A Comparative Evaluation of Pulmonary Artery Balloon Counterpulsation and a Centrifugal Flow Pump in an Experimental Model of Right Ventricular Infarction

Allen J. Taylor MD, Fred H. Edwards MD, Michael G. Macon MD, Brian Worley BS, Geoffrey M. Graeber MD

Division of Surgery, Walter Reed Army Institute of Research (MGM, BW, GMG), Departments of Medicine (AJT) and Cardiovascular Surgery (FHE), Walter Reed Army Medical Center, Washington DC, and the Uniformed Services University of the Health Sciences (GMG), Bethesda, MD

Keywords: Right ventricular failure, circulatory assistance, pulmonary artery balloon counterpulsation, centrifugal flow pump, swine.

Abstract

To compare the efficiency of pulmonary artery balloon counterpulsation and a centrifugal flow pump in reversing the hemodynamic consequences of acute right-sided heart failure, we employed both devices in 14 Yorkshire pigs in which right ventricular infarction was created via surgical ligation of branches of the right coronary artery. Pulmonary artery balloon counterpulsation improved some of the indicators of right heart failure, as manifested by significantly decreased right atrial pressure and increased mean systemic blood pressure. In contrast, the centrifugal flow pump consistently and significantly reversed all of the hemodynamic consequences of right ventricular infarction. In comparison to pulmonary artery balloon counterpulsation, the centrifugal flow pump resulted in lower right atrial pressures \( p = 0.020 \), lower mean pulmonary pressures \( p < 0.0001 \), increased left atrial pressures \( p = 0.026 \), increased cardiac output \( p < 0.0001 \), and increased mean systemic blood pressures \( p < 0.0001 \). Possible mechanisms to explain the superiority of the centrifugal flow pump include better hemodynamic unloading of the failing myocardium and independence from right ventricular output.

Introduction

Acute right heart failure, characterized hemodynamically by a rise in right atrial pressure, decreased left atrial, systemic and pulmonary pressures, and a fall in cardiac output, has been reported to occur in a variety of circumstances including right ventricular infarction (1, 2). The treatment of experimental right heart failure with mechanical assist devices has included pulmonary artery balloon counterpulsation (PABC), intraventricular balloon pumps, pneumatic assist devices and centrifugal flow pumps (3-8).

Previous efforts to study right heart assistance have been hampered by the lack of a satisfactory model of surgically-induced heart failure and technical limitations of the devices employed. PABC has met with some success, but has the drawback of its intrinsic reliance on adequate ventricular filling of the pulmonary vessels (2). The pneumatic pump has also been successful but the device is expensive, and its set-up and removal are time-consuming and may require directly cannulating the right ventricle. The use of roller pumps has been shown to cause pulmonary parenchymal damage (8). In a previous experimental trial, Gaines, et al. (5) compared four assist devices (including PABC) under conditions of profound right heart failure and found a pneumatic pump to be the most effective. In contrast to these other methods, centrifugal flow pumps are easy to use and set up, are relatively inexpensive, and are readily removed when no longer needed. When properly positioned, the pumps add no additional myocardial damage or arrhythmias (10).

We recently reported the successful development of a model of acute isolated right heart failure due to infarction via surgical ligation of branches of the right coronary artery (10). Right-sided circulatory support was successfully accomplished using two different models of centrifugal flow pumps. In the present trial, we have used the same model of experimental right heart failure to compare a centrifugal flow pump with the previously well-studied modality of PABC.

Materials and Methods

In conducting the research described in this report, the investigators adhered to the "Principles of Laboratory Animal Care," formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals," prepared by the National Academy of Sciences and published by National Institutes of Health (NIH Publication No. 80-23, revised 1978).

A total of 14 Yorkshire pigs were studied, with each pig...
studied as control, and then with both pulmonary artery balloon counterpulsation and the centrifugal flow pump in a sequential, randomly-ordered fashion. The animals were fasted overnight. They received 20 mg/kg Ketamine. When docile, an ear vein was cannulated and they were anesthetized with 30 mg/kg of sodium pentobarbital. After placing the animals in the supine position they were intubated with a number eight cuffed endotracheal tube and ventilated (Puritan Bennet 7200) at a rate of 12-16 breaths per minute, tidal volume 10-15 cc/kg with an FIO2 of 40% to maintain normal arterial blood gases. This was followed by placement of internal jugular venous and internal carotid arterial cannulas for fluid administration and measurement of systemic blood pressure.

The pigs were then shaved and scrubbed for median sternotomy. Once the heart was exposed, pressure transducer cannulas were placed in the right atrium, left atrium, and pulmonary artery and secured with purse string sutures. These transducers as well as limb ECG leads were connected to a Hewlett-Packard (7758B system) eight channel recorder and calibrated.

After systemic heparinization (100 U/kg), a straight Sarns (30F with basket) right atrial cannula was placed through the right atrial appendage and secured in place with a double purse string suture. A 12 mm polytetrafluoroethylene (PTFE) graft was anastomosed to the proximal pulmonary artery with 4-0 polypropylene suture through which another straight Sarns infusion cannula was secured with umbilical tape. Attached to this conduit was a PTFE sidearm in which a straight Sarns arterial cannula was secured with umbilical tape. Attached to this conduit was a PTFE sidearm in which a 40 cubic centimeter balloon was introduced and then tied off on its distal end. The infusion cannula was then connected to the centrifugal flow pump and the pulmonary artery balloon was connected to the balloon drive console (b). The purpose of this design (Figure I) was to ensure that both assist devices were meeting the same resistance and to allow facile switching between systems without the need for additional surgical procedures.

An electromagnetic flow probe, sized for the vessel, was placed around the ascending aorta and connected to an instantaneous cardiac output recorder (c) and calibrated. All measurements of right and left atrial pressures, pulmonary artery pressure, systemic arterial pressure and cardiac output were recorded on continuous graph paper.

The pigs were then pre-treated with 100 mg of lidocaine intravenously, followed by a lidocaine drip at 4 mg/min. Branches of the right coronary artery and collateral branches from the left anterior descending coronary artery were then occluded with suture ligation. The main right coronary artery and posterior descending vessels were preserved in order to maintain normal sinus rhythm. The right ventricular myocardium was seen to undergo hemorrhagic demarcation and paradoxical motion during systole, signifying ischemic dysfunction.

The trial of the assist devices began when enough branches were ligated in order to approximately double right atrial pressure and create paradoxical motion of the right ventricle. The order of the assist devices was determined by coin toss and initial baseline measurements were taken. The desired system was then isolated by opening the appropriate conduit off the pulmonary artery, and flow rates were adjusted to achieve optimum stable hemodynamic parameters. The device was then turned off, thereby returning the animal to unassisted right heart failure. Following stabilization with infusion of volume, the animal was placed on the other assist device and the above procedure repeated. Alternating assist-device trials were continued until the data generated was consistently reproducible. Following the final pump run, the animal was again returned to baseline failure to ensure that no further hemodynamic deterioration had occurred. At the end of the investigation, the animals were euthanised with intravenous sodium pentobarbital. Necropsies were performed on all pigs and showed varying degrees of right ventricular anterior and inferior wall infarction without septal infarction. In a few pigs in which flow rates on the centrifugal flow pump were rapidly increased, pulmonary alveolar hemorrhage was apparent (2 of 13 pigs in which necropsies were available). High flow rates, identical to those which produced hemorrhage, were well tolerated in other animals when attained gradually.

All measurements were recorded on continuous graph paper. The data were retrieved from these graphs and the values for each parameter were averaged. The means of right atrial pressure, pulmonary artery mean blood pressure, left atrial pressure, systemic mean blood pressure and cardiac output were compared for baseline vs. right heart failure, right heart failure vs. PABC, and right heart failure vs. centrifugal flow pump using paired, one or two tailed Student's t-test, as appropriate. P values less than 0.05 were considered statistically insignificant.

**Results**

**Baseline measurements vs. right heart failure:**

Shortly after ligation of the branches of the right coronary artery, right heart failure was clinically evident as right atrial dilation and paradoxical systolic motion of the right ventricle. Hemodynamically, the most marked change was increased right atrial pressure (from 7.33±1.81 mmHg to 16.74±1.71 mmHg; p=0.0009). Overall, cardiac output was unchanged, but tendencies were for heart rate to increase (mean increase 5.0±8.1 hpm; p=0.28) and stroke volume to decrease (from 54.5±4.8 ml to 42.2±4.8 ml; p=0.19). Mean pulmonary blood pressure increased from 17.23±1.46 mm Hg to 22.62±1.17 mm Hg (p=0.0009). Mean systemic blood pressure decreased from 100.46±7.25 mm Hg to 90.31±7.49 mm Hg (p=0.070). Left atrial pressure showed a slight tendency towards increasing (mean increase of 1.09±0.98 mm Hg) but this change was not significant (95% confidence interval (CI) -1.07 to 3.25; p=0.29).

**PABC vs. right heart failure:**

PABC improved some indicators of right heart failure to a mild but significant degree, as evidenced by a decrease in mean
**Figure 1.** Schematic representation of the assist devices.

**Figure 2.** Averages and standard errors of Right Atrial Pressure in mm Hg for Baseline, unassisted Right Ventricular Failure (RVF), Pulmonary Artery Balloon Counterpulsation (PABC) and Centrifugal Flow Pump (CFP).
Figure 3. Averages and standard errors of mean Systemic Blood Pressure in mm Hg for Baseline, unassisted Right Ventricular Failure (RVF), Pulmonary Artery Balloon Counterpulsation (PABC), and Centrifugal Flow Pump (CFP).

Figure 4. Change in hemodynamic parameters from unassisted Right Ventricular Failure Balloon Counterpulsation (PABC) and Centrifugal Flow Pump (CFP). Ax: = significant increase, Bl: = significant decrease, CO: = cardiac output, MBP: = mean systemic blood pressure, PI: = mean pulmonary blood pressure.
right atrial pressure (-2.92±1.33 mm Hg; 95% CI -5.79 to -0.06; p=0.023) and an increase in mean systemic blood pressure (4.21±2.21 mm Hg; 95% CI -0.57 to 8.99; p=0.040). Mean left atrial pressure was slightly increased (1.84±1.14 mm Hg; 95% CI -0.63 to 4.31; p=0.065) as was mean pulmonary blood pressure (0.65±0.52 mm Hg; 95% CI -0.48 to 1.78; p=0.12) but the changes were small and not statistically significant. Although mean cardiac output was not affected (-0.10±0.14 l/min; 95% CI -0.40 to 0.20; p=0.75), mean stroke volume tended to increase (1.3±2.6 ml; 95% CI -3.8 to 6.4; p=0.32).

Stratification of the data on mean right atrial pressure and mean stroke volume did not reveal any subgroups which were more or less likely to perform better with PABC (for example, pigs with higher stroke volumes did not necessarily have more marked improvements in right atrial or systemic blood pressures).

Centrifugal flow pump vs. right heart failure:

The centrifugal flow pump dramatically and significantly improved all hemodynamic parameters measured. Mean right atrial pressure decreased (-6.49±1.19 mmHg; 95% CI -9.05 to -3.92; p<0.0001); mean pulmonary blood pressure increased (9.57±1.02 mmHg; 95% CI 7.36 to 11.77; p<0.0001); mean left atrial pressure increased (5.37±0.64 mmHg; 95% CI 3.98 to 6.76; p<0.0001); cardiac output increased (1.40±0.11 l/min; 95% CI 1.16 to 1.64; p<0.0001); and mean systemic blood pressure increased (26.16±3.25 mmHg; 95% CI 19.14 to 33.17; p<0.0001).

PABC vs. centrifugal flow pump:

The centrifugal flow pump consistently and significantly outperformed PABC in improving all hemodynamic parameters (Figures 2, 3, and 4). Mean right atrial pressure was lower (mean difference -3.56±1.34 mmHg; 95% CI -6.52 to -0.55; p=0.020); mean pulmonary blood pressure was higher (mean difference 8.92±1.00 mmHg; 95% CI 6.76 to 11.08; p<0.0001); mean left atrial pressure was higher (mean difference 3.53±1.40 mmHg; 95% CI 0.49 to 6.56; p=0.026); cardiac output was higher (mean difference 1.50±0.12 l/min; 95% CI 1.23 to 1.77; p<0.0001); and mean systemic blood pressure was higher (mean difference 21.94±2.93 mmHg; 95% CI 15.61 to 28.28; p<0.0001).

Discussion

While pulmonary vascular hypertension and right ventricular hypertrophy place a patient at greater risk for acute right heart failure, failure does occur in the absence of these conditions, specifically in the case of right ventricular infarction and after cardiopulmonary bypass (2). Mild right ventricular failure is typically managed with conservative measures, including optimization of right ventricular preload, correction of acid-base status and oxygenation, and inotropic support (1, 2).

More profound right ventricular failure may require mechanical assistance. The purpose of right ventricular mechanical assistance devices is the maintenance of adequate pulmonary circulation for oxygenation, to provide left ventricular preload to optimize left ventricular performance, and to decrease myocardial work in the case of the ischemic heart.

Right ventricular assistance has been employed both clinically and experimentally using a variety of means including PABC, pneumatically-activated right atrial to pulmonary artery pumps and centrifugal flow pumps (2-18). PABC is a well-studied modality which has received both experimental and clinical usage. The balloon inflates during diastole to decrease afterload and therefore result in decreased systolic work. Its action relies upon right ventricular pumping to fill the pulmonary artery. However, after right ventricular infarction, a state of decreased contractility may result in poor ventricular function, which leads to poor performance of the device. Thus, in severe right ventricular depression, a mechanical pump should be considered. An additional technical limitation which we observed with the pulmonary artery balloon was a difficulty in electrocardiographic tracking in instances of supraventricular tachycardias, especially atrial fibrillation.

Centrifugal flow pumps offer several advantages over other assist devices. Unlike PABC, the centrifugal flow pump is not dependent upon right ventricular function, and it can reduce both the preload and the afterload of the right ventricle. In comparison to other pumps, including pneumatic and roller models, the centrifugal flow pump is relatively easy to use, low in cost, produces less hemolysis by virtue of its non-occlusive design, and has less risk for air pumping. We did observe two different complications. First, an excessively high flow rate could cause air pumping or collapse of the right atrium. Air pumping was avoidable by configuring the pump so the outflow was in a dependent position (see diagram). Right atrial collapse was preventable by placing the cannula in the inferior portion of the right atrium. Secondly, a rapidly-increased flow rate was capable of producing pulmonary alveolar hemorrhage.

Previous experimental comparisons of assist devices have been hampered by the lack of an adequate model of surgically-induced right heart failure. While there are models of right ventricular failure, they have used methods other than infarction or have not maintained normal sinus rhythm. Our model is the first to duplicate the clinical syndrome of right ventricular infarction and thus provides more information on the application of these devices in this setting.

As previously described (10), we were able to reliably create right ventricular infarction via selective ligation of branches of the right coronary artery, which resulted in isolated right heart failure hemodynamically characterized by increased right atrial pressure and decreased systemic blood pressures. With each pig serving as its own control for both PABC and the centrifugal flow pump, we have obtained information on the relative efficacy of these devices in reversing the hemodynamic consequences of right ventricular infarction.

Both devices resulted in significant hemodynamic improvement. The changes seen with PABC were limited to small, but statistically significant improvements in right atrial and mean systemic blood pressures. Whereas cardiac output did not change, this was in part explained by a trend toward increased stroke volume. However, in all parameters measured, the centrifugal flow pump consistently and significantly outperformed PABC. The centrifugal flow pump resulted in lower right atrial pressures (p=0.020), lower mean pulmonary
pressures (p<0.0001), increased left atrial pressures (p=0.026), increased cardiac output (p<0.0001), and increased mean systemic blood pressures (p<0.0001). The additional improvement seen with the centrifugal flow pump is presumably produced from a more favorable hemodynamic environment for the injured right ventricle with both afterload and preload reduced, as well as direct circulatory support and independence from right ventricular performance. An additional explanation for the inefficiency of PABC perhaps lies in the relatively high compliance of the pulmonary circulation enabling it to readily accommodate the volume displaced by the balloon.

Is the additional improvement seen with centrifugal flow pumps of clinical consequence? The answer to this question is unclear in the setting of mild to moderate right heart failure, but with severe right heart failure it almost certainly is since the pulmonary balloon system is dependent upon some ventricular systolic function for its operation. We observed no subgroups within the PABC data in which a more favorable response to this modality could be predicted. Furthermore, any additional insult, for example increased pulmonary vascular resistance or concomitant left ventricular or septal dysfunction, is likely to result in more profound right heart failure necessitating the more aggressive right-sided circulatory support which the centrifugal flow pump can provide. This, coupled with the ease of operation, and low cost of the centrifugal flow pump system, appear to make it a better system for right-sided circulatory support in the setting of right ventricular infarction.

In summary, we compared pulmonary artery balloon counterpulsation to a centrifugal flow pump for right heart failure resulting from experimentally induced right ventricular infarction in the pig. The centrifugal flow pump consistently and significantly outperformed PABC in improving the hemodynamic consequences of right ventricular infarction. This was felt to result from better hemodynamic unloading of the failing myocardium and independence from right ventricular output. In addition, the high compliance of the pulmonary vasculature may result in rapid dissipation of the balloon’s energy. Future research should include investigations into the changes of pulmonary compliance occurring with right ventricular infarction and clinical trials of the centrifugal flow pump in severe right heart failure.

Acknowledgements

The authors acknowledge and thank J. Robert Burge MS, Division of Biometrics, Walter Reed Army Institute of Research, for his outstanding statistical support.

References


The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.