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MANAGEMENT OF CARDIORENAL SYNDROME IN INTENSIVE CARE PATIENTS

Essay

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Contents

Title Page No.

List of Abbreviations

Abbreviation.	Full Name
A	Adenosine
AbCS	Abdominal compartment syndrome
ACC	American college of cardiology
ACE	Angiotensin-converting enzyme
ACEIs	Angiotensin-converting enzyme inhibitors
ACS	Acute coronary syndrome
ADH	Antidiuretic hormone
ADHF	Acute decompansated heart failure
ADMA	Asymmetric dimethyl arginine
ADPKD	Autosomal dominant polycystic kidney disease
AGEs	Advanced glycation end-products
AGEIs	Advanced glycation end-products inhibitors
AHA	American heart association
AKI	Acute kidney injury
AKIN	Acute kidney injury network
Ang II	Angiotensin II
ANP	Atrial natriuretic peptide
APP	Abdominal perfusion pressure
ARBs	Angiotensin receptor blockers
AT1	Angiotensin type 1
ATN	Acute tubular necrosis
AV	Atrioventricular
AVP	Arginine vasopressin
BNP	B-type natriuretic peptide
CAC	Coronary artery calcification
CEL	Carboxy ethyl lysine
CHF	Chronic heart failure
CI-AKI	Contrast-induced acute kidney injury
CKD	Chronic kidney disease
CML	Carboxy methyl lysine
CMR	Cardiac magnetic resonance
CPB	Cardiopulmonary bypass
CRP	C-reactive protein
CRRT	Continuous renal replacement therapy
CRS	Cardiorenal Syndrome
CSA-AKI	Cardiac surgery-associated acute kidney injury
CT	Computerized tomography

CVD	Cardio vascular disease
CVP	Central venous pressure
CVVH	Continuous veno -venous hemofiltration
DM	Diabetes mellitus
DN	Diabetic nephropathy
EBCT	Electron beam computed tomography
EC	Endothelial cell
ECFV	Extracellular fluid volume
ECM	Extra cellular Matrix
e-GFR	Estimated glomerular filtration rate
e-NOS	Endothelial nitric oxide synthase
EPO	Erythropoietin
ESAs	Erythropoiesis-stimulating agents
ESRD	End-stage renal disease
FABPs	Fatty acid–binding proteins
FGF-23	Fibroblast growth factor-23
FPE	Flash pulmonary edema
GFR	Glomerular filtration rate
GH	Growth hormone
Hcy	Homocysteine
HDL	high-density lipoprotein
HSS	Hypertonic saline solution
HTN	Hypertension
IAH	Intra-abdominal hypertension
IAP	Intra-Abdominal Pressure
ICAM-1	Intercellular adhesion molecule-1
ICU	Intensive care unit
IGF	Insulin-like growth factor
IL	Interleukin
IRAP	Insulin-regulated aminopeptidase
IVC	Inferior vena cava
KIM-1	Kidney injury molecule 1
LDL	Low density lipoprotein
LV	Left ventricle
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
MAP	Mean arterial pressure
MCP-1	Monocyte chemotactic protein-1
MSNA	Muscle sympathetic nerve activity
NAG	N-acetyl-beta-D-glucosaminidase
NEP	Neutral endopeptidase
NFkb	Nuclear factor kappa-b
NGAL	Neutrophil gelatinase associated lipocalin
NO	Nitric oxide
NPs	Natriuretic peptides

NYHA	New York Heart Association
PAI-1	Plasminogen-activation inhibitor-1
PCP	Propyl carboxypeptidase
PDGF	Platelet derived growth factor
PEP	Propyl endopeptidase
PKD	Polycystic kidney disease
PTH	Parathyroid hormone
PTHrP	Parathyroid-hormone-related protein
RAAS	Renin-angiotensin-aldosterone system
RAS	Renin–angiotensin system
RBF	Renal blood flow
ROS	Reactive oxygen species
RRT	Renal replacement therapy
SCD	Sudden cardiac death
SCR	Serum creatinine
SCUF	Slow continuous ultrafiltration
SNS	Sympathetic nervous system
SUN	Serum urea nitrogen
TGF	Tubuloglomerular feedback
TGF-b	Transforming growth factor beta
TNF-a	Tumor necrosis factor alpha
UO	Urine output
US	Ultrasonography
VCAM-1	Vascular cell adhesion molecule-1
VDR	Vitamin D receptor
VEGF	Vascular endothelial growth factor
VLDL	Very-low-density lipoprotein
VSMC	Vascular smooth muscle cells
WRF	Worsening renal function

List of Tables

List of Figures

INTRODUCTION

The cardiorenal syndrome (CRS) can be generally defined as a pathophysiologic disorder of the heart and kidneys, whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ ***(Ronco et al., 2010).***

The complex pathophysiologic interactions between heart and kidney depend on four potential cardiorenal connectors: inflammation, nitric oxide/reactive oxygen species balance, the sympathetic nervous system and renin - angiotensin-aldosterone system ***(Volpe and Testa, 2010).***

Numerous epidemiologic studies have shown an association between cardiovascular morbidity and mortality and decreased kidney function. Approximately 50% of deaths in patients with chronic kidney disease (CKD) are attributable to cardiovascular disease. Mortality rate in the 2-year interval after acute myocardial infarction is about 50 % in stage 5 CKD. In general, CKD patients have a 10 to 20 fold increased risk of cardiac death, when compared with age – gender – matched controls ***(Wall, 2010).***

In meta-analysis reported that 63% of heart failure patients had mild degree of renal impairment and that 29% of patients had moderate to sever degree of renal impairment ***(Volpe and Testa, 2010).***

The development of worsening renal function in congestive heart failure is associated with increased hospitalizations and death. So, the using of urinary biomarkers offer a rapid and non invasive method for detecting acute kidney injury more quickly and specifically than using of the serum creatinine. Urinary biomarkers able to identify patients at high risk for cardiorenal syndrome, establish prognosis and assess response to therapies ***(Comnick et al., 2011)***.

Understanding the complex interactive aspects of the cardiorenal relationship, i.e. from pathophysiology to epidemiology and diagnosis is essential to understand the mechanisms that linking chronic kidney disease (CKD) and chronic vascular disease (CVD) which is essential to have more clear perspectives on the future therapeutic approaches to this deadly association ***(Berbari et al., 2010).***

Without better understanding the pathophysiology of this complex interaction between the heart and kidney, the outcome for these patients remains poor ***(Sarraf et al., 2010).***

Aim of the Essay

The aim of this essay was to understand the pathophysiology, epidemiology, diagnosis and treatment of cardiorenal syndrome.

PHYSIOLOGY OF CARDIORENAL AXIS

1- Physiological functions of the kidney:

The kidneys perform their most important functions by filtering the plasma and removing substances from the filtrate at variable rates, depending on the needs of the body. The kidneys clear unwanted substances from the filtrate (and therefore from the blood) by excreting them in the urine while returning substances that are needed back to the blood. The kidneys play the central role in regulating the water content, inorganic-ion composition and volume of the internal environment. Second, the kidneys excrete metabolic waste products into the urine such as urea from the catabolism of protein, uric acid from nucleic acids, creatinine from muscle creatine, the end products of hemoglobin breakdown and many others like excretion of some foreign chemicals such as drugs. Also, the kidney share in acid-base control with lung. The third function is gluconeogenesis, during prolonged fasting. Finally, the kidneys act as endocrine glands, secreting some important hormones like erythropoietin, renin, **1,25**- dihydroxy vitamin **D3** and prostaglandin synthesis. Also, catabolism of polypeptide hormones (e.g parathyroid hormone, insulin) occurs in the kidney ***(Vander et al., 2001)***.

There are only two physiological functions that are routinely and easily measured in the ICU, which are unique to the kidney and which are considered clinically important: the production of urine and the excretion of water soluble waste

products of metabolism. Thus, clinicians have focused on these two aspects of renal function to help them define the presence of acute renal failure ***(Bellomo et al., 2012)***.

- ***Renal blood supply:***

Blood flow to the two kidneys is normally about 20 % of the cardiac output or 1100 ml/min. The renal artery enters the kidney through the hilum and then branches progressively to form the interlobar arteries, arcuate arteries, interlobular arteries and afferent arterioles which lead to the glomerular capillaries where large amounts of fluid and solutes (except the plasma proteins) are filtered to begin urine formation. The distal ends of the capillaries of each glomerulus coalesce to form the efferent arteriole which leads to a second capillary network, the peritubular capillaries, that surrounds the renal tubules. The peritubular capillaries empty into the vessels of the venous system, which run parallel to the arteriolar vessels and progressively form the interlobular veins, arcuate veins, interlobar veins and renal vein, which leaves the kidney beside the renal artery and ureter **(Figure 1)** ***(Guyton and Hall, 2006a)***.

Humoral influences on the renal vasculature are mediated by vasoconstrictors and vasodilators. Vasoconstrictors are angiotensin II, noradrenaline, thromboxane A2, B2, platelet-activating factor, endothelin-1 and vasopressin. Vasodilators are prostaglandins E_1, E_2, I_2, acetylcholine, bradykinin, nitric oxide and atrial natriuretic peptide (ANP) ***(Banerjee, 2001).***

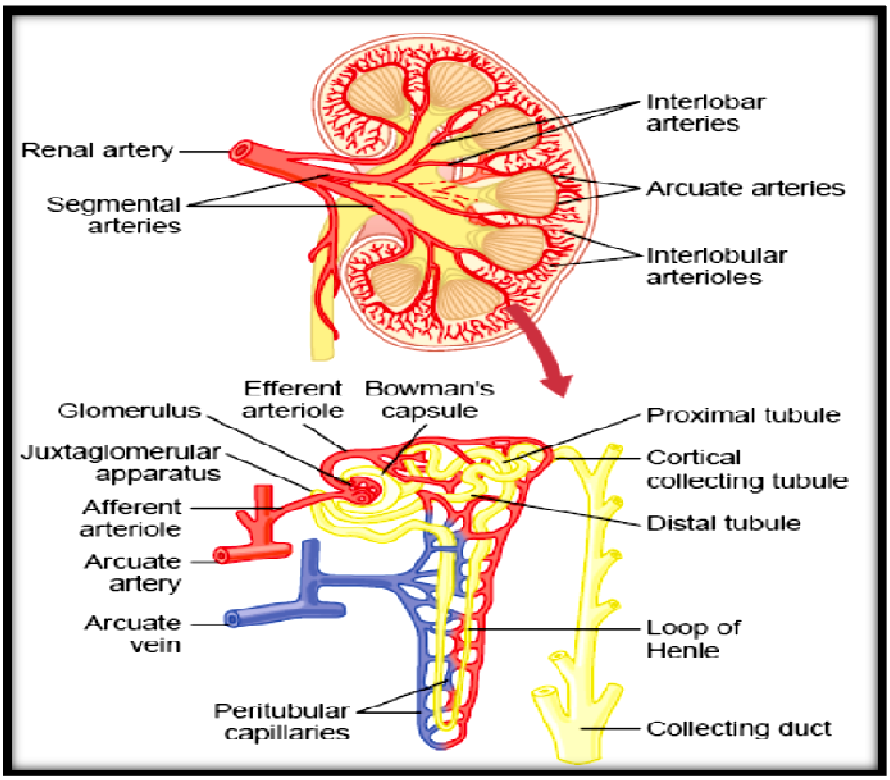

Figure (1): Section of the human kidney showing the major vessels that supply the blood flow to the kidney and schematic of the microcirculation of each nephron ***(Guyton and Hall, 2006 a).***

- ***Physyological steps of urine formation:***

1- Glomerular filteration:

The glomerular filtration barrier allows the filtration of small molecules but restricts the passage of macro molecules (e.g. the plasma proteins). The range of the glomerular filtration rate is 60–80 ml/min/m^2 or 100–140 ml/min per 1.73 m^2. The rate falls with increasing age by about 1 ml/min/ m^2 per year beyond the age of 40 years. Net glomerular filtration pressure = the glomerular capillary hydrostatic pressure(PGC) – Bowman