

ASSESSMENT OF LEFT VENTRICULAR VOLUME AND FILLING PRESSURE IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Thesis

*Submitted for Partial Fulfillment of Masters Degree
in Pediatrics*

By

Shereen Magdy Mahmoud Abdo Nassar

*M.B., B.Ch (2007)
Ain shams University*

Under The Supervision Of

Assist. Prof. Shereen Saad El Sayed

*Assistant Professor of Pediatrics
Ain Shams University*

Assist. Prof. Nevin Mohamed Mamdouh Habeeb

*Assistant Professor of Pediatrics
Ain Shams University*

Assist. Prof. Naglaa Hussein Shebrya

*Assistant Professor of Radiology
Ain Shams University*

**Faculty of Medicine
Ain Shams University
2012**

تقييم حجم الامتلاء و الضغط الانبساطي للبطين الايسر لعضلة القلب في الاطفال المصابين بداء الذئبة الحمراء

رسالة

توطئة للحصول على درجة الماجستير
في طب الاطفال

مقدمة من الطبيب

شيرين مجدي محمود عبده نصار

بكالوريوس الطب والجراحة

جامعة عين شمس

٢٠٠٧

تحت اشراف

أ.م.د / شيرين سعد السيد

أستاذ مساعد طب الاطفال

كلية الطب- جامعة عين شمس

أ.م.د / نيفين محمد ممدوح حبيب

أستاذ مساعد طب الاطفال

كلية الطب- جامعة عين شمس

أ.م.د / نجلاء حسين شبرية

أستاذ مساعد الاشعة التشخيصية

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٢

SUMMARY

Systemic lupus erythematosus (SLE) is an inflammatory autoimmune disease with multiorgan involvement, a wide variety of manifestations and an unpredictable course. Cardiac involvement in SLE is prevalent in more than 50% of that disease. The symptoms of myocardial involvement are usually clinically silent compared with other cardiac involvements.

Myocardial involvement (myocarditis) can provoke bilateral ventricular contractility and relaxation abnormalities inducing systolic and diastolic dysfunctions in SLE. Furthermore, it was reported that LV relaxation abnormality usually precedes systolic dysfunction in SLE.

This cross sectional study was carried out at the Pediatric Allergy and Immunology unit, Children's Hospital, Ain Shams University. It included 60 children classified into 2 groups. Group I, included 30 children who were diagnosed to have SLE. Group II, included 30 healthy, age and sex matched children as a control group. An informed consent was obtained from caregivers of each studied subject before enrollment in the study.

The studied children with SLE were subjected to clinical evaluation; they were classified into 2 groups. Group A, fifteen cases with hypertension, Group B, fifteen cases without hypertension. The disease activity index

List of Contents

<i>Title</i>	<i>Page No.</i>
List of Tables	ii
List of Figures	iii
List of Abbreviations	vi
Introduction	1
Aim of the work.....	3
<u>Review of Literature</u>	
• Cardiac Affection in Children with Systemic Lupus Erythematosus.....	4
• Diagnosis of Left Ventricular Volume and Filling Pressure in Systemic Lupus Erythematosus	19
• Treatment of Diastolic Dysfunction	54
Subjects and Methods	62
Results.....	72
Discussion	93
Summary	104
Conclusion	107
Recommendations.....	108
References	109
Appendix.....	129
Arabic Summary.....	---

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Clinical and pathological features in SLE patients with cardiovascular lesions:	7
Table (2):	Framingham Criteria for CHF.....	16
Table (3):	European Criteria for Diastolic Heart Failure:	17
Table (4):	Factors affecting LV filling	21
Table (5):	Definitions of cardiological terms.....	26
Table (6):	Illustrate different Echo and CMRI modalities and their parameters of diastolic function.	53
Table (7):	Systemic lupus erythematosus disease activity index (SLEDAI).....	63
Table (8):	Comparison between the studied patients and controls as regards the demographic data.	72
Table (9):	Descriptive data of clinical history of the studied patients	73
Table (10):	Descriptive laboratory data of the studied patients.....	73
Table (11):	Comparison between the studied patients and the control group as regards the echo-cardiographic parameters.....	74
Table (12):	Comparison between patients with affected Tei index and patients with normal Tei index as regards the echo cardiographic parameters.....	76
Table (13):	Comparison between patients with affected Tei index and patients with normal Tei index as regards the clinical history.....	77
Table (14):	Comparison between patients with affected Tei index and patients with normal Tei index as regards the laboratory data	78

List of Tables (Cont...)

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (15):	Comparison between the studied groups as regards the duration of illness	80
Table (16):	Comparison between the studied hypertensive patients (group IA) and non hypertensive patients (group IB) as regards the measured laboratory data.....	81
Table (17):	Descriptive echo-cardiographic data of the studied hypertensive patients (group IA) and non hypertensive patients (group IB).	82
Table (18):	Comparison between the different studied groups as regards the echo-cardiographic data.	84
Table (19):	Comparison between the studied patients and control group as regards the MRI parameters.	87
Table (20):	Descriptive MRI data of the studied hypertensive patients (group IA) and non hypertensive patients (group IB).....	88
Table (21)	Comparison between the different studied groups: hypertensive patients (group IA), non hypertensive patients (group IB) and control healthy children (group II) as regards the measured MRI data.	89
Table (22):	Correlation between the measured echocardiographic parameters and MRI parameters within the studied patients.....	90

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Fig. (1)	Section of visceral pericardium in a patient with recurrent pericarditis due to systemic lupus erythematosus.....	8
Fig. (2):	The 12-lead electrocardiogram in a patient with acute lupus pericarditis.....	10
Fig. (3):	Physiology of diastole.....	22
Fig. (4):	Model of the pathophysiology of diastolic heart failure.....	24
Fig. (5):	Doppler parameters in progressive diastolic dysfunction.....	27
Fig. (6):	Classification of diastolic dysfunction by Echocardiography.....	31
Fig. (7):	Doppler echocardiogram shows normal pattern of diastolic filling:	32
Fig. (8)	Doppler echocardiogram shows E/A reversal (stage I diastolic dysfunction)	34
Fig. (9):	Doppler echocardiogram shows pseudo normalization (stage II diastolic dysfunction) of the left ventricular filling pattern	35
Fig. (10):	Schematic diagram of the changes in mitral inflow in response to the transmitral pressure gradient.....	38
Fig. (11):	Estimation of LV filling pressures in patients with depressed EF	39
Fig. (12):	Estimation of LV filling pressures in patients with normal EF	39
Fig. (13):	Grading of diastolic dysfunction	40
Fig. (14):	Measurement of TMF.....	44
Fig. (15):	Measurement of PVF.....	44
Fig. (16):	Velocities obtained by echocardiogram and phase-contrast CMR.....	45
Fig. (17):	Analysis of volume time curve.....	48
Fig. (18):	LV filling volume versus time curve and its first derivative, the filling rate curve.....	48

List of Figures (Cont...)

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Fig. (19):	Measurement of myocardial TPC.	49
Fig. (20):	Diagram (a) and cardiac MR imaging findings (b) of myocardial TPC.	50
Fig. (21):	Analysis of myocardial TPC.	50
Fig. (22):	Sex distribution of the studied patients.	72
Fig. (23):	Comparison between studied groups as regards the studied echocardiographic parameters.	75
Fig. (24):	Comparison between patients with affected Tei index and patients with normal Tei index as regards the laboratory data.	79
Fig. (25):	Descriptive echo-cardiographic data of the hypertensive patients (group A), the non hypertensive patients (group B) and the control group (C).	83
Fig. (26a&26b)	Patient no. 13, Diagnosis: SLE	85
Fig. (27a&27b)	Patient no. 12, Diagnosis: SLE	86
Fig. (28):	Correlation between the e/a ratio and the echo cardiographic EDV within the studied patients.	91
Fig. (29):	Correlation between the EDV and the echo cardiographic E/e'ratio within the studied patients.	91
Fig. (30):	Correlation between the echocardiographic E/e'ratio and the MRI EDV within the studied patients.	92
Fig. (31):	Correlation between the echocardiographic E/e'ratio and the MRI E/EA ratio within the studied patients.	92

List of Abbreviations

ACE.....	Angiotensin – converting enzyme
ACEIs.....	Angiotensin converting enzyme inhibitors
ACR.....	American college of rheumatology
AOD.....	Aortic root diameter
AV block.....	Atrio-ventricular block
AV.....	Aortic valve
C3	Complement 3
CAD.....	Coronary arterial disease
CBC.....	Complete blood count
CHF.....	Congestive heart failure
CMRI.....	Cardiac magnetic resonance imaging
DE time.....	Deceleration time
DHF.....	Diastolic heart failure
e/a ratio	ratio between early diastolic transmitral flow and flow of atrial contraction.
E/e' ratio.....	ratio between early diastolic transmitral flow and early diastolic mitral annular velocity.
ECG.....	Electrocardiogram
EDV.....	End diastolic volume
EF	Ejection fraction
FS	Fractional – Shortening
Hb.....	Hemoglobin
HF.....	Heart failure
IVC	Inferior vena cava
IVSd	Inter ventricular septal diameter in diastole
LA.....	Left atrial
LAEDD	Left atrial end-diastolic diameter
LA-LV	Left atrial – Left ventricular
LAP	Left atrial pressure
LV.....	Left ventricle
LVEDD	Left ventricular end diastolic diameter

List of Abbreviations (Cont...)

LVEDd.....	Left ventricular external diameter in diastole
LVEDP.....	Left ventricular end diastolic pressure
LVEF.....	Left ventricular ejection fraction
LVH.....	Left ventricular hypertrophy
LVPWd	Left ventricular posterior wall diameter in diastole
MRI	Magnetic resonance imaging
MTPC.....	Myocardial tissue phase contrast
MV.....	Mitral valve
NBTE.....	Non-bacterial thrombotic endocarditis
PAWP.....	Pulmonary artery wedge
PLT.....	Platelet
PTE	Pulmonary thromboembolism
PVF	Pulmonary venous flow
RV.....	Right ventricle
RVEDD.....	Right ventricular end diastolic diameter
SD.....	Standard deviation
SLE.....	Systemic lupus erythematosus
SLEDAI	Systemic lupus erythematosus disease activity index
SPV.....	Superior vena cava
SSFP	Steady – state free precession
TDI	Tissue Doppler imaging
Tei index	Tei chuwa published in 1995 an index of myocardial performance (Tei index) that evaluates the ventricular systolic and diastolic function in combination
TLC	Total leukocyteic count
TMF.....	Transmitral flow
TPC	Tissue phase contrast
VHD	Valvular heart disease
VSD	Ventricular septal defect



*First and foremost, thanks are to **Allah**, the creator of the heavens and the earth and what's between them, to Him, whose knowledge is beyond all knowledge, for blessing this work until it has reached its end, as a part of His generous help throughout my life...*

*I am greatly honored to express my utmost thanks to **Assist. Prof. Shereen Saad El Sayed**, Assistant Professor of Pediatrics, Ain Shams University, for her constructive supervision, generous guidance & giving me such an honor to work under her supervision.*

*I would like to express my sincere gratitude & appreciations to **Assist. Prof. Nevin Mohamed Mamdouh Habeeb**, Assistant Professor of Pediatrics, Ain Shams University, for her close supervision, continuous help and the tremendous effect she has done in the meticulous revision of the whole work.*

*I am also greatly indebted to **Assist. Prof. Naglaa Hussein Shebrya**, Assistant Professor of Radiology, Ain Shams University, from whom I received faithful supervision, valuable suggestions and continuous guidance throughout this work.*

***Finally** yet importantly, I would like to express my endless gratitude to my dear patients for their kind co-operation in accomplishing my work, wishing them a good health.*

✍ Shereen Magdy Mahmoud Abdo Nassar



﴿وَأَنْزَلَ اللَّهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةَ وَعَلَّمَكَ مَا لَمْ
تَكُن تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا﴾

سورة النساء آية (١١٣)

صدق الله العظيم





To

My **Family**, My Beloved **Husband**
And My Daughter

*Who Gave Me Too Much
And Received Too Little*



INTRODUCTION

Systemic lupus erythematosus (SLE) is the prototypic inflammatory autoimmune disease with multiorgan involvement, a wide variety of manifestations and an unpredictable course. Cardiac involvement in SLE is prevalent in more than 50% of cases and includes myocarditis, valvular heart disease, coronary arterial disease, and conduction abnormalities (***Doria et al., 2005***).

Because the symptoms of myocardial involvement are usually clinically silent compared with other cardiac involvements, its prevalence in 7% to 10% of cases might have been underestimated (***Van de Veire and Sutter, 2006***).

Cardiac Magnetic resonance imaging (MRI) is a noninvasive test that helps to diagnose cardiac affection especially systolic dysfunction. Also, cardiac MRI showed a higher prevalence of myocarditis up to 40% - 70% (***Kim et al., 2005***).

Myocardial involvement (myocarditis) can provoke bilateral ventricular contractility and relaxation abnormalities inducing systolic and diastolic dysfunctions in SLE. Furthermore, it was reported that left ventricle (LV) relaxation abnormality usually precedes systolic dysfunction in SLE (***Olson et al., 2006***).

Considering the confounding effects of SLE involvements, such as pulmonary hypertension in the diastolic function of the right ventricle (RV), LV diastolic function can reflect myocardial inflammation due to SLE independently and relatively better than RV diastolic function. Thus, it is reasonable to assess the LV diastolic dysfunction to detect myocarditis in patients with early phase SLE (*Galie et al., 2005*).

There have been few reports on the morbidity and the mortality rates due to LV diastolic dysfunction in patients with SLE. However, in the general population, isolated LV diastolic dysfunction (elevated LV end-diastolic pressure with preserved LV systolic function) was reported to show that 45% of patients developed symptoms of congestive heart failure over a follow-up period of 5 years, and 25% of patients required hospitalization for these symptoms (*Paran et al., 2007*).

Furthermore, the mortality rate in patients with diastolic heart failure ranges from 5% to 8% annually, as compared with 10% to 15% in patients with systolic heart failure. Therefore, if we detect and correct LV diastolic dysfunction early, we can improve the prognosis in patients with SLE (*Lee et al., 2008*).