

Correlation Between Asymptomatic Intradialytic Hypotension and Regional Left Ventricular Dysfunction in Hemodialysis Patients

Reza Hekmat,¹ Mostafa Ahmadi,² Hedayatollah Fatehi³
 Bita Dadpour,¹ Afson Fazelenejad³

¹Department of Nephrology,
 Ghaem Hospital, Mashhad
 University of Medical Sciences,
 Mashhad, Iran

²Department of Cardiology,
 Vali-asar Hospital, Birjand
 University of Medical Sciences,
 Birjand, Iran

³Department of Cardiology,
 Ghaem Hospital, Mashhad
 University of Medical Sciences,
 Mashhad, Iran

Keywords. hemodialysis,
 hypotension, left ventricular
 dysfunction, myocardial
 stunning

Introduction. Cardiovascular disease and heart failure are common in dialysis patients. Recurrent subclinical myocardial ischemia is an important event which may lead to the heart failure. We examined whether this phenomenon occurs secondary to the intradialytic hypotension in hemodialysis patients.

Materials and Methods. Twelve patients prone to intradialytic hypotension who had been on maintenance hemodialysis for more than 12 months and 15 hemodialysis patients without any history of intradialytic hypotension were included in this study. Echocardiography was performed before hemodialysis (baseline), and at 60 minutes and 120 minutes during hemodialysis (climax), and 30 minutes postdialysis (recovery). Left ventricular end-diastolic diameter, left ventricular systolic diameter, left ventricular ejection fraction, fractional shortening of left ventricular, and regional wall motion abnormality score and index were measured during the four stages in all patients.

Results. Regional wall motion abnormality preceded reduction in the left ventricular ejection fraction and fractional shortening in patients with intradialytic hypotension. However, decreased systolic blood pressure and increased regional wall motion abnormality were accompanied.

Conclusions. This study showed that reversible myocardial dysfunction occurs during the hemodialysis. It may be contributed to the intradialytic hypotension. In addition, we showed that regional wall motion abnormality less frequently occurred in patients without intradialytic hypotension. This suggests that confronting with intradialytic hypotension may prevent cardiovascular dysfunction.

IJKD 2011;5:97-102
www.ijkd.org

INTRODUCTION

Cardiovascular disease, heart failure and death secondary to these disorders are common in dialysis patients.¹ Recurrent subclinical myocardial ischemia is an important event which may lead to the heart failure. It has long been suggested that myocardial ischemia may be precipitated by hemodialysis, with

the first report of silent ST segment depression during hemodialysis date back to 1989. However, the concept of the subclinical ischemia (occurring without acute rupture of atherosclerotic plaque) has received little attention, despite its theoretical plausibility. Short intermittent hemodialysis treatments exert significant hemodynamic effects,

and 20% to 30% of treatments are complicated by intradialytic hypotension (IDH). However, hemodialysis patients are particularly susceptible to the myocardial ischemia.²⁻⁴ We examined whether this phenomenon occurs secondary to the IDH in hemodialysis patients. We hypothesized that there is a correlation between IDH and changes in echocardiographic parameters during hemodialysis. We evaluated our hypothesis by comparing echocardiographic parameters between patients with and without IDH.

MATERIALS AND METHODS

Patients

Twelve patients prone to IDH (according to previous recorded data) who were on maintenance hemodialysis for more than 12 months were included as the case group in this study. More than 30 mm Hg reduction in systolic blood pressure without any accompanying clinical symptoms was defined as asymptomatic IDH. The control group contained 15 patients who were on maintenance hemodialysis without any history of IDH. Patients who were on maintenance hemodialysis for less than 12 months, patients with end-stage malignancies, and patients with significant valvular or pericardial diseases were excluded from the study. Demographic characteristics of the two groups are shown in Table 1.

Study Protocol

Echocardiography. Two-dimensional echocardiography was serially performed by an experienced assistant of cardiology throughout the hemodialysis session using a commercially available instrument (ATL HDI 5000, Bothel, WA,

USA). It was performed while the patients were in the supine position. Images were recorded before the beginning of hemodialysis (baseline), at 60 minutes and 120 minutes during hemodialysis (climax), and 30 minutes postdialysis (recovery). Standard apical 2-chamber and 4-chamber views (to visualize the left ventricular endocardial border in 2 planes, which were positioned in right angles) were recorded.

The mean fractional shortening was calculated, which is the percentage change in left ventricular (LV) dimensions in each LV contraction for all patients, using the following formula:

$$\text{Fractional Shortening} = \frac{\text{LVEDD} - \text{LVESD}}{\text{LVEDD}} \times 100$$

where LVED is the LV end-diastolic dimension and LVES is the LV end-systolic dimension).^{5,6} Ejection fraction (EF) was calculated by measuring LV volumes using the biplane disk method during the end-systolic and end-diastolic phases. Left atrial volume, which is used as a marker of diastolic function in hemodialysis patients, was calculated by using single-plane Simpson’s method from the apical 4-chamber view.

Regional Wall Motion Analysis. Regional contractility or wall motion of the LV is graded by dividing the LV into segments. In 1989, a 16-segment model was recommended by the American Society of Echocardiography.⁷ In this model, LV is divided into 3 levels (basal, mid or papillary, and apical levels). Each basal and mid level is further divided into 6 segments, including anteroseptum, anterior, lateral, inferolateral, inferior, and inferoseptal segments. Apex is divided into 4 segments as anterior, lateral, inferior, and septal segments. We used this model of myocardial segmentation for cardiac imaging in our study.⁷⁻⁹

A numeric scoring system has been adopted based on the contractility of the individual segments. In this scoring system, higher scores indicate more severe wall motion abnormality: (1) normal, (2) hypokinesia, (3) akinesia, (4) dyskinesia, and (5) aneurismal. Wall motion score index (WMSI) is derived by dividing the sum of the wall motion scores by the number of visualized segments. This index represents the extent of regional wall motion abnormalities. Normal WMSI is 1. Blood pressure was continuously controlled during the study using a noninvasive blood pressure monitor.

Table 1. Characteristics of Patients With and Without Intradialytic Hypotension*

Variables	Hemodialysis Patients		P
	With IDH	Without IDH	
Mean age, y	55.5 ± 16.0	43.1 ± 10.0	.06
Sex			
Male	6 (50.0)	10 (66.7)	
Female	6 (50.0)	5 (33.3)	.32
History of diabetes mellitus	5 (41.7)	3 (20.0)	.34
History of CCU admission	4 (33.3)	1 (6.7)	.21
History of coronary angiography	1 (8.3)	0	
History of hypertension	5 (42.7)	4 (26.7)	.08

*Values are numbers (%) except for age. IDH indicates intradialytic hypotension and CCU, cardiac care unit.

Statistical Analysis

Continuous variables with normal distribution were analyzed using the Student *t* test. The Mann-Whitney test was used for analyzing nonparametric variables. The calculated power of the study was 70%. *P* values less than .05 were considered significant.

RESULTS

Two hours after the beginning of hemodialysis, significant increment in the regional wall motion abnormality score was seen in IDH-prone patients compared to normotensive ones. Decrease in systolic blood pressure and increase in regional wall motion abnormality were accompanied.

There was no significant difference in the left ventricular end-diastolic diameters between the two studied groups during hemodialysis (Table 2). End-systolic diameters in the two studied groups are shown in Table 2. When evaluating the difference regarding the fractional shortening, only 30 minutes after hemodialysis, we found a nearly significant difference between the two studied groups (Table 3).

Ejection fraction did not show any significant difference before and during hemodialysis between

the two studied groups, except for the postdialysis period, which was significantly higher in patients without experiencing hypotension during a dialysis session (Table 4). Regional wall motion abnormality at 120 minutes of hemodialysis showed a significant difference between the two groups; it preceded any decrease in the LV EF (Table 5). The median regional wall scores were significantly higher in those prone to IDH at 120 minutes of dialysis (Table 6). The mean systolic blood pressure in different interval periods, including before, during, and after hemodialysis was significantly lower in the patients with IDH compared with the control group (*P* < .001). Regional wall motion abnormality preceded any reduction in the ejection fraction and fractional shortening. On the other hand, reduction in the mean systolic blood pressure and increment in regional wall motion abnormality were accompanied.

Table 2. Left Ventricular End-Diastolic and End-Systolic Diameters at Different Interval Periods*

Diameter, mm	Hemodialysis Patients		<i>P</i>
	With IDH	Without IDH	
End diastolic			
Before dialysis	48.66 ± 6.52	49.71 ± 5.13	.65
60 minutes	48.58 ± 6.58	50.42 ± 4.75	.43
120 minutes	48.33 ± 6.80	49.92 ± 5.01	.50
30 minutes after dialysis	48.83 ± 7.67	50.00 ± 5.42	.66
End systolic			
Before dialysis	34.16 ± 7.49	33.50 ± 5.90	.80
60 minutes	34.66 ± 7.52	34.35 ± 6.04	.91
120 minutes	35.16 ± 8.07	33.92 ± 6.52	.67
30 minutes after dialysis	36.41 ± 7.46	34.21 ± 6.50	.43

*IDH indicates intradialytic hypotension.

Table 3. Fractional Shortening at Different Interval Measurements*

Median Fractional Shortening, %	Hemodialysis Patients		<i>P</i>
	With IDH	Without IDH	
Before dialysis	31	33	.49
60 minutes	31	32	.40
120 minutes	31	32	.46
30 minutes after dialysis	26	32	.05

*IDH indicates intradialytic hypotension.

Table 4. Left Ventricular Ejection Fraction at Different Interval Measurements*

Median Ejection fraction, %	Hemodialysis Patients		<i>P</i>
	With IDH	Without IDH	
Before dialysis	67	68	.98
60 minutes	67	67	.71
120 minutes	63	66	.19
30 minutes after dialysis	50	65	.04

*IDH indicates intradialytic hypotension.

Table 5. Regional Wall Motion Abnormality at Different Interval Measurements*

Median RWMA Score	Hemodialysis Patients		<i>P</i>
	With IDH	Without IDH	
Before dialysis	16	16	.14
60 minutes	16	16	.12
120 minutes	22	16	.004
30 minutes after dialysis	24	16	.004

*IDH indicates intradialytic hypotension and RWMA, regional wall motion abnormality.

Table 6. Systolic Blood Pressure at Different Interval Measurements*

Blood Pressure, mm Hg	Hemodialysis Patients		<i>P</i>
	With IDH	Without IDH	
Before dialysis	154.4 ± 8.2	155.1 ± 16.5	.88
60 minutes	137.0 ± 15.3	161.5 ± 17.6	.001
120 minutes	115.8 ± 10.2	166.4 ± 17.3	< .001
30 minutes after dialysis	113.7 ± 8.0	164.5 ± 15.7	< .001

*IDH indicates intradialytic hypotension.

DISCUSSION

This study shows that remarkable abnormality in LV regional wall motion occurred during hemodialysis in hypotension-prone patients and it probably led to the LV dysfunction. The LV dysfunction that develops during hemodialysis is probably caused by myocardial ischemia. Previous studies suggested that hemodialysis may induce subclinical myocardial ischemia.^{4,10} We did not confirm the occurrence of subclinical myocardial ischemia by cardiac radioisotope scanning or cardiac angiography. However, our study showed that subclinical myocardial ischemia might lead to regional wall motion abnormality, which would precede intradialytic hypotension.

Left ventricular regional wall motion abnormality occurs following the physiological and/or pharmacological stress secondary to the ischemia. This precedes clinical symptoms and electrocardiographic changes. In this regard, the idea of stress echocardiography was formed, and it was used in clinical practice.¹¹⁻¹⁸ In our study, increased regional wall motion abnormality score and index 30 minutes after hemodialysis was consistent with the hypothesis of stunning occurrence. Unfortunately, we did not measure myocardial blood flow and LV function simultaneously during and after hemodialysis to confirm the occurrence of myocardial stunning. This is one of the limitations of our study.

Larger numbers of new regional wall motion abnormalities in patients prone to IDH could be explained by their demographic characteristics as suggested by the other studies.¹⁹ Although all patients prone to IDH had LV hypertrophy (LVH), and 5 of 12 patients had documented diabetes mellitus, these are not uncommon findings in long-term dialysis patients. The two groups of our study were not significantly different regarding the presence of LVH and history of diabetes mellitus. Therefore, these factors could not be an explanation for the high regional wall motion abnormality score preceding the occurrence of hypotension in the IDH-prone group.

Because we did not conduct a coronary angiography for the patients, establishing a correlation between the severity of a large coronary vessel disease and the echocardiographic data is impossible. Some other studies performed this assessment.²⁰⁻²⁴ Selby and McIntyre²⁵ showed

a significant number of regional wall motion abnormalities persisting at 30 minute postdialysis, when the conditions favoring to the development of ischemia during dialysis had been removed. This could be interpreted as preliminary evidence of dialysis-induced myocardial hibernation. Therefore, the occurrence of subclinical ischemia in response to the dialysis with sustained but reversible abnormalities in regional function could potentially contribute to the genesis of uremic cardiac failure, particularly if the ischemic insult is repeated up to 3 times per week. Several studies present different explanations for IDH; LVDD was proposed as a risk factor for IDH.²⁶ Barberato and colleagues found an association between left atrium enlargement and intradialytic hypotension,²⁷ while an excessive interdialytic weight gain, decreased ejection fraction, and low left ventricular volume were also mentioned independent risk factors for intradialytic hypotension.²⁸ One study reached the results that argued against a role for reduced myocardial contractility in the genesis of intradialytic hypotension.²⁹

In our study, EF did not significantly differ in the baseline, during hemodialysis, and half an hour after hemodialysis in patients prone to IDH compared to patients without IDH. This may be because myocardial stunning persists and somehow accentuates after hemodialysis. Furthermore, persistent hypotension and increased regional wall motion abnormality score and index are consistent with this hypothesis. The same theory may explain a significant difference in fractional shortening between the two groups, 30 minutes after hemodialysis. Ejection fraction did not decrease during the two hours of hemodialysis despite the development of regional wall motion abnormalities. This occurred perhaps because of increased LV fractional shortening during increased stress in the hypotensive group. In addition, this phenomenon was seen during hemodialysis, as reported by Selby and coworkers.²⁵ It corresponds to the better preservation of stroke volume and cardiac output during and after hemodialysis in IDH-prone patients. This may suggest that in regions without ischemia, function increases in short-term in response to the hemodynamic stress of dialysis. When this stress terminates, fractional shortening and ejection fraction decreases in all patients. This reduction is significantly more

pronounced in hypotensive patients compared to normotensive ones.

Our study has some limitations. Sample size was small; thus, such a study needs to be performed with a larger number of patients. In echocardiography, we used parasternal long and short axis views to determine the regional wall motion abnormality score and index. These all are operator-dependent. We did not evaluate subclinical myocardial ischemia, which may lead to the regional wall motion abnormality by cardiac radioisotope scanning or angiography. However, the study is repeatable and our results are quantitative. It was a short-term study. Therefore, any long-term effects of dialysis-induced regional wall motion abnormalities on cardiac dysfunction were undetermined.

CONCLUSIONS

This study shows that reversible myocardial dysfunction occurs during hemodialysis. It may be contributed to the IDH. In addition, we showed that regional wall motion abnormality was significantly less in patients without IDH. This suggests that confronting with IDH may prevent cardiovascular dysfunction. More studies with large sample sizes along with utilizing more accurate and sensitive modalities such as computed tomography angiography are required.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Weiner DE, Sarnak MJ. Cardiovascular disease in patients with chronic kidney disease. In: Pereira BJG, Sayegh MH, Blake P, editors. *Chronic kidney disease, dialysis and transplantation*. 2nd ed. Philadelphia: WB Saunders; 2005. p. 158-73.
- Boon D, van Montfrans GA, Koopman MG, Krediet RT, Bos WJ. Blood pressure response to uncomplicated hemodialysis: the importance of changes in stroke volume. *Nephron Clin Pract*. 2004;96:82-7.
- Daugirdas JT, Blake PG, Todd S, Hagerstown MD. *Handbook of dialysis*. 4th ed. Lippincott Williams and Wilkins. 2007. p. 482-3.
- Singh N, Langer A, Freeman MR, Goldstein MB. Myocardial alterations during hemodialysis: Insights from new noninvasive technology. *Am J Nephrol*. 1994;14:173-81.
- Oh JK, Steward JB, Tajik AJ. *The echo manual*. 3th ed. Philadelphia: Lippincott-Raven Publishers; 2006. p. 382.
- Fuster V, O'Rourke RA, Walsh RA, editors. *Hurst's the heart*. 11th ed. New York: McGraw-Hill; 2004. p. 1999-2007.
- Schiller NB, Shah PM, Crawford M, et al. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiography*. 1989;2:358-67.
- Cerqueira MD, Weissman NJ, Dilsizian V, et al. American Heart Association Writing Group on Myocardial Segmentation and Registration for Cardiac Imaging. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation*. 2002;105:539-42.
- Edwards WD, Tajik AJ, Seward JB. Standardized nomenclature and anatomic basis for regional tomographic analysis of the heart. *Mayo Clin Proc*. 1981;56:479-97.
- Mohi-ud-din K, Bali HK, Banerjee S, Sakhuja V, Jha V. Silent myocardial ischemia and high-grade ventricular arrhythmias in patients on maintenance hemodialysis. *Ren Fail*. 2005;27:171-75.
- Flachskampf FA, Rost C. Stress echocardiography in known or suspected coronary artery disease: an exercise in good clinical practice. *J Am Coll Cardiol*. 2009;53:1991-2.
- Cody DV, Tsicalas M, Davie AJ, Morton AR. Significance of prolonged left ventricular wall motion abnormalities after exercise echocardiography following non-Q-wave acute myocardial infarction. *Am J Cardiol*. 1997;80:1139-43.
- Barnes E, Dutka DP, Khan M, Camici PG, Hall RJ. Effect of repeated episodes of reversible myocardial ischemia on myocardial blood flow and function in humans. *Am J Physiol Heart Circ Physiol*. 2002;282:1603-8.
- Camici PG, Rimoldi OE. The contribution of hibernation to heart failure. *Ann Med*. 2004;36:440-7.
- Satyan S, Rocher LL. Impact of kidney transplantation on the progression of cardiovascular disease. *Adv Chronic Kidney Dis*. 2004;11:274-93.
- Wali RK, Wang GS, Gottlieb SS. Effect of kidney transplantation on left ventricular systolic dysfunction and congestive heart failure in patients with end-stage renal disease. *ACC Curr Rev*. 2005;14:38-9.
- Edwards NC, Hirth A, Ferro CJ, Townend JN, Steeds RP. Subclinical abnormalities of left ventricular myocardial deformation in early-stage chronic kidney disease: The precursor of uremic cardiomyopathy? *Journal of the American Society of Echocardiography*. 2008;21:1293-1298.
- Frangogiannis NG. The pathological basis of myocardial hibernation. *Histol Histopathol*. 2003;18:647-55.
- Rubinger D, Revis N, Pollak A, Luria MH, Sapoznikov D. Predictors of haemodynamic instability and heart rate variability during haemodialysis. *Nephrol Dial Transplant*. 2004;19:2053-60.
- Ichimaru K, Horie A. Microangiopathic changes of

- subepidermal capillaries in end-stage renal failure. *Nephron*. 1987;46:144-9.
21. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation*. 2005;111:472-9.
22. Mallamaci F, Tripepi G, Maas R, Malatino L, Boger R, Zoccali C. Analysis of the relationship between norepinephrine and asymmetric dimethyl arginine levels among patients with end-stage renal disease. *J Am Soc Nephrol*. 2004;15:435-41.
23. Converse RL Jr, Jacobsen TN, Jost CM, et al. Paradoxical withdrawal of reflex vasoconstriction as a cause of hemodialysis-induced hypotension. *J Clin Invest*. 1992;90:1657-65.
24. Nolan J, Flapan AD, Capewell S, MacDonald TM, Neilson JM, Ewing DJ. Decreased cardiac parasympathetic activity in chronic heart failure and its relation to left ventricular function. *Br Heart J*. 1992;67:482-5.
25. Selby NM and McIntyre CW. The acute cardiac effects of dialysis. *Semin Dial*. 2007;20:220-8.
26. Rostoker G, Griuncelli M, Loridon C, Benmaadi A, Illouz E. Left ventricular diastolic dysfunction as a risk factor for dialytic hypotension. *Cardiology*. 2009;114:142-9.
27. Barberato SH, Misocami M, Pecoits-Filho R. Association between left atrium enlargement and intradialytic hypotension: role of diastolic dysfunction in the hemodynamic complications during hemodialysis. *Echocardiography*. 2009;26:767-71.
28. Takeda A, Toda T, Fujii T, Sasaki S, Matsui N. Can predialysis hypertension prevent intradialytic hypotension in hemodialysis patients? *Nephron Clin Pract*. 2006;103:137-43.
29. Ie EH, Krams R, Vletter WB, Nette RW, Weimar W, Zietse R. Myocardial contractility does not determine the haemodynamic response during dialysis. *Nephrol Dial Transplant*. 2005;20:2465-71.

Correspondence to:
Reza Hekmat, MD
Department of Nephrology, Ghaem Hospital, Mashhad, Iran
E-mail: drhekmatreza@yahoo.com

Received February 2010
Revised July 2010
Accepted October 2010