Prediction of Hospital Outcome in Septic Shock: A Prospective Comparison of Tissue Doppler and Cardiac Biomarkers

Thesis
Submitted for Partial Fulfillment of
MD Degree in Critical Care

Investigator

Marwa Elsaid Abdelfattah

MB.B.CH, MSch

Supervisors Wahied Radwan MD.

Professor of Critical Care Medicine Critical care department, Cairo University

Khaled Hussein MD.

Asst. Professor of Critical Care, Critical Care Department, Cairo University

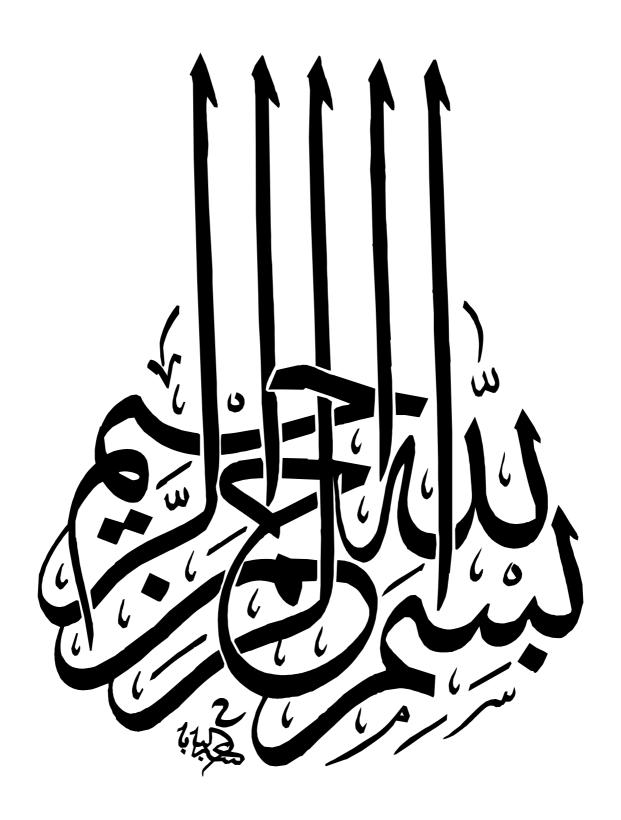
Emad El Deen Omar MD.

Asst. Professor of Critical Care, Critical Care Department, Cairo University

Mervat M. Khalaf MD.

Lecturer of Critical Care, Critical Care Department, Cairo University

Cairo University
2012



To

My Father, Mother, Sister and Brother

With special dedication to my husband Dr. Waleed Omar

&

My Sweet Heart, Maríam & Nour.

Acknowledgement

For **ALLAH** the merciful, the compassionate, I kneel to express my gratitude for all the countless gifts I have been offered, including those who gave their hands to enable me to fulfill this work.

No words are sufficient to express my deep appreciation and profound gratitude to **Prof. Dr. Sherif Mokhtar** and **Prof. Dr. Hossam Mowafi**, Professors of Critical Care Medicine, for offering all their students an inspirational role model, for showing us the excitement and joy of critical care medicine, for their dedication to education and for their encouraging attitude and invaluable advice made it possible for any one to overcome even the most difficult obstacles in preparing the research. I am really honored to belong to the school of these scientists.

I would like to send my deepest gratitude to **Prof. Dr. Alia Abd El-Fattah**, Professor of Critical Care Medicine and Chief of Critical Care Medicine Department for her abundant and fruitful encouragement, continuous support to her students, for her kindness, for her nonstop effort and endless giving to the running the department in the best way possible so as to maximize its performance.

No words are sufficient to express my deep appreciation and profound gratitude to, **Prof. Dr. Hassan Khaled** Professor of critical care medicine, Cairo University for his abundant encouragement, continuous support and endless giving.

My true appreciation is to **Dr. Waheed Radwan**, Professor of Critical Care Medicine for his meticulous supervision, for his kind guidance, valuable instructions and generous help. The time I worked under his supervision consolidated my knowledge, refined my experience and made me feel confident as a research student, because of the freedom he gives his students to express them selves no matter how inexperienced they might be. Thus, I really acknowledge that I consider my self lucky for ingoing the advantage of being supervised by such a great supervisor.

I am deeply thankful to **Dr.Khalid Hussien**, Asst, prof of Critical Care Medicine for his great help, outstanding support and active participation, for his sympathy, kindness and constructive advice and for treating me in a brotherly way.

I wish to thank **Dr. Emad Eldin Omer,** Asstist. professor; of Critical Care Medicine, for his great efforts and important contributions.

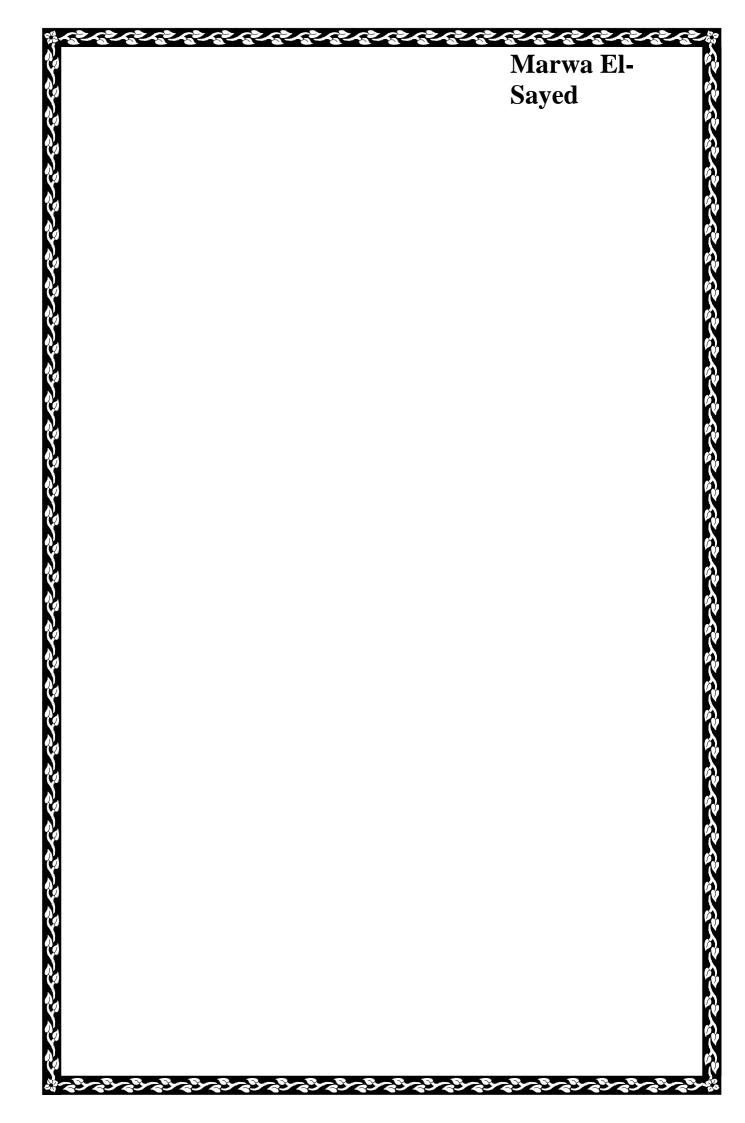
I would like to express my deep sense of gratitude to **Dr. Marvet Khalaf**, Lecturer of Critical Care Medicine who had spared no effort in guiding me through out the long and tiring task of writing this thesis and performing the echocardiographic part. I am truly indepted to her with all what I learned and still learning in echocardiography.

Prof. Dr. Sanaa Abd El Shafee Professor of Clinical & Chemical Pathology, Vice Dean of Faculty of Medicine, Beni Sueif University and all the laboratory team, for their great efforts and important contributions.

I wish to thank *Dr. Lamiaa Hamed, Critical Care Medicine Department*, for her great help in performing the statistical analysis of this work.

I wish to thank deeply **Mrs. Manal Youssef**, Critical Care Medicine Department for her patience and concentration in performing the computer work of this thesis.

Finally I am so thankful and honored to belong to the critical care medicine department, the land of imagination, innovation and fruitful research.



Abstract

Prediction of hospital outcome in septic shock; comparison of tissue Doppler and different biomarkers

Background: assessment of the diastolic dysfunction by tissue Doppler imaging (TDI) and cardiac biomarkers such as B-type natriutic peptide BNP together can be a good tools for prediction of hospital outcome in septic shock patients **Purpose:** to evaluate and compare the prognostic significance of (TDI) particularly E/é (peak early diastolic transmitral / peak early diastolic mitral annular velocity), cardiac biomarkers (N- terminal proBNP (NTproBNP); cardiac troponin I (cTnI)) and high sensitive C- reactive protein (hs CRP) in septic shock. **Methodology**: twenty eight patients with septic shock were involved in a prospective randomized clinical study (mean age were 62±9.3 yrs, 62% male) were divided into 2 groups according to mortality and were subjected to all fluid resuscitation, transthoracic echocardiography TTE and laboratory measurement of the mentioned cardiac biomarkers. **Results:** there were 20 pt (71.4 %) died Group A, 8 patients (28.6%) survived Group B. E/é ratio was significantly lower in survivors than non-survivors $(8.59\pm 2.29 \text{ vs.}12.32\pm 2.37, P\text{- value}=0.001)$, hs CRP was found to be significantly lower between survivals and non survivals (33.49 \pm 10.82 vs. 41.65 \pm 7.33, *P*-value =0.02). There was a strong positive correlation between E/e' and PMR, (P- value=0.002, and r= 0.6). There was a positive correlation between hs-CRP with PMR (P-value= 0.01 r=0.4). By cox regression analysis 5 parameters were found to be independent predictors of mortality in septic shock which were: E/e ratio, APACHE IV, SOFA 1, SOFA 3 and DT as P value (0.009, 0.002, 0.003, 0.007 and 0.0001) respectively. Conclusions: E/é and DT obtained by PW and TDI both offer independent and better prognostic prediction of hospital outcome in septic shock as compared with cardiac biomarkers (NT,proBNP & cTnI).

Key words: TDI, septic shock, mortality, pro BNP, hs CRP, cTnI

Table of Content

Item	Page
Introduction	1-3
Aim of Work	4
Review:	5-91
o Chapter I: Septic Shock	5-32
 Chapter II: Myocardial depression in sepsis and septic shock & echocardiographic evaluation 	33-58
o Chapter III: Cardiac Biomarkers & C-reactive protein	59-80
 Chapter IV: Different scoring system used in assessment of patients with septic shock 	81-91
Patients & Methods	92-100
Results	101-131
Discussion	132-142
Summary	143-146
Conclusion	147
References	148-176
Arabic Summary	4-1

List of Abbreviations

A:	Atrial peak velocity
a':	Peak active late diastolic septal mitral annulus velocity
ACCP:	The American College of Chest Physicians
ACS:	Acute coronary syndrome
ADP:	Adenosine diphosphate
AIS:	Abbreviated injury score
ALI:	Acute lung injery.
ANP:	A-type natriuretic peptide
APACHE:	Acute physiology and chronic health evaluation
APC:	Activated protein C
APS:	Acute Physiology Score
ARDS:	Adult respiratory distress syndrome.
ARF:	Acute renal failure
ATP:	Adenosine triphosphate
ATS:	The American Thoracic Society
AUC:	Area under the curve.
BNP:	Beta naturetric peptide,
bpm:	Beat per minute,

cGMP-	Cyclic guanosine monophosphate
CHF:	Congestive heart faluire.
CI:	Cardiac index
CNS:	Central nervous system
CO:	Cardiac output
CVP:	Central venous pressure
CWD:	Continuous wave Doppler
DBP:	Diastolic blood pressure
DIC:	Disseminated intravascular coagulopathy
DNA:	Deoxy ribonucleic acid
D Nase:	Deoxyribo nuclease
DT:	Deceleration time
E:	Peak early diastolic transmitral velocity
e':	Peak Early diastolic septal mitral annulus velocity
E/é	Peak early diastolic transmitral / peak early diastolic mitral annular velocity
ED:	Emergency department
EGDT:	Early goal directed therapy
ESICM:	European Society of Intensive Care Medicine
FiO ₂ :	Fraction of inspired oxygen
Fmol/l:	Ficomole/l

GCS:	Glasgow Coma Scale
G-CSF:	Granulocyte colony-stimulating factor
GIT:	Gastrointestinal tract
GM-CSF:	Granulocyte macrophage colony-stimulating factor
HR:	Heart rate
hs- CRP:	High sensitive C- reactive protein
ICU:	Intensive care unit
IL:	Interleukin
iNOS:	Inducible nitric oxide synthase
ISS:	Injury severity score
IVRT :	The isovolumic relaxation time
LA:	Left atrium
LAP:	Left atrial pressure
LOD:	The Logistic Organ Dysfunction
LOS:	Length of stay
LV	Left ventricle,
LVEDP:	Left ventricular end diastolic pressure
LVEDVI:	Left ventricular end diastolic volume index.
LVEF:	Left ventricular ejection fraction
LVESVI:	Left ventricular end systolic volume index.

LVSWI :	Left ventricular stroke work index
MAP:	Mean arterial blood pressure
MDS:	Myocardial depressant substance
MELD:	Model for end-stage liver disease
mg/dL:	Milligram per dicilitre
MHC:	The major histocompatibility complex molecules
MIF:	Macrophage inhibitory factor;
mL/kg:	Milliliter per killogram
mm Hg:	Millimeter mercury
mmol/L:	Millimole per litre
μL:	Micro liter
MODS:	Multiple organ dysfunction syndrome
MPM:	Mortality Probability Models
MR:	Mitral regurge
NADPH:	Nicotinamide adenine dinucleotide phosphate.
NK:	Natural killer cells
NTproBNP:	N terminal pro beta naturetric peptide,
OTD:	LV outflow tract diameter
PAC:	Pulmonary artery catheterization
PaCO ₂ :	Arterial carbon dioxide tension,
MR: NADPH: NK: NTproBNP: OTD: PAC:	Mitral regurge Nicotinamide adenine dinucleotide phosphate. Natural killer cells N terminal pro beta naturetric peptide, LV outflow tract diameter Pulmonary artery catheterization

PAF:	Platelet-activating factor
PAI-1:	Plasminogen activator inhibitor 1
PaO ₂ :	Arterial oxygen tension
PAWP:	Pulmonary artery wedge pressure
PCWP:	pulmonary capillary wedge pressure
Pmol/l:	Picomole/l
PVAR:	The pulmonary venous atrial flow reversal
PVD:	Pulmonary vein diastolic wave
PVR:	Pulmonary vascular resistance
PVS:	The pulmonary vein systolic flow
RNCA	Radionuclid coronary angiography.
R Nase:	Ribonuclease
RR:	Respiratory rate
RV:	Right ventricle
RVEDV:	Right ventricular end diastolic volume
RVEDVI:	Right ventricular end diastolic volume index
RVEF:	Right ventricle ejection fraction
RVSWI:	Right ventricular stroke work index
SAPS:	Simplified acute physiology score

SBP:	Systolic blood pressure
SCCM:	The Society of Critical Care Medicine
SIRS:	Systemic inflammatory response syndrome
SIS:	The Surgical Infection Society
SMR:	Standardized mortality ratio
SOFA:	Sequential organ failure assessment
SVI:	Stroke volume index
SVR:	Systemic vascular resistance
TAFI:	Thrombin activatable fibrinolysis inhibitor
TDI:	Tissue doppler imaging
TF:	Tissue factor
TISS:	Therapeutic intervention scoring system
TNF:	Tumor necrosis factor
TnI:	Troponin I
TnT:	Cardiac troponin T
t-PA:	Tissue plasminogen activator
TPN:	Total parenteral nutrition
TTE:	Transethroracic echocardiogram
VTI:	Velocity time integrity
WBC:	White blood cell,

List of Master Table Abbreviations

Pts No. Number

Sex: 1: Male

2: Female

DM: 0: no

1: yes

HTN: 0: No

1: Yes

BSA: Body surface area

HR: Heart rate

Ryth: Rhythm

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

MAP: Mean arterial pressure

RR: Respiratory rate

CVP: Central venous pressure on day one

BL bal/OA: Fluid balance after 24 hrs

CVP2: Central venous pressure after fluid resuscitation

NA n/kg/min: Noradrinaline dose mic/kg/min

Dop: Dopamine mic/kg/min

APS score: Acute physiology score

PMR: Predicting mortality rate

SOFA1: Sequential organ failure assessment on day one septic shock

SOFA2: Sequential organ failure assessment on day three septic shock

ICUdur: intensive care unit duration

ICU mort: intensive care unit mortality

28-D Mortality: 28 days mortality

DPDSS: Duration post developing septic shock

S of infection: source of infection

1: Chest 2: Bedsore 3: VTI

4: Abdominal 5: Wound 6: Obstetric

7: encephalitis

Cr-1: Serum creatinine on day one

Cr-2: Serum creatinine on day three

Plt.: Platelets count

Bl Trans: Blood transfusion

Plt: Platelets transfusion

VD/d: Duration of mechanical ventilation in days

VT: Tidal volume