Title: THE PEAK SYSTOLIC PRESSURE - END SYSTOLIC VOLUME RATIO CORRELATES WITH CHANGES IN THE EJECTION FRACTION IN A CANINE MODEL OF SEPTIC SHOCK

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Introduction. In humans and animals, recent studies of septic shock demonstrate a severe but reversible cardiovascular dysfunction during several days following the onset of hypotension[1,2]. Typically, the left ventricular ejection fraction (LVEF) falls to a nadir over the initial 2-3 days, this progressive fall in LVEF was associated with LV dilation and a normal or increased stroke volume and cardiac output. In a canine model that simulates human septic shock, these changes in LVEF correlate with downward and rightward shifts on the Frank-Starling curve (LV stroke work vs. end diastolic volume index). In surviving animals, these changes in LVEF and shifts in Frank-Starling plots returned toward normal in 7-10 days[2].

The LVEF and Frank-Starling relationship are load senstive measures of LV function. Some investigators feel that the load insensitive end systolic volume vs. pressure relationship more accurately reflects LV contractility.[3] The peak systolic pressure divided by end systolic volume index produces a ratio (PSPR) that has been found to be a sensitive and specific measure of systolic performance[3].

The purpose of this investigation is to examine the PSPR during septic shock, and evaluate the relationship between serial changes in PSPR and LVEF.

Methods. In awake, nonsedated animals hemodynamic parameters were measured at specific times immediately before and after volume infusion (80 ml/kg) over 30 minutes. Femoral artery catheters provided measurements of peak systolic pressure and heart rate; and pulmonary artery catheters were used to analyze cardiac index and stroke volume index. Radionuclide heart scans were obtained simultaneously and provided left ventricular end systolic volume index and LVEF. One-hundred-twenty animals were studied. Different bacteria and doses of bacteria (per kg body mass) were implanted in the peritoneal cavity within a fibrin clot. Fourteen control animals were implanted with a sterile clot. Hemodynamic measurements were determined prior to infection (baseline) and on days 1, 2 (bacteremia) and 10 (recovery) following clot implantation. Statistical comparisons were performed using the Student's t test at serial time points between the means of the corresponding septic and control groups.

Results. These data show (see table) that on day 2 of sepsis, infected dogs had profound decreases ($p<0.001$) in both LVEF and the PSPR (compared to baseline). Ventricular function returned to approximately baseline values in 7-10 days. Controls had no significant changes from baseline in either LVEF or the PSPR throughout. When infected dogs are compared to controls, these changes in LVEF and the PSPR were highly ($p<0.001$) significant on day 2 of septic shock.

| | LVEF (MEAN) - SEPSIS VS. CONTROL | | | | | |
|---|---|---|---|---|---|---|
| | B pre | B post | D2 pre | D2 post | D10 pre | D10 post |
| Sepsis | 0.65 | 0.68 | 0.45** | 0.48** | 0.59 | 0.62 |
| Control | 0.62 | 0.65 | 0.60 | 0.63 | 0.63 | 0.65 |
| | PSPR (MEAN) - SEPSIS VS. CONTROL | | | | | |
| | B pre | B post | D2 pre | D2 post | D10 pre | D10 post |
| Sepsis | 188 | 192 | 89** | 85** | 144 | 140* |
| Control | 162 | 180 | 144 | 151 | 155 | 229 |

p values compare control and sepsis dogs at each time point. * ($p<0.02$), ** ($p<0.001$), PSPR = PSP/EDVI in mmHG • $ml^{-1}$ • kg. B = baseline (presepsis), D2 = day 2 (sepsis), D10 = day 10 (recovery).

Discussion. This study demonstrates that a load independent (or insensitive) measure of LV performance (PSRP) documents a profound, reversible change in cardiac performance during severe sepis in a canine model[2] analogous to the human disease. Previous studies had documented these cardiac abnormalities using LVEF and ventricular function (Frank-Starling) curves, however this represents a demonstration of cardiac abnormalities using a measure of cardiac performance relatively independent of pre- and after-load. The three methods of evaluating cardiac function correlate temporally with one another. This data suggests that the day 2 ventricular dysfunction of septic shock represents a true intrinsic abnormality of the myocardial contraction mechanism.

References.

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