Rate of Decline of Forced Vital Capacity Predicts Future Arterial Hypertension

The Coronary Artery Risk Development in Young Adults Study

David R. Jacobs, Jr, Hiroshi Yatsuya, Mary O. Hearst, Bharat Thyagarajan, Ravi Kalhan, Sharon Rosenberg, Lewis J. Smith, R. Graham Barr, Daniel A. Duprez

Abstract—Lung function studies in middle-aged subjects predict cardiovascular disease mortality. We studied whether greater loss of forced vital capacity (FVC) early in life predicted incident hypertension. The sample was 3205 black and white men and women in the Coronary Artery Risk Development in Young Adults Study examined between 1985 and 1986 (Coronary Artery Risk Development in Young Adults year 0, ages 18–30 years) and 2005–2006 and who were not hypertensive by year 10. FVC was assessed at years 0, 2, 5, 10, and 20. Proportional hazard ratios and linear regression models predicted incident hypertension at years 15 or 20 (n=508) from the change in FVC (FVC at year 10 − peak FVC, where peak FVC was estimated as the maximum across years 0, 2, 5, and 10). Covariates included demographics, center, systolic blood pressure, FVC maximum, smoking, physical activity, asthma, and body mass index. Unadjusted cumulative incident hypertension was 25% in the lowest FVC loss quartile (Q1; median loss: 370 mL) compared with 12% cumulative incident hypertension in those who achieved peak FVC at year 10 (Q4). Minimally adjusted hazard ratio for Q1 versus Q4 was 2.21 (95% CI: 1.73–2.83), and this association remained significant in the fully adjusted model (1.37; 95% CI: 1.05–1.80). Decline in FVC from average age at peak (29.4 years) to 35 years old predicted incident hypertension between average ages 35 and 45 years. The findings may represent a common pathway that may link low normal FVC to cardiovascular disease morbidity and mortality. (Hypertension. 2012;59:219-225.) • Online Data Supplement

Key Words: forced vital capacity ■ hypertension ■ CARDIA ■ adults ■ cohort

As early as the 1960s, lower forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁) was found to be associated with all-cause and cardiovascular disease (CVD) death even in the absence of overt respiratory symptoms or disease. The association between lung function and CVD death has been consistently observed. Typical of these studies, Hole et al³ reported on 15,411 middle-aged men and women beginning in 1972–1976 and followed for 15 years. Relative risk for all-cause and ischemic heart disease death was inversely graded across FEV₁ levels. Specifically comparing the highest FEV₁ quintile as reference to the low-normal third quintile of FEV₁ (men: 87% to 96%; women: 90% to 100% of predicted FEV₁), all-cause death relative risks were 1.45 (95% CI: 1.26–1.68) in men and 1.21 (95% CI: 1.03–1.42) in women, with qualitatively similar findings for ischemic heart disease death. However, lung function did not predict nonfatal myocardial infarction in the Copenhagen City Heart Study. The Malmö Preventive Project found an association of a decline in FVC and FEV₁ with heart failure (ischemic and nonischemic) in 20,998 CVD-free men followed for 23 years, whereas there was little association with FEV₁/FVC, the latter restricted to smokers. Hypertension is a major cause of development of heart failure without preceding myocardial infarction. Reports have shown inverse cross-sectional associations between lung function measures (especially FVC and FEV₁ but not FEV₁/FVC) and blood pressure; however, analyses have been inconsistent. On the contrary, cohort studies have shown that lower lung function measures at baseline were consistently associated with higher incidence of subsequent hypertension, suggesting more rapid blood pressure elevation in persons who initially have lower lung function. This study aimed to assess whether steeper decline in lung function, even within the normal range, is associated with higher incidence of hypertension statistically controlling for level of baseline lung function. We hypothesized that greater rate of loss of lung function would predict future arterial hypertension in a general sample of young blacks and whites.
Materials and Methods

The Coronary Artery Risk Development in Young Adults Study

The Coronary Artery Risk Development in Young Adults (CARDIA) Study is a prospective epidemiological study of the evolution of CVD risk factors in young adults.\(^{13}\) Briefly, from 1985 to 1986, 5115 black and white individuals aged 18 to 30 years were examined in Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA. At the Birmingham, Minneapolis, and Chicago sites, participants were randomly selected from total communities or from specific census tracts. In Oakland, participants were randomly selected from the Kaiser Permanente Medical Care Program membership. Recruitment achieved nearly equal numbers at each site of race, sex, education (more than high school or high school or less), and age (18–24 years or 25–30 years). Fifty percent of invited individuals contacted were examined (47% of blacks and 60% of whites) and became the CARDIA cohort. Reexamination occurred after 2, 5, 7, 10, 15, and 20 years.

Lung Function

Lung function was measured at years 0, 2, 5, and 10 using a Collins Survey 8-L water-sealed spirometer and an Eagle II Microprocessor (W A Baum Co, Copiague, NY). At baseline through year 15 and using a digital BP monitor (OMRON HEM-705KL; Online Fitness, Santa Monica, CA) at the year 20 follow-up examination. A calibration study was performed, and values calibrated to the sphygmomanometric measures were used for the year 20 follow-up measurements, so that essentially no methodological artifacts between old and new machines; the average difference between the Collins Survey and OMI spirometer was 6 mL for FVC and 21 mL for FEV\(_1\). Standard procedures of the American Thoracic Society were followed at all of the examinations.\(^{14–17}\) Daily checks for leaks, volume calibration with a 3-L syringe, and weekly calibration in the 4- to 7-L range were undertaken to minimize methodological artifacts between exams. We analyzed FVC and FEV\(_1\) as the maximum of 5 satisfactory maneuvers. In almost all of the cases, the maximum and second highest maneuvers agreed to within 150 mL.

Considering the young age of some participants at baseline, the possibility that lung function had not yet reached the maximum at year 0, and the available data, we estimated an individual’s peak lung function as the maximum attained at year 0, 2, 5, or 10. This value was usually the highest achieved among the CARDIA measurements, because only 4% (138 of 3426 participants who had ≥1 FVC among years 0, 2, 5, and 10 and also had FVC measured at year 20) had their highest value at year 20, and in only 1.6% (55) was the year 20 the greatest by >100 mL. Change in lung function was calculated from peak lung function minus year 10 lung function. We divided participants into approximate quartile by this change of FVC from peak: at or less than −250 mL, −249 mL to −100 mL, −99 mL to −1 mL, and exactly 0 mL.

Hypertension

Blood pressure was measured on the seated participant’s right arm after a 5-minute rest at each examination, using a Hawksley random 0 sphygmomanometer (W A Baum Company, Copiague, NY) at baseline through year 15 and using a digital BP monitor (OMRON HEM-907XL; Online Fitness, Santa Monica, CA) at the year 20 follow-up examination. A calibration study was performed, and values calibrated to the sphygmomanometric measures were used for the year 20 follow-up measurements, so that essentially no machine bias remained (please see the online Data Supplement at http://hyper.ahajournals.org: CS = 3.74 + 0.96*OS and CD = 1.30 + 0.97*OD, where CS is calibrated systolic blood pressure, CD is calibrated diastolic blood pressure, OS is observed Omron systolic blood pressure, and OD is observed Omron diastolic blood pressure. Three measurements were taken at 1-minute intervals. Systolic and diastolic pressures were recorded as phase I and phase V Korotkoff sounds. The average of the second and third measurements was the pressure of record. We defined hypertension, consistent with the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or taking antihypertensive medication at that examination.\(^{18}\) Individuals free of hypertension at years 0, 2, 5, 7, and 10 were considered to have incident hypertension if they met 1 of the 3 criteria at either year 15 or 20.

Other Variables

Body weight was measured in light clothing to the nearest 0.1 kg with a calibrated balance beam scale, and height without shoes was measured to the nearest 0.5 cm using a vertical ruler. Body mass index (BMI) was computed as weight divided by height squared (kilograms per meter squared). Smoking status was classified as never, past, or current smoker. Physical activity was measured using an interviewer-administered questionnaire\(^{19}\) concerning the frequency of participation in 13 different activities during the past 12 months. Because participants were not asked specifically about duration of physical activity bouts, exact energy expenditure cannot be estimated, and the activity is expressed approximately in “exercise units.” We considered physician-confirmed asthma to be present from the time of the first examination in which the subject either was taking asthma medication (usually based on examination of medicine containers) or provided a positive response to, “Has a doctor or nurse ever said that you have asthma?”

Exclusions

In the present study, we first restricted the study sample to those with lung function measurements at year 10 and a value for peak lung function (n=3754). We excluded 68 participants for missing information on covariates (height, BMI, smoking status, physical activity, and systolic blood pressure all at year 10). We further excluded 41 subjects with physiologically implausible level of FVC change (−1 L or more decrease). Finally, participants who were ever classified as hypertensive through year 10 examination (n=440) were excluded, leaving 3205 for the present analyses.

Statistical Analysis

Age-, sex-, race-, and center-adjusted means and proportions among FVC change quartiles were calculated and tested by a general linear model. Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and their 95% CIs for incident hypertension in relation to quartiles of FVC change, beginning with a minimally adjusted model (age, sex, race, height, center, and education level), followed by an adjusted model with behavioral variables (physical activity and smoking) and systolic blood pressure at year 10, peak FVC, and history of asthma covariates. Time of occurrence of incident hypertension was taken to be the CARDIA examination year for those diagnosed by high blood pressure or else the previous year for those defined by use of medication. We also ran models that explored BMI as a common mechanism for changes in lung function and blood pressure. These models included year 10 BMI as a covariate in analyses using FVC loss through year 10 as the predictor of interest or year 20 BMI as a covariate in analyses using FVC loss through year 20 as the predictor of interest. We considered alterations in the coefficients for lung function loss by addition of BMI to the model to go beyond deconfounding, because those altered coefficients discount the potential importance of unmeasured variables that are in the causal pathway linking BMI to both lung function and hypertension. Parallel analyses were conducted using FEV\(_1\) and FEV\(_1\)/FVC instead of FVC. We also did several sensitivity analyses. Because the exclusion of those with physiologically implausible lung function change used rather arbitrary cut points, we carried out sensitivity analyses adding participants with FVC change >1.0 L but ≤1.5 L (n=3228) or deleting participants with FVC change ≥0.5 L (n=2999). The hazard proportionality assumption was ascertained graphically by examining whether the ln(–ln) survival curves were parallel by visual inspection. Second, we assessed robustness of the estimates by testing hierarchical models adding in changes from year 5 in BMI and waist circumference and pack years of cigarette smoking. Finally, we included diastolic blood pressure, heart rate, and systolic blood pressure at baseline and year...
medians of 370 mL (185 mL) of FVC from peak to year 10. Although those in the greatest FVC loss category (Q1) lost a median of 370 mL from their maximum attained value, they remained well within the normal range of FVC (Table 1). Those in the greatest loss category were more likely to be male, older, less physically active, a current smoker, have a higher BMI, and have higher systolic blood pressure at year 10.

During follow-up through year 20, hypertension developed in 508 cases (incidence density: 8.6 per 1000 person-years). Incidence density was >2-fold in subjects with largest FVC loss (Q1) compared with Q4 (13.9 versus 6.1 per 1000 person-years; Table 2). In the minimally adjusted model, HR for subjects in Q1 compared with Q4 was 2.21. Adjustment for confounders somewhat attenuated the magnitude of the association (HR for those in Q1 versus Q4 in model 2: 1.76).

**Results**

The study sample was (mean [SD]) 34.9 years old (3.7 years old) at year 10, 56% women, and 55% whites. Mean FVC at year 10 was 4.46 L (1.02 L). Peak FVC was achieved at age 29.4 years (4.62 years), with 27% of the sample achieving peak FVC at year 0, 18% at year 2, 27% at year 5, and 28% at year 10. Individuals who reached peak at year 10 experienced lung function decline from year 10 to 20 (mean decline: $-422 \pm 352$ mL). On average, participants lost 159 mL (185 mL) of FVC from peak to year 10. Although those in the greatest FVC loss category (Q1) lost a median of 370 mL from their maximum attained value, they remained well

### Table 1. Means and SDs or Percentages According to Quartiles of FVC Change From Peak to Year 10, CARDIA, 1995–1996 (n=3205)

<table>
<thead>
<tr>
<th>Y 10 Characteristics</th>
<th>Quartile of FVC Change From Peak to Y 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1 (n=787)</td>
</tr>
<tr>
<td>Range, mL</td>
<td>$-980$ to $-250$</td>
</tr>
<tr>
<td>Median, mL</td>
<td>$-370$</td>
</tr>
<tr>
<td>Women, %</td>
<td>41.6</td>
</tr>
<tr>
<td>White, %</td>
<td>54.5</td>
</tr>
<tr>
<td>Center, %</td>
<td></td>
</tr>
<tr>
<td>Birmingham</td>
<td>28.1</td>
</tr>
<tr>
<td>Chicago</td>
<td>17.0</td>
</tr>
<tr>
<td>Minneapolis</td>
<td>34.9</td>
</tr>
<tr>
<td>Oakland</td>
<td>20.0</td>
</tr>
<tr>
<td>Age, y</td>
<td>35.8 (3.4)</td>
</tr>
<tr>
<td>Education, y</td>
<td>15.4 (0.1)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>170.5 (0.3)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>30.7 (0.2)</td>
</tr>
<tr>
<td>ΔBody mass index, y 10 – y of peak FVC, kg/m²</td>
<td>1.94 (0.16)</td>
</tr>
<tr>
<td>ΔBody mass index, y 20 – y 10, kg/m²</td>
<td>3.95 (0.09)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>110.0 (0.3)</td>
</tr>
<tr>
<td>Physical activity, exercise units†</td>
<td>308 (10)</td>
</tr>
<tr>
<td>Smoking status, %</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>29.2</td>
</tr>
<tr>
<td>Past smoker</td>
<td>14.0</td>
</tr>
<tr>
<td>Asthma reported by y 10, %‡</td>
<td>14.3</td>
</tr>
<tr>
<td>Peak FVC, L</td>
<td>4.52 (0.02)</td>
</tr>
<tr>
<td>Y 10 FVC, L</td>
<td>4.10 (0.02)</td>
</tr>
<tr>
<td>Y 10 FVC, % predicted</td>
<td>97.5 (11.6)</td>
</tr>
<tr>
<td>Cumulative hypertension incidence by y 20, %§</td>
<td>24.8</td>
</tr>
</tbody>
</table>

FVC indicates forced vital capacity; CARDIA, Coronary Artery Risk Development in Young Adults. Peak is the highest FVC among whatever measurements were available at years 0, 2, 5, and 10 (participants were 18–30 y old at y 0; average: 25 y old).

*P values were derived from χ² test for sex, race, and center and 1-way ANOVA for age. General linear model adjusted for age, sex, race, and center was used to derive adjusted means, proportions, and P values (with 3 degree of freedom).

†Physical activity was measured using an interviewer-administered questionnaire concerning the frequency of participation in 13 different activities during the past 12 mo.

‡Data show ≥1 self-report of physician-confirmed asthma that was still active at the time of interview or history of medication use at year 0, 2, 7, or 10.

§Incident hypertension was defined when systolic blood pressure was ≥140 mm Hg or diastolic blood pressure was ≥90 mm Hg or use of antihypertensive medication was reported at either year 15 or 20.

10. All of the statistical analyses were performed by SAS 9.2 of the SAS System for Windows, and statistical significance was evaluated at a P value <0.05.
Thus, the direction of association was specific for lung function change predicting hypertension. Third, the addition of pack years, changes in BMI or waist circumference, diastolic blood pressure, or earlier measures of blood pressure did not substantively change the original findings.

Discussion

In this study of black and white American adults of the CARDIA Study, FVC change from peak to year 10 significantly predicted incidence of arterial hypertension during the 10-year follow-up (CARDIA years 10–20). The association was robust to adjustment and sensitivity analysis. These findings were consistent with previous studies that found that interindividual variation in lung function level in early adulthood to be associated with future development of hypertension.9,11,12 Our study extended this previous understanding of association between interindividual differences in lung function and hypertension to include intrindividual change of lung function from peak and hypertension in a

Table 2. Multivariable Analysis of Incident Hypertension (After Y 10) Related to FVC Change From Its Peak to Y 10, CARDIA, 1995–2006 (n=3205)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Quartile of FVC Change From Its Peak to Y 10</th>
<th>Continuous FVC Change From Its Peak to Y 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1 (n=787)</td>
<td>Q2 (n=811)</td>
</tr>
<tr>
<td>Range, mL</td>
<td>−980 to −250</td>
<td>−249 to −100</td>
</tr>
<tr>
<td>Median, mL</td>
<td>−370</td>
<td>−170</td>
</tr>
<tr>
<td>No. of cases</td>
<td>197</td>
<td>125</td>
</tr>
<tr>
<td>Incidence density per 1000 person-y</td>
<td>13.9</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Model 1 2.21 (1.73–2.83) 1.30 (1.00–1.69) 1.03 (0.77–1.38) 1 (reference) 1.32 (1.22–1.42)†
Model 2 1.75 (1.36–2.25) 1.18 (0.90–1.53) 1.00 (0.74–1.33) 1 (reference) 1.24 (1.15–1.34)
Model 3 1.37 (1.05–1.80) 1.03 (0.79–1.35) 0.95 (0.71–1.27) 1 (reference) 1.15 (1.06–1.26)

FVC indicates forced vital capacity; CARDIA, Coronary Artery Risk Development in Young Adults. Model 1 was adjusted for age, sex, race, height, center, and education level, all measured at baseline. Model 2 includes model 1 plus covariates systolic blood pressure at y 10, maximum FVC achieved either at y 0, 2, 5, or 10 exam, smoking (never, past, or current; y 10), physical activity (y 10), and history of asthma (y 10). Model 3 includes model 2 further adjusted for body mass index (y 10).

*Data show hazard ratio (95% CI).
†Data show hazard ratio (95% CI) per 1 SD (223 mL) decrement of FVC change from peak to y 10.

Table 3. Multivariable Analysis of Incident Hypertension (After Y 10) Related to FVC Change From Its Peak to Y 20, CARDIA, 1995–2006 (n=2980)

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Quartile of FVC Change From Its Peak to Y 20</th>
<th>Continuous FVC Change From Its Peak to Y 20</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Q1 (n=645)</td>
<td>Q2 (n=645)</td>
</tr>
<tr>
<td>Range, mL</td>
<td>−3110 to −740</td>
<td>−739 to −503</td>
</tr>
<tr>
<td>Median, mL</td>
<td>−338</td>
<td>−605</td>
</tr>
<tr>
<td>No. of cases</td>
<td>162</td>
<td>130</td>
</tr>
<tr>
<td>Incidence density per 1000 person-y</td>
<td>13.0</td>
<td>10.3</td>
</tr>
</tbody>
</table>

Model 1 2.67 (1.96–3.64)* 1.97 (1.46–2.67) 1.37 (1.00–1.88) 1 (reference) 1.41 (1.31–1.52)†
Model 2 1.98 (1.44–2.72) 1.50 (1.10–2.03) 1.16 (0.85–1.59) 1 (reference) 1.37 (1.25–1.50)
Model 3 1.49 (1.07–2.07) 1.24 (0.91–1.70) 1.03 (0.75–1.42) 1 (reference) 1.28 (1.16–1.42)

FVC indicates forced vital capacity; CARDIA, Coronary Artery Risk Development in Young Adults. Model 1 was adjusted for age, sex, race, height, center, and education level. Model 2 includes model 1 plus covariates systolic blood pressure at y 20, maximum FVC achieved at y 0, 2, 5, or 10 exam, smoking (never, past, or current; y 20), physical activity (y 20), and history of asthma (y 20). Model 3 includes model 2 further adjusted for body mass index (y 20).

*Data show hazard ratio (95% CI).
†Data show hazard ratio (95% CI) per 1 SD (398 mL) decrement of FVC change from peak to y 20.
generally healthy sample. Lung function deterioration can be seen as an independent factor associated with future hypertension incidence, even for those with low-normal lung function.

Although the relationship between reduced FVC and FEV₁ and the incidence of hypertension is clear, the mechanisms underlying these associations are less clear. We present several speculations and hypotheses that may help to focus future research. In the normal lung, once peak lung function is achieved, the changes leading to decreased elastic recoil of the lung include enlargement of airspaces (emphysema) and resultant loss of supporting tissue for peripheral airways. In an attempt to understand why reduced FVC and FEV₁ predisposed to heart failure, whereas reduced FEV₁/FVC did not, Engström et al. pointed to a decline in lung volume or reduced compliance of the lung tissue or chest wall rather than to airway obstruction. Our findings are in agreement with this view. Furthermore, the age-related reduction of lung elastic recoil is associated with a reduction in vital capacity. Although FEV₁ is more specifically affected by elastic recoil than is FVC, in our young, healthy sample, FEV₁ and FVC are highly correlated and statistically nearly interchangeable; thus, we cannot distinguish loss of elastic recoil from other causes of loss of lung volume within our data. The loss of lung elastic recoil could be paralleled by a nonatherosclerotic reduction in vascular elasticity. A decrease in arterial elasticity will result in an increase in arterial blood pressure.

In addition, there may be reduced chest wall compliance and decreased respiratory muscle strength, even without decline in elastic recoil. It is of particular interest in this regard that adjustment for BMI substantially attenuated the association between decline of lung function and increase in blood pressure. Because a common pathology might result from excess BMI to both decrease FVC and increase blood pressure, adjustment for BMI may discount any such factors that participate in this common pathology. Restrictive processes beyond physical restriction from impaired diaphragmatic motion likely play a role in loss of lung function with increasing central adiposity. For example, reduced lung function is associated with diabetes mellitus and insulin resistance. Engström et al. studied the relationship between FVC at baseline and the incidence of diabetes mellitus and insulin resistance in a follow-up examination after ≈12 years. After the follow-up examination, subjects with a moderately reduced FVC had an increased risk of developing insulin resistance and diabetes mellitus. It is well known that increases in both BMI and insulin resistance lead to a higher blood pressure.

Inflammation is also associated with reduced lung function. Epidemiological studies report associations between reduced lung function and increased levels of markers of inflammation in healthy subjects. Inflammation will also affect the arterial system. We demonstrated previously in asymptomatic subjects that high-sensitivity C-reactive protein is associated with increased arterial stiffness.

Other possibilities exist related to remodeling of the airway beyond that caused by inflammatory processes in the lung. External and environmental elements together with complex genetic factors propagate inflammation. This leads to active participation of structural elements, such as the airway epithelium and smooth muscle. Inflammation can occur in both the pulmonary and general vasculature and will aggravate endothelial dysfunction. Endothelial dysfunction leads to changes in arterial function, which, in turn, leads to vascular remodeling. Giannotti et al. noted that in vivo endothelial repair capacity of early endothelial progenitor cells is reduced in patients with prehypertension and hypertension. Endothelial progenitor cell senescence and impaired endothelial function likely represent early events in the development of hypertension. In the Multi-Ethnic Study of Atherosclerosis, a population-based study of an older cohort free of overt CVD at baseline, we described that structural and functional vascular abnormalities were independent predictors of incident hypertension. These findings are important for understanding the pathogenesis of arterial hypertension. Thus, it may be that the decline in lung function and the development of essential hypertension develop in parallel along a common pathophysiological pathway involving both functional and structural changes. Of note, changes in lung function predicted incident hypertension, but changes in blood pressure did not predict loss of lung function.

Increased blood pressure variability is associated with higher cardiovascular risk, as noted also by Engström et al. There is limited information regarding the association of lung function and blood pressure variability. In a population-based study, low FVC and FEV₁ was associated with short-term systolic blood pressure variability. It is suggested that high beat-to-beat variability in blood pressure could contribute to the increased cardiovascular risk in subjects with moderately reduced FEV₁. Further studies are necessary to explore the effect of the autonomic nervous system on lung function over time and the impact on blood pressure level and its variability over time. Hypoxia as a potential trigger for the incident hypertension is improbable, because these subjects had only a small decline in lung function over time, which was within normal limits, even when the lung function from peak through year 20 was considered.

There were several limitations of this study. As in all observational studies, unmeasured and residual confounding could be a problem. Loss to follow-up by year 20 was greater in black participants and current smokers, potentially distorting any observed association. There are limitations to our estimate of peak FVC, because measurement of lung function only occurred at years 0, 2, 5, 10, and 20. It is possible that the actual peak occurred between measurement years, and a few participants peaked after year 10. These sources of within-person variation would likely be nondifferential and tend to attenuate the observed associations. Although age at achievement of peak FVC is less critical to our argument, it would be less well estimated given an FVC plateau, small variations in lung function on repeat testing, and the fact that many participants may have reached peak before the year 0 examination. The strengths of the present analysis, other than its novelty in the study design, are that large numbers of participants were included, and the study was designed for the purpose of examining the relationship between lung function and incident hypertension.
generally healthy participants consisting of both blacks and whites and women and men had repeated measurements of high-quality spirometry data and excellent retention of the original cohort. The directional specificity of the association from lung function change to incident hypertension was strengthened by a sensitivity analysis in which change in blood pressure did not predict future lung function. The ability to identify the end of lung maturation and lung function decline soon thereafter was an additional strength of the study design.

Perspectives
Early detection of hypertension is a major diagnostic step in the scope of preventing future CVD. Unfortunately, CVD preventive assessment is started after the age of 40 years. With the major health-economic burden of noncommunicable diseases, it is important to consider prevention and early detection from a broader perspective. Our findings clearly demonstrated that spirometry, an easy and inexpensive test, can facilitate the prediction of hypertension in young apparently healthy individuals when there is a slight decline to a low-normal lung function. Given the interconnectedness of the lung and cardiovascular system, future research should explore the common pathways between changes in lung function and vascular behavior to improve the health of both systems.

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Disclosures
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Rate of decline of forced vital capacity predicts future arterial hypertension: The Coronary Artery Risk Development in Young Adults (CARDIA) Study
David R. Jacobs, Jr., Hiroshi Yatsuya, Mary O. Hearst, Bharat Thyagarajan, Ravi Kalhan, Sharon Rosenberg, Lewis J. Smith, R. Graham Barr, and Daniel Duprez

Clinical implication of switching in CARDIA from a random zero mercury sphygmomanometer to an Omron HEM907XL oscillometer (Online Fitness, Santa Monica, California)

The CARDIA study used a random zero mercury sphygmomanometer at year 0, 2, 5, 7, 10, and 15 examinations. At year 20, an Omron oscillometer was used, instead. At the year 20 examination, 906 persons were measured using both devices. Based on this blood pressure device calibration study, CARDIA is able to use blood pressure values calibrated to the sphygmomanometric measures: $CS = 3.74 + 0.96*OS$ and $CD = 1.30 + 0.97*OD$ where $CS$ is calibrated systolic blood pressure, $CD$ is calibrated diastolic blood pressure, $OS$ is observed Omron systolic blood pressure and $OD$ is observed Omron diastolic blood pressure.

The clinical implication is that after calibration, there is only a small bias between the random zero sphygmomanometric measure and this model of the Omron oscillometer. We do not claim that this specific calibration applies to all Omron devices or to the sphygmomanometer without random zero.

The range in the calibration study of observed random zero (RZ) systolic blood pressure was 79 to 219 mmHg and of observed RZ diastolic blood pressure was 43 to 133 mmHg. The Omron systolic was 0.5 mmHg too low at 80 mmHg, matched the RZ at 93.5 mmHg, was about 2 mmHg high at 140 mmHg, and about 5 mmHg at 200 mmHg. The Omron diastolic matched the RZ at 41 mmHg, was 1.4 mmHg too high at 90 mmHg, and was about 3 mmHg too high at 135 mmHg. Based on these calibrations, the Omron would sometimes classify a person as having high blood pressure when they actually just missed the cutpoint. In all 3521 people with blood pressure measured at CARDIA year 20, 788 were classified as hypertensive (CS>139 or DS>89 or treated). The Omron measurement placed 111 in OS = 140 or 141 or OD = 90 or 91. Of these 47 were not misclassified because they were taking medication (31 of these would be stated to be uncontrolled). Of the remaining 64, not taking antihypertensive medication, 15 had either OS>141 or OD>91, so were correctly classified, and 49 were misclassified (but only missed the cutpoint by 1-2 mmHg). Thus the Omron measure, at face value would liberalize by up to 2
mmHg the definition of HBP, increasing the number declared hypertensive by about 1.2% of the 3521 people, from n=788 to n=837.