شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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HANAA ALY

The use of Nuetrophil Gelatinase Associated Lipocalin (NGAL) as a novel marker in early diagnosis of Hepato Renal Syndrome in advanced cirrhotic patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Internal Medicine & Gastroentrology and Hepatology

By

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Ain Shams University
2021

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to ALLAH, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to Prof. Dr. Nevine Ibrahim Musa, Professor of Internal Medicine, Gastroentrololgy, Faculty of Medicine - Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to Dr. Ahmed Samir Abo Halima, Assistant Professor of Internal Medicine, Gastroentrololgy, Faculty of Medicine - Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I am deeply thankful to Dr. Ahmed Samir Allam, Lecturer of Internal Medicine, Gastroentrololgy, Faculty of Medicine - Ain Shams University, for his great help, active participation and guidance.

Amr Okasha

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List of Abbreviations

Abb.	Full term
ACLF	Acute-on-chronic liver failure
ADQI	Acute Dialysis Quality Initiative
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
ATN	Acute tubular necrosis
CKD	Chronic kidney disease
CRP	C-reactive protein
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
FeNa	Fractional excretion of sodium
HRS	Hepatorenal syndrome
HRS	Hepatorenal syndrome
IAC	International Ascites Club
iAKI	Intrinsic acute kidney injury
IL	Interleukin
KIM-1	Kidney injury molecule-1
L-FABP	Liver-type fatty acid-binding protein
LT	Liver transplantation
MDRD6	Modification of Diet in Renal Disease 6
NGAL	Neutrophil gelatinase-associated lipocalin
PRA	Prerenal azotemia
RRT	Renal replacement therapy
SBP	Spontaneous bacterial peritonitis
TIPS	Transjugular intrahepatic portosystemic shunting

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INTRODUCTION

Kidney dysfunction is a complex and common event in patients with liver cirrhosis. Although novel treatments have shown some promising results ***(Kaushal and Shah, 2014),*** acute kidney injury (AKI) remains a major complication of decompensated liver cirrhosis with high morbidity and mortality rates ***(Garcia-Tsao et al., 2008; Siew et al., 2009).*** AKI occurs in up to 19-20% of hospitalized patients with liver cirrhosis and among the most frequent causes are prerenal azotemia (PRA), hepatorenal syndrome (HRS), and acute tubular necrosis (ATN), with prevalence rates estimated around 68%, 25%, and 33%, respectively ***(Garcia-Tsao et al., 2008; Siew et al., 2009).***. Reports have shown that approximately 1% of cirrhotic patients with azotemia suffer from progressive parenchymal renal disease secondary to hepatic viral infections, immune or metabolic disorders (chronic glomerulonephritis, IgA nephropathy, diabetic nephropathy) ***(Garcia-Tsao et al., 2008; Hartleb and Gutkowski, 2012).***

Definitions of AKI and CKD

In 2011, after a joint debate, members of the Acute Dialysis Quality Initiative (ADQI) and the International Ascites Club (IAC) developed a new collection of diagnostic criteria for an improved evaluation of kidney impairment in liver cirrhosis ***(Wong et al., 2011; Choi et al., 2014).*** The term "Acute Kidney Injury (AKI)" is used to describe the abrupt

decline of the renal function indicated by a boost in serum creatinine level of >50% from baseline, or by an upward trend in serum creatinine level of ≥26.4 μmol/ L (≥0.3 mg/ dL) in less than 48 hours. Chronic Kidney Disease (CKD) can be defined by an estimated glomerular filtration rate (eGFR) below 60 ml/ minute for more than 3 months, by using the Modification of Diet in Renal Disease 6 (MDRD6) formula. Acute chronic kidney disease manifests as an overlapping of AKI on pre-existing chronic renal disease according to the previous definitions for AKI and CKD ***(Wong et al., 2011; Choi et al., 2014)***.

RIFLE classification

Gathered together in Vicenza (Italy) in May 2002, the members of ADQI group elaborated a new set of diagnostic and classification criteria for AKI: the RIFLE classification (published in May 2004). This classification system includes three classes for severity (Risk, Injury, Failure) and another two classes for outcome (Loss of kidney function, End-stage kidney disease) defined by perturbations in serum creatinine, glomerular filtration rate or urine output as described in Table 1 ***(Lopes and Jorge, 2013).***

Table (1): RIFLE classification by ADQI ***(Bellomo et al., 2004; Lopes and Jorge, 2013; Choi et al., 2014).***

Class	GFR criteria	UO criteria	
Risk	↑ SCr × 1.5 or ↓ GFR >25%	<0.5 mL/kg/h × 6 h	Severity classes
Injury	↑ SCr × 2 or ↓ GFR >50%	<0.5 mL/kg/h × 12 h	
Failure	↑ SCr × 3 or ↓ GFR >75% or if baseline SCr ≥353.6 μmol/ L (≥4 mg/ dL) ↑ SCr >44.2 μmol/ L >0.5 mg/ dL)	<0.3 mL/kg/h × 24 h or anuria × 12 h	
Loss of kidney function	Complete loss of kidney function >4 weeks		Outcome classes
End-stage kidney disease	Complete loss of kidney function >3 months		
GFR = glomerular filtration rate; UO = urine output; SCr = serum creatinine			

AKIN classification

After a meeting in Amsterdam (September 2005), the Acute Kidney Injury Network (AKIN) group developed a new set of criteria for AKI known as the AKIN classification (published in March 2007). This improved the classification system which consisted of 3 stages of severity and was based only on changes in serum creatinine (2 measurements within 48 h) and urine output as shown in **Table 2** ***(Lopes and Jorge, 2013).***

Table (2): AKIN classification ***(Lopes and Jorge, 2013; Choi et al., 2014).***

Stage	SCr criteria	UO criteria
1	↑ SCr ≥26.5 μmol/ L (≥0.3 mg/ dL) or ↑SCr ≥150-200% (1.5-2×)	<0.5 mL/kg/h (>6 h)
2	↑ SCr >200-300% (>2-3×)	<0.5 mL/kg/h (>12 h)
3	↑ SCr >300% (>3×) or if baseline SCr ≥353.6 μmol/ L (≥4 mg/ dL) an ↑SCr ≥44.2 μmol/ L (≥0.5 mg/ dL)	<0.3 mL/kg/h (>24 h) or anuria (>12 h)
SCr = serum creatinine; UO = urine output. * patients requiring RRT are included independent of the stage		

A common limitation of both classifications systems is their inability to provide any information on the cause of the renal dysfunction in liver cirrhosis. Existing data cannot support the superiority of AKIN classification to traditional criteria regarding risk prediction in patients with liver cirrhosis and renal failure ***(Arroyo, 2013).*** Fagundes et al. observed that a combination between AKIN classification and traditional criteria for kidney impairment might provide a better assessment of risk in patients with liver cirrhosis, compared with AKIN criteria alone ***(Fagundes et al., 2013).***