Age-Associated Increases in Pulmonary Artery Systolic Pressure in the General Population

Carolyn S.P. Lam, MBBS, MRCP; Barry A. Borlaug, MD; Garvan C. Kane, MD, PhD; Felicity T. Enders, PhD; Richard J. Rodeheffer, MD; Margaret M. Redfield, MD

**Background**—In contrast to the wealth of data on isolated systolic hypertension involving the systemic circulation in the elderly, much less is known about age-related change in pulmonary artery systolic pressure (PASP) and its prognostic impact in the general population. We sought to define the relationship between PASP and age, to evaluate which factors influence PASP, and to determine whether PASP is independently predictive of mortality in the community.

**Methods and Results**—A random sample of the Olmsted County, Minn, general population (n=2042) underwent echocardiography and spirometry and was followed up for a median of 9 years. PASP was measured from the tricuspid regurgitation velocity. Left ventricular diastolic pressure was estimated with Doppler echocardiography (E/e’ ratio), and arterial stiffening was assessed from the brachial artery pulse pressure. Among 1413 subjects (69%) with measurable PASP (age, 63±11 years; 43% male), median PASP was 26 mm Hg (25th to 75th percentile, 24 to 30 mm Hg) and increased with age (r=0.31, P<0.001). Independent predictors of PASP were age, pulse pressure, and mitral E/e’ (all P≤0.003). Increasing PASP was associated with higher mortality (hazard ratio, 2.73 per 10 mm Hg; P<0.001). In subjects without cardiopulmonary disease (any heart failure, coronary artery disease, hypertension, diabetes mellitus, or chronic obstructive lung disease), the age-adjusted hazard ratio was 2.74 per 10 mm Hg (P=0.016).

**Conclusions**—We provide the first population-based evidence of age-related increase in pulmonary artery pressure, its determinants, and any prognostic impact of elevated PASP in the general community. As in the systemic circulation,6 the pulmonary vasculature may be affected by age-associated arterial remodeling,7–13 leading to pulmonary vascular stiffening and increases in PASP. Pulmonary artery pressure also is directly affected by downstream left heart filling pressures, which may increase with age-related left ventricular diastolic dysfunction.14 The increasing prevalence of cardiopulmonary diseases with age also may contribute to increases in PASP. Previous studies examining the association between age and PASP have produced conflicting results and were conducted in patients referred for cardiac catheterization or echocardiography, leading to referral bias.15–20 Importantly, population-based data are lacking, and no studies have reported data on PASP and mortality in the community.

In the systemic circulation, age-related vascular stiffening contributes to isolated systolic hypertension in the elderly, promoting increased risk of cardiovascular morbidity and mortality.1–5 However, less is known about age-related changes in pulmonary artery systolic pressure (PASP), its determinants, and any prognostic impact of elevated PASP in the general community. As in the systemic circulation,6 the pulmonary vasculature may be affected by age-associated arterial remodeling,7–13 leading to pulmonary vascular stiffening and increases in PASP. Pulmonary artery pressure also is directly affected by downstream left heart filling pressures, which may increase with age-related left ventricular diastolic dysfunction.14 The increasing prevalence of cardiopulmonary diseases with age also may contribute to increases in PASP. Previous studies examining the association between age and PASP have produced conflicting results and were conducted in patients referred for cardiac catheterization or echocardiography, leading to referral bias.15–20 Importantly, population-based data are lacking, and no studies have reported data on PASP and mortality in the community.
on January 1, 1997, was enrolled and studied over 3 years ending September 30, 2000. Of 4203 invitees, 2042 subjects (47%) participated. As previously described, participants were uniformly white, and participation rates were similar in men and women and among persons with and without cardiovascular disease but were lower in persons with lung disease.23 Each subject underwent medical review, Doppler echocardiography, and pulmonary function testing.

The following cardiopulmonary diagnoses were recorded by trained nurses using established criteria14,24: heart failure, coronary artery disease, hypertension, diabetes mellitus, or chronic obstructive lung disease. Participants underwent focused physical examination that included measurement of height, weight, and brachial artery blood pressure. Pulse pressure, calculated as the difference between brachial systolic and diastolic blood pressures, was used as an index of systemic arterial stiffness.4 Systemic arterial stiffening results in the earlier return of reflected waves and thus increased systolic and decreased diastolic blood pressures, so pulse pressure is increased.6,25

Doppler Echocardiography
All echocardiograms were performed by registered diagnostic cardiac sonographers using standardized instruments and protocols and interpreted by an echocardiologist (M.M.R.) blinded to clinical data. All parameters were measured in triplicate and averaged. In addition to standard M-mode, 2-dimensional, and color Doppler imaging, continuous-wave Doppler examination of tricuspid flow, pulsed-wave Doppler examination of mitral inflow, and Doppler tissue imaging of the medial mitral annulus were performed in each subject.14 Left ventricular ejection fraction and cardiac output were derived by standard methods.14

Determination of Pulmonary Artery Pressures
PASP was estimated by Doppler echocardiography from the systolic right ventricular to right atrial pressure gradient using the modified Bernoulli equation (4 times the peak tricuspid regurgitant velocity squared). Right atrial pressure, assumed to be 5 mm Hg, was then added to the calculated gradient to yield PASP. None of the subjects had significant right ventricular outflow tract obstruction. Echocardiographic estimates of PASP obtained in this fashion have been shown to correlate well with invasively measured values over a wide range of values (correlation coefficients ranging between 0.89 and 0.97) in our institution26,27 and others.28,29

Determination of Left Ventricular Diastolic Pressures
The ratio of early transmitral flow velocity (E) to early mitral annular (medial) tissue velocity (e') was used as an echocardiography-derived estimate of left ventricular diastolic pressure.30 This index (E/e') has been shown to reliably detect elevated left ventricular diastolic pressure in patients with elevated echocardiography-derived PASP undergoing right heart catheterization.31

Pulmonary Function Testing
Spirometry was performed in accordance with recommended techniques32 using an automated pulmonary function testing system (MultiSpiro SX Spirometer [Creative Biomedics, Inc., San Clemente, Calif.] with Mayo Health Station Software [Mayo Foundation for Education and Medical Research, Mayo Clinic, Rochester, Minn.]). Measurements of forced expiratory volume in 1 second and forced vital capacity were standardized as percentages of predicted normal values.33

Follow-Up
Subjects were followed up from baseline echocardiography and spirometry at enrollment to death (all-cause mortality) or last contact, at which time they were censored. Vital status (March 2008) was determined from the Mayo Clinic registration database and the Rochester Epidemiology Project death database, in which mortality data on Olmsted County residents are routinely collected by review-
body mass index ($r=0.07$, $P=0.008$), even after adjustment for age ($P=0.001$).

### Association of PASP With Diastolic Dysfunction and Arterial Stiffening

PASP increased with increasing pulse pressure ($r=0.33$, $P<0.001$; Figure 3A) and increasing left ventricular diastolic pressure ($r=0.32$, $P<0.001$; Figure 3B), even after adjustment for age (age-adjusted $P<0.001$ for both). No interaction was found between age and pulse pressure ($P=0.58$) or between age and left ventricular diastolic pressure ($P=0.07$), implying a similar effect of pulse pressure or left ventricular diastolic pressure on PASP at all ages. Adjusting for medication use did not affect these results (not shown). PASP also varied directly, albeit modestly, with cardiac output ($r=0.11$, $P<0.001$) and inversely with forced expiratory volume ($r=-0.17$, $P<0.001$) and forced vital capacity ($r=-0.20$, $P<0.001$). No correlation with ejection fraction ($P=0.18$) was found.

In multivariate analysis, PASP was independently associated with age (28% increase for each 10.6 years; $P=0.003$), pulse pressure (42% increase for each 17.5 mm Hg; $P<0.001$), and echocardiography-estimated left ventricular diastolic pressure (58% increase for each 3.2 units of the mitral E/e' ratio; $P<0.001$) but not body mass index or lung function. No interaction was found between pulse pressure and left ventricular diastolic pressure ($P=0.14$). These associations remained highly significant ($P<0.001$) after adjust-

### Table 1. Characteristics of Subjects With Measurable PASP in the Whole Population

<table>
<thead>
<tr>
<th></th>
<th>Quartiles of Age</th>
<th>All</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>$P^*$</th>
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<tbody>
<tr>
<td>n</td>
<td>1413</td>
<td>380</td>
<td>348</td>
<td>349</td>
<td>336</td>
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<td>Age range, y</td>
<td>45–96</td>
<td>45–54</td>
<td>55–62</td>
<td>63–71</td>
<td>72–96</td>
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<td></td>
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<td>Male, %</td>
<td>43</td>
<td>44</td>
<td>44</td>
<td>46</td>
<td>37</td>
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<td>Height, m</td>
<td>1.67±0.11</td>
<td>1.69±0.10</td>
<td>1.68±0.12</td>
<td>1.67±0.10</td>
<td>1.63±0.94</td>
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<tr>
<td>Weight, kg</td>
<td>77.2±16.2</td>
<td>79.2±17.2</td>
<td>79.4±16.6</td>
<td>78.0±15.1</td>
<td>72.0±14.7</td>
<td></td>
<td>&lt;0.001</td>
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<td>Body mass index, kg/m²</td>
<td>27.8±7.9</td>
<td>27.8±9.1</td>
<td>27.9±5.2</td>
<td>28.4±10.6</td>
<td>26.9±4.9</td>
<td></td>
<td>0.110</td>
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<tr>
<td>Hypertension, %</td>
<td>36</td>
<td>16</td>
<td>32</td>
<td>46</td>
<td>55</td>
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<td>Coronary artery disease, %</td>
<td>14</td>
<td>2</td>
<td>8</td>
<td>20</td>
<td>28</td>
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<tr>
<td>Diabetes mellitus, %</td>
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<td>3</td>
<td>3</td>
<td>10</td>
<td>11</td>
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<tr>
<td>Heart failure, %</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
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<td>&lt;0.001</td>
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<tr>
<td>Chronic obstructive pulmonary disease, %</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>7</td>
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<tr>
<td>Medications, %</td>
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<td></td>
<td></td>
<td></td>
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<td>β-Blockers</td>
<td>17</td>
<td>7</td>
<td>14</td>
<td>24</td>
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<tr>
<td>Calcium channel blockers</td>
<td>7</td>
<td>2</td>
<td>5</td>
<td>9</td>
<td>13</td>
<td></td>
<td></td>
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<tr>
<td>ACE inhibitors</td>
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<td>7</td>
<td>11</td>
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<td>Angiotensin receptor blockers</td>
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<td>1</td>
<td>2</td>
<td>4</td>
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<td>Diuretics</td>
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<td>7</td>
<td>13</td>
<td>18</td>
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<td>Systemic blood pressure, mm Hg</td>
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<td>Systolic</td>
<td>131±22</td>
<td>121±15</td>
<td>128±19</td>
<td>135±21</td>
<td>143±25</td>
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<td>Diastolic</td>
<td>73±10</td>
<td>72±9</td>
<td>73±10</td>
<td>73±11</td>
<td>73±10</td>
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<td>0.670</td>
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<td>Pulse pressure</td>
<td>59±18</td>
<td>49±12</td>
<td>56±14</td>
<td>62±16</td>
<td>70±20</td>
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<td>Heart rate, bpm</td>
<td>65±11</td>
<td>64±9</td>
<td>65±10</td>
<td>64±11</td>
<td>67±12</td>
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<td>Doppler echocardiography</td>
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<td>Ejection fraction, %</td>
<td>63±7</td>
<td>63±5</td>
<td>63±6</td>
<td>64±7</td>
<td>63±9</td>
<td></td>
<td>0.231</td>
</tr>
<tr>
<td>Cardiac output, L/min</td>
<td>5.6±1.4</td>
<td>5.5±1.2</td>
<td>5.6±1.3</td>
<td>5.7±1.4</td>
<td>5.7±1.5</td>
<td></td>
<td>0.355</td>
</tr>
<tr>
<td>PASP, mm Hg</td>
<td>28±5</td>
<td>26±4</td>
<td>27±4</td>
<td>28±5</td>
<td>30±6</td>
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<tr>
<td>Mitral E/e' ratio</td>
<td>8.7±3.2</td>
<td>7.5±2.2</td>
<td>8.3±2.5</td>
<td>9.1±3.1</td>
<td>10.5±4.1</td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Left atrial volume index, mL/m²</td>
<td>25.5±11.2</td>
<td>22.3±5.2</td>
<td>23.9±7.3</td>
<td>25.5±7.9</td>
<td>31.1±18.7</td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Spirometry</td>
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<tr>
<td>Forced expiratory volume in 1 s, % predicted</td>
<td>94±18</td>
<td>99±15</td>
<td>95±16</td>
<td>93±18</td>
<td>88±21</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Forced vital capacity, % predicted</td>
<td>97±16</td>
<td>100±14</td>
<td>98±14</td>
<td>96±16</td>
<td>90±18</td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Ratio of forced expiratory volume to vital capacity, %</td>
<td>77±8</td>
<td>79±6</td>
<td>77±7</td>
<td>77±8</td>
<td>76±10</td>
<td></td>
<td>&lt;0.001</td>
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</tbody>
</table>

ACE indicates angiotensin-converting enzyme. Data are mean±SD when appropriate.

*P value for comparison among age quartiles.
ment for cardiac output. This suggests that age, vascular stiffening, and diastolic dysfunction each contributed independently to increasing PASP in the population.

Subset of Persons Without Cardiopulmonary Disease

Cardiopulmonary disease, defined as the presence of any heart failure, coronary artery disease, hypertension, diabetes mellitus, or chronic obstructive lung disease, was identified in 635 persons through the use of established criteria. When analysis was restricted to subjects without any cardiopulmonary disease (n = 778), median PASP was 26 mm Hg (25th to 75th percentile, 24 to 30 mm Hg). PASP increased across age quartiles (Table 2), as did indexes of systemic arterial stiffening, elevated left-sided filling pressures, and decreasing lung function, although absolute changes were smaller compared with findings in the whole population.

In univariate analysis, PASP still increased with age (r = 0.25, P < 0.001) and was positively correlated with pulse pressure (r = 0.28, P < 0.001), echocardiography-estimated left ventricular diastolic pressure (r = 0.25, P < 0.001), and cardiac output (r = 0.17, P < 0.001); PASP was negatively correlated, albeit weakly, with forced expiratory volume (r = −0.08, P = 0.035) and forced vital capacity (r = −0.12, P = 0.001). In multivariate analysis, similar to results in the whole population, age (38% increase for each 9.6 years; P = 0.001), pulse pressure (38% increase for each 14.4-mm Hg increase; P = 0.001), and left ventricular end-diastolic pressure (37% increase for each 2.6 units of the mitral E/e' ratio; P = 0.001) were significant predictors of PASP, even after adjustment for cardiac output. None of the interaction terms were significant.

Association of PASP With All-Cause Mortality

In the entire population, a total of 155 deaths occurred during a median follow-up of 9.0 years. By Kaplan-Meier analysis, increasing quintiles of PASP predicted poorer survival in the general population (P < 0.001). The pattern of increasing mortality risk was observed across the lower 4 quintiles and most strikingly in the highest 2 quintiles (Figure 4A). By Cox regression analysis, increasing PASP was strongly associated with mortality (unadjusted hazard ratio, 2.73 per 10 mm Hg; P < 0.001). When PASP, age, pulse pressure, ejection fraction, echocardiography-estimated left ventricular diastolic pressure, and spirometry values were included in stepwise modeling, PASP remained an independent predictor of mortality (adjusted hazard ratio, 1.46 per 10 mm Hg; P = 0.017), along with age, pulse pressure, ejection fraction, and forced expiratory volume. Forward and backward stepwise modeling gave the same results.

In the subset without cardiopulmonary disease, 36 deaths occurred over a median follow-up of 9.0 years. By Kaplan-Meier analysis, increasing tertiles of PASP similarly predicted poorer survival (P = 0.002; Figure 4B). Increasing

![Figure 1. Distribution of PASP in the general community. The cumulative frequency distribution of PASP in the population is shown. Values are median (25th to 75th percentiles). PASP was 26 mm Hg (24 to 30 mm Hg).](http://circ.ahajournals.org/)

![Figure 2. Association of systemic pressure and PASP with age. A, In the systemic circulation, brachial artery systolic blood pressure (SBP) increased with age. B, In the pulmonary circulation, PASP similarly increased with age in men (gray) and women (black) in the population. For each association, raw data points, the linear regression line, Pearson correlation coefficient, and the P value for the association are shown. C, Across age quartiles, the percentage increase in SBP (gray) and PASP (black) relative to the youngest quartile was strikingly similar in the systemic and pulmonary circulations.](http://circ.ahajournals.org/)
Pulmonary artery pressure also was strongly associated with mortality by Cox regression analysis (unadjusted hazard ratio, 4.65 per 10 mm Hg; \( P < 0.001 \)) and remained an independent predictor, along with age, in stepwise modeling (adjusted hazard ratio, 2.74 per 10 mm Hg; \( P = 0.016 \)). Forward and backward stepwise modeling yielded the same results.

**Discussion**

These are the first population-based data showing that pulmonary artery pressures increase with age in subjects from the general community. The increase in pulmonary artery pressure was coupled with increases in pulse pressure and estimated left heart filling pressures, suggesting that age-associated blood vessel stiffening and diastolic dysfunction contribute to changes in pulmonary artery pressure. Importantly, increasing PASP was associated with increased all-cause mortality independently of both age and the presence of clinically evident cardiopulmonary disease. As with systemic arterial hypertension, increasing blood pressure in the pulmonary circulation may serve as a cardiovascular risk factor and may potentially be a novel therapeutic target.

Pulmonary artery pressure is determined by the amount of blood flowing through the pulmonary circulation (cardiac output), the intrinsic properties of the vasculature (resistance, compliance, and impedance), and the left atrial pressure downstream of the pulmonary circuit (left ventricular diastolic pressure). Similar to the systemic circulation, high-output states and vascular stiffening may contribute to increases in systolic pressure in the pulmonary circulation. In contrast to the systemic circulation in which downstream venous pressure is very low compared with arterial pressure, pulmonary venous pressure is much greater in relation to pulmonary arterial pressures. Hence, increases in pulmonary venous pressures, determined primarily by left ventricular diastolic function, also may lead to increases in PASP. Furthermore, a reduction in left atrial compliance, such as that which may occur in advanced left ventricular diastolic dysfunction, also can contribute to increasing PASP independently of left ventricular filling pressures.

Previous cardiac catheterization-based studies have generally shown increasing pulmonary artery pressures at rest and/or with exercise among older volunteers compared with younger subjects, but these studies were relatively small and subject to referral bias in that, by definition, all participants had been referred for cardiac catheterization. More recently, McQuillan et al reported echocardiography-derived PASP values in 3790 normal subjects identified from a database of patients referred for echocardiography. In this large series, mean PASP was \( 28 \pm 5 \) mm Hg and increased with age and body mass, similar to the present findings. Although left heart filling pressures were not formally assessed, the authors noted a direct relationship between PASP and left ventricular wall thickness and left atrial diameter, suggesting an association with diastolic dysfunction and elevated left heart filling pressures. However, similar to earlier catheterization laboratory–based studies, this series was limited by selection bias, as acknowledged by the authors in their call for population-based studies. The present data therefore extend the previous findings by providing the first population-based evidence of age-associated increase in pulmonary artery pressures and its association with age-dependent diastolic dysfunction in the general population.

This is also the first study to show an association between PASP and mortality in the general population. The age-associated increases in PASP appear analogous to increases in systemic systolic blood pressure with aging, a phenomenon that is largely related to blood vessel stiffening in conduit arteries such as the aorta. Just as “isolated systolic hypertension” confers greater risk for cardiovascular events and mortality even with relatively small increases in systolic blood pressure, we show that even minor elevations in pulmonary artery pressure also predict greater risk. Although the relative accuracy of echocardiographic PASP measurement compared with brachial blood pressure measurement must be considered, it is notable that the relative increase in pulmonary and systemic pressures across age quartiles was strikingly similar after accounting for the baseline pressure differences between the 2 circulations. Furthermore, PASP may have been underestimated in the community because of the lower participation rates and lower feasibility of PASP measurements in persons with lung disease and because of the uniform assignment of a right atrial pressure of 5 mm Hg. Although this minimum assumed right atrial pressure is appropriate for most community-dwelling adults with normal...
PASP, it may be inappropriately low for subjects with elevated pulmonary pressures. The present data cannot discern how much of the age-dependent increase in PASP was related to changes in vascular tone (resistive load) compared with vascular stiffening. In the systemic circulation, mean vascular resistance remains stable with aging, and blood pressure elevations are predominantly related more to vascular stiffening with aging contributes and blood pressure elevations are predominantly related more to vascular stiffening. Age-associated arterial remodeling has similarly been reported in the pulmonary vasculature, and the significant association between PASP and brachial pulse pressure noted in the present study supports the notion that blood vessel stiffening with aging contributes to the increase in blood pressure in both pulmonary and systemic vascular beds.

Besides being a marker of diastolic dysfunction and vascular stiffening, the independent association of PASP with increased mortality suggests that PASP could ultimately prove to be a novel cardiovascular risk factor. Whether or how elevations in pulmonary artery pressure should be treated in such patients remains unknown, but given the importance of diastolic dysfunction, it is likely that treatments will need to focus on both the left heart and the pulmonary vasculature. These notions merit further study. The ease of assessing PASP and pulmonary venous hypertension noninvasively, the availability of an increasing number of pulmonary vasculature-modifying drugs, and ongoing trials involving agents targeting both diastolic dysfunction and pulmonary hypertension (Phosphodiesterase-5 Inhibition to Improve Clinical Status and Exercise Capacity in Diastolic Heart Failure [RELAX] trial; http://clinicaltrials.gov) all suggest that this may become possible.

**Study Strengths and Limitations**

Strengths of this study include the population-based approach, comprehensive echocardiographic characterization of diastolic function, uniform assessment of pulmonary function by spirometry, and outcome assessment in a large sample of the general community. The large number of subjects provided statistical power to detect even weaker (r<0.2) associations of potential physiological significance. Well-known examples of mathematically modest yet clinically important associations include the correlation between severity or duration of systemic hypertension and degree of left ventricular hypertrophy. In the present study, the large number of events also allowed adjustment for multiple covariates to yield clinically meaningful and robust results.

Although Doppler estimates of PASP correlate excellently with invasive measures, systematic overestimation may occur in low-risk populations, and invasive hemodynamic measurements remain the gold standard for verification of pulmonary hypertension. However, this study could not have been performed with an invasive approach. The contribution
of hypoxic pulmonary vasoconstriction to increases in PASP in the population cannot be ascertained from these data, although we postulate that in this community sample the contribution was small. We similarly lack data on potential genetic or molecular determinants of pulmonary pressures. The single time point measurement in this study precludes the evaluation of time-dependent covariance in survival analysis.

Conclusions

We provide the first population-based evidence of age-associated increases in pulmonary artery pressure, document the adverse prognostic implications of elevated pulmonary artery pressures in the general population, and provide data suggesting that increasing pulmonary artery pressure with age is related, at least in part, to age-associated vascular stiffening and pulmonary venous hypertension from left ventricular diastolic dysfunction. These findings need to be confirmed in other populations and, if proven, suggest that PASP may be a novel cardiovascular risk factor. The observation of increasing mortality provides rationale for future investigations into treatments targeting factors that lead to increased pulmonary artery pressure.

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Disclosures

None.

References

In contrast to the wealth of data on isolated systolic hypertension involving the systemic circulation in the elderly, much less is known about age-related change in pulmonary artery systolic pressure and its prognostic impact in the general population. Similar to the systemic circulation, vascular stiffening may contribute to increases in systolic pressure in the pulmonary circulation. Unlike the systemic circulation in which downstream venous pressure is very low compared with arterial pressure, pulmonary venous pressure is much greater in relation to pulmonary arterial pressures. Hence, increases in pulmonary venous pressures, determined primarily by left ventricular diastolic function, also may lead to increases in pulmonary arterial pressures. We provide the first population-based data showing that pulmonary artery pressures increase with age in subjects from the general community. The increase in pulmonary artery pressure was coupled with increases in pulse pressure and estimated left heart filling pressures, suggesting that age-associated blood vessel stiffening and diastolic dysfunction contribute to changes in pulmonary artery pressure. Importantly, increasing pulmonary artery systolic pressure was associated with increased all-cause mortality independently of both age and the presence of clinically evident cardiopulmonary disease. These findings need to be confirmed in other populations and, if proven, suggest that pulmonary artery systolic pressure may be a novel cardiovascular risk factor. The observation of increasing mortality provides rationale for future investigations into treatments targeting factors that lead to increased pulmonary artery pressure.

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