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Prolonged intra-aortic balloon pump support in biventricular heart failure induces right ventricular reverse remodeling

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ABSTRACT

Background: Right ventricular dysfunction is associated with high morbidity and mortality in candidates for left ventricular assist device (LVAD) implantation or cardiac transplantation.
Methods: We examined the effects of prolonged intra-aortic balloon pump (IABP) support on right ventricular, renal and hepatic functions in patients presenting with end-stage heart failure.
Results: Between March 2008 and June 2013, fifteen patients (mean age = 49.5 years; 14 men) with end-stage systolic heart failure (HF), contraindications for any life saving procedure (conventional cardiac surgery, heart transplantation, LVAD implantation) and right ventricular dysfunction were supported with the IABP. The patients remained on IABP support for a mean of 73 ± 50 days (median 72, range of 13–155). We measured the echocardiographic and hemodynamic changes in right ventricular function, and the changes in serum creatinine and bilirubin concentrations before and during IABP support. Mean right atrial pressure decreased from 12.7 ± 6.5 to 3.8 ± 3.3 ($P < 0.001$) and pulmonary artery pressure decreased from 35.7 ± 10.6 to 25 ± 8.4 mm Hg ($P = 0.001$), while cardiac index increased from 1.5 ± 0.4 to 2.2 ± 0.7 l/m^2/min ($P = 0.003$) and right ventricular stroke work index from 485 ± 228 to 688 ± 237 mm Hg × ml/m^2 ($P = 0.043$). Right ventricular end-diastolic diameter decreased from 34.0 ± 6.5 mm to 27.8 ± 6.2 mm ($P < 0.001$) and tricuspid annular systolic tissue Doppler velocity increased from 9.6 ± 2.4 cm/s to 11.1 ± 2.3 cm/s ($P = 0.029$). Serum creatinine and bilirubin decreased from 2.1 ± 1.3 to 1.4 ± 0.6 mg/dl and 2.0 ± 1.0 to 0.9 ± 0.5 mg/dl, respectively ($P = 0.002$ and $P < 0.001$, respectively).
Conclusions: Prolonged IABP support of patients presenting with end-stage heart failure and right ventricular dysfunction induced significant improvement in right ventricular and peripheral organ function.

1. Introduction

Right ventricular (RV) dysfunction, a common complication of heart failure (HF) patients undergoing a left ventricular device (LVAD) implantation, is associated with increased peri-operative mortality and decreased survival to cardiac transplantation (HTx) [1–3]. Consequently, patients at high risk of developing post-operative RV dysfunction are considered to be bad candidates for left ventricular (LV) support alone. While biventricular assist devices (BiVADs) are the only option for this subset of patients, their use is complicated and their implantation has been associated with a 55% 1-year survival, compared with 80% survival after 1 year of isolated LV mechanical support [4]. In another report, the 1-year survival of patients bridged to HTx with a BiVAD was 81% compared with 87% in patients who were bridged with an LVAD alone [5].

Several clinical and laboratory indices have been used to predict the incidence of RV dysfunction after LVAD implantation. Depressed RV contractility ascertained echocardiographically and hemodynamically, elevated central venous pressure and renal and hepatic dysfunction are all reliable predictors of post-operative RV dysfunction [6–8]. The contributions of the intra-aortic balloon pump (IABP) to the reversal of peripheral organ dysfunction in end-stage heart failure (HF) have been only anecdotally described, however, the duration of mechanical support reported in a study was based on the time needed to find a suitable donor rather than on a specific investigative protocol [9].

Abbreviations: RV, right ventricular; HF, heart failure; LVAD, left ventricular assist device; HTx, heart transplantation; LV, left ventricular; BiVAD, biventricular assist device; IABP, intra-aortic balloon pump; RA, right atrial; RVSWI, RV stroke work index; Sm, tricuspid annular systolic tissue Doppler velocity; EDD, end-diastolic diameter; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support.

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Furthermore, the effects of the IABP on RV function have not been studied in depth. A single experimental study reported an increase in RV ejection fraction mediated by the IABP in a sheep model of pressure overload-induced acute RV failure [10]. Similar results were reported in a small series of patients who developed low cardiac output syndrome with predominant RV failure immediately after HTx [11]. These observations, however, have not been systematically studied on the long term.

The present study was designed to investigate the potential of RV and peripheral organ function recovery by prolonged IABP support in patients suffering from end-stage HF.

2. Materials and methods

The Ethics Review Board of our institution approved this study, which conforms to the principles outlined in the Declaration of Helsinki, and all its participants granted an informed consent.

2.1. Study sample

Between March 2008 and June 2013, twenty two patients with end-stage HF (New York Heart Association HF functional classes IIIb or IV), severe LV systolic dysfunction and contraindications for other life saving procedures (conventional cardiac surgery, heart transplantation, LVAD implantation) were supported with the IABP in our tertiary university center as a bridge to decision making. All patients who additionally presented with ≥2 hemodynamic or/and echocardiographic indices of RV dysfunction, such as right atrial (RA) pressure > 8 mm Hg, RV stroke work index (RVSWI) < 500 mm Hg × ml/m^2, RA/pulmonary capillary wedge pressure ratio > 0.5, RV end-diastolic diameter (EDD) > 33 mm and tissue Doppler imaging velocity of tricuspid annular systolic motion (Sm) < 9 cm/s were identified in our database.

We included a total of 15 patients who fulfilled the study inclusion criteria, among who 12 patients presenting with non-ischemic dilated cardiomyopathy and 3 patients presenting with ischemic cardiomyopathy.

2.2. Study design

All patients underwent baseline clinical, hemodynamic, echocardiographic and laboratory investigations. They were on a regimen of medications for the management of HF administered in the highest tolerated doses, including intermittent inotropic support with dobutamine or levosimendan alone or together with norepinephrine. Their medical history, baseline clinical characteristics, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile, serum B-type natriuretic peptide and other laboratory investigations, including liver and renal function tests were recorded. All patients underwent percutaneous Doppler study of the lower-extremity arteries in order to exclude clinically significant peripheral vascular disease. A right heart catheterization and transthoracic echocardiogram were performed immediately before implantation of the IABP. Measurements of RV function indices including RVSWI, RV end-diastolic diameter at the mid-ventricular level and Sm were recorded. Myocardial isovolumic acceleration, a tissue Doppler-derived index of myocardial systolic function, which is less dependent on RV preload and afterload [12], was also calculated by dividing the peak isovolumic myocardial velocity by the time to peak velocity. All patients underwent monthly echocardiograms and laboratory screening tests throughout the study period. Right heart catheterizations were performed at 45 days of support and just before explantation of the IABP. Unfractionated heparin was administered intravenously for 24 h after implantation of the IABP, to reach an activated clotting time of 200 s, followed by the long-term, oral anticoagulants with a target value of international normalized ratio of 2. Due to the need for prolonged immobilization all patients wore lower extremity pressure stockings during IABP support.

A sheathless 8F intra-aortic balloon was inserted by catheterization of the common femoral artery under fluoroscopic guidance in all patients. A single dose of vancomycin at a dose of 15 mg/kg of body weight was administered prior to IABP implantation as chemoprophylaxis. Thereafter, antibiotics were administered only upon clinical indication. Standard AutoCAT 2 WAVE IABP systems (Arrow International Inc., Reading, PA) were used to drive the IABP. The rate of IABP function was 1:1 throughout the support period. In patients who derived significant hemodynamic benefit and were clinically stable, the device was synchronized to the blood pressure, to allow the removal of the electrocardiographic skin electrodes and maximize their comfort. Depending on the degree of clinical recovery, IABP support in these patients lasted between 13 and 155 days. Patients who became candidates for some permanent intervention were supported with the IABP until the procedure. A reduced IABP function test (operation of the IABP in 1:4 support mode for 24 h) was performed on a regular (usually monthly) basis in all study patients. The criteria used to ascertain potential for IABP weaning are described in Table 1.

The study patients were divided into two subgroups, according to their outcome while on IABP support: one group consisted of patients who were successfully bridged to LVAD implantation or were successfully weaned from the IABP and the second of patients who continued to deteriorate on the IABP and eventually died. The two groups were compared regarding their baseline characteristics and a survival curve analysis was also drawn in order to depict differences in outcome.

Table 1
Weaning criteria for IABP recipients (all measurements were obtained after 24 h with the IABP supporting 1 out of 4 cardiac cycles).

Clinical indices
- Administration of all medicine with anti-remodeling effects (b-blocker, ACE-I, mineralocorticoid receptor antagonist) or
- No symptoms or sign of HF or
- Furosemide discontinuation (stopped at least 3 days prior and not needed clinically during the test)

Echocardiographic indices
- LVEDD < 60 mm or
- LVEDD < 65 mm but reduced at least 3 mm compared to baseline or
- LVEF increased by more than 50%

Hemodynamic indices obtained after 24 h with the IABP assisting 1:4 cardiac beats
- PCWP < 12 mm Hg or
- Cardiac index ≥ 2.0 L/min/m^2

Laboratory indices obtained after 24 h with the IABP assisting 1:4 cardiac beats
- BNP ≤ 400 pg/ml or
- Reduced by more than 50% compared to baseline

2.3. Statistical analysis

The data are reported as means ± standard deviations or medians, when appropriate. Continuous variables measured before treatment with the IABP, during IABP support and at the time of IABP removal were compared, using Student's paired *t*-test or Wilcoxon's test for non-normally distributed variables. Between group differences and changes were compared using the independent *t*-test. Cumulative survival in the two study subgroups was estimated by Kaplan–Meier analysis and log rank test. A P value <0.05 was considered statistically significant for all differences.

3. Results

The demographic and baseline clinical, echocardiographic and hemodynamic characteristics of the study sample are presented in Table 2. All patients were in NYHA functional class IV, 8 were in INTERMACS profile 1 and 7 were in INTERMACS profile 2. The mean duration of IABP support was 73 ± 50 days (median 72, range of 13–155).