Introduction

Proteinuria is a common finding during the clinical outcome of thermally injured patients [1]. It has long been known that proteinuria appears shortly after severe burns, and is detectable for several weeks. Proteinuria quantitatively varies from 0.5 to 3 to 4 g/day is initially of mixed type, then, after a week, gradually changes to tubular proteinuria. The clinical role of proteinuria is still unclear, mainly due to a lack of data on its pathogenesis. Recent studies have demonstrated an association between proteinuria and incidence of inhalation injury, sepsis, acute kidney injury and mortality rate. Proteinuria is considered the mirror of increased systemic capillary permeability, and possibly a direct marker of glomerular and tubular injury. Circulating plasma inflammatory mediators and pro-apoptotic factors reflecting burn injury, sepsis and acute kidney injury can affect the viability and function of tubular cells and podocytes. These studies highlight that proteinuria in burn patients should receive due consideration.

Abstract

Hu and coworkers in the previous issue of Critical Care provide evidence for the clinical relevance of proteinuria in the outcome of burn patients. Proteinuria is a common finding after severe burns, appears within a short period and is detectable for several weeks. Proteinuria ranging from 0.5 to 3 to 4 g/day is initially of mixed type, then, after a week, gradually changes to tubular proteinuria. The clinical role of proteinuria is still unclear, mainly due to a lack of data on its pathogenesis. Recent studies have demonstrated an association between proteinuria and incidence of inhalation injury, sepsis, acute kidney injury and mortality rate. Proteinuria is considered the mirror of increased systemic capillary permeability, and possibly a direct marker of glomerular and tubular injury. Circulating plasma inflammatory mediators and pro-apoptotic factors reflecting burn injury, sepsis and acute kidney injury can affect the viability and function of tubular cells and podocytes. These studies highlight that proteinuria in burn patients should receive due consideration.

Studies using SDS polyacrylamide gel electrophoresis performed in the early 1980s demonstrated that the initial pattern of proteinuria is of mixed type, indicating a lesion of both glomerulus and tubule [2]. Then, after a week, the protein excretion pattern gradually changes to typical tubular proteinuria, and persists like this for several weeks [2]. Usually its duration and amount reflect the severity of burns: more severe burns lead to more proteinuria and worse patient outcome [2,3].

Proteinuria and clinical outcome in burn patients

In the past 10 years many reports have focused on the relationship between severe burns, acute kidney injury (AKI; staged using RIFLE or AKI classification) and proteinuria. These studies demonstrated a high incidence of AKI in burn patients, an association of AKI with dysfunction of other organs, a pathogenetic role of sepsis in AKI and, in particular, a direct correlation between AKI and mortality [4,5].

The study of Hu and coworkers [1] in the previous issue of Critical Care provides additional evidence on the clinical relevance of proteinuria on the outcome of burn patients. It explores in a large cohort of 369 severe burn patients (total burned surface area >30%) the determinants of proteinuria, and its influence on AKI staged according to the RIFLE classification and on clinical outcome. Proteinuria, evaluated as positive urine dipstick readings, was absent in 31.5% of patients, mild (5 to 20 mg/dl) in 45.5% and heavy (>100 mg/dl) in 23%. Patients with proteinuria were older, with a higher incidence of inhalation injury, more severe burns and more incidence of sepsis (67%) than in patients with mild (46%) or absent (15%) proteinuria. In addition, proteinuric patients were more prone to develop AKI (incidence of 55%). In contrast, none of the patients without proteinuria developed AKI, suggesting that the persistent absence of proteinuria excludes the development of AKI. The mortality rate of patients with AKI was 29%, significantly higher than that observed in patients without AKI (12.50%). Finally, patients with proteinuria had significantly longer mechanical ventilation durations, longer
ICU stays, and higher mortality rates (30.8%) than patients with mild (16.7%) or absent (0.8%) proteinuria.

Pathogenesis of proteinuria in burn patients
Proteinuria in thermally injured patients is considered the mirror of increased systemic capillary permeability [6]. However, proteinuria (or preferably proteinuria/creatininuria ratio to correct for variation of urinary flow rate) is possibly a direct marker of renal injury. In fact, it has been demonstrated that proteinuria negatively correlates with both decreased creatinine and urea clearance as an index of loss of glomerular function and positively correlates with both Na+ and K+ fraction excretion reflecting loss of tubular function [7]. A plethora of inflammatory mediators (cytokines, polypeptides, lipid mediators) targeting endothelial cells have been implicated in glomerular and peritubular capillary dysfunction [8]. Indeed, the plasma of burn patients contains pro-apoptotic factors at levels reflecting the presence of sepsis and AKI [7]. These circulating pro-apoptotic factors reduce the viability and function of tubular cells and podocytes by a mechanism dependent on up-regulation of pro-inflammatory and pro-apoptotic genes and down-regulation of apoptosis inhibitors. Moreover, they alter permeability by disrupting tight junctions and the polarity of tubular cells and by inducing nephrin loss in podocytes [7]. Therefore, proteinuria reflects a direct negative influence of plasma factors on renal parenchymal cells and requires further studies on new extracorporeal therapeutic approaches in burn patients [9-11].

In conclusion, the study of Hu and colleagues reminds us that proteinuria in burn patients should receive due consideration.

Abbreviations
AKI, acute kidney injury.

Competing interests
The authors declare that they have no competing interests.

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