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Letter to the Editor Open Access

Heart Attack and Kidney Attack: Evolution of Lay and Clinical Terms for Spontaneous, Acute Organ Injury Syndromes

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Dear Sir,

The term 'heart attack', inclusive of Acute Coronary Syndromes (ACS) and myocardial infarction (MI) is based on symptoms, Electrocardiographic (ECG) abnormalities and biomarkers. In an attempt to engage laypeople and non-experts, the term 'kidney attack' has been introduced to refer to Acute Kidney Injury (AKI) [1]. Acute kidney injury is a clinical syndrome associated with increased morbidity and mortality making early recognition critical in patient management. The consensus definition of AKI is based on changes in serum Creatinine (sCr) or urine output (UO) [2]. However, it has been long recognized that perturbations in sCr and UO can be induced by pathophysiologic processes that do not cause injury (e.g. volume depletion); just as cardiac output can be decreased by pathophysiologic process unrelated to cardiac ischemia (e.g. bradycardia or volume depletion). Similar to the approach used to differentiate ST-segment elevation myocardial infarction (STEMI) from non-ST-segment elevation myocardial infarction (NSTEMI), a new classification schema of AKI has been proposed. With the advent of robust novel AKI biomarkers, subclinical AKI (a rise in novel AKI biomarkers alone) is analogous to an NSTEMI, while clinical AKI (a rise in AKI biomarkers and significant perturbation in SCr or UO) is analogous to STEMI [3,4].

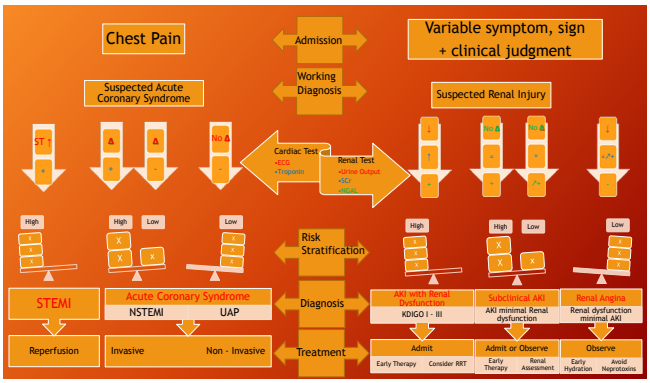
In patients with ACS, cardiac angina is a symptom complex that prompts care, is well codified, and helps clinicians assess pre-test probability for integration into diagnostic testing (i.e. a supportive

HEART ATTACK*						KIDNEY ATTACK						
	Sym	Bio	EKGST	Th	EF	MI		Sym	UO	SCr	Bio	RF	RI
STEMI	++	↑	↑	+++	↓↓	++	Clinical AKI with Kidney Dysfunction ➢ AKI KDIGO Stage 1 ➢ AKI KDIGO Stage 2 ➢ AKI KDIGO Stage 3	 - - -	 ↓ ↓↓ ↓↓↓	 ↑ ↑↑ ↑↑↑	 ↑ ↑↑ ↑↑	 ↓ ↓ ↓	 + ++ ++
NSTEMI	++	↑	↓	++	N/↓	±	Subclinical AKI with damage biomarker positive but dysfunction biomarker negative ➢ Damage Biomarker Trend ➢ Damage Biomarker Rise	 - -	 N N/↓	 ± ±	 ↗ ↑	 ± ±	 ± +
UNSTABLE ANGINA	+	-	±/↓	+	N/↓	-	Renal Angina Recognition of renal stressors (e.g. hypotension)	+	↓	N/↑	N	↓	-

Standard definition for all spectrum of myocardial ischemia/threat or "Heart Attack" are well established[9-14]. With the advent of diagnostic tools predominately biomarkers the definitions of "Heart Attack" has also evolved[9]. Similarly with the kidneys, the advent of renal injury biomarkers call for a new paradigm in AKI or "Kidney Attack". The lack of symptoms and delays in conventional AKI markers highlight a greater impetus for this term "Kidney Attack" within such a framework as we have highlighted. It is also stressed that injury and function in the renal and cardiac sense or not synonymous. In addition physiological differences highlight that injury is not always associated with loss of function and vice versa. It is thus important we introduce the term "attack" to categorize stages of heightened risk that may or may not be associated with early renal functional decline.

Bio = cardiac or renal biomarkers; EF = ejection fraction , surrogate for cardiac function; EKGST = electrocardiogram ST segment; MI = myocardial injury/infarction; N = Normal; RF = Renal Function; RI = renal injury/infarction; ST segments; Th = Thrombus; Sym = symptom; UO = urine output; ↑ increased; ↓ = decreased; ↓ = Trend; + = positive; - negative; ± equivocal

Figure 1: Proposed umbrella lay terms 'heart attack' and 'kidney attack' with parallel clinical syndromes.



Two clinical pathways are shown. Chest pain pathways are well established. Renal pathways are less well established. Urine output and SCr provide surrogate information on renal function. With the advent of AKI biomarkers, clinicians now have the ability to anticipate renal injury, with or without functional changes, as early as 2 hours from the insult. With more specific and comprehensive renal injury and function information we also begin the paradigm of reclassification the spectrum of "acute kidney syndromes". We have chosen the term "Kidney Attack" as it highlights firstly the urgency involved and secondly there are correlations with the lessons learnt from the heart. We emphasize that the role of AKI biomarkers are still partly in the research domain, and so to our understanding of "*acute kidney syndromes*". As such the schema proposed, has a degree of conjecture, however we feel that significant impetus is needed to highlight renal injury risks and as such the severity of the "Kidney Attack". We have chosen NGAL from the spectrum of renal biomarkers as it remains the most likely candidate for a "Renal Troponin". Renal injury biomarkers have a broader pathogenic base than serum troponin, for those discussion we point readers initially to Ref 15. (Diagram and concepts modified from ref 14, 15).

ABBREVIATIONS: AKI = acute kidney injury; ECG = electrocardiogram; EF = ejection fraction , surrogate for cardiac function. EKG = electrocardiogram; NGAL = neutrophil gelatinase associated lipocalin; NSTEMI = non ST elevation myocardial infarction; ST segments; STEMI = ST elevation myocardial infarction; Sym = symptom; UAP = unstable angina pectoris; UO = urine output;

SYMBOLS: ↑ increased; ↓ = decreased; ↗= Trend; + = positive; - negative; ± equivocal; Δ = changes; ↗+ range from equivocal to positive

Figure 2: Established chest pain pathway for 'heart attack' and proposed kidney injury pathway for 'kidney attack'.

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history for ACS). Because AKI does not cause visceral discomfort, the concept of Renal Angina (RA) or pathophysiologic stress on the kidneys, the parallel of cardiac angina, has been introduced in order to provide a similar construct to help direct the use and interpretation of AKI diagnostics [5]. Renal angina is currently undergoing validation in prospective studies of adults and children.

Thus, a new nomenclature for 'kidney attack' and AKI related syndromes with a wider spectrum of clinical criteria (clinical AKI, subclinical AKI, and renal angina) could be used for classification purposes (Figure 1 and Figure 2) [6-12]. The parallels between the terminology used in ACS and AKI is intentional, as we hope to use these familiar and accessible terms to help teach the non-experts how to appropriately integrate these new terms into the clinical vernacular. The public health burden of AKI is substantial. The population incidence of AKI is approximately 2,100 per million population and the case fatality rate is 25-50% [6]. Given the population of the developed world (USA, Canada, Western Europe, Japan, and Australia) of approximately 1 billion, there will be over 2 million cases of AKI this year, with 500,000 associated deaths and an expected 1.5 million AKI survivors. Of these patients, approximately 15-20% will progress to advanced stage CKD within 24 months, resulting in 300,000 cases of advanced CKD per year. With the increasing incidence of AKI in the aging population, the projected incidence of CKD associated with AKI is expected to increase [7,8].

In conclusion, the advances in consensus definitions and diagnostic biomarkers in AKI have led to an evolution in the nomenclature of the syndrome. Similar to the progress made in ACS and the lay term 'heart attack', AKI and 'kidney attack' hold promise. We believe that an educational campaign for awareness and alertness should be undertaken to prevent and improve early recognition of 'kidney attack' with use of novel, approved biomarkers and careful assessment of urine output. We think that the new terminology centered around 'kidney attack' will provide uniformity in the public health approach to AKI, and help to reveal what has been neglected and underestimated for too long simply because it was not clinically detectable.

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