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Cardiovascular

Reverse cardiac remodeling after fluid balance optimization in patients with end-stage renal disease

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Abstract
Background: In patients with end-stage renal disease (ESRD) undergoing hemodialysis, cardiovascular diseases, and in particular chronic heart failure are the leading causes of morbidity and mortality. Nevertheless, few data are available about the impact of fluid optimization on echocardiographic parameters of cardiac function in patients with ESRD.
Methods and Results: In five patients with ESRD undergoing hemodialysis who had developed nonischemic dilated cardiomyopathy, an optimal fluid volume management based on a strict bioelectrical impedance analysis-assisted dry weight target and dietary sodium and water restriction led to left ventricular reverse remodeling and improvement in hemodynamic parameters. The reverse remodeling further improved after kidney transplantation.
Conclusions: This case series supports the possible beneficial effect of volume status optimization on cardiac function and the potential reversibility of cardiac dysfunction after kidney transplantation.

KEYWORDS
cardiovascular disease, dialysis, echocardiography, heart failure

INTRODUCTION

In patients with end-stage renal disease (ESRD) undergoing hemodialysis, cardiovascular diseases, and in particular chronic heart failure (CHF) are the leading causes of morbidity and mortality.[1,2]

Despite the clinical relevance of this issue, few data are available on how the management of patients with ESRD with concomitant CHF affects the echocardiographic cardiac parameters. Here, we report a case series of five patients undergoing hemodialysis who had developed CHF, dilated cardiomyopathy, and mild-to-severe left ventricular (LV) systolic dysfunction, in whom the main therapeutic approach was based on optimal fluid volume management. Particularly, at the beginning of the observation, the dry weight of the patients was reassessed using bioelectrical impedance analysis (BIA) and set as low as possible. Thereafter, to minimize interdialytic weight gain, a low-sodium, and fluid-restricted (up to 750 ml/day) diet was prescribed.

Raffaella Ursi and Francesco Pesce equally contributed to this study.

METHODS

Among consecutive outpatients with CHF referred to the Heart Failure Unit of the University Polyclinic Hospital of Bari from 2014 to 2019,[3] we retrospectively evaluated those with ESRD and on the kidney transplant waiting list. Written informed consent was obtained from the patients for the publication of this case series and any accompanying images.

The first recorded medical visit was considered the baseline evaluation. Medical history taking, physical examination, 12-lead electrocardiography, mono- and two-dimensional echocardiography, and blood sample collection were performed. The presence of ischemic cardiomyopathy, arterial hypertension, atrial fibrillation, diabetes mellitus, and dyslipidemia, as well as the history of CKD and dialysis, were documented and recorded. These baseline evaluations were repeated at least every 6 months, according to the patients' management protocol at the heart failure unit. New York Heart Association class, anthropometric data, systolic and diastolic arterial pressures, and heart rhythm were also recorded.

Echocardiographic recordings were obtained using an echo-Doppler system (Vivid 7, GE Vingmed Ultrasound; General Electric) equipped with a phased-array, 4-MHz probe. Interventricular septal thickness, LV end-diastolic diameter, and posterior wall thickness were evaluated, and indexed LV mass was calculated.[4] LV end-diastolic volume, LV end-systolic volume, and LV ejection fraction (LVEF) were calculated using Simpson's rule. To estimate the right ventricular function, the tricuspid annular plane systolic excursion was evaluated. LV diastolic function was assessed by calculating the left atrial volume and through mitral pulsed Doppler and pulsed tissue Doppler imaging examinations. The peak early diastolic velocities (E') at the level of the septal and lateral mitral annulus, as well as the mean of these values, were calculated. The ratio between the peak early diastolic velocity in pulsed Doppler and the mean e' (E/e') was then calculated. Mitral regurgitation and tricuspid regurgitation were semiquantitatively evaluated using color Doppler, with arbitrary units ranging from 0 to 4. Pulmonary artery systolic pressure was estimated from the peak velocity of tricuspid regurgitation and the estimated central venous pressure.

RESULTS

A total of five patients with both nonischemic dilated cardiomyopathy and ESRD and on the kidney transplant waiting list were evaluated.

Patient 1 was a 52-year-old man who received a kidney transplant in 1996 after 6 years of hemodialysis. In 2003, chronic graft rejection occurred and hemodialysis was resumed. CHF with reduced LVEF was diagnosed in October 2012. Coronary angiography did not show obstructive coronary disease. A cardioverter defibrillator was implanted. In January 2014, he was assessed for eligibility for kidney retransplantation. He reported dyspnea on minimal exertion and poor adherence to sodium and water restriction.

Patient 2 was a 44-year-old man with a history of systemic hypertension, insulin-dependent diabetes mellitus, and ESRD requiring dialysis since 2012. In August 2013, he was admitted to our clinic for the evaluation of dilated cardiomyopathy. His coronary angiography results were normal. Considering the sustained reduced LVEF, a cardioverter defibrillator was implanted. He was evaluated for eligibility for kidney transplantation in September 2014. He reported poor adherence to sodium and water restriction, as well as excessive interdialytic weight gain.

Patient 3 was a 50-year-old man with hypertension and undergoing hemodialysis since May 2014. He was evaluated for nonischemic dilated cardiomyopathy in May 2015.

Patient 4 was a 22-year-old man with arterial hypertension and ESRD requiring hemodialysis since April 2017. In August 2018, he was admitted for acute pulmonary edema with negative coronary angiography.

Patient 5 was a 20-year-old man with poorly controlled systemic hypertension and ESRD requiring hemodialysis since April 2019.

Similar to the first two patients, patients 3–5 also reported poor adherence to sodium and water restriction.

Table 1 shows the clinical and echocardiographic characteristics of all patients before and after management. After dry weight reduction and sodium and water restriction, all patients showed progressive improvement in LVEF with reverse LV remodeling, reduced LV volume and left atrial volume, and significantly reduced estimated systolic arterial pulmonary pressure after a median time of 6 months (Table 1 and Figure 1). Patients 1 and 2, who had a longer history of CHF, showed improvements after a longer time. Additionally, cardiospecific therapy with beta-blockers or renin–angiotensin–aldosterone system inhibitors was reduced in three patients and discontinued in one patient. Patients 2 (November 2017), 3 (April 2017), and 4 (October 2019) showed further improvements after receiving a kidney transplant (Table 1).

DISCUSSION

This brief report describes the management of five patients with CHF who were undergoing hemodialysis.

TABLE 1 Clinical and echocardiographic characteristics of patients

	Patient 1		Patient 2			Patient 3			Patient 4			Patient 5	
	Baseline	After optimal fluid balance	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance
Clinical parameters													
Height, cm	165	165	179	179	179	180	180	180	172	172	172	163	163
Weight, kg	74	73	69	67	69	77	76	75.5	57	55	55	56	53.5
SAP, mmHg	120	110	130	150	140	155	105	125	175	160	127	150	123
DAP, mmHg	80	60	80	90	90	95	70	80	110	105	88	85	60
NYHA class	III	II	II	I	I	II	I	I	III	II	I	II	I
Carvedilol ED, mg	6.25	–	50	50	50	50	25	25	37.5	50	25	25	6.25
Valsartan ED, mg	–	–	160	80	–	160	–	80	80	160	–	–	160
Echocardiographic parameters													
LVEDD, mm	64	52	61	60	52	63	50	50	57	52	42	64	49
IVS, mm	9	12	12	12	13	12	14	15	12	11	14	12	12
PWT, mm	9	10	12	12	12	11	11	12	13	11	12	11	12
RWT	0.28	0.38	0.39	0.4	0.46	0.35	0.44	0.48	0.46	0.42	0.46	0.34	0.49
LVMI, g/m^2	133	122	179	168	141	164	129	134	173	134	122	207	145
LVEDV, mL	219	95	184	187	145	207	108	130	173	115	62	217	125
LVEF, %	20	50	35	40	48	43	44	52	30	47	55	43	60
Septal e'	3	5	8.3	4.4	7.6	7	7	7	6	6.7	6.9	6.9	8.9
Lateral e'	6.7	8	9	5.8	12	11	6	9	9	10.9	11.2	7	11.7
E/e'	13.4	8	10	8	7.5	10	6.6	7	10	11	9	16	6
LAV, ml	110	65	79	90	87	129	60	77	97	75	33	110	34
MR	Moderate–severe	Minimal	Mild–moderate	Mild	Mild	Moderate–severe	Mild	Mild	Moderate	Minimal	Minimal	Mild	–
TAPSE, mm	15	20	24	28	28	21	21	21	25	26	24	25	27
TR	Severe	Mild	Mild–moderate	Mild–moderate	Mild–moderate	Mild	Mild	Mild	Moderate	Minimal	Minimal	Moderate	–
IVC, mm	18	14	14	7	8	18	16	15	22	12	5	23	18
ePASP, mmHg	55	30	35	33	30	50	28	25	70	25	18	47	20

(Continues)

TABLE 1 (Continued)

Clinical parameters	Patient 1		Patient 2			Patient 3			Patient 4			Patient 5	
	Baseline	After optimal fluid balance	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance	After KT	Baseline	After optimal fluid balance
Time from baseline, months	0	12	0	12	18	0	6	18	0	6	20	0	6

Note: Data before and after optimization of fluid balance are shown for all patients, as well as after kidney transplantation for three patients. The optimal management of fluid and sodium imbalance in patients undergoing dialysis consisted of adjusting salt and fluid removal through dialysis (ultrafiltration and dialysate sodium) and by restricting salt intake and fluid gain between dialysis sessions.

Abbreviations: DAP, diastolic arterial pressure; ED, equivalent dose; ePASP, estimated pulmonary arterial systolic pressure; KT, kidney transplantation; IVS, interventricular septum; LAV, left atrial volume; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; IVC, inferior vena cava; MR, mitral regurgitation; NYHA, New York Heart Association; PWT, posterior wall thickness; RWT, relative wall thickness; SAP, systolic arterial pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

All patients were diagnosed with nonischemic dilated cardiomyopathy with mild-to-severe impairment of LVEF. After the optimization of fluid balance through sodium and water restriction and BIA-assisted adjustment of dry weight to the lowest possible target, significant reverse remodeling and improvement in hemodynamic parameters were observed. These improvements were further enhanced after kidney transplantation.

Patients with ESRD show myocardial structural changes mainly characterized by LV hypertrophy and diastolic dysfunction.[5] In more advanced stages, they can progress into a dilated phenotype, which is associated with greater mortality.[2] The underlying pathophysiologic mechanism is related to hemodynamic and nonhemodynamic factors. Increased LV afterload, which can be due to uncontrolled arterial hypertension, increased arterial systemic resistance, vascular calcification, and occasionally aortic stenosis, can promote concentric LV remodeling. Conversely, an increased preload, resulting from the expansion of intravascular volume due to fluid retention and to the high flow related to arteriovenous fistulas and anemia, can promote eccentric LV remodeling.[5] The dilated phenotype can also be caused by nonhemodynamic factors such as uremic toxins, oxidative stress, inflammatory status, hyperparathyroidism, hypovitaminosis D, hyperphosphatemia, and activation of the renin–angiotensin–aldosterone system.[6]

Despite its prognostic impact, the optimal medical management of heart failure with reduced LVEF and the role of dialysis treatment protocols in patients with ESRD remain controversial.[7,8] The impact of fluid balance on LV remodeling has been highlighted in a study with three patients treated with the intensive control of blood pressure and fluid and electrolyte intake.[9]

Our case series further supports the hypothesis that an optimal fluid management achieved by dietary salt and water restriction and a strict dry weight target may be beneficial in this clinical setting. All patients in our series showed reduced LV dilatation, improved systolic function, and reduced left atrial dilatation and pulmonary pressures.

Notably, the success of our therapeutic approach may be due to a shared phenotype. All patients were young, had no prior history of any heart disease, and had LV dilatation and reduced LVEF not related to an obstructive coronary disease. Moreover, all patients had fluid overload because of poor compliance to salt and fluid intake restriction, as well as excessive interdialytic weight gain.

The main role of optimal fluid balance in the observed improvements was also confirmed by the reduction (in three patients) or discontinuation (in one patient) of cardiospecific therapy with beta-blockers or renin–angiotensin–aldosterone system inhibitors (i.e., drugs with a reverse remodeling effect).

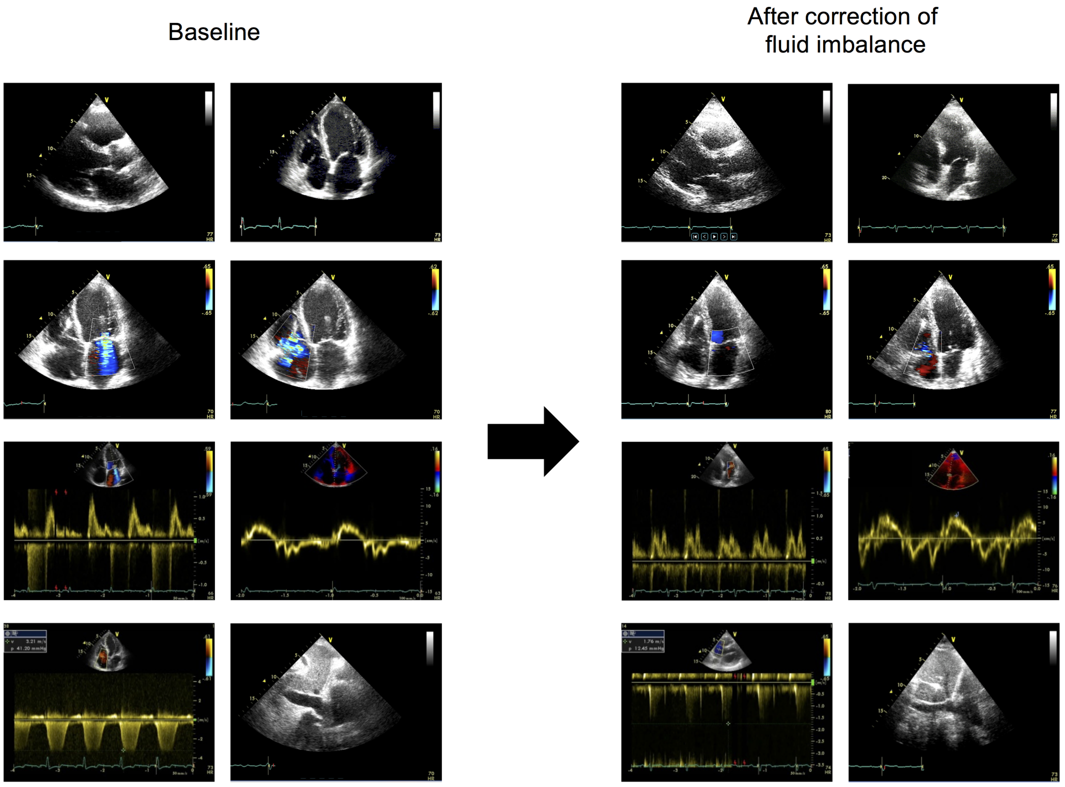

FIGURE 1 Echocardiographic examination of patient 1 before (left) and 12 months after (right) the correction of fluid imbalance. From top to bottom: Four-chamber view, mitral and tricuspid regurgitation, pulsed Doppler and tissue Doppler images obtained at the level of the mitral valve, and systolic velocity peak of tricuspid regurgitation and the inferiorvena cava [Color figure can be viewed at wileyonlinelibrary.com]

Finally, the observed improvements were even more noticeable after kidney transplantation in three patients. This was probably due to the combined role of better and continuous fluid balance control and effective clearance of uremic toxins.

In patients with ESRD, the accumulation of uremic toxins adversely affects cardiac performance because of their inotropic and chronotropic effects and their ability to cause myocyte fibrosis and apoptosis with long-term exposure.[10] In our three patients who received a transplant, the clearance of uremic toxins may have contributed to reverse cardiac remodeling. This is important because several studies have shown that kidney transplantation decreases cardiovascular mortality and the risk of CHF development compared with long-term dialysis therapy. Increasing evidence suggests that replacing renal function with a kidney graft in patients with CHF is associated not only with the reduction in LV hypertrophy but also with the reversal of cardiac dysfunction.[11]

Our clinical approach also has relevant consequences on the patients' eligibility for kidney transplantation. All patients were referred to the heart failure unit to exclude contraindications to kidney transplantation or to evaluate the option of kidney or heart transplantation. As we observed a dilated cardiomyopathy phenotype associated with fluid imbalance, none of the patients were determined to have had an absolute contraindication to kidney transplantation or an indication for heart transplantation. This decision was driven by the possibility of obtaining a significant improvement in cardiac function after the optimization of fluid balance. In our case series, kidney transplantation further improved the cardiac function of patients who received a transplant.

CONCLUSIONS

In patients with ESRD undergoing hemodialysis and with CHF due to nonischemic dilated cardiomyopathy, optimal fluid management can result in significant reverse remodeling, which can be further improved via kidney transplantation.

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CONFLICT OF INTEREST

No conflict of interests to declare.

ETHICS STATEMENT

All patients signed a written informed consent for publication of this case report and any accompanying images for writing.

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