The SCD, a novel biomimetic device

Immunomodulation with a selective cytopheretic device (SCD) improves myocardial contractility and renal sodium excretion in a canine model of congestive heart failure

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Abstract

Background: Cardiorenal syndrome (CRS), the most severe subset of patients with CHF, is characterized by diuretic resistance in volume overload and is a common problem faced by the critical care team. Current therapy is limited and new innovative approaches are needed. CHF is characterized by a proinflammatory state. The cytokines, TNF-□ and IL-6, inhibit mitochondrial respiration and depress cardiac contractility (CC). Monocytes and tissue macrophages are sources of systemic inflammation in CHF. Systemic monocyte levels correlate with poor outcome in CHF. The SCD, a novel biomimetic device, when placed in an extracorporeal circuit with regional citrate (c) anticoagulation has been shown to be an effective immunomodulatory device in acute multiorgan organ failure.

Method: To evaluate the acute effects of the SCD in a canine model of CHF, three groups of animals were evaluated during 4 hours of treatment: SCD-C, SCD-Heparin (H), and a sham control (S-C), n=2-5 in each group.

Results: Left ventricle (LV) ejection fraction (EF) increased substantially in the SCD-C group from 34 ± 2.3 to 48 ± 3.7% while SCD-H and S-C (n= 2-5) did not change. This effect was not due to a decline in systemic vascular resistance (SVR) which was similar in all groups. Ventriculograms demonstrated the SCD-C to convert viable but non-contracting myocardium to better contracting myocardium. The renal effects were also substantive. The fractional excretion (FE) Na nearly doubled in the SCD-C compared to SCD-H increasing from 2.2 ± to 0.8 to 5.3 ± 0.8% and FE urea went from 59 ± 3.1 to 81 ± 11.3%. No adverse events of arrhythmia or hypotension were observed during treatment. Isolated peripheral blood monocytes showed a decline in IL-6 and TNF-□ secretion at end of treatment compared to baseline demonstrating a change in proinflammatory phenotype.

Conclusions: These results demonstrate that immunomodulation with the SCD improves left ventricular function and improves natriuresis. Removal of the cardio depressant effects of the chronic inflammatory state of CHF may be a new innovative approach to the management of CRS in critically ill patients.

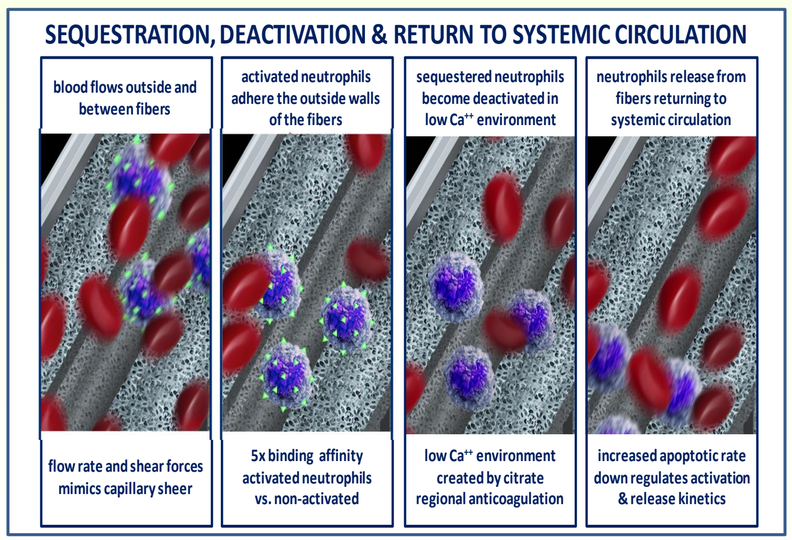


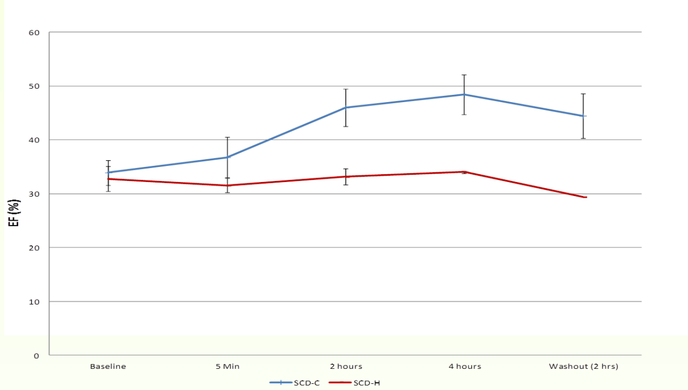
Fig 1: Putative mechanism of action of SCD

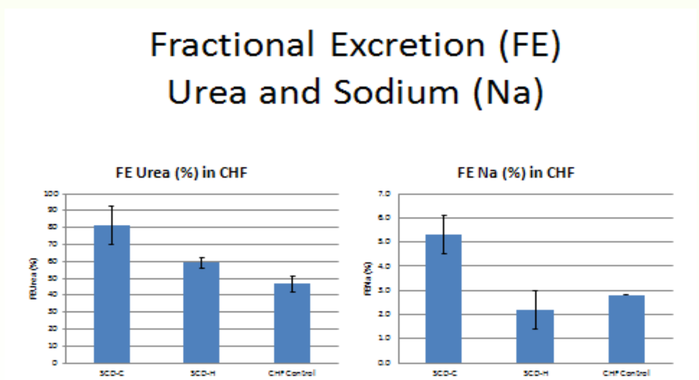
Objectives

To evaluate the acute effects of the SCD in a canine model of CHF on hemodynamic parameters.

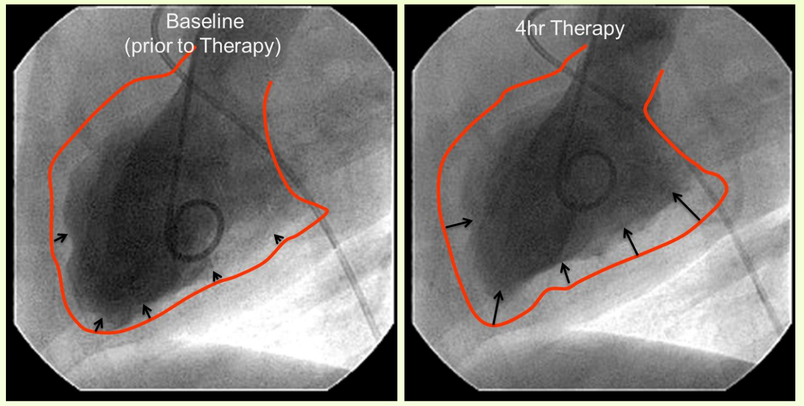
Methods

- In this model CHF is induced by multiple sequential intracoronary embolizations with polystyrene latex microspheres (~90µm in diameter) that lead to loss of viable myocardium.
- Five dogs with advanced CHF were used in the below study set:
- Two dogs were treated with a sham SCD circuit under systemic heparin (H) as the circuit anticoagulant and three dogs received SCD therapy in which regional citrate was used as the anticoagulant.
- In all studies, extracorporeal circuits were maintained for 4 hours.
- Hemodynamic and ventricular function parameters were measured and blood samples for the assessment of various biologic parameters taken at baseline, 2 and 4 hours after initiation of either sham or SCD therapy.





Results



Ventriculograms of a CHF dog heart are shown at baseline (before therapy) and at the end of the 4 hour therapy session. The red line depicts the border of the left ventricular diastolic silhouette (most relaxed state during filling) overlayed on the left ventricular systolic image (most contracted state), demonstrating improved contractility (black arrows) of the left ventricle after therapy.

- Under SCD/C therapy, overall cardiac function was enhanced, as indicated by increased ejection fraction (EF%) and cardiac output (CO); with a decrease in systemic vascular resistance in both groups.
- A strict control with only an extracorporeal circuit identical in volume of the SCD/H or C was similar to SCD/H animals showing similar degrees of SVR reduction but no change in EF.
- Stroke Volume (SV) from 26.7±4.9 to35.3±7.3 mL in the SCD/C group. SCD/C brought EF% to near normal levels of 50-55%.
- The fractional excretion (FE) sodium nearly doubled in the SCD group compared to the sham group increasing from 2.2 ± 0.8 to 5.3 ± 0.8% and FE urea went from 59 ± 3.1 to 81 ± 11.3%.
- With respect to safety profile, no episodes of arrhythmias or hypotension were observed during the treatment period.

Conclusions

These results demonstrate that immunomodulation with the SCD improves left ventricular function and improves natriuresis. Removal of the cardio depressant effects of the chronic inflammatory state of CHF may be a new innovative approach to the management of CRS in critically ill patients.