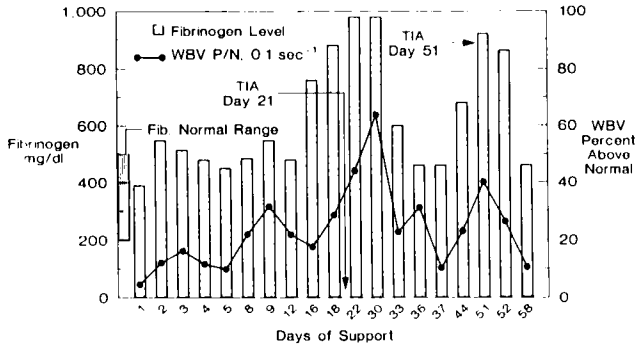

Figure 9. Plasma fibrinogen concentration and relative WBV at shear rate of 0.1 sec $^{-1}$ during Novacor support of Patient 2.

9, on which both were moderately increased, as shown in **Figure 9.** Patient 2 had significant increases in both plasma fibrinogen (820 + 85 mg/dl) and relative WBV (39% above normal) surrounding an incidence of neurologic deficit, which occurred on days 21–22. He suffered a second episode on day 51, coincident again with sharp rises in both plasma fibrinogen and relative WBV, with values of 920 mg/dl and 40% above normal, respectively. In addition, erythrocyte rigidity for this patient was quite high throughout the entire transplant period, ranging from 32–82% above normal.

Conclusions

Our studies indicate an association between abnormal hemorrheology and the occurrence of neurologic problems in artificial heart patients. The existence of these abnormalities and/or peaks prior to the clinical events indicate that they contributed to the patients' neurologic problems, and that improving the patients' hemorrheology may be a beneficial treatment avenue to pursue.

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The Real Impact of Mechanical Bridge Strategy in Patients with Severe Acute Infarction

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Results obtained in the past 3 years in patients referred with acute myocardial infarction (AMI) and cardiogenic shock for a mechanical bridge to urgent transplantation permit one to assess the real impact of the present strategy in clinical practice.

Ten patients (mean age = 49) were admitted in serious condition (CI = 1.8 ± 0.2 L/min/m^2, PCWP = 28 ± 6 mmHg, systolic aortic pressure = 88 ± 20 mmHg, urine output 11 ± 20 ml/hr) and were treated by maximal sympathomimetic support and i.v. enoximone. Two had to be implanted with a total artificial heart (TAH) and one with a left ventricular assist device (LVAD) for recurrent fibrillation despite hemodynamic improvement, within 8 hr. Two have received transplants and are living well after 20 months. Seven who initially improved markedly have been listed as urgent transplant candidates: two of these have been successfully transplanted, and three died suddenly after 6, 25, and 45 days, respectively. One has undergone successful coronary surgery. One patient (age 62, diabetic) was secondarily rejected for a transplant and died.

This experience clearly shows that despite initial spectacular hemodynamic improvement, which was due to opti-

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mized medical management, death rate before transplant because of sudden ventricular fibrillation remains unacceptably high. This should prompt early mechanical support, with less invasive systems, in patients with AMI.
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Cardiac transplantation in patients in cardiogenic shock is a lifesaving procedure which nevertheless carries a high risk of postoperative death. It may be performed either immediately or, in case of no donor graft availability, after a period of mechanical circulatory support (mechanical bridge)[1] or i.v. infusion of potent inotropic agents, such as phosphodiesterase inhibitors (pharmacologic bridge).[2] It appears, in many circumstances, to be a last chance procedure, which cannot be refused for obvious ethical reasons to patients in a desperate condition, as soon as they meet the usual criteria for heart transplantation (age < 65, pulmonary vascular resistance in the normal range, and lack of associated pathologic process).

Evaluation of the results of the bridge to transplantation strategy, in patients referred with an acute myocardial infarction (AMI) in cardiogenic shock who are potential candidates for cardiac transplantation, has been carried out since 1987 in a prospective fashion.

Protocol

The protocol was as follows: At the time of admission, the patients in cardiogenic shock complicating a recent (<3 weeks) AMI were immediately admitted to the intensive care unit (ICU) at the Henri Mondor hospital for complete hemodynamic evaluation (heart rate; systemic arterial, pulmonary arterial, and capillary wedge pressures; and cardiac index). Diuresis was monitored hourly. 2D Doppler echocardiographic examination was performed to evaluate the extent of akinetic myocardium. The treatment included optimal oxygen therapy, with eventual tracheal mechanical ventilation, optimal fluid balance, and sympathomimetics at maximal dose. The patients entering the protocol were those who did not improve despite this tailored medical therapy and were considered, *a priori*, as good candidates for immediate transplant. All met the criteria for immediate implantation of a mechanical circulatory support system, i.e., aortic systolic pressure < 80 mmHg; pulmonary wedge pressure > 25 mmHg; cardiac index < 2 L/min/m^2, urine output < 10 ml/hr, and no obvious contraindication to transplantation present. Patient and family consent for a cardiac transplant following a Jarvik 70 or a Symbion VAD was obtained.

At that stage, i.v. enoximone was administered according to our previously described protocol.[2] Clinical, electric, and hemodynamic parameters were monitored bi-hourly. In case of marked and continuous improvement, the decision to implant a mechanical device was postponed, and a transplant performed on the basis of maximal priority. Obviously, the decision could be changed immediately in case of either non-improvement, or rapid or progressive deterioration.

Clinical Experience

From 1987 to 1989, 10 patients entered the protocol. They were a minimal fraction of the total number of AMI patients admitted to the ICU during that period. Patients with ventricular septal rupture were excluded, while patients with functional mitral insufficiency were accepted.

Mean age was 49 ± 7 (40–62), all were men, and 6 had a history of previous infarct. The recent history started a mean of 2.5 days prior to admission (0–14) with an anterior infarction in 9 patients and a circumferential infarction in 1 patient. Seven patients received i.v. streptokinase within 4 hours (mean) following the first symptom. One patient, with no evidence of reperfusion, was treated successfully by early (<12 hr) PTCA. At time of admission, the clinical and hemodynamic signs confirmed the severity of the shock, despite optimal therapy **(Figure 1).** Enoximone was given by i.v. bolus, over 10 minutes. Thirty minutes later, the decision to perform an immediate implant was taken if hemodynamic indices were not improved, diuresis not increased, or if the risk of ventricular fibrillation, with ventricular tachycardia, caused us to expect major problems. The extent of the myocardial lesions and echocardiographic evaluation of right ventricular function facilitated selection of a Jarvik versus an IVAD.

Three patients received implants. Seven patients improved markedly in the first hours, and a rapid search for contraindication for transplantation was performed. Indication was confirmed in 6. The last patient, borderline because of his age (62) and physical condition (diabetes), was refused a transplant; he died within 3 days.

Evolution

Of the patients who had a device implanted, 2 improved rapidly, one with a Jarvik 70, one with an IVAD. The second

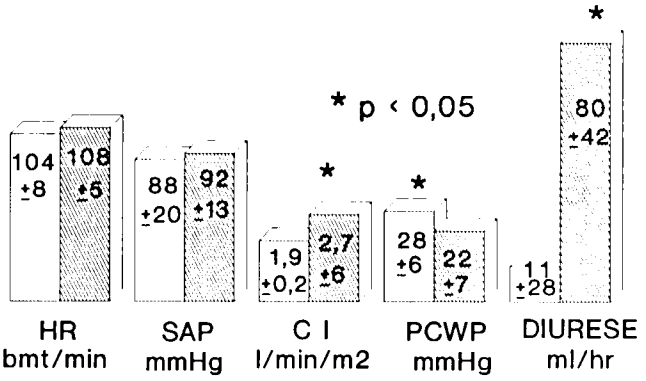

Figure 1. Hemodynamic indices and urine output at time of admission to ICU, with maximal sympathomimetic therapy (left column), and following i.v. enoximone bolus (right column) (HR: heart rate, SAP: systolic radial artery pressure, CI: cardiac index, PCWP: pulmonary capillary wedge pressure).

patient on a Jarvik initially improved dramatically, and was awake, with normal indices. After day 3, he developed a major drop in vasomotor tone, unresponsive to medical therapy and unexplained by any septic complication. This led to an impossible situation with an increasing flow, a low pressure, and progressive renal and cerebral deterioration. No evidence of sepsis could ever be found.

The 2 other patients were transplanted successfully, after 2 and 3 days, respectively. They are still doing well after 21 and 18 months, respectively.

The six patients greatly improved by i.v. enoximone were placed on the transplant list as maximal priority candidates. No graft could be obtained for two. They died at days 6 and 25, respectively. This last patient required a rare donor: group B, 100 kg body weight. Furthermore, a permanent fever (39° C), unexplained by numerous sterile blood and sputum cultures, was considered as a temporary contraindication for a Jarvik device. He was nevertheless unsuccessfully implanted with a Jarvik, for recurrent ventricular fibrillation. A third patient who stabilized, was given oral enoximone therapy and sent back home; he died suddenly at day 45. In the 3 others, the necessity for urgent transplantation disappeared. Two were transplanted on an elective basis, and aorto-coronary grafts were performed in the third. Decisions for transplantation or coronary reperfusion were based on the results of isotopic myocardial redistribution, under pharmacologic testing. Ejection fractions in these 3 patients were all 18%. They are doing well at 1 year; the 2 transplanted are free of any symptoms, while the third, with a CABG, is NYHA class II, with an ejection fraction increased to 35%.

In summary, 5 patients (50%) have benefitted from aggressive therapy and are long-term survivors, 2 with a transplant following mechanical support, 2 with elective transplantation, and 1 after bypass surgery. Deterioration under maximal medical therapy was due to arrhythmias.

Discussion

Implantation of a mechanical device (mechanical bridge), or i.v. phosphodiesterase inhibitor therapy (pharmacologic bridge) have been shown to permit survival in patients referred in cardiogenic shock, who are otherwise good candidates for transplantation, until a graft is available. The present study of acute ischemic patients clearly emphasizes the extremely high risk of sudden death under optimal intravenous therapy, the temporary nature of the clinical improvement initially achieved by the most recent inotropic drugs, and the rather infrequent evolution toward myocardial recovery.

Sudden death may occur independent of the extent of hemodynamic improvement, at any time in the evolution. It occurred, in our group of 10 patients, either initially or after a few days, with the patient still in the ICU or after discharge, when a marked improvement in pressures and cardiac index suggested that cardiac transplantation itself could be postponed. The acute arrhythmias occurred in each patient suddenly, and could not be reversed by cardioversion. This high risk of sudden death should consequently prompt the decision to implant a mechanical device as soon as the lack of major contraindications for transplantation has been recognized. This risk of rapid and sudden failure of pharmacologic support, which was not observed in our previous studies,[2] is nevertheless not a surprise when the patient selection of acute ischemic cases is recalled.

A second observation deals with the infrequent recovery of adequate myocardial function under maximal medical therapy. Despite the early management of the patient, early thrombolysis, and pharmacologic support, prolonged improvement in myocardial function has been observed in only 3 patients, and in 2, the extent of the recovery was rather limited and did not provide sufficient quality of life after a few weeks. In only 1 patient of the 10 entering the protocol, did isotopic myocardial studies after 3 months show the persistence of a significant mass of viable ischemic myocardium. This patient's ejection fraction was markedly improved after complete coronary revascularization.

The results obtained in the present study based on both mechanical and pharmacologic bridges compares favorably with the world experience with the Jarvik and bi-VAD bridge in unselected patients. The recent report (April 1990) of the ASAIO ISHT Registry shows an overall success rate of 34% in 178 TAH cases, and a 42% survival rate after a bi VAD bridge to transplantation. These data confirm the value of a careful selection process of candidates for mechanical bridge, and the benefits one may obtain from alternative strategy, in terms of both clinical efficacy and cost.

Nevertheless, the observation of both a high risk of sudden death, despite significant clinical and hemodynamic improvement, and the scarcity of myocardial recovery, lead us to suggest that cardiac transplantation gives the highest chances for survival in patients with AMI who are referred in cardiogenic shock. This conclusion should prompt the development of less invasive techniques of mechanical support.

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