KINETIC CHANGES OF HIGH-SENSITIVITY CARDIAC TROPONIN T IN ACUTE CORONARY SYNDROME WITH CHRONIC KIDNEY DISEASE

Thesis

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List Of Abbreviations

Abbrev.	Full term
Ab	: Antibody
ACS	: Acute coronary syndrome
Ag	: Antigen
AMI	: Acute myocardial infarction
BNP	: B-type Natriuretic Peptide
CK	: Creatine kinase
CK-MB	: Creatine kinase-MB fraction
CRP	: C-reactive protein
CT	: Computed tomography
cTnC	: Cardiac Troponin-C
cTnI	: Cardiac troponinI
cTnT	: Cardiac troponin T
ECG	: Electrocardiogram
ECL	: Electrochemiluminescence
ED	: Emergency departmrnt
eGFR	: Estimated glomerular filteration rate
ELISA	: Enzyme-Linked Immunosorbent Assay

List Of Abbreviations (Cont....)

Abbrev.	Full term
ESC/ACC	: European Society of Cardiology and the American College of Cardiology
FFAs	: free fatty acids
FFAu	: Free fatty acids unbound to albumin
GDF-15	: Growth differentiation factor-15
HDL-C	: High density Lipoprotein- Cholesterol
HF	: HEART failure
H-FABP	: Heart-Fatty Acid Binding Protein
hs-TnT	: High Sensitive Troponin T
HTN	: Hypertention
IL-6	: Interleukin 6
IMA	: Ischaemia modified albumin
MDRD	: Modification of Diet in Renal Disease
MEIA	: Microparticle Enzyme Immunoassay
MMP	: Matrix metalloproteinases
MPO	: Myeloperoxidase
MRI	: Magnetic resonance imaging

List Of Abbreviations (Cont....)

Abbrev.	Full term
MS	: Metabolic syndrome
NPV	: Negative predictive value
NSTEMI	: Non-ST segment elevation myocardial infarction
NT-proBNP	: N-terminal pro B-type natriuretic peptide
PAPP-A	: Pregnancy-Associated Plasma Protein-A
PE	: Pulmonary embolism
PLGF	: Placental Growth Factor
PPV	: Positive predictive value
ROC	: Receiver operating characteristic curve
SAA	: Serum amyloid A
sCD40L	: Soluble CD40 ligand
STEMI	: ST-segment elevation myocardial infarction
UA	: Unstable angina
UFFAs	: Unbound Free Fatty Acids
WBCHO	: Whole-blood choline
WHO	: World Health Organization

INTRODUCTION

INTRODUCTION

Acute coronary syndrome (ACS) is the obstruction of the coronary artery lumen with plaque disruption and acute myocardial ischemia as a consequence **(Nakata et al., 2003)**. This term covers a wide spectrum of clinical signs and symptoms, including unstable angina and both ST segment elevation (STEMI) and non-ST segment (NSTEMI) elevation myocardial infarction **(Nagesh and Roy, 2010)**. According to the World Health Organization (WHO) report dated January 2011; an estimated 7.2 million deaths per year worldwide are due to acute myocardial infarction (AMI) or other ischemic disorders of the heart **(Lotze et al., 2011)**.

The diagnosis for AMI was redefined by international guidelines of clinicians and laboratory scientists in: the detection of a rise and/or fall of preferably cardiac troponin (cTn) either T or I, with at least one value exceeding the upper reference limit (99^{th} percentile) measured in a cardio-healthy group together with clinical (history, physical exam) and imaging (electrocardiogram, echo) findings. Blood should be obtained at hospital presentation and 6-9 hours later. If previous measurements were not elevated

but the suspicion for AMI is high, serial sampling should be continued. Moreover, the upper reference limit should be provided with optimal precision defined by a coefficient of variation (CV) <10% **(Thygesen et al., 2007).**

However, at the time this universal definition was published, most cTn immunoassays that were commercially available were unable to detect cTn concentrations in the blood circulation of healthy individuals. In addition, these assays lacked analytical performance to measure the 99th percentile concentration with sufficient precision (CV<10%) **(Cobbaert et al., 2008)**.

Lately, improved sensitivity and accuracy in the lower detectable limit have been achieved, resulting in a new generation cTn immunoassays. These so called high sensitivity cTn (hs-cTn) immunoassays are characterized by measurable cTn concentrations in the circulation of healthy individuals (**Hollander, 2009)**. The hs-cTn assays are characterized by 10% CV at a lower 99th percentile upper reference concentration than conventional assays **(Jaffe and Apple, 2010).**These sensitive cTn assays increase the number of NSTEMI diagnosis and enables earlier detection of evolving NSTEMI **(Giannitsis et al., 2010)**.

The prevalence of coronary artery disease in patients with chronic kidney disease (CKD) is alarmingly high, and up to 38–62.5% of patients have significant stenosis **(Freda et al., 2002)**. Despite the advances in the diagnosis and treatment of coronary artery disease, the 5-year survival for dialysis patients is 33–34%. Death from AMI contributes to about half of those cases. The majority of the patients have multivessel disease. Often the first manifestation of atherosclerosis in a patient with CKD is sudden cardiac death or AMI, making it crucial to diagnose cardiac ischemia effectively **(Kanderian and Francis, 2006)**.

Diagnosing an AMI in CKD patients is often difficult though essential. Traditional diagnostic tools such as symptoms and electrocardiographic manifestations are not entirely helpful in patients with CKD, and physicians are often left to rely on laboratory analysis of biomarkers such as cardiac troponin. However, the diagnostic ability and prognostic value of cardiac troponin T and I in patients with CKD are uncertain in the emergency setting, making their interpretation problematic **(Kanderian and Francis, 2006)**.

Understanding the clinical significance of elevated cardiac troponin T and I in this patient population is extremely important as individuals with CKD have a higher likelihood for having AMI **(Han et al., 2005)**. Assessments of the standard and the high sensitivity troponin T assays in CKD patients, showed that 76% of dialysis patients had detectable troponin with the old assay but 100% of patients had detectable troponin T with the high sensitivity assay in the absence of clinical acute myocardial necrosis **(McGill et al., 2010)**.

Therefore, knowledge about the magnitude of concentration changes (δ) in AMI is essential to the definition of an optimal dynamic metric that allows discrimination of acute from chronic conditions and of AMI with CKD from CKD only that also causes cardiac troponin increases **(Javed et al., 2009)**.

AIM OF THE WORK