The Relation between Pulmonary Hypertension Measured by Standard Transthoracic Echocardiography and T Wave and R Wave Alternans in Electrocardiogram.

Thesis

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Ahmed Hendawy Radwan

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List of Abbreviations

Abb.	Full term
ASUH	Ain Shams University Hospitals
COPD	Chronic obstructive pulmonary disease
CTEPH	Chronic thromboembolic pulmonary hypertension
DM	Diabetes
ECG	Electrocardiogram
ECG	Electrocardiogram
EF	Ejection fraction
FS	Fractional shortening
HbA1c	Glycated hemoglobin
HFeRF	Heart failure with reduced ejection fraction
HTN	Hypertension
LHD	Left heart disease
LV	Left ventricle
LVD	Left ventricular dysfunction
LVD	Left ventricular dysfunction
mPAP	Mean pulmonary artery pressure
MR	Mitral regurge
MTW	Micro voltage T wave
PADP	Pulmonary artery diastolic pressure
PAH	Pulmonary arterial hypertension
PAH	Pulmonary arterial hypertension
PAOP	Pulmonary arterial occlusion pressure
PAP	Pulmonary arterial pressure
PASP	Pulmonary artery systolic pressure
PH	Pulmonary hypertension

List of Abbreviations Cont...

Abb.	Full term
PH-LHD	Pulmonary hypertension due to Left heart disease
PR	Pulmonary regurge
PTE	Pulmonary thromboendarterectomy
PVR	Pulmonary vascular resistance
QTc max	QTc maximum
QTc min	QTc minimum
QTcd	QTc dispersion
RA	Right atrium
RAP	Right atrial pressure
RHC	Right heart catheterization
RV	Right ventricle
RVH	Right ventricular hypertrophy
RVSP	Right ventricular systolic pressure
SCD	Sudden cardiac death
SGC	Soluble guanylate cyclase
sPAP	Systolic pulmonary artery pressure
TAPSE	Tricuspid annular plane systolic excursion
TR	Tricuspid regurge
TV	Tricuspid valve
TWA	T-wave alternans

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a progressive disorder with a complex pathology. It initially involves mostly the right ventricle, and eventually to its distension, dysfunction, and symptomatic insufficiency ***(Morell et al., 2009).***

PAH was first identified by Ernst von Romberg in 1891**.** ***PAH*** exact frequency is unknown, but the yearly new cases are about 1,000 cases in the United States. Females are more often affected than males and typically between 20 and 60 years of age ***(Rubin, 2016).***

However there is modern disease-specific therapy, patients with PAH is still characterized by a high overall mortality. Independent mortality risk factors include clinical characteristics (age, World Health Organization functional class, 6-min walk distance, etiology, family history), hemodynamic parameters (left atrial pressure, pulmonary pressure), echocardiography findings (pleural effusion), and laboratory tests (brain natriuretic peptide) ***(Galiè et al., 2016).***

Although sudden cardiac death (SCD) is a complication for 30%–40% of PAH patients, this issue has not been studied extensively ***(Batal et al., 2012).***

T-wave alternans (TWA) is a well-examined parameter for the risk stratification of sudden cardiac death (SCD) in patients with left ventricular dysfunction (LVD). However, the

role of TWA in pulmonary arterial hypertension (PAH) remains obscure. Consequently, the present study aimed to analyze the profile of TWA among PAH patients in comparison with healthy volunteers ***(Demerouti et al., 2013).***

R wave alternans is an electrocardiographic phenomenon of alternation of QRS complex amplitude or axis between beats and a possible wandering base-line. It is seen in cardiac tamponade and severe pericardial effusion.

QT dispersion is simply defined as the difference between the longest (QTCmax) and the shortest (QTCmin) QT intervals within a 12-lead ECG.

AIM OF THE WORK

To determine the correlation between ECG voltage variability (T wave alternans, R wave alternans and QT dispersion)and presence & severity of pulmonary hypertension.

Chapter 1
PULMONARY HYPERTENSION

Definition

Pulmonary hypertension (**PAH**) is a condition of increased blood pressure within the arteries of the lungs in which there is an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC) ***(Morell et al., 2009).***

Epidemiology

The exact frequency of the condition is unknown, it is estimated that about 1,000 new cases occur a year in the United States. Females are more often affected than males. Onset is typically between 20 and 60 years of age. It was first identified by Ernst von Romberg in 1891 ***(Morell et al., 2009).***

Causes and classification of pulmonary hypertension

Causes

Pulmonary hypertension is a pathophysiologic condition with many possible causes. Indeed, this condition frequently accompanies severe heart or lung conditions ***(Galiè et al., 2009).***

A 1973 World Health Organization meeting was the first attempted to classify pulmonary hypertension by its cause, and a distinction was made between primary PAH (resulting from a disease of the pulmonary arteries) and secondary PAH

(resulting secondary to other, non-vascular causes) ***(Rich et al., 2002).***

Primary PAH was divided in the "arterial plexiform", "veno-occlusive" and "thromboembolic" forms. In 1998, a second conference at Évian-les-Bains addressed the causes of secondary PAH. Subsequent third, fourth, and fifth (2013) World Symposia on PAH have further defined the classification of PAH. The classification continues to evolve based on improved understanding of the disease mechanism ***(Rich et al., 2002).***

Classification

According to WHO classification there are 5 groups of PAH, where Group I (pulmonary arterial hypertension) is further subdivided into Group I' and Group I" classes. The most recent WHO classification system (with adaptations from the more recent ESC guidelines shown in italics) can be summarized as follows: ***(Simonneau et al., 2013).***

- **WHO Group I – pulmonary arterial hypertension (PAH)**
  - Idiopathic
  - Heritable (BMPR2, ALK1, SMAD9, caveolin 1, KCNK3 mutations)
  - Drug- and toxin-induced (e.g., methamphetamine use)

- Associated conditions: connective tissue disease, HIV infection, portal hypertension, congenital heart diseases, schistosomiasis **(*Galiè et al., 2009).***

- **WHO Group II – pulmonary hypertension secondary to left heart disease**

- Left ventricular systolic dysfunction
- Left ventricular diastolic dysfunction
- Valvular heart disease
- Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathy
- Congenital/acquired pulmonary venous stenosis **(*Galiè et al., 2009).***

- **WHO Group III – pulmonary hypertension due to lung disease, chronic hypoxia**

- Chronic obstructive pulmonary disease (COPD)
- Interstitial lung disease
- Mixed restrictive and obstructive pattern pulmonary diseases
- Sleep-disordered breathing
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Developmental abnormalities ***(Simonneau et al., 2004).***

- **WHO Group IV – chronic arterial obstruction**
  - Chronic thromboembolic pulmonary hypertension (CTEPH)
  - Other pulmonary artery obstructions
    - Angiosarcoma or other tumor within the blood vessels
    - Arteritis
    - Congenital pulmonary artery stenosis
    - Parasitic infection (hydatidosis) ***(Simonneau et al., 2013).***
- **WHO Group V – pulmonary hypertension with unclear or multifactorial mechanisms**
  - Hematologic diseases: chronic hemolytic anemia (including sickle cell disease)
  - Systemic diseases: sarcoidosis, pulmonary Langerhans cell histiocytosis,lymphangioleiomyomatosis, neurofibromatosis, vasculitis
  - Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid diseases
  - Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic kidney failure, segmental pulmonary hypertension (pulmonary hypertension restricted to one or more lobes of the lungs) ***(Simonneau et al., 2013).***