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ARTICLE ORIGINAL

Impact of Hemodialysis on Left Ventricular Function: Echocardiographic study before and after hemodialysis

Impact de l'Hémodialyse sur la fonction ventriculaire Gauche : Etude échocardiographique avant et après hémodialyse

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Summary

Introduction : Chronic renal failure (CRF) and hemodialysis (HD) treatment can lead to cardiac dysfunction. Echocardiography plays a crucial role in identifying early alterations in cardiac structure and function. This study aimed to assess the immediate effect of HD on left ventricular (LV) function in chronic dialysis patients using conventional echocardiography and 2D strain and to identify predictive factors for the global longitudinal strain (GLS) alteration in HD patients.

Methods: A prospective, single-center, cross-sectional study involving CRF patients in the HD stage was conducted at Military Hospital of Tunis from July 2020 to March 2021. Standard two-dimensional echocardiography (2D Echo) with an assessment of longitudinal myocardial deformation of the LV was performed 30 minutes before and after HD sessions to compare LV systolic function and myocardial deformation using GLS.

Results: Thirty-five patients were included, with an average age of 58.89 years and a sex ratio of 1.18. Significant decreases were observed post-HD in LV end-diastolic and end-systolic diameters (p=0.029 and p=0.001, respectively). All patients exhibited left ventricular hypertrophy. LV mass decreased significantly post-HD (p=0.037). LV ejection fraction was preserved pre and post-HD. Significant improvements were observed in diastolic function (p=0.006) with a notable decrease in left atrial volume after hemodialysis (p<0.001)). The GLS was impaired before and after HD hemodialysis (HD), with a notable deterioration post-HD (p=0.041), decreasing from -17.9±4.2 to -15.1±1.3. The multivariate analysis identified male gender, age over 60, diabetes, and LV mass as predictive factors for GLS alteration.

Conclusions: This study demonstrated the impact of HD on LV systolic and diastolic functions and the importance of 2D strain in detecting subclinical cardiac dysfunction. Further research is needed to identify predictive factors for GLS alteration before a decrease in LV ejection fraction.

Keywords

Echocardiography; Hemodialysis; strain, left ventricle

Résumé

Introduction: L'insuffisance rénale chronique (IRC) et l'hémodialyse (HD) peuvent entraîner des dysfonctions cardiaques. L'échocardiographie joue un rôle crucial dans l'identification précoce des altérations de la structure et de la fonction cardiaques. Le but de cette étude était d'évaluer l'effet immédiat de l'HD sur la fonction du ventricule gauche (VG) chez les patients dialysés chroniques, en utilisant l'échocardiographie conventionnelle et le 2D strain, et d'identifier les facteurs prédictifs de l'altération du Strain Global Longitudinal (SLG) chez les patients hémodialysés.

Méthodes : Une étude prospective, monocentrique et transversale, incluant des patients atteints d'IRC au stade d'HD, a été menée à l'Hôpital Militaire de Tunis de juillet 2020 à mars 2021. Une échocardiographie bidimensionnelle standard (2D Echo) avec une évaluation de la déformation myocardique longitudinale du VG a été réalisée 30 minutes avant et après les séances d'HD. L'objectif était de comparer la fonction systolique du VG et la déformation myocardique en utilisant le GLS.

Résultats : Trente-cinq patients ont été inclus, avec un âge moyen de 58,89 ans et un rapport homme/femme de 1,18. Des diminutions significatives ont été observées après l'HD pour les diamètres télédiastolique et télésystolique du VG (p=0,029 et p=0,001, respectivement). Tous les patients présentaient une hypertrophie ventriculaire gauche. La masse du VG a diminué de manière significative après l'HD (p=0,037). La fraction d'éjection du VG était préservée avant et après l'HD. Des améliorations significatives de la fonction diastolique ont été observées (p=0,006), avec une diminution notable du volume de l'oreillette gauche **après l'hémodialyse (p<0,001). Le GLS était** altéré avant et après l'HD, avec une détérioration notable après l'HD (p=0,041), passant de-17,9±4,2 à-15,1±1,3. L'analyse multivariée a identifié le sexe masculin, un âge supérieur à 60 ans, le diabète et la masse du VG comme des facteurs prédictifs de l'altération du GLS.

Conclusion : Cette étude a démontré l'impact de l'HD sur les fonctions systolique et diastolique du VG et l'importance du strain 2D pour détecter une dysfonction cardiaque infraclinique. Des recherches supplémentaires sont nécessaires pour identifier les facteurs prédictifs de l'altération du SLG avant qu'une diminution de la fraction d'éjection du VG ne se manifeste.

Mots-clés

Hémodialyse, ventricule gauche, échocardiographie, strain

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INTRODUCTION

End-Stage Renal Disease (ESRD) presents a major global public health challenge due to its chronic nature, high morbidity and mortality rates in hemodialyzed patients, and substantial healthcare costs. The mortality rate in patients undergoing hemodialysis (HD) is alarmingly 10 to 20 times higher than that of the general population [1], primarily driven by cardiovascular disease (CVD), which accounts for up to 40% of all-cause mortality in this patient group [2].

Echocardiographic indicators such as left ventricular hypertrophy (LVH) and left ventricular (LV) systolic and diastolic dysfunctions have been identified as independent predictive factors for the progression of cardiovascular issues in HD patients [3]. Transthoracic echocardiography (TTE), an accessible and non-invasive method, can detect changes induced by HD sessions, offering the possibility for treatment monitoring and adjustment.

Compared to conventional echocardiography, speckle tracking echocardiography (STE) is a more sensitive, objective, and reproducible modality for assessing cardiac function. It is particularly useful in patients with heart failure with preserved LV ejection fraction (LVEF) and in ESRD patients, as it can detect subclinical left ventricular systolic dysfunction [4]. This technique could therefore significantly enhance our understanding of ventricular function alterations associated with HD.

The objective of this study was to assess the immediate effect of HD on left ventricular function using conventional Doppler echocardiography. We also aim to explore the utility of STE in the early detection of myocardial dysfunction compared to conventional echocardiography and to identify the predictive factors for an alteration in Global Longitudinal Strain (GLS) in these chronically dialyzed patients.

METHODS

This was a prospective, descriptive, single-center, cross-sectional study conducted at the Military Hospital of Tunis. The study was a collaborative effort between the dialysis unit and the non-invasive explorations unit of the cardiology department, and it was carried out from July 2020 to March 2021.

Patients

We included patients with End-Stage Renal Disease (ESRD) who were 18 years or older, had been on hemodialysis via an arteriovenous fistula (AVF) for more than nine months, and underwent three sessions per week using a highly biocompatible membrane.

Patients were not included if they were on peritoneal dialysis, dialyzed via a central venous catheter, or required emergency dialysis. Patients with a history of cardiomyopathy, coronary artery disease, arrhythmia, more than moderate mitral or aortic valvular disease, a history of chemotherapy, congenital heart disease, intra-cardiac devices or cardiac surgery were also not included

Finally, we also excluded patients who refused to participate in the study, had poor echocardiographic windows, or were found to have significant valvulopathy, LV dysfunction, or segmental kinetic disorders during the initial TTE.

Protocol

Demographic, medical history, anthropometric data, and HD session duration were collected from medical records and patient interviews. Before and after each HD session, a physical examination was conducted on all patients to record blood pressure (BP), heart rate (HR), and weight. Serum levels of N-terminal pro-brain natriuretic peptide (NT-pro BNP), hemoglobin (Hb), ionogram, urea, and creatinine were also measured before and after the session.

A transthoracic echocardiography (TTE) was performed on all patients both before and after the HD session, following the guidelines of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) [5]. A single experienced cardiologist, blinded to all clinical data, performed all echocardiographies using a Vivid E9 (General Electric Medical Systems) device equipped with a 3.5 MHz transducer. All echocardiographic data were stored on a central memory unit for post-processing, with measurements adjusted by averaging the results of three to five cardiac cycles using the General Electric Echopac software.

The echocardiographic evaluations included:

- Measurements of LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), interventricular septum end-diastolic thickness (IVS), and posterior wall end-diastolic thickness (PWTD), obtained in M-mode from the parasternal long-axis view.
- LV mass (LVM) estimation using the cube formula, indexed to body surface area (BSA).

- LVEF assessment using the biplane Simpson's method from the apical four-chamber and two-chamber views.
- Evaluation of transmitral flow with pulsed-wave Doppler, measuring peak early (E) and late (A) filling velocities and the E/A ratio.
- Tissue Doppler imaging (TDI) acquisition from the apical four-chamber view, measuring peak systolic velocity (S') and peak early diastolic velocity (E') of the mitral annulus [6].
- Global longitudinal myocardial deformation study by Speckle Tracking Imaging (STI): The myocardial deformation parameter studied was the GLS, corresponding to the average strain in the different LV segments, obtained on the apical 2C, 3C, and 4C views. The GLS provides a rapid and comprehensive assessment of overall LV function (the average of strains from the six walls: inferoseptal, anterolateral, inferolateral, anteroseptal, inferior, and anterior, in their apical, mid, and basal segments). A threshold of -18% was used, as recommended by the European and American cardiology societies [6, 7].

Statistical analysis

Data entry and statistical analysis were conducted using the «Statistical Package for the Social Sciences» (SPSS) software, version 20.0 (French-language version).

Simple and relative frequencies (percentages) were used to describe qualitative variables. Quantitative variables with a normal distribution were expressed as means and standard deviations, while those with a non-normal distribution were reported as medians and interquartile ranges.

For comparisons, we used the following tests:

- The Student's t-test for independent samples to compare means.
- The Chi-square test to compare percentages.
- Pearson's correlation coefficient to assess relationships between quantitative variables.

A multivariate analysis was performed using binary logistic regression with a step-down method to calculate adjusted odds ratios and to measure the unique contribution of each factor. The significance threshold for all statistical tests was set at $p < 0.05$.

Ethical Considerations

Les After approval of the Institutional Ethical Committee, the nature of the study and the purpose of our research were clearly explained to each patient. A written informed consent was obtained before inclusion.

RESULTS

Demographic, clinical, and biological characteristics:

A total of 35 patients were included in our study (Figure 1). The average age was 58.89 ± 14.4 years. The majority of the study population was male (n=19, 54.3%). The mean Body Mass Index (BMI) was 23 ± 4.2 kg/m². Regarding the duration of hemodialysis, 16 patients had been on HD for more than four years, 11 for two to four years, while the remaining patients had been on dialysis for less than two years.

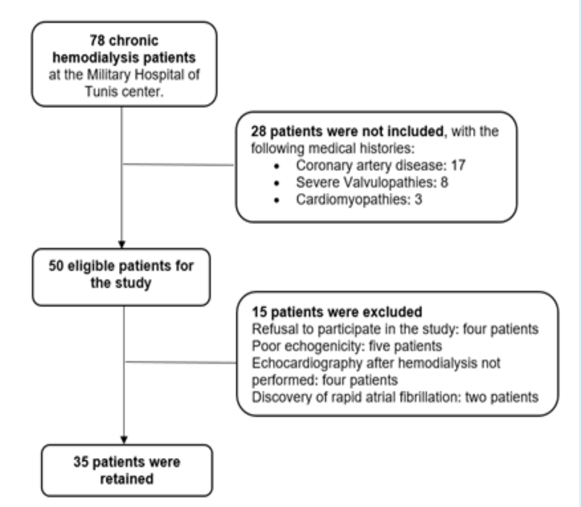

Figure 1. Patient Recruitment Flow Chart

Medical history and lifestyle habits of the study population are summarized in table 1.

Table 1. Medical history and lifestyle habits of the study population

	Number	Percentage (%)
Hypertension	31	88.6
diabetes mellitus	10	28.6
Dyslipidemia	5	14.3
Arteriopathy	1	2.9
Pulmonary pathology	3	8.6
Dysthyroidism	3	8.6
Stroke / TIA	2	5.7
Active smoking	4	11.4

TIA: transient ischemic attack

After the HD session, weight, systolic blood pressure (SBP), heart rate (HR), urea, potassium, and NT-pro BNP significantly decreased (Table 2).

Table 2. Comparison of clinical examination and biological parameters before and after hemodialysis

	Pre-dialysis	Post-dialysis	P
Weight (kg)	69.6±17.4	68.3±17.2	<0.001
SBP (mmHg)	13.5±1.8	12.9±2.1	0.041
DBP (mmHg)	7,2±1.1	7.2±2	0.810
HR (bpm)	71.1±10.8	74.1±10.6	0.020
Urea (mmol/L)	22.4±4.5	6.2±2.5	<0.001
NT-proBNP (ng/L)	4079 [2100- 15070]	2900 [1700-11200]	0.001
Na+(mmol/L)	136.2±2.7	135.4±2.1	0.044
K+ (mmol/L)	5.8±0.6	4.5±0.5	<0.001
Hemoglobin (g/dL)	10.6±1.2	10.2±1.1	0.944

SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; NT-pro BNP: N-terminal pro b-type natriuretic peptide; Na+: Sodium; K+: Potassium; results are presented as mean+/- SD

Echocardiographic characteristics

Echocardiographic measurements revealed significant changes in cardiac parameters following the HD session (Table 3).

Table 3. Comparison of echocardiographic parameters before and after hemodialysis.

	Pre-dialysis	Post-dialysis	P
LVEDD (mm)	51.3±6.3	49.4±7.9	0.029
LVESD (mm)	32.6±5.4	29.5±5.3	0.001
LVEDV (ml/m2)	132.8±29.9	121.1±26.7	0.021
LVESV (ml/m2)	43.1±12.1	36.9±14.2	0.003
IVS (mm)	10.7±1.9	10±2.3	0.053
PW (mm)	9.8±1.6	9.9±2.2	0.943
LVM (g/m2)	198.4±34.3	169.9±28.4	0.037
LVEF (%)	67.1±6.3	68.8±5.5	0.161
Lateral S' (cm/sec)	0.08±0.03	0.08±0.02	0.864
E wave (cm/sec)	0.76 ±0.31	0.68 ±0.21	0.324
A wave (cm/sec)	0.78 ± 0.19	0.81 ±0.20	0.336
E/A ratio	1.23 ± 0.69	0.83±0.24	0.292
E wave DT (cm/s)	182±61.4	214.6±51.2	0.143
E/E' ratio	9.4±4.7	7.3±2.4	0.006
LAVI (ml/m2)	69.9±26.2	61.2±22.5	0.006
PAPS (mmHg)	40.4±8.5	30.2±6.1	<0.001
IVC MAX (mm)	17.6±4.1	12.3±3.2	<0.001
IVC MIN (mm)	9.8±5	2.7±1.3	<0.001
LV GLS	-17.9±4.2	-15.1±1.3	0.041
Altered strain (%)	46.9	62.5	0.014

LVEDD: left ventricular end-diastolic diameter; LV: left ventricle; LVESD: left ventricular end-systolic diameter; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; IVS: interventricular septum; PW: posterior wall; LVM: left ventricular mass; LVEF: left ventricular ejection fraction; S' LAT: lateral S' wave; E-wave DT: E-wave deceleration time; LAVI: left atrial volume Index; PASP: pulmonary arterial systolic pressure; IVC MAX: maximum inferior vena cava diameter; IVC MIN: minimum inferior vena cava diameter; LV GLS: left ventricular global longitudinal strain

A significant reduction was observed in both LV end-systolic diameter (LVESD) and LV end-diastolic diameter (LVEDD) post-HD. While all patients exhibited LV hypertrophy before the session, this was significantly reduced post-HD, although it remained elevated compared to normal values.

The left ventricular ejection fraction (LVEF) remained preserved at both pre- and post-HD time points, with no significant change observed.

Regarding diastolic function, the E/A ratio was lower and the E-wave deceleration time was longer post-HD, but these changes were not statistically significant. However, the E/E' ratio showed a significant decrease after the HD session (p=0.01). The values for E and A waves showed no significant difference pre- and post-dialysis.

The distribution of LV diastolic dysfunction profiles changed markedly after the HD session. Before HD, patients presented with three grades of dysfunction: 48.5% had Grade 1, 45.5% had Grade 2, and 6.1% had Grade 3. Following the HD session, the distribution shifted to only Grade 1 (75.8%) and Grade 2 (24.2%), with no patients exhibiting Grade 3 dysfunction.

Post-HD, a significant decrease was noted in the left atrial volume (LAV), mean pulmonary artery systolic pressure (PASP), and the maximal and minimal diameters of the inferior vena cava (IVC).

The Global Longitudinal Strain (GLS) was impaired both before and after hemodialysis. A notable deterioration was observed post-HD (p=0.041), with the mean GLS decreasing from -17.9±4.2 to -15.1±1.3.

This finding suggests a worsening of subclinical myocardial function immediately following the session.

Predictive factors for global strain alteration after hemodialysis

In multivariate analysis, independent post HD GLS alteration predictors were male gender, age over 60 years, diabetes, and one echocardiographic factor: LVM (table 4).

Table 3. Comparison of echocardiographic parameters before and after hemodialysis.

	Pre-dialysis	Post-dialysis	P	OR [95%]
Age >60 (years)	15 (75%)	5 (41,7%)	0.044	2.333 [1.272-5.723]
Male gender	14 (70%)	3 (25%)	0.027	2.500 [1.187-5.266]
Diabetes mellitus	8 (40%)	1 (8.3%)	0.040	1.528 [1.028-2.271]
Hypertension	18 (90%)	11 (91.7)	0.876	
Dyslipidemia	4 (20%)	1 (8.3%)	0.626	
Active smoking	3 (15%)	1 (8.3%)	0.581	
Pre-HD Urea (mmol/L)	18 (100)	14 (100)	0.154	
Post-HD Urea (mmol/L)	1 (7.1)	0	0.249	
Pre-HD NT-proBNP(ng/L)	18 (100)	14 (100)	0.252	
Post-HD NT-proBNP(ng/L)	18 (100)	14 (100)	0.125	
Pre-HD Na+(mmol/L)	2 (11.1)	4 (28.6)	0.209	
Post-HD Na+(mmol/L)	8(44.4)	3(21.4)	0.174	
Pre-HD K+(mmol/L)	18 (100)	13(92.9)	0.249	
Post-HD K+(mmol/L)	7 (50)	7 (38.9)	0.530	
Pre-HD LVEF (%)	0	2 (14.3)	0.183	
Pre-HD LVM (g/m²)	18 (100)	9 (69.2)	0.035	0.692 [0.482-0.995]
Abnormal E/E' Pre-HD	6 (40)	5 (35.7)	0.812	
Post-HD LVEF (%)	0	0	0.524	
Post-HD LVM (g/m²)	2 (14.3)	4 (40)	0.170	
Abnormal E/E' Post-HD	16 (94.1)	9 (75)	0.141	

LVEF: Left Ventricular Ejection Fraction; LVM: Left Ventricular Mass;HD: hemodialysis;

DISCUSSION

This study reveals significant changes in cardiac structure and function in hemodialysis (HD) patients following a single session. We observed a significant decrease in both the left ventricular end-diastolic diameter (LVEDD) and end-systolic diameter (LVESD) post-HD. Similarly, while still elevated, left ventricular hypertrophy (LVH) significantly reduced after the session. These findings align with previous research by Ezziani et al [8] and Hung et al [9].

LVH in renal patients is a complex process influenced not only by traditional risk factors but also by factors specific to uremia, such as fluid retention, anemia, mineral-phosphorus metabolism disorders, inflammation, oxidative stress, and homocysteine [10, 11]. While LVH can initially be an adaptive response to volume and pressure overload, it eventually leads to maladaptive changes in uremic patients, including cardiomyocyte apoptosis, fibrosis, and myocardial calcifications. These pathological changes impair myocardial perfusion, ultimately leading to both diastolic and systolic dysfunction [12].

Our study showed that HD session influences the diastolic function of the left ventricle. Post-HD, there was a decrease in peak E and E/A ratio, but this was not significant. Similarly, no significant change was observed in peak A or the E-wave deceleration time (DT). Our findings align with prior research indicating that TDI measurements typically remain stable and do not show significant variations following HD sessions [12,13,14]. Indeed, the reduction in preload post-HD leads to a decrease in peak early filling velocities that may reveal delayed relaxation not apparent before HD.

Our study observed a significant reduction in the E/E' ratio post HD, supporting similar findings in previous studies [9,13,15]. A study by Ie et al [16] found that volume overload before HD underestimated the degree of diastolic dysfunction. Therefore, the assessment of LV diastolic function should be conducted under normovolemic conditions, mainly at the end of the HD session [12].

Several factors could explain the divergence of these results, such as methodological differences between studies, patient age, heart rate variations, and changes in preload and afterload during dialysis.

Our study observed no significant change in LVEF, which was preserved before and after HD. Our results are consistent with those reported by Hayashi et al. [17] and Charfeddine et al. [12]. It has been demonstrated that loading conditions impact the LVEF. Indeed, an increase in BP can lead to a decrease in LVEF, even with relatively normal contractility. Conversely, increased preload can enhance LVEF, which may be interpreted as improving myocardial function [18].

Furthermore, the value of LVEF is not considered a good index of myocardial function in patients with LVH. Indeed, subjective visual interpretation, semi-quantitative evaluation of left ventricular systolic contraction, and significant inter-observer variability complicate the evaluation of cardiac function by conventional echocardiography in patients ESRD [19].

Given its dependence on variations in loading conditions and its overestimation in hypertrophic cardiomyopathy, the study of LVEF in chronic hemodialysis patients represents a somewhat limited method [12]. Furthermore, LVEF reflects the sum of all regional shortening of the LV, and regional wall motion alteration may not affect LVEF unless multiple segments are involved [12]. Therefore, STE finds its interest in many cardiopathies where LVEF appears preserved and where the detection of subclinical deterioration of systolic function is sought.

We observed significant reductions in GLS values after the hemodialysis session (-17.9±4.2 vs -15.1±1.3; $p=0.041$). These results are consistent with those of Choi et al. [20]. This decrease in GLS can be explained by the fact that a heart with preserved systolic function follows the Frank-Starling law [21], meaning that a reduction in End-Diastolic Volume leads to a decrease in inotropism.

The findings of Mendes et al. [22] indicated that variations in preload did not influence systolic performance, regardless of the evaluation method. Other studies, including that of Abid et al. [15], noted a reduction in longitudinal strain in uremic patients, with an immediate improvement in GLS, a decrease in LVM, and an improvement in all volumetric parameters after a hemodialysis session [12, 15]. Early alterations in myocardial deformation can be attributed to LVH much like the situation observed in patients with hypertrophic cardiomyopathy and hypertensive cardiomyopathy. The improvement in myocardial deformation might result from the correction of the overhydration acquired during the interdialytic period [12].

«In our study, several risk factors influence post HD GLS values. These included male gender, age over 60, diabetes, and LVM. It has been observed that incident dialysis patients are increasingly older [23]. In our study, the mean age was 58.89 years. It was 60.7 years in the study by Collado et al [24], 64.5 years in the study by Breidthardt [25]. Collado et al. found a significant association between age and the occurrence of cardiovascular complications ($p<0.001$) [24]. This could be explained by the aging population, the presence of comorbidities in older individuals, aging of the cardiac muscle leading to the development of cardiac rhythm disorders, and also due to the duration of exposure to uremia directly involved in cardiovascular calcifications and uremic cardiomyopathy.

Our study also found a relationship between strain alteration and diabetes. Indeed, the incidence of cardiovascular-related deaths in dialysis is two to three times higher in diabetic patients than in non-diabetics [26].

We highlighted that LVM is a predictive factor for strain alteration. Indeed, Patients with ESRD exhibit characteristic myocardial alterations, including pathological myocardial fibrosis and cardiac hypertrophy. LVH is observed in about one-third of chronic renal failure patients, significantly increasing in those in the end-stage of the disease. The presence of LVH is an independent predictor of survival, even in the early stages of ESRD. Underlying mechanisms of LVH involve factors related to afterload and preload, as well as non-afterload, non-preload-related factors, implicating hemodynamic alterations and intracellular mediators. In addition to LVH, uremic cardiomyopathy is marked by the development of myocardial fibrosis independent of LVH, leading to maladaptive cardiac dilatation. [27

CONCLUSIONS

LVEF remains the cornerstone of evaluating LV systolic function, but it has limitations in reproducibility and sensitivity in early cardiopathies. Our study noted the importance of 2D strain in detecting latent alteration of the LV in hemodialysis patients with preserved ejection fraction. This technique should be integrated as a complement for monitoring systolic dysfunction. In light of the results reported in our study and the literature, STE could, in a few years, become part of the risk assessment tools for cardiovascular disease in hemodialysis patients. It may also help in the selection of the type of appropriate renal corrective therapy to improve survival.

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