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Journal

Hemodialysis International, 18(2)

ISSN

1492-7535

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Publication Date

2014-04-01

DOI

10.1111/hdi.12111

Peer reviewed

Published in final edited form as:
Hemodial Int. 2014 April ; 18(2): 396–405. doi:10.1111/hdi.12111.

Determinants of Hemodialysis-Induced Segmental Wall Motion Abnormalities

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Abstract

Background—Patients who demonstrate worsening of cardiac wall motion (WM) during hemodialysis have higher one-year mortality. We sought to identify risk factors for dialysis-induced WM abnormalities. Additionally, we examined the effects of hemodialysis on other parameters of cardiac function.

Methods—Forty patients underwent echocardiography directly before dialysis and during the last hour of dialysis (79 dialysis sessions). Candidate predictors for intradialytic worsening of WM included age, a history of heart failure (HF) or coronary artery disease, changes in blood pressure or heart rate, high sensitivity cardiac troponin T (hs-TnT) and N-terminal brain natriuretic peptide (NT-proBNP).

Results—Among 40 patients, WM worsened segmentally in 8 patients (20%), worsened globally in 1(3%), and improved segmentally in 4(10%). Diastolic function worsened in 44% of patients, and left ventricular ejection fraction was largely unchanged during dialysis. The case of globally worsened WM occurred in the setting of intradialytic hypertension in a patient without heart failure. Surprisingly, history of coronary artery disease, hemodynamics, and serologic factors were not associated with worsened segmental WM during dialysis. After adjustment for history of coronary artery disease and other cardiac risk factors, patients with a history of HF had a 3-fold higher risk of worsening segmental WM during dialysis (RR 3.1, 95%CI [1.1, 9], p=0.04).

Conclusions—In conclusion, patients with a history of clinical HF were at higher risk of intradialytic worsening of segmental WM. Further studies are needed to determine the mechanism of this association and whether cardioprotective medications could ameliorate this adverse cardiac effect of hemodialysis.

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Conflict of Interest Statement: Nelson Schiller is a consultant to Cardiocore for projects unrelated to the current manuscript. The other authors have no financial conflicts of interest to declare.

Keywords

heart failure; end stage renal disease; hemodialysis

Introduction

The mortality rate of persons with end-stage renal disease undergoing hemodialysis exceeds 25% during the first year following initiation of dialysis, and over one-third of these deaths are due to cardiovascular disease (1). Although hemodialysis provides vital control of blood volume and electrolytes, it also presents a distinct cardiovascular challenge. Prior studies have shown that myocardial stunning, seen as worsening of regional wall motion on echocardiography, can occur during dialysis and persist for at least 30 minutes after dialysis (2). Many patients with end-stage renal disease have wall motion (WM) abnormalities prior to initiation of renal replacement therapy. Intradialytic development of new WM abnormalities or worsening of pre-existing abnormalities is associated with long-term deterioration of left ventricular ejection fraction and higher overall mortality (2, 3); our group has shown that patients with worsening of WM during dialysis may be more prone to post-dialysis fatigue (4). A prior history of clinical heart failure (HF) is common among patients on hemodialysis (1, 5) and is also associated with higher mortality (1, 6). Whether a clinical history of HF is a risk factor for worsened WM during dialysis is unknown.

Our primary objectives were to describe the prevalence of dialysis-induced worsening of WM in a cohort of patients on stable thrice weekly hemodialysis and to identify risk factors and biomarkers of ischemia (high sensitivity troponin T (hs-TnT)) and wall stress (N-terminal brain natriuretic peptide (NT-proBNP)) that might be associated with dialysis-induced WM abnormalities. As a secondary objective, we evaluated other parameters of cardiac function during dialysis, including left ventricular ejection fraction and diastolic function. Identification of persons at risk for dialysis-induced WM abnormalities is important and timely, given the growing end-stage renal disease population. Such information might allow for more cost-effective application of potential therapies to reduce morbidity and mortality, including modifications of the dialysis procedure. Treatments that involve a more gradual removal of fluid (such as daily or nocturnal hemodialysis) may cause fewer WM abnormalities than thrice weekly dialysis (7). However, the cost of this therapy may prohibit widespread use; if effective, alterations of medication regimens may be a more accessible option for some patients.

Methods

Participants

We recruited and studied forty patients on chronic hemodialysis from the San Francisco Veterans Affairs Medical Center (SFVAMC), San Francisco General Hospital, and University of California San Francisco (UCSF)-Mt. Zion Hospital between February 2010 and February 2011. To be included, patients had to be on a stable chronic hemodialysis regimen. Exclusion criteria were as follows: NYHA class III or IV, significant valvular disease, current treatment for infection, major surgery within 1 month, newly diagnosed or metastatic cancer, myocardial infarction within the last 6 months, active angina, ongoing cocaine or intravenous drug use, current chemotherapy, or cognitive deficit limiting ability to give informed consent. Thirty-five eligible patients declined to participate, usually citing the difficulty of traveling to the SFVAMC for dialysis sessions. The protocol was approved by the UCSF Committee for Human Research and the SFVAMC Research and Development Committee, and patients gave written informed consent.

Protocol

Each participant underwent echocardiography before and during dialysis. Twenty-nine participants underwent echocardiography during two dialysis sessions; eleven had fewer or more sessions. Although patients were recruited from several dialysis centers, all patients received study-related dialysis at the SFVAMC Hemodialysis Unit, using their routine dialysis prescription comprising either 3 or 3.5 hours dialysis at standard temperature (37 °C). No patients were prescribed midodrine. Patients were studied during the 2nd or 3rd dialysis session of the week; we avoided the first dialysis session of the week, which follows a two-day break between dialysis sessions.

Measurements

Predictors—Data on demographics, comorbidities and medications were collected from the medical record. History of being hospitalized with HF was adjudicated by a physician (RD), who was blinded to intradialytic changes in WM. Hospitalization was deemed to be due to HF if this was the principal diagnosis on the discharge summary, if there was no diagnosis listed such as pneumonia, asthma, or other illnesses that could have led to shortness of breath, and if reduced left ventricular ejection fraction or diastolic dysfunction at or near the time of hospitalization for HF was documented on echocardiogram. HF with reduced left ventricular ejection fraction was defined as history of HF and left ventricular ejection fraction <55% on the echocardiogram performed closest to the date of hospitalization for HF; HF with preserved left ventricular ejection fraction was defined as history of HF with left ventricular ejection fraction ≥ 55% and abnormal diastolic function on the echocardiogram performed closest to the date of hospitalization. The echocardiogram closest to the date of hospitalization for HF was used because HF is a clinical diagnosis and we intended to describe the history of HF as systolic or diastolic. For all subsequent analyses, the pre-dialysis echocardiogram performed for this study was used to quantify left ventricular ejection fraction and diastolic function. Patients with a history of myocardial infarction, coronary stenting or bypass were considered to have a history of coronary artery disease. Intradialytic blood pressure, heart rate and ultrafiltration were abstracted from dialysis treatment records. Three parameters were used to estimate volume status: 'pre-dialysis weight – dry weight,' 'weight gain since last dialysis,' and inferior vena caval (IVC) index. IVC index was calculated as {(expiratory IVC diameter)-(inspiratory IVC diameter))/(expiratory IVC diameter)} × 100%. For all patients, routine monthly laboratory work processed at the patients' regular dialysis units was utilized for values of plasma calcium, phosphorus, parathyroid hormone, albumin and Kt/V (a measure of dialysis efficiency based on urea removal). Blood was collected directly before dialysis for measurement of NT-proBNP and hs-TnT. Assays for NT-proBNP and hs-TnT were performed at the University of Maryland Clinical Chemistry Laboratories. The Roche NT-proBNP assay (Roche Diagnostics, Indianapolis, Indiana) has an analytical range of 5 to 35,000 pg/ml and coefficient of variation of <10% within this range. The Roche Elecsys immunoassay for cardiac troponin T has an analytical range of 3 to 10,000 ng/L, and a coefficient of variation of 9% at 13.5 ng/L (the 99th percentile in a healthy reference group.) (8)

Outcomes—Left ventricular wall motion was scored from formal echocardiograms performed by a trained sonographer, immediately before dialysis and then during the last hour of dialysis on the same day using a Siemens Sequoia Model C512 with a 3.5 MHz transducer. Date, time and patient identification were removed from echocardiograms, which were then submitted in random order to an established reading center (Cardiocore Labs, Daly City CA). Echocardiograms were read by a single blinded reader (D.A.) who has demonstrated >90% intra-reader agreement in other cohorts. One set of echocardiograms was excluded for poor image quality, leaving 158 echocardiograms (79 dialysis sessions/40 patients) for analysis. The wall motion of each of the 16 myocardial segments was scored as

1 for normal, 2 for hypokinetic, 3 for akinetic, and 4 for dyskinetic. The sum score of all 16 segments represented the WM score for each echocardiogram. Pre- and post-dialysis echocardiograms were then matched by code and compared for WM score. If the score increased during dialysis, then it was described as "worsened;" if the score remained the same, "no change;" if the score decreased, "improved." Worsened WM scores were further classified as "segmentally worsened" if one or more segments in the same coronary territory worsened, and "globally worsened" if ≥15 segments worsened. Left ventricular mass was measured using a truncated ellipsoid technique (9), then indexed to body surface area calculated by Mosteller formula (10). End diastolic volume (EDV) and end systolic volume (ESV) were measured from images obtained in the parasternal short axis and apical two- and four-chamber views, and calculated according to the biplane method of discs (modified Simpson's rule) (9). ESV index was calculated as ESV/body surface area (ml/m^2), using the pre-dialysis ESV and weight. Diastolic function was determined from E to A ratio (E/A), mitral deceleration time, pulmonary vein flow, and Doppler tissue imaging using E to E′ ratio (E/E′). Impaired relaxation was defined as E/A < 1.0; pseudonormalization defined as E/A >1.0 with diastolic dominant pulmonary vein flow or E/E′ >10; restrictive diastolic function was defined as E/A > 1.5 with diastolic dominant pulmonary vein flow or E/E′>10 and mitral deceleration time <150 milliseconds. E/E′ measured by Doppler tissue imaging was also analyzed as a continuous variable; it has been shown to have a high correlation with left ventricular filling pressures (11, 12) and may be correlated with diastolic function.

Statistical Analysis

First, we described patient characteristics and summarized intradialytic changes in blood pressure, heart rate, biomarkers and cardiac function in the study cohort. In order to determine the prevalence of worsened, unchanged or improved WM score, we used the average change in WM score for patients who had more than one dialysis session. Of those that worsened, we identified which cases worsened globally and which worsened segmentally. We viewed the globally worsened case separately because we hypothesized that the mechanisms for this pattern of WM change would be different from that of segmental WM changes. For analysis of relative risk of segmentally worsened WM score, we excluded this globally worsened case, and utilized the remaining 78 dialysis sessions. Dialysis sessions were grouped as being associated with "improved or unchanged WM score" or "segmentally worsened WM score." We tested the relative risk of potential covariates with worsened segmental WM using generalized linear models, with a Poisson working model to account for clustering from participants with more than one dialysis session. Multivariable regression was carried out for covariates associated with the outcome with p≤0.2. We adjusted for these same covariates (age, history of heart failure, baseline heart rate, hemoglobin, use of angiotensin converting enzyme inhibitor or angiotensin receptor blocker (ACE/ARB), use of beta blockers, weekly epogen dose); in addition, we adjusted for history of coronary artery disease, given the plausible link with segmentally worsened WM; and we adjusted for change in mean arterial pressure during dialysis, given the previously observed association between hypotension and worsened WM (2). All analyses were performed using STATA 11 (StataCorp, College Station, TX, USA.)

Results

Characteristics of Study Participants

The mean age of our study cohort was 62 ±16 years; 45% of our participants had diabetes, 23% had a history of coronary artery disease (myocardial infarction, coronary stent, coronary artery bypass graft) and 45% had history of atherosclerosis (coronary artery disease, cerebral vascular attack, or peripheral vascular disease). Our cohort was 38% African American and 18% female. Six (15%) participants had a history of HF. Of the five

participants who had HF with reduced ejection fraction, average ejection fraction was 40%, and all had some degree of diastolic dysfunction. One participant had HF with preserved ejection fraction and pseudonormal diastolic function. Ten participants (25%) had segmental wall motion abnormalities at baseline. (Table 1)

Changes During Dialysis Among Study Participants

On average, mean arterial pressure decreased by 8 mmHg during dialysis, and heart rate was stable. No patients developed dyspnea or chest pain during dialysis. Among the forty participants, 8(20%) showed segmentally worsened WM, 1(3%) globally worsened WM, and 4(10%) improved WM. We evaluated intradialytic change in diastolic function in 32 patients (60 dialysis sessions). Using summary diastolic function (derived from E/A, mitral deceleration time, pulmonary veins and E/E′), diastolic function worsened in 14 (44%). Using E/E′ as a continuous variable, 10 (32%) patients had increased left ventricular filling pressures during dialysis compared to baseline. (Table 1) On average, changes in left ventricular ejection fraction were small; left ventricular ejection fraction improved in patients with improved WM score, but worsened in about half of patients with either unchanged or worsened WM score. The one patient with globally worsened WM was notable for an increase in mean arterial pressure during dialysis of +11 mmHg and decrease in left ventricular ejection fraction from 57% to 50%. This patient qualitatively had a more hypertensive response to dialysis than most other patients, although this did not reach statistical significance. Notably, this patient did not have a history of HF. (Table 2)

Association of Candidate Predictors with Segmentally Worsened WM Score

In univariate analyses, we found a strong association between history of HF and worsened segmental WM score (RR 3.4, 95%CI [1.4, 8.6], p=0.009). Left ventricular ejection fraction <45% and restrictive filling pattern were both associated with higher risk of WM abnormalities. The following covariates were not associated with worsened segmental WM: months on dialysis, history of coronary artery disease or diabetes, NT-proBNP, hs-TnT, or baseline WM abnormalities, change in mean arterial pressure or heart rate, or ultrafiltration. Surprisingly, volume status (measured either by patient weights or by IVC diameter) was not correlated with segmental WMA. Change in MAP was not associated with either worsened segmental WM or baseline WM (RR 0.99, 95% CI 0.97, 1.01, p=0.15). After multivariate adjustment, the associations of history of HF with higher risk of worsened WM and ACE/ARB and beta blockers with lower risk of worsened WM remained statistically significant. (Table 3) While we lacked power to detect an interaction between medications and a history of HF, we did perform analysis for univariate risk of segmental WM abnormalities in subgroups of patients with and without heart failure. Of the 6 patients with heart failure, 4 (67%) were on ACE/ARB, and 5(83%) had segmental WM. In patients with heart failure, two of the four on ACE/ARB had segmental WM (RR of segmental WM associated with ACE/ARB 0.56, 95% CI (0.25, 1.2), p=0.14). Of the 34 patients without HF, 12 (35%) were on ACE/ARB, and 4 (33%) had segmentally worsened WM. Of the patients without HF, none of those on ACE/ARB had dialysis-induced WM abnormalities (RR of segmental WM associated with ACE/ARB <0.001, 95%CI (4×10^{-8}, 3×10^{-7}), p<0.001).

Discussion

In this study, a history of heart failure was the only clinical factor associated with intradialytic development or worsening of segmental WM abnormalities; surprisingly, changes in blood pressure and heart rate, ultrafiltration, atherosclerotic disease, hs-TnT and NT-proBNP were not useful in identifying patients with dialysis-induced worsening of WM. Additionally, we demonstrated that WM may worsen in either segmental or global patterns during dialysis and that diastolic function may worsen during hemodialysis.

Prior investigators have demonstrated an association between worsening WM during dialysis and long-term deterioration in left ventricular ejection fraction (2). In our six patients with a history of HF and reduced left ventricular ejection fraction, 4 had been diagnosed with HF prior to initiation of dialysis. In these patients, pre-existing systolic failure may predispose to development or worsening of WM abnormalities during dialysis sessions. A potential explanation for this finding is that patients with systolic failure have increased wall stress and are more susceptible to myocardial ischemia due to the hemodynamic fluctuations and other perturbations related to hemodialysis. This adverse effect may be exacerbated by the increased neurohormonal activation during dialysis, including excess sympathetic stimulation. As myocardial oxygen consumption increases, these patients would become more vulnerable to cardiac ischemia. A plausible mechanism for a protective effect of beta blockers in these patients would be via a reduction in sympathetic stimulation. In patients with predominantly diastolic failure, a potential link between dialysis-induced WM abnormalities and HF would be through repeated ischemia, leading over repeated episodes to increased fibrosis and ventricle stiffening. Longitudinal studies are needed to elucidate the mechanism of association between history of HF and intradialytic worsening of segmental WM in patients with end-stage renal disease.

ACE/ARB use was associated with a lower risk of worsened WM during dialysis, even after adjustment for comorbidities and left ventricular mass index. Antagonists of the renin-angiotensin system are thought to be cardioprotective via reduction of cardiac hypertrophy and fibrosis caused by angiotensin II, as well as through beneficial effects on vascular endothelium caused by increasing levels of bradykinin, a potent stimulator of nitric oxide synthesis (13). Valsartan and ramipril have been shown to lower asymmetric dimethylarginine (ADMA) and improve endothelial function in persons with CKD (14, 15). By increasing bradykinin or lowering ADMA, ACE-inhibitors may improve coronary endothelial function and the ability of the heart to maintain perfusion during dialysis. Alternatively, our findings regarding ACE/ARB and BB may reflect a selection bias. Patients who are unable to tolerate ACE/ARB or beta blockers may have had these medications withdrawn because they were less able to tolerate hemodynamic fluctuations. This bias would confound the association between these medications and the lower rate of induced WM abnormalities. Nevertheless, our data raise the possibility that use of ACE/ARB or beta blockers could reduce the risk of worsened WM during dialysis. While daily (as opposed to thrice weekly) dialysis sessions may be associated with lower risk of worsened WM (7), alterations in medication regimen may be more feasible and cost-effective for some patients.

To our knowledge, we are the first to report that WM may improve during dialysis. Compared to participants with unchanged or worsened WM, those with improved WM tended to have an increase in ejection fraction. We interpret this as suggesting that some patients experience improved coronary perfusion during hemodialysis, possibly as a result of decreased afterload due to fluid removal. We hoped to reveal biomarker evidence of this by measuring baseline hs-TnT, but did not. In addition to changes in WM, we report on changes of diastolic function during dialysis. While on average, diastolic function (measured by E/E′) did improve, we found that worsening of diastolic function occurred in more patients than did worsened segmental WM. The prevalence of worsened diastolic function is in concordance with Assa's prior study (16). It is possible that intradialytic ischemia causes stiffening of the ventricle, thereby reducing E′. Worsened diastolic function was not correlated with worsened segmental WM.

The prevalence of dialysis-induced WM abnormalities in our cohort is comparable to a recent study by Assa *et al*. in which the prevalence of dialysis-induced WM abnormalities was 27%(3), but lower than the 64% prevalence observed by McIntyre's group (2). These

differences may be methodological; Assa *et al*. and our group manually read WM in 16 cardiac segments, whereas McIntyre *et al*. utilized automatic border detection and defined abnormal WM as a decline of >20% in shortening fraction compared to baseline (2, 17). Interestingly, additional similarities with Assa's study include the association of low baseline ejection fraction with WM abnormalities and the lack of association of intradialytic hemodynamic changes or ultrafiltration with development of WM abnormalities. Similarly to our findings, McIntyre's group has shown that pre-dialysis NT-proBNP levels do not predict worsening WM abnormalities in concurrent dialysis sessions (18). In contrast to our data on hs-TnT, McIntyre's group found that troponin T, assayed with the fourth generation troponin T assay, was associated with worsened WMA (19). Notably, both the troponin T assay and the method of measuring WM abnormalities were different in this prior cohort. Additional differences between the studies include the higher percentage of African Americans in our cohort, and the higher prevalence of WMA in the prior cohort. It is possible that the discordant findings related to troponin T in these two groups are due to methodology, differences in disease distribution, or racial differences in production of troponin T. Clarification of this issue would require further studies of troponin T production in racially diverse ESRD populations.

Strengths of our study include the rigor of echocardiographic measures, as well as the similarities between our cohort and the United States Renal Disease System end-stage renal disease population (particularly in regard to age, prevalence of diabetes or atherosclerosis, and high proportion of African Americans) (20). Baseline hs-TnT of 62 pg/ml (47–86) was comparable to that of an end-stage renal disease cohort of similar age (hs-TnT of 43 pg/ml (11–98)) (21). Prevalence of intradialytic WM was equivalent to prior work (3). Thus, we have no reason to believe our results would not generalize to other end-stage renal disease cohorts.

Important limitations of our study include the predominantly male cohort, and the sample size. Due to the cross-sectional design, we cannot assume causal relationships. The modest event rate (number of dialysis sessions with worsened WM) limited the number of covariates that we could include in multivariable analysis. We could not perform multivariable analysis for the risk ratio between nitrates and worsened WM, because no patients on nitrates had worsened WM. Residual renal function was not measured and could be an important risk factor for segmental WMA. Finally, atherosclerotic coronary disease was evaluated by medical history rather than left heart catheterization; therefore, we could not study the association between severity of atherosclerotic disease and resting or dialysis-induced WM abnormalities.

In conclusion, we found that history of HF was independently associated with worsened segmental WM during hemodialysis. ACE/ARB and beta blockers were associated with lower risk of worsened WM in our cohort, even after adjusting for comorbidities. Based on these findings, it is reasonable to speculate that patients with a history of HF, even once they are clinically compensated, are at risk for the negative prognostic impact of dialysis-induced WM abnormalities. These patients may benefit from therapies aimed at ameliorating cardiac ischemia during dialysis. Further studies are required to determine whether angiotensin antagonists or beta blockers are effective treatments in this setting. Additionally, as the mechanisms of dialysis-induced WM abnormalities are better understood, it will be important to consider whether the presence of worsened intradialytic WM is an indication for further cardiac diagnostic procedures.

Acknowledgments

Funding: Funding for this project came from the following sources. 1. Individual Investigator Grant, University of California San Francisco Academic Senate, San Francisco, CA 2. Grant Huntington Fund provided by the Research Evaluation and Allocation Committee in the University of California San Francisco, School of Medicine Dean's Office, San Francisco, CA. 3. National Institute of Diabetes and Digestive and Kidney Diseases, 1K24-DK085153-02 4. National Institute of Diabetes and Digestive and Kidney Diseases, 1K23-DK092354-01A1 5. UCSF Clinical and Translational Science Institute Grant Number UL1 TR000004 4. Roche Diagnostics Corporation (Indianapolis, Indiana) supplied reagents for the hs-TnT and NT-proBNP assays, but did not provide study funding.

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Table 1

Characteristics of Study Participants

Demographics and Comorbidities	N(%), Mean(±SD), Median (IQR)
Age (years)	62 (±16)
Women	7 (18%)
Race and ethnicity	
Non-Hispanic White	9 (23%)
African American	15 (38%)
Hispanic	6 (15%)
Filipino	4 (10%)
Other	6 (15%)
History of diabetes mellitus	18 (45%)
ESRD * **attributed to hypertension or diabetes**	25 (63%)
History of coronary artery disease †	9 (23%)
History of atherosclerosis ‡	18 (45%)
History of heart failure	7 (18%)
Months on dialysis	40 (14, 65)
Medications	
ACE-I or ARB §	17 (43%)
Beta blocker	30 (75%)
Statin	19 (48%)
Nitrates	5 (13%)
Epogen dose (units per week)	6000 (280, 13000)
Baseline measurements	
Systolic blood pressure (mmHg)	144 (±25)
Diastolic blood pressure (mmHg)	76 (±14)
Pre-dialysis weight – dry weight (kg)	2.6 (± 2.1)
Weight gain since last dialysis (kg)	2.0 (± 1.3)
Hemoglobin (g/dL)	11 (±1.2)
Kt/v ‖	1.5 (0.3)
Hs-TnT (pg/ml) #	62 (47, 86)
NT-proBNP (pg/ml) **	4040 (751, 10076)
Left ventricular ejection fraction	58% (±6)
Left ventricular mass index (g/m^2)	96 (81, 124)
IVC index (%) ¶	44% (±12)
Diastolic function	
Normal	12 (30%)
Impaired	17 (43%
Pseudonormal	4 (10%)
Restrictive	3 (8%)

Demographics and Comorbidities	N(%), Mean(±SD), Median (IQR)
Segmental wall motion abnormalities	10 (25%)
Intradialytic measurements	
Change in mean arterial pressure (mmHg)	−8(±16)
Change in heart rate (bpm)	0(±9)
Ultrafiltration (ml)	2461 (±1145)
Change in left ventricular ejection fraction (%)	0.0 (±4)
Change in E/E′ [#]	−1.3 (−2.7, 0)
Change in summary diastolic function (N, % of patients)	
Worsened	14 (44%)
Improved	15 (47%)
Change in wall motion (N, % of patients)	
Worsened, segmental	8 (20%)
Worsened, global	1 (3%)
Improved	4 (10%)

[*] end-stage renal disease

[†] defined as history of myocardial infarction, coronary stenting or coronary artery bypass graft

[‡] coronary artery disease, cerebral vascular attack, peripheral vascular disease

[§] angiotensin converting enzyme inhibitor or angiotensin receptor blocker

[||] K=clearance t=time on dialysis V=volume of distribution. Kt/V is a measure of dialysis adequacy

[#] high sensitivity troponin T

[**] N terminal prohormone of brain natriuretic peptide

[¶] IVC index = {((expiratory IVC diameter)-(inspiratory IVC diameter))/(expiratory IVC diameter)} × 100%

[#] E to E′ ratio

Table 2

Differences Among Patients Grouped by Average Change in Wall Motion Score*

		Change in wall motion score during dialysis				
		Improved	**No change**	**Worsened (segmental pattern)**	**Worsened (global pattern)**	**p-value (anova)**
Participants (N)		4	27	8	1	n/a
Change in WM† score (mean, (SD))		−0.3(0.6)	0.07(0.4)	1.8 (1.6)	16 (0)	<0.001
WM abnormality at baseline (%)		100%	19%	25%	0%	0.01
Change in WM occurred in a segment that		100%	n/a	13%	0%	n/a
was abnormal at baseline WM (%)						
Change in > 1 segment in same coronary artery territory (%)		25%	n/a	50%	100%	n/a
History of coronary artery disease‡ (%)		25%	22%	25%	0%	>0.99
History of heart failure (%)		0%	10%	38%	0%	0.2
MAP§ (mean, (SD))	baseline	110(4)	100(16)	100(23)	79(0)	0.3
	delta	−26(26)	−9(14)	−6(14)	11(0)	0.1
Heart rate (mean, (SD))	baseline	60(9)	68(10)	73(13)	73(0)	0.3
	delta	0(1)	0.4(8)	1(10)	6(0)	0.9
EDV‖ (mean, (SD))	baseline	160(22)	110(38)	120(50)	120(0)	0.2
	delta	−17(6)	−5(24)	−9(21)	−19(0)	0.8
ESV# (mean, (SD))	baseline	70(7)	47(20)	49(25)	52(0)	0.3
	delta	−13(4)	−0.9(12)	−5(9)	0(0)	0.3
LVEF (mean, (SD))**	baseline	55%(5)	58%(7)	60%(5)	54%(4)	0.5
	delta	+3%(2)	−0.02%(4)	+1%(4)	−7%(0)	0.5
E/E′	baseline	7.0(1.9)	8.1(3)	8(3.5)	6.8(1.6)	0.9
	delta	−0.7(0.9)	−1.3(2.3)	−0.8(1.2)	−1.8(0)	0.9

*If the participant had more than one dialysis session, the changes in score for the patient's dialysis sessions were averaged

†wall motion

‡defined as history of myocardial infarction, coronary stenting or coronary artery bypass graft

§mean arterial pressure

|| end diastolic volume

end systolic volume

** left ventricular ejection fraction

Table 3

Univariate and Adjusted Relative Risk of Segmentally Worsened Wall Motion Score*

	Univariate			Adjusted†		
	RR	**95% CI**	**p value**	**RR**	**95% CI**	**p value**
Demographics and comorbidities						
Age (years)	1.0	(0.98, 1.1)	0.2	1.0	(0.9, 1.0)	0.9
Months on dialysis	1.0	(0.99, 1.0)	0.4	---	---	---
History of coronary artery disease‡	1.3	(0.4, 3.7)	0.7	---	---	---
History of diabetes mellitus	0.8	(0.2, 2.4)	0.6	---	---	---
History of heart failure	3.4	(1.4, 8.6)	0.009	3.1	(1.1, 9)	0.04
Hemodynamics						
MAP§, pre-dialysis	1.0	(0.99, 1.0)	0.9	---	---	---
Change in MAP	1.0	(0.99, 1.0)	0.6	---	---	---
Heart rate, pre-dialysis	1.0	(0.99, 1.1)	0.2	1.0	(0.97, 1.1)	0.6
Change in heart rate	1.0	(0.99, 1.1)	0.6	---	---	---
Ultrafiltration (liter)	1.0	(0.6, 1.6)	>0.99	---	---	---
Pre-dialysis weight – dry weight (kg)	1.1	(0.91, 1.3)	0.4	---	---	---
Weight gain since last dialysis (kg)	1.1	(0.82, 1.5)	0.5	---	---	---
Medications						
ACE/ARB ‖	0.4	(0.95, 1.6)	0.2	0.16	(0.07, 0.4)	<0.001
Beta blocker	0.5	(0.18, 1.6)	0.2	0.29	(0.09, 0.9)	0.03
Aspirin	0.5	(0.15, 1.7)	0.3	---	---	---
Nitrates	<0.001	n/a	n/a	---	---	---
Weekly epogen dose (units)	1.0	(0.9, 1.0)	0.2	1.0	(0.99, 1.0)	0.4
Laboratory values						
Hemoglobin	1.5	(1, 2.1)	0.06	1.4	(0.8, 2.3)	0.2
Hs-TnT #	0.99	(0.98, 1.0)	0.3	---	---	---
NT pro-BNP **	0.99	(0.99, 1.0)	0.4	---	---	---
Baseline cardiac parameters						

	Univariate			Adjusted†		
	RR	**95% CI**	**p value**	**RR**	**95% CI**	**p value**
LV ¶ mass index	1.1	(0.9, 1.3)	0.3	---	---	---
IVC index	0.75	(0.007, 79)	0.9			
E/E′	0.9	(0.67, 1.2)	0.5			
LV ejection fraction >55%	ref	---	---	---	---	---
LV ejection fraction 46–55%	1.5	(0.5, 4.5)	0.5	---	---	---
LV ejection fraction <45%	3.4	(0.7, 15)	0.1	---	---	---
Normal diastolic function	ref	---	---	---	---	---
Impaired diastolic function	2.0	(0.4, 11)	0.4	---	---	---
Pseudonormal diastolic function	1.1	(0.1, 11)	0.9	---	---	---
Restrictive filling pattern	5.5	(1.3, 23)	0.02	---	---	---

*The patient with global changes (worsening in 16 segments) was excluded from analysis of relative risk

†Adjusted for age, history of coronary artery disease, history of heart failure, baseline heart rate, change in MAP, hemoglobin, use of angiotensin converting enzyme inhibitor or angiotensin receptor blocker, use of beta blockers, weekly epogen dose

‡defined as history of myocardial infarction, coronary stenting or coronary artery bypass graft

§mean arterial pressure

||angiotensin converting enzyme inhibitor or angiotensin receptor blocker

#high-sensitivity troponin T

**N terminal prohormone of brain natriuretic peptide

¶left ventricular