Evaluation of pulmonary artery pressure and resistance by pulsed Doppler echocardiography in patients with end-stage renal disease on dialysis therapy

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Background: Pulmonary hypertension (PH) is one of the most important comorbidities in patients undergoing hemodialysis (HD). The goal of the present work is to determine the possible etiologic factors for its occurrence.

Methods: The prevalence of PH was estimated by Doppler echocardiography in a cohort of 100 patients aged 49.3 ± 13.9 years on regular HD. Mean pulmonary artery pressure was estimated from pulmonary acceleration time by Mahan's regression equation. Pulmonary vascular resistance and pulmonary capillary wedge pressure were calculated. We focused on the effect of HD on left and right ventricle diastolic and systolic function. Right ventricle systolic function was assessed by tricuspid annular systolic excursion and pulsed Doppler myocardial performance index. Since impaired endothelial function was postulated as an underlying cause of PH, we studied the effects of HD on brachial artery endothelial function.

Results: The current study found that pulmonary hypertension was prevalent in 70% of patients on dialysis. Left atrium diameter, left ventricle mass indexed to body surface area, and mitral E/E′ were increased in the dialysis group (4.4 ± 0.2 cm, 126.5 ± 24.6 g/m^2, and 16.9 ± 4.4, respectively, $p < 0.001$ for all). Pulmonary artery systolic pressure was positively correlated to duration of dialysis and negatively correlated to glomerular filtration rate ($p < 0.001$ and $r = -0.991$). Pulmonary vascular resistance was significantly increased in dialysis patients (1.9 ± 0.2 Wood units vs. 1.2 Wood units in controls, $p < 0.001$). Endothelial dysfunction, defined as brachial artery flow mediated dilatation <6%, was found in 46% of dialysis group.

Conclusion: Increased pulmonary artery systolic pressure in the HD population could be attributed to left atrium dilatation and left ventricle diastolic dysfunction. Pulmonary vascular resistance was significantly increased in dialysis group. This might be explained by impaired endothelial nitric oxide synthesis that not only caused systemic vasoconstriction but also affected the pulmonary vasculature.

Keywords: Hemodialysis, End stage renal disease, Pulmonary artery pressure, Pulmonary vascular resistance, Pulsed Doppler echocardiography

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Introduction

Pulmonary hypertension (PH) is a complex hemodynamic alteration that may result from disparate causes. In the 2008 classification by the World Health Organization and in more recent guidelines by the European Society of Cardiology, for the first time attention was given to PH in dialysis patients classified in the fifth category gathering various forms of PH with unclear etiology [1].

The high prevalence of PH was attributed to high cardiac output secondary to the presence of arteriovenous fistula, anemia, and/or and to left ventricular (LV) disorders [2]. Moreover, sleep apnea, accumulation of endogenous inhibitors of nitric oxide synthase, insult to pulmonary microcirculation attributable to exposure to dialysis membranes is likely to contribute to the unique propensity of dialysis patients to PH [3]. Our aim was to study the contribution of left and right ventricle dysfunction to pulmonary hypertension. The second aim was to show that simple echocardiographic equations can be used to assess systolic, mean pulmonary artery pressure and pulmonary vascular resistance that might help in evaluation and risk stratification of patients on dialysis

Abbreviations

PH	pulmonary hypertension
HD	hemodialysis
PA	pulmonary artery
PAP	pulmonary artery pressure
PVR	pulmonary vascular resistance
TRV	tricuspid regurgitant velocity
TVI RVOT	right ventricular outflow tract time-velocity integral
PCWP	pulmonary capillary wedge pressure
FMD	flow mediated dilatation
LV	left ventricle
GFR	glomerular filtration rate
MDRD	formula Modification of Diet in Renal Disease formula
WHO FC	World Health Organization functional class
LVEF	left ventricular ejection fraction
LVMI	left ventricular mass index
EACVI	European Association of Cardiovascular Imaging
ASE	American Society of Echocardiography
LA	left atrium
LAVI	left atrium volume index
RV	right ventricle
TDI	tissue Doppler imaging
TAPSE	tricuspid annular plane systolic excursion
MPAP	mean pulmonary artery pressure
AT	pulmonary acceleration time
SPAP	pulmonary artery systolic pressure
RAP	right atrium pressure
TTE	transthoracic echocardiography
LVH	left ventricle hypertrophy
MPI	myocardial performance index
AVF	arteriovenous fistula
TPG	transpulmonary pressure gradient
RHC	right heart catheterization
CKD	chronic kidney disease

Patients and methods

Forty healthy controls and 100 adult patients aged 49.3 ± 13.9 years on regular hemodialysis (HD) for at least 12 months (range, 12–80 months) were referred from the Nephrology Department of Cairo University, Cairo, Egypt for echocardiography. Written consent was given by all the participants. The study protocol was approved by the Ethics Committee at Cairo University Hospital.

Inclusion criteria were: adults aged $\geqslant$18 years, stage 4 or 5 chronic kidney disease (CKD) defined as serum creatinine $\geqslant$2.26 mg/dL or glomerular filtration rate (GFR) $\leqslant$30 mL/min/1.73 m^2 assessed by MDRD4-formula [4] on HD, and in World Health Organization functional class $\geqslant$ II with dyspnea unexplained by other causes. Exclusion criteria were: pregnancy; LV ejection fraction (EF) <50%; mitral or aortic regurgitation > Grade 2; myocarditis; endocarditis; pericarditis; severe chronic obstructive pulmonary disease; lung fibrosis; and known pulmonary artery hypertension-reducing medication with prostanoids, endothelin receptor antagonists, or phosphodiesterase-5 inhibitors.

Patients were subjected to history taking, physical examination, and demographic parameters, including age, sex, and body mass index.

Echocardiography studies were performed using a commercial scanner (iE33; Philips Medical System, Andover, MA, USA) according to the recommendations of the American Society of Echocardiography [5].

M-mode echocardiography

LV dimensions, wall thickness and functions were studied. LV mass was calculated using the Devereux formula [6]:

$$\text{LV mass(g)} = 0.8 \times 1.04 \times [\text{LVID} + \text{PWT} + \text{IVST}]^3 - [\text{LVID}]^3 + 0.6\ \text{g}, \quad (1)$$

where LVID is the left ventricle internal dimension, PWT is the posterior wall thickness, IVST is the interventricular septal thickness, 1.04 is the specific gravity of the myocardium, and 0.8 is the correction factor. The LV mass index (LVMI, g/m^2) was defined as LV mass divided by body surface area (m^2). The reference ranges used to define LV hypertrophy (LVH) was LVMI >115 g/m^2 and 95 g/m^2 for men and women, respectively [5]. We tried refinements in image processing according