Results of mechanical circulatory support in France

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Abstract

Objective: To present the analyzed results on mechanical circulatory support (MCS) collected over a 7-year period, from 2000 to 2006, in France.

Methods: A cohort of 520 patients was analyzed. Mean age was 43.7 ± 13.6 years. The main causes of cardiac failure were ischemic cardiomyopathy (39%), idiopathic dilated cardiomyopathy (41.3%), or myocarditis (6.4%). Bridge to transplantation was indicated in 87.8% of patients, bridge to recovery in 9%, while destination therapy was proposed in 3.2% of patients.

Results: For patients in cardiogenic shock or advanced heart failure undergoing device implantation as bridge to transplantation or recovery (n = 458), overall mortality was 39% (n = 179). The main causes of mortality under MCS were multi-organ failure (MOF) (57.4%), neurological events (14.1%), or infections (11.9%). Heart transplantation was performed in 249 (54.3%) patients. The main causes of death following heart transplantation were primary graft failure (22.4%), MOF (14.3%), neurological event (14.3%), or infection (10.2%). Long-term survival in transplanted patients was 75 ± 2.8% at 1 year and 66 ± 3.4% at 5 years.

Conclusions: MCS is an essential therapeutic tool to save the life of young patients with cardiogenic shock or advanced cardiac failure. Early MCS implantation and the availability of a device that is adapted to the patient’s clinical status are prerequisites for reducing overall mortality rates.

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1. Introduction

Mechanical circulatory support (MCS) in France was, until recently, an activity performed by only a small number of surgical centers [1—5]. These pioneer centers, which have deployed much effort in terms of financial and organizational resources, have contributed to the development and credibility of this therapeutic tool among both health-care professionals and administrative authorities. As a result, MCS has established itself as a true therapeutic option for certain patients presenting a seriously compromised cardiac status. This was associated with a regular increase in the number of cardiac surgery centers involved in this activity. However, in spite of the progress made in both support device technology and medical management, MCS is still a cumbersome therapeutic tool that needs to be time-tested. In a joint effort to accelerate progress, French cardiac surgeons involved in MCS felt the need to share their experiences within a working group named ‘Reflection Group on MCS’ (the group’s abbreviation in French: GRAM). We herein report the MCS patient data collected by the French cardiac surgery centers participating in the GRAM working group.

2. Patients and methods

2.1. Data collection and analysis

Patient data were collected retrospectively by each of the cardiac surgery centers and centralized into an Access database.
database (Microsoft, France) specifically developed for the GRAM project. Exploratory and statistical analyses were performed using SPSS software (SPSS, France). The last date for data entry into the database was set as 15 January 2009. The chi-square test was used to compare qualitative variables. Survival curves were compared using the log-rank test. A $p$-value $< 0.05$ was considered statistically significant.

2.2. Patients

Cohort data of 520 patients from 16 cardiac surgery centers were collected over a 7-year period, from 2000 to 2006, and analyzed. The number of implants in relation to the year is shown in Fig. 1. The patients’ mean age was $43.7 \pm 13.6$ years (range: 8 months to 78 years). Patients aged between 40 and 60 years represented 58% of the population. Eleven children aged less than 15 years, representing 2.1% of the population, underwent device implantation. Of the patients, 83.8% were male ($n = 436$). The causes of cardiac insufficiency were idiopathic dilated cardiomyopathy (41.3%, $n = 215$), ischemic cardiomyopathy (39%, $n = 203$), myocarditis (6.4%, $n = 33$), cardiac valvulopathy (4.2%, $n = 22$), congenital cardiopathy (3.5%, $n = 18$), and other causes (5.6%, $n = 29$). MCS was implemented while awaiting cardiac transplantation ($n = 457$) or recovery ($n = 47$) in 87.8% or 9.0% of patients, respectively, or as destination therapy in 3.2% of patients ($n = 17$). The clinical context in which MCS was implemented was mostly cardiogenic shock or advanced heart failure (89%, $n = 463$), and less frequently post-cardiotomy (5.6%, $n = 29$), post-cardiac transplantation (3.5%, $n = 18$), or controlled device implantation (1.9%, $n = 10$).

2.3. Cardiac support devices

The different types of circulatory devices are provided in Table 1. The biventricular support mode was used in 72.9% of patients ($n = 379$), left univentricular assistance in 25.6% ($n = 133$), and right univentricular assistance in 1.5% of patients ($n = 8$). Yet, Fig. 1 shows that the number of patients undergoing biventricular support strongly decreased in 2006, in favor of left ventricular assistance.

3. Results

3.1. Overall mortality

The overall mortality rate under device support was 43% ($n = 224$). The mortality of patients undergoing first-line device support for cardiogenic shock was 40%. For patients undergoing device support in the post-cardiotomy state, the mortality rate was 69%, with a mortality rate of 72% in cases of post-cardiac transplantation. Evolution of patients in cardiogenic shock or advanced heart failure undergoing MCS as bridge to transplantation or recovery ($n = 458$). (Patients undergoing device support in the post-cardiotomy or post-cardiac transplantation state as well as those for whom destination therapy was proposed have been excluded.)

3.2. Mortality with device therapy

Overall mortality was 39% ($n = 179$). Mortality in relation to the year is shown in Fig. 2. Mortality rates remained stable.
over time. Statistical analysis showed that there were no differences in mortality rates between the different types of support devices used (Table 2). However, the mortality rates in patients with biventricular assistance were significantly lower than in those undergoing univentricular support (35.9% vs 48.2%, \( p = 0.022 \)). Actuarial survival according to the two support modes is shown in Fig. 3. The difference in survival rates can essentially be accounted for by a higher mortality observed during the first 10 days in patients undergoing left univentricular assistance. Mortality rate analysis in relation to the center is illustrated in Fig. 4. There is a wide disparity in mortality rates between centers, but only one center appears to exhibit a significantly higher mortality rate compared with the others. Concerning the time delay until death, the analysis shows that 40% of death cases occurred during the first 10 days following implantation. Monthly death rates of patients undergoing MCS are given in Fig. 5. As can be seen, mortality reached its lowest level during the fourth month and tended to increase from the seventh month onward. The causes of death were reported for 134 patients and mainly included multi-organ failure (57.4%), neurological events (14.1%), and infection (10.2%), and, less frequently, digestive complications (8.2%), support device failure (3.7%), or other complications (4.7%).

### 3.3. Transplanted patients

Cardiac transplantation was performed in 54.3% of patients (\( n = 249 \)). The waiting period until transplantation was less than 3 months for 56% of patients, whereas 18% of implanted patients had to wait for heart transplantation for at least 6 months. The early post-transplantation mortality rate for the first 60 days was 19.6% (\( n = 49 \)), the main causes of death being primary graft failure (22.4%, \( n = 11 \)), neurological events (14.3%, \( n = 7 \)), multi-organ failure (14.3%, \( n = 7 \)), infection (10.2%, \( n = 5 \)), and other or unknown causes (38.8%, \( n = 19 \)). Actuarial survival rates were 75 ± 2.8% at 1 year and 66 ± 3.4% at 5 years (Fig. 6).
3.4. Overall survival

For the entire study population, overall actuarial survival rates following MCS and cardiac transplantation were 47.6 ± 2.3% at 1 year and 39.5 ± 2.5% at 5 years.

4. Discussion

MCS is a relatively stable activity across the 16 French centers participating in this research project, with a mean number of 78 implanted patients per year. The patient population concerned comprises mainly young subjects, with a mean age of 43 years, the main causes of the patients’ cardiac insufficiency being ischemic cardiomyopathy and dilated cardiomyopathy. During the observation period, the device system used appeared to vary from one center to the other as well as over time, however, with a clear predominance of biventricular mode, even if there was a trend toward a higher use of univentricular support with axial flow pumps in 2006.

The number of biventricular assist devices implanted in France during the observation period was very high compared to international practice. One of the reasons is that the cost of external biventricular devices (Thoratec, Medos, Berlin heart, etc.) was lower than electrical left ventricle assist devices (Novacor, Heartmate I, Heartmate II, etc.). In France, since the 1990s until 2008, MCSs were bought by public heart surgery departments using private funds or by the hospital itself if possible. Since 2008, MCSs are supported by the French health insurance. Another reason is that many patients came to MCS too late with severe cardiogenic shock and multiple organ failure. Information on surgical strategies for advanced heart failure and cardiogenic shock was given to anesthesiologists and cardiologists in order to reduce the interval between end-stage heart failure diagnosis and MCS implantation. Improvement of patient clinical status before device implantation and emergence of new models of MCS as axial flow pump has led to a lesser use of biventricular devices in 2006.

This study shows that, despite the significant progress made in both the management of these patients over the last 20 years and the reliability of the support systems, overall mortality rates are still high. However, a distinction has to be made between different particular situations, one of which is MCS implementation for refractory cardiogenic shock occurring in the postoperative phase following conventional cardiac surgery or after cardiac transplantation with primary graft failure. In these specific settings, mortality rates are particularly high and in line with those reported in scientific literature [6]. As a result, we should use in this particular indication less expensive systems that are easy to implement such as long-term extracorporeal circulation, although this does not always lead to better results [7,8]. Nevertheless, more precise data than those contained in the GRAM registry are necessary in order to enable us to better define the exact indications for these patients.

For patients with cardiogenic shock receiving MCS as first-line therapy, the overall mortality rate following MCS is 39%. These mortality rates significantly varied between centers. The reasons for these variations are numerous, but the patient status upon implementation of circulatory support is likely to play a determinant role. Certain centers, particularly at the early stages of the learning curve, may exhibit two extreme tendencies, that is, either accept or wait for the patient to reach a severe state before implementing circulatory support so as to give medical treatment a maximum of chances to succeed, or, on the contrary, to implement circulatory support in patients with a ‘low’ severity level in order to guarantee maximum success, thereby excluding patients who are more severely affected and erroneously classified as ‘unfit’ for MCS implementation. This may explain why mortality rates may be twice as high in some of the centers, especially when taking into account those with low activity. However, as the patients are being treated first line in cardiology intensive care units or resuscitation units, the discussion on MCS between intensive care physicians, cardiologists, and surgeons must take place well before a situation of extreme gravity unfolds, such as multi-organ failure. It is, therefore, necessary today to encourage all physicians in charge of patients in cardiogenic shock to inform surgeons as early as possible. This strategy, which has been well established since the early 1990s, has allowed physicians in experienced centers to achieve better results with MCS [9]. Likewise, this probably accounts for the high survival rates following MCS that are currently published by North American research teams [10].

In our series, mortality rates were shown to be higher for univentricular support than for biventricular assistance. Due to the lack of data regarding the patient status prior to device implantation, we are not in a position to determine the reason for these higher mortality rates with univentricular devices but it seems likely that many patients with multi-organ failure or very severe cardiogenic shock and thus an unfavorable prognosis underwent univentricular assistance. Experienced teams tend to favor the use of biventricular support in severely ill patients, while favoring that of left univentricular support in less severely ill patients, which may account for the higher mortality rates found for biventricular support compared with univentricular support [10,11]. Furthermore, the presence of right ventricular insufficiency (RVI) upon implementation of left ventricular support might have been a relevant cause of mortality if right ventricular failure had not previously been diagnosed or only been diagnosed at a late time point. The overall frequency of RVI upon implementation of left ventricular support varies from 20% to 40%, while the frequency of RVI requiring complementary right ventricular mechanical support ranges from 6% to 13%. Even though RVI may be controlled by medications or secondarily by mechanical support, survival rates of these patients are markedly lower as compared with those having normal right ventricular function. Right ventricular dysfunction may lead up to 15% of death rates, in cases undergoing left ventricular assistance [12–17]. For this reason, comparing univentricular and biventricular support does not make sense, as of today; it seems more reasonable to select the support modality in relation to the patient status and, moreover, to favor biventricular support if there is no certainty as to the proper functioning of the right ventricle, particularly if certain parameters may predict the occurrence of right ventricular failure in the postoperative period (Matthews score) [18] or if the patient status deteriorates.
following the onset of left ventricular assistance. In this last case, temporary right ventricular support may be an interesting solution so as to allow hemodynamic parameters to stabilize in the postoperative period, while waiting for the recovery of right ventricular function, and, at a later time point, patients may benefit from the advantages of left ventricular support alone.

Another element to consider is the evolution of the patient’s risk of death over time while undergoing circulatory support. Despite progress made in the management of autonomous patients under circulatory support, especially with respect to anticoagulation therapy and the risk of infection, the incidence of death varies in relation to time. As shown in Fig. 5, the incidence of death is the lowest between 3 and 6 months, while beyond this time period, the risk of mortality increases, which may be accounted for by the occurrence of standard complications such as device infection, hemorrhagic or thromboembolic complications, and device dysfunction. A circulatory assistance period of long duration while waiting for heart transplantation may also be a risk factor for mortality following heart transplantation [19]. In France, since 2005, priority for heart transplantation was given to patients in advanced heart failure or ‘moderate’ cardiogenic shock, patients under extracorporeal life support, and those under MCS with device infection or neurological complication. This strategy has led to increase the waiting time for transplantation in patients with stable end-stage heart failure or rehabilitated patients under MCS. The 1-year survival rate for heart transplantation published by the French transplantation agency (Agence de Biomédecine) for the period 2005–2007 was 71%, while it was 77% for the period 2000–2004 [20]. As in other countries, lack of heart donors in France is a reality. Therefore, it seems reasonable to propose priority for heart transplantation to patients who have the best chance of survival as patients with stable end-stage heart failure, patients in advanced heart failure, and those under MCS who have been rehabilitated for more than 2 months before any complication.

Lastly, our study results show that the survival rates of patients who have been transplanted following MCS are similar to those of patients having undergone first-line heart transplantation. Indeed, according to the data provided by the Agence de Biomédecine, patient survival rates for the 2000–2004 period were 77% at 1 year and 69% at 5 years [20]. This may be accounted for by the fact that, following MCS, patients undergo heart transplantation after having achieved full organic and functional recovery. One may therefore consider that circulatory assistance is not a risk factor of mortality per se following heart transplantation.

In conclusion, MCS is an essential therapeutic tool capable of saving the lives of young patients. Improvement of results requires early discussion between cardiologists, physicians of the resuscitation unit, and surgeons; the selection of the appropriate circulatory support modality depending on the patient’s clinical status; and cardiac transplantation as soon as the patient’s rehabilitation has been achieved. A systematic prospective patient data collection will allow us to better target the indications for MCS and thereby improve the patients’ prognosis.

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References