Long-Term Clinical Use of the Novacor Left Ventricular Assist Device as a Bridge to Transplantation

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Abstract

The Novacor left ventricular assist device (NLVAD) is an implantable, electrically powered, pulsatile circulatory assist device undergoing clinical investigation. This report reviews the 33-day bridge-to-transplant course of a patient presenting in cardiogenic shock after acute myocardial infarction who could not be weaned from cardiopulmonary bypass following emergency coronary artery revascularization.

Cardiac output was satisfactory during the entire 33-day period: 4.2 ± 0.8 l/min (± SD) during the first week and 6.3 ± 0.9 thereafter. Haptoglobin remained low (30 ± 4 mg%), suggesting mild hemolysis, but plasma hemoglobin remained normal throughout and the patient required only 600 ml of blood after the first two postoperative days. Renal impairment (peak creatinine = 2.9 mg/dl on day three) was attributed to preoperative hypotension and resolved by day seven. The clinical course included pneumonia and hypoxic encephalopathy, both of which resolved. There were no thromboembolic complications or device-related infections. The patient underwent orthotopic cardiac transplantation on day 33.

This case demonstrates the long term clinical efficacy and safety of the NLVAD in the setting of cardiogenic shock after massive myocardial infarction as a bridge-to-transplant support system.

Introduction

Heart transplantation is appropriate, effective therapy for carefully selected patients with end-stage heart disease.[1] The unpredictability of hemodynamic deterioration coupled with the scarcity and equally unpredictable availability of donor hearts leave many candidates to die as they wait for transplantation.

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In the event of hemodynamic compromise during the waiting period for a donor heart, circulatory support can be maintained by a ventricular assist device, which is an accessory, prosthetic ventricle that assumes the work of the diseased ventricle.[2,3,4]

The purpose of this report is to review the 33-day performance of the only electrical, left ventricular assist device designed for permanent implantation currently approved for clinical use under Food and Drug Administration investigational protocol as a bridge to transplantation.

Materials and Methods

Protocols and Consents

In accordance with federal regulations and Investigational Device Exemption, permission for clinical use of the system was obtained from the Food and Drug Administration and from the Institutional Review Board of Vanderbilt University Medical Center. Informed consent was obtained from the patient's next of kin when all conventional therapy had been exhausted. The patient had no known contraindication to cardiac transplantation.

Description of Device

The Novacor Left Ventricular Assist Device (NLVAD)[a] is an electrically powered, mechanically actuated, pulsatile device which weighs approximately 0.78 kgs.[5,6] Although it has been designed for eventual permanent implantation, current clinical use is restricted to temporary placement as a bridge to transplantation or to postcardiotomy recovery.

The NLVAD is capable of producing a stroke volume of 72 ml and provides accurate, responsive tracking at heart rates up to 240 beats per minute.[7]

The operating cycle of the pump mechanism is illustrated in Figure 1. The one-piece, seamless polyurethane pump sac is filled passively via a vascular conduit (Figure 1, Panel A). Dual pusher plates are bonded to opposing sides of the pump sac, providing

a Novacor Medical Corporation, Inc., Oakland, CA 94621

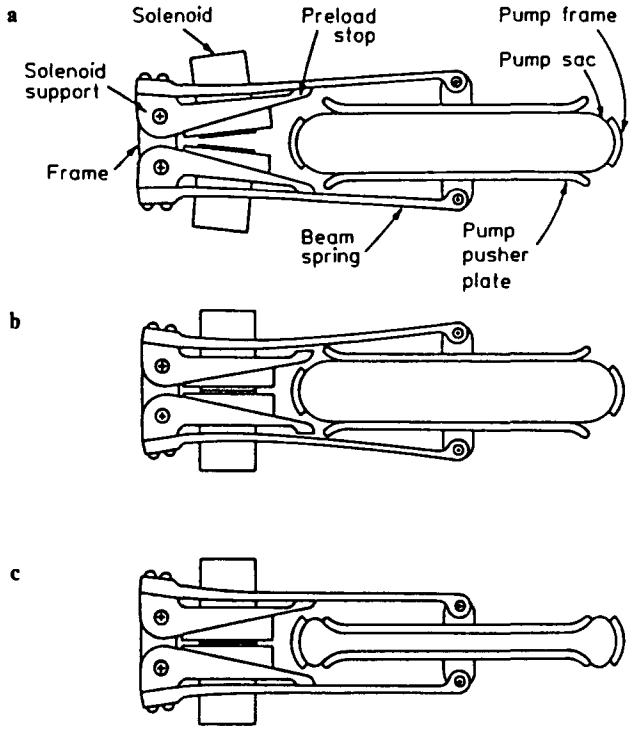

Figure 1. The energy converter operating cycle.
Panel A. Pump filled
Panel B. Solenoid closed and magnetically latched; start of ejection stroke
Panel C. End of ejection stroke

symmetrical deformation. Upon detection of a decrease in filling rate as sensed by position transducers within the pump, ejection is initiated. Solenoid closure transfers energy to the beam springs and in turn to the pusher plate mechanism (Figure 1, Panel B).[8] Blood is then ejected from the pump through a one-way valve in the outflow conduit (Figure 1, Panel C). Solenoid unlatching or deenergizing allows repetition of the entire cycle. The pump operates in synchronous counterpulsation with the heart.

The device is powered by an extracorporeal console consisting of a microprocessor, uninterruptable power supply, CRT terminal that displays beat by beat systems operation data, oscilloscope and physiologic monitor. Power and microprocessor control circuits are fully redundant.

As shown in Figure 2, the blood pump is implanted in the left upper quadrant subcutaneously, receiving inflow from the left ventricular apex. Blood is pumped into the ascending aorta via the outflow graft. Two pericardial valves are positioned at the junctions of the device with the inflow and outflow conduits. The external console is connected to the device by a single vent tube containing control and power cables.

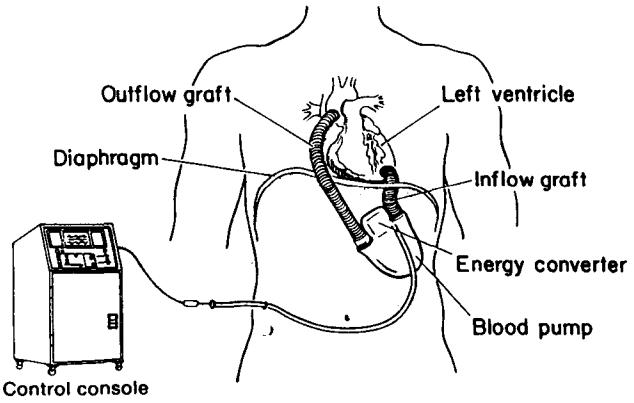

Figure 2. Novacor left ventricular assist system configuration. Device in left upper abdominal quadrant with percutaneous attachment to extracorporeal controller.

Patient Experience

A 47-year-old man was presented to another facility with severe chest pain, hypotension, and electrocardiographic changes of left ventricular ischemia. He was transported by helicopter to Vanderbilt University Medical Center and was taken directly to the catheterization laboratory where an intra-aortic balloon was placed. Two episodes of ventricular fibrillation each required external cardiac massage for resuscitation. Angiography documented an occluded left main coronary artery and a patent right coronary artery.

The patient underwent emergency coronary artery bypass revascularization to the left anterior descending artery and the first obtuse marginal artery. He could not be weaned from bypass in spite of maximal inotropic and intra-aortic balloon pump support. Consent was obtained, and the left ventricular assist device was implanted.

Implantation

A 22 mm Dacron graft was anastomosed to the ascending aorta, and the subcutaneous pocket was developed in the left upper quadrant. An elastomer sewing ring was sutured to the apex of the left ventricle and then connected to a 22 mm Dacron inflow graft. This conduit was tunneled beneath the costal margin through the diaphragm and attached to the blood pump (Figure 2). The pump was then connected to the outflow graft, air was evacuated, and the operation of the pump was begun. The patient was weaned from cardiopulmonary bypass with a flow of 4 L/min.

A Millar pressure transducer was inserted into the left ventricular cavity and a left atrial line placed through the right superior pulmonary vein. The transcutane-

ous cable was tunneled subcutaneously to exit adjacent to the right anterior superior iliac spine.

Postoperative Monitoring

Postoperative monitoring included left ventricular end-diastolic pressure as well as right and left atrial pressures. Cardiac outputs were determined from electronic calculations of stroke volume of the device. These measures correlated accurately with thermodilution cardiac outputs obtained during the first two postoperative days. Low dose dopamine and isoproterenol were maintained during the first week.

The anticoagulation regimen consisted of dextran 40 for 48 hours and dipyridamole thereafter, and sufficient intravenous heparin was administered to maintain the partial thromboplastin time at 1.5 times normal.

The left ventricular assist system operator was present during the entire 33-day course.

Results

Hemodynamic Functions

The pump output, which corresponds to the cardiac output, is summarized in Figure 3, panel A. Cardiac output immediately following implantation was 4.0 L/min, increasing to 4.5 L/min six hours after operation and remaining at that level for the first week. During the remaining weeks of support, the cardiac output remained in the six to seven L/min range.

Mean arterial pressure (Figure 3, Panel B) remained above 65 mmHg during the first week, increasing to a steady state of 80 mmHg thereafter.

Left atrial pressures, as well as left ventricular end-diastolic pressures, were monitored during the first week. The left ventricular end-diastolic pressure approximated that of the left atrial pressure. The right and left atrial pressures are depicted in Figure 3, Panel C. The right atrial pressure remained at approximately 17 mmHg during the first week, and approximately 14 mmHg thereafter.

Between day 2 and 4, the right atrial pressure was higher than the left atrial pressure, and a patent foramen ovale was confirmed by a bubble echocardiogram study. The shunt and associated hypoxia resolved by day 5.

Renal Function

As illustrated in Figure 4, Panel A, adequate urine output was achieved throughout the postoperative course. The patient's creatinine, which had been 1.1 mg/dl preoperatively, increased to 2.9 mg/dl on the third day. This deterioration in renal function was attributed to cardiogenic shock prior to implantation. By day 5 the serum creatinine had returned to normal. (Figure 4, Panel B)

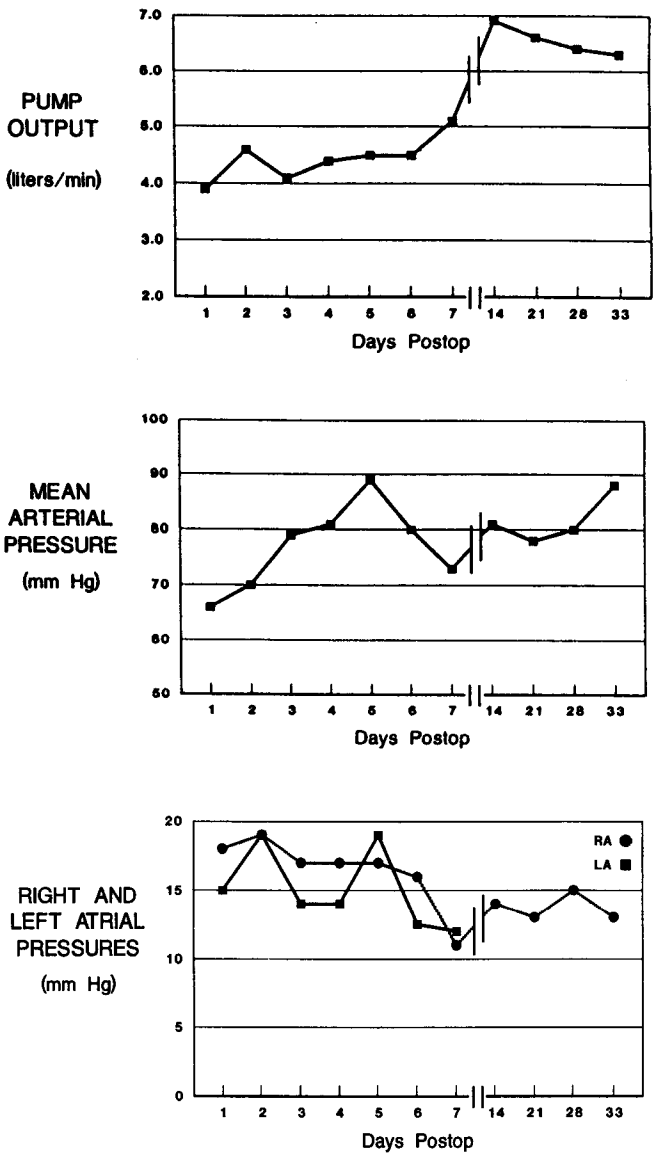

Figure 3. Hemodynamic parameters.
Panel A. Pump output
Panel B. Mean arterial pressure
Panel C. Right and left atrial pressures

Creatinine clearance, which was 50 ml/min on the fourth day, increased to 86 ml/min on day 11. For the remainder of the 33-day circulatory support period, renal function was normal.

Hemotologic Parameters

Figure 5 summarizes several of the hemotologic parameters monitored. Hematocrit was maintained in a satisfactory range throughout the support period. (Figure 5, Panel A) The patient was given 1200 ml of blood during the initial operation of coronary artery bypass grafting and implantation of the device. The

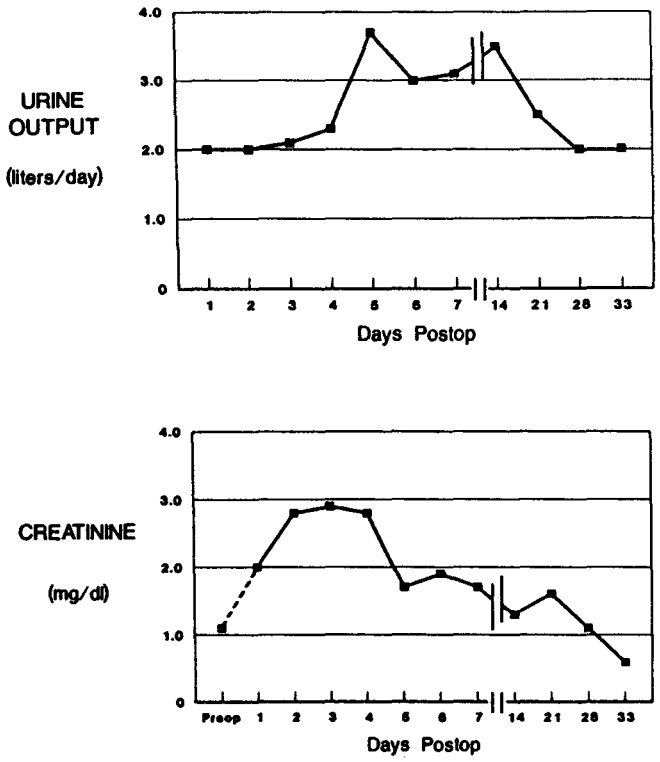

Figure 4. Renal parameters.
Panel A. Urine output
Panel B. Creatinine

total cardiopulmonary bypass time was 267 minutes. He was given an additional 600 ml of packed red blood cells during the first four days, requiring no transfusions thereafter.

Plasma free hemoglobin (Figure 5, Panel B) fell from 33 mg/dl on the first postoperative day to 0.8 mg/dl on the second day, remaining normal thereafter.

Platelet count (Figure 5, Panel C) remained approximately 100,000 during the first week, increasing during the third week at a time when a staphylococcus lung infection was diagnosed. Fibrinogen (Figure 5, Panel D) increased each day during the first five days. Over the next two weeks, the fibrinogen level fell towards normal, increasing again on the twenty-eighth postoperative day. Fibrin split products were normal throughout the postoperative period. Serum haptoglobin remained below normal (range 19 to 60 mg/dl) throughout the circulatory support course.

Postoperative Clinic Course

The patient had two clinical infections, both of pulmonary etiology. The first, an haemophilus influenza infection, occurred during the first week. During the fourth week the patient developed a staphylococcus aureus pneumonia which resolved with appropriate

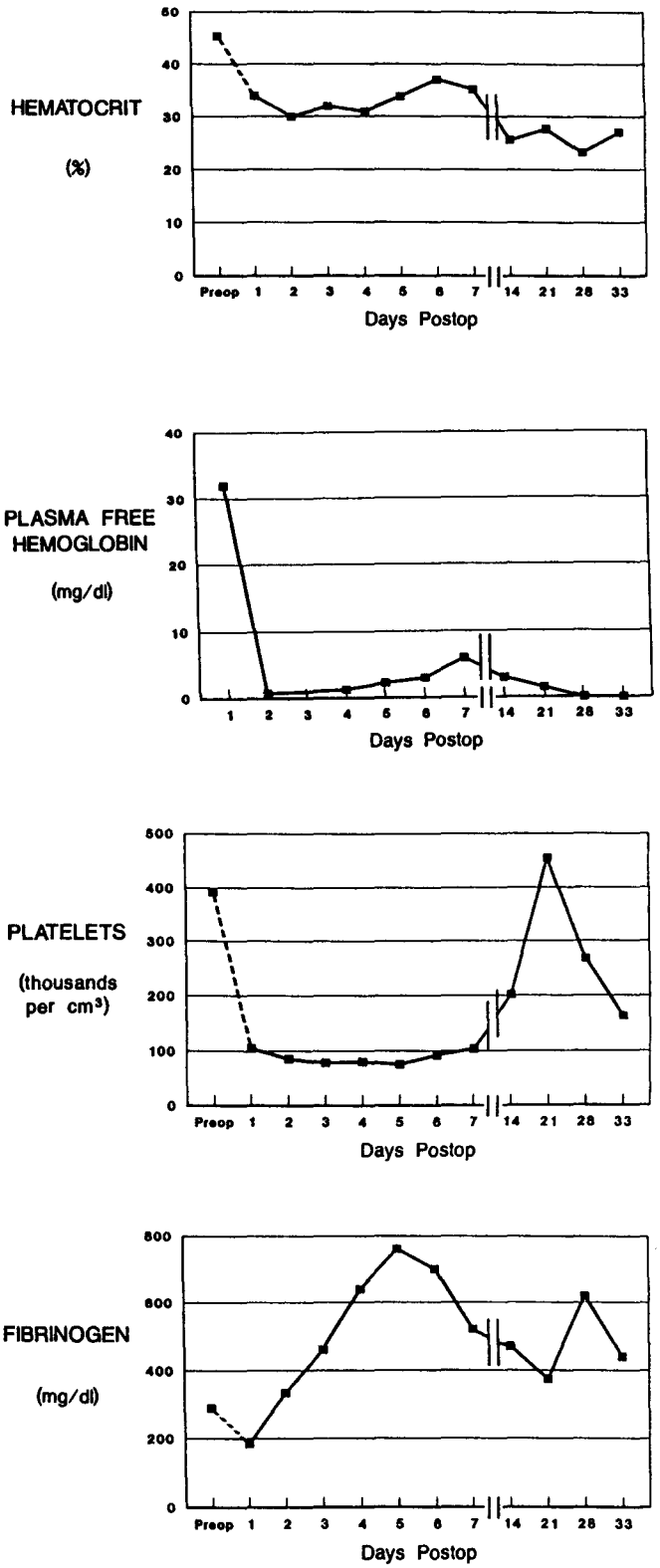

Figure 5. Hematologic parameters.
Panel A. Hematocrit
Panel B. Plasma free hemoglobin
Panel C. Platelets
Panel D. Fibrinogen

antibiotic treatment. It is important to note that there was no infection associated with the device or the transcutaneous line.

The patient had a cerebellar infarction documented by CT scan. It was attributed to the hypotensive preoperative course. He underwent cardiac transplantation on the thirty-third day. The ischemic time on the donor heart was four hours and five minutes. The patient died of graft failure.

Post-explant examination of the blood pump revealed smooth, normal blood contact surfaces with no evidence of thrombosis. There was a 3 × 4 × 2 mm fibrinous collection in the conduit just above the inflow valve. At autopsy, there was no evidence of embolic damage in any end organ, including the brain, kidneys, and spleen. There was evidence of a cerebellar infarction in the region supplied by severely atherosclerotic vessels.

Discussion

These results demonstrate that the NLVAD is a safe and clinically effective means to support the circulation as a bridge to transplantation in the setting of cardiogenic shock after massive myocardial infarction and coronary artery revascularization.

The NLVAD clearly provided sufficient cardiac output to resolve the early transient renal failure and provided satisfactory end-organ perfusion.

Thromboembolism is a major risk with prosthetic ventricles and hearts.[9] In this case, both post-explant examination of the blood pump and autopsy findings of organs confirmed no evidence of this potential problem. The cerebellar infarction occurred in a region distal to severe atherosclerosis.

Although the low haptoglobin suggested ongoing low-grade hemolysis, minimal transfusions were required after the first two days, and hematocrit and hemoglobin levels remained essentially constant. There were no complications associated with the anticoagulation regimen.

It is important to note that neither of the two observed clinical infections were device-related. The exit site of the transcutaneous lead remained infection free. The NLVAD is designed ultimately for total implantation without this transcutaneous lead. Elimination of this potential source of entry for infection as well as the complete internal placement of the Novacor LVAD potentially offer substantial advantages over other ventricular assist devices under current investigation.

Although this patient could have been managed with an orthotopic artificial heart, the potential comparative advantages of the NLVAD are several: 1) the natural heart is allowed the opportunity to recover, thereby preserving the option of device removal without transplantation,[3,11] and 2) there are no pulsating percutaneous cannulas or pneumatically-driven lines crossing the chest wall, which may increase susceptibility to infection over prolonged circulatory support periods.

The overall success of a bridge to transplant procedure includes appropriate selection of the recipient, successful surgical techniques of implantation, adequate device performance to sustain safely the circulation during the support period, and successful cardiac transplantation. In this case the patient died ultimately of cardiac graft failure, a complication of transplantation, not of the performance of the NLVAD.

The Novacor LVAD has been implanted as a bridge to transplant worldwide in 17 patients (median age, 43 years) for a median duration of 15 days (range 2–90 days). Nine patients died before transplantation, eight were transplanted, and 6 are alive following transplantation.

The true promise of this second-generation, electrically powered assist system is the potential for fully implantable and tether-free operation that would provide full rehabilitation with a high quality of life.

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