Clinical Experience With the Percutaneous Hemopump During High-Risk Coronary Angioplasty

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In 1988, Wampler et al[1] described a new catheter-mounted transvalvular left ventricular assist device, intended for surgical placement via the femoral artery. In animal experiments, this pump (Hemopump, 21Fr in outer diameter) had been shown to unload the left ventricle, leading to myocardial protection and hemodynamic stabilization in both cardiogenic shock and regional myocardial ischemia.[2–6] Clinical trials have demonstrated significant hemodynamic improvement in patients with cardiogenic shock[7,8] and in patients undergoing high-risk coronary angioplasty.[9] Recently, a new Hemopump system (Medtronic Inc., Minneapolis, Minnesota) (14Fr in outer diameter, flow rates of 1.5 to 2.2 L/min) has been developed for percutaneous insertion.[10,11] The focus of the present study is to describe the procedural results and short-term follow-up obtained during a multicenter investigation of the 14Fr Hemopump in patients undergoing high-risk coronary angioplasty.

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Patients were enrolled into this multicenter registry from May 1993 to December 1995. Selection criteria were in accordance with those suggested for use of percutaneous cardiopulmonary bypass support in patients undergoing high-risk coronary angioplasty.[12] All patients gave written informed consent to undergo the procedure. The design of the pump and the insertion technique have previously been described.[10] The inflow cannula is positioned across the aortic valve with the inlet residing in the left ventricle and the pump outlet positioned above the aortic valve. During Hemopump operation, the left ventricle is actively decompressed and blood is delivered to the ascending aorta (Figure 1).

Following placement of both the sheath for Hemopump introduction and the contralateral femoral artery sheath for angioplasty, patients received 5,000 to 15,000 U of heparin. Routine premedications consisted of nitrates and aspirin orally. Two patients received catecholamines intravenously. Before placement of the Hemopump, measurements of aortic pressures, pulmonary artery pressures, pulmonary artery wedge pressures, and of cardiac output (thermodilution technique) were performed. Following placement of the Hemopump inside the left ventricle, hemodynamic measurements were repeated during Hemopump operation with maximum pump speed. After these measurements, coronary angioplasty was performed with the Hemopump on maximum pump speed. During angioplasty, aortic pressures were continuously measured using the guiding catheter. Coronary angioplasty was considered successful if the residual stenosis was <50 % in all views. The Hemopump was removed immediately after coronary angioplasty in all patients, except 2. Sheath removal (manual compression and use of a compressor) was delayed for some hours until the activated clotting time was <200 seconds.

All data are expressed as the mean ± SD. To assess statistical significance, the chi-square test was used. Differences were considered statistically significant if the p value was <0.05.

There were 22 men and 10 women (mean age 67 ± 10 years, range 30 to 81). Thirty patients had had prior myocardial infarction. Previous coronary artery bypass graft surgery had been performed in 13 patients. The mean ejection fraction was 26 ± 11% (ejection fraction was $<25\%$ in 21 patients). All patients had functional class III or IV angina pectoris, 31 patients had 2- or 3-vessel coronary artery disease, and 2 patients had undergone left main coronary angioplasty. Mean duration of Hemopump support was 2.1 ± 1.0 hours (range 1.5 to 6.0).

Hemopump support on maximum pump speed led to a decrease in mean pulmonary artery wedge pressure from 15 ± 6 mm Hg to 13 ± 6 mm Hg ($p < 0.001$). Cardiac index. (2.2 ± 0.3 L/min/kg before and 2.3 ± 0.4 L/min/kg during Hemopump use; p = NS), mean aortic pressure (91 ± 13 mm Hg and 92 ± 12 mm Hg; NS), and systolic aortic pressure (124 ± 24 mm Hg and 119 ± 25 mm Hg; p = NS) did not change during support.

Balloon inflation during support led to an increase in mean pulmonary artery wedge pressure from 13 ± 6 mm Hg to 17 ± 7 mm Hg ($p < 0.001$) and a decrease in mean aortic pressure from 92 ± 12 mm Hg to 81 ± 13 mm Hg ($p < 0.001$). Fourteen patients (44%) developed significant hypotension during balloon inflation (defined as a decrease in mean aortic pressure of $\geq$10 mm Hg during supported angioplasty).

In a subgroup of 16 patients, balloon inflations were performed both with and without Hemopump support. In these patients, a decrease in mean pulmonary artery wedge pressure from 23 ± 6 mm Hg (without support) to 15 ± 7 mm Hg (with support) ($p < 0.001$) was observed during balloon inflation, indi-

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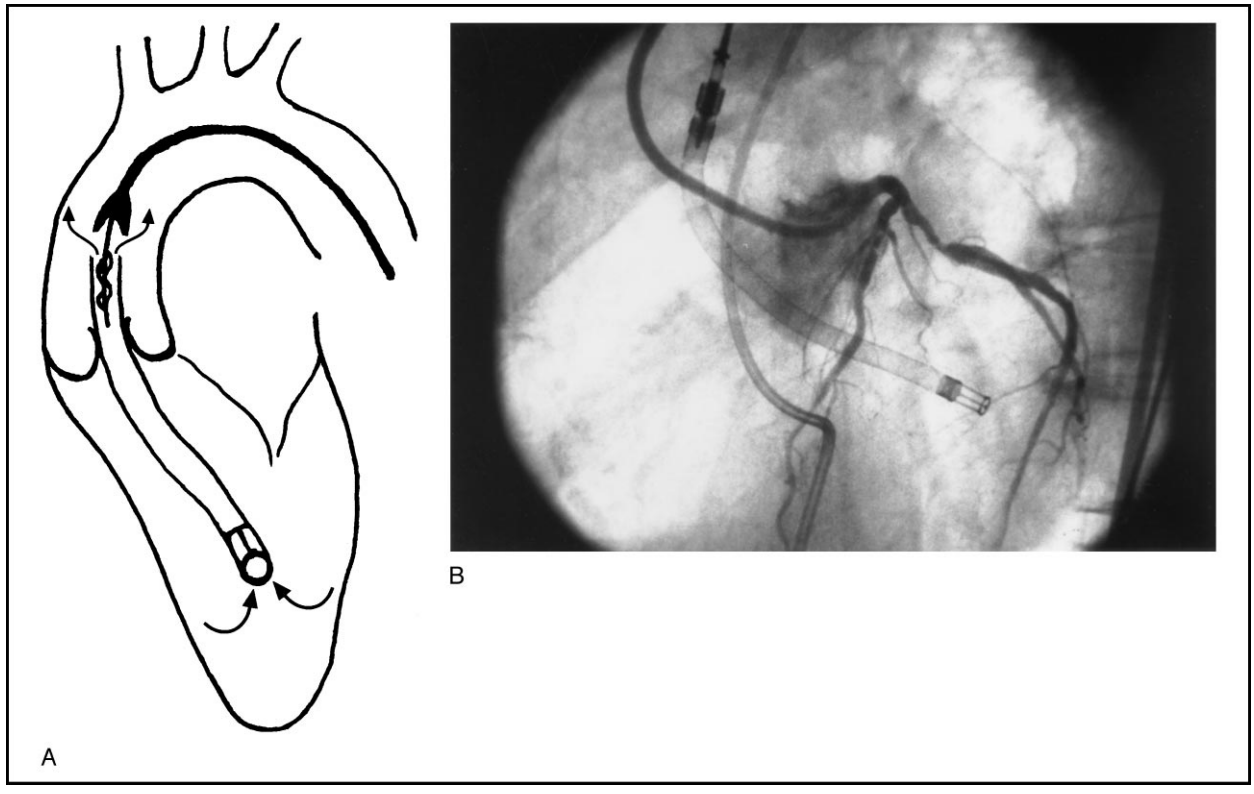

FIGURE 1. *A*, schematic diagram showing Hemopump inflow cannula in the left ventricle and body of flow rotary pump with lateral outflow 3 to 4 cm above the aortic valve. *B*, left coronary angiography during percutaneous transluminal coronary angioplasty (56-year-old patient): Hemopump inflow cannula within the left ventricle and pump body with lateral outflow in the ascending aorta (60° left anterior oblique position).

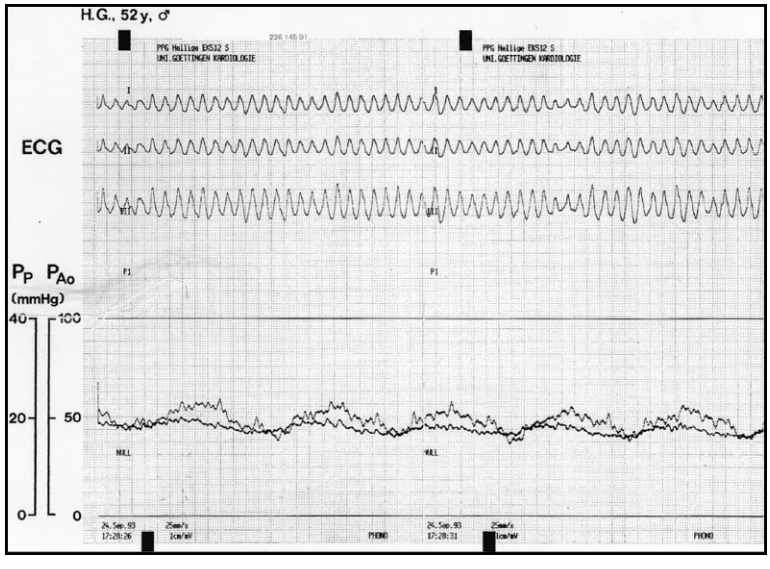

FIGURE 2. Original registration of electrocardiography (ECG; leads I to III), pulmonary pressure (P_P), and aortic pressure (P_{Ao}) in a 52-year-old man with Hemopump support during ventricular fibrillation.

cating Hemopump-related left ventricular unloading during ischemia. Simultaneously assistance led to an increase in mean aortic pressure from 79 ± 16 mm Hg (without) to 84 ± 10 mm Hg (with Hemopump) during balloon inflation (p = NS).

Three patients experienced periprocedural cardiac arrest. In these patients, mean aortic pressures were maintained at 45 to 50 mm Hg with Hemopump support during cardiac arrest and ventricular fibrillation was corrected by electrical cardioversion (Figure 2).

Multivessel coronary angioplasty was performed in 13 of the 32 patients. Successful balloon dilation was achieved in 46 of 50 vessels in which it was attempted. Stent implantation was performed in 6 patients and rotablation in 2 patients. Symptomatic improvement occurred in all of the 28 patients surviving hospitalization.

Limb ischemia, which was defined as leg pain, livid colored leg, coolness, or no palpable peripheral pulses of the limb ipsilateral to the Hemopump, occurred in 5 patients (16%). Ischemia resolved in all these patients after removal of the sheath. Two other patients developed femoral artery occlusion following removal of the sheath, necessitating surgical repair. One of these patients died after surgery.

A decrease in the hemoglobin value of >2 g% occurred in a total of 8 patients (25%); 4 patients required blood transfusion. In a subgroup of 9 pa-

tients, hemolysis parameters were analyzed before Hemopump support, immediately after assistance (mean operation time was 2.6 ± 1.1 hours), and 24 hours after the start of Hemopump operation. Plasma-free hemoglobin rose from 4.9 ± 2.8 mg/dl to 30.0 ± 21.7 mg/dl (normal range 0 to 10; $p < 0.001$). Simultaneously, there was a decrease in haptoglobin levels from 1.3 ± 0.9 g/L to 0.7 ± 0.5 g/L (normal range: 0.5 to 2.0; p = NS), and an increase in lactate dehydrogenase from 163 ± 35 U/L to 301 ± 103 U/L (normal range 90 to 200) ($p < 0.001$) immediately after assistance. Platelet counts showed a significant but mild decrease after Hemopump support (254 ± 105 before, and 232 ± 92 × 10^9/L after 24 hours; normal range 150 to 350; $p < 0.001$) in these patients.

The overall hospital mortality rate was 12.5% (4 of 32 patients). Two patients died of cardiogenic shock following reocclusion of the angioplasty vessel 1 and 3 hours after removal of the pump. One patient died after surgery for vascular repair after femoral occlusion and one 80-year old patient died 3 days after coronary angioplasty because of periprocedural stroke. Based on autopsy, ischemic stroke very likely was related to both a preexisting high-grade stenosis of the supplying left middle cerebral artery and prolonged cerebral hypoperfusion during the angioplasty maneuvers (balloon inflation had resulted in marked hemodynamic compromise with a decrease in systolic aortic pressure from 130 to 65 mm Hg in this patient). There was no histologic evidence of embolic material. Thus, procedure-related embolization of atheromatous or thrombotic material from the aorta or from the pump has been assessed to be unlikely.

Patients were followed for 12 to 36 months after discharge. An additional interventional procedure during subsequent hospitalization was required in 6 patients (1 required surgical repair for femoral artery stenosis 4 weeks after Hemopump, 4 patients underwent angioplasty, and 1 underwent bypass surgery). One patient died 10 days after coronary artery bypass grafting (8 month after Hemopump support). Three other patients died 2 and 14 months after discharge.

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The results of the present multicenter registry of supported coronary angioplasty demonstrate the beneficial effects of the percutaneous Hemopump during balloon inflation. First, in the subgroup of 16 patients in whom balloon inflation was performed both with and without Hemopump support, a decrease in mean pulmonary artery wedge pressure was observed during supported angioplasty, indicating Hemopump-related left ventricular unloading. Second, in each of the 3 patients with periprocedural cardiac arrest, mean aortic pressures of about 50 mm Hg were observed during ventricular fibrillation with Hemopump support. This level of stabilization during cardiac arrest should allow for revascularization maneuvers in case of angioplasty-related vessel closure in high-risk patients. In addition, the pump was easy to insert, safe during the procedure, and its use was not associated with major rhythm instability.

On the other hand, there were some significant procedure-related problems limiting the beneficial effects. First, introduction sheath-related leg ischemia occurred in 16% of patients. In 2 patients, removal of the sheath was followed by femoral artery occlusion. This complication was associated with the perioperative death of 1 patient. Second, in the present study we found a mortality rate of 12.5%, which is higher than that reported in other studies with supported high-risk coronary angioplasty.[12–15] On the one hand, this may be due to the unfavorable condition of these critically ill patients, however, on the other hand, it may reflect the high risk of the procedure per se. In 2 patients, both of whom died within a few hours after removal of the pump, death was probably due to postinterventional closure of the angioplasty vessel. This appears to be a central problem when using circulatory support during coronary angioplasty of critical lesions in general, and therefore, closure of the angioplasty vessel is not specifically related to the Hemopump.

Our preliminary experience suggests that the 14Fr percutaneous Hemopump device may be useful for selected patients undergoing high-risk coronary angioplasty, because it unloads the left ventricle and maintains cardiac output with mean aortic pressures of nearly 50 mm Hg during cardiac arrest. Because of the significant procedure-related morbidity rate, however, its application should be limited to patients in whom prior attempts of coronary angioplasty have led to immediate and severe hemodynamic compromise and to critically ill patients in whom careful risk stratification indicated a high probability of hemodynamic collapse in case of vessel closure.

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Effects of Changing the Availability of the Substrate for Nitric Oxide Synthase by L-Arginine Administration on Coronary Vasomotor Tone in Angina Patients With Angiographically Narrowed and in Patients With Normal Coronary Arteries

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Nitric oxide is a major component of the endothelium-derived relaxation factor and is synthesized from the amino acid L-arginine by nitric oxide synthase enzymes.[1] Its synthesis can be specifically and competitively antagonized by arginine analogs, such as N^G-monomethyl-L-arginine (LNMMA), which inhibit the enzymatic pathway in a process that can be reversed by increased availability of L-arginine.[2–4] Inhibition of nitric oxide synthesis with LNMMA has been shown to cause a decrease in the basal diameter of the distal segments of angiographically normal and diseased epicardial coronary arteries and coronary stenoses; it also contributes to the vasomotor tone of coronary resistance vessels.[5–8] It has been also shown that infusion of L-arginine into the brachial artery augments endothelium-dependent forearm vasodilation and reverses the defective endothelium-dependent vasodilation associated with an elevated plasma low-density lipoprotein level or hypercholesterolemia.[9–12] L-arginine administration improves the coronary blood flow response to acetylcholine in patients with normal coronary arteries and hypercholesterolemia,[13] enhances nitric oxide generation, and inhibits lesion formation after balloon angioplasty.[14] In hypercholesterolemic animals L-arginine administration prevents xanthoma development and inhibits atherosclerosis.[15–17] In the present study, we examined the effects of changing the substrate levels for nitric oxide synthase on coronary artery tone in patients with "normal" angiograms and in patients with coronary artery disease.

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Nine patients (8 men, 1 woman, mean age 57 ± 6 years) with chronic stable angina, coronary artery disease, and a positive treadmill exercise test result (≥0.1 mV ST-segment depression) between 5 and 7 METs using the modified Bruce protocol, and 6 patients (4 men, 2 women, mean age 54 ± 11 years) with atypical chest pain, risk factors for atherosclerosis, and "normal" coronary arteriograms were studied. These "normal" coronary arteries had a smooth angiographic outline in multiple projections with no irregularity or stenosis. Patients were excluded from the study if they had diabetes mellitus, recent myocardial infarction (<6 months), left ventricular hypertrophy (on echocardiography), left ventricular dysfunction (left ventricular ejection fraction <50%), or valvular heart disease. Antianginal medication was discontinued 24 hours before the study. The patients were allowed to use sublingual nitroglycerin as necessary, but no study was performed within 3 hours of its administration. The protocol was approved by the Research Ethics Committee and each patient gave written informed consent.

Following the diagnostic coronary angiogram, an optimal radiographic projection was selected and kept constant for subsequent angiograms. Two electrocardiographic leads were monitored continuously throughout the study. The following sequence of intracoronary infusions was administered in both groups: 0.9% saline (2 ml/min) for 2 minutes, 5.6 and 27.8 pmol/min of substance P in saline for 5 minutes each, 8 and 16 μmol/min of LNMMA in saline for 5 minutes each, and 50 μmol/min L-arginine for 8 minutes, using a syringe pump. Finally, an intracoronary bolus dose of nitroglycerin (250 μg in 2 ml of saline) was administered. Femoral arterial pressure and heart rate were recorded during the last 30 seconds of each infusion period. Angiography was performed with a