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**Echocardiographic assessment of aortic pulse wave
velocity as a new diagnostic parameter for left ventricular
diastolic dysfunction**

Thesis

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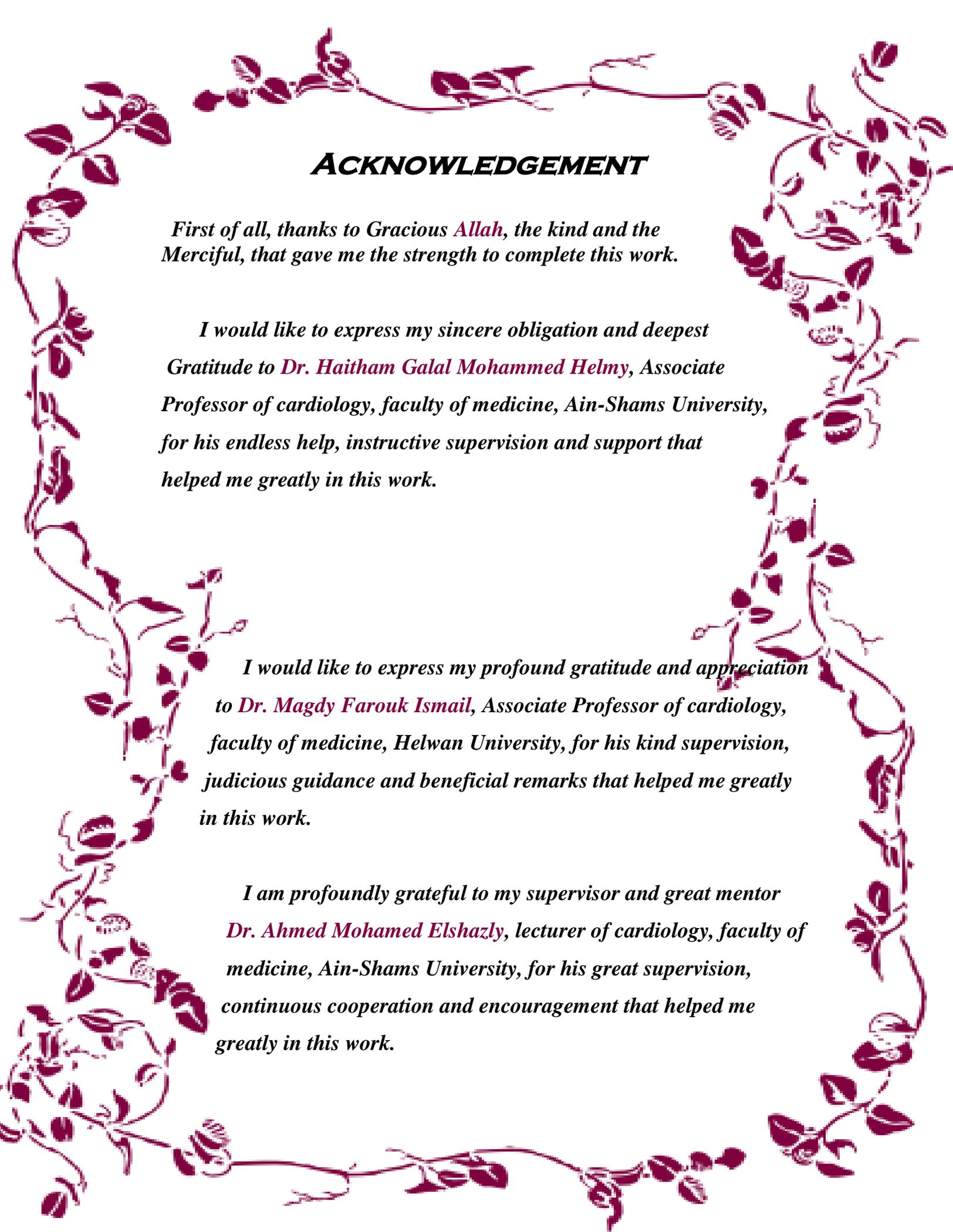
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LIST OF ABBREVIATIONS

BP	Blood Pressure
PWV	Pulse Wave Velocity
LV	Left Ventricle
BNP	Brain natriuretic peptide
NT-proBNP	N-Terminal proBNP
MP	Mean Pressure
cfPWV	Carotid-Femoral Pulse Wave Velocity
Zc	Characteristic Impedance
Pf	Forward Pressure Wave
AI	Augmentation Index
Pb	Backward Pressure Wave
RC	Reflection Coefficient
PP	Pulse Pressure
AP	Augmented Pressure
YM	Young's Modulus
CPP	Central Pulse Pressure
BSP	Brachial Systolic Pressure
ASP	Aortic Systolic Pressure
NO	Nitric Oxide
TNF	Tumor Necrosis Factor
COUP-TF	Chicken Ovalbumin Upstream Promoter Transcription Factor
CHF	Chronic Heart Failure
LVH	Left ventricular hypertrophy
MI	Myocardial Infarction

DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
MRI	Magnetic Resonance Imaging
ESH	European Society of Hypertension
ESC	European Society of Cardiology
baPWV	Brachial-ankle pulse wave velocity
ISH	Isolated Systolic Hypertension
IDH	Isolated Diastolic Hypertension
SDH	Systolic/Diastolic Hypertension
ATP	Adenosine Triphosphate
LA	Left Atrium
DD	Diastolic Dysfunction
LVEDP	Left Ventricular End Diastolic Pressure
LVEDV	Left Ventricular End Diastolic Volume
ROS	Reactive Oxygen Species
SR	Sarcoplasmic Reticulum
RyR	Ryanodine Receptor
NCX	Sodium-Calcium Exchanger
SERCA	Sarco/Endoplasmic Reticulum Ca ²⁺ ATPase
CaMK	Ca ²⁺ /Calmodulin Kinase
PK	Protien Kinase
MMPs	Matrix Metalloproteases
TIMBs	Tissue Inhibitors of Matrix Metalloproteases
cMyBP-C	Cardiac Myosin Binding Protein C
IVRT	Isovolumetric Relaxation Time
DHF	Diastolic Heart Failure

SHF	Systolic Heart Failure
EF	Ejection Fraction
CAD	Coronary Artery Disease
CMR	Cardiac Magnetic Resonance Imaging
STE	Speckle Tracking Echocardiography
HFpEF	Heart Failure with preserved Ejection Fraction
ANP	Atrial Natriuretic Peptide
CNP	C-type Natriuretic Peptide
NPR-A	Natriuretic Peptide Receptor Type A
RAAS	Renin Angiotensin Aldosterone System
SNS	Sympathetic Nervous System
NYHA	New York Heart Association
HFrEF	Heart Failure with reduced Ejection Fraction
NP	Natriuretic Peptide
AUC	Area Under the Curve
ROC	Receiver Operating Characteristic
PDE	Phosphodiesterase
ACEI	Angiotensin-Converting Enzyme Inhibitor
ARBs	Angiotensin II Receptor Blockers
IN	Sodium Current
HMG-CoA	Hydroxymethylglutaryl-Coenzyme A
BH4	Tetrahydrobiopterin
NOS	NO Synthase
CTGF	Connective Tissue Growth Factor
TGF	Transforming Growth Factor
CCU	Coronary Care Unit

CT	Computed Tomography
BMI	Body Mass Index
ECG	Electrocardiogram
ELISA	Enzyme Linked Immunosorbent Assay
2D	2-Dimension
LVIDs	Left Ventricular Internal Dimension During Systole
LVIDd	Left Ventricular Internal Dimension During Diastole
SWTd	Left Ventricular Septal Wall Thickness During Diastole
PWTd	Left Ventricular Posterior Wall Thickness During Diastole
TDI	Tissue Doppler Imaging
LAVI	Left Atrial Volume Index
SPSS	Statistical Package for the Social Sciences
N	Number
X	Mean
SD	Standard Deviation
r	Correlation Coefficient
TR	Tricuspid Regurge
CI	Confidence Interval
MAV	Mitral Annular Velocity
LVFP	Left Ventricular Filling Pressure
HTN	Hypertension
HBA1c	Glycated Hemoglobin
WHO	World Health Organization
ABI	Ankle-Brachial Index
ESRD	End Stage Renal Disease
CAVI	Cardio- Ankle Vascular Index

hf-PWV

Heart-Femoral Pulse Wave Velocity

hc-PWV

Heart-Carotid Pulse Wave Velocity

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ABSTRACT:

Background: The association between increased arterial stiffness and Left ventricular (LV) diastolic dysfunction (DD) has been well characterized, suggesting a close interaction between the arterial system and the left ventricle. Aortic pulse-wave velocity (PWV) is a measure of aortic stiffness, and it has an established prognostic role in cardiovascular diseases and in the general population.

Aim: Evaluation of aortic PWV assessed by echocardiography as a new diagnostic parameter for LV DD by correlation with current echocardiographic LV DD indices, and also evaluation of aortic PWV prognostic value in patients with DD by correlation with Brain natriuretic peptide (BNP).

Methods: This study was conducted at Ain-Shams and Helwan University hospitals from December 2017 to December 2018. It included 100 subjects aged from 55 to 60 years; they were divided into two groups, 1st group (case group): 80 patients with asymptomatic LV DD with preserved ejection fraction $\geq 50\%$, 2nd group (control group): 20 patients with normal diastolic function. All patients were subjected to full history and thorough physical examination. BNP, ECG and full echocardiography with assessment of aortic PWV were done.

Results: A total of 100 patients were enrolled, 38 (47.5%) males in case group vs. 9 (45%) in control group. Hypertension, diabetes and dyslipidemia were significantly higher in case vs. control (P-values: <0.001 , 0.005, 0.002 respectively). Aortic PWV has significant positive correlation with both age and body mass index ($r=0.422$, $r=0.847$ respectively with $P<0.001$ for both). Aortic PWV has significant positive correlation with E/e' ($r=0.957$, $P<0.001$), tricuspid regurgitation velocity ($r=0.941$, $P<0.001$), and left atrial volume index ($r=0.947$, $P<0.001$), but it has significant negative correlation with septal e' ($r=-0.970$, $P<0.001$) and lateral e' ($r=-0.932$, $P<0.001$). Aortic PWV has significant positive correlation with plasma BNP level ($r=0.958$, $P<0.001$). Aortic PWV was significantly higher in case vs. control group with mean values (15.5 ± 1.32 vs. 10.11 ± 0.78 m/s respectively; $P<0.001$). The area under the ROC curve for aortic PWV to detect DD was 0.86 (95% CI, 0.76–0.98; $P<0.001$) and the optimal cutoff point of 12.5 m/s produced 92.3% sensitivity and 75.0% specificity (the positive and negative predictive values were 93.5 and 72.7%, respectively with an accuracy of 89.0%).

Conclusion: Aortic PWV assessed by echocardiography appears not only to be a highly sensitive, reliable, easy, rapid and practical parameter for LV DD detection but also has a promising prognostic value in patients with LV DD.

Key words: Aortic pulse wave velocity, diastolic dysfunction, BNP.

Introduction

INTRODUCTION

The capacity of the body to augment cardiac output, to regulate systemic blood pressure (BP) and to respond appropriately to changes in pre and afterload depends on the properties of the heart and the vasculature. Normal ventricular–arterial coupling matches these properties, so that (near) maximal cardiac work, power, and chamber efficiency are achieved and BP and cardiac output are maintained within a physiological range. Stiffening of the large arteries is a common feature of aging, leads to isolated systolic hypertension and is exacerbated by many common disorders such as hypertension and diabetes mellitus.¹

Increased arterial stiffness is an indicator of diastolic dysfunction.² From what is known as the Windkessel effect, when blood is ejected from the heart to the aorta, the transient expansion of the aorta transmits pulse waves to peripheral arteries. This pulse wave is reflected at the bifurcation of the common iliac artery, whereas the retrograde reflection pulse wave amplifies arterial BP when it returns to the ascending aorta. The return of the reflection pulse wave to the ascending aorta happens during diastole when pulse wave velocity (PWV) is slow and during late systole when PWV is fast due to arterial stiffness. This change in loading sequence amplifies systolic BP and increases pulse pressure.³ As a result, left ventricle (LV) afterload is increased and the heart adapts by both hypertrophy and LV stiffening.¹ In addition, this change reduces the time constant τ , an indicator of LV relaxation, which is a component of LV diastolic function and significantly correlates with the development of LV diastolic dysfunction. When PWV is fast, the arrival of the reflection pulse wave during late systole causes a reduction in diastolic pressure and may correlate with LV diastolic dysfunction due to endomyocardial ischemia secondary to a reduction in coronary perfusion pressure.³

Aortic pulse-wave velocity (PWV) is a measure of aortic stiffness, and it has an established prognostic role in cardiovascular diseases and in the general population. Several studies have shown that increased PWV independently predicts cardiovascular outcomes, including cardiovascular or all-cause mortality in patients with renal