بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

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قسم

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Evaluation of RNA Based Biomarker Expression in Acute Kidney Injury after ESWL

Thesis

Submitted for Partial Fulfillment of Master Degree in Urology

By

Mohamed Sahab Emam

Bachelor of Medicine and Surgery

Supervised by

Prof. Dr. Mohamed Mohamed Yassin

Assistant Professor of Urology

Faculty of Medicine- Ain Shams University

Prof. Dr. Amr El Kholy

Assistant Professor of Urology

Theodor Bilharz Research Institute

Dr. Waleed Mousa

Lecturer of Urology

Faculty of Medicine - Ain Shams University

Prof. Dr. Marwa Matboli Sayed

Assistant Professor of Biochemistry

Faculty of Medicine - Ain Shams University

Faculty of Medicine

Ain Shams University

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Mohamed Sahab

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List of Abbreviations

Abb.	Full term
5-ASA	5-aminosalicylic acid
ACEi	Angiotensin-converting enzyme inhibitor
ADQI	Acute Dialysis Quality Initiative
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
ARB	Angiotensin receptor blockers
ATP	Adenosine triphosphate
B2M	B-2-microglobulin
BGAL	B-galactosidase
CAGE	Cap analysis gene expression
CKD	Chronic kidney disease
CT	Computerized tomography
DM	Diabetes munities
DNA	Deoxyribonucleic acid
EAU	European Association of Urology
eGFR	Estimated glomerular filtration rates
ESRD	End-Stage Renal Disease
ESWL	Extracorporeal shockwave lithotripsy
FeNa	Fractional excretion of sodium
FeUr	Fractional excretion of urea
GFR	Glomerular filtration rate
HAR	Human accelerated regions
HGP	Human Genome Project
HTN	Hypertension
ICU	Intensive care unit
IGFBP-7	Insulin-like growth factor binding protein 7

List of Abbreviations Cont...

Abb.	Full term
KDIGO	Kidney Disease: Improving Global Outcomes
KIM-1	Kidney injury molecule-1
L-FAB	Liver fatty acid-binding protein
MRI	Magnetic resonance imaging
NAG	N-acetyl-β-d-glucosaminidase
ncRNAs	Noncoding RNAs
NGAL	Neutrophil gelatinase-associated lipocalin
NIH	National Institute of Health
NO	Nitric oxide
O2	Oxygen
P.A	Postero-anterior
PC	Protein-coding
PCG	PC gene
RIRS	Retrograde intra-renal surgery
ROS	Reactive oxygen species
RRT	Renal replacement therapy
sUr	Serum urea
SW	Shock waves
TapSAKI	TrAnscript predicting survival in AKI
TE	Transposable elements
TIMP2	Tissue inhibitor metalloproteinase 2
TSS	Transcription start
TTS	Termination
XIST	X inactive specific transcript

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INTRODUCTION

Urinary stone prevalence is estimated at 3% in all individuals, and it affects up to 12% of the population during their lifetime. Urinary stone recurrence rates approach 50% at 10 years ***(Preminger et al., 2007).***

The European Association of Urology (EAU) guidelines recommend the use of less invasive modalities such as extracorporeal shockwave lithotripsy (ESWL) or retrograde intra-renal surgery (RIRS), for stones less than 2 cm ***(Turk et al., 2013).***

ESWL has gained rapid acceptance worldwide because of its ease of use, noninvasive nature, high efficacy in treating kidney and ureteral stones, and wide availability of lithotriptors. ESWL acts via a number of mechanical and dynamic forces on stones such as cavitation, shear, spalling and cavitation ***(Moody et al., 2012).***

However, the destructive forces generated when the cavitation bubbles can cause trauma to thin-walled vessels in the kidneys and adjacent tissues, which result in a broad spectrum of vascular kidney damage, ranging from self-limited hematuria to perinephric/nephric hematomas, although most hematomas resolve, some may cause life-threatening hemodynamic instability and acute renal failure, In the long term, animal and human studies have suggested that these acute

hemorrhagic lesions may progress to scar formation and complete atrophy of the renal papillae ***(Wang et al., 2021).***

Also, SWL cause release of cytokines/inflammatory cellular mediators, and infiltration of tissue by inflammatory response cells ***(Connors et al., 2013).***

Most of our knowledge about urological therapeutic modalities injury to the kidney is based on experimental animal studies where invasive methods were used to assess for tissue damage ***(Fahmy et al., 2013).***

This is due to almost of the standard metrics used to define and monitor the progression of renal damage, such as serum creatinine and blood urea nitrogen levels, are insensitive, nonspecific, and change significantly only after significant kidney injury and then with a substantial time delay ***(Bryniarski et al., 2012).***

As regard imaging modalities, there is no existing adequate imaging modality available to assess parenchymal injury, the absence of hematoma detection by conventional imaging techniques does not rule out the occurrence of potentially significant injury to the SWL-treated kidneys which rises the need to find a noninvasive diagnostic test that can reliably identify kidney injuries, especially in certain populations such as children, patients with preexisting renal disease, or those undergoing multiple SWL treatments ***(Dede et al., 2015).***

There is no consistent dependable urinary or circulatory marker to permit detection of significant renal injury. Therefore, several new urinary and serum biomarkers promise to address the gap associated with the use of serum creatnine ***(Schmid et al., 2015).***

More than 80% of the human genome is transcribed into RNA transcripts without protein-coding potential. These so-called noncoding RNAs (ncRNAs) are arbitrarily separated into long ncRNAs (lncRNAs) >200 nucleotides and small ncRNAs (<200 nucleotides) on the basis of their size ***(Djebali et al., 2012).***

However, little is known about the functional role of lncRNAs. lncRNAs play a critical role in several important cellular processes, such as the regulation of imprinting and X-chromosome inactivation. In the nucleus, lncRNAs "fine-tune" chromatin architecture by interacting with chromatin remodeling complexes to regulate the expression of genes residing on the same chromosome(incis) or on another chromosome (in trans) ***(Ponting et al., 2009).*** Emerging studies in the cancer and cardiovascular field have demonstrated that lncRNAs can be detected in body fluids of patients ***(Kumarswamy et al., 2014).***

Circulating or urinary lncRNAs may thus be fascinating novel biomarkers that reflect intra-nuclear processes noninvasively and may therefore be a better estimate of