

Characteristics and Prognostic Associations of Echocardiographic Pulmonary Hypertension With Normal Left Ventricular Systolic Function in Patients ≥ 90 Years of Age



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The high prevalence of pulmonary hypertension (PH) in elderly patients is well known. However, much remains unknown about those population. We sought to find the clinical characteristics of echocardiographic PH and the prognostic factors in patients ≥ 90 years of age. We retrospectively reviewed 310 patients ≥ 90 years of age (median age 92 years, 64% women) diagnosed as echocardiographic PH (peak systolic pulmonary arterial pressure ≥ 40 mm Hg) with normal left ventricular systolic function. We defined left heart disease (LHD) as significant left-sided valve diseases, left ventricular hypertrophy and left ventricular diastolic dysfunction by using echocardiography. The endpoint was all-cause death at 2,000 days after diagnosis. LHD was found in 92% of patients. During the median follow-up of 367 days (interquartile range, 39-1,028 days), 151 all-cause deaths (49%) occurred. Multivariable Cox regression analysis demonstrated that right ventricular fraction area change $< 35\%$ (adjusted hazard ratio [HR]: 2.31; $p < 0.001$), pericardial effusion (adjusted HR: 2.28; $p < 0.001$), serum albumin < 3.5 g/dL (adjusted HR: 1.76; $p = 0.001$), chronic obstructive pulmonary disease (adjusted HR: 1.93; $p = 0.001$) and New York Heart Association (NYHA) class $\geq II$ (adjusted HR: 1.73; $p = 0.004$) were associated with mortality after adjusted for age. In conclusion, LHD was significantly associated with echocardiographic PH in most patients ≥ 90 years of age. Also, the co-morbid factors at diagnosis (right ventricular systolic dysfunction, pericardial effusion, hypoalbuminemia, chronic obstructive pulmonary disease, and NYHA class $\geq II$) were independently associated with mortality. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;129:95–101)

Recently, in developed countries, pulmonary hypertension (PH) was increasingly recognized in the elderly population and associated with a worse outcome compared to the younger population.^{1–3} There were a few comparative epidemiological data on the prevalence of the different groups of PH in elderly patients. A previous study of PH in elderly patients (mean age of 72) showed that the postcapillary PH due to left heart disease (LHD) was the most common type (28% of cohort).⁴ Furthermore, other/mixed type with postcapillary PH and precapillary PH or more than one cause of PH (e.g., LHD and chronic lung disease) was also common (17% of cohort) diagnoses in elderly patients.⁴ Understanding the cause and prognostic factors of PH is important for therapeutic adjustments in extremely elderly patients who have many co-morbidities. However, much remains to be learned about PH in patients ≥ 90 years of age. We hypothesized that LHD was strongly associated

with PH in patients ≥ 90 years of age. This study also aimed to investigate the prognostic factors in those patients.

Methods

We retrospectively reviewed the transthoracic echocardiography database of 317 patients ≥ 90 years of age with echocardiographic PH (peak systolic pulmonary arterial pressure [SPAP] ≥ 40 mm Hg) and normal left ventricular systolic function at Cedars-Sinai Medical Center between May 2012 and May 2014. We excluded patients with insufficient images of B-mode ($n = 6$), no medical record ($n = 1$). The remaining 310 patients were analyzed in this study. The Cedars-Sinai Institutional Review Board approved this retrospective study with the requirement for individual patients informed consent waived (Institutional Review Board No. 00000483).

We reviewed patient age, sex, body size, and clinical information from the medical records. Hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, atrial fibrillation, chronic obstructive pulmonary disease (COPD), interstitial lung disease, and obstructive sleep apnea were confirmed by medical records. New York Heart Association (NYHA) functional classification was assessed at baseline.⁵ Pulmonary embolism was diagnosed by contrast-enhanced computed tomography ($n = 2$), pulmonary ventilation/perfusion scan

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($n = 1$), the physician's diagnosis ($n = 1$). Chronic kidney disease was defined as an estimated glomerular filtration rate ≤ 60 mL/min/1.73 m² by Chronic Kidney Disease Epidemiology Collaboration equation.^{6,7}

A comprehensive 2-dimensional transthoracic echocardiography was performed in all patients using an ultrasound system (S5-1 probe, IE33; Philips, Andover, Massachusetts). The trained echocardiographers obtained resting transthoracic echocardiograms in all patients. Left ventricular end-diastolic, interventricular septal and posterior wall thickness were measured at the parasternal long-axis view, and left ventricular mass was determined as recommended.⁸ The biplane method of disks was used to assess left ventricular ejection fraction.⁸ Pulsed-wave Doppler was performed in the apical 4-chamber view to obtain mitral inflow velocities to assess left ventricular filling. Left ventricular hypertrophy was defined as an indexed left ventricular mass >115 g/m² in men and >95 g/m² in women.⁸ Measurements of mitral inflow included the peak early filling (E-wave), late diastolic filling (A-wave) velocities, and the E/A ratio. Early diastolic mitral annular velocity (e') was obtained from the lateral aspect of the mitral annulus, and E/e' was calculated for identifying diastolic dysfunction.⁹ Right atrial area was assessed from the apical 4-chamber view at end-systole, on the frame just prior to tricuspid valve opening, by tracing the right atrial blood-tissue interface, excluding the area under the tricuspid valve annulus.⁸ Right ventricular end-diastolic diameter at the base was measured from the right ventricular focused apical 4-chamber view. Right ventricular fractional area change was defined as (end-diastolic area – end-systolic area)/end-diastolic area obtained by tracing the right ventricular endocardium including the trabeculae in both systole and diastole.⁸ Right ventricular systolic dysfunction was defined as right ventricular fractional area change $<35\%$.⁸ Indexed left atrial volume was calculated using the biplane area-length method at end-systole on apical 4- and 2-chamber views with indexing by body surface area.⁸ SPAP was measured by using the following formula: $4 \times (\text{peak tricuspid regurgitation jet velocity [m/s]}^2 + \text{right atrial pressure (mm Hg)})$. Right atrial pressure was estimated from the inferior vena cava diameter and changes as follows: 3 mm Hg (inferior vena cava diameter <2.1 cm, collapse with sniff $>50\%$), and 15 mm Hg (inferior vena cava diameter ≥ 2.1 cm, collapse with sniff $<50\%$), and 8 mm Hg (inferior vena cava diameter and collapse do not fit previously mentioned paradigm).¹⁰ We used the best envelope and the highest velocity of tricuspid regurgitation as current guideline recommended¹⁰ and defined PH as SPAP ≥ 40 mm Hg,¹¹ severe PH as ≥ 60 mm Hg.¹² Except for peak tricuspid regurgitation jet velocity, other measurements were averages of 5 beats in patients with atrial fibrillation.⁸ Pericardial effusion was defined as a distinct systolic and diastolic separation of pericardial layers posterior to the heart on the parasternal long-axis and short-axis views, as previously reported.^{13,14}

We defined the severity of valvular heart disease by using the semiquantitative and quantitative parameters according to the criteria of the American Society of Echocardiography and the European Association of Echocardiography.^{15,16} Concerning left heart diastolic dysfunction, the current guideline includes peak tricuspid regurgitation

jet velocity as a parameter of diastolic dysfunction.⁹ However, we excluded the parameter of peak tricuspid regurgitation jet velocity for the evaluation of diastolic dysfunction in this study because all patients had high tricuspid regurgitation jet velocity. Therefore, we defined left ventricular diastolic dysfunction with elevated left atrial pressure as 2 or 3 positive findings among following echocardiographic parameters; left atrial volume index >34 mL/m², lateral e' velocity <10 cm/s, lateral E/e' >13 .⁹

We categorized patients into 3 groups; (1) PH with only LHD (PH-LHD), (2) PH with LHD and chronic lung disease (COPD, interstitial lung disease, obstructive sleep apnea) or pulmonary embolism (PH-combined), (3) PH without LHD (PH-no LHD). LHD included left-sided valve diseases with the severity of moderate or severe, left ventricular hypertrophy, and left heart diastolic dysfunction with elevated left atrial pressure. The follow-up information was obtained from medical records and the endpoint was all-cause death at 2,000 days after diagnosis.

Data were expressed as mean and standard deviation, median (interquartile range), or frequencies and percentages. All variables were tested for normal distribution with the Kolmogorov-Smirnov test and the histogram analysis. Chi-square test or Fisher exact test was used to compare the proportions of categorical variables among groups. We used one-way analysis of variance or Kruskal-Wallis analysis to compare the normal distributed and skewed variables among 3 groups, respectively. If overall significance was reached among 3 groups, Bonferroni post hoc was applied by using Student's *t* test for normally distributed variables and Mann-Whitney U-test for non-normally distributed variables. Differences in categorical variables were analyzed using Chi-square test or Fisher exact test, as appropriate. Predictors of all-cause death were identified using univariable Cox-proportional hazards models. A multivariable model adjusted for age was built to identify the factors independently associated with the occurrence of all-cause death at follow-up. All covariates with a statistically significant association with all-cause death at the univariable Cox regression model (p value <0.10) were included in the final model. A probability value (p value) <0.05 was considered to indicate a significant difference. All p values were 2 sided. All statistical analyses were performed with Easy R version 3.5.2 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).¹⁷

Results

In all patients, 92% of patients had LHD (Figure 1). Also in subgroup analysis, the most common type of PH was PH-LHD (73%), followed by PH-combined (19%) and PH-no LHD (8%) (Figure 1). Examples of echocardiographic images in patients with PH with and without LHD were shown in Figure 2. Table 1 shows the clinical characteristics of all patients and 3 groups at diagnosis of PH. The median age was 92 years (interquartile range, 91 to 95 years), and 65% were women. Age, sex, body surface area, and systemic blood pressure were similar among the groups. Compared with PH-no LHD, PH-LHD, and PH-combined had a higher prevalence of NYHA \geq II. COPD

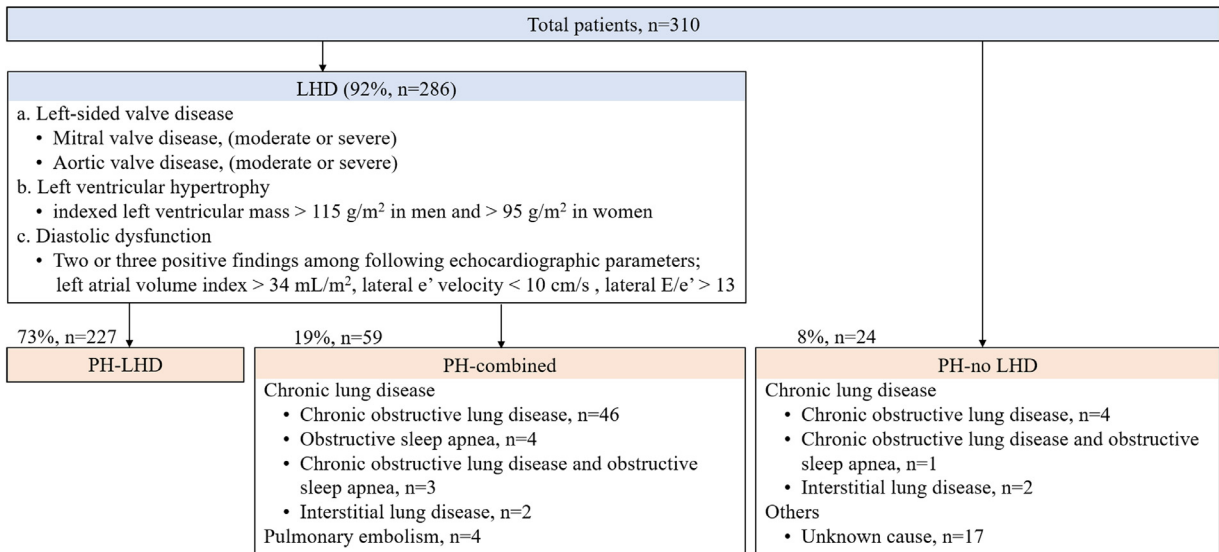


Figure 1. Flowchart of the study population. LHD = left heart disease; PH = pulmonary hypertension; PH-LHD = PH with only left heart disease; PH-combined = PH with left heart disease and chronic lung disease or pulmonary embolism; PH-no LHD = PH without left heart disease

was more frequently found in PH-combined than PH-no LHD. In this study, none of the patients had connective tissue disease. Laboratory results (hemoglobin, serum albumin, glomerular filtration rate, brain natriuretic peptide) were not different among groups.

Table 2 showed the echocardiographic characteristics at diagnosis of PH. The proportion of valvular heart disease was not different between PH-LHD and PH-

combined. Median SPAP in all patients was 50 mm Hg (interquartile range, 45 to 58 mm Hg). Although PH-combined had other causes of PH in addition to LHD compared with PH-LHD, SPAP was similar among groups.

During the median follow-up of 367 days (interquartile range, 39-1028 days), 151 all-cause deaths (49%) occurred. Univariate Cox regression analysis revealed 6 potential risk

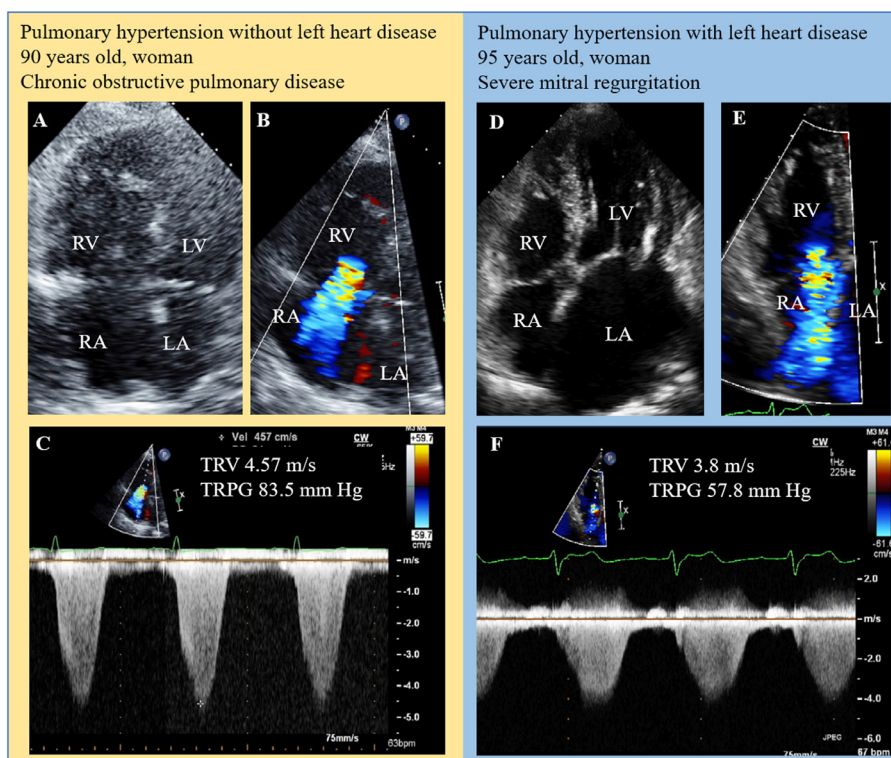


Figure 2. Representative cases in pulmonary hypertension with and without left heart disease. Right ventricular enlargement (A), moderate TR (B), high velocity of TR (C). Left atrial enlargement (D), moderate TR (E), high velocity of TR (F). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; TR = tricuspid regurgitation, TRV = tricuspid regurgitation peak velocity; TRPG = tricuspid regurgitation peak gradient

Table 1
Clinical characteristics at diagnosis of PH

Variable	All patients (n=310)	PH-LHD (n=227)	PH-combined (n=59)	PH-no LHD (n=24)	p Value
Age (years)	92 [91, 95]	92 [91, 95]	92 [91, 95]	93 [91, 94]	0.876
Women	201 (65%)	151 (67%)	36 (61%)	14 (58%)	0.576
Body mass index (kg/m ²)	23.7 ± 4.6	23.8 ± 4.6	24.2 ± 4.6	22.5 ± 4.5	0.307
Heart rate (beats/minute)	77 ± 19	77 ± 20	76 ± 18	81 ± 19	0.55
Systolic blood pressure (mm Hg)	134 ± 23	135 ± 23	131 ± 20	135 ± 22	0.504
Diastolic blood pressure (mm Hg)	62 ± 16	62 ± 17	58 ± 13	66 ± 15	0.062
New York Heart Association Class ≥ II	192 (62%)	144 (63%)	41 (70%)	7 (30%)	0.002* [†]
Systemic hypertension	250 (81%)	185 (82%)	47 (80%)	18 (75%)	0.729
Coronary artery disease	124 (40%)	88 (39%)	27 (46%)	9 (38%)	0.6
Dyslipidemia	146 (47%)	112 (49%)	27 (46%)	7 (29%)	0.166
Diabetes mellitus	67 (22%)	48 (21%)	14 (24%)	5 (21%)	0.908
Atrial fibrillation	164 (53%)	124 (55%)	30 (51%)	10 (42%)	0.452
Connective tissue disease	0	0	0	0	NA
Chronic obstructive pulmonary disease	54 (17%)	0	49 (83%)	5 (21%)	<0.001* ^{†,‡}
Obstructive sleep apnea	8 (3%)	0	7 (12%)	1 (4%)	<0.001 [‡]
Interstitial lung disease	4 (1%)	0	2 (3%)	2 (8%)	0.004*
Pulmonary embolism	4 (1%)	0	4 (7%)	0	0.001 [‡]
Hypothyroid	84 (27%)	63 (28%)	16 (27%)	5 (21%)	0.861
Chronic kidney disease	143 (46%)	106 (47%)	26 (44%)	11 (46%)	0.937
Hemoglobin (g/dL), (n=299)	11.0 ± 1.7	10.9 ± 1.8	11.1 ± 1.7	11.3 ± 1.7	0.496
Serum albumin (g/dL), (n=274)	3.5 ± 0.6	3.6 ± 0.6	3.6 ± 0.5	3.4 ± 0.5	0.288
GFR (mL/min/1.73 m ²), (n=303)	47.7 ± 21.1	47.0 ± 20.4	48.8 ± 21.4	52.0 ± 26.7	0.491
Brain natriuretic peptide (pg/mL), (n=238)	377 [248, 674]	412 [247, 693]	358 [276, 627]	286 [201, 486]	0.356

GFR = glomerular filtration rate; LHD = left heart disease; NA = not available; PH = pulmonary hypertension; PH-LHD = pulmonary hypertension with only left heart disease; PH-combined = pulmonary hypertension with left heart disease and chronic lung disease or pulmonary embolism; PH-no LHD = pulmonary hypertension without left heart disease.

Continuous variables are presented as mean ± standard deviation unless otherwise noted as median [interquartile range]; categorical variables are summarized as n (%).

Dyslipidemia was defined as low-density lipoprotein cholesterol >130 mg/dL and/or triglyceride >150 mg/dL and/or high-density lipoprotein cholesterol <40 mg/dL; men or <50 mg/dL; women without lipid-lowering treatment or receiving lipid-lowering treatment.

* p < 0.05 (post hoc, Bonferroni correction), PH-LHD versus PH-no LHD.

† p < 0.05 (post hoc, Bonferroni correction), PH-combined versus PH-no LHD.

‡ p < 0.05 (post hoc, Bonferroni correction), PH-LHD versus PH-combined.

factors for all-cause death (NYHA ≥II, COPD, coronary artery disease, right ventricular fractional area change <35%, pericardial effusion, serum albumin <3.5 g/dL; Table 3). Subsequent multivariate Cox regression analysis adjusted for age and using variables with p < 0.10 identified by univariate analysis showed that right ventricular fractional area change <35%, pericardial effusion, COPD, serum albumin <3.5 g/dL, and NYHA ≥II were significant risk factors for all-cause death at the 2,000 days of follow-up (Table 3). Severe PH (SPAP ≥60 mm Hg) and women were not significant predictors of all-cause death in this study.

When analyzed as patients with and without pericardial effusion, patients with pericardial effusion had lower serum albumin, and similar right atrial and right ventricular remodeling and function compared with patients without pericardial effusion (Tables S1 and S2 in the Data Supplement).

Discussion

This study showed 2 findings; in patients ≥90 years of age with echocardiographic PH and normal left ventricular systolic function (1) most patients (92%) had LHD as a cause of PH, (2) the comorbid factors at diagnosis (right ventricular fractional area change <35%, pericardial effusion, hypoalbuminemia, COPD, and NYHA class ≥II)

predicted worse outcomes. To our knowledge, this is the first report of the causes and prognosis in patients ≥90 years of age with echocardiographic PH.

In a previous invasive study of elderly patients aged ≥65 years with PH (n = 246, mean age of 72 years), the most frequent (45%) diagnosis was PH due to elevated left ventricular filling pressure by LHD; 28% in PH due to only LHD, 17% in PH due to LHD and other precapillary causes.⁴ This previous study included patients referred for evaluation of pulmonary arterial hypertension.⁴ Therefore most patients had no significant valvular heart disease.⁴ This predominance of LHD as a cause of PH was in agreement with our study. However, the prevalence of LHD in our study was much higher than that of this previous study. In our study, we included the significant left-sided valve diseases as LHD, and 53% of total patients had left-sided valve diseases. The difference in the inclusion criteria may reflect the high prevalence of LHD in more advanced aged patients (≥90 years old) in our study compared with patients (≥65 years old) in the previous study.

Several previous studies showed that the existence of pericardial effusion was an independent predictor of adverse outcome in patients with primary PH.^{14,18} And authors also suggested that pericardial effusion was a manifestation of right heart failure, and probably resulted from impaired venous lymphatic drainage due to elevated right

Table 2
Echocardiographic characteristics at diagnosis of PH

Variable	All patients (n=310)	PH-LHD (n=227)	PH-combined (n=59)	PH-no LHD (n=24)	P value
Aortic valve stenosis (moderate) [¶]	73 (24%)	54 (24%)	19 (32%)	0	0.185 ^{*,†}
Aortic valve regurgitation (moderate) [¶]	15 (5%)	14 (6%)	1 (2%)	0	0.259
Mitral valve stenosis (moderate) [¶]	29 (9%)	25 (11%)	4 (7%)	0	0.181
Mitral valve regurgitation (moderate) [¶]	95 (31%)	77 (34%)	18 (31%)	0	<0.001 ^{*,†}
Tricuspid valve regurgitation (moderate) [¶]	151 (49%)	111 (49%)	30 (51%)	10 (42%)	0.745
SPAP (mm Hg)	50.0 [45.0, 58.0]	50.0 [45.0, 58.0]	50.0 [45.1, 57.0]	51.3 [41.0, 57.8]	0.77
SPAP 60 mm Hg	65 (21%)	45 (20%)	14 (24%)	6 (25%)	0.71
Right ventricular diastolic dimension (cm)	3.8 ± 0.7	3.7 ± 0.7	3.9 ± 0.7	3.8 ± 0.7	0.489
Right ventricular FAC (%)	44.5 ± 9.6	44.3 ± 9.7	44.8 ± 8.8	45.9 ± 10.6	0.692
Right ventricular FAC < 35%	49 (16%)	37 (16%)	8 (14%)	4 (17%)	0.87
Right atrial area (cm ²)	21.2 ± 8.1	21.3 ± 8.5	21.7 ± 7.1	19.3 ± 6.9	0.446
Right atrial pressure (mm Hg)	3.0 [3.0, 8.0]	3.0 [3.0, 8.0]	5.5 [3.0, 8.0]	3.0 [3.0, 9.7]	0.952
Left ventricular diastolic dimension (cm)	4.0 ± 0.7	4.0 ± 0.7	4.1 ± 0.7	3.9 ± 0.7	0.498
Left ventricular ejection fraction (%)	64.0 ± 8.3	64.1 ± 8.5	64.9 ± 7.1	61.4 ± 8.6	0.22
Left ventricular mass index (g/m ²)	99.1 ± 33.9	100.9 ± 34.1	102.1 ± 35.1	76.0 ± 15.7	0.002 ^{*,†}
Left atrial volume index (mL/m ²)	52.9 ± 21.5	56.5 ± 21.8	49.4 ± 15.0	27.2 ± 11.3	<0.001 ^{*,†}
Lateral E/e', (n=304)	15.3 ± 7.2	16.1 ± 7.3	15.2 ± 6.5	8.0 ± 2.6	<0.001 ^{*,†}
Diastolic dysfunction	270 (87%)	214 (94%)	56 (95%)	0	<0.001 ^{*,†}
Pericardial effusion	45 (15%)	32 (14%)	10 (17%)	3 (13%)	0.822

Continuous variables are presented as mean ± standard deviation unless otherwise noted as median [interquartile range]; categorical variables are summarized as n (%). FAC = fractional area change; PH = pulmonary hypertension; PH-LHD = pulmonary hypertension with only left heart disease, PH-combined = pulmonary hypertension with left heart disease and chronic lung disease or pulmonary embolism; PH-no LHD = pulmonary hypertension without left heart disease, SPAP = systolic pulmonary arterial pressure.

[¶] "≥ moderate" was identified using the semiquantitative and quantitative parameters according to the criteria of the American Society of Echocardiography and the European Association of Echocardiography.

* P < 0.05, PH-LHD versus PH-no LHD;

† P < 0.05, PH-combined versus PH-no LHD

atrial pressure. In contrast, we found that right atrial and right ventricular remodeling and function were similar among patients with and without pericardial effusion. However, the serum albumin was lower in patients with pericardial effusion than those without in our study. Therefore

hypoalbuminemia might be a cause of pericardial effusion in our study as previously reported.¹⁹

Hypoalbuminemia was known as an independent prognostic factor in elderly patients with and without surgery.^{20,21} A previous community-based study (mean

Table 3
Predictors of mortality in patients with PH

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	Adjusted HR (95% CI)*	p value
Women	0.83 (0.60-1.15)	0.270		
Body mass index > 30 kg/m ²	0.99 (0.95-1.03)	0.603		
Hypertension	1.01 (0.65-1.57)	0.972		
NYHA Class ≥ II	2.10 (1.47-2.99)	<0.001	1.73 (1.19-2.52)	0.004
Left-sided valve disease	1.30 (0.94-1.79)	0.114		
COPD	2.27 (1.56-3.3)	<0.001	1.93 (1.30-2.87)	0.001
Coronary artery disease	1.46 (1.06-2.01)	0.021	1.26 (0.89-1.78)	0.184
Atrial fibrillation	1.09 (0.79-1.50)	0.589		
Diabetes mellitus	0.74 (0.49-1.12)	0.162		
Chronic kidney disease	0.97 (0.71-1.35)	0.880		
RV FAC <35 %	2.68 (1.73-4.06)	<0.001	2.31 (1.47-3.61)	<0.001
Diastolic dysfunction	1.02 (0.59-1.74)	0.979		
SPAP >60 mm Hg	1.25 (0.86-1.82)	0.240		
Pericardial effusion	1.99 (1.39-2.84)	<0.001	2.28 (1.53-3.38)	<0.001
Serum Alb <3.5 g/dL	1.82 (1.30-2.55)	<0.001	1.76 (1.25-2.48)	0.001
BNP >300 pg/mL	1.34 (0.93-1.93)	0.115		

Alb = albumin; BNP = brain natriuretic peptide; CI; confidence interval; COPD = chronic obstructive pulmonary disease; HR = hazard ratio; NYHA = New York Heart Association; PH = pulmonary hypertension; RV FAC = right ventricular fractional area change; SPAP = systolic pulmonary arterial pressure.

* Multivariate analysis was adjusted with age.

follow-up of 3.7 years) showed that hypoalbuminemia (<3.5 g/dL) was an independent risk factor for all-cause mortality in older persons aged ≥ 71 years ($n = 4,116$).²⁰ Furthermore, in patients ≥ 90 years of age who underwent general emergency surgery ($n = 4,724$), Kongwibulwut et al reported the prognostic impact of preoperative hypoalbuminemia.²¹ Our results are consistent with these reports. Additionally, we showed that hypoalbuminemia was associated with the worse outcomes even in the longer follow-up than the previous study²¹ (2,000-day and 30-day mortality, respectively).

Previous studies have provided evidence of the association between right ventricular dysfunction and poor prognosis in patients with LHD.^{22–25} In agreement with these studies, right ventricular dysfunction was an independent prognostic factor in our study in which most elderly patients with PH had LHD. Zafir et al showed that the severe heart failure (NHYA \geq III) was associated with elevated 2-year mortality in patients with heart failure and PH (mean age of 77 years).²⁶ As opposed to the previous study, we found that even NYHA \geq II had a worse outcome in extremely advanced aged patients with PH as compared with those with NYHA I. In a large cohort study ($n = 47,784$, mean age of 59 years), Huston et al reported that COPD was an independent prognostic factor in patients with echocardiographic PH.²⁷ Our finding was consistent with this study despite the age difference between their study and ours.

The prognostic value of gender in patients with PH is controversial. Huston et al showed that women were associated with increased mortality risk at any given SPAP in patients who were referred for echocardiography.²⁷ In contrast, men were known to have increased mortality in pulmonary arterial hypertension.²⁸ We did not find a gender difference in outcome in our patients. Our study population who were much advanced aged may explain this difference.

Our study has some limitations. (1) This study was retrospectively conducted in a single-center, and we studied the patients only referred for echocardiography. Therefore, this analysis may not be generalizable to the community. (2) We could not differentiate between precapillary, postcapillary and mixed PH because this study was based on echocardiography. (3) The co-morbidities were confirmed by medical records. We could not assess the relationship between the severity of the comorbidities and the severity of PH and the prognosis.

In conclusion, echocardiographic PH in patients ≥ 90 years of age was significantly associated with LHD. And the right ventricular systolic dysfunction, pericardial effusion, hypoalbuminemia, COPD, and NYHA class \geq II at diagnosis were independently associated with mortality.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2020.05.031>.

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