Circulatory support for fulminant myocarditis: consideration for implantation, weaning and explantation

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Abstract

Objective: Fulminant myocarditis (FM) is an uncommon but life-threatening condition for which a mechanical circulatory support (MCS) device can be life-saving. However, device selection, weaning and explantation procedures remain poorly defined. Methods: Four patients were bridged to recovery using the Thoratec® biventricular support device. All four were in a state of cardiogenic shock with rapid deterioration of their clinical status despite increasing doses of inotropes. Three patients required mechanical respiratory support, three were anuric and one was dialyzed. Echocardiography showed a mean ejection fraction of 12 ± 8%. Results: Each Thoratec implantation was performed on cardiopulmonary bypass with a beating heart. Three patients underwent biventricular cannulation. The fourth patient underwent left ventricular and right atrial cannulation. All patients manifested evidence of moderate to severe end organ dysfunction after device implantation. However, by explantation, end organ function had recovered in all patients. After a mean duration of 17 ± 10 days, all the patients showed evidence of myocardial recovery. Recovery was confirmed on echocardiography which showed opening of the aortic valve and contraction of both ventricles. The weaning process was performed in 2–5 days by setting the device in a fixed mode and increasing the rate. Device explantation was uneventful in the four patients. At the 6 months echocardiography follow-up, all had normal systolic function. Conclusion: In patients with FM, biventricular support allows full circulatory support and unloads both ventricles until recovery occurs. In this set of patients, weaning and removal procedures are straight-forward. These results suggest an aggressive stance toward implantation of MCS in patients with FM.

Keywords: Myocarditis; Circulatory support; Biventricular assist device; Bridge to recovery; Cardiogenic shock

1. Introduction

Fulminant myocarditis (FM) is characterized by rapid and extensive hemodynamic compromise occurring in a previously healthy patient [1]. However, if the patient survives the acute phase of heart failure, recovery occurs in a few weeks with a good long-term prognosis [2]. Since the risk of death during the acute phase is high, bridge to recovery with circulatory support devices is often useful in these patients. However, type of device, technique of implantation and explantation in addition to weaning protocol remain unclear. We report our experience of four patients with FM recently bridged to recovery with mechanical circulatory support (MCS).

2. Patients

From April 2001 to March 2002, four patients with FM (two males, two females, mean age: 31 ± 4 years) were bridged to recovery. Each had a 2–5-day history of fever, myalgia and malaise and were hospitalized due to symptoms of biventricular heart failure with chest pain and EKG anomalies. One patient had a previous history (3 years prior) of medically treated acute myocarditis with complete recovery as assessed by serial echocardiography. On admission, the four patients underwent coronary
angiography which demonstrated an absence of coronary artery disease. Each patient developed cardiogenic shock requiring inotropic support. After 2–4 days, the patients were transferred to our institution as a result of deteriorating hemodynamic status despite maximal medical therapy. Three of them required mechanical respiratory support. All patients were treated with dobutamine and two also had an infusion of epinephrine. Echocardiographic examination showed major alteration of the cardiac function with a mean ejection fraction of 12 ± 8%. Laboratory results are summarized in Table 1.

The four patients underwent circulatory support implantation 2–12 h after transfer to our institution. One had a cardiac arrest in the OR requiring external and internal cardiac resuscitation prior to institution of CPB.

3. Device management

The four patients underwent biventricular circulatory support with the Thoratec® (TCI®) pneumus device. Implantation was performed on a beating unloaded heart with no aortic cross-clamp. The first patient underwent an apical left ventricle and right atrial cannulation for inflows. The three others underwent left and right ventricle cannulation [3]. Before sternal closure, in order to prevent formation of adhesions, the anterior wall of the heart was covered with an expanded polytetrafluoroethylene (ePTFE) membrane (Preclude Pericardial Membrane, Gore and Associates, Flagstaff, AZ, USA) and the right atrium with a Seprafilm membrane (Genzyme Corp.).

Anticoagulation was managed as previously described [5]. Myocardial recovery was assessed with transthoracic echocardiography or transesophageal echocardiography if the patient was intubated. Weaning of circulatory support device was performed as described by Slaughter et al. [6]. Removal of the Thoratec was performed on a beating heart using cardiopulmonary bypass (CPB). Ventricular orifices were closed using a synthetic circular patch (Vasculitek). Ejection tubes were completely removed from the great vessels.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Creatinine (µmol/l)</th>
<th>Total bilirubin (µmol/l)</th>
<th>SGOT (U/l)</th>
<th>Lactates (mmol/l)</th>
<th>Troponin Ic (µg/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal values</td>
<td>60–110</td>
<td>&lt;17</td>
<td>17–27</td>
<td>1–2</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Patient 1</td>
<td>117</td>
<td>18</td>
<td>114</td>
<td>6.3</td>
<td>12.6</td>
</tr>
<tr>
<td>Patient 2a</td>
<td>419</td>
<td>19</td>
<td>9295</td>
<td>7.35</td>
<td>96.5</td>
</tr>
<tr>
<td>Patient 3</td>
<td>100</td>
<td>16</td>
<td>35</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Patient 4</td>
<td>60</td>
<td>4</td>
<td>22</td>
<td>3.2</td>
<td>1.39</td>
</tr>
</tbody>
</table>

SGOT, serum glutamic oxaloacetic transaminase.

a This patient was dialyzed.

4. Results

In the patient who underwent right atrial cannulation, attempts to close the chest were associated with a loss of the filling signal on both sides and hemodynamic compromise, despite many attempts to improve the position of the right atrial cannula. In this patient, the chest was left open and ePTFE membrane was sutured to the skin. Left device outflow was 5.6 l/min corresponding to a 3.5 l/min per m². After 9 days, the patient developed a fever and required norepinephrine to treat a sudden vasoplegia. She underwent right ventricular assist device removal and the chest was closed. During the days which followed, she developed right ventricular dysfunction requiring epinephrine for 1 week. Moreover, she developed a hypoxemia (PaO₂: 50 mmHg with FIO2 at 100%) related in part to a right to left shunt due to a patent foramen oval. The hypoxemia resolved after a few days, when the right ventricle improved. This episode of hemodynamic instability led to acute renal failure. The patient was finally extubated 13 days after right pneumatic device removal.

In the three other patients, the mean CPB time was 113 ± 24 min. The Thoratec device was set up in an automatic mode immediately after the CPB discontinuation in two patients and after 24 h in a third one. In these patients, the left and right outflow averaged 6.2 ± 1.2 l/min (mean cardiac index of 3.2 ± 0.6 l/min per m²) and 5.3 ± 0.4 l/min, respectively.

The three patients required norepinephrine for a brief period after implantation. One patient underwent reoperation for tamponade at day 15. Two patients could not be weaned from mechanical ventilation due to excessive agitation requiring sedation. The fourth patient was extubated at day 7. The patient who was dialyzed before implantation required continuous veno-venous hemodiafiltration for 1 week before recovery of renal function. While on circulatory support, each patient received on average: packed red blood cells (PRBC) 18 (range 11–32), fresh frozen plasma 8 (2–14) and single donor platelets 13 units (7–22).

All patients manifested evidence of moderate to severe end organ dysfunction after device implantation, as shown in Table 2. However, by explantation, end organ functions had recovered in all patients. Troponin Ic increased in three patients after implantation, peaked between day 2 and 4 and then decreased to reach normal values around day 15.

Myocardial biopsies were available in three patients. Biopsies demonstrated myocardial infiltrates of monocellular cells in interstitial as well as perivascular tissues. Infiltrates were associated with myonecrosis in two patients.

After a mean duration of 17 ± 10 days (mean ± standard deviation), all of the patients showed evidence of myocardial recovery, with native left ventricle activity clearly seen on the arterial pressure wave. Interestingly, in the three patients who still had biventricular support at that time, the setup of the right pneumatic ventricle had to be turned to an asynchronous mode because of competition...
with the native ventricle. Recovery was confirmed on echocardiography which showed opening of the aortic valve and contraction of both ventricles. In the first patient, the weaning process took four steps in 5 days. In the three other patients, weaning was performed in a two-steps/2-days process (Table 3). Finally, the mean duration of support was 24 ± 13 days (43, 23, 18 and 12 days, respectively).

Reoperation for device explantation was uneventful in the four patients with a mean CPB time of 72 ± 16 min for the three patients with biventricular cannulation. Post-recovery biopsies showed normal myocardial tissue. No adverse event occurred after explantation. Mean time for extubation was 33 ± 20 h. One patient required a small dose of dobutamine which was discontinued after 4 days. The four patients left the intensive care unit after 1 week. Since serum hemoglobin was low before explantation (8.7 ± 0.7 g/dl), three of the patients required transfusion (2–8 PRBC) during the 12 h following surgery. After a follow-up of 8.8 ± 4.9 months, the four patients are doing well, back to full-time work. Six-month echocardiography examination showed normal ventricular function in all patients.

### 5. Discussion

Lieberman et al. [1] proposed a classification of idiopathic myocarditis in four different groups parallel to the viral hepatitis classification: fulminant, acute, chronic active and chronic persistent. Patients with the fulminant form have a well characterized clinical presentation. The onset of cardiac involvement is distinct and heralded by non-specific flu-like illness. The patient rapidly develops profound hemodynamic compromise. All of our patients had these clinical criteria. Moreover, in three of them, myocardial biopsies were available and revealed unequivocal active myocarditis in two and borderline myocarditis in one by the Dallas criteria. Finally, all of them had complete myocardial recovery in less than 1 month. Complete resolution is another characteristic of the fulminant form. As shown by McCarthy et al. [2], if the patient does not die during the acute episode, long-term prognosis is good with 100% freedom from death or transplantation at 12 years for the patients who were discharged from hospital.

The high risk of death during the acute phase and the very good long-term prognosis of FM are important arguments for physicians to use aggressive treatments. In a randomized clinical trial, Mason et al. [7] demonstrated the absence of any beneficial effect of immunosuppressive therapy in most patients with myocarditis. Lieberman even hypothesized that immunosuppressive therapy could aggravate FM [1]. Even if i.v. inotropes can stabilize the hemodynamic status of patients with FM, the risk of rapid deterioration of the clinical condition should lead physicians to take an aggressive stance toward implantation of MCS.

During the acute phase of FM, MCS has two inter-related objectives: assuming the role of the heart as a pump and unloading of the ventricles avoiding distension. Moreover, the device must be easy to remove. Extracorporeal membrane oxygenation (ECMO) can fulfill these objectives and good results have been reported particularly in children [8,9]. ECMO is easy to implant and to explant, its cost is much lower than other devices and if recovery does not occur, it is always possible to switch toward another device. However, ECMO does not always allow to reach adequate output in adults. This is why we feel more confident in the efficacy of a pulsatile biventricular device. In our opinion, intracorporeal left ventricular assist devices (LVADs) (Novacor®, TCI®) are less suited to support patients with FM since they are more difficult to implant and explant, and are more expensive than extracorporeal VADs (Thoratec®, Abiomed®). Although case-reports have shown good results with LVADs [10,11], myocarditis generally involves both ventricles. As such we systematically used biventricular support in our four patients. This is consistent with the review of literature and voluntary registry published by Acker [12] who reported a 70–75% use of biventricular...
assist devices (BIVADs) in the series of Thoratec or Abiomed. Secondary right ventricular failure in patients with a LVAD may be associated with a higher morbidity/mortality rate than the use of a BIVAD by itself. In a multicenter review, Farrar et al. reported that patients who required biventricular support had more severe illness with higher creatinine, total bilirubin, greater mechanical ventilation support needs. BIVADs were more often placed under emergency conditions and following intra-aortic balloon pump counterpulsation [13]. However, most of the patients of the series had chronic heart failure. In patients with acute hemodynamic compromise as it occurs in FM, those pre-operative markers might less accurately reflect the severity of illness or right ventricular involvement.

In our patients, recovery occurred in less than 3 weeks in the patients who had full biventricular support. This result is consistent with other reports in which duration of support is from 15 to 45 days [10–12,14]. In our patients, recovery was obvious and native left ventricle ejection could be seen on the arterial pressure wave even with the device set up in an automatic mode. Echocardiography performed on demand easily confirmed recovery of myocardial function and was used to monitor myocardial contractility during the weaning process. In many reports on fulminant myocarditis, assessment of recovery is performed on clinical and echocardiographic findings [10,11,14]. This shows that the recovery assessment might be easier in this set of patients than in patients with dilated cardiomyopathy. In the latter group, there are almost no criteria to assess recovery and weaning remains challenging. When recovery is doubtful, other tools can be used to assess recovery such as exercise testing with simultaneous hemodynamic and echocardiographic measurements. As recently reported by Maybaum et al., myocardial biopsy can be useful by showing ongoing myocardial inflammatory infiltrate [15]. On the other hand, in a patient with a clinical history of FM, Houel et al. [16] pointed out the difficulty of predicting success after explantation. Interestingly, duration of support for their patient (50 days) was longer than support typically required for FM. Rapidity of recovery might be a good prognosis criteria in patients with FM.

As recovery was clinically evident, weaning was performed in only 2 days in the last three patients. We used the concept described by Slaughter et al. [6] which consists of increasing the rate of the device so that filling decreases, allowing a drop in output to approximately 2 l/min with no blood stagnation. In our opinion, this method is better than decreasing the rate of the device, since it limits the risk of thrombus formation without requiring a full heparinization and allows a more profound reduction in device output.

Reoperation for device removal is technically straightforward. Since we use a beating heart technique, we prefer bicaval cannulation. This ensures complete emptying of the ventricles and lessens the risk of entraining air into the circuit. Closing the ventricular cannulation site with a synthetic patch is efficacious and avoids cavity size reduction in comparison to primary closure.

6. Conclusion
BIVADs offer an efficient and clinically straightforward means of bridging patients with FM to recovery. Recovery occurs after few weeks, allowing quick weaning from the device. These results suggest an aggressive stance toward implantation of MCS in patients with FM.

References

[14] Chen YS, Wang MJ, Chou NK, Han YY, Chiu IS, Lin FY, Chu SH,
