Right Ventricular Functions in Hemodialysis Patients: Tissue Doppler Study

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Abstract

Background: Cardiovascular disease is the leading cause of mortality in patients undergoing dialysis, accounting for 50% of deaths. In particular, heart failure is the most common finding in these patients and is associated with poor prognosis. Hemodialysis (HD) which is usually carried out via a surgically created native Arteriovenous Fistula (AVF) has been associated with an increased risk of pulmonary hypertension, a condition reported as a predictor of mortality in these patients.

Aim of the Work: The aim of this study is to assess right ventricular function in patients with end stage renal disease on hemodialysis using tissue Doppler imaging of the right ventricle.

Subjects and Methods: The study population consisted of 40 patients with end-stage renal disease on a regular dialysis program and 20 normal subjects as a control group (mean age 54.9±12.7 years, male/female: 33/27. The study group comprises 40 HD patients with brachial AVF. Patients were receiving HD sessions 3 times per week. Each session lasted for 4 hours and used bicarbonate-buffered dialysate. Standard Kt/V (K= in vitro clearance of dialysate, t=time of dialysis and V=volume distribution of blood urea nitrogen) was calculated. The study was done in the period between January 2013 and July 2014 in Urology and Nephrology Center and Mansoura Specialized Hospital in Mansoura, Egypt. All subjects underwent clinical evaluation with special concentration upon cardiovascular system, laboratory evaluation, ECG and tissue Doppler examination.

Results: HD patients were older than control subjects; however the difference was not statistically significant. Heart rates were significantly higher in dialysis patients as compared to controls. There was significant deterioration of systolic and diastolic function of the RV in the dialysis group either using conventional echocardiography or tissue Doppler imaging. Patients on HD presented higher right ventricular diameters and volumes than control group. Right ventricular ejection fraction was significantly reduced in HD patients as compared to control group. TDI indices of diastolic and systolic function were significantly lower in patients undergoing HD. Ea velocity, measured at both lateral and septal tricuspid annulus was significantly and progressively reduced in controls and HD patients. Compared to control group, HD patients showed a prolonged isovolumic relaxation time. TDI indices of systolic function showed that lateral and septal Sa velocities were progressively reduced among HD patients as compared to control group.

Conclusion: Hemodialysis is associated with right ventricular dysfunction with significantly lower RV ejection fraction by using conventional Doppler echocardiography and significantly higher TDMP1 at both lateral and septal tricuspid annulus which is independent to high systolic pulmonary artery pressure. So, we recommend the use of TDI evaluation of right ventricular function for early detection of preclinical dysfunction in hemodialysis patients.

Key Words: Tissue Doppler – Right ventricular function – Hemodialysis.

Introduction

CARDIOVASCULAR disease is the leading cause of mortality in patients undergoing dialysis, accounting for 50% of deaths [1]. In particular, heart failure is the most common finding in these patients and is associated with poor prognosis [2]. Hemodialysis (HD) which is usually carried out via a surgically created native Arteriovenous Fistula (AVF) has been associated with an increased risk of pulmonary hypertension [3-6], a condition reported as a predictor of mortality in these patients [7].

The incidence of pulmonary hypertension in HD patients ranges from 17 to 60% and is associated with the presence of AVF [3-6].

The leading mechanism underlying pulmonary hypertension development in these patients is the volume/pressure overload imposed by the shunt which increases right ventricular output and pulmonary pressures. On the other hand, AVF determines a chronic increase in preload which may
impair right ventricular performance independently of post-load conditions [8].

Although patients undergoing chronic dialysis exhibit an increased prevalence of pulmonary hypertension during treatment, data on the development of Right Ventricular Dysfunction (RVD) are lacking. Moreover, in patients with pulmonary hypertension, survival has been related to cardiac function rather than pulmonary pressure values [9]. Importantly, RVD may also affect left ventricular filling via inter ventricular interaction [8].

Assessment of RV function by tissue Doppler Imaging (TDI) is an accurate and reproducible method to detect preclinical ventricular abnormalities and has been considered as a reliable predictor of prognosis [9].

Aim of the work:

The aim of this study was to assess right ventricular function in patients with end stage renal disease on hemodialysis using tissue Doppler imaging of the right ventricle.

Subjects and Methods

This is a prospective (comparative) study between End Stage Renal Disease (ESRD) patients on hemodialysis and age and gender matched control group. The study population consisted of 40 patients with end-stage renal disease on a regular dialysis program and 20 subjects as a control group (mean age 45.9±12.7 years, male/female: 33/27). The study group included 40 HD patients with brachial AVF. Patients were receiving HD sessions 3 times per week. Each session lasted for 4 hours and used bicarbonate-buffered dialysate. Standard Kt/V (K= in vitro clearance of dialystae, t=time of dialysis and V=volume distribution of blood urea nitrogen) was calculated [10]. The study was done in the period between January 2013 and July 2014 in Urology and Nephrology Center and Mansoura Specialized Hospital in Mansoura, Egypt.

Exclusion criteria:

• Any clinical condition that might predispose to pulmonary hypertension e.g.: Chronic obstructive pulmonary disease, interstitial pneumopathy, connective tissue disorders, chronic thromboembolic disease, congenital left-to-right shunts and coronary artery bypass graft.

• Clinical or echocardiographic evidence of manifest left ventricular systolic dysfunction with EF lower than 40%, valvular heart disease or previous renal transplantation.

All patients were subjected to a thorough clinical evaluation, laboratory evaluation and radiological assessment.

A- Clinical evaluation:

• History: Thorough history taking with stress on age, sex, history of hypertension and antihypertensive medications, diabetes mellitus and its treatment, smoking history and cardiovascular symptoms.

• Clinical examination: Thorough clinical examination was done with special stress on pulse rate, blood pressure measurement, sings of valvular affection, sings of pulmonary hypertension and signs of heart failure.

B- Laboratory evaluation: All patients were subjected to the following investigations: Serum creatinine, blood sugar, serum calcium, serum phosphorus, serum sodium and potassium, lipid profile, serum uric acid, liver function tests, complete blood count and viral status.

C- Echocardiographic assessment:

Left ventricular volumes were estimated [11]. Ejection fraction of the left ventricle was calculated using the Teicholz formula and further confirmed with Simpson’s technique in the 4-chamber view [12]. Pulsed-wave Doppler of mitral inflow velocity was performed [13].

The maximal tricuspid regurgitation velocity was measured by continuous wave Doppler echocardiography from the apical 4-chamber view. The highest peak velocity was recorded and the average peak velocities from 3 beats were calculated. Systolic pulmonary pressure was calculated as follows: 4 X (tricuspid systolic jet)² + right atrial pressure. Pulmonary hypertension was defined as a value of mean systolic pulmonary pressure >25mmHg at rest. Right ventricular diameters were measured in the long axis view. Ejection fraction of the right ventricle was calculated by using the Simpson’s formula from the apical 4-chamber view [14].

Early (E) and late (A) right ventricular inflow velocities were measured with pulse-wave Doppler by placing the sample volume in between the tips of the tricuspid valve in the apical 4-chamber window. The TDI spectral signal was acquired from the apical 4-chamber view, with the sample volume placed along the lateral and septal tricuspid annulus [21]. Sa (systolic annular velocity), Ea (proto diastolic annular velocity) and late peak diastolic annular velocity (Aa) were measured. The E/Ea ratio, an index of ventricular filling pressure, was calculated [13].
Ejection Time (ET), Isovolumic Relaxation Time (IVRT) and Isovolumic Contraction Time (IVCT) were also measured. Regional TDI Myocardial Performance Index (MPI) was calculated [15]. Average regional TDI MPI for the right ventricle was calculated as follows: (MPI lateral + MPI septal)/2 [15,16]. RVD was defined by an average regional MPI value >2 SD from the mean of the values derived from a group of 20 healthy subjects (MPI >0.51).

Statistical analysis:

Data were tabulated, coded then analyzed using the computer program SPSS (Statistical package for social science) version 17.0 to obtain:

Descriptive statistics were calculated in the form of:

- Mean ± Standard Deviation (SD) for quantitative parametric data.
- Frequency (number-percent).

Analytical statistics: In the statistical comparison between different groups, the significance of difference was tested using one of the following tests:

- Student's t-test: Used to compare between mean of two groups of numerical (parametric) data.
- Inter-group comparison of categorical data was performed by using chi square test ($\chi^2$-value).

The sensitivity and specificity of RV-EF and average TDI-MPI to differentiate between hemodialysis and control group were examined at different cutoff points using ROC curve analysis to determine the best cutoff point as well as the diagnostic power of each test. A $p$-value <0.05 was considered statistically significant in all analyses.

Results

Hemodialysis patients were older than control subjects; however, the difference was not statistically significant. No significant difference regarding gender between study and control subjects (age and gender matched control group). Heart rate was statistically higher in hemodialysis patients when compared to control subjects.

Conventional Doppler echocardiographic examination of right ventricular diameters and functions revealed higher RVEDD, higher RVESD and higher RV/LV diameter in hemodialysis patients when compared to control subjects, lower E/A ratio and lower RV ejection fraction in hemodialysis patients when compared to control subjects and all these results were statistically significant ($p<0.001$ for each) (Table 2).

TDI indices of right ventricular function at lateral tricuspid annulus in the studied population (N=60) revealed significantly higher Aa, IVRT, E/Ea ratio, IVCT and lateral TDI MPI in hemodialysis group when compared to control subjects ($p<0.001$) and significantly lower Ea, Ea/Aa ratio and Sa in hemodialysis patients when compared to control subjects ($p<0.001$) (Table 3).

TDI indices of right ventricular function at septal tricuspid annulus in the studied population revealed significantly higher Aa, IVRT, Ea/Aa ratio, IVCT, septal TDI MPI and average TDI MPI in hemodialysis patients when compared to control subjects ($p<0.001$) and significantly lower Ea, E/Ea ratio, ET and Sa in hemodialysis patients when compared to control subjects ($p<0.001$) (Table 4).

Linear regression analysis adjusted for age, gender, heart rate showed that HD treatment was independently associated with average TDI MPI of the right ventricle ($p<0.001$) (Table 5). Average TDI MPI has more sensitivity and specificity than RV EF in determining RVD among dialysis patients (100.0 & 90.0 vs 75.0 & 70.0 respectively) Figs. (1,2).
Hypertension:
ET : Ejection Time.
Ea : Peak velocity during early diastole.
Aa : Peak velocity during atrial contraction.
IVRT
Lateral TDI MPI : Tissue Doppler myocardial performance index at
E/Ea ratio : An index of ventricular filling pressure.
ET, ms
Ea/Aa ratio
IVRT, ms
Aa, m/s
Ea, m/s

Table (3): TDI indices of right ventricular function at lateral tricuspid annulus in the studied population.

<table>
<thead>
<tr>
<th></th>
<th>Control (N=20)</th>
<th>Hemodialysis group (N=40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Ea, m/s</td>
<td>0.19</td>
<td>0.02</td>
<td>0.12</td>
</tr>
<tr>
<td>Aa, m/s</td>
<td>0.17</td>
<td>0.03</td>
<td>0.21</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td>64.99</td>
<td>7.94</td>
<td>90.52</td>
</tr>
<tr>
<td>Ea/Aa ratio</td>
<td>1.11</td>
<td>0.18</td>
<td>0.63</td>
</tr>
<tr>
<td>E/Ea ratio</td>
<td>4.23</td>
<td>0.59</td>
<td>5.39</td>
</tr>
<tr>
<td>IVCT, ms</td>
<td>62.94</td>
<td>5.44</td>
<td>76.48</td>
</tr>
<tr>
<td>ET, ms</td>
<td>281.79</td>
<td>12.67</td>
<td>284.53</td>
</tr>
<tr>
<td>Sa, m/s</td>
<td>0.17</td>
<td>0.01</td>
<td>0.13</td>
</tr>
<tr>
<td>Average TDI MPI</td>
<td>0.45</td>
<td>0.04</td>
<td>0.59</td>
</tr>
</tbody>
</table>

SD : Standard Deviation.
p : Probability.
IVRT : Isovolumic Relaxation Time.
IVCT : Isovolumic Contraction Time.
Aa : Peak velocity during atrial contraction.
Ea : Peak velocity during early diastole.
ET : Ejection Time.
Sa : Peak velocity during ejection period of systole.
E/Ea ratio : An index of ventricular filling pressure.
Average TDI MPI : Average Tissue Doppler myocardial performance index at lateral tricuspid annulus.

Discussion

Echocardiography is an established method for the assessment of LV and RV function. Most conventional echocardiographic parameters of LV and RV systolic and diastolic function are known to be load-dependent [17]. Also TDI systolic and diastolic velocities of the tricuspid annulus correlated with RV global systolic and diastolic function. Assessment of RV function by Tissue Doppler Imaging (TDI) is an accurate and reproducible method to detect preclinical ventricular abnormalities and has been considered as a reliable predictor of prognosis [9].

In HD patients, AVF causes left-to-right shunt leading to chronic volume overload, independently of the increase in total body water. However, while most available studies focused their attention on left ventricular function in dialysis patients [19,20], the impact of different dialysis treatments on the development of RVD has not been investigated. In last years, TDI has emerged as a powerful diagnostic tool in detecting subclinical abnormalities of cardiac function and has been shown to predict mortality [21].
It is important to note, however, that in patients with similar pulmonary pressure values, chronic volume overload may induce different adaptations of the right ventricle, thus accelerating or delaying the progression toward systolic dysfunction [8].

The aim of this study was to assess function of right ventricle in patients on hemodialysis compared to control group. To achieve this target, the present study included 60 patients who were divided into 2 groups (40 HD, 20 controls). They were subjected to careful history taking, thorough clinical examination, laboratory investigations and assessment of cardiac functions using conventional and tissue Doppler echocardiography.

Comparative analysis of echocardiographic Doppler parameters of both systolic and diastolic right ventricular function and TD parameters revealed a significant difference in these parameters ($p<0.001$).

Our results are in accordance with the results of Paneni et al., [18] who found statistically significant differences between the dialysis and control groups regarding both left and right ventricular functions using conventional Doppler echocardiography.

Yiegla et al., (2008) reported that HD treatment was associated with RVD independently of pulmonary pressure values. It has been previously reported that patients on chronic dialysis treatment display a higher prevalence of pulmonary hypertension, ranging 56% in patients treated with HD [4].

Myocardial Performance Index (MPI) is one of the most accurate indices of ventricular performance since it includes parameters relative to both cardiac contraction and relaxation. Moreover, MPI estimation based on tissue Doppler analysis is relatively independent from intravascular volume reduction after HD [22].

In this study, TDI indices of right ventricular systolic and diastolic function were significantly reduced in HD patients compared to control group. These data confirm that TDI evaluation is more accurate in detecting subclinical abnormalities of right ventricular function. These results also demonstrated that HD treatment was an independent predictor of RVD. Interestingly, HD treatment was associated with increased MPI of the right ventricle independently of systolic pulmonary pressure, suggesting that AVF-dependent volume overload by itself plays a crucial role in triggering RVD in patients undergoing chronic HD.

Piazza et al., (2005) reported that chronic volume overload is known to affect right ventricular function independently from post-load conditions. MPI of the right ventricle negatively correlated with left ventricular ejection fraction ( $r=-0.33$, $p<0.05$), confirming that RVD also impairs left ventricular filling [8]. Also, Said et al., (2012) concluded that subclinical RV dysfunction-as estimated by TDI derived MPI is highly prevalent among ESRD patients even before starting dialysis therapy and pulmonary hypertension is not significantly associated with RV dysfunction in these patients [23].

Conclusions:

End-stage renal disease and arteriovenous fistula are associated with right ventricular dysfunction with significantly lower RV ejection fraction by using conventional Doppler echocardiography and significantly higher TDIMPI at both lateral and septal tricuspid annulus which is independent to high systolic pulmonary artery pressure. So, we recommend the use of TDI evaluation of right ventricular function for early detection of preclinical dysfunction in hemodialysis patients.

References


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الملخص العربي

تهدف هذه الدراسة إلى تقييم وظيفة البطين الأيمن للقلب في مرضى الفسيل الدموي والجموعة الضابطة وترتبط النتائج مع بعض النتائج السريرية والعملية.

وتحقيق هذا الهدف شملت هذه الدراسة 100 مريضًا تم تقسيمهم إلى 40 مريضًا الفسيل الدموي و20 متطوعًا كمجموعة ضابطة. وقد خضعوا للفحص السريري الفيتيق، والفحوصات العملية وتقييم وظيفة القلب باستخدام الهدايا فوق الصوتية العادية والدوهار النسيجي.

ظهرت الدراسة الجلياء أن مرضى الفسيل الدموي كانوا أكثر سنًا بصورة ذات دلالات إحصائية كبيرة من المجموعة الضابطة. وأن ضغط الدم الانسياسي ومعدل ضربات القلب أعلى قيمة بصورة ذات دلالات إحصائية كبيرة في مرضى الفسيل الدمويمقارنة مع المجموعة الضابطة.

كشفت هذه الدراسة عند المقارنة بين مرضى الفسيل الدموي والجموعة الضابطة بالنسبة لمؤشرات الهدايا فوق الصوتية للقلب عن وجود اختلافات مهمة ذات دلالات إحصائية كبيرة.

كشفت هذه الدراسة عن وجود تدهور كبير واتخاذ في الوظيفة الانتقائية والانسياسية للبطين الأيمن للقلب ذو دلالات إحصائية سلبية في مرضى الفسيل الدموي باستخدام الهدايا فوق الصوتية العادية أو الدوهار النسيجي.

كما بينت ان ابعاد احجام البطين الأيمن للقلب كانت أكبر بصورة ذات دلالات إحصائية إيجابية في مرضى الفسيل الدموي من المجموعة الضابطة.

معامل الارتفاع للبطين الأيمن للقلب كان أعلى بصورة ذات دلالات إحصائية سلبية في مرضى الفسيل الدموي مقارة بالمجموعة الضابطة.

معامرات الوظيفة الانتقائية والانسياسية للفسيل الدموي باستخدام تصوير الارضي النسيجي كانت أقل بصورة ذات دلالات إحصائية سلبية في مرضى الفسيل الدموي.

سرعة الكرة والثاني التي قياسها عند المنطقة البارزة والمنطقة الجدارية لدارة الصمام ثلاثي الشفاف انخفضت بصورة ذات دلالات إحصائية سلبية في مرضى الفسيل الدموي مقارة بالمجموعة الضابطة.

معيقات الدراسة:
• صعوبة تقييم مرضى الفسيل الدموي خلال ساعة واحدة من جراحة الفسيل.
• العدد القليل نسبة للمرضى في هذه الدراسة.
• في النتيجة وجد أن معدل انتشار اختلاف وظيفة البطين الأيمن للقلب كان أكبر بصورة ذات دلالات إحصائية إيجابية في مرضى الفسيل الدموي مقارة بالمجموعة الضابطة مما يدل على أن الزيادة المزمنة لسوائل الجسم في مرضى الفسيل الدموي لوجود الوعاء ربما تؤدي إلى تدهور وظيفة البطين الأيمن للقلب في هذه الملاحظات تدعم استخدام تصوير الارضي النسيجي لتقدير وظيفة البطين الأيمن للقلب لتشخيص المرحلة قبل السريرية لتدهور وظيفة القلب في مرضى الفسيل.