Long-term mechanical circulatory support with the wearable Novacor left ventricular assist system

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Abstract

Objective: As of July 1st 1999, 36 European patients have lived for more than 1 year supported by the Novacor wearable electric left ventricular assist system (LVAS). All were unresponsive to maximum medical therapy, prior to implantation. These patients offer an unique opportunity to evaluate the feasibility of long-term ambulatory mechanical circulatory support as a therapeutic option for patients in profound cardiac failure.

Methods: Data was obtained from the Novacor European Registry.

Results: At the time of implantation, median age was 55 (18–67) years. Aetiology was ischemic (9, 25%) or idiopathic (26, 72%) cardiomyopathy, and myocarditis (1, 3%). Median duration of LVAS support was 1.49 (1.03–4.10) years. Eight recipients had LVAS support times >2 years, of which two were >3 years and one >4 years. The median time spent outside the hospital was 1.27 (0.58–3.83) years, representing 82% of the duration of LVAS support. No mechanical failure was observed during the entire observation period. One pump was replaced electively after 3.67 years due to pump driver wear-out. Twelve patients (33%) are currently on support while 17 were transplanted (14, 39%) or weaned (3, 8%). Seven (19%) patients died after a median of 1.24 years circulatory support.

Conclusions: Experience with long-term Novacor LVAS recipients has demonstrated effective rehabilitation in this group of patients with refractory advanced heart failure. This suggests that LVAS therapy may offer a safe and realistic option for patients for whom no other effective therapy is available. The patient sub-population that would benefit most from this therapy remains to be defined. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Cardiac failure; Mechanical circulatory support

1. Introduction

There have been significant advances in the medical management of patients with advanced heart failure over the last decade. However, this group of patients still require multiple hospital admissions and have a dismal prognosis. Currently, the only effective therapy available for those patients who inevitably become refractory to medication is transplantation. However, many of these patients have contra-indications to transplantation, the most prevalent being age above 60–65 years. Epidemiological studies show a steep increase in the number of patients older than 60 with advanced heart failure, exacerbating the already huge disparity between the demand for transplantation and the supply of donor organs [1]. Clearly, alternative therapeutic options are urgently required.

Prolonged mechanical circulatory support represents one of these options. The left ventricular assist system (LVAS) should be capable of providing an extended bridge to transplantation (BTT), allowing full rehabilitation of the patients before definitive therapy: elective cardiac transplantation; a bridge to the recovery of native left ventricular function (depending on underlying cardiac disease) [2], or permanent implantation (when cardiac transplantation is contra-indicated).

The Novacor LVAS, initially designed for permanent use, has been utilized in the bridge to transplantation application since 1984 [3]. Progressive refinements in the technology have resulted in the first implantation of a wearable, implanted version in 1993 [4]. Since then, support times have steadily increased. For the first time in the history of
mechanical circulatory support, a significant experience has been accumulated in patients supported for more than one year. These recipients offer an unique opportunity to evaluate the feasibility of long-term ambulatory mechanical circulatory support as a therapeutic option for patients in advanced cardiac failure, and they represent the basis of this report.

2. Materials and methods

Between March 1993 and July 1999, 469 European patients that have received the Novacor wearable electrical LVAS. Of these, 36 (8%) of patients had lived for more than one year supported by the Novacor LVAS. The data were obtained from the Novacor European Registry, a voluntary registry of each active European center, organized as an initiative of the surgeon and cardiologist investigators (Appendix A).

Patient characteristics at the time of implantation are summarized in Table 1. Hemodynamics and biological markers of secondary organ dysfunction are listed in Table 2. These data were obtained following optimal medical therapy, and underline the degree of cardiac decompensation prior to implant.

The intention to treat, with the Novacor LVAS has been, in most cases, as a bridge to transplantation (26, 72%). In five (14%) cases, implantation was as an alternative to transplantation in patients who were not transplant candidates. In a subset of patients (five, 14%) recovery of native left ventricular function, following extended support, allowed weaning and device explant. Surgical implantation techniques and patient management protocols varied, to some extent, between centers [4–6], however these differences were not thought to be significant. Clinical outcome was analyzed in three time frames: the first month following LVAS implantation, 1–12 months, and longer than 1 year. Continuous variables are expressed as medians with range. Binary variables are described by frequency distributions. Clinical complication data are presented as linearized rates.

3. Results

At the time of implantation, median age was 55 (18–67) years. Body surface area was 1.94 (1.64–2.32) m². The majority of patients were male (32, 89%). Aetiology was ischemic (nine, 25%) or idiopathic (26, 72%) cardiomyopathy, and myocarditis (one, 3%).

Median duration of LVAS support was 1.49 (1.03–4.10) years. Eight recipients had LVAS support times >2 years, of which two were >3 years and one >4 years. The median duration of hospitalization before discharge was 72 (28–510) days; the median time spent outside the hospital was 1.27 (0.58–3.83) years, representing 82% of the duration of LVAS support.

The incidence of complications during the three time intervals is shown in Fig. 1. Surgically-related bleeding (9/36, 25%) was the predominant complication in the initial period. Neurological events (neurological deficit which is sudden in onset, clinically relevant and persists for more than 24 h) were diagnosed in 6/36 (17%) patients and occurred predominantly in the first 2–3 months. Infection, particularly following the first month, was the most important complication. Most infections were minor, representing either driveline exit-site or pump pocket infections. However, some were more serious systemic infections or endocarditis of the valved conduit. The overall freedom from these infections was 75% at 1 year, 67% at 1.5 years and 58% at 2 years on LVAS. The most significant organism

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Patient status at the time of implantation</th>
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<tbody>
<tr>
<td><strong>Patients</strong></td>
<td></td>
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<tr>
<td>Previous thoracic surgery</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>Intra-aortic counterpulsation</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Renal dialysis</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Post cardiotomy</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Other ventricular assist device</td>
<td>2 (6%)</td>
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* Centrifugal pump in one patient, extracorporeal membrane oxygenation in another patient.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Hemodynamics, renal and hepatic function at implantation</th>
</tr>
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<tbody>
<tr>
<td><strong>Median (range)</strong></td>
<td></td>
</tr>
<tr>
<td>Central venous pressure (mm Hg)</td>
<td>11 (3–25)</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure (mm Hg)</td>
<td>36 (11–57)</td>
</tr>
<tr>
<td>Pulmonary capillary wedge pressure (mm Hg)</td>
<td>28 (11–36)</td>
</tr>
<tr>
<td>Cardiac index (/min per m²)</td>
<td>1.9 (1.3–3.4)</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.35 (0.7–8.4)</td>
</tr>
<tr>
<td>Sodium (meq/l)</td>
<td>135 (122–153)</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>1.6 (0.6–5.2)</td>
</tr>
</tbody>
</table>

Fig. 1. Linearized rates (new events per recipient per month) are calculated in three time bands: (1) the first 30 days following LVAS implant; (2) from 1 to 12 months and (3) after 1 year of LVAS support. Non-surgical bleeding represents gastro-intestinal tract bleeding and cerebral bleeding. Device pocket and drive line infections were culture positive infection requiring intravenous antibiotics and local lavage.
was *Staphylococcus aureus* (Fig. 2). Infections were treated with systemic and local anti-microbial therapy and lavage. In three patients, the infected valved conduit was replaced. No infection of the blood contact surface of the LVAS pump was diagnosed.

No mechanical defect of the LVAS pump system was observed during the entire observation period. In one recipient the pump was replaced electively after 3.67 years due to normal end-of-life pump driver wear-out. Two patients underwent cardiac transplantation at day 664 and 1297, respectively, when device wearout was predicted to occur (prematurely, secondary to uncontrolled hypertension in the first) within the following 2 months. Device-related complications including valved conduit replacement secondary to endocarditis, connector wear and drive-line repair are shown in Fig. 3. The complications accounted for unscheduled re-hospitalizations in 23/36 (64%) recipients.

At the time of the study, 12 patients (33.3%) are currently on support while 17 have been transplanted (38.9%) or weaned (three, 8.3%) (Table 3). Seven (19.4%) patients died, one during explant, three due to cerebral bleeding, two of multi-organ failure and sepsis, and one of lung cancer.

### 4. Discussion

This report describes, for the first time, a significant cohort of patients supported by an LVAS for more than one year. Analysis provides valuable information from which the feasibility of truly chronic LVAS support can be inferred. The trend towards extended LVAS support times is multi-factorial: a reduction in LVAS-related morbidity; demonstrable high reliability and durability, improvement in LVAS supported quality of life, and increasing transplant waiting times. This trend has resulted in increasing difficulty in differentiating between a prolonged BTT and permanent implantation. It is also pertinent to point out that there is currently no other similar experience reported in the literature.

One of the main features of the current LVAS recipients’ lives, is the large proportion of time spent within their own community of friends and relatives, leading self reliant lives. This was not initially expected as evidenced by the requirement for a qualified care-giver as part of the United States’ Food and Drugs Administration pre-market study. However, the autonomy of the Novacor LVAS, coupled with the high level of system reliability has made the requirement for a care-giver unnecessary. This has had an important impact on both quality of life and overall resource use. Whilst there have been no prospective, scientific quality

### Table 3

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Recipients</th>
<th>Percentage</th>
<th>Years on LVAS support</th>
</tr>
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<tbody>
<tr>
<td>Valve replacement (endocarditis)</td>
<td>12</td>
<td>33</td>
<td>1.72</td>
</tr>
<tr>
<td>Connector wear</td>
<td>14</td>
<td>39</td>
<td>1.58</td>
</tr>
<tr>
<td>Drive line repair</td>
<td>3</td>
<td>8</td>
<td>1.15</td>
</tr>
<tr>
<td>Died</td>
<td>7</td>
<td>19</td>
<td>1.24</td>
</tr>
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of life studies carried out in this cohort of patients, the individual center experiences are replete with anecdotal accounts supporting a significantly-improved quality of life [7]. This is also a consequence of the user-friendly system design, the relatively low risk of life threatening complications and the quality of physical rehabilitation of the recipients after only a few weeks.

The results presented here do not imply that the therapy is perfect. The frequency of unscheduled re-hospitalizations impacts on life quality and on resource use, and efforts are underway to reduce complication rates, particularly with respect to infection and embolism. Limitations in system biocompatibility, implant size, dead spaces and the percutaneous lead contribute to device-related infection. Patient selection and optimal implant timing also impact on infection since long-stay ICU patients, with significant secondary organ failure are exposed to nosocomial infections [8]. Meticulous surgical practice, analogous to that used with large orthopaedic prostheses, also have a role to play.

The risk of embolic events remains a continuing concern. The rate of neurological events in the total cohort of patients has been reduced by 50%, when compared to the earlier experience [6,9]. This is due to the identification of one of the main sources of embolism, associated with the inadequate healing process in the original inflow conduit [10]. The development of a friable, easily detachable neo-intima has been substantially reduced by changes in the physical characteristics of the new inflow conduit: reduced compliance, elimination of graft crimp and shorter length, which result in improved flow characteristics at the luminal wall [11]. In addition, anticoagulation and anti aggregant therapies have been adjusted to the specific requirements of prolonged activation of the biological cascades. Further reductions in the risk of embolism should be obtained by the ongoing use of more biocompatible blood contacting surfaces.

The present experience suggests a new device-assisted medical therapy is evolving for patients with advanced cardiac failure. Analysis of patient selection and implant timing have has demonstrated that significant improvements in current long term results are easily attainable [12]. This suggests that one-year survival rates of Novacor LVAS recipients should compare favorably with those obtained with optimal medical therapy [13]. While quality of life has been substantially improved, the remaining clinical debate revolves around continuing medical therapy and selection of patients who are most likely to benefit from this therapeutic intervention.

Appendix A

Novacor European Registry data was provided by the following Centers:

University Hospital Graz, Austria (K.-H. Tscheleissnigg), University Hospital Helsinki, Finland (J. Sipponen), Hospital La Timone, Marseilles, France (T. Mesana), Hospital Broussais, Paris, France (A. Carpentier), Hospital Henri Mondor Creteil, France (D.Y. Loisance), Hospital La Pitié Salpétriére, Paris, France (Pavie), Heart Center North Rhine Westfalia, Bad Oeynhausen, Germany (R. Koerfer), German Heart Center Berlin (A. Hetzer), Humboldt University Hospital Charité Berlin, Germany (W. Konertz), University Hospital Freiburg, Germany (F. Beyersdorf), Hospital Grollhäusern, Munich, Germany (B. Reichart), Westfalian Wilhelms University Hospital Münster, Germany (H.H. Scheld), IRCCS Policlinico S. Matteo, University of Pavia, Italy (M. Vigano), University Hospital Verona, Italy (G. Faggian), Hospital Niguarda Ca’ Granda, Milano, Italy (E. Vitali), University Hospital Padova, Italy (D. Casarotto).

References

Appendix B. Conference discussion

Dr R. Koerfer (Bad Oeyhausen, Germany): In this group of long-term patients, are there some who had previously a right heart support?

Dr Loisance: There were a few who were on balloon pumping, but none of them went on another type of mechanical support system.

Dr Koerfer: Because I think we have at least one who had been about 100 days on the Novacor prior to transplantation and he had about, maybe, 28 or 30 days of the right heart support, and I thought that there should be some.

Dr Loisance: Right heart support at the same time as the Novacor?

Dr Koerfer: Yes.

Dr Loisance: But not before the implantation?

Dr Koerfer: No, no, not before.

Dr Loisance: Yes, but in a 5-min talk I cannot give every detail of the clinical material, and you will find your patient in the manuscript.

Dr G. Tedy (Beirut, Lebanon): What is your anticoagulation protocol for the long term?

Dr Loisance: Every patient is maintained long-term on anticoagulation and antiaggregation therapy, and there are variations between the various centers. But basically they are fully anticoagulated with the INR which targets 2.5–3.5. They are also antiaggregated, and the dose of aspirin varies from each center to another, (150–400 mg/day), it depends.

Dr F. Rosenfeldt (Melbourne, Australia): You mentioned that the pocket infections in your series of patients were trivial. In Melbourne we had one patient who had an absolutely disastrous pocket infection that went on for several months and severely impacted on the recovery of the patient. The patient eventually recovered but the pocket infection was impossible to control with antibiotics.

Dr Loisance: Yes, it’s totally true. But there are the patients who live one year and more. So the patient with major pocket infection usually has been transplanted before. So there is a bias in the evaluation of the actual risk of pocket infection in a Novacor recipient presented today.