Health Insurance and Racial Disparities in Pulmonary Hypertension Outcomes

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ABSTRACT

OBJECTIVES: Pulmonary hypertension portends a poorer prognosis for blacks versus white populations, but the underlying reasons are poorly understood. We investigated associations of disease characteristics, insurance status, and race with clinical outcomes.

STUDY DESIGN: Retrospective cohort study of patients presenting for initial pulmonary hypertension evaluation at 2 academic referral centers.

METHODS: We recorded insurance status (Medicare, Medicaid, private, self-pay), echocardiographic, and hemodynamics data from 261 patients (79% whites, 17% blacks) with a new diagnosis of pulmonary hypertension. Subjects were followed for 2.3 years for survival. Adjustment for covariates was performed with Cox proportional hazards modeling.

RESULTS: Compared with white patients, blacks were younger (50 ± 15 vs 53 ± 12 years; *P* = .04), with females representing a majority of patients in both groups (80% vs 66%; *P* = .08) and similar functional class distribution (class 2/3/4: 30%/52%/16% blacks vs 33%/48%/14% whites; *P* = .69). Blacks diagnosed with incident pulmonary hypertension were more frequently covered by Medicaid (12.5% vs 0.7%) and had less private insurance (50% vs 61%; *P* = .007) than whites. At presentation, blacks had more right ventricular dysfunction (*P* = .04), but similar mean pulmonary arterial pressure (46 vs 45 mm Hg, respectively; *P* = .66). After adjusting for age and functional class, blacks had greater mortality risk (hazard ratio [HR], 2.06; 95% confidence interval [CI], 1.18-3.44), which did not differ by race after additional adjustment for insurance status (HR, 1.74; 95% CI, 0.84-3.32; *P* =.13).

CONCLUSIONS: In a large cohort of patients with incident pulmonary hypertension, black patients had poorer right-side heart function and survival rates than white patients. However, adjustment for insurance status in our cohort removed differences in survival by race.

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Pulmonary hypertension (defined as mean pulmonary artery pressure ≥25 mm Hg) encompasses a broad spectrum of diseases and patient populations. Prior efforts to characterize patients with pulmonary hypertension focused on the subset of those with "pure" pulmonary vascular disease, defined as pulmonary arterial hypertension (pulmonary capillary wedge pressure ≤15 mm Hg and pulmonary vascular resistance ≥3 Woods units). Given the dismal 5-year survival rate of 34% in the National Institutes of Health pulmonary arterial hypertension cohort 3 decades ago,[1] therapeutic advances targeting functional capacity, disease progression, and mortality have led to the availability of endothelin receptor antagonists (ERAs),[2-7] prostacyclins or their analogs,[8-10] phosphodiesterase 5-inhibitors,[11-13] and soluble guanylate cyclase stimulators.[14,15] These advances in disease management have improved the care of patients with pulmonary arterial hypertension, but are expensive: the approximate annual costs are sildenafil, $12,761; bosentan, $55,890; ambrisentan, $56,736; iloprost, $92,146; epoprostenol (70 kg patient), $33,153; and treprostinil (70 kg patient), $97,615.[16] Furthermore, 5-year survival, incorporating advances in modern therapies, remains low at 58% for patients with pulmonary arterial hypertension,[17] and the development of pulmonary hypertension is among the most significant predictors of poor outcomes in patients with chronic heart failure and lung disease.

Although there is a similar prevalence of pulmonary hypertension in black (6.6%) and white populations (6.8%),[18,19] Black individuals have been shown to have a worse prognosis.[20-23] Furthermore, age-standardized death rates for pulmonary arterial hypertension patients from 2 separate epidemiological studies, from 1980 to 1984 and 2000 to 2002, have diverged between whites (increasing from 5.0%-5.3%) and blacks (increasing from 4.8%-7.3%),[21] with little insight into why these racial disparities currently exist. However, the Registry to Evaluate Early and Long-term Pulmonary Arterial Hypertension Disease Management (REVEAL) registry of patients with pulmonary arterial hypertension in the United States reported no difference in time-to-recognition of disease from symptom

onset by race.[24] We sought to investigate the association of race with survival in a population of patients referred to 2 large tertiary care centers for invasive evaluation of pulmonary hypertension. Additionally, given that cost may be a barrier to pulmonary arterial hypertension medications, associated equipment for intravenous/inhaled administration, and specialized care, we investigated the role of insurance status on mortality.

TAKEAWAY POINTS

Black race was associated with a 2-fold mortality risk in patients with incident pulmonary hypertension after adjustment for age and functional class. However, this relationship was no longer observed after additional adjustment for insurance.

- A total of 261 consecutive patients with pulmonary hypertension were included in our cohort at time of first evaluation at 2 large tertiary referral centers (Duke University Medical Center and Cleveland Clinic).
- African American patients had more severe pulmonary vascular disease at presentation and greater than a 2-fold risk of death over study follow-up.
- Pulmonary hypertension is a fatal disease and access to medications is a public health issue due to high costs and racial disparities.

METHODS

Consecutive patients who were evaluated at 2 pulmonary hypertension referral centers for initial hemodynamic assessment between 1998 and 2009, and found to have mean pulmonary artery pressure of at least 25 mm Hg, were prospectively entered in a database. Each patient underwent a diagnostic work-up, including echocardiography and cardiac catheterization with vasodilator testing, if indicated. Only patients with known insurance type were included in our study. The study was approved by the institutional review boards at Duke University Medical Center and the Cleveland Clinic Foundation.

Right heart catheterization was performed by the same experienced cardiologist (RAK) in the cardiac catheterization laboratories at the 2 medical centers, using a single end-hole, balloon flotation catheter (either Bard Pulmonary Wedge Catheter [Medtronic; Minneapolis, Minnesota] or Balloon Wedge Pressure Catheter [Arrow International, Inc; Cleveland, Ohio]). Contrast injections during left heart catheterization, if performed, followed all hemodynamic measurements. Standard hemodynamic measurements from right heart catheterization were obtained, including mean right atrial pressure, right ventricular, systolic and diastolic pressures, pulmonary artery systolic, diastolic and mean pressures, and mean pulmonary capillary wedge pressure. Mean arterial blood pressure, cardiac index, pulmonary vascular resistance, systemic vascular resistance, and response to vasodilator challenge were also recorded in the database when indicated.

All echocardiograms were performed within 30 days of cardiac catheterization using a phase-arrayed scanner with a 4- or 8-MHz transducer, depending on body habitus and image quality. Standard 2-dimensional images were obtained in the parasternal long- and short-axis views, apical 2- and 4-chamber views, and subcostal view, and Doppler gradients were obtained to estimate valvular gradients. Assessment of right ventricular size was reported as a grade from 0 to 3, where 0 = normal, 1 = mildly enlarged, 2 = moderately enlarged, and 3 = severely enlarged. Right ventricular function was graded on a 4-point scale for systolic dysfunction, where 0 = no dysfunction, 1 = mild dysfunction, 2 = moderate dysfunction, and 3 = severe dysfunction. The degree of tricuspid regurgitation was determined using color-flow Doppler and assigned a grade from 0 to 4+, depending on the extent of color flow relative to the right atrial area. Estimated right ventricular pressures were obtained by applying continuous wave Doppler to the tricuspid regurgitation jet to the Bernoulli equation and added to the estimated right atrial pressure. If tricuspid regurgitation velocity could not be adequately visualized by color Doppler, saline microbubbles were injected to improve image quality. Saline microbubble injection was also used to assess for intracardiac shunting if flow across the interatrial septum was noted by color Doppler on subcostal imaging. Assessments were made by experienced imaging cardiologists at both academic medical centers.

Pulmonary hypertension work-up for all patients also included chest radiography, (chest computed tomography if chest radiography was abnormal), ventilation-perfusion scanning, full pulmonary function testing, electrocardiography, and echocardiography, in addition to catheterization. Test results, demographics, and medical histories were obtained from medical records and entered in the database. Insurance status at the time of the assessment was recorded as either Medicare, Medicaid, private, or self-pay, and confirmed by appointment schedulers at the time of the initial appointment. Race was self-reported at the time of catheterization. Long-term survival was assessed using electronic health records and confirmed using the Social Security Death Index. Variables of interest included the following: idiopathic pulmonary arterial hypertension (no attributable etiology of pulmonary hypertension), New York Heart Association (NYHA) class (functional class 1: no symptoms and class 4: severe symptoms), systemic hypertension and atrial fibrillation (by medical history), serum sodium and creatinine (venous laboratory values drawn at time of heart catheterization), and arterial oxygen saturation (obtained by femoral arterial blood sample at time of heart catheterization).

Only white and black patients were included in our study; patients who self-identified as other races were excluded. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and as a percentage for discrete variables. Comparison of categorical variables was performed using

TABLE 1. Demographic and Clinical Characteristics[a]

Demographics	Whites (n = 205)	Blacks (n = 45)	*P*
Median age, years	57.7 ± 15.4	52.6 ± 12.3	.02
Female, %	65.9	80.0	.08
Idiopathic PAH, %	41.9	28.6	.12
Female			.003
WHO group classification			
1, %	59.5	40.0	
2, %	11.7	17.8	
3, %	19.5	15.6	
4, %	3.9	4.4	
5, %	5.3	22.2	
NYHA class[b]			.69
2, %	29.7	33.3	
3, %	52.0	47.6	
4, %	16.3	14.3	
Systemic hypertension, %	39.0	42.2	.74
Diabetes, %	18.5	35.6	.02
Atrial fibrillation, %	21.0	11.1	.15
Serum sodium (mg/dL)	139.1 ± 3.2	138.4 ± 3.5	.21
Serum creatinine (mg/dL)	1.0 ± 0.4	1.0 ± 0.5	.69
Arterial O_2 saturation	89.6 ± 14.7	89.0 ± 8.4	.85
Insurance status			.007
Medicaid, %	0.74	12.5	
Medicare, %	31.2	33.3	
Private, %	61.6	50.0	
Self-pay, %	7.4	4.2	

NYHA indicates New York Heart Association; O_2, oxygen; PH, pulmonary arterial hypertension; WHO, World Health Organization.
[a]Data presented as mean ± standard deviation or frequency (%).
[b]Functional classes range from 1 to 4, with 4 having the most severe symptoms.

the χ^2 test or Fisher's exact test, where appropriate. Comparisons of continuous variables between groups were performed using 2-sided *t* tests and 1-way analysis of variance. Statistical significance was assumed with $P < .05$. Survival analyses were performed using the Kaplan-Meier and Cox proportional hazards regression methods. Two proportional hazards models were utilized to investigate the effect of demographics, hemodynamics, echocardiographic measurements, and insurance status. Each model was constructed in a forward step-wise manner, investigating the effect of each covariate and potential interactions individually. Potential covariates included in the adjustment models were variables with baseline differences having $P < .20$, including known predictors of death in the pulmonary hypertension population (including right atrial pressure, pulmonary artery pressure, pulmonary vascular resistance, right ventricular function, cardiac index, functional status), and race. Based on the size of the cohort, the maximum number of covariates included in each model was predetermined to be 5 to limit overfitting. Differences in the survival functions were assessed for significance using the Wilcoxon test. All analyses were performed using JMP version 12.0 software (SAS Institute; Cary, North Carolina).

RESULTS

A total of 250 patients (82% white, 18% black) were included in the study. An additional 11 patients self-identified as Asian/Pacific Islander, Hispanic, or Native American were excluded from the analysis. The median follow-up period was 2.3 years (whites: 2.0; interquartile range [IQR], 1.1-2.0 years; blacks: 1.7 years; IQR, 0.9-1.7; $P = .02$). Overall, black patients were younger, more likely to have diabetes, and coverage with Medicaid versus private insurance compared with white patients (**Table 1**). Etiology of pulmonary vascular disease was idiopathic pulmonary arterial hypertension in 42% of whites, but only 29% in blacks. Functional class distribution was similar for both races.

Comparison of pulmonary hypertension characteristics was also performed using invasive hemodynamics and echocardiography at presentation. Black individuals had higher right atrial pressure, decreased right ventricular function, and more severe tricuspid regurgitation than whites. Other markers of pulmonary hypertension severity, including pulmonary vascular resistance, cardiac index, and right ventricular size, did not differ by race (**Table 2**).

No drug prescribing differences were seen between black and white patients. During follow-up, 55% of patients received at least 1 pulmonary arterial hypertension-specific therapy (ERA, prostanoid or phosphodiesterase 5-inhibitor) and 16% received combination pulmonary hypertension-specific therapy. The most commonly utilized pharmacologic agents in descending order of frequency included sildenafil (used in 29.6% of patients), bosentan (16.8%), epoprostenol (15.8%), treprostinil (6.8%), and iloprost (2.8%). None of these agents were associated with improved survival by univariate analysis.

Differences in baseline characteristics between patients who survived and those who died were examined (**Table 3**). Older age, worse functional class, diabetes, serum sodium and creatinine values, and insurance status were associated with death by completion of the study follow-up period. Analysis by race revealed that 20 of 45 (44%) black patients and 67 of 205 (33%) white patients had died at the end of the 2.3-year follow-up period (**Figure**). With adjustment for baseline differences in age and NYHA functional class, blacks had increased risk for death (hazard ratio, 2.06; 95% confidence interval [CI], 1.18-3.44; $P = .012$) (**Table 4**). However, when insurance status was added to the model, blacks and whites had no statistically significant difference in survival rates ($P = .13$).

TABLE 2. Hemodynamics and Echocardiographic Measurements of Whites and African Americans at Initial PH Evaluation[a]

Variable	Whites (n = 205)	Blacks (n = 45)	*P*
Invasive hemodynamics			
Right atrial pressure (mm Hg)	10.3 ± 5.7	13.4 ± 8.6	.02
Mean PA pressure (mm Hg)	44.7 ± 16.0	45.8 ± 15.2	.66
PCW pressure (mm Hg)	13.5 ± 6.9	13.1 ± 7.5	.73
Cardiac index (L/min/m^2)	2.5 ± 0.9	2.5 ± 0.9	.79
PVR (Wood units)	8.6 ± 7.0	10.2 ± 7.5	.26
Systolic blood pressure (mm Hg)	96.5 ± 15.2	103.6 ± 15.3	.03
SVR (Wood units)	22.1 ± 9.7	22.4 ± 6.0	.86
Echocardiography			
RV size (grade)[b]	1.5 ± 1.2	1.8 ± 1.2	.09
RV function (grade)[c]	1.1 ± .1	1.5 ± 1.2	.04
RV systolic pressure (mm Hg)	70.5 ± 25.5	68.9 ± 24.7	.73
LV ejection fraction, %	56.3 ± 6.7	57.9 ± 5.4	.15
LV systolic dysfunction, %	9.3	6.8	.69
TR (grade)[d]	2.0 ± 1.1	2.5 ± 1.2	.009

LV indicates left ventricular; PA, pulmonary artery; PCW, pulmonary capillary wedge; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RV, right ventricular; SVR, systemic vascular resistance; TR, tricuspid regurgitation.
[a]Data presented as mean ± standard deviation for continuous variables and median ± interquartile range for categorical variables.
[b]RV size grade: 0 = normal, 1 = mildly enlarged, 2 = moderately enlarged, 3 = severely enlarged.
[c]RV function grade: 0 = normal, 1 = mild dysfunction, 2 = moderate dysfunction, 3 = severe dysfunction.
[d]Tricuspid regurgitation grade: 0 = none, 1 = trivial, 2 = mild, 3 = moderate, 4 = severe.

TABLE 3. Demographic and Clinical Characteristics, Cohorts Separated by Survivors and Nonsurvivors at End of Study Follow-up Period[a]

Characteristic	Surviving (n = 163)	Nonsurviving (n = 87)	*P*
Median age, years	53.3 ± 14.7	63.3 ± 13.3	<.001
Female	68.7	66.7	.74
Race			.13
White	84.7	77.0	
Black	15.3	23.0	
Follow-up interval, years	2.3 ± 0.2	1.2 ±0 .8	<.001
Pulmonary hypertension WHO group classification			.33
1	55.2	57.5	
2	14.7	9.2	
3	16.0	24.1	
4	4.3	3.4	
5	9.8	5.7	
NYHA class[b]			<.001
2	40.0	14.1	
3	47.2	58.8	
4	10.7	25.9	
Systemic hypertension	36.8	44.8	.22
Diabetes	16.0	32.2	.003
Atrial fibrillation	16.6	24.1	.15
Serum sodium (mg/dL)	139.4 ± 2.8	138.1 ± 4.0	.006
Serum creatinine (mg/dL)	0.9 ± 0.4	1.2 ± 0.5	<.001
Arterial O_2 saturation, %	90.0 ± 13.7	88.4 ± 14.0	.50
Insurance status, %			.004
Medicaid	1.9	3.5	
Medicare	21.4	47.4	
Private	69.9	42.1	
Self-pay	6.8	7.0	

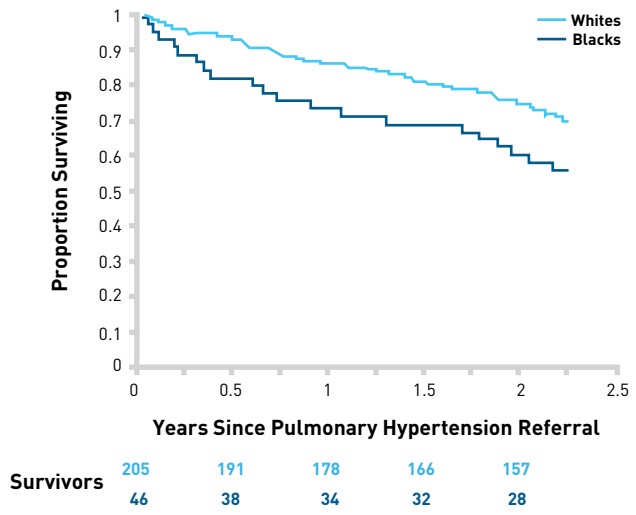
NYHA indicates New York Heart Association; O_2, oxygen; WHO, World Health Organization.
[a]Data presented as mean ± standard deviation, mean (range), or frequency (%).
[b]Ranging from class 1 to 4, with 4 reflecting the most severe symptoms.

DISCUSSION

Among 250 patients referred to 2 large pulmonary hypertension referral centers, blacks had worse survival from time of evaluation. However, additional adjustment for insurance status attenuated the association of race with outcomes, suggesting that insurance status plays an important role in pulmonary hypertension outcomes. blacks with pulmonary hypertension had more markers of advanced pulmonary vascular disease, decreased right ventricular function, and were more likely to have diabetes compared with whites. Patients who died were also more likely to have diabetes, which may be a marker for endothelial dysfunction and the resulting pulmonary venous hypertension.[25] Despite increased disease severity and diabetes, pulmonary hypertension etiology (including pulmonary hypertension secondary to left-sided heart failure) did not vary between patients who survived and those who died. Finally, the percentage of our subjects lacking insurance was lower than that of the general US population.

The association of race and health outcomes in pulmonary hypertension, which carries a high mortality as an isolated disease and when associated with obstructive lung disease, pulmonary fibrosis, and left-sided heart failure,[26-35] has not been well understood. This is the largest study to date to examine the association between insurance and racial disparities in outcomes for pulmonary hypertension, and the only study to examine this association among patients with pulmonary hypertension in WHO groups 2 to 5. Prior studies examining racial differences in pulmonary arterial hypertension have consistently shown that blacks have poorer outcomes, but the studies had significant limitations. Lilienfield et al found clear racial differences in pulmonary arterial hypertension survival using data from the CDC, but all diagnosis and disease characterization was based on *International Classification*

FIGURE. Survival of Patients With Newly Diagnosed Pulmonary Hypertension by Race Over 2.3-Year Follow-up



of Diseases, Ninth Revision, Clinical Modification (*ICD-9-CM*) codes.[23] Furthermore, their analysis used data from 1979 to 1996 in the absence of many new pulmonary arterial hypertension therapies that have emerged in the last 2 decades, and are more difficult to interpret in the context of current management practices. A more recent study of pulmonary arterial hypertension prognosticators identified race as one of the most significant variables associated with death, with an adjusted survival hazard ratio of 4.3 for nonwhites compared with whites.[22] However, further exploration of this strong association was limited by a small sample size of nonwhite patients (15 nonwhites, including 6 blacks), and socioeconomic and insurance status was not reported.

In the United States, blacks experience more life-years lost as a result of hypertension, HIV, diabetes, and trauma,[34] and they are also less likely to undergo procedures for heart disease—including angiography and coronary artery bypass surgery—resulting in poorer outcomes following cardiothoracic surgery.[33,36,37] These findings persist after controlling for socioeconomic factors. Thus, racial disparities in healthcare have been well established, and our study extends these findings to pulmonary hypertension.[28,29,31,32,34,35] Hypotheses regarding discrepancies for other disease states have cited differences in genetics, income, education, access to medical insurance and providers, affordability of medical care, geography, and psychological biases among patients and providers.[38-45]

In our population, blacks had poorer right ventricular function, but overall, no significant differences in clinicians' assessment of functional class compared with whites. Right ventricular function is a known key determinant of outcome in pulmonary hypertension, and black patients without private insurance may have been referred later in their disease course, and presented with more difficult to treat disease. This discrepancy also suggests that clinical ascertainment of functional class, which is often used to base management decisions, may also be subject to important inaccuracies, as shown in heart failure populations.[46]

Our results highlight the need for further public health study in understanding how to manage pulmonary hypertension most effectively. Although time-from-symptom onset to pulmonary arterial hypertension diagnosis likely does not differ by race,[24] the poorer right ventricular function observed in blacks on presentation may

TABLE 4. Proportional Hazards Regression Models

Model	Age β Value[a]	NYHA Functional Class β-Value[b]	Insurance Status β Value[b]	Survival Hazard Ratio (black vs white)	95% CI	*P*
Model A[c]	−0.04 (*P* <.001)	• Class 1: 0.99 (*P* = .23) • Class 2: 0.48 (*P* = .19) • Class 3: −0.37 (*P* = .25) • Overall *P* = .003	N/A	2.06	1.18-3.44	.01
Model B[d]	−0.03 (*P* = .006)	• Class 1: 0.91 (*P* = .27) • Class 2: 0.54 (*P* = .16) • Class 3: −0.35 (*P* = .30) • Overall *P* = .005	• Medicaid: −0.97 (*P* = .24) • Medicare: −0.07 (*P* = .86) • Private: 0.79 (*P* = .03) • Overall *P* = .05	1.74	0.84-3.32	.13

CI indicates confidence interval; NYHA, New York Heart Association.
[a]Beta value is the standard regression coefficient used in the statistical model.
[b]Ranging from class 1 to 4, with 4 reflecting the most severe symptoms. NYHA functional class β value is relative to NYHA class 4 and insurance status β value.
[c]Adjusted for age and NYHA functional class.
[d]Adjusted for age, NYHA functional class, and insurance status.

be due to genetic factors, comorbid conditions, or fewer interactions with healthcare providers, leading to more aggressive disease at presentation to the pulmonary hypertension referral center. blacks are less likely to have private insurance, and we found that the type of insurance at the time of referral may interact with race for survival. Insurance may be a surrogate for overall socioeconomic status, and it also may have implications for ease of access to referral centers and potential pulmonary hypertension therapies.

Limitations

The granularity of our analysis is limited by lack of data on modes of death. However, distribution of pulmonary hypertension etiology did not significantly differ between survivor and nonsurvivor groups, and so it is less likely that our findings are driven by a single pulmonary hypertension subtype or associated comorbid conditions. Patient adherence rates and physician likelihood to prescribe pulmonary arterial hypertension therapies when indicated were not assessed, but, given their relationship with insurance status, would be difficult to interpret in the context of this study. Once the decision to prescribe pulmonary arterial hypertension therapy was made, we were able to assess that specific pulmonary arterial hypertension therapies did not differ by race alone. Finally, we noted a weak correlation between age and Medicare status in our population in our model: due to the discrete information provided by each variable and lack of significant multi–co-linearity, we kept both variables in the adjustment model.

Clinical Implications

Clinicians caring for patients with pulmonary hypertension should recognize that insurance status is an important prognosticator of increased mortality after adjustment for age and functional class, regardless of pulmonary hypertension WHO classification. Patients with pulmonary hypertension who are lacking private insurance represent a high-risk subpopulation that would benefit from further public health research and thorough evaluation of insurance options if necessary monitoring and treatments are not available.

CONCLUSIONS

Blacks referred for evaluation of pulmonary hypertension have worse right heart function and subsequent prognosis compared with whites after initial diagnosis. However, adjusting for insurance status weakens the racial outcomes disparities. Pulmonary hypertension workup and management often require multiple tests for diagnosis and monitoring, specialist care, and, if warranted, costly therapies. A better understanding of varying options available to patients with newly diagnosed pulmonary hypertension across the spectrum of insurance types may identify public health measures that would improve detection and morbidity and mortality associated with the disease. ■

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