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ORIGINAL ARTICLE

Structure and Function of the Kidney in Septic Shock

A Prospective Controlled Experimental Study

Matthew J. Maiden[1,2], Sophia Otto[3], John K. Brealey[3], Mark E. Finnis[1,2], Marianne J. Chapman[1,2], Tim R. Kuchel[4], Coralie H. Nash[2], Jason Edwards[1], and Rinaldo Bellomo[5]

[1]Intensive Care Unit, Royal Adelaide Hospital, Adelaide, Australia; [2]Discipline of Acute Care Medicine, University of Adelaide, Adelaide, Australia; [3]Department of Pathology, SA Pathology, Adelaide, Australia; [4]Preclinical, Imaging and Research Laboratories, South Australian Health and Medical Research Institute, Gilles Plains, Australia; and [5]University of Melbourne, Parkville, Australia

ORCID ID: 0000-0003-4345-3213 (M.J.M.).

Abstract

Rationale: It is unclear how septic shock causes acute kidney injury (AKI) and whether this is associated with histological change.

Objectives: We aimed to determine the nature and extent of changes in renal structure and function over time in an ovine model of septic shock.

Methods: Fifteen sheep were instrumented with a renal artery flow probe and renal vein cannula. Ten were given intravenous *Escherichia coli* to induce septic shock, and five acted as controls. Animals were mechanically ventilated for 48 hours, while receiving protocol-guided parenteral fluids and a norepinephrine infusion to maintain mean arterial pressure. Renal biopsies were taken every 24 hours or whenever animals were oliguric for 2 hours. A renal pathologist, blinded to tissue source, systematically quantified histological appearance by light and electron microscopy for 31 prespecified structural changes.

Measurements and Main Results: Sheep given *E. coli* developed septic shock, oliguria, increased serum creatinine, and reduced creatinine clearance (AKI), but there were no changes over time in renal blood flow between groups ($P > 0.30$) or over time within groups ($P > 0.50$). Renal oxygen consumption increased only in nonseptic animals ($P = 0.01$), but there was no between-group difference in renal lactate flux ($P > 0.50$). There was little structural disturbance in all biopsies and, although some cellular appearances changed over time, the only difference between septic and nonseptic animals was mesangial expansion on electron microscopy.

Conclusions: In an intensive care–supported model of gram-negative septic shock, early AKI was not associated with changes in renal blood flow, oxygen delivery, or histological appearance. Other mechanisms must contribute to septic AKI.

Keywords: acute kidney injury; histology; pathophysiology; animal models

Acute decreases in renal function define acute kidney injury (AKI). AKI occurs in up to two-thirds of intensive care unit (ICU) patients and is independently associated with health-care use and mortality (1–3). Sepsis is the most common condition associated with AKI, and increasing sepsis severity is associated with more severe AKI (4–6).

Several mechanisms have been proposed to explain septic AKI. Systemic hypotension during septic shock has been thought to decrease renal blood flow and impair renal function (7–10). However, reliable measures of renal blood flow during septic shock are not available in humans (11) and relevant animal studies have contradicted this theory, revealing that blood flow to the

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Correspondence and requests for reprints should be addressed to Matthew J. Maiden, B.Sc., B.M. B.S., Ph.D., Royal Adelaide Hospital, North Terrace, Adelaide, South Australia, Australia 5000. E-mail: mjmaiden@ozemail.com.au

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