Diagnostic and prognostic value of serum concentration of cardiac troponin I in severe congestive heart failure

Thesis submitted for partial fulfilment of Master degree in Cardiology

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CONTENTS	Page

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBRRVIATIONS

ACE	Angiotensin converting enzyme
AF	Atrial fibrillation
AHF	Acute heart failure
ARBs	Angiotensin receptor blockers
BB	Beta blockers
BNP	Beta natriuretic peptide
CAD	Coronary artery disease
CCU	Cardiac Care Unit
CHF	Congestive heart failure
CRP	C_Reactive protein
cTnI	Cardiac troponin I
cTnT	Cardiac troponin T
DCM	Dilated cardiomyopathy
ECG	Electrocardiogram
EF	Ejection fraction

HCM	Hypertrophic Cardiomyopathy
HF	Heart Failure.
H_FABP	Heart type fatty acid binding protein.
HR	Heart rate.
LAD	Left atrial diameter.
LVEDD	Left Ventricular End Diastolic Diameter
LVESD	Left Ventricular End Systolic Diameter
MI	Myocardial infarction
PKA	Protein kinase A
PKC	Protein kinase C
STEMI	ST segment elevated myocardial infarction
TEE	Transesophageal echocardiography
TEA	Transient ischemic attack
TSH	Thyroid stimulating hormone
TTE	Transthoracic echocardiography

Introduction

Heart failure (HF) is a condition in which a problem with the structure or function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs Common causes of heart failure include myocardial infarction and other forms of ischemic heart disease, hypertension, valvular heart disease and cardiomyopathy. Heart failure can cause a large variety of symptoms such as shortness of breath, coughing, ankle swelling and reduced exercise capacity. (McMurray et al, 2005)

Heart failure is a common, costly, disabling and deadly condition. In developing countries, around 2% of adults suffer from heart failure, but in those over the age of 65, this increases to 6—10%. **(Dickstein et al, 2008)**

Heart failure is associated with significantly reduced physical and mental health, resulting in a markedly decreased quality of life. With the exception of heart failure caused by reversible conditions, the condition usually worsens over time. **(Juenger et al, 2002)**

The troponin proteins are found in cardiac and skeletal muscle tissue as products of separate genes. They are located in the myofibril, where they regulate the interaction of actin monomers with the myosin

heavy chain. The cAMP-dependent phosphorylation of troponin I at two adjacent serine residues in the amino-terminal of the molecule causes a decrease in the affinity of calcium for the calcium-binding troponin C and inhibition of actin-myosin interactions. **(Wattanapermpool et al, 1995)**

Troponin I exist in three isoforms: slow skeletal, fast skeletal and cardiac muscle–specific isoforms. **(Cummins et al, 1978)**

The cardiac muscle isoform of troponin I is a 24-kD protein uniquely expressed in the adult human heart. It differs from the slow-twitch and fast-twitch skeletal muscle isoform in that (1) it possesses 31 additional amino-terminal residues and (2) the remaining amino acid sequence shows 40% dissimilarity from both the slow and fast skeletal muscle isoform. **(Wilkinson et al, 1978)**

Importantly, the skeletal muscle does not express cardiac troponin I throughout ontogeny, during regenerative muscle disease, or in response to pathological stimuli, which confers to the cardiac isoform absolute specificity for the myocardium. **(Adams et al, 1993) and (Bodor et al, 1995)**

A new-generation, highly sensitive immunoenzymo-luminometric assay for quantitative determination of the cardiac muscle isoform of troponin I in human serum has recently been

developed. The assay operates at the picomolar concentration range and allows for the measurement of extremely low concentrations of cardiac troponin I. The lower limit of detection is 3 pg/mL. **(Setsuta et al, 1999)**

A fundamental hypothesis were been particularly interested; whether the use of an immunoassay with high analytical performance could provide evidence for cardiac troponin I release in congestive heart failure due to systolic dysfunction of the left ventricle, reflected in a severely compromised left ventricular ejection fraction. This hypothesis is consistent with a basic biological phenomenon in the failing human myocardium, namely, myofibrilolysis, and relates to the pathophysiology of congestive heart failure **(Setsuta et al, 2002)**

In the past decade, it has been recognized that elevated concentrations of cardiac troponin also are detectable in patients with HF in the absence of unstable coronary syndromes. In 1997, Missov and colleagues used a highly sensitive research assay to demonstrate elevated concentrations of troponin I in 35 patients with advanced HF. Subsequent reports extended these observations to troponin T. **(Sato et al, 2002)**

For instance, in a Japanese study, troponin T was detectable by a second-generation assay (detection limit, 0.02 ng/mL) in 30 of 58

patients (52%) with chronic HF compared with 4% of healthy control subjects. **(Setsuta et al, 2002)**

Cardiac cell death has been shown to occur in heart failure and has been implicated as one of the mechanisms responsible for progression of the disease. Cardiac Troponin I (cTnI) represents a highly sensitive marker for myocardial cell death. Based on previous studies reporting that cTnI may be detected in patients with heart failure, it was evaluated the clinical correlates and prognostic implications of detectable cTnI in a consecutive series of patients with severe heart failure. And it was suggested that cTnI is detected in the blood of 25% to 33% of patients with severe heart failure; its presence may help to identify a high-risk sub-group who faces very poor short-term prognosis. **(Luigi et al, 2000)**

Cardiac troponin I (cTnI), a sensitive and specific marker of myocardial cell injury, is useful in diagnosing and assessing prognosis in acute coronary syndromes. Small studies report that cTnI is elevated in severe heart failure and may predict adverse outcomes**.** **(Tamara et al, 2003)**

CTnI is associated with impaired haemodynamic, elevated BNP levels, and progressive left ventricular dysfunction in patients with HF. cTnI may be a novel, useful tool in identifying patients with HF

who are at increased risk for progressive ventricular dysfunction and death. **(Tamara et al, 2003)**

Aim of work

In this study we will evaluate the diagnostic and prognostic rule of serum concentration of cardiac troponin I in severe congestive heart failure.