

TITLE: THE PERIPHERAL EFFECTS OF DOBUTAMINE IN THE POST-OP LOW-CARDIAC-OUTPUT STATE

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It has been reported, that when used at doses of 7.5 ug/kg/min, dobutamine will increase cardiac index without increasing pulmonary capillary wedge pressure, mean arterial pressure, or pulmonary vascular resistance in patients following coronary artery bypass surgery.^{1 2} The purpose of this study was to determine the systemic and pulmonary vascular effects of a dobutamine infusion, in the absence of the natural myocardium, by utilizing the Jarvik-7, Total Artificial Heart (TAH).

Methods. Following approval by the institutional animal resources committee, five Holstein calves weighing 70-90 kg were studied. Under halothane anesthesia, a 7 Fr introducer was placed in the right external jugular vein along with an 18 gauge right femoral arterial catheter. The animals were allowed to recover from the anesthesia and were extubated. Six hours post-extubation a pulmonary artery catheter was placed and baseline measurements were obtained. Dobutamine infusion was then begun through the sheath introducer at a rate of 2.5 ug/kg/min. Measurements were obtained after 30 min and the infusion rate was increased to 10 ug/kg/min. After an additional 30 minutes, measurements were again taken and the infusion was turned off. Data was lastly collected, 30 minutes after discontinuation of the infusion. Hemodynamic measurements obtained included heart rate (HR), systemic blood pressure (SBP), mean arterial pressure (MAP), pulmonary artery pressure (PAP), central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and cardiac output. Systemic (SVR) and pulmonary vascular resistance (PVR) and stroke volume (SV) were calculated from the above data. The following day the calves underwent placement of a TAH.

On post-operative day 2, following collection of baseline measurements, a protocol identical to the above was implemented with the exception that left atrial pressure (LAP) was measured rather than PCWP. Cardiac output was determined by the Cardiac Output Monitoring Diagnostic Unit (COMDU) which monitors the performance of the TAH.³ The operational drive parameters and HR of the TAH were held constant throughout the period of study.

Statistical analysis of the data was performed with a two-way ANOVA and Student's *t*-test for unpaired and paired data. Significance was set at *p* < 0.05.

Results. The results are shown in Table 1 (Pre- and Post TAH). The results reveal that there are significant differences pre-operatively vs. post-operatively with respect to HR, CO, SVR, and PVR. It should also be noted that dobutamine (10 ug/kg/min) produced a significant increase in HR in the pre-TAH study, but had no significant effect on any other parameter measured. Post-TAH, however, when the dobutamine was infused at a dose of 10 ug/kg/min, a significant decrease in MAP and

SVR was seen.

Discussion. Many of the significant differences between the Pre-TAH and the Post-TAH measurements can be attributed to the fact that in the Pre-op period the animals were healthy with an intact myocardium, whereas Post-op the animals were 2 days Post-TAH implantation and have a TAH (Jarvik-7) that can maintain only a low normal cardiac output for the calf. However, it is interesting to note that dobutamine at a dose of 10 ug/kg/min significantly decreased SVR and MAP in the Post-TAH period, but did not during the Pre-TAH period. These findings suggest that the ability of dobutamine to produce a decrease in peripheral resistance may depend on the presence or absence of an intact, innervated myocardium or on the degree of vascular tone present when it is administered. Further study is warranted to elucidate this important distinction.

References

1. Salomon KW, Plachetka JR, Copeland JG: Ann Thorac Surg 33:48-54, 1982.
2. Sonnenblick EH, Frishman WH, Lejemtel TH: N Engl J Med 300:17-22, 1979.
3. Willshaw P, Nielsen SD, Nanas J, et al: Artif Organs 8:215, 1984.

TABLE 1
PRE- AND POST-TAH

	Baseline	2.5 ug/kg/min	10 ug/kg/min	OFF
HR (beats/min)	Pre 98±15 ⁺ Post 100±4	127±11 ^x 100±4	206±7 ^x 100±4	102±15 100±4
MAP (mm Hg)	Pre 113±10 Post 131±9	118±13 120±2	110±11 106±8	117±4 123±3
PCWP (mm Hg)	Pre 5.4±0.9 Post 10.2±2.8	4.5±2.9 10.6±3.0	4.2±2.5 12.0±2.6	7.2±1.3 9.8±2.4
C.O. (liters/min)	Pre 11.6±1.4 ^x Post 6.8±0.7 ^x	12.7±1.0 ^x 6.8±0.7 ^x	14.4±1.0 ^x 7.0±0.7 ^x	10.1±1.2 ^x 6.6±0.8 ^x
SVR (dynes-sec cm ⁻⁵)	Pre 787±7.3 ^x Post 1438±147 ^x	764±125 ^x 1307±95 ^x	610±99 ^x 1051±40 ^x	955±110 ^x 1395±132
PVR (Wood Units)	Pre 0.99±0.16 ^x Post 3.27±0.87 ^x	1.1±0.18 3.20±0.97	0.83±0.18 ^x 2.88±0.85 ^x	1.4±0.22 ^x 3.50±0.76 ^x

n = 5
^x significantly different from baseline *p* < 0.05.
^y significantly different from post-artificial heart group
⁺ *p* < 0.05.
mean ± S.E.