Prolonged QT Interval and Troponin Level as Predictors of Clinical Outcome in Spontaneous Intra-cerebral Hemorrhage

Thesis

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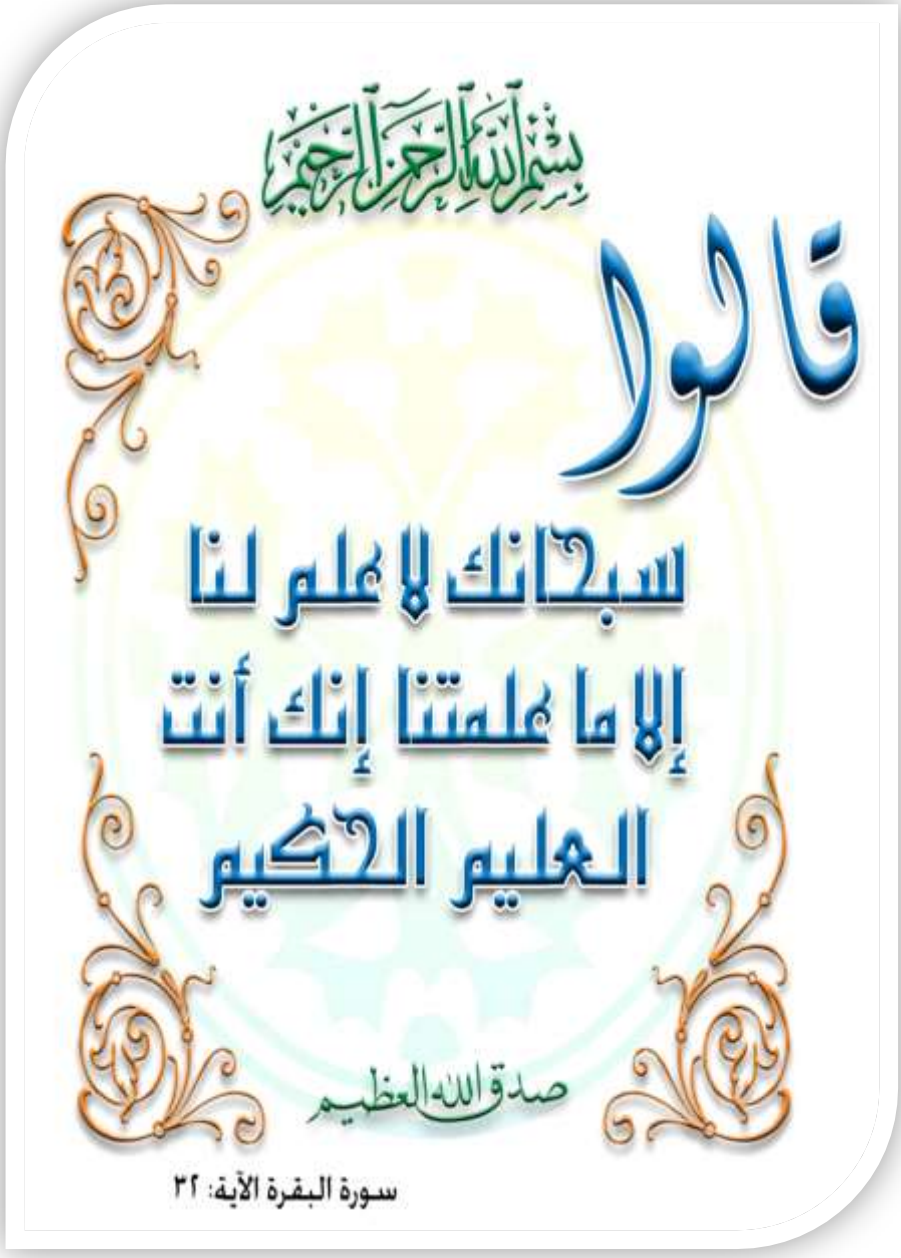
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List of Abbreviations

Abbrev.	Full-term
ACS	**:** Acute coronary syndrome
AF	**:** Atrial fibrillation
AV	**:** Atrioventricular
BNP	**:** B-type natriuretic peptide
CAD	**:** Coronary artery disease
CBN	**:** Contraction band necrosis
CM	**:** Capture myopathy
CMO	**:** Cardiomyopathy
CNS	**:** Central nervous system
cTnT	**:** Troponin T
ICP	**:** Intracranial pressure
ICU	: Intensive Care Unit
MCA	**:** Middle cerebral artery
MRI	**:** magnetic resonance imaging
NIHSS	**:** National Institute of Health Stroke Scale
RWMA	**:** Regional wall motion abnormality
SA	**:** Sinoatrial
SUDEP	**:** Sudden unexpected death in epilepsy
VF	**:** Ventricular fibrillation
VT	**:** Ventricular tachycardia

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Abstract

Background: Spontaneous intracerebral hemorrhage (ICH) accounts for approximately 20% of all strokes among the Western population. Although huge progress has been made in the management of ischemia, ICH remains a major cause of morbidity and mortality worldwide. The case fatality rate of ICH at 1 month is around 10% to 50%, and less than one survivor out of two is independent at 1 year.

Aim of this study to detect the prognostic value of prolonged QTc interval and Troponin level in clinical outcome of patients with spontaneous intracranial hemorrhage.

Patients and Methods: This prospective randomized observational study was conducted on fifty adult patients, admitted to ICU of Al Arish general hospital, North Sini, Egypt, presented with acute intracranial hemorrhage diagnosed by non-contrast CT brain. Measurement of serum Troponin level was done at admission then after 24 hours. A 12-lead resting ECG examination was done within 30 min of emergency department admission and then after 24 hours. The QT interval was measured manually by a single person, from the onset of the QRS complex to the point at which the T wave ends. It was measured for 3 to 5 consecutive beats and averaged. Lead II was chosen for this purpose as most normal reference ranges are based upon measurements from this limb lead. Full assessment for all patients at discharge from intensive care unit according to modified RANKIN scale (MRS).

Results: our study showed 43 cases (86%) were diagnosed as intracranial hemorrhage and 7 cases (14%) were diagnosed as subarachnoid hemorrhage and the mean of age was [61.38±6.87]. Hypertension was diagnosed in 40 patients (80%) and diabetes was diagnosed in 20 patients (40%).

In this study, long QT syndrome was present in only 21 cases (42%) and troponin elevated in 6 cases only (12%).

Conclusion: Prolonged QT interval has a poor predictive value of intracranial hemorrhage prognosis. On the other side Troponin has a very significant predictive value of poor prognosis.

Key words: Prolonged QT Interval and Troponin Level as Predictors of Clinical Outcome in Spontaneous Intra-cerebral Hemorrhage

Introduction

Spontaneous intracranial hemorrhage accounts for about 20%of all strokes, but they are often devastating, accounting for a disproportionately large proportion of morbidity and mortality among stroke patients. There are two types of hemorrhagic stroke; intra-parenchymal hemorrhage (IPH) which is characterized by bleeding within the brain itself, whereas subarachnoid hemorrhage (SAH) is characterized by vessel rupture in the cerebrospinal fluid (CSF)–filled subarachnoid space surrounding the brain **(Bernstein, 2012)**.

Intracranial hemorrhage (ICH) is associated with considerable morbidity and mortality, with estimates of 30-day mortality ranging from 10 to 52% **(Ahn and Lee, 2004; Martí-Fàbregas et al., 2003)**.

Troponin is a highly sensitive and specific marker for myocardial necrosis that is used in the diagnosis and prognosis of patients with acute coronary syndrome (ACS). However, troponin elevation has been documented in multiple clinical settings in the absence of ACS **(Agewall et al., 2011)**.

In a study of a heterogeneous group of patients with strokes, head injuries, and seizures, elevated troponin levels were observed in 19% of the patients and correlated with poor prognosis **(Dixit, 2000)**. It has been suggested that elevated

troponin may be a marker of increased mortality in patients with acute ischemic stroke (**Di Angelantonio et al., 2005)**.

However, only a few studies have examined the relation between troponin and prognosis of intracranial hemorrhage, and results were largely inconclusive **(Hays and Diringer 2006)**.

According to international guidelines, all patients with acute stroke need an ECG performed at the moment of admission to document any heart abnormalities **(Popescu et al., 2012)**. The association between heart-rate corrected QT (QTc) interval and cardiovascular morbidity and mortality is well established **(Zhang et al., 2011)**.

A multitude of ECG changes have been observed in patients who presented with acute strokes, both ischemic and hemorrhagic. In particular, repolarization changes, such as prolongation in the QTc interval, have been noticed in as much as 90% of unselected stroke victims; these may well result in a management and diagnostic dilemma, both to physicians and neurologists. Another concern is that these cardiac electrophysiological changes might be responsible for sudden death in stroke sufferers **(Amin et al., 2014).**

QTc intervals (QT intervals corrected for heart rate) in excess of 429 msec and QTc dispersion measurements in excess of 65 msec are considered significant elevations that place such populations at risk ***(*Wu et al., 2005)**.

Aim of the Work

The aim of this study is to detect the prognostic value of prolonged QTc interval and troponin level in clinical outcome of patients with spontaneous intracranial hemorrhage.

Neurocardiology

Introduction

The capacity for the brain to injure the heart has been well recognized throughout history, but has only recently gained attention in the field of neurocardiology **(van der Wal and Gilst, 2013)**. The central nervous system (CNS) has an extensive physiologic influence on the cardiovascular system, and the cardiovascular system in turn has both physiologic and, all too frequently, pathologic influences on the CNS (such as cardioembolic stroke and cerebral hypoperfusion **(Samuels, 2007a).**

The emphasis of this chapter will be on the pathologic CNS influences on the cardiovascular system, focusing on the most common vascular pathologies seen in the intensive care setting, specifically, aneurysmal subarachnoid hemorrhage (SAH), ischemic stroke and intracerebral hemorrhage (ICH), along with a discussion of epilepsy in relationship to sudden unexplained death in epilepsy (SUDEP). Commonly encountered pathologic neurocardiac manifestations in this setting are subendocardial ischemia, repolarization abnormalities, arrhythmias, autonomic dysfunction, and sudden cardiac death. In this chapter there is a particular focus on stress-related cardiomyopathy syndromes, which include "neurogenic stunned myocardium" and takotsubo cardiomyopathy.

Basic Anatomy and Physiology of Neurocardiology

Although a complete understanding of the anatomy and pathology involved in neurocardiac dysregulation has not yet been achieved, much is known. A brief review of the pertinent anatomy and physiology of the CNS, autonomic nervous system, and the cardiovascular system is needed prior to a discussion of pathologic processes. The autonomic nervous system has significant influence on the cardiovascular system due to its ability to modulate heart rate and conduction velocity, as well as cardiac contractility. These effects are mediated primarily via parasympathetic and sympathetic nervous system innervation of the sinoatrial (SA) and atrioventricular (AV) nodes, and these systems are subject to supratentorial influence as well **(Gordan et al., 2015).** Pathologic disruption at various points in this axis has a variety of clinical manifestations; the general categories are subendocardial ischemia, repolarization abnormalities, arrhythmias, sudden cardiac death, and cardiovascular autonomic dysfunction; takotsubo cardiomyopathy and neurogenic stunned myocardium are most commonly described in patients with aneurysmal subarachnoid hemorrhage, but can also occur in patients diagnosed with intracranial hemorrhage and ischemic stroke **(Amaral, 2012).**

The cardiovascular system has afferent connections with the CNS which are critical in providing regulatory feedback

on cardiac rate and contractility. The afferent system begins with chemoreceptors and baroreceptors **(Pereira et al., 2013),** with the ascending afferent information transmitted primarily by cranial nerves IX and X. These travel caudally to the nucleus of the solitary tract and dorsal vagal nucleus, and onwards to the parabrachial nucleus. From this nucleus, afferent pathways continue to the central nucleus of the amygdala, hypothalamus, infralimbic cortex (located in the ventromedial prefrontal cortex), as well as ventral basal thalamus. The infralimbic cortex and basal thalamus (specifically, the paraventricular nucleus) have ipsilateral and contralateral afferent connections to the insular cortex. Communication throughout the ascending pathways is mediated by the neurotransmitter *N*-methyl-D-aspartate, along with contributions from alpha-adrenergic and gamma-aminobutyric acid receptors and modulation by multiple peptides.

The descending pathway continues with parasympathetic ganglia and sympathetic pathway afferent signaling through the intermediolateral column of the spinal cord to the cardiac plexus. Cardiac sympathetic innervation consists of superior, middle, and inferior cervical sympathetic cardiac nerves along with innervation from the thoracic sympathetic ganglia. The cardiac plexus, along with the SA node and AV node, are the final targets of the descending autonomic system **(Figure 1)**