Original Contribution

Cardiorespiratory Fitness Is an Independent Predictor of Hypertension Incidence among Initially Normotensive Healthy Women

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The authors examined the association between cardiorespiratory fitness and incident hypertension in women who were normotensive and free of cardiovascular disease at baseline in the Aerobics Center Longitudinal Study (Dallas, Texas), 1970–1998. A total of 4,884 women performed a maximal treadmill exercise test and completed a follow-up health survey. During an average follow-up of 5 years, 157 incident cases of self-reported, physician-diagnosed hypertension were identified from the health surveys. The cumulative incidence of hypertension was 3.2%. Compared with the rates of low-fit women, crude hypertension rates were 60% and 79% lower among women in the moderate and high fitness categories, respectively ($p < 0.001$). After adjustment for several potential confounders, the odds ratios for hypertension were 1.0, 0.61 (95% confidence interval (CI): 0.30, 1.21), and 0.35 (95% CI: 0.17, 0.73) in low-, moderately, and highly fit women, respectively ($p_{trend} < 0.01$). Each 1-metabolic equivalent increment in treadmill performance was, on average, associated with a 19% (95% CI: 10, 27; $p < 0.001$) lower odds of incident hypertension. The pattern and strength of association between fitness and hypertension persisted in analyses stratified on body mass index, age, and the presence of prehypertension at baseline. An active lifestyle should be promoted for the primary prevention of hypertension in women.

cohort studies; hypertension; motor activity; physical fitness; women

Abbreviations: CI, confidence interval; MET, metabolic equivalent; PAR, population attributable risk.
major emphasis on modifying adverse lifestyle behaviors such as physical inactivity (11–13).

It is well established that physical activity is associated with lower cardiovascular morbidity and mortality (14, 15). Accumulating evidence indicates that regular moderate-to-vigorous physical activity significantly lowers resting blood pressure in normotensive and hypertensive adults (16–18). Prospective observational studies consistently show that higher levels of self-reported physical activity are associated with lower hypertension incidence in men (19–24). Data in women, however, are equivocal (21, 23–26), which may be partly explained by imprecise assessment of physical activity in women when using activity recall instruments developed and validated among men (27, 28).

Cardiorespiratory fitness, assessed with maximal exercise testing, is stronger than self-reported physical activity as a predictor of cardiovascular outcomes, most likely because fitness assessment provides a more objective and reliable index of recent activity habits than do self-reported data (29). Fitness may also be better than recalled activity as a predictor of health outcomes, because factors other than activity may influence both fitness levels and health status through shared biologic pathways (30). Few prospective studies have related a baseline fitness exposure to the development of hypertension in initially normotensive individuals (31–33). Reporting on 3,350 middle-aged Japanese men, Sawada et al. (32) observed a 90 percent higher 5-year age- and covariate-adjusted incidence of hypertension for men in the lowest compared with the highest quintile of fitness estimated from submaximal cycle ergometry. Carnethon et al. (33) reported that, after adjustment for age, sex, and other confounding factors, each 1-minute decrease in maximal treadmill performance was associated with a 19 percent higher 15-year risk of incident hypertension among men and women. An early analysis of 6,039 men and women from our cohort showed a 52 percent higher 4-year age-, sex-, and covariate-adjusted incidence of hypertension for individuals with low versus high maximal treadmill exercise tolerance (31). A relatively small number of women precluded sex-specific analysis in our previous report.

Given the recent attention to the growing health burden of hypertension (1), the recent increases in hypertension among women (2), and the current emphasis on increasing population levels of physical activity in the primary prevention of hypertension (12), we set forth to examine the association between cardiorespiratory fitness and incident hypertension in a large cohort of women who were normotensive and healthy at baseline.

MATERIALS AND METHODS

Women in the current study received a preventive medical examination at the Cooper Clinic in Dallas, Texas, during 1970–1998 and responded to at least one follow-up mail survey conducted in 1982, 1986, 1990, 1995, or 1999 as part of the Aerobics Center Longitudinal Study. Participants were excluded if at baseline they reported a personal history of hypertension (n = 666), cardiovascular disease (n = 44), diabetes (n = 89), or cancer (n = 215); had a measured resting blood pressure of ≥140 mmHg systolic or ≥90 mmHg diastolic (n = 138); had an abnormal resting or exercise electrocardiogram (n = 403); or achieved less than 85 percent of their age-predicted maximal heart rate during graded treadmill exercise testing (n = 211). These criteria resulted in 4,884 women aged 20–79 years for analysis.

Clinical examination

The baseline examination was conducted following a 12-hour fast and has been described in detail elsewhere (31, 34). Briefly, body mass index (kg/m²) was computed from measured height and weight. Waist girth (cm) was measured with the umbilicus following a normal exhalation. Resting blood pressure was auscultated as the first and fifth Korotkoff sounds according to a standard sphygmomanometer protocol (35). Serum samples were analyzed for lipids and glucose by use of automated bioassays in accord with the Centers for Disease Control and Prevention Lipid Standardization Program.

Cardiorespiratory fitness was quantified as the duration (minutes) of a maximal graded treadmill exercise test using a modified Balke protocol as previously described (31, 34). Exercise duration from this protocol correlates highly (r = 0.94) with measured maximal oxygen uptake in women (36) and explains a large proportion of the variation (R² = 0.60–0.80) in physical activity habits in our population sample (37, 38). Study participants were placed into age-specific fitness categories defined by the distribution of maximal exercise duration for all women in the Aerobics Center Longitudinal Study (31, 34) according to the following age groups: 20–39, 40–49, 50–59, and 60 or more years. The least-fit 20 percent of women in each age-specific distribution of maximal exercise duration were classified as having low fitness, the next 40 percent as having moderate fitness, and the remaining 40 percent as having high fitness. Low fitness by this definition is consistently an independent predictor of morbid and mortal events in the Aerobics Center Longitudinal Study population (39–41), and it is analogous to conventional definitions of hypertension or obesity in epidemiologic work. To standardize the estimate of cardiorespiratory fitness, we computed maximal metabolic equivalents (METs) (1 MET = 3.5 ml of oxygen uptake per kg of body mass per minute) from the final treadmill speed and grade (42). Table 1 shows the maximal exercise duration and estimated METs according to the age-specific fitness categories in women from the Aerobics Center Longitudinal Study.

Morbidity surveillance

The incidence of hypertension was ascertained from the 1982, 1986, 1990, 1995, and 1999 mail-back health surveys. A case-finding question for physician-diagnosed illness was used to identify cases of hypertension. Women were asked if a physician had ever told them they had hypertension. If yes, respondents were asked to report the year of diagnosis. For women who completed multiple surveys, the first survey in which hypertension was reported was used in analyses. This method of case ascertainment has been used in other large,
population-based epidemiologic studies of hypertension (20, 31, 43). We previously verified the accuracy of self-reported, physician-diagnosed hypertension in this cohort and observed 98 percent sensitivity and 99 percent specificity (31).

Statistical analysis

The primary exposure variable in the current study was cardiorespiratory fitness, defined categorically as low, moderate, and high. Once a case was identified, additional follow-up on subsequent surveys for this individual was not undertaken. To account for differences in survey response patterns among study participants, we created indicator variables (yes/no) for each survey period. To standardize for surveillance and period and length of follow-up, we entered these variables, as well as the year of the baseline examination, into our analyses as covariates. Cumulative incidence rates were computed by dividing the number of hypertension cases by the population at risk for the total sample and within categories of fitness. Because the data included in this analysis were from periodic surveillance with unknown or uncertain event times, logistic regression was used to compute odds ratios and 95 percent confidence intervals for incident hypertension according to categories of cardiorespiratory fitness. Adjusted models controlled for the potential confounding effects of baseline age (years), smoking (yes/no), alcohol intake (drinks/week), systolic and diastolic blood pressure (mmHg), family history of hypertension (yes/no), waist girth (cm), glucose (mg/dl), and triglycerides (mg/dl). Tests for linear trend of the fitness-hypertension association were conducted by entering the three-category fitness variable into the regression model as an ordinal term.

To examine potential modifying effects of select variables on the fitness-hypertension association, we conducted logistic regression analyses according to strata of body mass index (<25 vs. ≥25 kg/m²), age (<55 vs. ≥55 years), and baseline prehypertension (present-absent). The population attributable risk (PAR) of hypertension was estimated for fitness and selected risk factors to quantify the influence that changing these risk factors might have on hypertension incidence in our population sample. PAR was computed as $P_r(1 - 1/OR_{adj})$, where $P_r$ is the prevalence of a risk factor among hypertension cases, and $OR_{adj}$ is the multivariable adjusted odds ratio for hypertension associated with the specified risk factor (44). All $p$ values are two sided, with an alpha level of 0.05.

RESULTS

Study participants were mostly Caucasian (>95 percent) and from middle to upper socioeconomic strata. Women who developed hypertension were somewhat older and less physically fit and had a higher prevalence of being 55 or more years of age and prehypertensive at baseline than women who remained normotensive through follow-up (table 2). Significant ($p < 0.01$) Spearman correlations were observed with systolic and diastolic blood pressure, respectively, for age ($r = 0.27$ and $r = 0.24$), body mass index ($r = 0.23$ and $r = 0.21$), waist girth ($r = 0.21$ and $r = 0.19$), triglycerides ($r = 0.19$ and $r = 0.16$), glucose ($r = 0.19$ and $r = 0.16$), and maximal METs ($r = -0.18$ and $r = -0.17$). A total of 157 women reported developing hypertension during an average of 5 years’ follow-up, which resulted in a 3.2 percent cumulative incidence of hypertension. A steep inverse gradient ($p < 0.001$) was observed across the rates of hypertension and cardiorespiratory fitness (figure 1). Crude incidence rates were significantly lower among women with moderate and high fitness than among women with low fitness ($p < 0.05$ each).

Odds ratios were used to quantify the strength of association between cardiorespiratory fitness and incident hypertension (table 3). Women in the low fitness category were the referent group. Unadjusted analyses demonstrated an inverse dose-response relation ($p < 0.0001$) between fitness and hypertension. Women in the moderate and high fitness categories, respectively, had a 61 percent (95 percent confidence interval: CI: 43, 73) and 81 percent (95 percent CI: 71, 87) lower relative odds of developing hypertension when compared with their low-fit counterparts. The strength and pattern of association persisted with increasing control of potential confounding influences. In the fully adjusted model, each 1-MET increment in maximal exercise performance was, on average, associated with a 19 percent (95 percent CI: 10, 27) lower odds of incident hypertension ($p < 0.001$).

We examined the influence of fitness on hypertension incidence within strata of known hypertension antecedents (table 4). Higher levels of fitness were associated with lower incidence of hypertension in women who were normal weight ($p < 0.01$) and overweight ($p = 0.02$). When stratified according to age, an inverse gradient for incident

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TABLE 1. Age-specific cardiorespiratory fitness classifications among women, Aerobics Center Longitudinal Study, Dallas, Texas, 1970–1998

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Fitness category</th>
<th>Maximal treadmill time (minutes)*</th>
<th>Maximal METs †</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–39</td>
<td>Low</td>
<td>&lt;10.3</td>
<td>&lt;8.2</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>10.3–15.0</td>
<td>8.2–10.4</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>&gt;15.0</td>
<td>&gt;10.4</td>
</tr>
<tr>
<td>40–49</td>
<td>Low</td>
<td>&lt;8.9</td>
<td>&lt;7.6</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>8.9–11.0</td>
<td>7.6–9.4</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>&gt;11.0</td>
<td>&gt;9.4</td>
</tr>
<tr>
<td>50–59</td>
<td>Low</td>
<td>&lt;6.9</td>
<td>&lt;6.7</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>6.9–10.7</td>
<td>6.7–8.5</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>&gt;10.7</td>
<td>&gt;8.5</td>
</tr>
<tr>
<td>≥60</td>
<td>Low</td>
<td>&lt;5.5</td>
<td>&lt;5.8</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>5.5–9.0</td>
<td>5.8–7.6</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>&gt;9.0</td>
<td>&gt;7.6</td>
</tr>
</tbody>
</table>

* Modified Balke treadmill protocol: 3.3 mph (5.311 km/hour), 0% for first minute, 2% for second minute, plus 1% for each additional minute to 25%, and then plus 0.2 mph (0.3219 km/hour) for each additional minute until exhaustion. † METs, metabolic equivalents, estimated from the final treadmill speed and grade (42).
hypothesis across levels of fitness was seen in women aged less than 55 years ($p < 0.0001$). A similar pattern of association was present at baseline in 63.1 percent of women who became cases, compared with 35.8 percent ($\chi^2_{1df} = 46.3; p < 0.0001$) of women who remained hypertension free. The age-adjusted odds ratio of incident hypertension was 2.8 (95 percent CI: 1.9, 3.9) in women with prehypertension at baseline. However, an inverse association between fitness and hypertension was observed in women both with and without prehypertension at baseline ($p < 0.01$).

The relative importance of low fitness and other hypertension risk factors is shown in table 5. After adjustment for each risk factor shown in the table, low cardiorespiratory fitness was a significant predictor of incident hypertension on the same or higher order of magnitude as having prehypertension, being overweight, and being 55 or more years of age. To place the risk of hypertension for each exposure category in the context of population-disease burden, we computed PAR estimates based on the prevalence and strength of association with hypertension for each exposure. Accordingly, if all unfit women in our population sample became fit, a reduction in new-onset hypertension of 22 percent might be expected.

**DISCUSSION**

The data reported here show an inverse dose-response association between cardiorespiratory fitness and 5-year incidence of hypertension in initially normotensive and healthy middle-aged women. The association persisted after extensive adjustment for potential confounding factors and when stratified on the presence of known hypertension precursors, including baseline prehypertension. Strengths of the study are use of maximal exercise testing to quantify cardiorespiratory fitness, women free of hypertension and other forms of cardiovascular disease at baseline, and a large sample with extensive follow-up for incident cases. We believe this is the first study of cardiorespiratory fitness and hypertension in women that meets all of these criteria.

There are three principal findings from the current study. First, the inverse gradient of hypertension rates across fitness categories persisted through extensive control for confounding factors and when stratified on the presence of known hypertension precursors, including baseline prehypertension. Strengths of the study are use of maximal exercise testing to quantify cardiorespiratory fitness, women free of hypertension and other forms of cardiovascular disease at baseline, and a large sample with extensive follow-up for incident cases. We believe this is the first study of cardiorespiratory fitness and hypertension in women that meets all of these criteria.

There are three principal findings from the current study. First, the inverse gradient of hypertension rates across fitness categories persisted through extensive control for confounding factors including age, smoking status, baseline blood pressure, family history of hypertension, waist girth, and metabolic risk factors known to synergize in the development of hypertension (45, 46). The general pattern of association was for substantially lower relative odds of incident hypertension in women with moderate levels of
cardiorespiratory fitness. Adjusted odds ratios showed a 39–55 percent lower incidence of hypertension in moderately fit women compared with women in the low fitness category. Women with higher levels of fitness category had even lower relative odds of hypertension than did moderately fit participants. The observation that moderate and higher levels of cardiorespiratory fitness were associated with lower incidence of hypertension in our cohort of initially normotensive and healthy women has clinical and public health importance. The national prevalence of hypertension has risen significantly in women (2), and hypertension is a potent risk factor for new and recurrent cardiovascular disease events in women (7, 10). Experimental studies suggest that exercise training-induced reductions in blood pressure are most pronounced in individuals with established hypertension (13, 16). The prospective data reported here indicate that higher cardiorespiratory fitness may be an important homeostatic factor that contributes to the regulation and maintenance of healthy blood pressure levels. Our findings underscore the importance of promoting increases in physical activity and higher levels of fitness as a primary method of preventing hypertension in women (11–13).

TABLE 3.  Odds ratios and 95% confidence intervals for incident hypertension by level of cardiorespiratory fitness among women, Aerobics Center Longitudinal Study, Dallas, Texas, 1970–1998

<table>
<thead>
<tr>
<th>Fitness level</th>
<th>Low (n = 609)</th>
<th>Moderate (n = 1,795)</th>
<th>High (n = 2,480)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Multivariable†</td>
<td>Multivariable‡</td>
</tr>
<tr>
<td></td>
<td>Odds ratio</td>
<td>95% confidence interval</td>
<td>Odds ratio</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.39, 0.57</td>
<td>0.19, 0.29*</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.45, 0.68</td>
<td>0.27, 0.43*</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.47, 0.72</td>
<td>0.31, 0.50*</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.61, 1.21</td>
<td>0.35, 0.73**</td>
</tr>
</tbody>
</table>

* \( p_{\text{trend}} < 0.0001; \)** \( p_{\text{trend}} < 0.01. 
† Adjusted for age, examination year, and survey response pattern.
‡ Adjusted for the above variables and smoking, alcohol intake, systolic and diastolic blood pressure, and family history of hypertension.
§ Adjusted for the above variables and waist girth, glucose, and triglyceride concentration. Note: the results of the third multivariable model were materially unchanged when body mass index was substituted for waist girth.

TABLE 4.  Odds ratios and 95% confidence intervals for incident hypertension according to body mass index level, age, and prehypertension status by cardiorespiratory fitness level among women, Aerobics Center Longitudinal Study, Dallas, Texas, 1970–1998

<table>
<thead>
<tr>
<th>Fitness level</th>
<th>Low (n = 609)</th>
<th>Moderate (n = 1,795)</th>
<th>High (n = 2,480)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body mass index (kg/m²)†</td>
<td>Odds ratio</td>
<td>95% confidence interval</td>
</tr>
<tr>
<td></td>
<td>&lt;25</td>
<td>1.0</td>
<td>0.59, 1.05</td>
</tr>
<tr>
<td></td>
<td>≥25</td>
<td>1.0</td>
<td>0.41, 0.79</td>
</tr>
<tr>
<td></td>
<td>Age (years)‡</td>
<td>&lt;55</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>≥55</td>
<td>1.0</td>
<td>0.46, 1.2</td>
</tr>
<tr>
<td></td>
<td>Prehypertension§</td>
<td>Present</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Absent</td>
<td>1.0</td>
</tr>
</tbody>
</table>

* \( p_{\text{trend}} = 0.004; \)** \( p_{\text{trend}} = 0.02; \)** \( p_{\text{trend}} < 0.01; \)** \( p_{\text{trend}} = 0.22. 
† Adjusted for age, examination year, survey response pattern, current smoking, family history of hypertension, and baseline blood pressure.
‡ Adjusted for examination year, survey response pattern, current smoking, family history of hypertension, body mass index, and baseline blood pressure.
§ Adjusted for age, examination year, survey response pattern, current smoking, family history of hypertension, and body mass index.
A second major observation from our analyses was the consistent inverse gradient between hypertension and cardiorespiratory fitness within various strata of other hypertension predictors (table 4). Body mass index is a predictor of hypertension in women (23, 25, 26, 31, 43, 45). Whether classified as normal weight or overweight on the basis of their body mass index, women with moderate and high cardiorespiratory fitness in our study had relative odds of hypertension 41–61 percent lower compared with their low-fit peers. Our finding is similar to the pattern of association between recalled physical activity and incident hypertension reported across the strata of body mass index in a cohort of Finnish women (23) and previously reported in men (19, 20, 23). Body fat per se may not be the principal vector of hypertension risk; rather, overweight in the presence of physical inactivity and low fitness may represent the high-risk phenotype. Although overweight and obesity are significant population health concerns associated with hypertension (47), the results from our study and those reported by others (19, 20, 23) emphasize the importance of physical activity and fitness in preventing hypertension among individuals with normal weight as well as individuals who are overweight or mildly obese. Additional studies in more diverse population samples of women and men with objective measures of physical activity, fitness, and body fat are needed to better understand this complex issue.

Data from the Framingham Heart Study indicate that women who are normotensive at age 55 years have greater than a 90 percent risk of developing hypertension during their remaining years of life (3). The older segment of the US population is rapidly increasing (48). It is, therefore, conceivable that most adults living beyond their sixth decade would require pharmacotherapy for hypertension, which is costly and potentially hazardous (1). Our analyses show a significant inverse association between fitness and hypertension incidence in women aged less than 55 years and a similar, albeit nonsignificant ($p = 0.22$), pattern of association in women aged 55 or more years, which may be attributed to the small number of cases ($n = 9$) in the high-fitness category. It appears as though moderate and higher levels of fitness may prevent the development of hypertension in young and older women alike.

It has become apparent that even high normal blood pressure increases the risk of developing hypertension (8) and cardiovascular events (5). Accordingly, national blood pressure guidelines now include prehypertension (systolic blood pressure of 120–139 mmHg or diastolic blood pressure of 80–89 mmHg) as the first category of abnormal blood pressure to be targeted with therapeutic intervention (1). Prehypertension was present at baseline in 63 percent of women who became hypertensive during follow-up. The relative odds of developing hypertension were threefold higher in women with prehypertension at baseline. However, even in women with prehypertension at baseline, the incidence of hypertension was 29 percent and 58 percent lower among moderately and highly fit women, respectively, compared with low-fit women. Current guidelines recommend intensive lifestyle modifications, including increased physical activity, as the primary therapy for prehypertension (1, 12). Our prospective data indicate that higher levels of fitness confer substantial protection against clinically manifest hypertension in women who are at risk because of the presence of prehypertension.

The third major finding from our study was the substantial strength and independence of low cardiorespiratory fitness as a predictor of incident hypertension (table 5). The 2.3-fold increase in the multivariable odds of incident hypertension associated with low fitness was slightly lower than that observed for prehypertension and higher than the adjusted odds ratios associated with a body mass index of greater than 25, age of 55 or more years, family history of hypertension, current smoking, and high levels of metabolic antecedents (45, 46) for hypertension. After extensive adjustment for potential confounders, the strength of association between

### Table 5. Odds ratios and population attributable risk of incident hypertension for low cardiorespiratory fitness and selected hypertension risk factors among women, Aerobics Center Longitudinal Study, Dallas, Texas, 1970–1998

<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>Population attributable risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted†</td>
<td></td>
</tr>
<tr>
<td>Low fitness</td>
<td>15.5</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td>Family history of hypertension</td>
<td>44.2</td>
<td>1.3</td>
<td>1.4</td>
</tr>
<tr>
<td>Current smoker</td>
<td>9.5</td>
<td>1.2</td>
<td>0.95</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>36.7</td>
<td>3.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Body mass index $\geq 25$ kg/m²</td>
<td>16.7</td>
<td>3.1</td>
<td>1.8</td>
</tr>
<tr>
<td>Glucose $\geq 110$ mg/dl</td>
<td>4.3</td>
<td>2.1</td>
<td>0.95</td>
</tr>
<tr>
<td>Triglyceride $\geq 150$ mg/dl</td>
<td>7.5</td>
<td>2.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Age $\geq 55$ years</td>
<td>14.1</td>
<td>2.2</td>
<td>1.9</td>
</tr>
</tbody>
</table>

* Prevalence among the entire population sample.
† Adjusted for examination year, survey response pattern, and the other variables in the table.
‡ Computed as $P_c(1 - 1/OR_{adj})$, where $P_c$ is the prevalence among hypertension cases, and $OR_{adj}$ is the multivariable adjusted odds ratio (44). P_c (ordered as listed in the table) was 39.5, 49.7, 10.8, 63.1, 36.9, 6.1, 7.1, and 26.1.
low fitness and incident hypertension in our cohort of women was higher than reported among Japanese men (relative risk \( \approx 1.8 \)) (32), higher than the sex- and covariate-adjusted association previously reported in our cohort of healthy women and men (relative risk \( \approx 1.5 \)) (31), and similar to the sex- and covariate-adjusted association (hazard ratio \( \approx 2.4–3.0 \)) reported in men and women from the Coronary Artery Risk Development in Young Adults Study (33). Clearly, low levels of cardiorespiratory fitness should be seen as a potent risk factor for hypertension development. Increasing population levels of fitness through greater physical activity should be a cornerstone element in the primary prevention of hypertension.

We computed PAR values to estimate the burden of hypertension attributable to low fitness and other risk predictors. We observed that 22 percent of incident hypertension cases might be averted or delayed if all unfit women in our population sample became fit. Our PAR for low fitness and hypertension is consistent with the 21 percent recently reported for men and women combined in the Coronary Artery Risk Development in Young Adults Study (33). In our study, the PAR associated with low fitness was second in magnitude only to prehypertension (PAR = 39 percent); however, our data also indicate that moderate and higher levels of fitness protect against hypertension development even in women with prehypertension. Experimental evidence indicates that most women can achieve moderate levels of cardiorespiratory fitness (e.g., 6–9 METs) through regular participation in moderate intensity activities like brisk walking or bicycling (49, 50). Although genetic susceptibility is an important contributor, other mechanisms underlie hypertension such as architectural changes in the vascular wall, altered endothelial cell function, increased activity of the sympathetic nervous system, hyperinsulinemia, hypertriglyceridemia, and increased sodium retention (51), each of which may be favorably modified by regular physical activity (13). Unlike antihypertensive drugs, which are costly, largely limited to blood pressure control, and often have adverse effects, physical activity is a relatively safe and inexpensive therapy with favorable effects on a broad spectrum of cardiovascular disease antecedents and outcomes, including hypertension (15).

Similar to other large, prospective, epidemiologic studies, the Aerobics Center Longitudinal Study has limitations that should be considered. The external validity of our findings is specific to women with demographics similar to those enrolled in the Aerobics Center Longitudinal Study. The homogeneity of our cohort enhances the internal validity of our findings because it lowers the likelihood of confounding by these characteristics. Further, our study participants are very similar on key clinical variables such as lipids, glucose, and blood pressure to participants in other large epidemiologic studies in the United States (34, 43). While we urge caution against overgeneralizing the results reported herein, we are not aware of published data suggesting that the health benefits of enhanced fitness would be any less among women of other races/ethnicities or socioeconomic disposition.

Lack of sufficient data on nutrient intake, menopausal status, and medication use precluded examination of their influences on the association between fitness and hypertension risk in our population sample of women. However, because the women included in this report were relatively young and apparently healthy at baseline, it is not likely that menopausal issues or medication use explained a large proportion of the observed associations reported herein. Nonetheless, these issues should be addressed in future prospective analyses on fitness and hypertension risk.

Although cardiorespiratory fitness was predicted from maximal exercise test performance rather than measured with indirect calorimetry, correlations between predicted and measured fitness levels in women are large \((r = 0.94)\) (36). Recent evidence of only a modest genetic contribution (25–45 percent) to cardiorespiratory fitness (52), a high correlation \((r = 0.70–0.90)\) between cardiorespiratory fitness and detailed records of usual physical activity habits (37, 38), reported training gains of up to 30 percent (42), and rapid detraining-related losses (53) illustrate the plasticity of cardiorespiratory fitness and should temper arguments of genetic transmission as its principal determinant.

The presence of subclinical disease at baseline could have affected treadmill performance or increased the incidence of hypertension during follow-up. We attempted to account for this by excluding women with abnormal resting or exercise electrocardiograms, women who did not achieve at least 85 percent of the age-predicted maximal heart rate during the treadmill exercise test, and women with known or suspected cardiovascular disease and cancer at baseline. Baseline risk factor profiles (table 2) were similar between women who remained hypertension free and women who developed hypertension in follow up. This adds confidence to our assertion that undetected subclinical disease is not the underlying difference in hypertension incidence between fit and unfit women. The independent dose-response gradient between fitness and hypertension also supports a causal inference.

In conclusion, our prospective findings in a large cohort of initially normotensive and healthy middle-aged women show that cardiorespiratory fitness is an independent predictor of incident hypertension in women. Even small reductions in blood pressure associated with modest increases in physical activity and fitness may have a substantial public health impact on hypertension prevalence and related health sequelae. We believe physicians should counsel sedentary patients to become physically active and to improve their cardiorespiratory fitness for the primary prevention of hypertension.

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