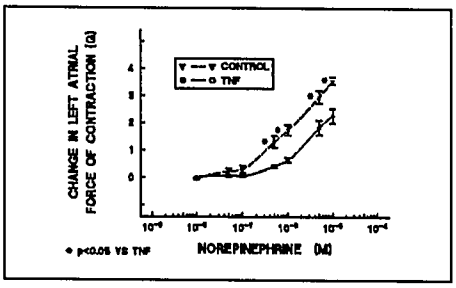
TITLE: TUMOR NECROSIS FACTORα INJECTED IN VIVO CAUSES EX VIVO LEFT ATRIAL DYSFUNCTION IN GUINEA PIGS.

AUTHORS: SO Heard, M.D., MW Perkins, B.S. and MP Fink, M.D.

AFFILIATION: Departments of Anesthesiology and Surgery. University of Massachusetts Medical Center. Worcester MA 01655.

Cardiac dysfunction occurs during sepsis and endotoxicosis. The pathophysiology of this phenomenon is not well delineated, but human recombinant tumor necrosis factor α (hrTNFα) has been implicated as being a key mediator in many of the cardiovascular derangements observed in sepsis. We tested the hypothesis that hrTNFα causes myocardial dysfunction in guinea pigs.

Methods. Albino Hartley guinea pigs were anesthetized with 2-2.5% halothane in 30% O_2 and 70% N_2O. Group I (n=5) was injected with normal saline (1.5 ml) and group II (n=6) was injected with hrTNFα (1 mg/kg, Asahi) via the jugular vein. Twenty-four hours later, the animals were reanesthetized and the hearts were removed and immersed in warmed (37° C), oxygenated Krebs-Henseleit (KH) solution. The atria were carefully dissected, separated, attached to force displacement transducers and suspended in tissue baths of warmed, oxygenated KH buffer. The right atrium (RA) was allowed to beat spontaneously; the left (LA) was field stimulated at a rate of 1 hertz. Force of contraction (FOC) at 1 gram preload was recorded for both preparations. The responses to graded doses of norepinephrine (NE, 10^{-8} - 10^{-5} M) were evaluated. Data are expressed as mean±SE and were analyzed using ANOVA.



Results. There was no difference in RA rate or FOC between the two groups. LA FOC (in g/g LA weight) was significantly lower in the animals given hrTNFα (39.0±5.4 [Group I] vs 20.1±4.1 [Group II], p=0.02). The sensitivity of the LA contractile response to NE was significantly diminished (figure).

Conclusions. 1) Ex vivo LA contractility was reduced by injecting guinea pigs with hrTNFα 24 hours before study; 2) the sensitivity of LA tissue to the inotropic effect of NE was also significantly diminished; 3) these data suggest that hrTNFα is an important mediator of sepsis-induced myocardial dysfunction.

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Title HEMODYNAMIC AND OXYGENATION CHANGES WITH CONTINUOUS VENOUS-VENOUS HEMODIALYSIS (CVVHD)

Authors: W. Gerard MD, C. Patel MD, J. Mohr MD, B. Johnson, MD.

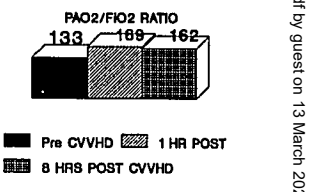
Affiliation Departments of Anesthesiology and Surgery, Maricopa Medical Center, University of Arizona Integrated Residency Program/Phoenix Campus, Phoenix AZ 85008

Introduction Acute renal failure (ARF) in the critically ill patient is fairly common. The modes of dialysis available include hemodialysis; continuous arterio-venous hemofiltration and hemodialysis. Hemodialysis is associated with unstable hemodynamics and oxygenation. CVVHD is a new method of dialysis in which one double lumen dialysis catheter is inserted into a central vein, and a dialysis membrane is interposed in a circuit between the two ports of the catheter. The blood is kept moving by a roller pump. Our goal in this study was to analyze the hemodynamic, oxygenation, and metabolic changes associated with CVVHD.

Method After obtaining informed consent , 8 patients with acute renal failure (ARF) in the intensive care unit (ICU) were studied. Hemodynamic and pulmonary parameters were recorded at 1 hour before, 1 hour after and 8 hours after institution of CVVHD. Blood urea nitrogen (BUN), creatinine and coagulation profile were examined the morning before starting CVVHD as well as the morning after and two days after the start of CVVHD.

Results Hemodynamically, the patients remained stable with CVVHD (see table). The P_aO_2/F_IO_2 ratio, improved significantly ($p<.05$) at 1 and 8 hours post institution of CVVHD (See figure). The BUN and creatinine fell. The platelet count fell significantly from a mean of 154K to 118K after 12 hours.

	Mean values ± SD		
	-1 Hr.	+1 Hr.	+8 Hrs.
HR	104±16	102±12	100±13
BP	88±18	83±12	80±9
PCWP	21±7	18±6	16±5
CI	4.5±.8	4.2±1	4.0±.7
SVR	605±169	683±231	683±209



Conclusion The use of CVVHD in the ICU is an option in the patient with ARF. Our study patients tolerated the volume shifts well, as evidenced by hemodynamic stability. There is preliminary evidence that CVVHD may improve oxygenation.