Effect of acute kidney injury on weaning from mechanical ventilation in critically ill patients

Thesis

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David Mamdouh Saleh Rizq

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List of Abbreviations

ADQI	:Acute Dialysis Quality Initiative
AECOPD	:Acute Exacerbations Of Chronic Obstructive Pulmonary Disease
AHPE	:Acute Hypertensive Pulmonary Edema
AKI	:Acute Kidney Injury
AKIN	:Acute Kidney Injury Network
ALI	:Acute Lung Injury
ATN	:Acute Tubular Necrosis
ATP	:Adenosin Tri-Phosphate
APACHE	:Acute Physiology And Chronic Health Evaluation
ARDS	:Adult Respiratory Distress Syndrome
ARF	:Acute Renal Failure
CKD	:Chronic Kidney Disease
COPD	:Chronic Obstructive Pulmonary Disease
CPAP	:Continuous Positive Airway Pressure
CHF	:Congestive Heart Failure
DM	:Diabetes Mellitus
ESKD	:End Stage Kidney Disease
ESRD	:End Stage Renal Disease
FEV1	:Forced Exhalation Volume in 1 second
FiO_2	:Fraction of Inspirated Oxygen
FVC	:Forced Vital Capacity
GFR	:Glomerular Filtration Rate
GN	:Glomerulonephritis
HCL	:Hydrochloric Acid
HFNC	:High Flow Nasal Canula
HO	:Hemeoxygenase
HTN	:Hypertension
HUS	:Hemolytic Uremic Syndrome

ICU	:Intensive Care Unit
IHD	:Ischemic Heart Disease
IL	:Interleukin
IRI	:Ischemic Reperfusion Injury
KC	:Kemochines
KDIGO	:Kidney Disease: Improving Global Outcomes
MBC	:Maximal Breathing Capacity
MDRD	:The Modification of Diet in Renal Disease
MV	:Mechanical Ventilation
NE	:Neutrophil elastase
NIV	:Non Invasive Ventilation
NO	:Nitric Oxide
NPE	:Nephrogenic Pulmonary Edema
PaCO2	:Partial Carbon Dioxide arterial Pressure
PaO_2	:Partial Oxygen Arterial Pressure
PEEP	:Positive End Expiratory Pressure
RIFLE	:Risk, Injury, Failure; Loss and End-stage kidney disease
RRT	:Renal Replacement Therapy
SBT	:Spontaneous Breath Trial
sCr	:Serum Creatinen
STARRT-AKI	:Standard Versus Accelerated Initiation of RRT in AKI
TNF	:Tumour Necrosis Factor
TTP	:Thrombocytopenic Purpura
UO	:Urine Output

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Abstract

Acute Kidney Injury (AKI) is a frequently encountered condition in hospitalized patients specially critically ill patients in ICUs. This condition is not a single organ failure but it is a multi-organ syndrome as AKI negatively affects many other organs. In our study we chose to investigate the effect of AKI on respiratory system. Specifically on the mechanically ventilated patients and how AKI would affect the weaning of these patients. Our study sample was 150 mechanically ventilated patients. They were divided into 2 groups according to their renal function: **Group A:** 50 patients with normal kidney function; **Group B:** 100 patients suffered from AKI at any point during their admission. Serum Creatinin (SCr) and urine output was routinely recorded at admission and every 24 hours. Duration of MV, duration of weaning, rate of weaning failure and mortality rates were recorded among other data such as demographic data, SAPS score at admission, cause of admission and co-morbidities. These data were statistically analyzed between the 2 groups. As regard demographic data, SAPS score, cause of admission and co- morbidities, they all showed no statistical significant difference between the 2 groups. As regard duration of MV and duration of weaning (length of time elapsed from the moment the patient reached weaning criterion to the time the patient was extubated), there were significant statistical difference between the two groups. As the group of patients suffered from AKI lasted longer on MV and had longer duration of weaning. As regardrate of weaning failure, it was significantly higher in AKI patients (Group A). While successful first time weaning was higher in non AKI patients (Group B). Mortality rate was also significantly higher in patients was AKI (Group A) than non AKI patients (Group B). In conclusion, AKI has significant deleterious effect on respiratory system. Which is clearly seen in our resulted. As AKI significantly worsened the outcome of mechanically ventilated patients regarding days of MV, weaning failure and up to mortality rates.

Keywords: Effect; acute kidney injury; mechanical ventilation; ill; patient

Introduction

Acute kidney injury (AKI) is the most common cause of organ dysfunction in critically ill adults, with a single episode of AKI, despite of stage, carrying a significant morbidity and mortality risk ***(Doyle and Forni, 2016)***. Both clinical and translational laboratory studies have demonstrated very complex mechanisms of inter-actions between the injured kidney and distant organs such as the lung, heart, liver, gut, brain, and hematologic system ***(White et al., 2011)***.

AKI imparts a dim outcome on different settings of critically ill patients ***(Lassnigg et al., 2004).*** Decreased renal function is accompanied by immune depression and disturbances in homeostasis of acid– base and volume status that can adversely affect respiratory function ***(Hoste and De Waele, 2005)***.

Besides that, the prescence of AKI in critically ill patients frequently contributes to depression of mental status and accumulation of several drugs' metabolites, which can further compromise the level of consciousness which can further delay weaning from mechanical ventilation ***(Rabb et al., 2003).***

Lung and kidney function are intimately related in both health and disease. Respiratory changes help to mitigate the systemic effects of renal acid-base disturbances, and the reverse is also true (***Pierson, 2006).***

Acute kidney injury

History:

For a lot of years in medical performance, the expressions acute tubular necrosis (ATN) and acute renal failure (ARF) were used interchangeably. Because of histological proof for irregular necrosis of renal tubules at autopsy, acute tubular necrosis (ATN) was the expression that was used to express this clinical entity ***(Mirzoyan et al., 2017).*** First to bring in the term Acute Renal Faliure is Homer W. Smith in 1951 in a chapter on Acute renal failure connected to traumatic injuries in his text-book The kidney Structure and Function in Health and Disease. Only lately, an exact biochemical definition for ARF was recognized. As a consequence there was no union on the diagnostic criteria, resulting in various different definitions ***(Kellum et al., 2002)***.

Conventionally, importance was given to the most severe acute decrease in kidney function, as manifested by severe azotaemia and regularly by oliguria or anuria. Yet, recent data suggests that even fairly mild injury or impairment of kidney function manifested by minute changes in serum creatinine (sCr) and/or urine output (UO), is prophetic of grave clinical consequences ***(Chertow et al., 2005)***.

The recent diagnostic approach of Acute Kidney Injury (AKI) is derived from an acute decrease of Glomerular Filtration Rtae (GFR), as reflected by an acute

increase in sCr levels and/or a decreas in UO over a given time period. Recently several bio-markers have been projected for the diagnosis of AKI and these are in different stages of progress and confirmation ***(Vanmassenhove et al., 2013).***

Terminology and definitions:

Acute kidney injury is a syndrome character-ised by the fast failure of the kidney's excretory function and is classically diagnosed by the buildup of end products of nitrogen metabolism (urea and creatinine) or reduced urine output, or both ***(Bellomo et al., 2012).***

The term Acute Kidney Injury (AKI) was used intially by William MacNider in 1918 in a situation of acute mercury poisoning, but became the favored term in 2004 when ARF was redefined with the now widely established consensus criteria recognized as: Risk, Injury, Failure; Loss and End-stage kidney disease classification (RIFLE) ***(Makris and Spanou, 2016).***

Acute Kidney Injury (AKI) is the expression that has lately replaced the term ARF. AKI is defined as an abrupt (within hours) decrease in kidney function, which encompasses both injury (structural damage) and impairment (failure of function). It is a syndrome that seldom has a solitary and distinctive pathophysiology. Many patients with AKI have a diverse aetiology where the presence of sepsis, ischaemia and nephrotoxicity frequently co-exist and complicate diagnosis and treatment. Furthermore, the syndrome is quite frequent among patients

without critical illness and it is necessary that health care professionals, mainly those without specialisation in renal disorders, detect it easily ***(Makris and Spanou, 2016).***

Categorization of AKI includes pre-renal AKI, acute post-renal obstructive nephropathy and intri-nsic acute kidney diseases. Among these, only 'intrinsic' AKI represents true kidney disease, whereas pre-renal and post-renal AKI are the conse-quence of extra-renal diseases leading to the declined glomerular filtration rate (GFR). If these pre- and/or post-renal conditions continued, they will ultimately develop to renal cellular damage and consequently intrinsic renal disease (***KDIGO Acute Kidney Injury Work Group, 2012)***

RIFLE classification:

Diagnostic criteria for AKI was recognized later from several consensus groups, first was in 2002 the Acute Dialysis Quality Initiative (ADQI) group, they developed the Risk, Injury, Failure; Loss and End-stage kidney disease (RIFLE) system for diagnosis and categorization of a wide variety of acute impairment of kidney function through a large consensus of experts ***(Bellomo et al., 2004).***

The RIFLE classification (Table 1) is derived from sCr and UO determinants, and considers three severity modules of AKI (Risk, Injury and Failure), in proportion to the variations in sCr and/or UO, and two conclusion classes (loss of kidney function and end-stage kidney disease). The patient should be classified via the criteria (sCr and/or UO) which leads to the worst classification (maximum RIFLE),

for illustration, if a patient was in the Risk group according to the UO but in the Injury group according to sCr measurement, then the worst criteria (sCr) should be used for judging the severity of AKI in this patient (***Lopes and Jorge, 2013)***

Table 1: RIFLE classification *(Lopes and Jorge, 2013)*:

Rifle criteria

category	GFR criteria	Urine output criteria
Risk	GFR reduction >25% or increased creatinine 1.5x	<0.5ml/kg/hr x 6hrs
Injury	GFR reduction >50% or increased creatinine 2x	<0.5ml/kg/hr x 12hrs
Failure	GFR reduction >75% or increased creatinine 3x	<0.3ml/kg/hr x 24hrs or anuric x 12hrs
Loss	Persistent ARF = complete loss of renal function >4 weeks	
ESKD	Complete loss of renal function > 3mths	

Strengths and weaknesses of the RIFLE classification:

RIFLE has been fundamentally validated in terms of shaping the incidence of AKI and its predictive stratification in several settings of hospitalized patient ***(Reddy et al., 2014).*** Moreover, it has been revealed that the RIFLE enables monitoring the progression of AKI severity throughout hospitalization and RIFLE classes are strongly related with increased lengths of residency, renal replacement therapy (RRT) requirement, renal function resurgence and release from hospital to a care facility ***(Mallhi et al., 2016).***

In spite of its clinical use, the RIFLE classi-fication has a numeral important restrictions.

First, baseline sCr is essential to define and organize AKI; this baseline value is often unidentified in clinical practice ***(Jannot et al., 2017).***

Second, The Modification of Diet in Renal Disease (MDRD) method, used in estimation of the GFR, has been verrified in Chronic Kidney Disease (CKD) patients with stable renal function, not in AKI patients ***(Nguyen et al., 2009).***

Third, sCr was used to define and stage AKI and determination of renal function using sCr has some other limits as:

i. The endogenous production and serum release of Cr are changeable, and it is subjective to several factors, specifically age, gender, diet, and muscle mass; ***(Srisawat and Kellum, 2011)***.
ii. 10% to 40% of Cr removal is performed by tubular secretion and this mechanism is augmented as the GFR diminishes, therefore, over-estimating renal function in AKI patients will occur ***(Lopez and Jorge, 2013).***
iii. Lots of medications inhibit tubular secretion of Cr (i.e. trimethoprim, cimetidine), causing a brief increase in sCr ***(Shahrbaf and Assadi, 2015).***
iv. Variety of factors can interfere with sCr value (i.e. acetoacetate accumulated in diabetic ketoacidosis can interfere with the alkaline picrate technique), resulting into a false rise in sCr ***(Syal et al., 2013).***

Lastly, diminish in the UO is sensitive and common in AKI; on the other hand, it also has some important restrictions in defining and staging AKI:

i. Sensitivity and specificity of UO can be considerably distorted by the use of diuretics, and this matter is not specifically considered in the RIFLE classification ***(Ricci et al., 2008).***

ii. The UO can just be determined by means of a bladder catheter in place, which, although being common in ICU patients, is uncommon in other hospitalized patients ***(Lopez and Jorge, 2013);***

The Acute Kidney Injury Network (AKIN) classification:

The AKIN classification is an update of the RIFLE classification with some changes, it is defined by a rise in absolute sCr of at least 26.5 μmol/L (0.3 mg/dL) or by a percentage increase in sCr ≥50% (1.5× baseline value), or by a decrease in the UO (documented oliguria <0.5 mL/kg/h for more than 6 h) (***Mehta et al., 2007)***

Strengths and weaknesses of the AKIN classification:

The AKIN classification has added benefits and limits associated with the modifications introduced to the RIFLE classification. As for the benfits: First, the AKI definition is only measured after an sufficient status of hydration is reached. Therefore, the AKIN classification, dissimilar from RIFLE, adds important aetiological data. Second, the AKIN classification does not necessitate baseline sCr. And for the restrictions: the AKIN