



Right Ventricular Dysfunction in Patients with End-Stage Renal Disease on Regular Hemodialysis

MSc Thesis

Submitted in Partial Fulfillment of the Master Degree in Cardiology

By

Rabei Zaid Yahya Al-Ansi, M.B. B.CH.

Under the supervision of:

Yasser Abd Al-Azeem Sharaf, MD.

Professor of cardiology,
Cairo University

Hesham Salah Eldin Taha , MD.

Professor of cardiology,
Cairo University

Mohammed Momtaz Mohammed, MD

Lecturer of internal medicine,
nephrology division,
Cairo University

Faculty of Medicine
Cairo University
2012

محضر

اجتماع لجنة الحكم على الرسالة المقدمة من
الطبيب / ديع زكي النسي
توطئة للحصول على درجة الماجستير / الدكتوراه
فى

تحت عنوان : باللغة الإنجليزية :
Right Ventricular Dysfunction in Patients with End-Stage Renal disease on Regular Hemodialysis
باللغة العربية : أعراض البطين الأيمن لدى مرضى
المرحلة النهائية للفشل الكلوى المعالجين بالدياليزه المنتظمة

بناء على موافقة الجامعة بتاريخ ٦ / ١٢ / ٢٠١١ تم تشكيل لجنة الفحص والمناقشة
لِلرسالة المذكورة أعلاه على النحو التالي :-

١. د. ياسر عبد العظيم شريف عن المشرفين
٢. د. رئيس الطوبى عاشور ممتحن داخلي
٣. د. حاتم عبد المازن أحمد ممتحن خارجي

بعد فحص الرسالة بواسطة كل عضو منفردا وكتابة تقارير منفردة لكل منهم انعمت اللجنة
مجتمعة فى يوم الجمعة بتاريخ ٢ / ١٢ / ٢٠١٢ بقسم تقديم الطبي مدرج ١
بكلية الطب - جامعة القاهرة وذلك لمناقشة المالماب فى جلمة علمية فى موضوع الرسالة والنتائج
التي توصل اليها وكذلك الأسس العلمية التي قام عليها البحث ،

قرار اللجنة :

تمت الرسالة

وتنصح ويتم تدويناها

المجلة

توقيع أعضاء اللجنة :-

المشرف للممتحن

ياسر عبد العظيم شريف

الممتحن الداخلي

رئيس الطوبى عاشور

الممتحن الخارجي

حاتم عبد المازن أحمد

Abstract :

Background : Hemodialysis (HD) has been associated with an increased risk of pulmonary hypertension . Ateriovenous fistula determines a chronic increase in preload which may impair right ventricular performance independently of post-load conditions

Aim of study : The study was a *prospective* study that was designed to investigate the impact of chronic dialysis therapy on right ventricular function by echocardiography in patients with ESRD treated by regular hemodialysis.

Methods : Study population consisted of 50 (31 male and 19 female) patients with ESRD treated with hemodialysis. The control group was consisted of 24 age and gender matched healthy subjects (15 male and 9 female) without history of cardiovascular or renal dysfunction . All subjects in the HD and control groups underwent detailed history and physical examination as well as electrocardiography (ECG), echocardiography, and biochemical and hematological analysis.

Results : The mean age of the patients was 37.3 ± 12.9 years in the HD group and 39.6 ± 12.6 years in control group. LV mass index was increased in HD patients in comparison to control group (117.43 ± 46.72 gm/m² vs 80.13 ± 13.40 gm/m, p value $< .001$) so the study found the prevalence LVH was 52% (26/50). The pulmonary hypertension with SPAP values > 35 mmHg was found in 34% (17/50) of patients receiving HD (mean \pm SD = 32.75 ± 10.11 mmHg). There was statistically significant decrease in RV function parameters in HD compared to control group (RV FAC ; $37.54 \pm 9.86\%$ vs $43.5 \pm 4.8\%$, p value < 0.001 , TAPSE ; 2.09 ± 0.49 cm vs 2.61 ± 0.36 cm , p value < 0.001 , lateral TDIS⁰ ; 11.86 ± 2.86 cm/s vs 16.04 ± 3.60 cm/s, p value < 0.001) .

Conclusion, RV dysfunction is highly prevalent among ESRD patients on regular hemodialysis and RV dysfunction was independent of LV hypertrophy, diastolic dysfunction of the LV and pulmonary hypertension.

Key words:

Right Ventricular Dysfunction in Patients with End-Stage Renal Disease on Regular Hemodialysis

Acknowledgments

FIRST OF ALL, THANKS TO ALLAH

In these few lines, I would like to express my deep gratitude, appreciation and sincere thanks to the main supervisors of this thesis, ***Dr. Yasser Abd Al-Azeem Sharaf, Professor of Cardiology, Cairo University***, for his supervision, valuable remarks, until this work was fulfilled.

I would like to express my special deep gratitude, appreciation and sincere thanks to ***Dr. Hesham Salah Eldin Taha , Professor of Cardiology, Cairo University***, for his continuous support, meticulous supervision, great valuable remarks, encouragement and assistance until this work was fulfilled.

I would like to express my special deep gratitude, appreciation and sincere thanks to ***Dr., Mohammed Momtaz Mohamed , Lecturer of internal medicine , nephrology department ,Cairo University***, for his continuous support, meticulous supervision, great valuable remarks, encouragement and assistance until this work was fulfilled.

Also I would like to express my deepest gratitude to ***Dr. Heba Farouk***, and ***Dr. Dina Osama*** who have assisted me greatly in conducting the echocardiographic studies in this research.

Finally, I would like to express my special deep thanks and gratitude to my family especially my father, my mother, and my wife for their continuous support and encouragement and without them the completion of this work would have not been possible

Rabei Zaid Al-Ansi

Abbreviations

ASE	American Society of Echocardiography
AVF	Ateriovenous fistula
AT	Acceleration time
CAD	Coronary artery disease
CKD	Chronic kidney disease
CMR	Cardiac magnetic resonance
CRT	Cardiac resynchronizing therapy
DBP	Diastolic blood pressure
Ecclx	LV eccentricity index
EF	Ejection fraction
ET	Ejection time
ESRD	End stage renal disease
FAC	Fractional area change
IVA	Isovolumic acceleration
IVC	Inferior vena cava
IVCT	Isovolumic contraction time
IVRT	Isovolumic relaxation time
HD	Hemodialysis
LVEDD	Left ventricular end-diastolic diameter
LVEDS	Left ventricular end-systolic diameter
LVH	Left ventricular hypertrophy
LVMI	Left ventricular mass
K/DOQI	National Kidney Foundation Dialysis Outcome Quality Initiative
MBF	Myocardial blood flow
MI	Myocardial infarction
MPI	Myocardial performance index
MRI	Magnetic resonance imaging
LTDIS'	Lateral tricuspid(tissue Doppler image)systolic excursion velocity
LV	Left ventricle
PA	Pulmonary artery
PD	Peritoneal dialysis
PADP	Pulmonary artery diastolic pressure
PH	Pulmonary hypertension
PLAX	Parasternal long-axis
PSAX	Parasternal short-axis
PWT	Posterior wall thickness
PVR	Pulmonary vascular resistance
RA	Right atrium
RVEDD	Right ventricular end-diastolic diameter

RVESD	Right ventricular end-systolic diameter
RV dp/dt	Rate of pressure rise of right ventricle
RV IVA	Right ventricle isovolumic acceleration time
RIMP	Right ventricular index of myocardial performance
RV	Right ventricle
RV EF	Right ventricle ejection fraction
RV FAC	Right ventricle fractional area change
RVH	Right ventricular hypertrophy
RVOT	Right ventricular outflow tract
RVSP	Right ventricular systolic pressure
RVS^o	Right ventricle systolic excursion
SBP	Systolic blood pressure
SD	Standard deviation
SPAP	Systolic pulmonary artery pressure
STDIS'	Septal tricuspid(tissue Doppler image)systolic excursion velocity
SWT	Septal wall thickness
TAM	Tricuspid annular motion
TAPSE	Tricuspid annular plane systolic excursion
TDI	Tissue Doppler Imaging
TDIS	Tricuspid annular systolic excursion velocity
TR	Tricuspid regurgitation
USRDS	Unite State Renal Data System
2D	Two-dimensional
3D	Three-dimensional

Table of contents

Title	Page
Abbreviation list	ii
Table of tables	iv
Table of figures	iv
Introduction and aim of the study	1-3
Review of literature	3-60
Chapter I: Anatomy and physiology of right ventricle	3-13
Chapter II: Echocardiographic assessment of right ventricle	14-39
Chapter III: Cardiovascular complications of hemodialysis	40-58
Chapter IV : Right ventricle dysfunction in hemodialysis	59-60
Subjects and methods	61-72
Results	73-95
Discussion	96-103
Conclusion	104
Limitations	105
Summary	106-108
References	109-135
Arabic summary	136

Table of tables

Table	Title	Page
Table 1	Normal values of RA pressure on basis of IVC diameter and collapse	17
Table 2	Summary of reference limits for recommended measures of right heart structure and function	71
Table 3	Comparison between HD group and control group according to patients characteristics	74
Table 4	Comparison between HD and control groups according laboratory data	75
Table 5	Comparison between HD and Control group according to left side echocardiographic parameters	76
Table 6	Sensitivity and Specificity of ECG for determination of LVH	77
Table 7	Comparison between HD and control group according to right ventricular dimensions	79
Table 8	Prevalence of increase of RV dimensions in HD group.	80
Table 9	Ccomparison of right ventricle function parameters between HD and control groups	81
Table 10	Correlations between RV indices and clinical data	85
Table 11	Correlations between RV indices and hypertension and DM.	86
Table 12	Correlations between RV indices and laboratory data.	87
Table 13	Correlations between RV indices and left ventricle indices	89
Table 14	Comparison between HD and control group according to PSAP	92
Table 15	Correlation between SPAP and RV parameters	93
Table 16	Correlation between SPAP and LV parameters	94
Table 17	Prevalence of RV dysfunction in patients on regular hemodialysis	103

Table of figures

Figure	Title	Page
Figure 1	The inlet, trabeculated apical myocardium and infundibulum of the Right Ventricle.	5
Figure 2	Anatomic landmarks within the right ventricle	7
Figure 3	Simultaneous ECG, right ventricular dP/dt, phasic pulmonary artery (PA) flow	9
Figure 4	Graphic representation of the echocardiographic views used for evaluating the right ventricle	15
Figure 5	Tracing of the right atrium	16
Figure 6	Inferior vena cava (IVC) view & Measurement of the IVC	17
Figure 7	RV free wall thickness measurement in the subcostal 4-chamber view	18
Figure 8	Right ventricular, basal (RVD1), mid cavity (RVD2) and longitudinal dimension (RVD3)	19
Figure 9	Measurement of right ventricular outflow tract (RVOT) dimensions	20
Figure 10	RV FAC measurement	22
Figure 11	Parasternal short-axis views at the mid-ventricular level illustrating measurements of left ventricular diameters for calculation of the eccentricity index (EccIx)	23
Figure 12	Measurement of the tricuspid annular plane systolic excursion	12
Figure 13	Relationship of tricuspid annular plane systolic excursion and right ventricular ejection fraction in patients with mild (a), moderate (b), and severe (c) tricuspid regurgitation (TR).	27
Figure 14	Calculation of right ventricular myocardial performance index (RVMPI) pulsed tissue Doppler	30
Figure 15	Normal Doppler tissue imaging (DTI) waveform	34
Figure 16	Pulsed-wave Doppler at the tricuspid level of the right ventricular free wall in a normal individual (A) and in a patient with pulmonary hypertension (B)	36
Figure 17	Doppler tissue velocities and time intervals obtained at lateral tricuspid valve annulus	38

Figure	Title	Page
Figure18	Causes of death in hemodialysis according to US Renal Data System	41
Figure 19	Pathophysiology of Cardiomyopathy and ischemic heart disease in chronic Uremia	45
Figure 20	Physiological responses to hemodialysis and the pathogenesis of IDH	46
Figure 21	Risk for the development of de novo cardiovascular disease according to age at the start of dialysis	48
Figure 22	Measurement of right ventricular outflow tract (RVOT) dimensions at the proximal (RVOT-Proximal) and at the distal (RVOT-distal)	65
Figure 23	Apical 4-chamber image showing the right ventricular (RV) basal (RVD1) and mid cavity (RVD2) and the RV longitudinal dimension (RVD3)	66
Figure 24	Right ventricular fractional area change (RV FAC).	67
Figure 25	Tracing of the right atrium to obtain RA area, and RA minor dimensions	67
Figure 26	Measurement of tricuspid annular plane systolic excursion (TAPSE)	68
Figure 27	Tricuspid annular tissue Doppler imaging.	69
Figure 28	Measurement of systolic pulmonary artery pressure SPAP	70
Figure 29	Inferior vena cava (IVC) view & measurement	70
Figure 30	Gender distribution among HD and control groups	75
Figure 31	Comparison of LV EF% (mean) between HD and control groups	77
Figure 32	Significant increase in IVST and PWT in HD group comparing to control group	78
Figure 33	LV mass index between HD and controls	78
Figure 34	The mean values of RV diameters (cm) between HD and control groups	80
Figure 35	Comparison of TAPSE values (mean) between HD and control groups	82
Figure 36	Distribution of TAPSE values(cm) between HD and control groups	82
Figure 37	Comparison of RV fractional area changes (mean) values between HD and control groups	83
Figure 38	Distribution of RV FAC values between HD and controls	83

Figure	Title	Page
Figure 39	Significant decrease in mean values (cm/s) of lateral and septal tricuspid systolic waves	84
Figure 40	Distribution of lateral TDI S' wave values (cm/s) between HD and control groups	84
Figure 41	A; negative correlation between LVEF% and RV FAC. B: negative correlation between LVEF% and TAPSE	90
Figure 42	A; negative correlation between LV mass index and RV FAC. B ; negative correlation between LV mass index and TAPSE	91
Figure 43	A: negative correlation between E/A ratio and TAPSE B; negative correlation between E/A ratio and RVFAC	91
Figure 44	Systolic pulmonary artery pressure (SPAP) values (mean) across the groups	92
Figure 45	Systolic pulmonary artery pressure (SPAP) values (mmHg) across HD and controls.	93
Figure 46	A: correlations between SPAP and RV FAC .B; correlations between SPAP and TAPSE	94
Figure 47	A; Positive correlation between systolic pulmonary artery pressure SPAP and left atrium (LA)B; positive correlation between systolic pulmonary artery pressure and E/A ratio	96



Introduction & Aim of the work

Introduction

Chronic renal failure (CRF) is associated with significantly increased morbidity and mortality. Chronic renal failure affects almost every system of the body and results in various functional and structural abnormalities. Cardiovascular complications are the main cause of death in patients with chronic kidney disease (CKD) undergoing hemodialysis therapy. ^(1,2) accounting for 40% of deaths in international registries. ⁽³⁾ The traditional risk factors for cardiovascular disease do not completely explain this excess risk, which seems to be influenced by the so-called non-traditional risk factors associated with CKD. ⁽⁴⁾ This set of factors accelerates the course of coronary artery disease (CAD) ⁽⁵⁾ and is associated with a higher prevalence of ventricular hypertrophy, myocardial fibrosis, valvulopathies, arrhythmias and sudden death. ⁽⁷⁾ The prevalence of clinical manifestations of cardiac disease at the start of end-stage renal disease (ESRD) therapy is high and these manifestations independently predict death. ^(8,10) More than 50% of the individuals starting a dialysis program present some type of pre-existent cardiovascular disease. ⁽¹¹⁾ Clinical manifestations of cardiovascular disease were highly prevalent at the start of ESRD therapy: 14% had coronary artery disease, 19% angina pectoris, 31% cardiac failure, 7% dysrhythmia and 8% peripheral vascular disease. ⁽¹²⁾

There is increasing evidence of the pivotal role of echocardiography in the improvement of quality of global clinical evaluation of advanced CKD patients. Current literature and clinical practice have emphasized the usefulness of the method for the diagnosis of clinical and subclinical cardiac dysfunction, the prediction of cardiovascular risk, and in the orientation and follow-up of treatment strategies. Guidelines recommend the echocardiogram for all dialysis patients 1–3 months after the start of renal replacement therapy and in intervals of 3 years subsequently, irrespective of the symptoms. ⁽¹³⁾

End-stage renal disease is associated with a variety of cardiac alterations including left ventricular hypertrophy (LVH), LV dilation, and reduction in systolic and

diastolic function, with only 16% of new dialysis patients presenting with normal cardiac morphology and function. ⁽¹⁴⁾

On echocardiography 15% had systolic dysfunction, 32% left ventricular dilatation and 74% left ventricular hypertrophy. ⁽¹⁵⁾ Patients undergoing chronic dialysis exhibit an increased prevalence of pulmonary hypertension during treatment 15-20 % ^(1,2).

However, while most available studies focused their attention on left ventricular function in dialysis patients, the impact of dialysis treatments on the development of right ventricular dysfunction (RVD) has not been fully investigated. But recently a retrospective study in which Paneni et al. ⁽¹⁶⁾ investigated the impact of different dialysis treatments on right ventricular function, showed that Compared to peritoneal dialysis, hemodialysis increases the risk of RVD, particularly in the presence of brachial arteriovenous fistula (AVF) ⁽¹⁷⁾. A limitation of this study is represented by its *retrospective* design.