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Mechanical ventilation and thoracic artificial lung assistance during mechanical circulatory support with PUCA pump: In silico study

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ABSTRACT

Patients assisted with left ventricular assist device (LVAD) may require prolonged mechanical ventilatory assistance secondary to postoperative respiratory failure. The goal of this work is the study of the interdependent effects LVAD like pulsatile catheter (PUCA) pump and mechanical ventilatory support or thoracic artificial lung (TAL), by the hemodynamic point of view, using a numerical simulator of the human cardiovascular system. In the simulator, different circulatory sections are described using lumped parameter models. Lumped parameter models have been designed to describe the hydrodynamic behavior of both PUCA pump and thoracic artificial lung. Ventricular behavior atrial and septum functions were reproduced using variable elastance model. Starting from simulated pathological conditions we studied the effects produced on some hemodynamic variables by simultaneous PUCA pump, thoracic artificial lung or mechanical ventilation assistance. Thoracic artificial lung was applied in parallel or in hybrid mode. The effects of mechanical ventilation have been simulated by changing mean intrathoracic pressure value from −4 mmHg to +5 mmHg. The hemodynamic variables observed during the simulations, in different assisted conditions, were: left and right ventricular end systolic (diastolic) volume, systolic/diastolic aortic pressure, mean pulmonary arterial pressure, left and right mean atrial pressure, mean systemic venous pressure and the total blood flow. Results show that the application of PUCA (without mechanical ventilatory assistance) increases the total blood flow, reduces the left ventricular

Abbreviations: LVAD, left ventricular assist device; PUCA, pulsatile catheter pump; TAL, thoracic artificial lung; REMATCH, randomized evaluation of mechanical assistance for the treatment of congestive heart failure; HF, heart failure; VADs, ventricular assist devices; ICUs, intensive care units; MV, mechanical ventilation; CVS, cardiovascular system; LVESV (LVEDV), left ventricular end systolic (diastolic) volume; RVESV (RVEDV), right ventricular end systolic (diastolic) volume; PAP, mean pulmonary arterial pressure; TBF, total blood flow (TBF = left ventricular output flow + PUCA output flow); MCS, mechanical circulatory support; QT, interval time between the onset of ventricular depolarization and the end of ventricular repolarization (in electrocardiogram ECG); PQ, interval time between the beginning of atrial depolarization and the beginning of ventricular depolarization (in ECG); QRS, combination of three of the graphical deflections seen on a typical electrocardiogram; HR, heart rate; CO, cardiac output; LAP (RAP), mean left (right) atrial pressure; NL, natural lung; P–V, pressure–volume.

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end systolic volume and increases the diastolic aortic pressure. Parallel TAL assistance increases the right ventricular end diastolic (systolic) volume reduction both when PUCA is switched "ON" and both when PUCA is switched "OFF". By switching "OFF" the PUCA pump, it seems that parallel thoracic artificial lung assistance produces a greater cardiac output (respect to hybrid TAL assistance).

Results concerning PUCA and TAL interaction produced by simulations cannot be compared with "in vivo" results since they are not presented in literature. But results concerning the effects produced by LVAD and mechanical ventilation have a trend consistent with those presented in literature.

1. Introduction

According to the landmark study randomized evaluation of mechanical assistance for the treatment of congestive heart failure (REMATCH), conducted from May 1998 through July 2001, end-stage heart failure (HF) patients who received a left ventricular assist device (LVAD) had a 52.1% chance of surviving one year, compared with a 24.7% survival rate for patients on medical management [34,47]. Insertion of an LVAD can significantly improve performance and quality of life in patients with end-stage HF. Also patients who experience postoperative ventricular dysfunction or who suffer from postcardiotomy cardiogenic shock can benefit from the ventricular assist devices (VADs). During the initial period after the device implantation, the patients are managed in intensive care units (ICUs). At that time, they are frequently supported by mechanical ventilation (MV) [34,44]. MV is the standard treatment for acute lung disease. In patients affected by acute and/or chronic pulmonary dysfunction, thoracic artificial lung (TAL) can be used as a medical device instead of MV. TAL is designed to take over or to supplement the respiratory function of the lung by oxygenating the blood and by removing carbon dioxide [1,40,63]. Respiratory support with TAL has recently reached the stage of being submitted to human clinical trials. The pulsatile catheter (PUCA) pump is a minimally invasive intra-arterial left ventricular assist device [38,59].

The management of patients simultaneously assisted with PUCA pump and with MV is not simple and clinical studies results are not yet available. LVAD in conjunction with MV can improve left ventricular function but could bring the right ventricle prone to failure. To minimizing the right ventricular failure the solution can be the use of TAL lung that is capable to reduce pulmonary arterial pressure and pulmonary vascular resistances.

It is very difficult make an evaluation of these speculations "*in vivo*", but some "*in vitro*" or "*in silico*" simulations allow us to acquire important messages and results. In silico modeling of the cardiovascular system (CVS) can help both in understanding pharmacological or pathophysiological process and in providing information which could not be obtained by means of traditional clinical research methods due to practical or ethical reasons. The numerical simulators are a great tool to facilitate the study of the interaction between mechanical circulatory and mechanical ventilatory assist devices [6,31]. In silico simulator allows to study the different effects produced by two different ventilatory strategies during LVAD assistance: mechanical ventilation with positive pressure and thoracic artificial lung.

Considering the interest shown by researchers regarding the effects induced on hemodynamic variables by the interaction among cardiovascular system, LVAD and MV [6,41,44,51,55], we studied the effect produced by the joint action of PUCA pump and MV (or TAL) in patients with HF. In order to study the effects produced by these assistances on CVS flow, pressures and ventricular volumes, we used the software simulator CARDIOSIM© [5,9,10]. CARDIOSIM© is a numerical simulator of the cardiovascular system in which the PUCA pump and thoracic artificial lung numerical models are implemented [4,21]. In the simulator, the mean intrathoracic pressure value can be changed in order to reproduce the effects of MV. The hemodynamic variables observed during the simulations, in different assisted conditions, were: left ventricular end systolic volume (LVESV), left ventricular end diastolic volume (LVEDV), right ventricular end systolic volume (RVESV), right ventricular end diastolic volume (RVEDV) systolic/diastolic aortic pressure, mean pulmonary arterial pressure (PAP), left and right mean atrial pressure, mean systemic venous pressure and the total blood flow (TBF = left ventricular output flow + PUCA output flow). The results obtained during the simultaneous application of PUCA pump and MV show that the mechanical circulatory support (MCS) increases the total blood flow, increases the diastolic aortic pressure, reduces the left ventricular end systolic (diastolic) volume and increases the right ventricular end systolic (diastolic) volume. Parallel TAL assistance in conjunction with LVAD produces an increase of the left ventricular end diastolic (systolic) volume and a reduction in the right ventricular end diastolic (systolic) volume.

The results obtained using the numerical simulator allow us to highlight the trend of some hemodynamic variables in conditions that are hardly repeatable and measurable in a hospital setting during assistances not easily manageable. These results may be a first step to help clinicians (i.e. anesthetists) in the management of patients undergoing to the simultaneous action of different mechanical circulatory and ventilatory devices.

2. Materials and methods

The "*in silico*" cardiovascular simulator (CARDIOSIM©) is a modular software package that can be assembled in different way. It can be used to simulate the effects produced by PUCA