzed by planimetry (Hewlett Packard Digitizer model 9864 A, together with Hewlett Packard 9821 A Series calculator) from the dynamic pressure curves. At each hemodynamic measuring, six parallel cardiac output (CO) determinations were made by the thermodilution technique. The highest and lowest values were excluded and the mean of the remaining four was calculated. Average standard deviation of CO measurements was 4.8%. CO computations were performed with an Edwards CO computer (model 9510) using melting frozen 5% dextrose directly from an infusion vial.

Derived hemodynamic parameters were calculated as follows: MPAP = (2 × PASP + 3 × PAEDP)/5, CI = CO/BSA, SI = CI/HR, CWI = CI × (MAP – PCWP) × 0.0136, LVSWI = 1000 × CWI/HR, SVR = 80 × (MAP – RAP)/CO, PVR = 80 × (MPAP – PCWP)/CO, R-P-P = SBP × HR, where MPAP is mean pulmonary arterial pressure, PASP and PAEDP are pulmonary arterial systolic and end-diastolic pressures (mm Hg), respectively, CI is the cardiac index (1/min/m²), CO is cardiac output (1/min), BSA is body surface area, SI is the stroke index (ml/min/m²), HR is heart rate (beats/min), CWI is the cardiac work index (kg/m²/min), MAP is mean arterial pressure, PCWP is pulmonary capillary wedge pressure, LVSWI is the left ventricle stroke work index (g-m/m²), SVR and PVR are the systemic and pulmonary vascular resistances (dyne-sec-cm⁻⁵), respectively, RAP is right arterial pressure, R-P-P is the rate-pressure-product (mm Hg beats/min), and SBP is systolic blood pressure.

Investigation Program

The first 10 patients chosen for the study were investigated preoperatively and all 20 patients postoperatively. The thermodilution catheter and arterial cannula were inserted percutaneously at least 6 hours before the preoperative patients came into the investigation unit and the patients lay quietly with all the monitoring devices connected to them for at least 1 hour before the initial (control) preoperative measurements. Postoperative control measurements were initiated 8 hours after the end of extracorporeal circulation.

The investigation program was the same preoperatively and postoperatively. Through the whole investigation period measurements in each patient of HR, AP, PAP, PCWP, RAP and CO were repeated at 10–15-minute intervals (during the volume loading periods, after every 2 mm Hg increase of PCWP). After the initial hemodynamic measurements (stage 1), PCWP was increased with 3.8% plasma protein liquid (PPL, Finnish Red Cross) 6–7 mm Hg above the initial level. During this stepwise elevation of LVp the control left ventricular function curve was constructed. The hemodynamic values obtained during minimal preload effect are documented under stage 2. Immediately after these measurements, plasma infusion was discontinued and 0.01% NP (Nipride, Roche)-infusion was started at a rate of 0.2 
μg/kg/min via an infusion flow controller (Ivac 501, Ivac Corporation, San Diego, California). The infusion rate of NP was increased by 0.25 
μg/kg/min increments until PCWP did not decrease more than 0.5 mm Hg between two successive measurements. The final rate of NP infusion was 1.2 
μg/kg/min (range 0.25–2.0 
μg/kg/min), and the hemodynamic values measured during this maximal NP effect are documented as stage 3. The maximal NP flow rate was continued steadily while PCWP was again increased stepwise 6 mm Hg with plasma. During this restoration of LVFP the second left ventricular function curve was constructed. The hemodynamic values achieved during maximal preload effect under the in-
fluence of NP are documented as stage 4. The mean total amount of plasma used during both volume loading periods was 1.8 l for each patient. This volume loading diluted mean hemoglobin postoperatively from 131 g/l to 109 g/l.

The results were analyzed by means of t test for paired data.

**Results**

**Preoperative Day**

The control hemodynamic values (stage 1) revealed that all the patients had preoperatively normal myocardial performance at rest (CI over 2.6 l/min/m² at normal PCWP).

**Preload**

The 6.2 mm Hg increase of PCWP augmented CI and CWI by 0.90 l/min/m² and 0.97 kg-m/m², respectively (P < 0.001), in accordance with the Frank-Starling mechanism (figs. 1 and 2). Also, SL and LVSWI increased very markedly (18% and 17% respectively, P < 0.005). The volume loading with plasma decreased SVR by 21% (table 1).

**Afterload**

NP infusion decreased PCWP and RAP to a level that did not differ from the initial (table 1). The MAP decreased by 18%, to a level below the control (P < 0.01). NP infusion decreased CI nonsignificantly; however, at stage 3 CI was significantly greater than initially (P < 0.001) (table 1 and fig. 1). In patients with normal myocardial performance the moderate reduction in MAP caused by NP when PCWP was unchanged was associated with very marked increase in CI, as shown in figure 3 (the continuous line connecting the triangles shows the change from stage 1 to stage 3). In six patients the increase in tissue blood flow was accompanied by very clear flushing on the upper chest and face.

During NP infusion CWI and R-P-P (an indirect indication of myocardial oxygen consumption, MVO₂) decreased along the very line constructed during the control preload elevation (in fig. 4 the triangles at stages 1, 2 and 3 lie on the same line). This is because the decrease produced by NP in the pressure component of cardiac work (MAP-PCWP) at the initial filling pressure level was accompanied by such a reflex increase in HR (from 71.0 at stage 1 to 79.7 at stage 3, P < 0.005) that both R-P-P and CWI increased slightly between the initial stage and stage 3 (fig. 4). After the maximal afterload reduction, SVR and PVR had fallen 27% and 28%, respectively, from the initial levels (P < 0.05) (table 1).

**Afterload and Preload**

The stepwise 5.9 mm Hg elevation of PCWP during continuous NP infusion increased CI and CWI by 0.82 l/min/m² and by 0.71 kg-m/m², respectively (P < 0.005) (figs. 1 and 2, table 1). The left ventricular function curves constructed with and without NP were almost parallel. If CI is the ordinate, the mean 1.2 μg/kg/min rate of NP infusion moved the ventricular function curve 0.86 l/min/m² upwards (fig. 1). At each measurement during the stepwise plasma infusions, MAP was lower with than without NP at the same PCWP levels. Thus, the reductive effect on afterload produced by NP was maintained despite the increase in preload. The very marked increase in CO and only moderate decrease in MAP induced by afterload reduction at elevated preload level was proportionate to the changes seen at the initial preload level (fig. 3). During preload restoration LVSWI increased precisely along the function curve previously constructed (in fig. 5, triangle 4 lies on the same line as stages 1, 2 and 3). The second preload elevation reduced SVR and PVR progressively, so that at the end of the investigation the levels of SVR and PVR
were 39% and 45% lower, respectively, than initially \( P < 0.001 \).

Postoperative Period

The maximal postoperative steady state hemodynamic changes observed during preload elevation, NP infusion and preload elevation with continuous NP infusion are shown in table 2. Initial measurements revealed that 12 patients had severe pump failure and five patients had moderate pump failure (CIs less than 2.1 and 2.6 l/min/m², respectively, at normal filling pressures). The mean values of CI and PCWP in these patient groups were 1.85 l/min/m² at 8.4 mm Hg and 2.36 l/min/m² at 9.9 mm Hg, respectively.

Preload

The mean stepwise 7.2 mm Hg elevation of PCWP increased CI from the initial level of 2.11 l/min/m² to a maximum of 2.77 l/min/m² \( P < 0.001 \) (fig. 1). The improvement of pumping performance was followed by highly significant increases in systemic and pulmonary arterial pressures and decreases of SVR and PVR (table 2).

Afterload

NP at a mean infusion rate of 1.2 \( \mu g/kg/min \) diminished both PCWP and RAP to their initial levels (table 2). MAP decreased on the average to a level 17% lower than the initial level (MAP 67.9 mm Hg vs 74.1 mm Hg, \( P < 0.001 \)). NP also decreased systolic and diastolic pressures in both systemic and pulmonary vasculatures \( P < 0.001 \); however, the systolic pressures decreased only to the initial levels, while the diastolic pressures fell to significantly lower levels than those observed at stage 1 (table 2). Systemic and pulmonary vascular resistance decreased progressively with NP infusion, and they reached values which were respectively 34% and 38% lower than initially \( P < 0.001 \).
In different patients the effect of NP on CI was very different. Although the mean postoperative change in CI was a nonsignificant increase from 2.77 to 2.88 l/min/m², three kinds of reactions of CI to NP were observed: first, in four patients CI decreased more than 5% (the mean decrease was 0.57 l/min/m²); second, in eight patients CI remained unchanged within the limits of ±5% (the mean change was an increase of 0.05 l/min/m²) and third, in eight patients CI increased more than 5% (the mean increase was 0.52 l/min/m²) (fig. 6). In all groups NP decreased PCWP from 14.5-15.9 mm Hg to between 7.8 and 8.9 mm Hg. The hemodynamic parameter that best distinguished the groups from each other was the angle coefficient of the slope of the control left ventricular function curves constructed during plasma infusion. Very clear differences were observed: in the first, second and third patient groups the angle coefficients were 0.174, 0.088 and 0.054, respectively (CI in l/min/m² and PCWP in mm Hg). When comparing the CI values without NP at the same PCWP levels as

![Figure 3](https://circ.ahajournals.org/lookup/suppl/doi:10.1161/01.CIR.81.6.819/-/DC1/fig_3.png)

**Figure 3.** Changes in mean arterial pressure (MAP) and cardiac index (CI) produced by sodium nitroprusside at unchanged left ventricular filling pressure levels pre- and post-operatively. Stages as in figure 1. At constant filling pressures, the optimum afterload reductive dosage of nitroprusside decreases MAP in normal hearts very markedly, while the increase in CI is greatest in patients with moderate or severe pump failure. The elevation of filling pressure moves these curves upwards and to the right (change from solid lines to broken lines).

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**Table 1. Hemodynamic Data During Preload and Afterload Changes, Preoperative Day**

<table>
<thead>
<tr>
<th></th>
<th>1. Initial</th>
<th>P&lt;0.05</th>
<th>2. Plasma infusion</th>
<th>P&lt;0.05</th>
<th>3. Nitroprusside infusion</th>
<th>P&lt;0.05</th>
<th>4. Plasma + NP infusion</th>
<th>P&lt;0.05</th>
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<tbody>
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<td>SBP</td>
<td>151.5 ± 3.3</td>
<td>0.001</td>
<td>169.7 ± 4.4</td>
<td>0.005</td>
<td>143.0 ± 5.6</td>
<td>0.025</td>
<td>158.6 ± 5.1</td>
<td>NS</td>
</tr>
<tr>
<td>DBP</td>
<td>71.6 ± 2.1</td>
<td>NS</td>
<td>75.5 ± 2.2</td>
<td>0.005</td>
<td>63.5 ± 1.9</td>
<td>NS</td>
<td>63.7 ± 1.2</td>
<td>0.02</td>
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<td>MAP</td>
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<td>NS</td>
<td>94.3 ± 2.4</td>
<td>0.001</td>
<td>77.6 ± 1.9</td>
<td>NS</td>
<td>81.5 ± 1.8</td>
<td>0.01</td>
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<td>PASP</td>
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<td>0.001</td>
<td>20.9 ± 2.1</td>
<td>0.001</td>
<td>15.5 ± 1.2</td>
<td>0.005</td>
<td>21.6 ± 1.4</td>
<td>0.01</td>
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<tr>
<td>PAEDP</td>
<td>7.3 ± 1</td>
<td>0.001</td>
<td>12.2 ± 1.3</td>
<td>0.001</td>
<td>5.1 ± 1</td>
<td>0.005</td>
<td>10.1 ± 1.3</td>
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<td>MPAP</td>
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<td>9.2 ± 1</td>
<td>0.005</td>
<td>14.7 ± 1.3</td>
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<td>PCWP</td>
<td>4.4 ± 1</td>
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<td>10.6 ± 1.2</td>
<td>0.001</td>
<td>2.8 ± 0.9</td>
<td>0.001</td>
<td>8.7 ± 1.2</td>
<td>NS</td>
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<td>RAP</td>
<td>1.5 ± 0.6</td>
<td>0.005</td>
<td>4.7 ± 1</td>
<td>0.001</td>
<td>0.6 ± 0.7</td>
<td>0.005</td>
<td>3.4 ± 1</td>
<td>NS</td>
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<td>76.5 ± 2.4</td>
<td>NS</td>
<td>79.7 ± 3.1</td>
<td>NS</td>
<td>80.1 ± 2.8</td>
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<td>4.66 ± 0.22</td>
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<tr>
<td>SI</td>
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<td>55.4 ± 1.4</td>
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<td>58.2 ± 1.8</td>
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<td>SVR</td>
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<td>886 ± 35</td>
<td>NS</td>
<td>815 ± 35</td>
<td>0.02</td>
<td>678 ± 23</td>
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<td>CWWI</td>
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<td>LVSVI</td>
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<td>R-P-P</td>
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<td>11.33 ± 0.50</td>
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<td>12.66 ± 0.49</td>
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</table>

Values are mean ± SEM; n = 10.

P* refers to comparison between stages and denote values lower than those documented.

For abbreviations see Materials and Methods section. NS = not significant (P > 0.05).
at stage 3 to those observed after NP infusion, it was found that the calculated increase in CI was 0.58 l/min/m², 0.67 l/min/m² and 0.95 l/min/m² in the first, second and third patient groups, respectively (fig. 6).

NP reduced total cardiac work nonsignificantly, from 2.55 to 2.40 kg-m/m² (figs. 2 and 4), because when the volume component of CWI (CI) increased slightly, the pressure component (MAP-PCWP) decreased by only 11%. NP reduced LVSWI more markedly than it reduced CWI, yet the reduction of LVSWI was only symptomatically significant ($P < 0.1$) (fig. 4). In those patients with decreasing CI response to NP, LVSWI decreased to the initial level along the previously constructed function curve. In those patients with increasing CI response to NP, LVSWI was also enhanced during NP infusion.

After these measurements, rethoracotomy was performed on one patient who had normal myocardial performance at stage 3, because of continuing bleeding from minor side branches of the internal mammary artery.

Figure 4. Mean effects of preload elevation, afterload reduction and preload restoration on the relationship between total cardiac work (kg-m/m²) and myocardial oxygen consumption (reflected as rate-pressure-product (R-P-P) (mm Hg beats/min) pre- and postoperatively. Stages as in figure 1. Note that only postoperatively, the reduction of afterload made it possible for the left ventricle to do more work at constant R-P-P. The work of the heart was more economical during vasodilation than without.

Figure 5. Changes in the relationship between mean pulmonary capillary wedge pressure (PCWP) and left ventricular stroke work index (LVSWI) induced by preload elevation, afterload reduction and preload restoration pre- and postoperatively. Stages as in figure 1. Preoperatively, sodium nitroprusside did not change the relation between LVSWI and PCWP, while postoperatively the optimum vasodilation moved LVSWI upwards.
### Table 2. Hemodynamic Data During Preload and Afterload Changes, Postoperatively

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<td>DBP</td>
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<td>RAP</td>
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<td>94.8 ± 2.9</td>
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<td>91.8 ± 2.5</td>
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<td>3.46 ± 0.16</td>
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<td>0.001</td>
<td>892 ± 36</td>
<td>0.001</td>
<td>792 ± 45</td>
<td>0.001</td>
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<td>PVR</td>
<td>119 ± 9</td>
<td>0.001</td>
<td>57 ± 6</td>
<td>0.025</td>
<td>74 ± 7</td>
<td>0.001</td>
<td>60 ± 6</td>
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<tr>
<td>CWI</td>
<td>1.90 ± 0.11</td>
<td>0.001</td>
<td>2.55 ± 0.20</td>
<td>NS</td>
<td>2.40 ± 0.17</td>
<td>0.001</td>
<td>2.93 ± 0.18</td>
<td>0.001</td>
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<tr>
<td>LVSWI</td>
<td>20.6 ± 1.5</td>
<td>0.001</td>
<td>28.8 ± 2.3</td>
<td>0.1</td>
<td>25.3 ± 1.9</td>
<td>0.001</td>
<td>32.0 ± 1.9</td>
<td>0.001</td>
</tr>
<tr>
<td>R-P-P</td>
<td>10.12 ± 0.41</td>
<td>0.001</td>
<td>11.86 ± 0.63</td>
<td>0.01</td>
<td>10.52 ± 0.44</td>
<td>0.001</td>
<td>12.40 ± 0.52</td>
<td>NS</td>
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</table>

Values as mean ± SEM; n = 20.
P's refer to comparison between stages and denote values lower than those documented.

For abbreviations see Materials and Methods section. NS = not significant (P > 0.05).

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**Figure 6.** Postoperative groups with decreasing, unchanged and increasing response of cardiac index (CI) to sodium nitroprusside (NP) after maximum volume expansion. Stages 2 and 3 are the same as in figure 1, whereas points 1 locate on groups' mean control left ventricular function curves at the same pulmonary capillary wedge pressure (PCWP) levels as stages 3. The direction and magnitude of changes in CI produced by NP are shown on the right. Note from the left that at identical PCWP levels (stages 1 and 3), optimum vasodilation increased CI in every patient group; left ventricular function curves have moved in every patient upwards parallel to the control curves.
Afterload and Preload

The filling pressures of the left and the right ventricles obtained during preload restoration (14.8 mm Hg and 11.7 mm Hg, respectively) did not differ from the values achieved during the first preload elevation (table 2). The directions of the first and the second ventricular function curves were nearly parallel (fig. 6); NP had moved the function curve 0.76 l/min/m² upwards on the average (fig. 1). The increase in SI was proportionate to the increase in CI, since HR was not affected by NP at constant filling pressures. Figure 3 shows (by following the broken line connecting the circles) that with a constant elevated PCWP level of 15 mm Hg, NP produced a very small decrease in MAP (7%) while CI increased very markedly (25%).

Because both the pressure generated in the left ventricle during each systole and the volume ejected by the heart increased during preload restoration, CWI increased highly significantly. The amount of work done by the heart at stage 4 was greater than at stage 2 (P < 0.01); also, LVSWI was greatest at maximal preload level during NP infusion. Thus, during the postoperative period, the work done by the left ventricle in every systole and also in any time period was greater with NP than without, at identical PCWP levels. Preload elevation during constant vasodilator infusion increased the product of SBP and HR highly significantly, but only to the same level that was observed at stage 2 (table 2), which means that under the influence of NP, CWI was constantly greater at any R-P-P level (fig. 4).

During the whole postoperative investigation period, CI increased by 64% (from the initial depressed value of 2.11 l/min/m² to a normal 3.46 l/min/m²) and CWI increased by 54% (from 1.90 to 2.93 kg·m/m²). Nevertheless, mean SI remained at 15% and mean LVSWI at 38% lower than the initial preoperative values. The seven patients who had steady dopamine infusion during the time of investigation did not differ in their reactions from the other patients when preload and afterload were altered. The infusion rate of NP was doubled in five patients after the measurements at stage 4. The result was that CI increased above the second cardiac function curve, whereas PCWP decreased.

Postoperative Low Output Patients

The three patients who after the first preload elevation still had severe pump failure (CI less than 2.1 l/min/m² at maximum filling pressure level) are considered as the true postoperative low CO patients. During extracorporeal perfusion these patients had had total aortic closure longer than all the other patients, with a mean of 91 minutes (the average for all patients was 70 minutes, and for those three patients with normal initial myocardial performance, 55 minutes). Selected steady state hemodynamic changes observed in these patients during the postoperative investigation period are summarized in table 3. Although statistical analysis of the data is not possible, some characteristic features can be seen. At a PCWP of 18.3 mm Hg, these patients had CI of 1.95 l/min/m²; the mean left ventricular function curve was very horizontal, with an angle coefficient of approximately 0.034. With NP infusion, both CI and CWI, and even LVSWI, were enhanced (fig. 2). The effect of NP on MAP and CI at the initial (approximately 10 mm Hg) and elevated (approximately 19 mm Hg) PCWP levels is shown in figure 3. The responses were very similar to those of the whole postoperative patient population, but with the coordinates used, at a lower level. After the second preload elevation, CI had increased by 53% (to 2.57 l/min/m²), but SI and especially LVSWI were still abnormally low. During the investigation period, SVR and PVR decreased progressively, as among the other patients. Four days after the operation, the patient who had had aortic valve replacement and two coronary bypasses died because of an irreversible low CO state, due to acute myocardial infarction.

Although the left ventricular pumping capacity had increased very profoundly between the initial stage and stage 4, it will be seen from figure 2 that preoperative, postoperative and low output patients can easily be distinguished from each other by their CWI. This is, first, because with preload elevation and with afterload reduction (using NP) it was possible to increase only the volume component of CWI, and, second, because the more severe the heart failure, the more reduced also the pressure component of CWI.

Discussion

The investigation program that was carried out on each of the patients made it possible 1) to clarify the actual effects of NP on hemodynamics when both preload and afterload were reduced from stage 2 to stage 3. 2) by constructing the left ventricular function curves both with and without NP at identical LVFPs, it was possible to demonstrate the hemodynamic changes that afterload reduction alone could produce when filling pressure was unchanged. Because PCWP correlates highly significantly with left ventricular end-diastolic pressure in the absence of mitral stenosis or pulmonary vascular abnormalities even during intermittent positive pressure ventilation with moderate

<table>
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<th>TABLE 3. Hemodynamic Data of Postoperative Low Output Patients</th>
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<td>LVSWI</td>
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<td>SVR</td>
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*Values as mean; n = 3.*

*For abbreviations see Materials and Methods section.*
PEEP,21 we considered PCWPs at different times to present real left ventricular filling pressure levels. Although it has been shown that NP moves left ventricular diastolic pressure-volume curve downwards and to the left,22 very little information exists on the effects of preload and/or afterload on left ventricular compliance. The volume loading increases left ventricular preload, but whether NP decreases preload in relation to filling pressure or does not change the myocardial end-diastolic fiber length at all in relaxing the myocardium itself is not known. For this reason, the real preload level may be greater with NP infusion than without at identical filling pressures.

Several investigators have shown that NP is very effective for enhancing myocardial performance, especially if the LVFP is markedly elevated and the basic myocardial function is diminished.1,2,5-14 It has also been shown that myocardial performance often deteriorates when NP is infused into patients with normal cardiac function or into patients with low or normal preload levels.5-7 During the preoperative day, even though every patient studied had normal pumping performance initially, and although NP infusion in fact decreased SI, the function curves constructed during continuous steady NP infusion were, in every patient, at a higher level than the control curves. Thus, in these patients with severe coronary artery disease, NP augmented the volume pumping capacity of the left ventricle at constant PCWP levels even preoperatively when both CI and the LVFP were normal initially. The 15% hemodilution produced by plasma infusions during the 3-hour investigation period could, to a minor degree, enhance these results.

Postoperatively, it was possible to distinguish three patient groups according to the change in CI produced by NP: in the first group CI decreased, in the second it was unchanged and in the third it increased. There was no single hemodynamic parameter at stage 2 to distinguish the groups from each other, but the angle coefficient of the upstroke of the control left ventricular function curves enabled a clear distinction to be made: in the second and third groups the angle coefficients were one-half and one-third, respectively, of that of the first group. In every patient group, the function curves constructed at reduced afterload level were nearly parallel but always above the control curves. If the two imagined function curves are parallel and very steep, and if NP infusion causes marked reduction in PCWP while the observation point moves to the upper curve, the only possible change in CI can be a decrease in CI. On the other hand, if the function curves are nearly horizontal, while PCWP decreases and the observation point moves to the upper curve by NP the only possible change in CI can be an increase in CI. This is exactly what we observed in every patient group. The difference in the level of the two curves can be independent of the degree of the reduction in filling pressure produced by NP, but the steeper the curves and/or the more the decrease in preload, the greater is the lowering in CI, although vasodilation has moved the function curve upwards and to the left. In several patients CIs were similar at stage 2, as were PCWPs, but the steepness of the control left ventricular function curves along which these values lay were nevertheless dissimilar. It may not be possible on the basis of these results to judge whether NP reduces myocardial performance of the patient (as expressed in function curves), although CI falls, if we do not know the steepness of the ventricular function curves along which preload and afterload are altered.

In clinical practice, there may be many ways of moving from the lower function curve to the upper one. One way would be to go straight upwards, by administering volume expanders at the same time as NP infusion and thus not letting the LVFP (and possible the CI) decrease at all. NP decreased both systemic and pulmonary arterial pressures very markedly, as has been reported also by numerous other investigators. Because volume depletion or preload decrease generally causes reduction of pressure in systemic and pulmonary vasculatures, especially if myocardial function is reduced, only some of the observed systemic arterial pressure reduction during NP infusion was due to afterload reduction, with the rest due to the dilation of capacitance vessels. When we compared systemic arterial pressures at identical PCWP levels with and without NP, we found that systolic pressures remained unchanged, while mean and diastolic pressures were significantly reduced with NP both pre- and postoperatively. NP decreased MAP pre- and postoperatively 18% and 17%, respectively, but these reductions were only 13% and 8% if LVFPs were unchanged.

If in clinical practice the aim of NP therapy is enhancement of myocardial performance and not reduction of pressures in systemic or pulmonary vasculatures, the smallest reduction of pressures can be achieved by keeping the preload level constant with fluid infusions while increasing NP dosage stepwise. However, diastolic and mean pressures would decrease, and as a consequence disadvantages may arise because of possible reduction in both coronary arterial perfusion pressure and coronary blood flow. The perfusion pressure gradient across the left ventricular wall (diastolic blood pressure-left ventricular end-diastolic pressure) becomes progressively lower the more preload is elevated and the more afterload is reduced, and as a consequence the myocardial blood flow (and oxygen supply) may deteriorate and the left ventricular wall (most prominently endocardially) may begin to suffer because of lack of oxygen. Wyatt et al.29 have indeed shown that the myocardial oxygen supply-demand ratio becomes more favorable if afterload is increased rather than decreased. Chiariello et al.24 have shown that NP increases the electrocardiographic ischemic injury in patients with acute myocardial infarction, while Awan et al.26 have shown NP to decrease the injury. During the present investigation, there was no clinical sign of any decrease in myocardial oxygen supply. At constant filling pressure NP produced an enhancement of left ventricular pump performance equal to that caused by a 7 mm Hg increase in PCWP.
Stinson et al. observed that NP infusion and preload restoration within 2 hours after aortic-coronary bypass grafting in patients with an MAP of over 100 mm Hg caused simple downward and upward displacement of LVSWI upon a theoretically single function curve. Our preoperative measurements revealed a similar situation, because at constant PCWP level the mean 13% reduction of the pressure component of LVSWI (MAP-PCWP) and the mean 14% increase in the volume component of LVSWI (SI) resulted in an almost unchanged SWI (87% times 114% is more than 99%). On the other hand, during the postoperative measurements in myocardial performance was moderately or severely reduced in most patients, the decrease in MAP-PCWP (8%) was clearly less than the increase in SI (28%). The product of these changes increased by 18%, which means that at identical filling pressures LVSWI was 18% higher during NP than without. Taken together these results show that LVSWI is increased by NP at constant LVFP only if myocardial function is reduced and the reduction is not due to elevated arterial pressures. As discussed above, the left ventricular volume can be greater during NP infusion than without at identical filling pressure levels. Hence, during the construction of the second function curves the preload levels could have been higher than the control curves. The most favorable effect of NP on LVSWI in failing heart with normal arterial pressures may be due to improved ventricular compliance produced by NP. The enhancement of LVSWI must not be associated with increasing MVO₂, but as discussed above it may be connected with a less favorable oxygen supply-demand ratio.

We used the R-P-P as an indirect indication of MVO₂ instead of tension-time-index, because the latter correlates less well with MVO₂ than R-P-P. When R-P-P as an index of MVO₂ was set against CI, it was found that preoperatively, preload elevation, afterload reduction and preload restoration caused only upward and downward movements along the same MVO₂-CWI curve. This means that when myocardial performance is normal, NP is unable to change MVO₂ from what can be predicted as resulting from total cardiac work. Postoperatively, when myocardial performance was reduced, NP made it possible for the left ventricle to do more work with the same R-P-P; if CI was not changed by NP, R-P-P was reduced. This means 1) NP decreases the MVO₂ when both afterload and preload are reduced; and 2) at identical filling pressures, MVO₂ of the failing heart is the same both along the upper ventricular function curve constructed under the influence of NP and along the lower control curve, whether the ordinate is CI, SI, CWI, or LVSWI. If NP changes the myocardial fiber length disproportionately to LVFP, the R-P-P values attained during NP infusions can reflect levels of MVO₂ lower than the actual, because left ventricular volume is one of the important determinants of MVO₂. On the other hand, the possible effects of changing ventricular compliance on MVO₂ are not known; the improved compliance may decrease MVO₂, making the concept of oxygen consumption more complex.

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Chronic Aortic Regurgitation: The Effect of Aortic Valve Replacement on Left Ventricular Volume, Mass and Function

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with the technical assistance of L. M. Woodbury

SUMMARY Serial echocardiographic left ventricular (LV) studies were performed in 19 patients before (preop) and after (postop) aortic valve replacement (AVR) for chronic aortic regurgitation (AR); the effect of AVR on LV volume, mass and function was determined from the echocardiographic data. In the 12 patients who were considered to have successful surgical results, the average LV end-diastolic dimension fell from a preop value of 6.9 ± 0.2 cm to 5.5 ± 0.2 cm (P < 0.01) at the time of the early postop study (seven to 10 days). Muscle cross-sectional area (CSA) derived from dimension and wall thickness data was used as an index of LV muscle mass (preop CSA = 26 ± 1.3 cm²); CSA was unchanged at the early postop study, but subsequently fell to near normal within six months after AVR (20 ± 1 cm², P < 0.01). There was a trend toward improvement in systolic performance by the late postop studies (12+ months). In two out of three patients with postop paravalvular AR, LV dimension increased after an initial fall. Four patients without paravalvular AR failed to show a significant reduction in LV dimension in the postop studies. In this group the preop studies showed a tendency toward a large end-diastolic dimension and decreased fractional shortening, but the single preop parameter which differentiated these four from the successfully treated group was an end-diastolic radius-to-wall thickness (R/Th) ratio ≥ 4.

Thus, successful AVR for chronic AR results in the normalization of LV volume and a decrease in LV muscle mass to near normal. The R/Th ratio has important prognostic value which appears to be independent of fractional shortening in some patients with chronic AR.

OPTIMUM TIMING of valve replacement in patients with chronic left ventricular (LV) volume overload is a difficult and challenging problem. While aortic valve replacement often results in striking symptomatic and hemodynamic improvement in patients with chronic aortic regurgitation, in some instances surgical correction does little to alter the course of the disease. Furthermore, the extent to which clinical improvement is associated with regression of hypertrophy and abnormalities of ventricular function is not known.1-4

The present study was designed to examine the time course of changes in LV volume, mass and systolic performance in patients undergoing aortic valve replacement for chronic aortic regurgitation. In addition, preoperative data were examined in an effort to identify parameters which might predict which patients could expect a good result from surgery and which might not.

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