Impacts of Residual Renal Function on Cardiac Morphology and Function in Haemodialysis Patients

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Abstract: The aim of this work was to clarify the beneficial effect of residual renal function on cardiovascular morphology and function in hemodialysis patients. This study was conducted on sixty (60) patients with chronic renal failure on regular HD selected from Nephrology Units of Al-Azhar University Hospital New Damietta, Kafr-Saad Hospital and Alzarka General Hospital and were divided into two groups according to presence of residual renal function (RRF) in to thirty patients with residual renal function (group1) and thirty patients without RRF (group 2). For all patients, full medical history, thorough clinical examination and laboratory investigations were done including: ECHO-Cardiography and ECG. **Results:** There was statistically significant difference between group 1 and group 2 as regard to LVEDD, ESD, however values of both groups were within normal ranges, and in spite of that, there were better contraction and good capacity of left ventricle in group1.PWT and SWT were higher in group 2 than group 1, and this indicate left ventricular hypertrophy in group2. But there was no difference in ejection fraction (EF) of both groups. The study revealed significant decrease of CRP in group 1 in comparison to group 2 (2.56±1.16 vs. 6.99±4.11 respectively), and significant decrease of cholesterol in group 1 in comparison to group 2. **Conclusion:** there were beneficial effect of RRF on cardiac morphology and function.
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1. Introduction

Residual renal function (RRF) is defined as the residual glomerular filtration rate (GFR) in patients with Chronic Kidney Disease (CKD) stage 5. A progressive decrease in RRF is commonly observed in dialyzed patients as functional renal parenchyma is lost. The rate of decrease depends on several factors such as etiology of CKD, treatment modalities, and exposure to nephrotoxic agents **(Marron *et al.,* 2008).**

RRF has been a concept in evolution since the first reference to its importance in hemodialysis patients by **Ahmad *et al.* (1979)** who studied the effect of RRF on the development of dialysis neuropathy and found that RRF played a major determinant role in dialysis requirements. **Marron *et al.* (2008)** studied that RRF would be a marker, but not a determinant of survival. However, other evidence indicates that the absence or rapid loss of RRF had a specific impact on the clinical condition of dialytic patients, particularly influencing the cardiovascular outcome of these patients.

General benefits of residual renal function preservation:

Residual renal function (RRF) has been associated with multiple beneficial effects including:

1-Preservation of RRF is associated with better long-term survival (lower relative risk of death) in dialysis patients **(Wang *et al.*, 2005).**
2- RRF plays an important role in the reduction of the blood pressure (BP) **(Menon *et al.*, 2001).**
3- RRF decreases the occurrence of left ventricular hypertrophy (LVH) **(Wang *et al.*, 2004).**
4- RRF increases sodium removal **(Ates *et al.*, 2001).**
5- RRF improves fluid status **(Konings *et al.*, 2003).**
6- RRF improves the serum hemoglobin level **(Wang *et al.*, 2005).**
7- RRF associated with better nutritional status **(Wang *et al.*, 2005).**
8- RRF decreases circulating inflammatory markers (**Pecoits *et al.*, 2003).**
9- RRF associated with more favorable lipid profile (**Kagan *et al.*, 1997).**

Cardiovascular disease is the main cause of death in CKD stage 5 patients **(Ates *et al.*, 2001).** In patients with CKD on HD, left ventricular hypertrophy (LVH) is related to the increase in total peripheral vascular resistance and volume overload **(Salustiano–*et al.*, 2011).** Morbidity and mortality from cardiac disease in chronic uremia usually result from cardiomyopathy and/or ischemic heart disease **(Wood *et al.*, 1980).** The severity of LVH, a strong independent predictor of mortality in dialysis patients, inversely correlates

with the presence of RRF **(Wang *et al.*, 2004).**

Residual GFR was calculated as an average of the 24-hour urine urea and creatinine clearance (CCr) **(Van Olden *et al.*, 1996)**.

2. Patients

The present study included sixty (60) patients with CKD stage 5 on regular HD selected from Nephrology Units of Al-Azhar University Hospital New Damietta, Kafr-Saad Hospital and Alzarka-General Hospital. Patients divided into two groups according to presence of RRF into: **Group1:** thirty (30) patients with RRF **Group 2:** thirty (30) patients without RRF. **Group1:** Included14 males (23.3%) and 16 (26.6%) females. Age ranged from (25.0 to 64.0) years. **Group2:** included 13 males and 17 females. Age ranged from (29.0 to 60.0) years.

HD was performed for 4 hours, three times weekly using conventional heparin. Vascular access was through arterio-venous fistula. Blood flow rate was usually 300 – 350ml/min with a dialysate flow rate of 500 ml /min. Ultrafiltration varied according to patient's actual weight. The membrane used was high flux polysulphone with surface area suitable for each patient. Bicarbonate was the buffer used throughout the study for all patients. Erythropoietin was taken for each patient according to the body weight (80 – 120IU/kg/ week).

Exclusion criteria:

1- Patients with duration less than six months on regular hemodialysis.

2- Diabetic patients.

3- Patients with previous cardiovascular disease.

4- Uncontrolled hypertension.

5- Recent major cardiovascular surgery.

6- Connective tissue disease.

7- Chronic liver disease.

II- Methods

All patients were subjected to the following:

1- Medicolegal consent.

2- History taking with emphasis on:

History of cardiovascular symptoms and Diabetes mellitus.

Etiology of renal failure.

History of long standing hypertension before dialysis.

History of connective tissue diseases.

Past history of anti-diabetic drugs and nephrotoxic medication.

Family history of cardiac diseases, premature coronary heart disease or sudden death.

3- Complete clinical examination to assess the condition and reviewing other systems of the body.

4- Laboratory investigations, included;

Complete blood count (CBC).

Renal functions tests (blood urea, serum creatinine, creatinine clearance and serum uric acid).

Erythrocyte sedimentation rate (ESR).

C - reactive protein (CRP).

Fasting and 2 hours postprandial blood glucose level.

Urine analysis.

Serum albumin, Bilirubin, ALT, AST.

Lipid profile including, Serum cholesterol, and triglycerides.

5-Assessment of residual renal function by calculation of 24h interdialytic (between dialysis sessions) urine volume ≥100 cc (**Salustiano *et al.*, 2011**).

6- Electrocardiogram

7- Echo-cardiography: Resting Trans-Thoracic Echo-cardiography was done; M-mode, 2-D echo and Doppler were performed for all patients using Esaote Biomedical apparatus. A wide angle mechanical sector scanner with a 3.5 MHz transducer was used to obtain M-mode and 2-D echo tracing, while Doppler studies were performed using 3.25 MHz duplex mechanical sector scanner.

Echo-cardiography was done at interdialytic period and all patients were studied in left lateral position. The following parameters were specially looked for:

Left ventricular end diastolic diameter (EDD)

Normally: (3.7-5.6) cm (**Lang *et al.*, 2006.**

Left ventricular end systolic diameter (ESD)

Normally: (2.3–4.0) cm (**Lang *et al.*, 2006.**

Fractional shortening (FS)

Normally: (25-40%) (**Lang *et al.*, 2006.**

Ejection fraction:

Normally it is ≥55 % (**Lang *et al.*, 2006.**

Left atrium diameter (LA)

Normally: (2.7–4.0 cm) (**Lang *et al.*, 2006**).

Posterior wall thickness (PWT)

Normally: (0.7-1.1cm) (**Lang *et al.*, 2006**).

Aortic root diameter:

Normally: 1.7–2.5 cm (**Triulzi *et al.*, 1984**).

Septal wall thickness (SWT): Normally (0.7-1.1cm) (**Lang *et al.*, 2006**).

Statistical analysis of data:

The collected data was organized, tabulated and statistically analyzed using Statistical Package for Social Science (SPSS) version 15 (SPSS Inc, Illinois, and Chicago, USA). For quantitative data, mean, standard deviation (SD), minimum and maximum were calculated and for comparison between two groups, the students (t) test was used. For comparison between the same group at two different points of time (i.e. before and after dialysis), paired samples (t) test*was used.

For qualitative (categorical data), frequency and percent distribution were calculated, and for

comparison between groups, the Chi square (x2) was calculated.

For interpretation of results, *p* value less than or equal to 0.05 was considered significant.

3. Results

Table (2) showed that, there was statistically significant decrease of duration of dialysis in group 1 in comparison to group 2 (30.93±20.74 vs 57.60±14.57 month respectively).

Table (2) revealed that, there was statistically significant difference between group 1 and group 2 as regard LVEDD, LVESD, PWT, SWT and LA, while,

there was statistically non-significant difference between group 1 and group 2 as regard FS, EF and AO root.

Table (3) revealed that, there was statistically significant decrease of cholesterol in group 1 in comparison to group 2 (150.50±21.79 vs 164.63±12.45 respectively). On the other hand, there was statistically non-significant difference between group 1 and group 2 as regard triglycerides.

Figure (1) showed that, there was statistically significant decrease of CRP in group 1 in comparison to group 2.

Table (1): statistical evaluation of dialysis duration (months) of group1 (RRF) in comparison to group 2 (without RRF).

	Mean	±S. D	Minimum	Maximum	T	*P*
Group 1	30.93	20.74	8.00	84.00	5.76	<0.001*
Group 2	57.60	14.57	36.00	84.00		
Total	44.26	22.28	8.00	84.00		

Table (2): statistical evaluation of echocardiography results of group1 (RRF) in comparison to group 2 (without RRF).

		MEAN	S. D	MINIMUM	MAXIMUM	T	*P*
LVEDD	Group 1	5.07	0.14	4.50	5.20	8.63	<0.001*
	Group 2	4.63	0.24	4.10	5.10		
	Total	4.85	0.29	4.10	5.20		
LVESD	Group 1	3.34	0.19	2.70	3.60	12.03	<0.001*
	Group 2	2.67	0.23	2.30	3.20		
	Total	3.00	0.39	2.30	3.60		
PWT	Group 1	0.98	0.10	0.80	1.40	10.12	<0.001*
	Group 2	1.31	0.14	1.00	1.50		
	Total	1.15	0.21	0.80	1.50		
SWT	Group 1	0.98	0.11	0.80	1.40	10.21	<0.001*
	Group 2	1.31	0.14	1.00	1.50		
	Total	1.15	0.21	0.80	1.50		
FS%	Group 1	30.53	1.27	29.00	32.00	0.61	0.54(NS)
	Group 2	30.33	1.26	29.00	32.00		
	Total	30.43	1.26	29.00	32.00		
EF%	Group 1	66.14	0.84	65.00	67.20	0.60	0.55(NS)
	Group 2	66.27	0.86	65.00	67.50		
	Total	66.21	0.85	65.00	67.50		
AO root	Group 1	3.17	0.19	2.80	3.80	0.88	0.38(NS)
	Group 2	3.13	0.15	2.90	3.60		
	Total	3.15	0.17	2.80	3.80		
LA	Group 1	3.55	0.28	3.10	4.30	5.48	<0.001*
	Group 2	3.98	0.31	3.50	4.60		
	Total	3.76	0.36	3.10	4.60		

Table (3): statistical evaluation of cholesterol and triglycerides of group1 (RRF) in comparison to group 2 (withoutRRF).

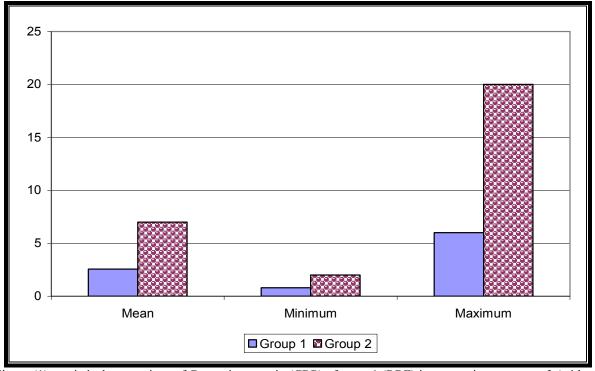|		Mean	±S. D	Minimum	Maximum	t	p
cholesterol	Group 1	150.50	21.79	110.00	184.00	3.08	0.003*
	Group 2	164.63	12.45	139.00	185.00		
	Total	157.57	18.98	110.00	185.00		
TG	Group 1	122.87	15.90	99.00	150.00	1.26	0.21(NS)
	Group 2	128.23	16.78	90.00	155.00		
	Total	125.55	16.43	90.00	155.00		

Figure (1): statistical comparison of C-reactive protein (CRP) of group1 (RRF) in comparison to group 2 (without RRF).

4. Discussion

The present study was designed to clarify the beneficial effect of residual renal function on cardiac morphology and function in hemodialysis patients. **Levin et al. (1999)** reported that residual renal function may play a role in limiting cardiac hypertrophy by improving the overall removal of uremic toxins. While **Wang et al. (2002)** suggested that worsening the volume control with loss of residual renal function may be one of the important contributing factors for the adverse cardiovascular outcomes observed in anuric patients. In CKD patients, RRF progressively decreased with time in replacement therapy. In this study, the group without RRF (RD-ve) spent more time in HD treatment than the group with RRF (RD+ve), and the loss of urine volume only happened in patients with the longest time of HD.The duration of dialysis in **group 1 (RRF+ve)** (30.93±20.74) in comparison to **group 2(RRF-ve)** (57.60±14.57) month. The reasons for losing the RRF may be explained by the changes related to the underlying disease that caused the CKD or by a continuous inflammatory process, anemia and associated co-morbidities **(Jacobs et al., 2010).**This in

agreement with the study by **Salustiano *et al.* (2011)** who reported that there was decrease in duration of dialysis in HD patient with **(RRF+ve)** and mean duration was (27.5 ± 3.8) month in comparison to HD patient with**o**ut **(RRF-ve)** and mean duration was (69.0 ± 10.9) month. **Motohashi and Nishi (1991)** observed that, dialysis patients may be associated with either; Cardiomyopathy which may be manifest as; concentric left ventricular (LV) hypertrophy (that results from pressure overload), left ventricular dilatation (that results from volume overload), or systolic dysfunction (a reflection of diminished myocardial contractility). **Wood *et al.* (1980)** reported that morbidity and mortality from cardiac disease in chronic uraemia usually result from cardiomyopathy and/or ischaemic heart disease**.** Also **Wang *et al.* (2004)** reported that cardiac hypertrophy is an important predictor of mortality in dialysis patients. In the present study, there was statistically significant increase of left ventricular end diastolic diameter (LVEDD) in group 1(RRF+ve) (5.07 ± 0.14) and decrease of (LVEDD) in group 2(RRF-ve) (4.63 ± 0.24) by echo-cardiography, however values of both groups were within average ranges and inspite of that, there was better contraction and good capacity of the left ventricle in group 1 (RRF+ve) .This in agreement with the study by **Salustiano *et al.* (2011)** who reported that, there was increase of left ventricular end diastolic diameter (LVEDD) in group 1(5.2 ± 0.79) and decrease of (LVEDD) in group2 (48 ± 1.12). In this study, there was statistically significant increase of left ventricular end systolic diameter (LVESD) in group1 (RRF+ve) and statistically significant decrease of (LVESD)in group2 (RRF-ve). Also, there was statistically significant decrease of posterior wall thickness (PWT) ingroup1 (RRF+ve) (0.98± 0.10) and statistically significant increase of (PWT) in group 2 (RRF-ve) (1.31 ± 0.14).As regard to, Septal wall thickness (SWT) there was statistically significant decrease in group1 (RRF+ve) (0.98 ± 0.11) and statistically significant increase of (SWT) in group2 (1.31 ± 0.14) and this indicate left ventricular hypertrophy in this group. **Lang *et al.* (2005)** reported that relative wall thickness constitutes one of the variables used to define the geometric pattern of the left ventricle. Thus, **Salustiano *et al.*, (2011)** observed that the patients in groups RD+ and RD- had different values of relative wall thickness, and suggested that both groups would have distinct ventricular morphologies and the load resistance and volume imposed on the left ventricle would be of different magnitudes. Relative wall thickness (RWT) is measured in clinical studies as: (2 multiplying to posterior wall thickness) divided by (LV diastolic diameter) or, (septal wall thickness + posterior wall thickness) divided by (LV diastolic diameter) **(Lang *et al.*, 2005)**. In this study as

regard to, left atrium (LA) there was non-significant difference between group 1(3.55 ± 0.28) and group 2(3.98 ± 0.31). As regard to, fractional shortening (FS) in group1 (30.53 ± 1.27) and in group2 (30.33 ± 1.26) there was no difference of both groups. And regard to, ejection fraction (EF) in group 1 (66.14± 0.84) and in group2 (66.27± 0.86) there was no difference of both groups. This in agreement with the study by **Salustiano *et al.* (2011)** who reported that, there was no difference of ejection fraction (EF)in patients on hemodialysis with and without residual renal function. As regard to, aortic root (AO) in group1 (3.17 ± 0.19) and in group2 (3.13 ± 0.15) and there was no difference of both groups. On the other hand **Faguli *et al.* (2003)** demonstrated LVH in the majority of the HD patients studied, but did not exclude patients with pathologies that could interfere with the myocardium remodeling process such as diabetes mellitus, ischemic cardiomyopathy or systemic arterial hypertension; further, they did not correlate their findings with the residual urinary Volume. But in our study, the morpho-functional cardiac changes could not be attributed to the blood pressure levels found, because both groups demonstrated similar diastolic and systolic blood pressure values. **Feldman *et al.* (1988)** reported that, Persistent hypocalcemia is considered a pathogenic factor in the reduction of left ventricular systolic function. However, serum calcium in this study remained at normal values. In the present study, as regard to S. Cholesterol, there was statistically significant decrease of cholesterol in group 1 (RRF+ve) in comparison to group 2(RRF-ve) (150.50±21.79 vs 164.63±12.45 respectively). These in agreement with the study by **Kagan *et al.* (1997)** who reported that levels of serum total cholesterol, were significantly lower in patients with preserved RRF. **Chung *et al.* (2003)** reported that patients with low RRF have high C-reactive protein levels. **Panichi *et al.* (2000)** reported that the RRF declines after the start of dialysis in most end‑stage renal disease patients and this might result in less efficient removal of inflammatory mediators and also reported that CRP was inversely related to renal function. In the present study, there was significant decrease of CRP in group 1 (RRF+ve) in comparison to group 2 (RRF-ve) (2.56±1.16 vs 6.99±4.11 respectively).These in agreement with the study by **Shin *et al.* (1999)** who reported the association between reduction in RRF and high serum CRP. **Wang *et al.* (2005)** reported that the loss of residual renal function was associated with an increased inflammatory response as denoted by C-reactive protein or soluble vascular cell adhesion molecules (VCAM-1) in peritoneal dialysis patients.

Conclusion:

The RRF have beneficial effect on cardiac morphology and function in hemodialysis patients as it decrease the occurrence of left ventricular hypertrophy (LVH) and so decrease mortality. Also Residual renal function decreases the circulating inflammatory markers as (CRP) and associated with better serum cholesterol level.

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