

## The changes in cardiac dimensions and function in patients with end stage renal disease undergoing hemodialysis

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**Background :** *It is absolutely necessary to evaluate cardiac function on starting and during hemodialysis in patients with end stage renal disease. In this study, we tried to determinate the changes of cardiac function associated with hemodialysis.*

**Methods :** *Twenty patients with end stage renal disease, who had been in a hemodialysis program from February, 1997 to August, 1999 in Pusan National University Hospital, were enrolled. They were examined with echocardiography and gated blood pool scintigraphy on starting hemodialysis and after follow-up. The data were analyzed by paired t-test.*

**Results :** *The patients were  $46.2 \pm 16.8$  years old and male to female ratio was 8 : 12. The underlying diseases were diabetes mellitus ( $n=10$ ), hypertension<sup>1)</sup>, glomerulonephritis<sup>2)</sup> and others<sup>1)</sup>. The duration of symptoms associated with end stage renal disease and underlying diseases was  $3.4 \pm 2.6$  years and the duration of hemodialysis was  $13.8 \pm 7.0$  months. The LVEDID, LVESID and RVC decreased significantly ( $-6.10$ ,  $-7.80$  and  $-20.00\%$ , respectively,  $p < 0.05$ ) with no significant changes for LAD, IVS, PWT and EF ( $p > 0.05$ ). In ten cases associated with diabetes, LVEDID decreased ( $-7.90\%$ ,  $p < 0.05$ ). In twelve cases associated with cardiac diseases, LVEDID and LVESID decreased ( $-8.60$  and  $-10.50\%$ , respectively,  $p < 0.05$ ). In four cases associated with diabetes without cardiac diseases, LAD decreased ( $-5.10\%$ ,  $p < 0.05$ ) and in four cases associated with cardiac diseases without diabetes there were no significant changes in cardiac dimensions and EF. In seven cases associated with diabetes and cardiac diseases, LVEDID decreased ( $-10.50\%$ ,  $p < 0.05$ ). The EF on gated blood pool scintigraphy decreased ( $-0.9\%$ ,  $p < 0.05$ ) as a whole while it increased ( $5.90\%$ ,  $p < 0.05$ ) in the cases associated with diabetes and cardiac diseases.*

**Conclusion :** *During the early hemodialysis stage of end stage renal disease, we found a change of concentric left ventricular hypertrophy and relatively preserved left ventricular function. Furthermore, we can expect that adequate hemodialysis - with dry weight as low as possible - may prevent progression to eccentric left ventricular hypertrophy and dilated cardiomyopathy.*

**Key Words :** *End stage renal disease, Hemodialysis, Echocardiography, Cardiac function*

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## INTRODUCTION

It is absolutely necessary to evaluate the cardiac function on starting and during hemodialysis in patients with end stage renal disease as it plays an important role in deciding the therapeutic procedures and judging the therapeutic effects. In this study, we tried to determine the changes of cardiac function associated with hemodialysis. The average survival in patients with end stage renal disease is just one-third or one-fourth compared with one in normal people of similar age and it is often followed by such cardiac diseases as vessel disease, congestive heart failure, arrhythmia, myocardial infarction, pericarditis and cardiac arrest. Cardiac diseases before and after hemodialysis frequently occur and the mortality, thereby, is high. Therefore, the cardiac disease is an important prognosis for the death of patients with end stage renal disease. Especially, the classification by left ventricular dimensions and mass on echocardiography is a strong prognosis for death within 2 years from the start of hemodialysis. It is expected that echocardiography is used to observe changes in dimensions of each atrium and ventricle in order to preserve and enhance renal and heart functions through hemodialysis, which would decrease the mortality by the end stage renal disease and incidence of cardiac diseases.

This study used echocardiography and gated blood pool scintigraphy for the patients undergoing hemodialysis at Pusan National University Hospital to measure the changes in cardiac dimensions and ejection fraction before and after hemodialysis for comparison. In addition, it aimed to observe the changes of cardiac function according to hemodialysis with comparative analysis for the presence of risk factors like diabetes mellitus and hypertension.

## MATERIALS AND METHODS

### 1. Patients

20 patients with end stage renal disease in the hemodialysis program of Pusan National University Hospital from February, 1997 to August, 1999 were tested.

### 2. Methods

The patients with end stage renal disease were evaluated for the cardiac function by echocardiography

(SONOS 2500 of Hewlett Packard Co., 2-dimensional Echocardiography) before hemodialysis. After starting hemodialysis, echocardiography was repeated to measure left atrial dimension (LAD), left ventricular end diastolic internal dimension (LVEDID), left ventricular end systolic internal dimension (LVESID), interventricular septum thickness (IVS), right ventricular cavity (RVC), left ventricular post wall thickness (PWT) and ejection fraction (EF) for comparative analysis between the results before hemodialysis and during the follow-up. Also, gated blood pool scintigraphy using VERTEX (EPIC) gamma camera with dual detector of ADAC Co. was carried out as a subsidiary device for measuring ejection fraction. The dialyzer was AK-95 of B/brown Dialog, GSD 2000, Gambro Co. and Hemophan was used for the dialysis membrane.

### 3. Statistical method

Cardiac dimensions and ejection fraction before hemodialysis were calculated into mean  $\pm$  standard deviation. Each increase and decrease was expressed in percentage and paired *t*-test was used to evaluate the statistical significance.

## RESULTS

Patients were 22-76 years old and the average age was  $46.2 \pm 16.8$ . They were 8 males and 12 females. The underlying diseases of end-stage renal disease were diabetes mellitus (n=10), hypertension<sup>7)</sup>, glomerulonephritis<sup>2)</sup> and others<sup>1)</sup>. The cardiovascular complications associated with hemodialysis were hypertension (n=20), hypertensive heart disease<sup>7)</sup>, congestive heart failure<sup>7)</sup>, dilated cardiomyopathy<sup>4)</sup>, valvular heart disease<sup>2)</sup> and ischemic heart disease<sup>1)</sup>. The duration of symptoms associated with renal failure to starting hemodialysis was mean  $3.4 \pm 2.6$  years and the follow-up period after hemodialysis was mean  $13.8 \pm 7.0$  months (Table 1).

The results by echocardiography and gated blood pool scintigraphy at the start of hemodialysis and after follow-up were compared and analyzed (Table 2). As a result, LVEDID decreased from  $5.51 \pm 0.48$  cm to  $5.17 \pm 0.59$  cm, LVESID from  $3.84 \pm 0.59$  cm to  $3.54 \pm 0.49$  cm, RVC from  $1.28 \pm 0.47$  cm to  $1.02 \pm 0.42$  cm, which were statistically significant as -6.10%, -7.80%, -20.00%, respectively ( $p < 0.05$ ). On the other hand, there were no significant changes in LAD, IVS, PWT, ET, which increased or decreased by 0.50%, -3.80%, -3.40%,

**Table 1. Clinical characteristics of hemodialysis patients who had echocardiography and gated blood pool scintigraphy**

Age (years)	22 - 76 (46.2 ± 16.8)			
Sex (M : F)	8 : 12			
Duration of symptom (years)*	1 - 10 (3.4 ± 2.6)			
Duration of hemodialysis (months)†	7 - 31 (13.8 ± 7.0)			
Cardiovascular Cx.§	Underlying diseases†			
	Diabetic (n=10)	Hypertensive (n=7)	Glomerulonephritic (n=2)	Others (n=1)
HT	10	7	2	1
CHH	3	4	0	0
CHF	2	5	0	0
DCMP	1	3	0	0
VHD	1	1	0	0
IHD	1	0	0	0

\* Period from referral due to associated diseases or uremic symptom to starting hemodialysis

† Period from starting hemodialysis to Aug, 1999

‡ Underlying diseases causing CRF : diabetic, hypertensive, glomerulonephritic and others

§ Cardiovascular complications associated with the underlying diseases and CRF  
HT, hypertension; CHH, chronic hypertensive heart; CHF, congestive heart failure;  
DCMP, dilated cardiomyopathy; VHD, valvular heart diseases; IHD, ischemic heart diseases

**Table 2. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy**

	Pre-dialysis* (cm)	Post-dialysis† (cm)	Changes (%)‡	p-value§
LAD	3.97 ± 0.47	3.93 ± 0.61	0.5	0.709
LVEDID	5.51 ± 0.48	5.17 ± 0.59	-6.1	0.004
LVESID	3.84 ± 0.59	3.54 ± 0.49	-7.8	0.021
IVS	1.17 ± 0.16	1.13 ± 0.13	-3.8	0.087
PWT	1.18 ± 0.16	1.14 ± 0.10	-3.4	0.209
RVC	1.28 ± 0.47	1.02 ± 0.42	-20.0	0.019
EF	64.28 ± 12.30	63.28 ± 9.60	-1.6	0.767
REF	73.40 ± 9.03	72.69 ± 10.53	-0.9	0.039

LAD, Left atrial dimension; LVEDID, Left ventricular end-diastolic internal dimension; LVESID, Left ventricular end-systolic internal dimension; IVS, Interventricular septum thickness; PWT, Left ventricular posterior wall thickness; RVC, Right ventricular cavity; EF, Ejection fraction; REF, Ejection fraction on gated blood pool scintigraphy (RVG)

\* measurements at starting hemodialysis

† measurements after follow-up

‡ difference between measurements of pre- & post-dialysis

§ statistically significant when  $p < 0.05$

- 1.60%, respectively ( $p > 0.05$ ).

In Table 3, 10 diabetic cases showed a significant decrease of LVEDID (from  $5.42 \pm 0.38$  cm to  $4.99 \pm 0.46$  cm, -7.90%) in dimensions after dialysis ( $p < 0.05$ ), whereas

there were no significant changes in LAD, LVESID, IVS, PWT, RVC, EF, which showed -1.80%, -7.60%, -4.20%, -5.60%, -14.30%, -1.30%, respectively ( $p > 0.05$ ).

In 12 cardiac diseases like congestive heart failure,

**Table 3. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy in patients with diabetes mellitus**

	Pre-dialysis (cm)	Post-dialysis (cm)	Changes (%)	<i>p</i> -value
LAD	3.90 ± 0.31	3.38 ± 0.34	- 1.8	0.299
LVEDID	5.42 ± 0.38	4.99 ± 0.46	- 7.9	0.027
LVESID	3.68 ± 0.70	3.40 ± 0.48	- 7.6	0.193
IVS	1.18 ± 0.19	1.13 ± 0.10	- 4.2	0.272
PWT	1.19 ± 0.20	1.12 ± 0.11	- 5.6	0.141
RVC	1.26 ± 0.54	1.08 ± 0.58	- 14.3	0.149
EF	66.00 ± 16.22	65.11 ± 7.52	- 1.3	0.881
REF	74.28 ± 8.12	73.18 ± 10.37	- 1.0	0.722

**Table 4. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy in patients with heart diseases**

	Pre-dialysis (cm)	Post-dialysis (cm)	Changes (%)	<i>p</i> -value
LAD	3.97 ± 0.43	4.05 ± 0.58	2.0	0.464
LVEDID	5.73 ± 0.43	5.24 ± 0.74	- 8.6	0.007
LVESID	4.08 ± 0.62	3.65 ± 0.54	- 10.5	0.043
IVS	1.15 ± 0.19	1.14 ± 0.14	- 0.8	0.778
PWT	1.15 ± 0.20	1.15 ± 0.14	- 0.8	0.821
RVC	1.36 ± 0.46	1.09 ± 0.51	- 20.0	0.062
EF	61.09 ± 14.17	60.91 ± 8.14	- 0.3	0.972
REF	72.92 ± 9.27	76.32 ± 9.89	4.7	0.079

**Table 5. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy in patients with diabetes mellitus without heart diseases**

	Pre-dialysis (cm)	Post-dialysis (cm)	Changes (%)	<i>p</i> -value
LAD	3.90 ± 0.37	3.70 ± 0.39	- 5.1	0.016
LVEDID	5.25 ± 0.24	4.75 ± 0.50	- 9.5	0.267
LVESID	3.60 ± 0.68	3.13 ± 0.29	- 13.2	0.334
IVS	1.18 ± 0.10	1.13 ± 0.10	- 4.3	0.182
PWT	1.18 ± 0.10	1.13 ± 0.05	- 4.3	0.182
RVC	0.95 ± 0.37	0.83 ± 0.26	- 12.6	0.412
EF	66.50 ± 15.15	67.25 ± 8.26	1.1	0.892
REF	78.60 ± 7.51	70.23 ± 13.72	- 10.6	0.130

**Table 6. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy in patients with heart diseases without diabetes mellitus**

	Pre-dialysis (cm)	Post-dialysis (cm)	Changes (%)	p-value
LAD	4.30 ± 0.42	4.58 ± 0.45	6.5	0.273
LVEDID	6.00 ± 0.45	5.78 ± 0.78	-3.7	0.266
LVESID	4.30 ± 0.24	4.05 ± 0.31	-5.8	0.127
IVS	1.08 ± 0.13	1.08 ± 0.13	0.0	
PWT	1.08 ± 0.13	1.13 ± 0.10	4.7	0.182
RVC	1.28 ± 0.49	0.88 ± 0.05	-31.2	0.228
EF	62.25 ± 5.62	56.00 ± 7.79	-10.0	0.132
REF	71.03 ± 11.42	70.28 ± 8.14	-1.1	0.773

**Table 7. The changes in cardiac dimensions and ejection fraction on echocardiography and gated blood pool scintigraphy in patients with heart diseases and diabetes mellitus**

	Pre-dialysis (cm)	Post-dialysis (cm)	Changes (%)	p-value
LAD	3.83 ± 0.32	3.82 ± 0.40	-0.4	0.849
LVEDID	5.57 ± 0.39	4.98 ± 0.58	-10.5	0.045
LVESID	3.88 ± 0.79	3.50 ± 0.54	-9.9	0.242
IVS	1.17 ± 0.23	1.13 ± 0.10	-2.9	0.576
PWT	1.18 ± 0.24	1.12 ± 0.13	-5.6	0.328
RVC	1.45 ± 0.52	1.18 ± 0.67	-18.4	0.148
EF	62.00 ± 18.98	62.33 ± 7.06	0.5	0.971
REF	73.47 ± 9.32	77.80 ± 8.79	5.9	0.036

dilated cardiomyopathy, hypertensive heart disease, ischemic heart disease and cardiac valvular disease (Table 4), LVEDID significantly decreased from 5.73 ± 0.43 cm to 5.24 ± 0.74 cm (-8.60%) and LVESID from 4.08 ± 0.62 cm to 3.65 ± 0.54 cm (-10.50%) ( $p < 0.05$ ). However, there were no significant changes in LAD, IVS, PWT, RVC, EF (2.00%, -0.80%, -0.80%, -20.00%, -0.30%, respectively,  $p > 0.05$ ).

In 4 cases associated with diabetic mellitus without cardiac diseases (Table 5), LAD significantly decreased from 3.90 ± 0.37 cm to 3.70 ± 0.39 cm by -5.10% ( $p < 0.05$ ), whereas there were no significant changes in 4 cases associated with cardiac diseases without diabetes mellitus ( $p < 0.05$ ).

In 7 cases associated with diabetes mellitus and cardiac diseases (Table 7), LVEDID showed a significant decrease of -10.50% from 5.57 ± 0.39 cm to 4.98 ± 0.58 cm ( $p < 0.05$ ).

On the whole, a significant change in EF on

echocardiography was not observed, but EF measured by gated blood pool scintigraphy (RVG) (hereafter as REF) showed a decrease of -0.90% from 73.40 ± 9.03 cm to 72.69 ± 10.53 cm ( $p < 0.05$ ). In cases of patients with diabetes mellitus and cardiac diseases, REF showed a significant increase of 5.90% from 77.47 ± 9.30 cm to 77.80 ± 8.79 cm ( $p < 0.05$ , Table 2, 7)

## DISCUSSION

The changes in cardiac dimensions and function by long-term hemodialysis in patients with end stage renal disease are important indices for an effective maintenance and improvement of renal and heart functions. Also, they are important prognoses for prevalence and mortality.

Jürgen et al. performed a follow-up of changes in cardiac dimensions by M-mode echocardiography for

2.5 years in chronic renal failure patients undergoing a long-term hemodialysis therapy. As a result, LAD ( $38.26 \pm 5.42$  vs.  $42.52 \pm 6.27$  mm) and IVS ( $14.34 \pm 3.02$  vs.  $16.44 \pm 3.38$  mm) showed statistically significant increases, but LVESID ( $35.80 \pm 60.4$  vs.  $34.31 \pm 6.42$  mm) showed a significant decrease. No significant changes were observed in LVEDID and stroke volume. The cause of LAD increase is not certain, but it is assumed that it is attributed to left ventricular diastolic failure by left ventricular hypertrophy. LVEDID and LVESID decreases are related to preload and afterload, which indicates decreases in dimensions by the concentric left ventricular hypertrophy.

Deligiannis et al. performed a follow-up in 10 patients with end stage renal disease for 22 months and observed increases in LVEDID from  $52 \pm 3.0$  to  $54 \pm 3.0$  mm and IVS from  $12 \pm 2.0$  to  $13 \pm 2.0$  mm, which showed an eccentric left ventricular hypertrophy finding.

Left ventricular hypertrophy by end stage renal disease is a process of adapting to myocardial load increase, in which pressure overload causes left ventricular wall thickening and induces concentric left ventricular hypertrophy by reducing cavity volume, whereas volume overload increases the internal dimension with left ventricular wall thickness to cause the eccentric left ventricular hypertrophy. In the state of such chronic overloads, left ventricular hypertrophy and fibrosis proceed continuously to yield dilated cardiomyopathy and heart failure. Therefore, in case of left ventricular hypertrophy by end stage renal disease, the left ventricular internal dimension decreases in the early stage and increases gradually, of which change is more accelerated with inadequate hemodialysis. As the blood flow volume is directly related to the left ventricular diameter, it is said that the left ventricular diastole may be prevented if the dry weight is maintained as low as possible. Also in the patients with end-stage renal disease, hemodialysis through arteriovenous shunt induces higher blood flow volume, which causes left ventricular hypertrophy and dilatation.

This study tested patients of mean  $46.2 \pm 16.8$  years of age with end stage renal disease in the early stage of hemodialysis therapy, of which average duration was  $13.8 \pm 7.0$  months. It is judged that decreases in LVEDID and LVESID are attributed to the decreased finding of the left ventricular internal diameter by concentric left ventricular hypertrophy. No change in left atrial volume reflects a mild left ventricular diastolic failure by left ventricular hypertrophy.

Hypertension is an independent determinant causing concentric left ventricular hypertrophy. There were 7 hypertensive end stage renal disease patients in this study and every subject had hypertension as an underlying disease or a complication, which was being controlled by calcium-channel blocker,  $\alpha$ -adrenergic blocker and angiotensin converting enzyme inhibitors.

As compared with diabetes mellitus as another risk factor for cardiac diseases, as well as a main cause of chronic renal failure, a complicated cases with diabetes mellitus and cardiac diseases of 10 diabetic end stage renal patients showed a volume decrease of -10.5% in LVEDID, which assumed that the concentric left ventricular hypertrophy proceeded most among the other cases. In case of diabetes mellitus without cardiac disease or cardiac disease without diabetes mellitus, LVEDID decreased 9.5% and 3.7%, respectively and it is judged that no statistical significances are attributed to few patients and a relatively short prevalence or hemodialysis period.

Gated blood pool scintigraphy is useful to evaluate the left ventricular function by radionuclide venoclysis for equilibrium in blood and then for collecting electrocardiograms repeatedly during the heart beat cycle to image the changes of blood pool within the heart. With echocardiography, the gated blood pool scintigraphy was used to assay the left ventricular function quantitatively in measuring the ejection fraction. This study displayed a difference in measuring the ejection fraction by echocardiography and gated blood pool scintigraphy, which assumed that it is due to each method using left ventricular volume or radioactive value during the cardiac cycle to yield some differences in measurement and accuracy.

Finally, end stage renal disease patients in the early stage of hemodialysis showed the concentric left ventricular hypertrophy finding, whereas the left ventricular function was relatively well maintained. It is considered that adequate hemodialysis, preserving dry weight as low as possible, may prevent progression to eccentric left ventricular hypertrophy and dilated cardiomyopathy. Also, it is expected to reduce death due to heart failure and ischemic heart disease caused by left ventricular hypertrophy and dilated cardiomyopathy. A long-term follow-up should be required for mortality and prognosis according to changes in cardiac function and a long-term study should also be required for risk factors of cardiac diseases like hypertension and diabetes mellitus.

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