Perioperative Acute Kidney Injury in Patients Undergoing General Surgery

An Essay Submitted For Partial Fulfillment of Master Degree In

Anesthesiology

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The Acute Dialysis Quality Initiative (ADQI) group proposed a standard definition and classification system for the syndrome of acute renal failure. The classification system coins the acronym RIFLE and has three levels: Risk, Injury, and Failure; and two outcomes: Persistent acute renal failure (termed Loss) and End stage kidney disease classically, the causes of AKI have been subdivided into three groups: prerenal, intrinsic, and post renal. While there is considerable overlap between these, especially the first two, it remains a useful clinical guide.

Current diagnostic parameters for AKI are limited by reliance on serum creatinine, which is affected by age, gender and muscle mass. It is not so helpful in early detection of AKI as elevations in serum creatinine may occur several days after the actual injury. The search for AKI biomarkers has focused on identifying alternatives to serum creatinine. Urinary neutrophil gelatinase associated lipocalin (NGAL) and interleukin-18 may provide insights into the cause of AKI. Similarly, serum NGAL, serum cystatin C and urinary kidney injury molecule-1 (KIM-1) may facilitate the early diagnosis of AKI.

Detection of risk factors predisposing to AKI in every patient is so important in anticipation and using of preventive strategies in such patients: age, emergency surgery, liver disease, BMI, high risk surgery, peripheral vascular occlusive disease and chronic obstructive pulmonary disease, sever hemodynamic derangement and use of nephrotoxic medications.

Management is directed at treating any life threatening features, attempting to halt or reverse the decline in renal function, and if unsuccessful providing support by renal replacement therapy anticipating

renal recovery. Hyperkalemia, pulmonary edema, and severe acidosis require immediate attention. Fluid balance, the treatment of less severe acidosis, the use of diuretics and dopamine, as well as the relief of obstruction are all issues in the further management of the patient some more controversial than others. Provided the patient can be maintained through the period of non-function, and no further insults accrue, the kidney is remarkable in its ability to recover its normal homoeostatic role.

Pharmacological interventions in AKI have targeted the prevention of renal ischemia or modulation of the ongoing inflammatory or hormonal insults. Low dose dopamine, historically thought to improve renal perfusion and thus prevent AKI, has recently been shown to have no effect on mortality and RRT requirement. Similarly, atrial natriuretic peptide (ANP), a vasoactive endogenous hormone that increases glomerular filtration by dilating afferent and constricting efferent arterioles, was felt to be a promising therapeutic option.

Intermittent hemodialysis (IHD), continuous renal replacement therapies (CRRT) and sustained low efficiency dialysis (SLED) are the principal RRT modalities that are used in the acute setting. Although institutional policies may determine the local availability of these modalities, CRRT and SLED tend to be used in patients with greater hemodynamic instability. There is likely substantial intercenter variability with respect to how each of these forms of RRT is utilized and prescribed.

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List of Abbreviations

^{99m}Tc-DMSA	**T**echnetium-**L**abeled **D**imer**c**apto**s**uccinic **A**cid
^{99m}Tc-DTPA	**T**echnetium-**L**abeled **D**iethylene**t**riamine **P**enta **A**cetic acid
ACEIs	**A**ngiotensin **C**onverting **E**nzyme **I**nhibitors
ADH	**A**nti-**D**iuretic **H**ormone
AKI	**A**cute **K**idney **I**njury
AKIN	**A**cute **K**idney **I**njury **N**etwork
ALI	**A**cute **L**ung **I**njury
ANP	**A**trial **N**atriuretic **P**eptide
ARBs	**A**ngiotensin **R**eceptor **B**lockers
ARF	**A**cute **R**enal **F**ailure
ASA	The **A**merican **S**ociety of **A**nesthesiologists
ATN	**A**cute **T**ubular **N**ecrosis
ATP	**A**denosine **Tri**phosphate
BMI	**B**ody **M**ass **I**ndex
BMP7	**B**one **M**orphogenetic **P**rotein **7**
BUN	**B**lood **U**rea **N**itrogen
Ca^{+2}	**Ca**lcium
CCBs	**C**alcium **C**hannel **B**lockers
CKD	**C**hronic **K**idney **D**isease
Cl^{-}	Cloride
CNS	**C**entral **N**ervous **S**ystem
CPB	**C**ardio- **P**ulmonary **B**ypass

CRRT	**C**ontinuous **R**enal **R**eplacement **T**herapy
CT	**C**omputed **T**omography
CVVH	**C**ontinuous **V**eno**v**enous **H**emofiltration
CVVHD	**C**ontinuous **V**eno**v**enous **H**emo**d**ialysis
CVVHDF	**C**ontinuous **V**eno**v**enous **H**emo**d**ia**f**iltration
Da	**D**alton
DCT	The **D**istal **C**onvoluted **T**ubule
ECF	**E**xtra**c**ellular **F**luid
ECG	**E**lectro**c**ardio**g**ram
EGF	**E**pidermal **G**rowth **F**actor
ELISA	**E**nzyme **L**inked **I**mmuno **S**orbent **A**ssay
ENaC	**E**pithelial Sodium **C**hannel
EP2 - EP4	**E P**rostanoid receptors
ESF	**E**rythropoiesis **S**timulating **F**actor
FDA	**F**ood and **D**rug **A**dministration
FE_{Na}	**F**ractional **E**xcretion of sodium
FGF-1	**F**ibroblast **G**rowth **F**actor-1
GFR	**G**lomerular **F**iltration **R**ate
GLUT2	**Glu**cose **T**ransporter **2**
H^+	Hydrogen
H_2O	Water
HCO_3^-	Bicarbonate
HD	**H**emo**d**ialysis
HGF	**H**epatocyte **G**rowth **F**actor
HIT	**H**eparin-**I**nduced **T**hrombocytopenia
HMG CoA	3-**H**ydroxy-3-**M**ethyl-**G**lutaryl-Co**A**
ICU	**I**ntensive **C**are **U**nit

Ig	**I**mmuno**g**lobulin
IGF-1	**I**nsulin like **g**rowth **F**actor-1
IHD	**I**ntermittent **H**emo**d**ialysis
IL-18	**I**nter**l**eukin-18
IV	**I**ntra**v**enous
IVP	**I**ntra**v**enous **P**yelogram
JGA	**J**uxta**g**lomerular **A**pparatus
K^+	Potassium
K_{ATP}	ATP sensitive potassium channel
KIM-1	**K**idney **I**njury **M**olecule -1
MAP	**M**ean **A**rterial Blood **P**ressure
Mg^{+2}	Magnesium
MRI	**M**agnetic **R**esonance **I**maging
mRNA	**M**essenger **R**ibo**n**uclei**c** **A**cid
MSCs	**M**esenchymal **S**tromal **C**ells
Na^+	Sodium
NAC	**N**-**A**cetyl **C**ysteine
NGAL	**N**eutrophil **G**elatinase-**A**ssociated **L**ipocalin
NHE3	**N**a-**H** **E**xchanger isoform 3
$NKCC_2$	**N**a-**K**-**C**l **C**otransporter 2
NSAIDs	**N**on-**S**teroidal **A**nti **I**nflamatory **D**rugs
PCT	**T**he **P**roximal **C**onvoluted **T**ubule
PD	**P**eritoneal **D**ialysis
PGD_2	**P**rosta**g**landin D_2
PGE_1	**A**lprostadil
PGE_2	**P**rosta**g**landin E_2
PGI_2	**P**rostacyclin

Ph^{-3}	Phospahte
PO	**P**er **O**ral
RBCs	**R**ed **B**lood **C**ells
RBF	**R**enal **B**lood **F**low
RBP	**R**etinol-**B**inding **P**rotein
RCRI	**R**evised **C**ardiac **R**isk **I**ndex
RCT	**R**andomized **C**ontrolled **T**rial
RIFLE	**R**isk, **I**njury, **F**ailure, **L**oss, **E**nd stage
RPF	**R**enal **P**lasma **F**low
RRT	**R**enal **R**eplacement **T**herapy
S.Cr	**S**erum **Cr**eatinine
SGLT	**S**odium **Gl**ucose co**t**ransporter
SLED	**S**ustained **L**ow **E**fficiency **D**ialysis
TAL	**T**hick **A**scending **L**imb
Tx	**T**ransplantation
UFH	**U**n**f**ractionated **H**eparin
UO	**U**rine **O**utput
USA	**U**nited **S**tates of **A**merica
UTI	**U**rinary **T**ract **I**nfection
WBCs	**W**hite **B**lood **C**ells

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Acute kidney injury (AKI) has now replaced the term acute renal failure and a universal definition and staging system has been proposed to allow earlier detection and management AKI. The new terminology enables healthcare professionals to consider the disease as a spectrum of injury. This spectrum extends from less severe forms of injury to more advanced injury when acute kidney failure may require renal replacement therapy (RRT) ***(Praught and Shlipak, 2005).***

Clinically, acute kidney injury is characterized by a rapid reduction in kidney function resulting in a failure to maintain fluid, electrolyte and acid-base homeostasis. There have previously been many different definitions of AKI used in the literature which has made it difficult to determine the epidemiology and outcomes of AKI. Over recent years there has been increasing recognition that relatively small rises in serum creatinine in a variety of clinical settings are associated with worse outcomes ***(Praught and Shlipak, 2005).***

Acute kidney injury occurs in approximately one to five percent of all hospitalized patients and is increasingly prevalent. The development of acute renal failure (ARF) is known to increase cost, duration of stay, and mortality ***(Kheterpal et al., 2007).***

Acute kidney injury is a common clinical problem encountered in critically ill patients and characteristically portends an increase in morbidity and mortality ***(Uchino et al., 2005).***

Acute kidney injury is no longer considered to be an innocent bystander merely reflecting co-existent pathologies. It has been demonstrated to be an independent risk factor for mortality ***(Levy et al., 1996)***.

Anatomy of the Kidney

Location

The kidneys are located in the paravertebral gutter and lie in a retroperitoneal position at a slightly oblique angle. There are two, one on each side of the spine. The asymmetry within the abdominal cavity caused by the liver typically results in the right kidney being slightly lower than the left, and left kidney being located slightly more medial than the right ***(Cotran et al., 2005).***

Surface anatomy of the kidney

The left kidney is approximately at the vertebral level T_{12} to L_3. The right kidney lies just below the diaphragm and posterior to the liver, the left kidney below the diaphragm and posterior to the spleen. Resting on top of each kidney is an adrenal gland. The upper (cranial) parts of the kidneys are partially protected by the eleventh and twelfth ribs, and each whole kidney and adrenal gland are surrounded by two layers of fat (the perirenal and pararenal fat) and the renal fascia ***(Cotran et al., 2005).***

Structure of the Kidney

The substance, or parenchyma, of the kidney is divided into two major structures: superficial is the renal cortex and deep is the renal medulla. Grossly, these structures take the shape of 8 to 18 cone-shaped renal lobes, each containing renal cortex surrounding a portion of

medulla called a renal pyramid (of Malpighi). There are projections of cortex between the renal pyramids called renal columns (of Bertin). Nephrons, the urine-producing functional structures of the kidney, span the cortex and medulla. The initial filtering portion of a nephron is the renal corpuscle, located in the cortex, which is followed by a renal tubule that passes from the cortex deep into the medullary pyramids. Part of the renal cortex, a medullary ray is a collection of renal tubules that drain into a single collecting duct ***(Giebisch and Windhager, 2004).***

The tip, or papilla, of each pyramid empties urine into a minor calyx, minor calyces empty into major calyces, and major calyces empty into the renal pelvis, which becomes the ureter ***(Giebisch and Windhager, 2004).***

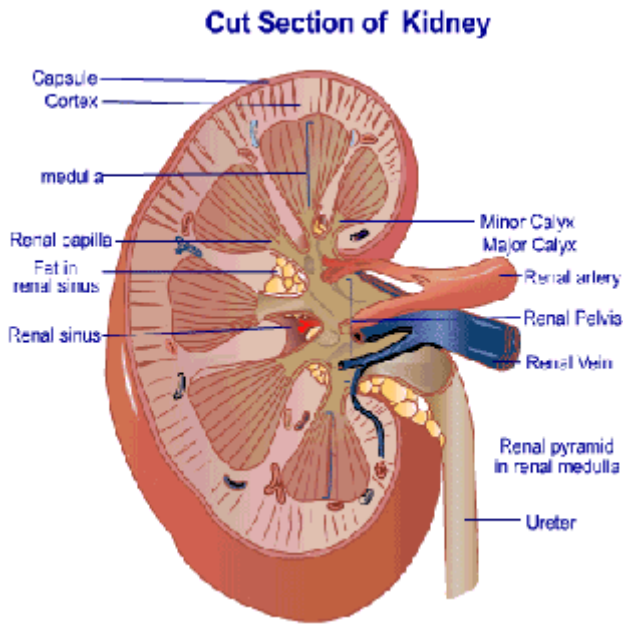

Fig. 1 : Structure of the kidney

(Cotran et al., 2005).

Renal circulation

The renal arteries branch laterally from the aorta just below the origin of the superior mesenteric artery. The paired renal arteries take 20% of cardiac output to supply organs that represent