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CLINICAL RESEARCH

Long-term outcome of heart transplantation performed after ventricular assist device compared with standard heart transplantation

Évaluation à long terme de la transplantation cardiaque effectuée après assistance ventriculaire comparativement à la transplantation cardiaque standard

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KEYWORDS
Advanced heart failure therapies;
Heart failure;
Heart failure with

Summary
Background. — Data on the long-term outcome of heart transplantation in patients with a ventricular assist device (VAD) are scarce.
Aim. — To evaluate long-term outcome after heart transplantation in patients with a VAD compared with no mechanical circulatory support.

Abbreviations: Bi-VAD, biventricular assist device; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; MCS, mechanical circulatory support; OR, odds ratio; VAD, ventricular assist device.

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reduced ejection fraction;
Heart transplantation;
Left ventricular assist device

Methods. — Consecutive all-comers who underwent heart transplantation were included at a single high-volume centre from January 2005 until December 2012, with 5 years of follow-up. Clinical and biological characteristics, operative results, outcomes and survival were recorded. Regression analyses were performed to determine predictors of 1-year and 5-year mortality.
Results. — Fifty-two patients with bridge to transplantation by VAD (VAD group) and 289 patients transplanted without a VAD (standard group) were enrolled. The mean age was 46 ± 11 years in the VAD group compared with 51 ± 13 years in the standard group ($P = 0.01$); 17% of the VAD group and 25% of the standard group were women ($P = 0.21$). Ischaemic time was longer in the VAD group (207 ± 54 vs 169 ± 60 minutes; $P < 0.01$). There was no difference in primary graft failure (33% vs 25%; $P = 0.22$) or 1-year mortality (17% vs 28%; $P = 0.12$). In the multivariable analysis, preoperative VAD was an independent protective factor for 1-year mortality (odds ratio 0.40, 95% confidence interval 0.17—0.97; $P = 0.04$). Independent risk factors for 1-year mortality were recipient age > 60 years, recipient creatinine, body surface area mismatch and ischaemic time. The VAD and standard groups had similar long-term survival, with 5-year mortality rates of 35% and 40%, respectively ($P = 0.72$).
Conclusions. — Bridge to transplantation by VAD was associated with a reduction in 1-year mortality, leading critically ill patients to similar long-term survival compared with patients who underwent standard heart transplantation. This alternative strategy may benefit carefully selected patients.

MOTS CLÉS
Insuffisance cardiaque ;
Insuffisance cardiaque à fraction d'éjection altérée ;
Transplantation ;
Cardiaque ;
Traitements de l'insuffisance cardiaque avancée (dispositifs d'assistance ;
Ventriculaire gauche, Cœur artificiel total)

Résumé
Contexte. — Peu de données sont disponibles concernant le devenir des patients transplantés après l'implantation d'un dispositif d'assistance ventriculaire (DAV).
Objectifs. — Évaluer le devenir à long terme après transplantation cardiaque des patients implantés d'un DAV, comparativement aux patients transplantés sans dispositif.
Méthodes. — Tous les patients consécutifs qui ont bénéficié d'une transplantation cardiaque entre janvier 2005 et décembre 2012 ont été inclus au sein d'un unique centre à haut volume, avec un suivi de 5 ans. Les caractéristiques cliniques, biologiques, les résultats opératoires, le devenir et la mortalité totale ont été relevés. Des analyses de régression ont été effectuées pour déterminer les facteurs prédictifs de mortalité à 1 et 5 ans.
Résultats. — Cinquante-deux patients « DAV » et 289 patients « standards » transplantés sans DAV ont été inclus. L'âge moyen était de 46 ± 11 ans dans le groupe DAV vs 51 ± 13 ans dans le groupe standard ($p = 0,01$) et 17% des patients DAV étaient de sexe féminin vs 25% ($p = 0,21$). Le temps d'ischémie froide était plus long dans le groupe DAV (207 ± 54 vs 169 ± 60 min, $p < 0,01$). Il n'y avait pas de différence de défaillance primaire du greffon (33% vs 25%, $p = 0,22$) ou de mortalité à 1 an (17% vs 28%, $p = 0,12$). Le DAV pré-transplantation était un facteur protecteur indépendant de mortalité à 1 an (OR 0,40 [0,17-0,97], $p = 0,04$). Les facteurs de risque indépendants de mortalité à 1 an étaient l'âge du receveur>60 ans, la créatinine de receveur, le mismatch de surface corporelle et la durée d'ischémie. Les patients DAV et standards avaient une survie à long terme similaire, avec une mortalité à 5 ans respectivement de 35% et 40% ($p = 0,72$).
Conclusions. — Le pont vers la transplantation par un DAV était associé à une réduction de la mortalité à 1 an, conduisant les patients les plus critiques à une survie à long terme comparable à celle des patients transplantés de façon standard. Cette stratégie alternative est susceptible de bénéficier à une population de patients sélectionnés.

Background

Heart transplantation was first performed in 1967, and has become the best available treatment for symptomatic end-stage heart failure refractory to optimal medical care in young patients with no co-morbidities [1,2]. The outcome of these patients is improved, especially when heart transplantation is performed in a relatively stable situation, with no concomitant organ failure. In acute settings or because of cardiac graft shortage, mechanical circulatory support (MCS) is an alternative option, and is considered as a ''bridge to transplantation'' when it eventually leads

to heart transplantation [3]. With an increasing population of patients awaiting heart transplantation worldwide, and a lack of available or suitable organs, the number of candidates for the bridge to transplantation strategy is growing.

Simultaneously, the development of new implantable devices for circulatory support (reduced size; increased biocompatibility and haemodynamic support) and improvements in surgical techniques for device implantation have reduced postoperative complications [4]. MCS by ventricular assist device (VAD) has emerged as the reference standard for mid-term circulatory support in this setting [5,6]. Carefully selected patients with maximal medication and single-organ failure transplanted in optimal conditions are known to have the best outcome and survival rate [1,7—10]. However, data on the outcome of patients with bridge to transplantation compared with standard heart transplantation are still scarce and conflicting [11—13]. To date, only two unmatched studies have reported acceptable post-transplantation outcome in patients bridged by a continuous-flow left ventricular assist device (LVAD) [14]. In this study, we report the outcome of patients with VAD as a bridge to transplantation compared with stable patients with standard heart transplantation at a single centre.

Methods

Study population

We conducted a single-centre retrospective observational study in a single high-volume French centre (Pitié-Salpêtrière Hospital, AP—HP, Paris, France). All stable patients who underwent orthotopic heart transplantation between January 2005 and December 2012 were included in this study; patients who underwent cardiac transplantation in an urgent setting were excluded from the analysis. Demographics, clinical characteristics of recipients and donors, type of VAD, operative results, outcome after heart transplantation and survival were recorded. Patients transplanted after stabilization by the implantation of a VAD were compared with those transplanted without previous circulatory support. Donor and recipient data were obtained from ''Cristal'', the database of the French regulatory agency for transplantation (l'Agence de la Biomédecine). Patients were managed as indicated in the care protocol shown in Fig. 1.

Type of VAD

The VADs included LVADs and biventricular assist devices (Bi-VADs). The LVADs were either continuous-flow pumps (HeartMate II®, Thoratec Corp., Pleasanton, CA, USA; HeartWare®, HeartWare International Inc., Framingham, MA, USA; Jarvik 2000®, Jarvik Heart Inc., New York, NY, USA) or a pulsatile-flow pump (PVAD®, Thoratec Corp., Pleasanton, CA, USA). The Bi-VADs were CardioWest® total artificial heart (SynCardia Systems Inc., Tucson, AZ, USA), or PVAD® (Thoratec Corp., Pleasanton, CA, USA). The principles of these devices and their surgical implantation have been detailed previously [5,15,16].

Patient management

All patients included in our study were receiving maximal medical treatment regarding standards for heart failure therapy, considering the medical knowledge at the time of heart transplantation. Biventricular pacing and a defibrillator were part of the baseline treatment for eligible patients. Added to standard and maximal heart failure medical and instrumental therapy, all patients in the VAD group received aspirin and anticoagulation with a vitamin K antagonist (warfarin or fluindione); they all underwent standard a postoperative rehabilitation programme after device placement, and further close routine follow-up in our centre.

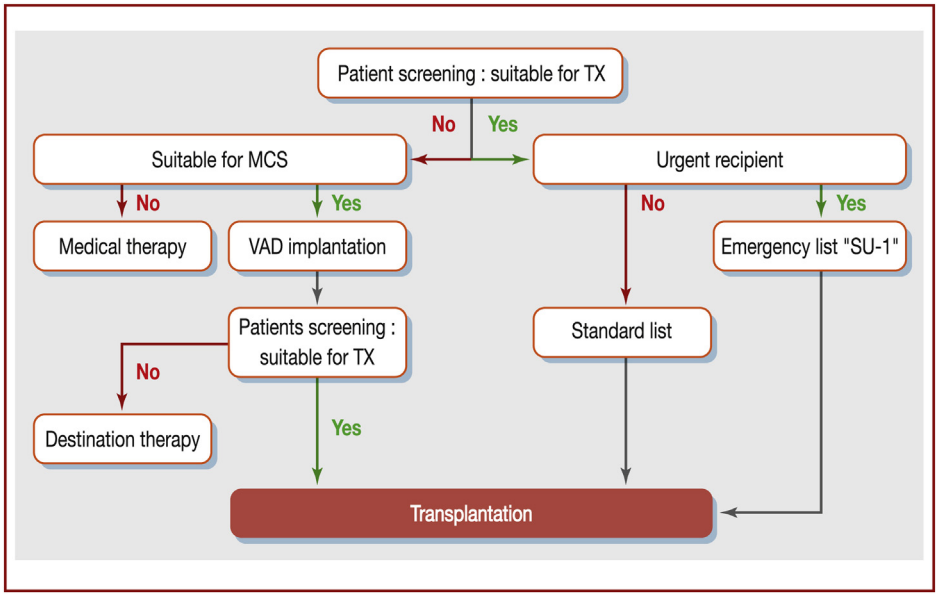

Figure 1. Care protocol. MCS: mechanical circulatory support; N: no; SU: super urgent; TX: transplant; VAD: ventricular assist device; Y: yes.

Contrary to standard heart transplantation, based on the on-call chronological waiting list in compatible patients, patients where scheduled for VAD because of haemodynamic instability resulting from worsening heart failure or acute heart failure. The other indication was a lack of a suitable graft when listed on the national top priority (''super emergency'' list). Contraindications were linked to co-morbidities, especially severe renal failure or any disease that reduced life expectancy to less than 1 year.

Management post-transplantation

All patients who underwent transplantation received immunosuppressive therapy according to a standard protocol implemented in our centre. Early postoperative immunosuppressive induction therapy included an initial 1000 mg prednisolone intravenous loading dose and thymoglobulin 1.5 mg/kg/day for 4 days. Intravenous immunoglobulin at 1.5 g/kg/day for 5 days, daily plasmapheresis for 5 days and a single dose of 375 mg/m^2 rituximab were gradually administered and combined according to the severity of alloimmunization, reflected in the mean fluorescence index score of donor-specific antibodies. Immunosuppressive maintenance therapy combined a 1 mg/kg prednisone taper (targeting 20 mg/day at 3 months, then 5—10 mg/day at 6 months), cyclosporin 2—5 mg/kg/day started at postoperative day 3 (targeting an initial serum residual concentration of 250 mg/L) and mycophenolate mofetil 1500 mg twice a day.

Evaluation of outcomes

Follow-up and close monitoring of all these patients are routinely performed life-long after heart transplantation, with evaluation through outpatient appointments or short in-hospital stays, monthly during the first 6 months, then each 6-month period at a minimum. Baseline and follow-up data were collected, and subgroup analyses were performed to assess the outcome depending on the presence of VAD before cardiac transplantation. Major clinical events after transplantation (acute graft failure, in-hospital death) and long-term survival were reported in both subgroups. This study was approved by our hospital's institutional review board.

Statistical analysis

Data collection was realized prospectively and analysed retrospectively. Comparisons were performed for continuous variables using analysis of variance or the *t* test, and for categorical variables using the χ^2 test or Fisher's exact test. A stepwise logistic regression was performed to determine predictors of 1-year mortality, with a cut-off of $P = 0.10$. To measure model discrimination, the C-statistic (area under the receiver operating characteristic curve) was used, and the Hosmer—Lemeshow test was used for goodness-of-fit assessment. The Kaplan-Meier method was used for survival analysis, and survival curves were compared using the log-rank test. Cox proportional hazard regression was performed to assess predictors of 5-year mortality.

Data are expressed as means ± standard deviations for continuous variables, and numbers (percentages) for qualitative variables. All *P* values were two-tailed.

All statistical analyses were performed with the StatView® statistical package, version 5 (SAS Institute Inc., Cary, NC, USA).

Results

Clinical characteristics

A total of 341 patients were included in this study: 52 received a VAD as a bridge to transplantation, and 289 underwent standard heart transplantation. Clinical characteristics of the cohort are summarized Table 1. The mean age was 50 ± 13 years in the overall cohort, and 76% of patients were male. VAD group patients were younger ($P = 0.01$), with a smaller proportion of women (17% vs 25%; $P = 0.21$) and older patients. The underlying cardiomyopathy resulted from various aetiologies, but idiopathic dilated cardiomyopathy and ischaemic cardiomyopathy were the most represented, accounting for 74% of the overall cohort; this proportion reached 92% in the VAD group. The presence of the device meant that all VAD group patients had undergone a previous sternotomy, which was noted in less than a quarter of the standard group, and was mainly driven by previous coronary artery bypass graft. Of the 54 patients in the VAD group, 25 received an LVAD and 27 received a Bi-VAD (Table 2). LVADs included continuous and pulsatile-flow pumps, but nearly all patients received the HeartMate II® device. In the Bi-VAD subgroup, all patients but two received the CardioWest® total artificial heart. Preoperative clinical status regarding inotropes and mechanical ventilation was similar in both VAD and standard groups.

Donors were male in 58% of cases, with a mean age of 47 ± 13 years. The VAD group were transplanted with younger donors ($P = 0.02$). However, donors were old, as 46% were aged > 50 years, and 17% were aged > 60 years. No significant body surface area mismatch was observed between the two groups ($P = 0.09$). The waiting time for heart transplantation was higher in the VAD group than the standard group but did not reach statistical significance (191 ± 314 and 164 ± 286 days, respectively; $P = 0.54$).

Short-term outcome post-transplantation

Compared with the standard group, the VAD group had an increased ischaemic time (207 ± 54 vs 169 ± 60 minutes; $P < 0.01$). Primary graft failure leading to postoperative circulatory assistance by peripheral venoarterial extracorporeal membrane oxygenation (ECMO) occurred in 26% of the overall cohort, without significant difference between the two groups ($P = 0.22$). In-hospital events including infection, weaning duration from mechanical ventilation, bleeding complications and renal replacement therapy were not collected exhaustively.

The 30-day operative mortality rate was 12% in the VAD group compared with 16% in the standard group ($P = 0.39$). The 1-year mortality rate was 26% in the overall cohort. The VAD group had a non-significant lower mortality rate than the standard group at 1-year follow-up (17% vs 28%, respectively; $P = 0.12$) Multivariable analysis showed that VAD implantation was associated with a reduced mortality rate at 1 year (odds ratio [OR] 0.399, 95% confidence interval [CI]

Table 1 Clinical demographics.

	All ($n=341$)	Standard group ($n=289$)	VAD group ($n=52$)	P
Recipient				
Age (years)	50 ± 13	51 ± 13	46 ± 11	0.01
Age > 50 years	220 (34)	195 (67)	25 (48)	< 0.01
Age > 60 years	88 (25)	82 (28)	6 (11)	0.01
Waiting time (days)	168 ± 290	164 ± 286	191 ± 314	0.54
Female sex	82 (24)	73 (25)	9 (17)	0.21
Aetiology				
Ischaemic cardiomyopathy	110 (32)	91 (31)	19 (36)	0.47
Dilated cardiomyopathy	145 (42)	116 (40)	29 (56)	0.03
Previous sternotomy	121 (35)	69 (24)	52 (100)	< 0.01
Implantable cardioverter defibrillator	152 (45)	134 (46)	18 (35)	0.12
Serum creatinine (μmol/L)	113 ± 57	112 ± 50	123 ± 96	0.54
Creatinine clearance (mL/min)	79 ± 40	76 ± 37	96 ± 51	0.01
Diabetes	56 (16)	48 (17)	8 (16)	0.87
Preoperative ventilation	3 (0.9)	1 (0.3)	2 (4)	0.06
Preoperative inotropes	24 (7)	22 (8)	2 (4)	0.55
Donor				
Age (years)	47 ± 13	47 ± 12	43 ± 14	0.02
Age > 50 years	158 (46)	138 (48)	20 (38)	0.69
Age > 60 years	59 (17)	51 (18)	8 (15)	0.01
Female sex	144 (42)	129 (44)	15 (29)	0.03
Male recipient/female donor	88 (26)	77 (27)	11 (21)	0.40
Weight mismatch > 0.15	40 (12)	29 (10)	11 (21)	0.02
Body surface area mismatch > 0.15	12 (3.5)	8 (2.8)	4 (8)	0.09
Operative results				
Ischaemic time (minutes)	174 ± 60	169 ± 60	207 ± 54	< 0.01
Primary graft failure	89 (26)	72 (25)	17 (33)	0.22
1-year mortality	89 (26)	80 (28)	9 (17)	0.12

Data are expressed as mean ± standard deviation or number (%). VAD: ventricular assist device.

Table 2 Ventricular assist devices used ($n=52$).

LVAD	25 (48)
Continuous-flow pump	
HeartMate II®[a]	22 (42)
HeartWare®[b]	1 (2)
Jarvik 2000®[c]	1 (2)
Pulsatile-flow pump	
PVAD®[a]	1 (2)
Bi-VAD	27 (52)
CardioWest® total artificial heart[d]	25 (48)
PVAD®[a]	2 (4)

Data are expressed as number (%). Bi-VAD: biventricular assist device; LVAD: left ventricular assist device; VAD: ventricular assist device.
[a] Thoratec Corp., Pleasanton, CA, USA.
[b] HeartWare International Inc., Framingham, MA, USA.
[c] Jarvik Heart Inc., New York, NY, USA.
[d] SynCardia Systems Inc., Tucson, AZ, USA.

0.165—0.967; $P=0.04$). Factors associated with increased 1-year mortality were recipient age > 60 years, recipient serum creatinine, body surface area mismatch > 0.15 and prolonged ischaemic time (Table 3).

Long-term outcome post-transplantation

The overall survival rate at 5 years was 61%, with no statistically significant difference between the VAD and standard groups (65% vs 60%, respectively; $P=0.72$) (Fig. 2). Independent risk factors for 5-year survival were recipient age > 60 years (OR 1.570, 95% CI 1.052—2.343; $P=0.02$), recipient creatinine (OR 1.005, 95% CI 1.002—1.008; $P=0.02$) and ischaemic time (OR 1.004, 95% CI 1.001—1.007; $P=0.01$) (Table 3).

Discussion

Interpretation of results in light of recent evolution in heart failure management

Our study reports data from a series of patients transplanted after bridge by VAD at a single centre, and shows that these

Table 3 Risk-adjusted multivariable analysis for death risk.

Risk factor	OR (95% CI)	*P*
At 1 year		
VAD group	0.399 (0.165—0.967)	0.04
Recipient age > 60 years	2.353 (1.339—4.135)	< 0.01
Recipient creatinine	1.005 (1.001—1.010)	0.02
Body surface area mismatch > 0.15	4.847 (1.340—17.536)	0.02
Ischaemic time	1.005 (1.001—1.010)	0.02
At 5 years		
VAD group	0.668 (0.364—1.226)	0.19
Recipient age > 60 years	1.570 (1.052—2.343)	0.02
Recipient creatinine	1.005 (1.002—1.008)	0.02
Ischaemic time	1.004 (1.001—1.007)	0.01

CI: confidence interval; OR: odds ratio; VAD: ventricular assist device.

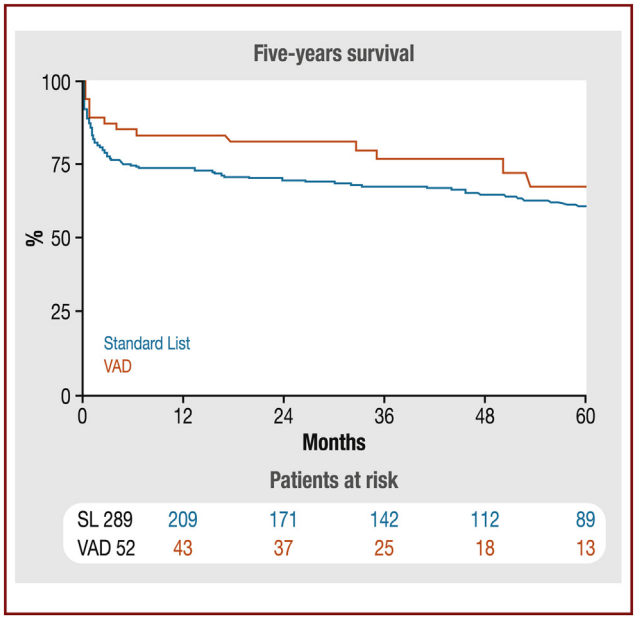

Figure 2. Kaplan—Meier curve of survival after heart transplantation, with or without ventricular assist device. Overall mortality at 5 years in 52 patients transplanted after bridge by ventricular assist device (VAD) versus 289 with no assistance. SL: standard list.

patients have an acceptable outcome, with good long-term survival. The results of this study even suggest that bridge to transplantation by VAD is associated with long-term survival that is similar to conventional heart transplantation. Moreover, VAD was identified as a major protective factor, reducing 1-year mortality by 60%.

The profile of patients with heart failure has changed over the past decade. Eligibility for heart transplantation is now discussed after optimized medical treatment for heart failure, including beta-blockers, renin — angiotensin system antagonists, aldosterone receptor blockers, ivabradine, digoxin and diuretics. Most patients receive an implantable cardioverter defibrillator to prevent sudden death from malignant ventricular arrhythmias; they are also screened for cardiac resynchronization therapy, and a significant proportion may benefit from biventricular pacing. Cardiac rehabilitation increases survival, and also has a growing place in the management of these patients. Unresponsiveness to such treatments may occur later in the natural history of heart failure.

Post-transplantation management and immunosuppressive therapies have also improved greatly. Technical improvements in circulatory support devices are of great significance. Implantable continuous-flow devices demonstrated convincing results and good outcome in 2007, so the use of pulsatile-flow devices stopped in our centre thereafter [5,17,18]. Surgical skills and techniques in implanting circulatory devices have improved simultaneously. All of these factors may have had an impact on the long-term results of cardiac transplantation.

French specificities regarding heart transplantation and indication for VAD

The number of patients who undergo heart transplantation in France reaches 400 each year and has remained stable over the past 4 years; more than 20% of these procedures are performed in our centre. The number of candidates for heart transplantation is gradually increasing year after year, and they may benefit from circulatory support as a bridge to transplantation, a bridge to decision or even as a destination therapy. The indication for VAD in our centre is a bridge to transplantation for advanced heart failure refractory to conventional management (class 2 or 3 of the INTERMACS classification [19]) and an indication for heart transplantation. Contraindications are ongoing cardiogenic shock, defined as class 1 in the INTERMACS classification, because the high early postoperative mortality outweighs the expected long-term benefits [20], associated co-morbidities or severe organ failure and lack of expected compliance. The rate of mortality or clinical worsening while on the waiting list for transplantation was reported at 13% between 2015 and 2016 by the l'Agence de la Biomédecine in France. In patients with mid-term MCS, the mortality rate while waiting for heart transplantation was 6.4% between 2015 and 2016.

In unstable situations with multiple organ failure, heart transplantation is no longer performed. MCS should be preferred [21], to supply the impaired circulation and target a ''single organ failure'' situation as an objective. Patients with severe refractory heart failure, such as INTERMACS 1 (crash and burn) should be screened for peripheral venoarterial ECMO, even at the bedside, but not for a VAD [22]. A VAD is usually implanted in case of refractory heart failure and haemodynamic compromise, when heart transplantation cannot be performed [23]. Associated organ failure is common, and heart transplantation in such a context has a poor prognosis, and hence becomes contraindicated temporarily. The shortage of cardiac grafts adds to this medical issue.

Outcomes of heart transplantation after VAD

MCS using a VAD may stabilize haemodynamics, and has become our routine practice when the patient has no evidence of persisting contraindication to heart transplantation [24]. These patients are supposed to have a worse post-transplantation prognosis compared with patients who undergo standard heart transplantation [3,25—27], which was not confirmed by the results of our study. Counterintuitively, our data highlight an improvement in outcome with a ''VAD as a bridge to transplantation'' strategy compared with standard medical management. A possible explanation for this finding may be that restoring haemodynamics and reversing metabolic, cellular and nutritional compromises help the recovery of associated organ failure before heart transplantation, leading to better postoperative outcome. It should be remembered that standard heart transplantation is performed in patients with severe chronic heart failure, whereas transplantation bridged by a VAD is performed in patients with durably restored heart failure and normalized cardiac output.

Another explanation may lie in the technological progress, with the development of more biocompatible, smaller and more reliable devices for cardiac assistance. Portable control units and prolonged battery life allows mobility for the patient, with the ability to go back home and get involved in a rehabilitation programme. The increased waiting time to transplantation in the VAD group also provides more time to choose better-fitting donor grafts for the recipients, as suggested by the younger mean age of the donors and the lower prevalence of elderly donors in the VAD group; this may translate into better post-transplantation outcome.

Third, it must be underlined that the 1-year mortality rate in the standard group was unexpectedly high. Mean post-transplantation 1-year mortality rate has been reported as being between 15% and 20%, but the rate in our cohort reached 28% [28,29]. Part of the explanation may be attributed to the older age of both donors and recipients. In our series, the proportion of donors aged > 60 years was 18%, and recipients aged > 60 represented 28% of the patients. On top of this, male recipients with female donors may have played a role, and this situation was seen frequently, in 27% of cases. These positive aspects of VADs should not obscure the increased initial morbidity, including the prolonged waiting time for heart transplantation, surgical concerns caused by the VAD, leading to a prolonged ischaemic time of nearly 40 minutes, and by the high rate of weight mismatch, and more frequent primary graft failure.

Study strengths

Our study has several strengths. It was conducted recently, and only included patients since 2005; this was because post-transplantation ECMO was used routinely from that time. Moreover, it also corresponds to the emergence and validation of implantable continuous-flow LVAD devices, such as HeartMate II® [30] and HeartWare® [5,18,31,32], for long-term circulatory support. Over the past decade, dramatic improvements have been made in terms of circulatory assist devices and surgical techniques for performing heart transplantation, as well as in device implantation and the management of patients immediately after the operation and during long-term follow-up. Other aspects to consider are the single-centre design and the relatively short period over which the study was conducted. This reflects contemporary surgical experience and up-to-date skills, with more homogenous results and uniform practices. As a result, nearly all VADs were represented by HeartMate II® and the CardioWest® total artificial heart. Consequently, a temporal effect was avoided in our present work, unlike in many previous studies on this topic.

Study limitations

Nevertheless, our study has some limitations. This study was not randomized and was limited to a small number of patients in the VAD group compared with multicentre studies. As this study was not randomized, it was impossible to assess the superiority of one management over another, and the very critical status of the VAD group patients has to be kept in mind. Despite the multivariable analysis suggesting improved survival in the VAD group, only a randomized trial can perfectly address this question. However, there were study-consistent practices regarding circulatory assistance and perioperative and postoperative management. Although donors and recipients are selected uniformly in such a single-centre study, criteria may vary across countries, and therefore may influence the long-term outcome of transplanted patients. A single-centre study has the limitation of less strict inclusion and exclusion criteria, but has the strength of homogenous practices, and large number of patients undergoing heart transplantation, unlike small series of patients pooled together from multiple centres. Different types of VAD were used, but the results were mainly driven by Heart-Mate II® and the CardioWest® total artificial heart. Focusing on patients with continuous-flow VADs only, such as Heart-Mate II®, would have selected a very small cohort, with no opportunity to perform comparisons that make sense or valid statistical analyses. Other limitations of our present study are the lack of data regarding pretransplantation mortality and morbidity in the VAD group, post-transplantation infection and rejection, weaning duration from mechanical ventilation, bleeding complications and renal replacement therapy.

Finally, VADs may not be used routinely in all countries, given their high cost and the reimbursement policies of local health authorities. All of these socioeconomic aspects must be carefully taken into account, and further cost-effectiveness studies are mandatory.

Conclusions

Our study has demonstrated that bridge to transplantation by VAD reduces 1-year mortality and improves the long-term survival rate after heart transplantation compared with standard management, with similar survival, despite having increased post-transplantation morbidity as a price to pay. We identified VAD as a major factor in reducing long-term post-transplantation mortality in carefully selected patients.

Patients with symptomatic end-stage heart failure who become candidates for heart transplantation are a

growing population that is expected to increase exponentially in future decades. Medical and technological progress over the past 10 years have led to reduced waiting times for heart transplantation and better long-term outcomes. Circulatory assist devices have dramatically changed the prognosis of the most critically ill patients, by increasing their probability of being transplanted in a stabilized haemodynamic situation with better functional status and improved quality of life. Our experience brings consistent data to support the strategy of a VAD as a bridge to transplantation for eligible patients, as it was associated with favourable outcome and similar survival compared with patients undergoing conventional transplantation. These observations need to be confirmed by further large prospective clinical and cost-effectiveness studies.

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