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Original Paper

Clinical and Echocardiographic Factors Associated with Right Ventricular Systolic Dysfunction in Hemodialysis Patients

Juan Manuel López-Quijano[a, b] Antonio Gordillo-Moscoso[b, c]
Jesús Antonio Viana-Rojas[b] Jorge Carrillo-Calvillo[a, b]
Peter B. Mandeville[b, c] Alejandro Chevaile-Ramos[a, b]

[a]Department of Cardiology, Hospital Central 'Dr. Ignacio Morones Prieto', and [b]Faculty of Medicine and [c]Department of Clinical Epidemiology, Universidad Autónoma de San Luis Potosí, San Luis Potosí, México

Key Words
Tricuspid annular plane systolic excursion · Right ventricular dysfunction · Hemodialysis · Chronic kidney disease

Abstract
Background: Chronic kidney disease is a disorder of epidemic proportions that impairs cardiac function. Cardiovascular diseases are the leading cause of death in hemodialysis patients, and the understanding of new nontraditional predictors of mortality could improve their outcomes. Right ventricular systolic dysfunction (RVSD) has recently been recognized as a predictor of cardiovascular death in heart failure and hemodialysis patients. However, the factors contributing to RVSD in hemodialysis patients remain unknown. The aim of this study was to evaluate the clinical and echocardiographic factors associated with RVSD in hemodialysis patients. ***Methods:*** A cross-sectional study was conducted in which 100 outpatients with end-stage renal disease on chronic hemodialysis were evaluated. A transthoracic echocardiographic examination was performed at optimal dry weight. Right ventricular systolic function was evaluated using tricuspid annular plane systolic excursion (TAPSE). Clinical and echocardiographic data were recorded for each patient. A multivariate linear logistic regression was created using RVSD (TAPSE <14 mm) as the dependent variable. ***Results:*** Fifteen patients with RVSD and 85 patients without RVSD were analyzed. TAPSE had a positive correlation with left ventricular ejection fraction (LVEF) and myocardial relaxation velocity. Independent contributors to RVSD were LVEF (OR 1.14, 95% CI 1.05–1.26), left ventricular mass index (OR 1.02, 95% CI 1.00–1.04), and myocardial relaxation velocity (OR 1.81, 95% CI 1.18–3.19). ***Conclusions:*** Echocardiographic factors were significant contributors to RVSD. These measurements could be included as part of the routine workup in all end-stage renal disease patients on hemodialysis.

Antonio Gordillo-Moscoso, MD, PhD
Department of Clinical Epidemiology, Universidad Autónoma de San Luis Potosí
Av. Venustiano Carranza No. 2405
San Luis Potosí, SLP 78240 (México)
E-Mail gordillo@uaslp.mx

Introduction

Chronic kidney disease is a multisystemic disorder of epidemic proportions that negatively affects cardiac function (type 4 cardiorenal syndrome) [1, 2]. The incidence of structural heart disease is high in end-stage renal disease (ESRD) patients [3] and has been reported to be more frequent in hemodialysis patients [4].

Cardiovascular diseases are the leading cause of death in chronic kidney disease patients on hemodialysis. Traditional risk factors do not completely explain this high risk [5]; thus, an understanding of new nontraditional predictors of mortality could improve treatment and increase the survival of chronic kidney disease patients.

Right ventricular systolic dysfunction (RVSD) has recently been shown to be a predictor of cardiovascular death in patients with chronic systolic heart failure and coronary artery disease [6–8]. Moreover, right ventricular systolic function has been shown to inversely correlate with glomerular filtration rate in chronic kidney disease patients [9] and has been poorer in hemodialysis patients than in healthy controls [10]. However, it remains unknown which factors contribute to RVSD in ESRD patients on hemodialysis.

The aim of this study was to evaluate the clinical and echocardiographic factors associated with RVSD in ESRD patients on hemodialysis.

Methods

Study Population

A cross-sectional study was conducted between April 2013 and January 2014 in the Cardiology and Nephrology Departments of the Hospital Central 'Dr. Ignacio Morones Prieto' in San Luis Potosí, México. An evaluation was performed on a total of 100 outpatients with ESRD on chronic hemodialysis (minimum 3 months).

Exclusion criteria were a history of renal graft, a history of heart failure, a history of ischemic heart disease, presence of a prosthetic heart valve, moderate to severe aortic or mitral valve disease, pericardial effusion, and oxygen-dependent lung disease. Clinical and echocardiographic data were recorded for each patient. Every participant provided informed consent, and all procedures were approved by our institute's Bioethics Committee (reference 30-13).

Clinical Data Collection

Previous to echocardiographic evaluation, participants were interviewed about some clinical data. Age, gender, diabetes diagnosis, hemodialysis time, and arteriovenous fistula time (length of time the fistula was in place) were recorded. All patients were dialyzed in the same center with bicarbonate dialysate solution (NaturaLyte 4000, Fresenius Medical Care). Medical records were reviewed to confirm the data obtained.

Echocardiographic Evaluation

Transthoracic echocardiographic examination was performed with a Philips IE 320 ultrasound instrument and a 3.5-MHz transducer. Echocardiography was performed after hemodialysis while the patients were at optimal dry weight. Dry weight was ascertained by clinical examination. Left ventricular ejection fraction (LVEF) was calculated from apical two- and four-chamber views using the modified Simpson's rule. Right ventricular systolic function was evaluated using tricuspid annular plane systolic excursion (TAPSE) [11, 12]. TAPSE was assessed by M-mode at the junction of the tricuspid valve and right ventricle free wall in the apical four-chamber view (fig. 1). Left ventricular mass index was calculated as recommended by the American Society of Echocardiography [13]. Myocardial relaxation velocity was evaluated by tissue Doppler ultrasound, calculating the mean value between the septum and left ventricle free wall (E' wave). Estimated pulmonary artery systolic pressure was obtained from the apical four-chamber view by calculating the pressure gradient between the right ventricle and the right atrium through tricuspid regurgitation flow and by adding the estimated value of pressure in the right atrium.

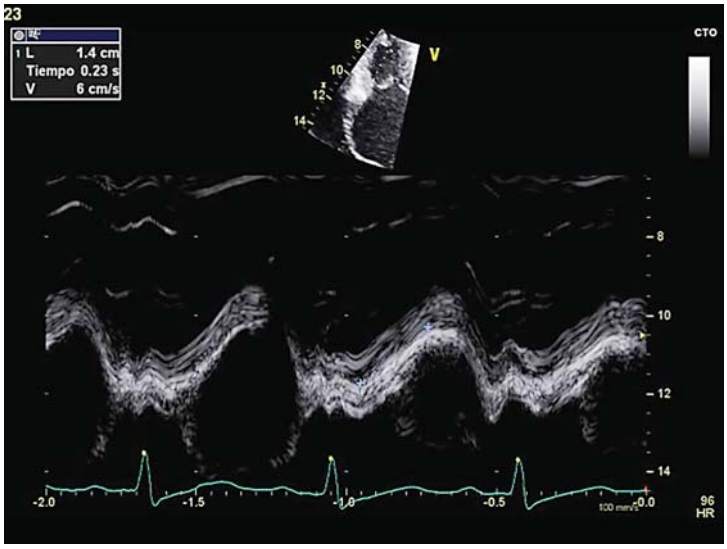

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Fig. 1. Low TAPSE assessed by M-mode transthoracic echocardiography.

Reproducibility

Prior to the study, echocardiographic measurements were repeated by two echocardiography cardiologists in 16 ESRD subjects to assess interobserver agreement. The Linn correlation coefficient was 0.94 for LVEF, 0.99 for pulmonary artery systolic pressure, 0.97 for left ventricular mass index, and 0.86 for TAPSE.

Statistical Analysis

Descriptive methods were used with continuous variables presented as means ± SD and categorical variables presented as frequency (%). Patients were divided into two groups: RVSD (TAPSE <14 mm) and normal right ventricular systolic function (TAPSE ≥14 mm), as has been established previously [7, 9]. Differences between the groups were tested using the χ^2 test for categorical variables and the Student t test for continuous variables. Correlation between TAPSE and other parameters was performed using the Spearman rank correlation test and the Pearson correlation test, as appropriate. A multiple linear regression model was created using TAPSE as the dependent variable. Curved linear relationships of the covariates were tested and then quadratic terms added if appropriate. A multivariate linear logistic regression was also created using RVSD as the dependent variable. Both models were tested for multicollinearity. Statistical analysis was performed using R version 3.1.0 for Windows [14]. A value of $p < 0.05$ was considered statistically significant.

Results

The analysis included 15 patients with RVSD (TAPSE <14 mm) and 85 patients without RVSD (TAPSE ≥14 mm). The mean age of the study population was 41.2 ± 18 years, the mean time on hemodialysis was 36.3 ± 35 months, and there were 56 males (56%). Clinical and echocardiographic characteristics of the study population are shown in table 1. Compared with the group of normal TAPSE, patients with low TAPSE had less time with their arteriovenous fistula, lower values of LVEF, and a lower myocardial relaxation velocity. Other clinical and echocardiographic characteristics between the groups were not statistically significant.

Correlation between TAPSE and other Parameters

TAPSE had a positive correlation with LVEF and myocardial relaxation velocity. There was a negative correlation between TAPSE and diabetes. Correlations between TAPSE and other parameters were not statistically significant (table 2).

Table 1. Clinical and echocardiographic characteristics of the study population

	TAPSE <14 mm (n = 15)	TAPSE ≥14 mm (n = 85)	p
Age, years	40.8±16.1	41.3±18.4	0.92*
Gender, male	8 (53.3)	48 (56.4)	0.82†
Diabetes	7 (46.6)	23 (27.0)	0.22†
HD time, months	37.9±32.3	36.1±35.7	0.85*
AVF time, months	4.2±9.6	17.8±25.2	0.04*
PASP, mm Hg	34.1±13.7	34.9±13.3	0.82*
PAH	8 (53.3)	52 (61.1)	0.77†
LVEF	42.4 (11.3)	53.4 (11.5)	0.001*
Left ventricular mass index, g/m^2 CS	162.4±60.1	167.2±48.2	0.73*
Myocardial relaxation velocity, cm/s	4.9±1.6	6.3±1.7	0.004*
TAPSE, mm	11.5±1.3	20.4±3.6	<0.0001*

Categorical variables are reported as frequency (%) and continuous variables as means ± SD. HD = Hemodialysis; AVF = arteriovenous fistula; PASP = pulmonary artery systolic pressure; PAH = pulmonary artery hypertension (PASP >30 mm Hg); CS = corporal surface. * Student's t test; † χ^2 test.

Table 2. Correlation between TAPSE and other parameters

	r (95% CI)	p
Diabetes	–0.26 (–0.43 to –0.06)	0.008*
LVEF	0.24 (0.05 to 0.42)	0.01†
Myocardial relaxation velocity	0.46 (0.28 to 0.60)	<0.0001*

* Spearman rank correlation test; † Pearson correlation test.

Clinical and Echocardiographic Factors Associated with Right Ventricular Systolic Function

Clinical and echocardiographic data that could contribute to right ventricular systolic function were entered into the multiple linear regression model. The final model is shown in table 3. Independent contributors to right ventricular systolic function were LVEF, left ventricular mass index, and myocardial relaxation velocity. The R^2 of the model was 0.38, and 0.35 with Bootstrap validation. Other covariates were not statistically significant.

Known risk factors for RVSD were entered into the multivariate linear logistic regression model. The final model is shown in table 4. Independent contributors to RVSD were arteriovenous fistula time, LVEF, left ventricular mass index, and myocardial relaxation velocity. Other covariates were not statistically significant. The accuracy of the model by cross validation was 87%.

Discussion

Cardiovascular complications are the leading cause of death in chronic hemodialysis patients. Being elderly, smoking status, diabetes, hypertension, and left ventricular heart failure are major contributors recognized. However, nontraditional risk factors for cardiac disease (such as RVSD) have been poorly addressed.

Table 3. Multiple linear regression showing factors independently associated with right ventricular systolic function

	Regression coefficient (β)	95% CI of β	ε^2	p
LVEF	17.15	8.24 to 26.06	0.07	<0.001
$LVEF^2$	–8.16	–15.74 to –0.59	0.02	0.03
Left ventricular mass index	0.03	0.01 to 0.05	0.10	<0.001
Myocardial relaxation velocity	1.26	0.82 to 1.70	0.20	<0.001

Covariates entered in the initial model: age, gender, diabetes, hemodialysis time, quadratic term of hemodialysis time, arteriovenous fistula time, quadratic term of arteriovenous fistula time, pulmonary artery systolic pressure, LVEF, $LVEF^2$, ventricular mass index, and myocardial relaxation velocity. Validated R^2 = 0.38, $p < 0.001$. $LVEF^2$ = Quadratic term of left ventricular ejection fraction.

Table 4. Logistic regression showing factors independently associated with RVSD

	Regression coefficient (β)	OR (95% CI)	p
AVF time	0.05	1.05 (1.00–1.14)	0.002
LVEF	0.13	1.14 (1.05–1.26)	0.003
Myocardial relaxation velocity	0.59	1.81 (1.18–3.19)	0.01
Left ventricular mass index	0.02	1.02 (1.00–1.04)	0.02

Covariates entered in the initial model: age, gender, hemodialysis time, AVF time, pulmonary artery systolic pressure, ejection fraction, ventricular mass index, and myocardial relaxation velocity. Validated accuracy of the model = 87%. AVF = Arteriovenous fistula.

RVSD is a significant predictor of mortality in heart failure patients, regardless of left ventricular systolic dysfunction and valvular disease [7, 15, 16]. However, it has been poorly studied in hemodialysis patients.

In our study, it was found that LVEF, left ventricular mass index, and myocardial relaxation velocity are major contributors to right ventricular systolic function measured as TAPSE. Additionally, arteriovenous fistula time, LVEF, left ventricular mass index, and myocardial relaxation time were found to be independent factors associated with RVSD in hemodialysis patients.

Hemodialysis therapy increases the risk of RVSD, particularly in the presence of brachial arteriovenous fistula. The arteriovenous fistula causes a left-to-right shunt, leading to chronic volume overload and right ventricle function impairment [10, 17].

The left ventricular mass index contributes to left ventricular diastolic dysfunction, and delayed myocardial relaxation velocity is an expression of it. Left ventricular diastolic function impairment produces an increase in left ventricular pressure and in pulmonary pressure and, therefore, a decrease in right ventricular function [18, 10]. Through these mechanisms, left ventricular dysfunction (systolic and diastolic) could be the main contributor to RVSD.

Strengths and Limitations

The validation and reproducibility of echocardiographic measurements and the statistical analysis without missing data are some significant strengths of this study. However, our study also has several limitations. First, it is a single-center study. Second, the cross-sectional design does not allow assuming causal relationships between echocardiographic factors and RVSD. Finally, a low rate of RVSD was observed in the study population; so, the logistic regression analysis could be performed only as an approximation.

Conclusion

In our study, only echocardiographic factors were significant contributors to RVSD. The evaluation of LVEF, left ventricular mass index, and myocardial relaxation velocity are simple and noninvasive measurements performed by transthoracic echocardiography. These parameters should be included and reported in every patient on hemodialysis.

Disclosure Statement

The authors have no conflicts of interest to declare.

References

1 Iyngkaran P, Schneider H, Devajaran P, Anavekar N, Krum H, Ronco C: Cardio-renal syndrome: new perspective in diagnostics. Semin Nephrol 2012;32:3–17.
2 House A, Anand I, Bellomo R, Cruz D, Bobek I, Anker S: Definitions and classification of cardio-renal syndromes: workgroup statements from the 7th ADQI Consensus Conference. Nephrol Dial Transplant 2010;25:1416–1420.
3 House AA: Cardio-renal syndrome type 4: epidemiology, pathophysiology and treatment. Semin Nephrol 2012;32:40–48.
4 Cheung AK, Sarnak MJ, Yan G, Berkoben M, Heyka R, Kaufman A, Lewis J, Rocco M, Toto R, Windus D, Ornt D, Levey AS; HEMO Study Group: Cardiac diseases in maintenance hemodialysis patients: results of the HEMO study. Kidney Int 2004;65:2380–2389.
5 Foley RN, Parfrey PS, Sarnak MJ: Epidemiology of cardiovascular disease in chronic renal disease. J Am Soc Nephrol 1998;9(12 suppl):S16–S23.
6 Polak JF, Holman BL, Wynne J, Colucci WS: Right ventricular ejection fraction: an indicator of increased mortality in patients with congestive heart failure associated with coronary artery disease. J Am Coll Cardiol 1983;2:217–224.
7 Kjaergaard J, Akkan D, Iversen KK, Kober L, Torp-Pedersen C, Hassager C: Right ventricular dysfunction as an independent predictor of short- and long-term mortality in patients with heart failure. Eur J Heart Fail 2007;9:610–616.
8 Engstrom AE, Vis MM, Bouma BJ, van den Brink RB, Baan J Jr, Claessen BE, Kikkert WJ, Sjauw KD, Meuwissen M, Koch KT, de Winter RJ, Tijssen JG, Piek JJ, Henriques JP: Right ventricular dysfunction is an independent predictor for mortality in ST-elevation myocardial infarction patients presenting with cardiogenic shock on admission. Eur J Heart Fail 2010;12:276–282.
9 Dini FL, Demmer RT, Simioniuc A, Morrone D, Donati F, Guarini G, Orsini E, Caravelli P, Mazilli M, Colombo PC: Right ventricular dysfunction is associated with chronic kidney disease and predicts survival in patients with chronic systolic heart failure. Eur J Heart Fail 2012;14:287–294.
10 Momtaz M, Al-Fishawy H, Mabid-Aljarhi U, Al-Ansi RZ, Megid MA, Khaled M: Right ventricular dysfunction in patients with end-stage renal disease on regular hemodialysis. Egypt J Intern Med 2013;25:127–132.
11 Kaul S, Tei C, Hopkins JM, Shah PM: Assessment of right ventricular function using two-dimensional echocardiography. Am Heart J 1984;107:526–531.
12 Ghio S, Recusani F, Klersy C, Sebastiani R, Laudisa ML, Campana C, Gavazzi A, Tavazzi L: Prognostic usefulness of the tricuspid annular plane systolic excursion in patients with congestive heart failure secondary to idiopathic or ischemic dilated cardiomyopathy. Am J Cardiol 2000;85:837–842.

13 Lang R, Biering M, Devereux R, Flachskampf FA, Foster E, Pellikka PA, et al: Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guideline and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–1463.
14 R Core Team: R: A Language and Environment for Statistical Computing. Vienna, R Foundation for Statistical Computing, 2014. http://www.R-project.org/.
15 Di Salvo TG, Mathier M, Semigran MJ, Dec GW: Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. J Am Coll Cardiol 1995;25:1143–1153.
16 Testani JM, Khera AV, St John Sutton MG, Keane MG, Wiegers SE, Shannon RP: Effect of right ventricular function and venous congestion on cardiorenal interactions during the treatment of decompensated heart failure. Am J Cardiol 2010;105:511–516.
17 Paneni F, Gregori M, Ciavarella GM, Sciarretta S, De Biase L, Marino L, Tocci G, Principe F, Domenici A, Luciani R, Punzo G, Mene P, Volpe M: Right ventricular dysfunction in patients with end-stage renal disease. Am J Nephrol 2010;32:432–438.
18 Santamore WP, Dell'Italia LJ: Ventricular interdependence: significant left ventricular contributions to right ventricular systolic function. Prog Cardiovasc Dis 1998;40:289–308.