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Assessment of the Prevalence of Pulmonary Hypertension and Volume Status in Regular Hemodialysis Patients

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Abstract

Background: Cardiovascular disease is well-acknowledged as a significant cause of death among individuals diagnosed with chronic renal disease. It constitutes ~50% of mortality cases among those undergoing dialysis treatment. In recent studies, it has been discovered that the presence of pulmonary hypertension (PH) serves as a robust and autonomous prognostic indicator for mortality among those undergoing hemodialysis.

Aim: To assess the prevalence of PH and its relation to volume status in hemodialysis patients.

Patients and methods: A prospective comparative study that was conducted on 50 patients on regular hemodialysis in the Nephrology Unit of Kobry Al-Qobba Military Hospital.

Results: There were 23 (46.0%) patients with no PH and 27 (54.0%) patients with PH. 85.2% of patients with PH were mild and 14.8% were moderate. No statistically significant disparity was observed between non-PH and PH in terms of dialysis vintage hypervolemia as determined by clinical technique. A substantial statistical difference was seen between non-PH and PH in terms of e' (m/s), MR, and LVSD.

Conclusion: Patients undergoing hemodialysis exhibit a significantly elevated prevalence of PH. The pH levels were notably elevated in conjunction with e' (m/s), MR, and LVSD, although no discernible differences were observed with the remaining parameters.

Keywords: Assessment, Hemodialysis, Pulmonary hypertension

1. Introduction

Chronic kidney disease (CKD) poses significant challenges for healthcare practitioners and represents a substantial burden on the healthcare system. Cardiovascular disease is well-acknowledged as a significant and consequential cause of death among those diagnosed with chronic renal disease. It constitutes ~50% of mortality cases among those undergoing dialysis treatment. In addition to coronary artery disease, chronic renal disease is associated with a high prevalence of various other kinds of cardiovascular disease. Hemodialysis patients have been shown to have

pulmonary hypertension (PH). The condition is characterized by a gradual deterioration, leading to higher rates of illness and death.¹

In recent studies, it has been discovered that the parathyroid hormone (PTH) exhibits a robust capacity to independently forecast death among individuals undergoing hemodialysis. The occurrence of PH has been observed to be common in individuals diagnosed with end-stage renal disease (ESRD), and this association seems to be unrelated to the frequency of cardiovascular illness.²

PH is an increase in pulmonary arterial pressure (PAP), which may arise from many conditions

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affecting the heart, lungs, or systemic system. When the PAP is at or above 25 mmHg at rest or 30 mmHg during activity, it is called PH. Furthermore, those with PH have left ventricular end-diastolic pressure of at least 15 mmHg and mean pulmonary-capillary wedge pressure of the same amount.³

The measurement of pH is typically utilized as a diagnostic tool to assess the presence and severity of pulmonary vascular disease, which has the potential to worsen over time and result in mortality. A wide range of disorders might potentially lead to the development of PH. The problems that are commonly noticed include left heart failure and chronic hypoxic lung disorders. These conditions may be more prevalent among patients with collagen vascular diseases and a history of thromboembolic episodes.⁴

The average yearly occurrence of PH in the whole population is recorded at 15.9 new cases per million individuals per year. Additionally, the average prevalence of PH ranges from 15 to 50 cases per million people.⁵ The prevalence of PH exhibits variability according on the approach employed for estimation. The prevalence of PH in patients undergoing hemodialysis ranges from 12 to 49%. This variation can be attributed to different factors such as the specific threshold used to define PH based on PAP, the inclusion criteria employed in various studies (which may encompass individuals diagnosed with congestive heart failure or other comorbidities associated with increased pulmonary artery pressure), and the specific modality of extracorporeal dialysis utilized (either hemodialysis or peritoneal dialysis).⁶

Various factors can contribute to elevated pulmonary pressures. This includes conditions such as chronic volume overload, metabolic disruptions that impact the pulmonary vasculature, alterations in calcium and phosphate metabolism that contribute to metastatic calcification of the pulmonary artery, and persistent elevation in blood flow caused by an arteriovenous fistula (AVF) or arteriovenous graft. The issue is frequently disregarded and inadequately attended to, resulting in the eventual development of irreparable heart failure and mortality.⁷

2. Patients and methods

This prospective comparative study was conducted on 50 patients on regular hemodialysis in the Nephrology Unit of Kobry Al-Qobba Military Hospital.

2.1. Inclusion criteria

The study population consisted of individuals diagnosed with ESRD who had undergone regular hemodialysis treatment for a minimum duration of 6 months. The age range of the participants was between 18 and 60 years.

2.2. Exclusion criteria

The study excluded patients who had the following conditions: the patient presents with a medical history. This encompasses chronic obstructive lung illness, diseases affecting the chest wall or lung tissue, a history of pulmonary embolism, collagen vascular disorders, significant mitral or aortic valve abnormalities, as well as obstructive sleep apnea and cardiac or hepatic insufficiency.

2.3. Ethical consideration

An informed oral and written consent was taken from all participants before the start of the study. The steps of the study were explained to all the participants, and everyone had the right to leave at any time with no explanation.

2.4. Methods

Patients were subjected to the following.

2.4.1. Clinical characteristics

Age, sex, smoking habits, hypertension, a history of a cerebrovascular accident, and the cause of ESRD, and the occurrence of ischemic heart disease were the variables taken into account in this study.

2.4.2. Dialysis-related factors

Examples of factors that may be considered include the existence of AVF, the flow rates of AVF, the duration of dialysis treatment, the amount of residual urine output, the individual's volume status, and the rate of ultrafiltration each dialysis session.

2.4.3. Analysis of the volume status

The evaluation of quantity status across all patients was conducted using the standard clinical approach recommended by the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. This method encompasses the assessment of peripheral edema, blood pressure monitoring, and jugular venous pressure rise. For each session, the

ultrafiltration rate was computed, and all participants had dialysis until their target dry weight was achieved.

A full battery of laboratory investigations was administered to all patients, comprising the following tests: the laboratory tests conducted included a complete blood count, assessment of liver and kidney function, determination of serum albumin levels, measurement of calcium and phosphorus levels, analysis of PTH, quantification of C-reactive protein, and evaluation of brain natriuretic peptide (BNP).

2.4.4. Echocardiography and ECG

All participants' ECG and echocardiograms were evaluated 1 h after hemodialysis. A strain pattern in the right atrium, right ventricular, and left ventricular, as well as right ventricular hypertrophy, were all present, and any abnormalities in wall motion were all looked for on the electrocardiogram, which was examined for signs of PH.

2.5. Variable definitions

According to the recommendations made by the American Society of Echocardiography, the pulmonary artery systolic pressure (PASP) was calculated using the modified Bernoulli equation and the tricuspid systolic jet. To calculate the PASP, multiply the transvalvular regurgitant velocity by 4, squared, and add the predicted right atrial pressure.

The estimated right atrial pressure was 5, 10, and 15 mmHg in cases where the right atrium exhibited normal, mild enlargement, and severe enlargement, respectively.

PH is characterized by a PASP exceeding 35 mmHg, whereas individuals with a PASP below 35 mmHg are classified as typical non-PH patients, as per the guidelines set forth by the American Society of Echocardiography and corroborated by several research (19–22).

The group with significantly elevated PASP has been identified as having a PASP measurement beyond 50 mmHg. On the other hand, a PASP measurement ranging between 36 and 50 mmHg is regarded to indicate a slight increase in PASP. Patients falling within the normal PASP range have been categorized based on the guidelines provided by the American Society of Echocardiography and other relevant research studies.

2.6. Statistical analysis

The data was gathered, updated, coded, and entered into IBM SPSS (Nasr City, Cairo, Egypt),

version 20, by the researchers. Numbers and percentages were used to provide qualitative data, whereas means, SDs, and ranges were used to display quantitative data, provided that their distribution was parametric.

The analysis involved comparing two groups with qualitative data. The χ^2 test was utilized, except when the expected count in any cell was below 5, in which case the Fisher exact test was employed as an alternative to the χ^2 test.

The analysis involved doing an independent *t* test to compare two independent groups with quantitative data that followed a parametric distribution.

The confidence interval was established at a 95%, with a corresponding margin of error of 5%. The *P* value was deemed statistically significant based on the following analysis. In statistical analysis, a *P* value more than 0.05 is considered nonsignificant, a *P* value less than 0.05 is considered significant, and a *P* value less than 0.001 is considered highly significant.

3. Results

Table 1.

This prospective comparative study will be conducted on 50 patients on regular hemodialysis in the Nephrology Unit of Kobry Al-Qobba Military Hospital. The study included 33 men and 17 women. The mean age was 44.46 ± 12.47 (Fig. 1).

Table 2 shows the etiology, as there were 21 (42.0%) patients with hypertension, nine (18.0%) patients with diabetes mellitus, six (12.0%) patients with glomerulonephritis, five (10.0%) patients with APKD, five (10.0%) patients with interstitial, and four (8.0%) patients with other (Fig. 2).

Table 3 shows that there were 23 (46.0%) patients with no PH and 27 (54.0%) patients with PH (Fig. 3).

Table 4 shows that there were 41 (82.0%) patients with hypertension, 18 (36.0%) patients with cerebrovascular accident, 31 (62.0%) patients with smoking, and 12 (24.0%) patients with ischemic heart disease (Fig. 4).

Table 5 shows that there were 46 (92.0%) patients with AVF. The mean AVF flow rates were

Table 1. The present study examines the distribution of cases under investigation based on age and sex.

	All cases (N = 23)
Age	
Mean \pm SD	44.46 \pm 12.47
Range	20–68
Sex [n (%)]	
Female	17 (34.0)
Male	33 (66.0)

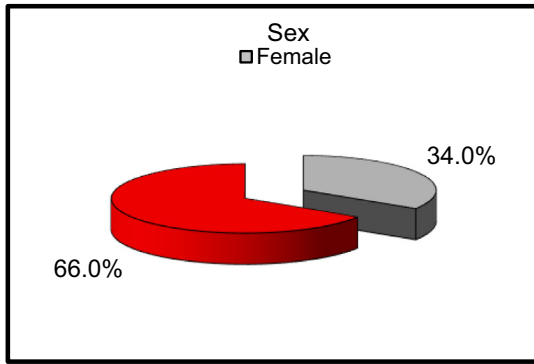


Fig. 1. The distribution of the cases under study is categorized based on sex.

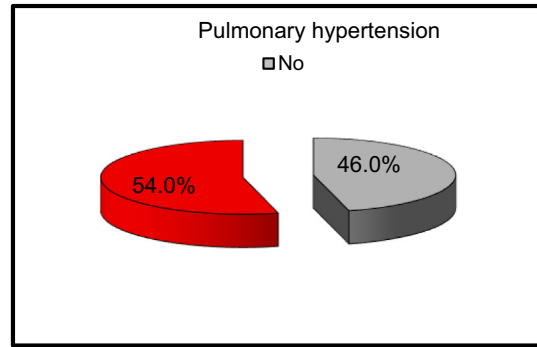


Fig. 3. The cases under investigation were categorized based on the distribution of pulmonary hypertension.

Table 2. The cases under investigation were categorized based on their etiology.

Etiology	All cases [n (%)]
HTN	21 (42.0)
DM	9 (18.0)
Glomerulonephritis	6 (12.0)
APKD	5 (10.0)
Interstitial	5 (10.0)
Other	4 (8.0)

DM, diabetes mellitus; HTN, hypertension.

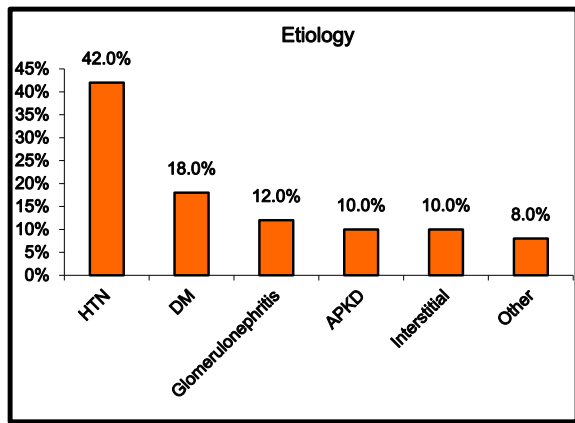


Fig. 2. The cases under investigation were categorized based on etiology.

764.53 ± 80.34, and the residual urine output ranged from 49.77 to 90.72 with mean of 73.39 ± 7.75.

Table 6 shows that there were 44 (88.0%) patients with hypervolemia by clinical method. The mean

Table 3. The cases under investigation were distributed based on the classification of pulmonary hypertension.

Pulmonary hypertension	All cases [n (%)]
No	23 (46.0)
Yes	27 (54.0)
Mild	23 (85.2)
Moderate	4 (14.8)

Table 4. The distribution of the cases under study is categorized depending on the existence of ischemic heart disease, smoking, hypertension, and a history of a vascular accident.

	All cases [n (%)]
Hypertension	41 (82.0)
Cerebrovascular accident	18 (36.0)
Smoking	31 (62.0)
IHD	12 (24.0)

IHD, ischemic heart disease.

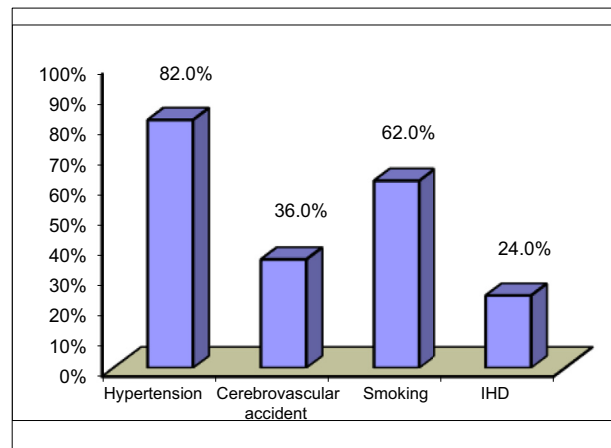


Fig. 4. Distribution of the studied cases according to hypertension, cerebrovascular accident, smoking, and IHD. IHD, ischemic heart disease.

Table 5. Distribution of the studied cases according to arteriovenous fistula, arteriovenous fistula flow rates, and residual urine output.

	All cases (N = 23)
AVF	46 (92.0)
AVF flow rates	
Mean ± SD	764.53 ± 80.34
Range	592.64–925.45
Residual urine output	
Mean ± SD	73.39 ± 7.75
Range	49.77–90.72

AVF, arteriovenous fistula.

Table 6. Distribution of the studied cases according to volume state vintage hypervolemia by clinical method, and ultrafiltration rate per session.

	All cases (N = 23)
Vintage on dialysis (years)	
Mean ± SD	3.30 ± 0.42
Range	2.5–4.3
Hypervolemia by clinical method	44 (88.0)
Ultrafiltration rate per session	
Mean ± SD	1.45 ± 0.24
Range	1–1.90

vintage on dialysis (years) were 3.30 ± 0.42 , and the ultrafiltration rate per session ranged from 1 to 1.90 with mean of 1.45 ± 0.24 (Table 7).

The mean hemoglobin were 8.75 ± 1.76 , the mean calcium were 7.63 ± 0.91 , the mean phosphorus were 6.27 ± 1.65 , the mean PTH (pg/ml) were 341.36 ± 191.29 , the serum ferritin (mg) ranged from 600 to 1900 with mean 1226.60 ± 352.82 , the mean creatinine were 6.89 ± 2.16 , the mean estimated

Table 7. The distribution of the cases under study is categorized based on hemoglobin, calcium, phosphorus, parathormone (pg/ml), serum ferritin (mg), creatinine, estimated glomerular filtration rate (ml/min), protein, albumin (g/dl), pro-brain natriuretic peptide (pg/ml), and left atrial dimension (cm).

	All cases (N = 23)
Hb	
Mean ± SD	8.75 ± 1.76
Range	5.4–13.32
Calcium	
Mean ± SD	7.63 ± 0.91
Range	5.61–9.59
Phosphorus	
Mean ± SD	6.27 ± 1.65
Range	3.21–11.02
PTH (pg/ml)	
Mean ± SD	341.36 ± 191.29
Range	100–800
Serum ferritin (mg)	
Mean ± SD	1226.60 ± 352.82
Range	600–1900
Creatinine	
Mean ± SD	6.89 ± 2.16
Range	1.8–11.08
EGFR (ml/min)	
Mean ± SD	13.70 ± 4.87
Range	0.63–25.9
Protein	
Mean ± SD	6.59 ± 0.83
Range	5.1–9.45
Albumin (g/dl)	
Mean ± SD	3.49 ± 0.58
Range	2.04–5.02
Pro-BNP (pg/ml)	
Mean ± SD	15484.69 ± 472.48
Range	14 399.05–16 519.65

BNP, brain natriuretic peptide; EGFR, estimated glomerular filtration rate; Hb, hemoglobin; PTH, parathyroid hormone.

Table 8. The distribution of the instances under study is organized based on their respective categories to LAVI (ml/m²), E (m/s), A (m/s), e' (m/s), E/e' ratio, LVEDD (cm), LVEDV (ml), LVMI, LVEF, and EF (%).

	All cases (N = 23)
LAVI (ml/m ²)	
Mean ± SD	42.09 ± 11.52
Range	21.33–75.32
E (m/s)	
Mean ± SD	0.82 ± 0.36
Range	0.16–1.45
A (m/s)	
Mean ± SD	1.09 ± 0.35
Range	0.27–1.75
e' (m/s)	
Mean ± SD	0.06 ± 0.01
Range	0.04–0.08
E/e' ratio	
Mean ± SD	17.27 ± 5.30
Range	6.98–26.78
LVEDD (cm)	
Mean ± SD	5.06 ± 0.42
Range	3.82–5.88
LVEDV (ml)	
Mean ± SD	149.38 ± 30.80
Range	85.63–213.01
LVMI	
Mean ± SD	122.62 ± 27.56
Range	59.24–187.48
LVEF	
Mean ± SD	65.22 ± 6.98
Range	55.27–83.19
EF (%)	
Mean ± SD	61.80 ± 6.82
Range	50–79
LA dimension (cm)	
Mean ± SD	4.62 ± 0.52
Range	3.01–5.71

glomerular filtration rate (ml/min)] were 13.70 ± 4.87 , the mean protein were 6.59 ± 0.83 , the mean albumin (g/dl) were 3.49 ± 0.58 , the pro-BNP (pg/ml) ranged from 14399.05 to 16519.65 with mean 15484.69 ± 472.48 (Table 8).

The mean LAVI (ml/m²) were 42.09 ± 11.52 , the mean E (m/s) were 0.82 ± 0.36 , the mean A (m/s) were 1.09 ± 0.35 , the mean e' (m/s) were 0.06 ± 0.01 , the E/e' ratio ranged from 6.98 to 26.78 with mean 17.27 ± 5.30 , the LVEDD (cm) ranged from 3.82 to 5.88 with mean 5.06 ± 0.42 , the mean LVEDV (ml) were 149.38 ± 30.80 , the mean LVMI were 122.62 ± 27.56 , the mean LVEF were 65.22 ± 6.98 , and the EF (%) ranged from 50 to 79 with mean 61.80 ± 6.82 and the LA dimension (cm) ranged from 3.01 to 5.71 with mean 4.62 ± 0.52 .

4. Discussion

Predialysis and dialysis-dependent individuals are equally predisposed to PH, however it is often overlooked and underestimated. PH is distinguished

by modification of the medial and intimal layers of the pulmonary vasculature as well as endothelial dysfunction. These changes lead to constrictive and occlusive vascular lesions.⁸

The pulmonary artery pressure typically falls between 14 and 17 mmHg, with a maximum threshold of 20 mmHg. Nevertheless, if the average chest artery pressure surpasses 25 mmHg when in a state of rest, it is classified as PH. The WHO classifies the pH in individuals with chronic renal failure as 'category 5: PH with unknown multifactorial etiology'.⁹

The impact of AVF on the development of PH in patients undergoing hemodialysis is contingent upon several factors, including the specific type of AVF, the length of time during which it is used, as well as the rates at which blood flows through the AVF. The probable explanation for this phenomena might be a rise in cardiac output, leading to heightened pulmonary artery pressures. Nevertheless, it is imperative to acknowledge that additional research is required to establish a conclusive correlation.¹⁰

The impact of AVF on the progression of PH in individuals on hemodialysis is contingent upon several factors. This study aims to provide detailed information regarding the precise type of AVF utilized, the duration of its utilization, and the blood flow rates that traverse the AVF. The likely explanation for this phenomenon is increased cardiac output, resulting in heightened pulmonary artery pressures. Nevertheless, further research is required to definitively prove this correlation, in the study of Nagaraju *et al.*⁶ The identity of the researcher who conducted an analysis into the prevalence of PH, its risk factors, its association with inflammation and oxidative stress, as well as its impact on cardiac irregularities, has not been released. According to their analysis, the prevalence of mild PH was found to be 54%, with the majority of cases falling under this category.

Prior research has indicated a notable prevalence of PH in individuals with ESRD, with rates reaching up to 39% in patients diagnosed with stage 5 chronic kidney disease. Furthermore, the occurrence of PH among those undergoing hemodialysis has been estimated to be ~68.8%.^{11,12}

In the current study, there was no statistically significant difference found between non-PH and PH regarding age and sex.

This comes in agreement with Nagaraju *et al.*⁶ The study findings indicated that the average age of individuals diagnosed with Huntington's disease and PH was 56.5 ± 9.3 years. Furthermore, the majority of these individuals were male. The analysis did not

reveal any significant association between age or sex and the prevalence of PH in hemodialysis patients.

The study by Tarrass *et al.*¹³ The sample size for this investigation was 200, with a probability of success (P) of 0.37. This study yielded results comparable to a previous study, as no significant association between and the prevalence of PH was detected.

The findings of this study indicate that there was no statistically significant distinction observed between individuals with non-PH and those with PH in relation to hypertension, diabetes mellitus, glomerulonephritis, autosomal dominant polycystic kidney disease, interstitial disease, and other factors.

Furthermore, no statistically significant distinction was observed between individuals with non-PH and those with PH about the prevalence of hypertension, cerebrovascular accident, smoking, and ischemic heart disease.

This was in accordance with Nagaraju *et al.*⁶ The investigators noted that their study did not identify a statistically significant association between various possible risk factors, including diabetes, hypertension, smoking, cerebrovascular accident, and ischemic heart disease, and the prevalence of PH.

The present investigation demonstrated that no statistically significant distinction was observed between non-PH and PH regarding AVF and AVF flow rates.

The study by Pabst *et al.*¹⁴ on a sample size of 62 individuals showed a decrease in the prevalence of PH immediately following dialysis. This reduction was related to the process of ultrafiltration.

The findings of this study indicate that there was no statistically significant distinction observed between individuals without PH and individuals with PH in terms of their levels of hemoglobin, calcium, phosphorus, serum ferritin (mg), parathormone, creatinine, estimated glomerular filtration rate (ml/min), protein, albumin (g/dl), pro-BNP (pg/ml), and LA dimension (cm).

This agrees with Nagaraju *et al.*,⁶ who reported that there was no significant association observed between laboratory risk variables such as anemia, serum calcium, phosphorus, albumin, PTH, and ferritin with PH.

The present study showed that, there was no statistically significant difference found between non-PH and PH. Regarding LAVI (ml/m^2), E (m/s), A (m/s), E/e' ratio, LVEDD (cm), LVEDV (ml), LVMI, LVEF, and EF (%), a substantial statistical difference was observed between individuals with non-PH and PH in relation to the variable e' (m/s).

Also Zhang *et al.*,¹⁵ findings, patients with PH exhibited elevated levels of left atrial, right atrial, left ventricular end-diastolic diameter, and pulmonary

artery measurements, while demonstrating diminished left heart function.

Numerous studies have demonstrated a strong correlation between PH and alterations in cardiac morphology. The alterations in the right atrium can potentially result in secondary tricuspid regurgitation. The occurrence of tricuspid regurgitation resulted in an additional increase in the size of the right atrium, functioning as a negative feedback mechanism. Both of the aforementioned diseases have the potential to trigger the development of PH.^{16,17}

Moreover Zhang *et al.*,¹⁵ a relationship has been discovered between left atrium and PH, indicating the need for more cohort studies to validate the involvement of the left heart in PH within the specific subgroup of ESRD patients undergoing maintenance dialysis. The hemodynamics of the left and right heart, altered by dialysis, may potentially contribute to the pathogenesis of PH.

4.1. Conclusion

Patients undergoing hemodialysis exhibit a significantly elevated prevalence of PH. The pH exhibited a statistically significant increase in the presence of e' (m/s), MR, and LVSD, although no significant differences were seen with the other parameters. The present investigation did not identify any significant disparities in conventional risk factors and factors associated to hypertensive disease between the two groups, namely those with and without PH.

4.2. Recommendation

Further studies with a large number of patients should be done to support our results for better outcome.

Conflicts of interest

There are no conflicts of interest.

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