RIGHT VENTRICULAR DYSFUNCTION IN CHRONIC KIDNEY DISEASE STAGES 3 AND 4

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ABSTRACT

BACKGROUND

Cardiovascular diseases form the major cause of death in patients with end-stage renal disease, among which heart failure predominates the list. Right ventricular dysfunction significantly contributes to the cause of morbidity and mortality in chronic kidney disease patients. We observed for the presence of right ventricular dysfunction in stages 3 and 4 of chronic kidney disease patients.

MATERIALS AND METHODS

We enrolled 100 patients with chronic kidney disease stages 3 and 4 with glomerular filtration rate of 15-60 mL/mins./1.73 sq. m. based on MDRD formula. Two dimensional and M-mode echocardiography was performed in these patients. TAPSE values were used to assess right ventricular dysfunction and Right Ventricular End-Diastolic Diameter (RVEDD) was used to identify the presence of RV dilatation.

CONCLUSION

Right ventricular dysfunction and pulmonary hypertension start early and progresses as the chronic kidney disease progresses. Hence, early detection of RV dysfunction by TAPSE and measurement of SPAP for pulmonary hypertension by echocardiogram, which is a noninvasive and cost-effective modality could help in prognostication and better management of these patients.

RESULTS

35% of the study group had TAPSE value less than 16 mm suggestive of right ventricular dysfunction. 24 patients had right ventricular end-diastolic diameter more than 26 mm denoting the presence of RV dilatation. TAPSE values had a positive correlation with GFR. Renal parameters like urea, creatinine, calcium, phosphorus were significantly higher among the patients with right ventricular dysfunction compared to patients with no evidence of right ventricular dysfunction.

KEYWORDS

RV Dysfunction, PHT, CKD, Heart Failure in CKD.

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BACKGROUND

Cardiovascular diseases are the leading cause for mortality among patients with chronic kidney disease contributing to almost 50% of the deaths.[1] Cardiac failure in particular has a poor prognosis when coexisting with chronic kidney disease.[2] Patients with CKD are prone to develop pulmonary hypertension whose incidence increases as the disease progresses. Survival of these patients, however, depends on the cardiac function rather than the pulmonary pressures.[3] Right ventricular dysfunction may also affect the filling of left ventricle via interventricular interaction.[4] Right ventricular function assessment by tissue Doppler imaging can be used to detect preclinical abnormalities in the cardiac functioning.[5] Data on the prevalence of right ventricular dysfunction among patients with chronic kidney disease is well established among end-stage renal disease patients.[6] This study was designed to screen for the presence of right ventricular dysfunction among patients with chronic kidney disease stages 3 and 4 in order to establish early development of right ventricular dysfunction among them, which will help in prognostication of the patients.

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AIMS

To study right ventricular function by tricuspid annular plane systolic excursion (TAPSE) in patients with CKD stages 3 and 4 (GFR 15-60 mL/min. calculated by modification of diet in renal disease formula) and study the correlation between right ventricular function with GFR.

MATERIALS AND METHODS

The study was carried over a period of one year during 2015. It was an analytical study involving 100 patients with CKD stages 3 and 4 having GFR 15-60 mL/min./1.73 sq. m. based on MDRD formula who visited the medical outpatient

department. The patients with cardiac diseases, systemic connective tissue disorders, COPD, pulmonary tuberculosis, interstitial lung disease, patients with deep vein thrombosis, HIV positive patients and patients with EF <55% have been excluded from the study in order to avoid the known confounding factors.

A detailed history and clinical examination was carried out. GFR was calculated using the MDRD formula.

GFR (mL/min./1.73 sq. m.) = 175 × (s. creatinine)-(1.154 × age) - (0.203 × 0.742 if female or 1.212, if African American).

Two-dimensional and M-mode echocardiography were performed in these patients. Cardiac dimensions were estimated by adhering to the American Society of Echocardiography Guidelines. TAPSE was measured by the distance of systolic excursion of the RV annular segment along its longitudinal plane. TAPSE was assessed using the M mode in apical four chamber window. Patients with TAPSE less than 16 mm were considered to be having RV dysfunction. RV End-Diastolic Diameter (RVEDD) was also estimated by M mode. RVEDD diameter more than 26 mm was considered as presence of RV dilatation. Ejection fraction was estimated in all patients by using Simpson's formula.

STATISTICAL ANALYSIS

Descriptive statistical analysis has been carried out in the present study. The proportion is computed for categorical data. Chi-square test has been used to find the statistical significance between two groups of proportions. The mean and standard deviation are computed for continuous data. The independent t-test was used to find statistical significance between the groups of mean. Correlation coefficient was computed to assess the linear relationship between continuous variables. All analyses was two tailed and p ≤0.05 was considered significant. SPSS version 16.0 was used for data analysis.

RESULTS

Among the 100 study population, 26% were more than 60 yrs. of age, 24% patients were in 40-49 years age group, 19% in 50-59, 18% in 30-39 and 13% were less than 30 years of age. Of these, 67 patients were male and 33 were female patients. The aetiology of chronic kidney disease among the study patients was diabetes mellitus in 46, systemic hypertension in 31, glomerulonephritis in 14 and chronic interstitial nephritis in 9 patients, respectively. Table 1 shows the age distribution among the patients with and without RV dysfunction. The p value was 0.147, which is statistically insignificant, tells that both the groups had similar age group distribution. Table 2 shows the sex distribution among the patients with pulmonary hypertension.

35% patients had TAPSE less than 16 mm suggestive of RV dysfunction while 65% patients had normal TAPSE values. Among the 35 patients with RV dysfunction, 14 were females (40%) and 21 were males (60%). The TAPSE values ranged between 11.8 and 24.0 with a mean of 18.441 and standard deviation of 3.11685. Table 3 shows native kidney disease distribution among patients with and without RV dysfunction. The p value was 0.053, which shows no significant difference among the two groups. 24 patients had RV dilatation with RV end-diastolic diameter more than 26 mm while 76 patients had normal RV dimensions. 11 patients had RV dysfunction in spite of no RV dilatation.

Table 4 shows the biochemical parameters and GFR among the study group. Table 5 shows the correlation between SPAP, TAPSE and GFR. TAPSE and GFR have a positive correlation of 0.751 while SPAP had a negative correlation with both TAPSE and GFR. Table 6 shows the biochemical parameters in patients with and without RV dysfunction. Urea, creatinine, serum calcium, serum phosphorus were significantly higher in patients with RV dysfunction while GFR was low among them. Mean urea and creatinine were higher in the pulmonary hypertension group with p value of 0.002 and 0.005, respectively. Serum calcium and phosphorus were also higher among these group of patients whereas the GFR was significantly lower in them.

Among the patients with RVD, 17 patients were having pulmonary hypertension and 7 had normal pulmonary hypertension. P value of 0.00 shows RVD is more common in patients with pulmonary hypertension as is shown in table 7.

			TAPSE			**SPAP**	
Age Group			<16 mm	>16 mm	<35 mm	>35 mm	Total
	<30	No.	3	10	0	13	13
		%	8.6%	15.4%	0%	17.3%	13%
	30-39	No.	5	13	2	16	18
		%	14.3%	20.0%	8%	21.3%	18%
	40-49	No.	6	18	4	20	24
		%	17.1%	27.7%	16.0%	26.7%	24%
	50-59	No.	11	8	8	11	19
		%	31.4%	12.3%	32%	14.7%	19%
	7160	No.	10	16	11	15	26
		%	28.6%	24.6%	44%	20.0%	26%
	Total	**No.**	**35**	**65**	**25**	**75**	**100**
		%	**100.0%**	**100.0%**	**100.0%**	**100%**	**100%**

Table 1. Age Distribution in Patients With and Without RV Dysfunction and Pulmonary Hypertension

			TAPSE		SPAP		Total
			<16 mm	>16 mm	>35 mmHg	≤35 mmHg	
Sex	Male	No.	21	46	16	51	67
		%	31.3%	68.7%	23.9%	76.1%	100%
	Female	No.	14	19	9	24	33
		%	42.4%	57.6%	27.3%	72.7%	100%
Total		**No.**	**35**	**65**	**25**	**75**	**100**
		%	**35%**	**65%**	**25%**	**75%**	**100%**

Table 2. Sex Distribution Among the Patients With RV Dysfunction and Pulmonary Hypertension

			TAPSE			SPAP	
Native Kidney Disease (NKD)			**<16 mm**	**>16 mm**	**>35 mm**	**<35 mm**	**Total**
		No.	22	24	18	28	46
	DM	%	47.8%	52.2%	39%	60.9%	100%
		No.	7	24	6	25	31
	SHT	%	22.6%	77.4%	19.4%	80.6%	100%
		No.	5	9	1	13	14
	GN	%	35.7%	64.3%	7.1%	92.9%	100%
		No.	1	8	0	9	9
	CIN	%	11.1%	88.9%	0%	100%	100%
		No.	35	65	25	75	100
	Total	**%**	**35.0%**	**65.0%**	**25.0%**	**75%**	**100%**

Table 3. Native Kidney Disease Distribution in Patients With and Without RV Dysfunction and Pulmonary Hypertension

Parameter	No.	Minimum	Maximum	Mean	Standard Deviation
Age	100	16.0	84.0	48.5	16.92318
Haemoglobin	100	7.8	12.0	9.885	1.06774
Urea	100	4.5	129.0	72.575	25.04263
Creatinine	100	1.2	4.2	2.79	0.88209
Calcium	100	7.2	11.3	9.0410	0.86993
Phosphorus	100	2.3	5.2	3.6320	0.56816
GFR	100	15.0	59.2	27.363	11.85725
TAPSE	100	11.8	24.0	18.4410	3.11685
Valid N	100				

Table 4. Variation of Biochemical Parameter, GFR and TAPSE Among the Study Group

		TAPSE	GFR	SPAP
TAPSE	Pearson correlation	1	0.751**	-.611**
	Sig. (2 tailed)		0.000	.000
	N	100	100	100
GFR	Pearson correlation	0.751	1	-.427**
	Sig. (2 tailed)	0.000		.000
	N	100	100	100
	Pearson correlation	-.611**	-.427**	1
SPAP	Sig. (2 tailed)	.000	.000	
	N	100	100	100

Table 5. Correlation Between TAPSE, SPAP and GFR

**Correlation is significant at the 0.01 level (2-tailed).

TAPSE with GFR showed a positive correlation of 0.751.

TAPSE and GFR showed a negative correlation with SPAP (-.611 and -.427, respectively).

Parameter	TAPSE	N	Mean	Std. Dev.	P value	SPAP	N	Mean	Std. Dev.	P value
Haemoglobin	<16 mm	35	9.7171	1.08451	0.251	>35 mmHg	25	9.764	1.03677	0.516
	≥16 mm	65	9.9754	1.05594		≤35 mmHg	75	9.9253	1.08168	
Urea	<16 mm	35	87.4286	22.08311	0.000	>35 mmHg	25	85.88	25.03051	0.002
	≥16 mm	65	64.5769	22.92161		≤35 mmHg	75	68.14	23.58102	
Creatinine	<16 mm	35	3.4286	0.39747	0.000	>35 mmHg	25	3.368	0.41102	0.000
	≥16 mm	65	2.4462	0.88124		≤35 mmHg	75	2.5973	0.91415	
Calcium	<16 mm	35	8.5829	0.62190	0.000	>35 mmHg	25	8.492	0.65949	0.000
	≥16 mm	65	9.2877	0.88803		≤35 mmHg	75	9.224	0.85769	
Phosphorus	<16 mm	35	3.8314	0.70576	0.024	>35 mmHg	25	4.076	0.65909	0.000
	≥16 mm	65	3.5246	0.44862		≤35 mmHg	75	3.484	0.44964	
GFR	<16 mm	35	18.1114	2.12697	0.000	>35 mmHg	25	18.084	2.58838	0.000
	≥16 mm	65	32.3446	11.96104		≤35 mmHg	75	30.456	12.12996	

Table 6. Variation of Biochemical Parameters and GFR Among the Patients With and Without RV Dysfunction and Pulmonary Hypertension

			Pulmonary Hypertension		Total
			SPAP >35 mmHg	SPAP ≤35 mmHg	
RV Dilatation	RVEDD >26 mm	No.	17	7	24
		%	70.8%	29.2%	100%
	RVEDD <26 mm	No.	8	68	76
		%	10.5%	89.5%	100%
	Total	**No.**	**25**	**75**	**100**
		%	**25%**	**75%**	**100%**

Table 7. Correlation Between RV Dilatation and Pulmonary Hypertension

DISCUSSION

There are several studies on the prevalence and management of pulmonary hypertension in ESRD patients, but only a few studies on the incidence of pulmonary hypertension and RV dysfunction in early stages of CKD.[7-11]

In patients with similar pulmonary pressure values the key factor for the progression of systolic dysfunction is the presence of chronic volume overload, which may induce various adaptations in the right ventricle.[4] Hence, patients with chronic kidney disease should be watched for development of right ventricular dilatation and dysfunction beginning early in the disease course as volume overload is commonly encountered.

In our study, 35% had TAPSE less than 16 mm with mean TAPSE values of 18.44±3.11, while in the study by Floccari et al, among 202 patients, TAPSE was mildly depressed (less than 18 mm) in 44.5% of patients, moderately depressed (less than 15 mm) in 10.3% of patients. According to the American Society of Echocardiography, TAPSE less than 16 mm suggests right ventricular dysfunction, hence, TAPSE of less than 16 mm was taken as the cutoff for RV dysfunction in our study. LV ejection fraction was normal in all patients.[12,13]

No difference in haemoglobin levels were noted among patients with or without RV dysfunction. The urea and creatinine levels were higher among patients with low TAPSE values. Similarly, GFR was low in patients with RV dysfunction.[14]

There was a positive Pearson correlation between TAPSE and GFR in our study, while in the study by Floccari et al, there was no correlation between TAPSE and GFR while the study by Frank L. Dini et al showed a significant linear relationship between TAPSE and GFR.

To assess the chamber dilatation, RV end-diastolic diameter was used. A value more than 26 mm was considered dilated.[9,15,16,17] RV dilatation was observed among 24% of the study patients. Floccari et al reported RVEDD more than 26 mm in 107 patients (52.9%) and more than 30 mm among 6 (14.8%) patients.

The mean age of patients in our study was 48.5±6.92 years with no difference in distribution among patients with and without RV dysfunction and a slight male predominance.

However, PHT was more common among older age groups, which was in contrast to the observations made by Floccari et al. Considering the native kidney disease, diabetes mellitus was the commonest aetiology followed by

systemic hypertension, glomerulonephritis and chronic interstitial nephritis with no significant difference in kidney disease distribution among patients with and without RV dysfunction, which was similar to the observations made in the previous studies.[18] No difference in native kidney disease distribution was seen between RV dysfunction and non-RV dysfunction groups while pulmonary hypertension was more among in patients with diabetes. No such difference in pulmonary hypertension incidence was observed among the diabetics and normoglycaemics in the study by Floccari et al.

LIMITATIONS

- Right heart catheterisation was not performed to confirm the presence of pulmonary hypertension.
- The study population was a select group from a tertiary centre so there could be higher incidence of complicated and sick cases.
- TAPSE as a measure of right ventricular dysfunction can be misinterpreted in cases of severe tricuspid regurgitation, but none of our patients had severe tricuspid regurgitation.

CONCLUSION

Right ventricular dysfunction and pulmonary hypertension start early and progresses as the chronic kidney disease progresses. Hence, early detection of RV dysfunction by TAPSE and measurement of SPAP for pulmonary hypertension by echocardiogram, which is a noninvasive and cost-effective modality could help in prognostication and better management of these patients.

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