The Prevalence of Pulmonary Hypertension in the United States

Adult Population Estimates Obtained from Measurements of Chest Roentgenograms from the NHANES II Survey

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Because a definitive diagnosis of pulmonary hypertension requires cardiac catheterization, there have been no data on the prevalence of pulmonary hypertension in the general population. The diameter of the right descending pulmonary artery, as measured from chest roentgenograms, has been used by clinicians as a noninvasive indicator of pulmonary hypertension. Chest roentgenograms from the Second National Health and Nutrition Examination Survey, a sample survey of the US civilian noninstitutional population, were used in conjunction with estimates of sensitivity and specificity of this technique determined from patients who underwent right heart catheterization to estimate the prevalence of pulmonary hypertension (mean pulmonary artery pressure > 20 mm Hg at rest) in the US population aged 25 years and older. The prevalence is estimated to be very low in the population at large, primarily because of the low prevalence in women of all ages. The prevalence in men is 13.4 percent above age 34, and increases to 28.2 percent above age 64. Thus, in elderly men, pulmonary hypertension is relatively common and may have an important impact in the management of this age group.

(Chest 1989; 96:236-41)

Pulmonary hypertension is a complication of congenital and acquired heart disease, diseases of the lung and pulmonary vasculature, and thromboembolic disease. It is occasionally associated with collagen vascular diseases, diseases of the liver, residence at high altitudes, and abuse of drugs. Rarely, it seems to be idiopathic. Patients with severe pulmonary hypertension, be it primary or secondary, generally develop right ventricular hypertrophy and death from right heart failure.

Because the definitive diagnosis of pulmonary hypertension requires right heart catheterization, little is known about the prevalence of this condition in the general population. There have been studies suggesting that an enlarged right descending pulmonary artery (RDPA) identified on a chest roentgenogram correlates with pulmonary artery pressure as measured by catheterization.1-3 Since chest radiography is often used in screening defined populations of apparently healthy individuals, it is our contention that known epidemiologic relationships involving the frequency of positive findings of a screening test (in this instance the chest roentgenogram), the sensitivity and specificity of the screening test, and the prevalence of the condition interest in the population can be used to gain some insight into estimating the prevalence of this condition. With this in mind, we report an estimate of the prevalence of pulmonary hypertension in the US noninstitutional population based on chest roentgenograms taken in a sample survey of that population.

Methods

The Second National Health and Nutrition Examination Survey (NHANES II) was a cross-sectional survey conducted by the National Center for Health Statistics (NCHS) in 1976-80 on a probability sample of 27,801 persons residing in 64 areas of the United States. Because of the sampling design, estimates obtained from this survey can be extrapolated to the US civilian noninstitutional population aged 6 months to 74 years. The survey included a battery of interviews, medical examinations, and numerous laboratory measurements including chest roentgenograms on subjects 25 years of age and above. The roentgenograms were performed at a 4.5-in target-film distance with the subjects upright and at full inspiration. The sampling design, interview, examination, and laboratory procedures are detailed in an NCHS monograph.4

Selection of the Chest Roentgenograms

The chest roentgenogram from approximately 10,000 NHANES

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This study was supported in part by a contract awarded to the University of Illinois at Chicago by the National Center for Health Statistics.

Manuscript received October 17, 1988; revision accepted January 3, 1989.

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Prevalence of Pulmonary Hypertension in the US (Rich et al)
FIGURE 1. Schematic diagram of a chest roentgenogram showing the hilum and RDPA. The width of the RDPA measured in this study (arrows) was taken as its widest portion before the bifurcation of the lateral segment of the right middle lobe.

II subjects 25 to 74 years of age were screened by two radiologists, each unaware of the findings of the other, for a variety of abnormalities. One of the items on the checklist of abnormalities was "enlargement of the pulmonary arteries." All roentgenograms in which one or both of the initial readers subjectively noted an enlargement of any of the pulmonary arteries were sent to the University of Illinois at Chicago for further evaluation. In each of these (326 in number), an attempt was made to measure the diameter of the RDPA. Because the two reviewers disagreed with each other on 396 (91.8 percent) of these 326 chest roentgenograms, it was considered highly probable that many subjects who had pulmonary artery enlargement could have been screened as "negative" by both of the initial reviewers. To capture these individuals, we also chose a sample from among those subjects initially screened as negative for pulmonary artery enlargement by both reviewers. In this second sample, blacks were oversampled in order to obtain more reliable estimates by race. Thus, 288 chest roentgenograms (selected in such a way as to obtain an approximately equal number of black and white subjects) were randomly taken from those subjects who were indicated initially by neither of the two radiologists as having pulmonary artery enlargement.

Measurement of RDPA Width

The RDPA was measured directly by ruler in the posteroanterior view at its widest portion, free from pulmonary vein, before the bifurcation of the lateral segment of the right middle lobe (Fig 1). Only roentgenograms where the borders of the RDPA were distinct were used (574 of the 614 sent). The width was measured by two investigators, with consensus from a third if there was any disagreement.

Compilation of Other Variables

For each of the subjects whose chest roentgenograms were evaluated, the following information was extracted from NHANES II data files: age; race; sex; systolic blood pressure (SBP); diastolic blood pressure (DBP); and NHANES II sample weight.

The NHANES II sample weight is the reciprocal of the probability of the subject's being selected in the NHANES II sample and characterizes the number of persons in the United States represented by any subject sampled.

Estimation of the Distribution of RDPA Diameter in the Target Population

The target population of the NHANES II survey is the US noninstitutional population 1976-80. Statistical procedures used here to estimate characteristics of the distribution of RDPA diameter in this population took the following into consideration: (1) the complex cluster sampling design used in the NHANES II, (2) the original screening of each roentgenogram by two radiologists, followed by a measurement made at the University of Illinois at Chicago of RDPA width on all chest roentgenograms screened as having any pulmonary artery enlargement (by one or both of the original readers), and (3) selection of a stratified sample of 288 chest roentgenograms from those NHANES II subjects not identified by the original readers as having pulmonary artery enlargement. The particular algorithms for ratio estimation were developed using standard methods of estimation appropriate for data from complex sample surveys and have the following form:

\[ r = \frac{\sum x_i}{\sum w_i} \]

where

- \( r \) is an estimated mean level of a characteristic (e.g., mean RDPA width) or prevalence of a characteristic (e.g., enlarged RDPA in the target population, US civilian noninstitutional population 25 to 74 years of age, or specified subgroups thereof.
- \( w_i \) is sample weight for the ith subject in the study. This particular weight is the original NHANES II sample weight for the 326 subjects originally screened as showing enlargement of the pulmonary artery, and is the product of the original NHANES II sample weight, and the race specific inverse of the sampling fraction for the 288 subjects who had been screened by the original readers as not having pulmonary artery enlargement.

- \( x_i \) is level of attribute \( X \) for the ith subject in the study.

Estimation of Standard Errors

Standard errors of estimates were obtained based on the features of the sampling design noted above. To take into consideration the complex cluster sampling used in the NHANES II design, standard errors obtained by methodology appropriate for stratified random sampling were multiplied by a factor equal to the square root of \( 1 - \frac{2}{N} \), so that resulting inferences would be conservative. The factor used is based on the size of design effects found for similar variables in complex sample surveys conducted by the National Center for Health Statistics. The statistical significance of differences between groups with respect to means and prevalence rates were evaluated by use of the normal distribution applied to the ratio of observed differences to the estimated standard error of these differences. Confidence intervals were also obtained by use of the normal distribution. All p values reported are two-sided.

The Sensitivity and Specificity of RDPA Measurements

Although previous studies attempted to determine the sensitivity and specificity of RDPA measurements from chest roentgenograms as a screening test for pulmonary hypertension, the populations in those studies consisted of persons known to have lung disease and it was thought that the findings might not be generalizable to presumed healthy populations such as the NHANES II. Therefore, we sought to reestablish the sensitivity and specificity of the RDPA measurement as a screen for pulmonary hypertension based on roentgenograms of patients seen recently at the University of Illinois, with the measurements of the roentgenograms made by the same investigators that measured the roentgenograms from the NHANES II study. A sample of chest roentgenograms from 100 patients who underwent cardiac catheterization at the University of Illinois Hospital was selected in such a way that approximately equal numbers of persons with normal, mildly, moderately, and severely elevated pulmonary artery pressures (as determined during catheterization) would be included. Measurements of the RDPA diameter were made as described above, and the readers of the roentgenograms were blinded to any knowledge of the pulmonary
artery pressure. Two roentgenograms were excluded because of indistinct borders of the RDPA. Of the remaining 98 patients, the mean age was 50.8 ± 13.5 years, with 40 males and 58 females. The pulmonary artery mean pressure averaged 27.5 ± 19.6 mm Hg and ranged from 9 to 100 mm Hg.

Previous investigators suggested that gender influences the normal size of the pulmonary arteries, women having an upper limit of normal measurement for RDPA of 15 mm and men of 16 mm. A likely explanation for this difference, however, is the fact that men on average are larger than women and that differences in RDPA diameter might reflect differences in size. To test this, we used multiple regression to examine the independent influence of gender on RDPA diameter from the roentgenograms of the University of Illinois patients and found no significant relationship between gender and the diameter of the RDPA. Consequently, we chose not to segregate by sex the measurements of RDPA for the determination of sensitivity and specificity from the University of Illinois roentgenograms, or the measurements made of the roentgenograms from the NHANES II study.

The sensitivity and specificity of the RDPA measurement from chest roentgenograms will be influenced by the level of pulmonary artery pressure used to define pulmonary hypertension, and the upper limit of normal size used for the RDPA measurements. We thus tabulated the sensitivity and specificity of RDPA diameter using as cutoff points RDPA measurements ranging from 14 mm to 19 mm. In addition, although a mean pulmonary artery pressure of 20 mm Hg or above is considered abnormal, we recognize that 1 or 2 mm Hg elevations above this probably have little clinical significance. Consequently, we also tabulated the sensitivity and specificity of the RDPA measurement for mildly (greater or equal to 20 mm Hg), moderately (greater or equal to 25 mm Hg), and severely (greater or equal to 30 mm Hg) elevated pulmonary artery pressure. The relationship between the RDPA diameter and mean pulmonary artery pressure was tested with the Pearson product moment correlation coefficient.

Estimation of the Prevalence of Pulmonary Hypertension and its Standard Error

The prevalence of pulmonary hypertension in the target population and in subgroups of it was estimated by means of the equation (1) shown below, involving the true prevalence of a condition, the prevalence of a positive screening test (in this instance, RDPA enlargement) for that condition, the sensitivity of the screening test, and its specificity. This relationship was derived by Levy and Kast6 by means of the method of maximum likelihood and is applicable in situations where the specificity is high relative to the prevalence:

\[ P' = \frac{P + S_s - 1}{S_s + S_p - 1} \]  

(1)

where

- \( P' \) = the prevalence of pulmonary hypertension
- \( P \) = the estimated prevalence of RDPA enlargement
- \( S_s \) = the sensitivity of the screening test-probability of a person with pulmonary hypertension (as defined above) having RDPA enlargement (also as defined above)

and

- \( S_p \) = the specificity of the screening test (probability of a person without pulmonary hypertension not having RDPA enlargement)

In instances when the numerator in the right-hand side of equation (1) was negative, the resulting estimates of prevalence were set at zero.

The standard error of the estimated prevalence, \( P' \), of pulmonary hypertension was approximated according to standard statistical methodology by the following expression:

\[ \text{SE} (P') = \frac{\text{SE} (P) \times S_s}{\sqrt{S_s + S_p - 1}} \]  

(2)

where

- \( \text{SE} (P') \) = standard error of estimated prevalence of pulmonary hypertension

SE \((P') = \text{standard error of estimated prevalence of RDPA enlargement}\)

RESULTS

Sensitivity and Specificity of Chest Roentgenograms for Determination of Pulmonary Hypertension

The measurements of RDPA from the roentgenograms of patients at the University of Illinois were correlated with the actual values of mean pulmonary artery pressure at the time of catheterization (Table...
Table 2—Determination of the Sensitivity and Specificity of Pulmonary Hypertension Using RDPA Measurements from University of Illinois Patients (n = 98)

<table>
<thead>
<tr>
<th>RDPA (mm)</th>
<th>Mild (PAP≤20 mm Hg)</th>
<th>Moderate (PAP≥25 mm Hg)</th>
<th>Severe (PAP≥30 mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sens</td>
<td>Spec</td>
<td>Sens</td>
</tr>
<tr>
<td>14</td>
<td>87.3</td>
<td>44.2</td>
<td>91.9</td>
</tr>
<tr>
<td>15</td>
<td>80.0</td>
<td>53.5</td>
<td>89.2</td>
</tr>
<tr>
<td>16</td>
<td>60.0</td>
<td>65.0</td>
<td>75.7</td>
</tr>
<tr>
<td>17</td>
<td>50.9</td>
<td>79.1</td>
<td>67.6</td>
</tr>
<tr>
<td>18</td>
<td>56.4</td>
<td>88.4</td>
<td>56.8</td>
</tr>
<tr>
<td>19</td>
<td>34.5</td>
<td>93.0</td>
<td>43.2</td>
</tr>
</tbody>
</table>

Abbreviations: See beginning of text. Sens, sensitivity; Spec, specificity.

1) The mean RDPA diameter was 17.1±3.7 mm and ranged from 9 to 30 mm. There was a significant correlation between RDPA diameter and mean pulmonary artery pressure (r = 0.51, p = 0.001) (Fig 2). The sensitivity and specificity of the RDPA measurement was determined for a range of RDPA diameters, using from 14 to 19 mm as the upper limit of normal (Table 2). To keep the test relatively specific, we selected 18 mm as the upper limit of normal for RDPA diameter. Using this parameter, the sensitivity and specificity for the detection of mildly elevated pulmonary artery pressure were 56.4 and 88.4 percent, respectively. For moderately elevated pulmonary artery pressure, they remained similar at 56.8 and 86.9 percent, respectively. For severely elevated pulmonary artery pressure, the sensitivity and specificity increased to 75.0 and 88.6 percent.

Distribution of Right Descending Pulmonary Artery Diameter

The estimated distribution of RDPA diameter was determined for the target population as a whole and by sex (Fig 3). RDPA diameters ranged from 9 mm to 37 mm, with an overall mean of 14.47 mm and a median of 13.18 mm, which indicates a positively skewed distribution. Approximately 10 percent (±2.2 percent) of the population are estimated to have RDPA diameters above 17.9 mm and 1 percent (±0.6 percent) above 22.6 mm. The estimated prevalence of RDPA diameters of 19 mm or larger is 6.4 percent (±1.4 percent) overall, 9.7 percent (±1.8 percent) in males and 3.7 percent (±1.5 percent) in females with significant differences between males and females in both mean RDPA diameter and prevalence of RDPA enlargement (p<0.01). When stratified by race, the differences were significant between white males and white females, but not between black males and black females.

In males the estimated prevalence of RDPA enlargement (19 mm or greater) increased after age 34. No relationship was found between RDPA diameter and systolic or diastolic blood pressure.

Projected Prevalence of Pulmonary Hypertension

Based on the relations shown in equations (1) and (2) involving the prevalence of RDPA enlargement and the sensitivity and specificity of this measurement with respect to the diagnosis of pulmonary hypertension, prevalences of pulmonary hypertension were projected for the US noninstitutional population 25 to 74 years of age from 1976 to 1980 and for defined subgroups of it (Table 3). The overall prevalence of pulmonary hypertension was too low to project within reasonable confidence limits. This was largely due to the low prevalence in women at all ages. However, it was between 8.3 percent (±3.1 percent) and 13.4 percent (±5.0 percent) for men ages 35 to 44, depending on the severity, and increased to 20.1 percent (±7.4 percent) for severe pulmonary hypertension and 28.2 percent (±11.2 percent) for mild pulmonary hypertension.
Table 3—Prevalence per 100 Persons of Mild, Moderate, and Severe Pulmonary Hypertension*

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male, age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>13.4</td>
<td>10.3</td>
<td>8.3</td>
</tr>
<tr>
<td>45-54</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>21.9</td>
<td>19.0</td>
<td>15.7</td>
</tr>
<tr>
<td>65-74</td>
<td>28.2</td>
<td>25.4</td>
<td>20.1</td>
</tr>
<tr>
<td><strong>Female, all ages</strong></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

*From the NHANES II population sample.
†Number is too low to describe the prevalence within reasonable confidence limits.

pulmonary hypertension for men aged 65 and older.

**DISCUSSION**

This study integrates radiologic findings on RDPA diameter from a national survey along with determinations of the sensitivity and specificity of the chest roentgenogram on the relationship between RDPA diameter and pulmonary artery pressure to provide an estimate of the prevalence of pulmonary hypertension among US adults. Currently, the prevalence of pulmonary hypertension, mild or severe, in the general population is unknown. It has been reported to occur in 5 to 40 percent of patients with COPD* and has been estimated to account for approximately 10 percent of the cases of heart disease in the United States. The chest roentgenogram is an attractive screening test because it is widely available, noninvasive, and relatively inexpensive, and has been widely used for the subjective assessment of cardiopulmonary diseases.

Based on the sensitivity and specificity of predicting pulmonary hypertension from RDPA measurements made from roentgenograms of patients at the University of Illinois Hospital who had direct measurements of pulmonary artery pressure, and the RDPA diameters from the NHANES II population, we estimate the prevalence of mild pulmonary hypertension to be extremely small in the general population. When stratified by sex, the prevalence appears to be very low in women at any age. In men, however, the prevalence of mild pulmonary hypertension is 13.4 percent above age 34, and increases to 28.2 percent for men above the age of 64. For severe pulmonary hypertension, the prevalence is 8.3 percent for men above age 34, and 20.1 percent for men above age 64. The relationship between pulmonary hypertension and age is not surprising, since many pulmonary and cardiovascular diseases associated with pulmonary hypertension are also age related (eg, chronic lung disease, valvular heart disease, and coronary artery disease). In the initial group of 327 chest roentgenograms that were reviewed, 35 percent had abnormal-

*Chang reported an upper limit of normal diameter for the right descending pulmonary artery of 16 mm in men and 15 mm in women, but his study did not confirm normality with direct measurements of pulmonary artery pressure. The assumption that RDPA size is influenced by gender, however, likely relates to body size rather than other gender influences. We were unable to find an influence of sex on RDPA measurement in our series of “normal” patients. Other investigators have used 16 mm as the upper limit of normal for the determination of enlarged pulmonary arteries with no stratification based on gender. From our data, using 16 mm as the upper limit of normal would enhance the sensitivity of the test, but yield a specificity too low to be appropriate for the determination of prevalence in a large population where the prevalence of the disease is considered to be low. For that reason we used 18 mm as the upper limit of normal, and 19 mm or greater as an RDPA diameter reflecting pulmonary hypertension.

Matthay et al suggested that the chest roentgenogram could provide a sensitivity of 93 percent and a specificity of 87 percent for the detection of pulmonary hypertension. However, their population consisted of patients with COPD, and thus were not a reflection of the population at large. In addition, the relative hyperlucency of the lung fields on roentgenograms in this group of patients might allow a more accurate measurement of the RDPA diameter than the population at large. Clearly, the sensitivity and specificity of any test depends on the definition of the abnormal finding. When using 20 mm Hg or greater as an indication of pulmonary hypertension and an upper limit of normal of 18 mm for RDPA diameter, we obtained a sensitivity of 56.4 percent and specificity of 88.4 percent. These parameters improved as the definition of abnormal pulmonary artery pressure became stricter. Thus, the sensitivity increases to 75 percent, and specificity is maintained at 86.6 percent for the detection of a mean pulmonary artery pressure greater than 30 mm Hg.

One factor that could affect the predictive accuracy of the RDPA diameter in screening for pulmonary hypertension is that pulmonary artery size is influenced by flow as well as pressure. In the patients selected from the University of Illinois Hospital, pulmonary blood flow was normal or reduced in all subjects. In the NHANES II sample population, however, no measurement was made of pulmonary blood flow, and thus it remains unknown as to how conditions that cause increased pulmonary blood flow (primarily congenital heart disease) might also affect the estimates of the overall prevalence of pulmonary hypertension.

Prevalence of Pulmonary Hypertension in the US (Rich et al)
hypertension.

The chest roentgenogram is a relatively imprecise test for the determination of mean pulmonary artery pressure. The best noninvasive test to estimate the level of pulmonary artery pressure appears to be Doppler echocardiography. Results of previous studies on select populations suggest a correlation from 0.77 to 0.97 between indices of right-sided Doppler flow and pulmonary artery pressure,¹⁻⁵ which is considerably better than the correlation of 0.51 obtained in our study. However, Doppler echocardiography is relatively expensive, is not as widely available as chest radiography, and thus is not a practical screening test for this disease entity at this time.

The prevalence of pulmonary artery hypertension in the population at large seems to be small but is greater in men than women and increases with age. Men older than 34 years have a prevalence of mild pulmonary hypertension of 13.4 percent, which increases to 21.9 percent for men above age 54. The prevalence of pulmonary hypertension in women appears to be low at all ages.

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