Risk Factors and Early Diagnosis of Acute Renal Impairment in Patients with Sepsis

An essay Submitted for partial fulfillment of Master Degree in Intensive Care

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List of Figures

List of Tables

List of Abbreviations

ACE inhibitors	:	Angiotensin converting enzyme inhibitor
RRT	:	renal replacement therapy
AIIRA	:	angiotensin II receptor antagonists
AIN	:	Acute interstitial nephritis
FSGS	:	focal segmental glomerulosclerosis
AKI	:	acute kidney injury
anti-TNF	:	anti Tumor necrosis factor
ARF	:	acute renal failure
ATN	:	acute tubular necrosis
ATN	:	Acute tubular necrosis
CHF	:	congestive heart failure
CIN	:	Contrast-induced nephropathy
CKD	:	chronic kidney disease
CRRT	:	Continuous Renal Replacement Therapy
ECM	:	extracellular matrix

eGFR	:	estimated glomerular filtration rate
NICE Guidelines	:	National Institute for Health and Care Excellence
eNOS	:	endothelial nitric oxide synthase
ERK	:	extracellular signal–regulated kinase
FENa	:	fraction of excreted Na
GFR	:	glomerular filtration rate
HAART	:	Highly Active AntiRetroviral Therapy
HIV	:	Human immunodeficiency virus
HRS	:	Hepatorenal syndrome
IAP	:	intra-abdominal pressure
ICAMs	:	inter cellular adhesive molecules
ICU	:	intensive care unit
ADQI	:	Acute Dialysis Quality Initiative group
IHD	:	Intermittent hemodialysis
IL-1	:	Interluekin 1
IL-18	:	Interluekin 18
IL-6	:	Interluekin 6

iNOS	:	inducible nitric oxide synthase
NO	:	nitric oxide
JNK	:	Jun N-terminal kinase
KIM-1	:	kidney injury molecule- 1
LDH	:	lactic dehydrogenase
L-FABP	:	L-type fatty acid–binding protein
L-NAME	:	L-NG-Nitroarginine Methyl Ester
MMP-9	:	Matrix metallopeptidase 9
MRSA	:	methicillin resistant Staphylococcus aureus
NGAL	:	neutrophil gelatinase-associated lipocalin
nNOS	:	neuronal NO synthase
NSAID	:	non steroid anti inflamatory drug
NSF	:	Nephrogenic systemic fibrosis
RBC	:	red blood cell
RBF	:	renal blood flow
THP	:	Tamm-Horsfall protein
TLRs	:	Toll-like receptors

TNF-α	:	Tumor necrosis factor- α
αMSH	:	α-melanocyte–stimulating hormone

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List of contents

Pathophysiology of Acute Kidney Injury and Sepsis

Introduction:

The development of acute renal failure (ARF) continues to be a problem that markedly affects outcome in critically ill patients. Despite advances in treatment, development of ARF continues to be associated with high mortality rates, ranging from 40% to 90% ***(Mehta et al., 2007).***

In addition, ARF is a major risk factor for non renal complications. Factors that may influence the high mortality rates include the increasing age of the population of patients and the existence of comorbid conditions (e.g. diabetes, heart disease, preexisting renal disease, preexisting vascular disease, sepsis and respiratory failure) ***(Levy et al., 1996)***.

Additional evidence indicates that even milder forms of acute kidney injury (AKI), not just ARF requiring renal replacement therapy, are associated with excess mortality ***(Venkataraman et al., 2008).***

Numerous studies have shown that ARF in patients in the intensive care unit (ICU) is associated with high short- and long-term case fatality rates, dialysis dependence, and reduced quality of

life. Until recently, no uniform standard for diagnosing and classifying ARF was available ***(Hoste et al., 2006).***

More than 35 different definitions of acute renal failure were used in clinical practice. A need for clear definitions of renal injury and renal failure has led to the request for measurable criteria ***(Kellum et al., 2002).***

A consensus on the need for a definition and a classification system to enable more accurate diagnosis of kidney injury was reached by the Acute Dialysis Quality Initiative group(ADQI), AKI refers to a sudden decline in kidney function that causes disturbances in fluid, electrolyte, and acid-base balances because of a loss in clearance of small solutes and a decreased glomerular filtration rate (GFR) ***(Dennen et al., 2010).***

Therefore, the term AKI has replaced the term ARF, with the understanding that AKI has a broad spectrum and encompasses the entire syndrome in all patients, not just patients who require renal replacement therapy but also patients with minor changes in renal function ***(Hoste et al., 2003).***

AKI Classification

Classification criteria for AKI include assessment of 3 grades of severity: risk of acute renal failure, injury to the kidney, and failure of renal function. The 2 outcome classifications are loss

of kidney function and end-stage renal disease. This 5-point system (Risk of injury, Injury, Failure, Loss of function, and End-stage renal failure) is known as the RIFLE classification system (Table 1-1) ***(Kellum et al., 2008).***

In several investigations on use of the RIFLE system in different populations of patients, RIFLE criteria correlated with outcome. Consequently, the RIFLE classification is being used to identify kidney injury and improve patients' outcome ***(Hoste et al., 2003).***

Table 1-1 RIFLE classification system for acute kidney injury

Criteria		
RIFLE category	**Glomerular filtration rate**	**Urine output**
Grades of severity		
Risk	Serum creatinine level increased 1.5 times or glomerular filtration rate decreased >25%	<0.5 mL/kg for 6 hours
Injury	Serum creatinine level increased 2 times or glomerular filtration rate decreased >50%	<0.5 mL/kg for 12 hours
Failure	Serum creatinine level increased 3 times or glomerular filtration rate decreased >75% or serum creatinine level >4 mg/dL	<0.3 mL/kg for 24 hours or anuria for 12 hours