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Impact of short-term mechanical circulatory support with extracorporeal devices on postoperative outcomes after emergency heart transplantation: Data from a multi-institutional Spanish cohort

Eduardo Barge-Caballero [a,b,*], Luis Almenar-Bonet [c], Adolfo Villa-Arranz [d], Félix Pérez-Villa [e], Javier Segovia-Cubero [f], Juan Delgado-Jiménez [g], Francisco González-Vilchez [h], Nicolás Manito-Lorite [i], Luis De-la-Fuente-Galán [j], Vicens Brossa-Loidi [k], Jose L. Lambert-Rodríguez [l], Domingo Pascual-Figal [m], Ernesto Lage-Gallé [n], Jose M. Arizón-Del-Prado [o], Marisa Sanz-Julve [p], Javier Muñiz-García [b,q], Marisa Crespo-Leiro [a,b]

[a] Complejo Hospitalario Universitario A Coruña, A Coruña, Spain
[b] Instituto de Investigación Biomédica de A Coruña (INIBIC), A Coruña, Spain
[c] Hospital Universitario Politécnico La Fe. Valencia, Spain
[d] Hospital Gregorio Marañón, Madrid, Spain
[e] Hospital Clinic i Provincial, Barcelona, Spain
[f] Hospital Puerta de Hierro, Madrid, Spain
[g] Hospital Doce de Octubre, Madrid, Spain
[h] Hospital Marqués de Valdecilla, Santander, Spain
[i] Hospital de Bellvitge, Hospitalet de Llobregat, Spain
[j] Hospital Clínico Universitario de Valladolid, Valladolid, Spain
[k] Hospital Santa Creu i Sant Pau, Barcelona, Spain
[l] Hospital Universitario Central de Asturias, Oviedo, Spain
[m] Hospital Virgen de la Arrixaca, Murcia, Spain
[n] Hospital Virgen del Rocio, Sevilla, Spain
[o] Hospital Reina Sofía, Córdoba, Spain
[p] Hospital Miguel Servet, Zaragoza, Spain
[q] Instituto Universitario de Ciencias de la Salud, Universidad de A Coruña, A Coruña, Spain

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ABSTRACT

Objectives: We sought to investigate the potential impact of preoperative short-term mechanical circulatory support (MCS) with extracorporeal devices on postoperative outcomes after emergency heart transplantation (HT).
Methods: We conducted an observational study of 669 patients who underwent emergency HT in 15 Spanish hospitals between 2000 and 2009. Postoperative outcomes of patients bridged to HT on short-term MCS (n = 101) were compared with those of the rest of the cohort (n = 568). Short-term MCS included veno-arterial extracorporeal membrane oxygenators (VA-ECMOs, n = 23), and both pulsatile-flow (n = 53) and continuous-flow (n = 25) extracorporeal ventricular assist devices (VADs). No patient underwent HT on intracorporeal VADs.
Results: Preoperative short-term MCS was independently associated with increased in-hospital postoperative mortality (adjusted odds-ratio 1.75, 95% CI 1.05–2.91) and overall post-transplant mortality (adjusted hazard-ratio 1.60, 95% CI 1.15–2.23). Rates of major surgical bleeding, cardiac reoperation, postoperative infection and primary graft failure were also significantly higher among MCS patients. Causes of death and survival after hospital discharge were similar in MCS and non-MCS candidates. Increased risk of post-transplant mortality affected patients bridged on pulsatile-flow extracorporeal VADs (adjusted hazard-ratio 2.21, 95% CI 1.48–3.30) and continuous-flow extracorporeal VADs (adjusted hazard-ratio 2.24, 95% CI 1.20–4.19), but not those bridged on VA-ECMO (adjusted hazard-ratio 0.51, 95% CI 0.21–1.25).
Conclusions: Patients bridged to emergency HT on short-term MCS are exposed to an increased risk of postoperative complications and mortality. In our series, preoperative bridging with VA-ECMO resulted in comparable post-transplant outcomes to those of patients transplanted on conventional support.

* Corresponding author at: Servicio de Cardiología, Complejo Hospitalario Universitario A Coruña, As Xubias, 84, 15006 A Coruña, Spain. Tel.: +34 649280319; fax: +34 981178299.
E-mail address: eduardo.barge.caballero@sergas.es (E. Barge-Caballero).

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1. Introduction

The number of patients bridged to heart transplantation (HT) under mechanical circulatory support (MCS) is growing worldwide [1]. In this setting, the goal of MCS is not only to increase patient's life expectancy, but also to improve their quality of life, end-organ function and nutritional status, so favoring better post-transplant outcomes. However, the potential benefits of MCS may be counteracted by device-related complications [2] such as infection, embolism, bleeding, or immune sensitization.

Intracorporeal left ventricular assist devices (LVADs) constitute the current standard-of-care to provide long-term MCS to HT candidates whose clinical status deteriorates while waiting for an organ donor. According to the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS), 1-year and 2-year survival rates of patients who currently receive a continuous-flow intracorporeal LVAD as a bridge-to-transplantation respectively exceed 80% and 70% [3]. In a pooled analysis of 12 observational studies, patients bridged to HT on intracorporeal LVADs showed comparable post-transplant survival to candidates bridged on optimal medical therapy, including intravenous inotropes [4]. A propensity-score-matched analysis of the United Network for Organ Sharing (UNOS) database reached a similar conclusion [5].

The implantation of an intracorporeal LVAD, however, is not the best therapeutic option for all HT candidates that require MCS. Postoperative mortality after LVAD surgery is significantly increased when the device is implanted in severely acute decompensated patients [6], or in the presence of right ventricular failure [7]. In most of these cases, the implantation of a short-term extracorporeal device constitutes a more suitable initial approach. Short-term MCS usually results in a rapid hemodynamic stabilization, and favors the recovery of the end-organ function, allowing the patient to undergo a destination procedure such as HT or long-term VAD implantation with a reasonable expectancy of survival [8]. Worldwide, the use of short-term extracorporeal devices as a direct bridge to HT is an uncommon strategy, as it implies that a suitable organ donor must become available for the patient within a few days. In Spain, however, it is frequently resorted to, as the use of long-term intracorporeal LVADs is subject to tight economic restrictions.

The potential impact of preoperative short-term extracorporeal MCS on post-transplant outcomes has been less studied than in the case of intracorporeal LVADs. Previous analyses included a small number of patients supported on short-term devices, and showed conflicting results. Some authors found that patients bridged to HT on extracorporeal MCS were exposed to an increased risk of post-transplant mortality [4,9], but others reported that they have similar post-transplant outcomes to candidates bridged on intravenous inotropes [10]. The potential impact of different extracorporeal devices on post-transplant outcomes has not yet been determined.

In view of gaps in knowledge, we sought to study the impact of preoperative short-term MCS on post-transplant outcomes. For this purpose, we analyzed in-hospital postoperative complications, long-term survival, and causes of death of patients who underwent emergency HT in Spain during the past decade after being supported with short-term extracorporeal VADs or veno-arterial extracorporeal membrane oxygenators (VA-ECMOs), and compared them with a control group of patients who underwent emergency HT without preoperative MCS during the same period.

2. Methods

2.1. Setting of the study

We conducted a multi-institutional, observational study based on a historical cohort of patients who underwent first, single-organ HT under a high-emergency status – the so-called status 0 – in the Spanish organ donor allocation system (Organización Nacional de Trasplantes, ONT) between January 1st, 2000 and December 31st, 2009.

During the study period, listing criteria for ONT status 0 required permanent hospitalization due to a non-reversible cardiac disease with an imminent risk of death, and either continuous dependence on short-term extracorporeal MCS, an intra-aortic balloon pump (IABP), or invasive mechanical ventilation together with intravenous inotropes, or the presence of recurrent life-threatening ventricular arrhythmias despite optimal medical therapy. Heart transplant candidates listed under ONT status 0 had priority over all other candidates to get the first suitable donor heart available in the system. Long-term intracorporeal VADs were not available in Spain during the study period.

2.2. Short-term mechanical circulatory support

In this study, the definition of short-term MCS refers to extracorporeal devices intended for left ventricular, right ventricular, or biventricular circulatory assistance for a maximum period of a few weeks (usually < 30 days). This included continuous-flow extracorporeal VADs (Levitronix Centrimag, Medtronic Biomedicus, Medos HIA-VAD, Jostra Rotaflow and Impella 5L), pulsatile-flow extracorporeal VADs (Abiomed BVS5000, Abiomed AB5000, Berlin Heart Excor, and Thoratec), and VA-ECMO (Maquet PLS, Maquet Cardiohelp, Medos Deltastream, and Medtronic Biomedicus). Patients bridged to emergency HT solely under IABP support were included in the control group.

2.3. Data collection and variables

Data for the study were extracted from a multicentre database [11] that contains detailed clinical information about all consecutive patients aged > 18 years who underwent emergency HT between 2000 and 2009 in 15 out of the 16 Spanish hospitals that had an active HT program at that time. This database was assembled with data collected from the prospective Spanish National Heart Transplantation Registry [12] and completed on the basis of an individualized review of clinical records. For the present analysis, patients who underwent re-transplantation or double-organ transplantation were not considered. The institutional review board approved the study protocol.

2.4. Post-transplant outcomes

In-hospital postoperative outcomes of the study were major surgical bleeding, need for cardiac reoperation, need for dialysis, postoperative infection, primary graft failure, isolated right ventricular failure and in-hospital postoperative mortality. Long-term outcomes were post-transplant survival and discharge-conditioned post-transplant survival. Causes of death were collected from autopsy studies or, if not available, from medical certificates of death. Specific definitions of study outcomes have been detailed previously [11] and are provided as Supplementary data.

2.5. Statistical analysis

In this manuscript, categorical variables are presented as proportions and compared by means of the Chi-squared test, while continuous variables are presented as mean ± standard deviation and compared by means of the T-Student test.

Post-transplant survival curves of patients bridged to HT with or without short-term MCS were estimated by means of the Kaplan–Meier method and compared by means of the log-rank test, both in the entire cohort and in the subcohort of individuals who survived the early postoperative period and were discharged alive from hospital. Follow-up was censored at the time of death or the last clinical visit, up to a maximum of 5 years after HT.

Adjusted hazard-ratios (HRs) for overall post-transplant mortality and discharge-conditioned post-transplant mortality were obtained by means of backward stepwise multivariable Cox's proportional hazards models. Candidate variables that entered multivariable analyses were those that showed a statistically significant association ($p < 0.05$) with each one of these outcomes in univariable analyses and others considered as potential confounders on the basis of previous literature and clinical experience. In a similar manner, the association between short-term MCS and in-hospital postoperative outcomes was assessed by means of backward stepwise multivariable logistic regression models.

In view of the asymmetric distribution of MCS and non-MCS patients over the study period, this was arbitrarily divided into two eras, the early era (years 2000 to 2006), and the recent era (years 2007 to 2009). Specific subanalyses about the impact of short-term MCS on post-transplant survival during both eras were conducted.

Statistical significance was set as a p-value < 0.05, and all contrasts were two-tailed. Statistical analysis was performed with SPSS Statistics 20.

3. Results

3.1. Study population

According to the Spanish National Heart Transplantation Registry, 2956 patients aged > 18 years underwent HT in our country between 2000 and 2009. Seven hundred and twenty-four patients underwent HT under ONT status 0, with 711 of them at the 15 hospitals participating in the study. After the exclusion of 29 patients who underwent re-transplantation and 13 patients who underwent simultaneous double-organ transplantation, the final study sample comprised 669 patients.

One hundred and one (15%) patients were bridged to HT on short-term MCS. Twenty-five patients from 9 centers were supported on