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Reduced residual urine volume is independently associated with left ventricular systolic and diastolic dysfunction in Congolese patients on maintenance hemodialysis: A post hoc analysis

Yannick Mompango Engole[1], Yves Simbi Lubenga[2], François Bompeka Lepira[1], Aliocha Nkodila[1], Yannick Mayamba Nlandu[1], Jean Robert Rissassy Makulo[1], Vieux Momeme Mokoli [1], Marie France Ingole Mboliasa[1], Evariste Mukendi Kadima[1], Cedric Kabemba Ilunga[1], Tresor Swambulu Mvunzi[2], Nazaire Mangani Nseka[1], Ernest Kiswaya Sumaili[1]

1. Department of Nephrology Unit, University Hospital of Kinshasa, DRC, Kinshasa, Congo

2. Department of Cardiology Unit, University Hospital of Kinshasa, DRC, Kinshasa, Congo

*Corresponding author: Engole YM, Department of Nephrology Unit, University Hospital of Kinshasa, DRC, Kinshasa, Congo; Tel No: 243811495588; E-Mail: yannickengole@yahoo.fr

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ABSTRACT

Objective

Cardiac dysfunction, valvular calcification (VC) and decrease residual renal function are known independently associated with cardiovascular complications and all-cause mortality in chronic hemodialysis. But, little is known whether residual urine volume (RUV) may contributed to occurrence of cardiac dysfunction or VC. This study aimed to investigate whether RUV was associated with VC, left ventricular systolic and diastolic dysfunction in hemodialysis in Kinshasa between March 2016 and October 2017.

Methods

A cross sectional study including patients on maintenance hemodialysis for at least 6 months in 4 hd centers. vc were defined as a luminous echo of more than 1 mm on 1 or more cusps of the valve, lvsd (lvef <55%) and lvdd (e / a < 1 or > 2, e / a between 1-2 with e / e '>13) were investigated by doppler echocardiography performed 24 hours after the hd session. urine collection was performed during the interdialytic period. the determinants were investigated by logistic regression analyses.

Results

71 patients (mean age 51.7 ± 16.6 years, 38 with reduced RUV). The determinants associated with: VC were HT (p=0,026), age > 60 years (p=0,012), tobacco (p=0,039), hyperphosphoremia; LVSD: HT (p= 0.016), hyperphosphoremia (p=0.003); RUV (p=0,017); ABI (p=0.025) and LVDD: diabetes mellitus (p= 0.025), tobacco (p=0.015), SBP (p=0.020) and RUV (p=0,019).

Conclusion

In this study, reduced RUV is independently associated with systolic and diastolic dysfunction as opposed to VC.

Keywords: Systolic and diastolic dysfunction, residual diuresis, hemodialysis, valvular calcification

Introduction

Cardiovascular disease is the leading cause of death in patients with end-stage renal disease (ESRD) [1-2]. However, traditional cardiovascular risk factors do not fully explain the elevated mortality rates of cardiovascular disease seen in patients with ESRD. Non-traditional risk factors such vascular calcification (VC) greatly contributes to the exceedingly high cardiovascular disease mortality in ESRD population (3). Indeed, VC is a common pathologic finding among patients with ESRD that has a variety of forms, including the deposition of calcium in the intimal and/or medial vessel layer [3-4]. Patients with chronic kidney disease (CKD), especially in hemodialysis, frequently develop widespread cardiac and vascular calcifications [5]. Previous reports have demonstrated the association between vascular calcification and cardiac changes in ESRD patients, including arterial stiffness [6], stroke volume [7], and left ventricular (LV) diastolic dysfunction [8]. Heart failure is one of the most common cardiac complications in patients with ESRD on hemodialysis. Chronic pressure and volume overload, as well as oxidative stress and inappropriate activation of the renin - angiotensin - aldosterone system, lead to the development of systolic and diastolic left ventricular (LV) dysfunction [9]. Due to the interdependent influences between malnutrition, inflammatory state, atherosclerosis and calcium-phosphorus metabolic disorders, the incidence of cardiac valve

calcification is significantly higher in ESRD patients than in general population [10] and is also a key factor impacting their prognosis [11]. Although many factors, including age, hyperphosphatemia, microinflammatory state and β2-microglobulin elevation, are independent risk factors for cardiac valve calcification in hemodialysis patients [11], there is controversy regarding the independent risk factors for cardiac valve calcification in peritoneal dialysis patients [11]. Residual urine volume (RUV) assists in the purification of low- to medium-molecular-weight substances, allowing for even greater liquid removal 1 and improvement of the patient's nutritional state [12-13] and quality of life [14], in addition to maintaining the endocrine functions of the kidney. RUV may contribute to better anemia and volume control, lower inflammation degrees, malnutrition, and calcium-phosphorous products, and greater solute clearance [14–17].

Thus, these beneficial effects explained the lower overall and cardiovascular mortality in dialysis patients with residual renal function (RRF). In this regard, increasing evidence suggests that the preservation of RRF contribute in favorable way on the predictors of mortality in HD such as hypervolemia [18], left ventricular hypertrophy (LVH) and congestive heart failure [19, 20], heart rhythm disorders [21] and ischemic strokes [22]. Thus, patients on hemodialysis (HD) had more rapid reductions in their RRF than those on peritoneal dialysis (PD).The progressive reduction in renal function is associated with LVH and greater cardiovascular mortality in PD patients [23, 24]. Causes of LV diastolic dysfunction are impaired active LV relaxation or decreased LV compliance. These changes are reflected in low diastolic volume for a given diastolic pressure, meaning reduced passive LV filling. The decrease in peak E velocity, with a resultant decrease in the E/A ratio, occurs due to a decrease in ventricular preload leads. This could have an effect on the obtained decrease of E/A ratio after hemodialysis (HD) [25]. Indeed, Ma and Ding [21] found, in a case-control study, that the frequency of LVH and systolic dysfunction was significantly lower in patients with preserved RRF (defined as RUV ≥200 mL/day) compared to those having lost RRF (RUV <200 mL/day) [26]. Little is known about valvular calcification and cardiac function according to RUV expressed as mL in patients on hemodialysis. Here we hypothesis that RUV is associated with VC and cardiac function and it affected cardiovascular events. Therefore, we investigated the correlation between RUV and VC, the cardiac dysfunction in patients on hemodialysis [27]. Despite the multiple benefits of the preservation of RUV in patients on maintenance hemodialysis (HD), available data on the preservation of the RUV in sub-Saharan Africa are scarce [28]. Hence, there is a need to fill this gap by acquiring reliable data that inform the development of policy and rational and adapted strategies as regards extrarenal purification to better survival of chronic HD patients [28]. The present study aimed to investigate the impact of the decline of RUV on valvular calcification and systolic and diastolic LV dysfunction in our hemodialysis patients.

Methods

Design, setting and study period

We conducted a cross-sectional study among patients with RUV under maintenance hemodialysis for 6 months, between March 2016 and October 2017, in four hemodialysis centers existing in Kinshasa at the epoch.

Data collection Parameters of interest were the following: Demographic (age, financing of treatment, level of studies), clinical (weight, height, waistline, initial nephropathy, complications of CKD (encephalopathy, pericarditis, hypervolemia, acidosis, anemia, hypocalcemia, etc.), comorbidities associated with CKD (antecedent Stroke and AIT, arrhythmias, heart failure, coronary heart disease, cirrhosis, viral hepatitis C, HIV, diabetes, hypertension, respiratory failure, etc.), systolic blood pressure (SBP), diastolic blood pressure (DBP) and the pulsating pressure that is the differential of SBP and DBP) and biochemical (BUN, creatinine, serum kaliemia, uric acid, alkaline reserve, calcium, phosphorus, cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, hemoglobin and hematocrit, C-reactive protein (CRP), ProBNP, Troponine, Vitamin D, Parathormon (PTH), albumin and total protein) data obtained from medical records. We performed ankle brachial index (ABI) as well as echocardiographic data 24 hours after the beginning of week hemodialysis session and collection of urine in interdialytic period. The Kt/V index was used to assess the adequacy of dialysis. The effective clearance plasma Kt (K: urea clearance, t: effective dialysis duration) was delivered by automatic measurements and calculations.

Operational definitions

- Measurement of residual urine volume:
- Reduced RUV was defined as: RUV < 500 mL, preserved RUV: RUV ≥ 500 mL;
- Echocardiographic measurements

Comprehensive echocardiographic measurements were performed using an ultrasound machine (Vivid 7; GE Vingmed Utrasound AS, Boston, USA, 2007) with a 3.5 MHz probe, based on the imaging protocol in the American Society of Echocardiography guideline [27]. Left ventricular ejection fraction (LVEF) was estimated using the modified biplane Simpson's method in apical two and four-chamber views. LV mass was determined using the method described by Devereux et al. and LV mass index (LVMI) was calculated by dividing the LV mass by the body surface area. Observed left ventricular mass was calculated by the following equation: Without measuring the major axis of the LV, LV mass is obtained from the LV short-axis dimension and a simple geometric cube formula. The following equation provides a reasonable determination of LV mass in grams: 1.04× [(LVID+PWT+ IVST)3-LVID3)] × 0.8+0.6 [29] Cardiac valve calcification was defined by bright echoes of more than 1 mm and more cups of the mitral valve, mitral annulus or aortic valve [30]. Mitral inflow was assessed with Doppler echocardiography from the apical four-chamber view. The mitral inflow profiles were used to measure the peak mitral inflow velocities at the early (E), late (A) diastole, and its deceleration time (DT). Doppler tissue imaging of the mitral annulus was also obtained. From the apical four-chamber view, the early (E') and late (A') diastolic peak velocities were evaluated. Moderate to severe diastolic dysfunction was defined as E/A < 1 or > 2 and

between1-2, we complete with E/E'>15 [31]. Relaxation anomaly according to Appleton: Type I: E / A <1, TDE> 200 ms, TRIV> 100 ms, Type II: E / A between 0.75 and 2, and / or TDE between 150 to 200 ms, Type III: E / A> 2, and / or TDE <150 ms; systolic dysfunction: LVEF< 55%.

- Ankle brachial index measurement
- Peripheral artery disease was defined as ABI < 0.9
-

The ideal weight has been defined by the Lorentz formula (Charlson T):
Woman: ideal weight (Kg): size-100-(size-150)/2.5
Male: ideal weight: height - 100 - (size - 150) / 4

Statistical analyses

The statistical analysis was carried out using SPSS 21 for windows. Quantitative variables were expressed as mean ± SD and qualitative variables as a percentage. Student t-test and Pearson's chi-square were used to compare quantitative and qualitative variables, respectively. The determinants of VC, LV systolic and diastolic dysfunction in HD patients were identified using univariate and multivariate stepwise logistic regression analysis. The threshold of statistical significance was set at α= 0.05.

Ethics statement

The study protocol was approved by the Clinical Research Ethics Committee of Kinshasa School of Public Health (number ESP/CE/013/2016).

RESULTS

71 patients (incident and prevalent) on maintenance hemodialysis were included.

Baseline characteristics according to residual urine volume

Baseline characteristics of all patients studied according to median RUV (reduced and preserved) are shown in Table 1. The median RUV was 518.9 ± 338.6 mL (259.8 ± 121.8 mL for RUV reduced and 775.8 ± 326.3 mL for RUV preserved). The average ankle index was 1.02 ± 0.2. Their mean age was 51.7 ± 16.6 years old and 55 (67.1%) were men. The median duration of dialysis was 12 months (interquartile range, 7-15.7). The underlying cause of IRT was diabetes in 25 patients (35.2%). Compared with patients with preserved RUV (RUV ≥ 500 mL), those with reduced RUV (RUV <500 mL) had longer hemodialysis duration (p=0.007), higher mean interdialytic weight gain (p=0.006), greater likelihood of taking ACE inhibitors (p=0.014) and diuretics (p=0.036). In addition, valvular calcification [15 (40.5) vs 10 (30.3), p = 0.026] was significantly higher in patients with reduced RUV than in those having preserved RUV. P x Ca (p=0.024) and kaliemia (p=0.033) were also significantly higher in patients with reduced RUV (Table 2). Although IVC, E / A and E / E 'were higher in patients with reduced RUV than those with RUV preserved, there was no statistically significant difference in the echocardiographic parameters (Table 3).

Variables	Whole	Reduced RUV	Preserved RUV	P value
	n=71	n=38	n=33	
Age, years old	51.7±16.6	52.8±15.7	50.5±17.7	0.558
Male, sex	48 (67.1)	27 (70.3)	21 (63.6)	0.368
Duration of HD, month	12.0 (7.0-15.7)	12.0 (8-22.0)	12.0 (6.5-15 .0)	0.007
Kt/v	1.14±0.2	1.11±0.2	1.16±0.2	0.365
Dry Weight, Kg	68.4±15.6	69.3±16.1	67.4±15.2	0.598
IWG, Kg	2.06±0.83	2.31±0.87	1.77±0.69	0.006
SBP, mmHg	156.5±17.6	154.2±16.3	159.1±18.8	0.247
DBP, mmHg	86.4±14.4	84.3±15.5	88.9±12.9	0.191
PP, mmHg	70.0±16.8	69.8±16.0	70.1±17.9	0.94
ABI	1.02±0.2	1.0±0.2	1.04±0.2	0.45
Ideal weight, kg	61.8±6.0	60.4±4.6	63.7±7.1	0.032
BMI, kg/m2	26.0±9.0	27.6±11.0	24.1±5.5	0.102
RUV, mL	518.9±338.9	259.8±121.8	775.8±326.3	<0.001
eGFR initial, MDRD	7.4±3.1	7.7±3.2	7.1±3.0	0.421
Initial nephropathy				
Glomerulo nephritis	20 (28.1)	8(21.1)	12 (36.4)	0.187
Hypertensive nephrosclerosis	22 (31.0)	11(28.9)	11 (33.3)	0.443
Diabetes mellitus	25 (35.2)	17 (44.7)	8 (24.2)	0.059
Polycystic kidney	2 (2.8)	1 (2.6)	1 (3.0)	0.717
Obstructive uropathy	2 (2.8)	1 (2.6)	1 (3.0)	0.717
Medication				
Vit D + CaCO3	32(45.1)	14(36.8)	18(54.5)	0.104
Phosphorus chelators	5(7.0)	2(5.3)	3(9.1)	0.432
Insuline	9(12.7)	4(10.5)	5(15.2)	0.409
Oral antidiabetic	6(8.5)	3(7.9)	3(9.1)	0.593
Diuretic	36(50.7)	15(39.5)	21(63.6)	0.036
Anticalcic	51(71.8)	27(71.1)	24(72.7)	0.544
EPO	50(70.4)	25(65.8)	25(75.8)	0.256

CEA inhibitor	26(36.6)	9(23.7)	17(51.5)	0.014
ARAII	12(16.9)	5(13.2)	7(21.2)	0.279
β blockers	12(16.9)	6(15.8)	6(18.2)	0.517
Fer	55(77.5)	28(73.7)	27(81.8)	0.298
AAS junior	62(36.6)	14(36.8)	12(36.4)	0.582
Statine	10(14.1)	4(10.5)	6(18.2)	0.28
Cardiac abnormalities				
VC	25(35.7)	15(40.5)	10(30.3)	0.026
Systolic dysfunction	18(25.7)	7(18.9)	11(33.3)	0.135
Diastolic dysfunction	21(29.6)	13(34.2)	8(24.2)	0.256
Pericardial effusion	7(10.0)	3(8.1)	4(12.1)	0.435

Table 1: Clinical characteristics of the study population according to residual urine volume status.

Variables	Whole	Reduced RUV	Preserved RUV	p
S.Creatinin, mg/dL	9.2 (8.5-10.0)	8.9 (8.2-9.4)	10.0 (8.6-10.9)	0.465
BUN mg/dL	141.8±53.2	145.6±49.9	137.4±57.3	0.523
PxCa2, mg2/dL2	45.1±17.6	49.5±19.4	40.1±13.8	0.024
Calcium, mg/dL	8.8±1.6	9.7±2.7	7.9±1.14	0.323
Vit D, ng/mL	25.3 (23.9-30.0)	24.7 (23.9-29.8)	27.9 (13.4-35.0)	0.995
PTH, pg/mL	497 (259.8-623.9)	623.9 (321.9-1308.6)	436.6 (80.7-538.0)	0.084
Troponine,	16.4 (7.2 – 32.0)	20.8 (3.7 – 34.0)	9.3 (6.7 – 32.0)	0.53
ProBNP, ng/mL	735.5 (340.9-1157)	454.8 (270.3-911.1)	222.2 (150.9-250)	0.055
Albumin g/L	36.1±6.2	35.7±6.2	36.6±6.2	0.511
Total Protein, g/dL	66,0±10.1	65.6±9.1	66.5±11.2	0.715
Hemoglobin g/dL	9.4±3.9	9.9±5.1	8.8±1.6	0.264
Phosphorus,mg/dL	6.9±1.5	8.4±1.5	5.1±1.5	0.216
Glucose, mg/dL	109.3±31.1	103.1±26.5	116.5±34.7	0.071
CRP, mg/L	12.0 (8.0-13.2)	12.0 (8.0-17.0)	12.0 (7.0-15.7)	0.706
Cholestérol, mg/dL	175.2±39.2	170.3±35.5	180.8±42.8	0.264
HDL-c, mg/dL	47.1±16.9	45.1±17.6	49.3±16.1	0.298
LDL-c, mg/dL	107.8±34.5	106.5±34.2	109.4±35.2	0.726
Triglycerid, mg/dL	109.5±36.6	109.1±37.3	109.9±36.4	0.921
Kaliemia, mmol/L	6.1±2.7	7.5±1.7	4.6±0.5	0.033
Iron, µg/dL	32.4±11.5	30.7±8.9	33.8±11.5	0.647

Table 2: Biological characteristics of the study population according to residual urine volume status.

Variables	Whole	Reduced RUV	Preserved RUV	p
LVEF, %	64.3±9.2	65.7±9.7	62.8±8.4	0.174
LVedd, cm	50.3±5.9	49.8±6.5	50.9±5.2	0.429
LMVi, g/m2	395.7±142.6	399.7±145.4	391.1±141.5	0.802
IVC, mm	14.9±5.4	15.1±5.4	14.6±5.5	0.722
E/A	1.1±0.8	1.15±0.8	1.04±0.8	0.552
E/E'	10.8±5.7	11.1±5.2	10.5±6.2	0.69
LVPWd	12.1±1.9	12.0±1.9	12.3±2.0	0.546
IVSd	13.3±2.4	13.1±2.3	13.5±2.5	0.547
DT, cm	225.5±69.4	225.5±75.9	225.4±62.2	0.998
Volume of OG, cm3	21.4±5.7	21.3±6.8	21.6±4.3	0.81
Volume of OD cm3	15.7±3.6	15.9±4.2	15.5±2.9	0.626
SPAP, mmHg	27.7±10.3	28.2±10.4	27.1±10.3	0.681
TDI cms	14.1±2.3	14.3±2.2	14.0±2.4	0.639
Aorte initiale, mm	30.8±3.9	30.3±3.7	31.4±4.2	0.24
LVeds	19.2±4.0	19.1±4.1	19.3±4.0	0.81

Variables	Whole	Reduced RUV	Preserved RUV	p
LVEF, %	64.3±9.2	65.7±9.7	62.8±8.4	0.174
LVedd, cm	50.3±5.9	49.8±6.5	50.9±5.2	0.429
LMVi, g/m2	395.7±142.6	399.7±145.4	391.1±141.5	0.802
IVC, mm	14.9±5.4	15.1±5.4	14.6±5.5	0.722
E/A	1.1±0.8	1.15±0.8	1.04±0.8	0.552
E/E'	10.8±5.7	11.1±5.2	10.5±6.2	0.69
LVPWd	12.1±1.9	12.0±1.9	12.3±2.0	0.546
IVSd	13.3±2.4	13.1±2.3	13.5±2.5	0.547
DT, cm	225.5±69.4	225.5±75.9	225.4±62.2	0.998
Volume of OG, cm3	21.4±5.7	21.3±6.8	21.6±4.3	0.81

Volume of OD cm3	15.7±3.6	15.9±4.2	15.5±2.9	0.626
SPAP, mmHg	27.7±10.3	28.2±10.4	27.1±10.3	0.681
TDI cms	14.1±2.3	14.3±2.2	14.0±2.4	0.639
Aorte initiale, mm	30.8±3.9	30.3±3.7	31.4±4.2	0.24
LVeds	19.2±4.0	19.1±4.1	19.3±4.0	0.81

Table 3: Echocardiographic parameters of the study population according to residual urine volume status

Factors associated with valvular calcification in hemodialysis patients

	Univariate analysis		**Multivariate analysis**	
Variables	p	OR (95%CI)	p	aOR (95%CI)
Age (years)				
≤60		1		1
>60	0.003	6.7 (1.93-23.7)	0.012	4.48 (1.67-6.10)
Tobacco (No vs Yes)	0.016	4.85 (1.55-42.86)	0.039	4.57 (1.15-13.36)
RUV				
≥500 mL		1		
<500 mL	0.374	1.57 (0.58-4.22)	-	-
DBP* mmHg	0.041	2.96 (1.91-9.98)	0.574	1.02 (0.95-1.09)
PP* mmHg	0.02	5.61 (1.01-11.05)	0.335	1.03 (0.97-1.10)
ABI*	0.04	11.24 (1.06-13.85)	0.534	0.26 (0,14-17,82)
P* mg/dL	0.012	5.71 (1.11-22.32)	0.011	2.17 (1.83-5.65)
CRP* mg/L	0.014	3.96 (1.90-10.15)	0.23	0.95 (0.88-1.03)
HT (No vs Yes)	0.014	26 (1.79-8.51)	0.026	3.96(1.24-15/7)

Table 4: Univariate and multivariate factors associated with cardiac vascular calcifications according to residual volume urine status in logistic regression analysis

In multivariate analysis (Table 4), hypertension (adjusted OR 4, 95% CI [1.24-15.7]), age> 60 years (adjusted OR 4, 95% CI [1.67-6.10]), tobacco (adjusted OR to 5, 95% CI [1.15-13.36]), phosphoremia (adjusted OR 2, 95% CI [1.83-5.65]) were independently associated with valvular calcifications. However, RUV is not associated with valvular calcifications

Factors associated with systolic and diastolic function in hemodialysis patients according to residual urine volume.

Factors independently associated with systolic dysfunction (Table 5) found were the following: HT [adjusted OR 6, (2.11-7.49), p= 0.016], hyperphosphatemia [adjusted OR 8 (2.13-11. 58), p=0.003]; RUV [adjusted OR 2 (1.69-4.76), p=0,017]; ABI [adjusted OR 7 (2.10 – 8.58) p=0.025] for systolic dysfunction of LV and diastolic (Table 6): diabetes mellitus [adjusted OR 8 (1.89 - 17.15), p= 0.025], tobacco [adjusted OR 6 (1.20 - 8.57), p=0.015], SBP [adjusted OR 3 (1.09 - 5.66), p=0.020] and RUV [adjusted OR 3 (1.61 - 5.19), p=0,019].

	Univariate analysis		**Multivariate analysis**	
Variables	P	OR (95%CI)	p	ORa (95%CI
HT (No vs Yes)	0.007	4.70 (2.89-7.25)	0.016	5.88 (2.11-7.49)
Hyperphosphoremia(No vs Yes)	0.014	7.67 (1.53-11.07)	0.003	8,17 (2.13-11.58)
RUV				
>500 ml		1		1
<500 ml	0.025	3.88 (1.65-5.43)	0.017	2.31 (1.69-4.76)
Duration in HD* month	0.042	2.07 (1.91-12.71)	0.81	1.01 (0.95-1.06)
Kt/v* weekly	0.035	11.63(1.01-15.14)	0.76	1.59 (0.82-3.72)
PP* mmHg	0.002	2.07 (1.98-6.17)	0.998	1.12 (0.95-1.43)
ABI*	0.23	7.78 (1.05-8.19)	0.025	6.67 (2.10-8.58)
P* mg/dl	0.276	2.69 (1.66-4.31)	0.354	1.05 (0.95-1.17)
CRP* mg/l	0.047	6.12 (1.92-9.99)	0.799	1.01 (0.97-1.04)

Table 5: Univariate and multivariate factors associated with LV systolic dysfunction in logistic regression analysis

	Univariate analysis		**Multivariate analysis**	
Variables	p	OR (95%CI)	p	ORa (95%CI)
Diabetes (No vs Yes)	0.043	3.60 (1.04 - 12.48)	0.025	7.26 (1.59 - 10.15)
Tobacco (No vs Yes)	0.014	3.60 (1.65 - 19.84)	0.015	6.15 (1.20 - 8.57)
RUV				
≥500 ml		1		1
<500 ml	0.014	2.59 (1.73 – 9.22)	0.019	2.75 (1.61 – 5.19)

Duration* in HD month	0.015	11.3 (1.96 - 16.30)	0.125	1.16 (0.96 - 1.39)
KT/V* weekly	0.033	2.86 (1.21 – 39.59)	0.239	0.59 (0.14 – 4.15)
SBP mmHg	0.049	4.10 (1.01 - 10.84)	0.02	2.76 (1.04 - 5.66)
eGFR*	0.002	0.57 (0.39 – 0.82)	0.607	1.11 (0.74 – 1.67)
Créat* mg/dl	0.013	3.10 (1.06 - 16.19)	0.985	1.04 (0.68 - 1.48)
P* mg/dl	0.007	13.41 (1.97– 18.57)	0.277	1.98 (0.58 – 6.80)

Table 6: Univariate and multivariate factors associated with LV diastolic dysfunction in logistic regression analysis

DISCUSSION

This study showed that the presence of valvular calcifications, a high value of phosphocalcic product, the lower use of diuretics and ACE inhibitors and prolonged duration in HD were independently associated with a deterioration of the RUV. In addition, the proportion of left ventricular diastolic dysfunction was higher in patients with reduced RUV than in those with preserved RUV, although this was not statistically significant.

In the present study, VC were seen in nearly 4 out of 10 HD patients. This discrepancy can be justified by the low use of phosphorus chelators, the abusive use of vitamin D + calcium carbonate without proper control of monitoring parameters. This value is however lower that of 46% and 50% found by Selcoki in Turkey [32] and Sanchez Perales et al. in Spain, respectively [33].

Duration of hemodialysis therapy seems to be another risk factor for VC [30, 33 - 35]. Disturbance of Ca × P product is a well-known contributor to the development of cardiac VC in patients on HD. In addition, uncontrolled hyperphosphatemia is an established risk factor for cardiovascular calcifications [36]. Elevated Ca × P product was predictive parameter for VC in studies of Maher et al, and Salgueira et al. [34, 35].

In the present study traditional (aging, tabacco use and hypertension) as well as uremic-specific (hyperphosphatemia) risk factors were both associated with VC. In general, very little RRF can effectively control blood volume to minimize the effect of dialysis. In addition, RRF can produce a certain amount of erythropoietin and active Vit D3 and promote hematopoietic function, which maximizes and maintains the calcium and phosphorus balance and nutritional status. In our study, phosphorus and serum calcium in reduced RRF group were higher than those in preserved RRF group. These results confirmed the effect of RRF on endocrine system [21], even though RUV does not emerge as a determinant of valve calcification. Indeed, aging process is a well-known vascular risk factor through associated-insulin resistance and subsequent clustering of multiple risk factors to vascular wall remodeling [37]. Hypertension is an important risk factor for atherosclerosis and its association with cardiac valvular calcification in HD patients has been already reported [30, 32, 38]. Tabacco use may induce vascular remodeling and subsequent atherosclerosis through oxidative stress and subsequent inflammation activation sympathetic nervous system and renin angiotensin system [39].

Therefore, high interdialytic weight gain induced by deterioration of residual renal function is associated with increased vascular stiffness in patients on hemodialysis. Taken together, following the decrease in residual renal function of dialysis patients, the accumulation of proinflammatory cytokines and β2-microglobulin, and high interdialytic weight gain may induce the increase of vascular calcification and stiffness.

Diastolic dysfunction has been observed in patients receiving RRT for ESRD in many studies [40, 41]. The residual urinary volume is associated in this study with systolic and diastolic dysfunctions of the ventricle contrary to the results of Faguli et al. [42].

The survival benefit is likely connected to advantages in fluid management, because frequently volume-overloaded HD patients are at high risk of hypertension, LVH and CHF [43]. In agreement with this, we noted in this study a significant association between the loss of RRF and diastolic and systolic cardiac dysfunction, and that was found to be significant.

Of note, left ventricular diastolic dysfunction is known as an ongoing cardiovascular challenge and may be an independent predictor of cardiovascular events in dialysis patients [44]

In fact, the adverse influence of SBP, diabetes mellitus and tobacco on diastolic function was evidenced by the finding of left ventricular mass and deceleration time higher in the group in patients with reduced RRF; however, an inappropriate left ventricular mass was not correlated with the severity of diastolic dysfunction. Our study indicated that LVM and E / E 'were reduced in patients with RUV reduced but not significant. These results suggest that RRF has a certain protective effect on the left ventricular structure and corroborate those of Ma T et al. [21]

In conclusion, although the patients with retained residual renal function had a much shorter hemodialysis duration, they showed that the presence of valvular calcifications, the decrease in the consumption of diuretics, ACE inhibitors, were associated to a deterioration of the residual renal function. Furthermore, we have not established that residual urinary volume is also an independent factor in valvular calcification, unlike left ventricular systolic and diastolic dysfunctions as predictive of cardiovascular events. Cardiovascular risk factors such as hypertension, diabetes mellitus, tobacco and hyperparathyroidism are independently associated with systolic and diastolic dysfunction. However, these results also make it difficult to confirm the causal link between cardiovascular events and residual renal function.

Limitations

Our study has certain limitations that must be acknowledged. First, limiting the study to only 4 HD centers leads to selection

bias and does not allow the generalization of our results to all hypertensive individuals. Second, the cross-sectional design of our study prevents the establishment of any causal relationship. Third, the small sample size does not give enough power to statistical tests to detect potential associations. Fourth, VC were evaluated using echocardiography, a tool that is less sensitive than electron beam tomography (EBCT), and does not accurately quantify calcium deposited on heart valves and absence of certain parameters such as FGF 23, Klotho. Fifth, the simple evaluation of residual renal function from residual renal diuresis only without taking into account the residual clearance of renal urea calculated from the concentration of urea in the blood and urine. Sixth, the absence of the echocardiography 2D-strain which is a new evaluation technique and better tool for evaluation of LV systolic function by measuring Strain (S) and Strain Rate (SR), a reflection of myocardial deformity during the cardiac cycle.

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