Cardiorespiratory fitness reduces the risk of incident hypertension associated with a parental history of hypertension.

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CARDIORESPIRATORY FITNESS REDUCES THE RISK OF INCIDENT HYPERTENSION ASSOCIATED WITH A PARENTAL HISTORY OF HYPERTENSION

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Abstract

Family history of hypertension increases the risk of an individual to develop hypertension, while moderate to high cardiorespiratory fitness has the opposite effect. However, the joint association of each on the development of hypertension is not well understood. We studied fitness and incident hypertension in 6,278 participants who were given a preventative medical examination. Thirty-three percent reported a parent with hypertension and there were 1,545 cases of incident hypertension after a mean of 4.7 years. The presence of parental hypertension was associated with a 28% higher risk of developing hypertension after adjustments for age, gender, and examination year. After further adjustments for smoking, alcohol intake, resting systolic and diastolic blood pressure, hypercholesterolemia, body mass index, physical inactivity, and fitness there was a 20% higher risk associated with parental hypertension. After adjusting for age, gender, and examination year, both moderate and high levels of fitness were associated with lower risk for developing hypertension by 26% and 42%, respectively. In the joint analysis, individuals with both a low level of fitness and a parent with hypertension exhibited a 70% higher risk for developing hypertension compared with high fit individuals with no parental history (p=0.004). However, individuals with a high level of fitness and a parent with hypertension only experienced a 16% higher risk of developing hypertension compared to fit individuals with no parental history (p=0.03). The significantly lower risk of developing hypertension when progressing from low to high fit groups among those with a parental history of hypertension has important clinical implications.

Key words: Exercise, fitness, blood pressure, hypertension, family history, risk factors
**Introduction**

It is well established that regular physical activity and being moderately fit are associated with a reduced risk of developing hypertension.\cite{1,2,3} Indeed, the National High Blood Pressure Education Program lists ‘Engaging in moderate physical activity’ as one of six effective strategies for the primary prevention of hypertension.\cite{4} Over 40 years ago, Paffenbarger et al. reported parental hypertension to be the strongest sociofamilial influence in the development of hypertension in the College Alumni Health Study.\cite{5} Subsequent work has supported this and it is estimated a parental history accounts for 35-65% of the variability in blood pressure among offspring,\cite{6,7,8} with varying levels of risk based on which parent developed hypertension\cite{9,10} and the age of that onset.\cite{9,10}

Despite the protective benefits of high levels of cardiorespiratory fitness (CRF) and the elevated risk associated with a history of parental hypertension, the joint association of each on the development of hypertension is not well understood. Identifying modifiable risk factors such as CRF could help clinicians promote preventative strategies that may offset non-modifiable risk factors such as familial history. The present study examines the independent and combined effects of fitness and parental history of hypertension in men and women in the development of hypertension.

**Methods**

*Study population.* The Aerobics Center Longitudinal Study (ACLS) is an ongoing cohort study that investigates the relationship of cardiorespiratory fitness, physical activity, and other factors to chronic diseases.\cite{11} Data were obtained from patients of the Cooper Clinic in Dallas, Texas. Many participants were sent by their employers for the examination, some were referred
by their personal physicians, whereas others were self-referred. The present study consists of 6,278 men and women aged 20–80 years who completed a baseline examination at the Cooper Clinic during 1988–2005. The sample was predominantly Caucasian, well-educated and from the middle and upper socioeconomic strata. At baseline, all participants included in the analysis were free of known cardiovascular disease, cancer, abnormal resting or exercise electrocardiogram, diabetes, and were able to achieve an exercise test to at least 85% of their age-predicted maximal heart rate \((220 – \text{age})\). They also reported no diagnosis of hypertension by a physician and had resting blood pressure of <140/90 mmHg at baseline. The study protocol was approved annually by the institutional review board of the Cooper Institute.

_Baseline examination._ The baseline clinical examination was administered after receiving written informed consent from each participant for both the baseline examination and follow-up assessments. Baseline measures included resting blood pressure, fasting blood chemistry analyses, personal and family health history, anthropometry, and electrocardiogram. The baseline examination has been previously described in detail elsewhere.\(^2\) \(^{11}\) \(^{12}\) Resting blood pressure was measured by trained technicians using auscultatory methods in the seated position, and was recorded as the first and fifth Korotkoff sounds after at least 5 min of sitting quietly using mercury sphygmomanometers. Two readings separated by 1 min were averaged. If the first two readings differed by >5 mm Hg, additional readings were obtained and averaged. Serum samples were analyzed for glucose and total cholesterol using standardized automated bioassays. Diabetes mellitus was defined as fasting plasma glucose concentration of 126 mg/dl or greater, a history of physician diagnosis, or insulin use. Hypercholesterolemia was defined as total cholesterol of 240 mg/dl or greater or a history of physician diagnosis.\(^{13}\) Height and weight were
measured and BMI was calculated as weight in kilograms divided by height in meters squared. Information on parental history of hypertension, smoking habits (never, former, or current smoker), alcohol intake (drinks per week), and physical activity habits (physically inactive or not) were obtained from a standardized questionnaire. Consuming >14 drinks/wk for men and 7 drinks/wk for women was defined as heavy alcohol drinking. Physically inactive was defined as reporting no leisure-time physical activity in the three months before the examination. Participants were asked to select from a list of existing parental health problems.

CRF was quantified as the total time of a symptom limited maximal treadmill exercise test, using a modified Balke protocol. Total treadmill endurance time of the test on this protocol correlates highly with measured maximal oxygen uptake (VO2max) in both men ($r=0.92$) and women ($r=0.94$). We have defined low, moderate, and high CRF exposures according to the lowest 20%, the next 40%, and the upper 40%, respectively, of the age- and sex-specific distribution of maximal exercise duration in the overall ACLS population. We use this approach because a widely accepted clinical categorization of CRF does not exist and this cut point has been used as a standardized fitness classification method, which has shown low fitness to be an independent risk factor of morbidity and mortality. Because unhealthy individuals who had a history of hypertension, diabetes, heart attack, stroke, or cancer or an abnormal electrocardiogram at baseline were excluded, the number of participants in this study classified as having a low fitness level was <20%, compared with the entire ACLS cohort.

Ascertainment of hypertension. Hypertension was ascertained by presence of resting blood pressure criteria of the National High Blood Pressure Education Program: a self-report
history of physician diagnosis or a measured resting systolic or diastolic blood pressure of ≥140 or ≥90 mm Hg, respectively, at a follow-up clinic evaluation. Participants with hypertension at baseline by any of these criteria were excluded from the current study. This method of case ascertainment is similar to those used in other well-known epidemiological studies on hypertension.19-21

Statistical analysis. Descriptive statistics were calculated for each variable using Chi-square tests, or t-tests. The primary exposure variable was parental hypertension and CRF defined categorically as low, moderate, and high as described above. Follow-up time was computed as the difference between the date of the baseline examination and the date of first hypertension event, or the last clinic visit through the end of 2005. Cox proportional hazards regression analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of hypertension events according to exposure categories. To test effect modification by gender on the associations between parental hypertension or CRF and incident hypertension, we compared risk estimates in the gender-stratified analyses and checked interaction terms in the Cox regressions. There were similar trends in developing hypertension between men and women, and no significant interactions were observed. Thus, we presented the results of pooled analyses. Inspection of empirical cumulative hazards plots (log–log [survival function] vs. log [time] across number of health-risk factors) indicated that the proportional hazards assumption was justified. All statistical analyses were performed by Statistical Analysis Systems Software (SAS Institute, Cary, NC) and all P values are two-sided, with an α-level of 0.05.

Results
There were 1,545 cases of incident hypertension among 6,278 participants after a mean of 4.7 follow-up years, with 33% of the sample reporting a parent with hypertension. The baseline characteristics of the study population are presented in Table 1. Study participants were middle-aged (44.7±8.7 years), mostly male (76.1%), slightly overweight (BMI 25.2±3.3 kg/m²), predominantly active (79.2%), and non-smokers (88.3%). Participants with parental hypertension were younger, had lower total cholesterol, had higher resting blood pressure, and shorter maximal treadmill duration.

Table 2 shows the individual associations between parental hypertension or CRF and incident hypertension. This relationship was explored using three different models: after adjusting for age, gender, and examination year (model 1), further adjusting for smoking status, alcohol intake, resting blood pressure, presence of hypercholesterolemia, BMI, and physical inactivity (model 2), and further adjusting for each of the other variables in the table (model 3). The presence of parental hypertension was associated with significantly higher the risk of developing hypertension in each model, with 28% higher in the initial model and 20% in the full model. After adjusting for age, gender, and examination year, both moderate and high levels of CRF were associated with lower risk for developing hypertension by 26% and 43%, respectively. The risk reduction for moderate levels of CRF was not maintained after further adjustment for variables in model 2 and 3 (p=0.15 and p=0.16, respectively). However, the high level of CRF remained significantly protective for the development of hypertension after adjustments for variables in both models 2 and 3 (HR=0.75 [0.58, 0.96] for each model).
Figure 1 displays the joint association between parental hypertension, CRF, and incident hypertension after adjustment for the same covariables in the independent association analyses. Individuals who were in the lowest fitness category and had a parent with hypertension exhibited a 70% higher risk for developing hypertension compared to individuals in the highest fitness category with no parental history of hypertension (p=0.0041). However, individuals who had a parent with hypertension and a high level of CRF only experienced a 16% increased risk of developing hypertension compared to fit individuals with no parental history of hypertension (p=0.03). In an additional analysis among only those individuals with parental history of hypertension, moderately and highly fit individuals had 21% (HR=0.79 [0.54-1.15]) and 34% (HR=0.66 [0.45-0.97]) lower risks of developing hypertension, respectively, compared to low fit individuals.

Discussion

In this sample of middle-aged men and women, we found both parental hypertension and CRF were independently associated with the development of hypertension. The primary finding from this study is the risk for developing hypertension among individuals with a parental history of hypertension is lower for those who are fit compared to those who are not. While the protective influence of CRF on the development of hypertension has been previously shown, to our knowledge this is the first examination of this joint association among individuals with a parental history of hypertension. Previous research has estimated the increase in risk of developing hypertension among those whose parents also had hypertension to be 1.3-2.4.9, 10, 22-24 In our fully adjusted model, the risk for developing high blood pressure if their parent had hypertension was 34% lower among highly fit individuals compared to low fit individuals. By
identifying the role of modifiable risk factors such as CRF on the development of hypertension, clinicians may promote preventative strategies such as regular physical activity to offset non-modifiable risk factors such as family history.

Physical activity has been previously shown to lower blood pressure in normotensive and hypertensive adults, and higher levels of CRF are associated with lower risk of developing hypertension. Despite this association, CRF has rarely been examined in previous research on the risk of hypertension associated with parental hypertension. While most studies on parental hypertension fail to adjust for physical activity levels, those that do have relied on self-report measures, which are subject to misclassification. To our knowledge, this is the first study to include objectively assessed CRF on the risk of hypertension associated with parental hypertension.

Individuals in our cohort reporting a parent with hypertension had a 20% higher risk of developing hypertension themselves compared to those without a history of parental hypertension. This value is similar to or slightly lower than those reported elsewhere, though the reporting methods of identifying parental hypertension, type of study design, and socioeconomic characteristics of the sample likely explains a portion of any difference. The predictive strength of family history on offspring hypertension varies with the type of family history that is present. In the Johns Hopkins Precursor Study, level of risk varied by parent (mother only, HR=1.5; father only, HR=1.8; both, HR=2.4) and age of onset (one parent, late onset, HR=1.5; both parents, early onset, HR=6.2). Our study only reports if a parent has hypertension, resulting in the inability to categorize risk to the level reported elsewhere. Additionally, the ACLS population in this study is comprised of those who are relatively fit and
physically active. As we have shown, a high level of fitness reduces the risk of developing hypertension after adjusting for a family history of hypertension (HR=0.75, Table 2), which may explain lower hypertension rates compared to other studies.

The significantly lower risk of developing hypertension in highly fit individuals compared to low fit individuals with a parental history of hypertension is worth further discussion and has important clinical ramifications. Previous analysis on the ACLS population found walking an average of 130 minutes/week for men and 150 minutes/week for women was associated with a moderate level of fitness (representing the 21-60 percentile of the overall ACLS population). This attainable level of physical activity closely resembles the 2008 Physical Activity Guidelines for Americans of 150 minutes/week and the recommendations from the National High Blood Pressure Education Program for the primary prevention of hypertension.

Strengths of the study include the valid and diverse measurements of exposure and outcome variables. CRF and BMI were objectively measured during the medical examinations at baseline. In many previous studies, the effect of family history on incident hypertension has been determined without inclusion of physical activity or CRF in the analytic models, or with self-reported physical activity that has limitations not found with objectively measured CRF. This study also benefits from a large sample size with high internal validity and an extended follow-up period.

The current study has limitations that deserve mention. The majority of participants were well educated white men, of middle to upper class socioeconomic status, relatively fit and physically active, which limits the generalizability of the findings. Family history of
hypertension was assessed through self-report, which may be subject to recall bias. We only measured baseline levels of CRF and family history, and these may have changed during follow-up. However, the mean age of the sample makes a change in family history highly unlikely, as most of the participant's parents would have been at an age where chronic diseases were already present and diagnosed.

**Perspectives**

The present study demonstrates that high levels of CRF are associated with a lower risk of developing hypertension among a large cohort of men and women with a parental history of hypertension. Individuals in our sample population who had a parent with hypertension yet were high fit were at a 34% lower risk of becoming hypertensive themselves compared to low fit individuals with the same parental history. Our findings support current recommendations to engage in moderate levels of physical activity to prevent the development of hypertension, particularly among individuals at an elevated risk for the disease due to parental history of hypertension.
Acknowledgments

We thank the Cooper Clinic physicians and technicians for collecting the baseline data and staff at the Cooper Institute for data entry and data management.

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Disclosures

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References


Figure 1. Hazard ratios of incident hypertension associated with parental hypertension and cardiorespiratory fitness.

Adjusted for age, gender, examination year, smoking status (never, past, current), alcohol intake (heavy drinking, yes or no), resting systolic and diastolic blood pressure, hypercholesterolemia (present or not), BMI, and physical inactivity (yes or no). *p<0.03
Novelty and Significance

What is new?

- This is the first attempt to explore the relationship between cardiorespiratory fitness and family history of hypertension on incident hypertension.

What is relevant?

- It is clinically relevant to understand the relationship between a non-modifiable risk factor such as family history and a modifiable risk factor such as cardiorespiratory fitness on incident hypertension.

Summary

- The primary finding from this study is the risk for developing hypertension among individuals with a parental history of hypertension is lower for those who are fit compared to those who are not.
### Table 1. Baseline characteristics according to sex and parental hypertension category, ACLS database, 1988-2005

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Sex</th>
<th>Parental Hypertension</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (n=6278)</td>
<td>Males (n=4781)</td>
<td>Females (n=1497)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>23.9</td>
<td>29.6</td>
<td>21.0</td>
</tr>
<tr>
<td>Age (years)</td>
<td>44.7±8.7</td>
<td>44.7±8.6</td>
<td>44.5±9.0</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.2±3.3</td>
<td>26.0±2.9</td>
<td>22.8±3.3</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>200.4±37.4</td>
<td>202.5±37.6</td>
<td>193.5±35.8</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>25.7</td>
<td>27.7</td>
<td>19.4</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>96.0±8.4</td>
<td>97.3±8.2</td>
<td>92.0±7.6</td>
</tr>
<tr>
<td>Resting blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>115.1±10.0</td>
<td>116.9±9.0</td>
<td>109.4±10.9</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>76.9±7.1</td>
<td>78.0±6.5</td>
<td>73.7±7.7</td>
</tr>
<tr>
<td>Maximal treadmill time (min)</td>
<td>18.8±4.8</td>
<td>19.9±4.4</td>
<td>15.2±4.2</td>
</tr>
<tr>
<td>Cardiorespiratory fitness (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.3622</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.3</td>
<td>4.5</td>
<td>3.7</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>29.6</td>
<td>31.2</td>
<td>24.5</td>
</tr>
<tr>
<td>High</td>
<td>66.1</td>
<td>64.3</td>
<td>71.9</td>
</tr>
<tr>
<td>Physically inactive (%)&lt;sup&gt;*&lt;/sup&gt;</td>
<td>20.8</td>
<td>21.2</td>
<td>19.6</td>
</tr>
<tr>
<td>Smoking status (%)&lt;sup&gt;&lt;/sup&gt;</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>64.4</td>
<td>62.7</td>
<td>69.8</td>
</tr>
<tr>
<td>Former</td>
<td>23.9</td>
<td>23.8</td>
<td>24.5</td>
</tr>
<tr>
<td>Current</td>
<td>11.6</td>
<td>13.5</td>
<td>5.7</td>
</tr>
<tr>
<td>Heavy alcohol drinking (%)&lt;sup&gt;†&lt;/sup&gt;</td>
<td>11.1</td>
<td>9.2</td>
<td>17.2</td>
</tr>
</tbody>
</table>

<sup>*</sup>Participants reporting no leisure-time physical activity in the 3 months before the examination.  
<sup>†</sup>Consuming >14 drinks/wk for men, >7 drinks/wk for women, as defined by the National Institute on Alcohol Abuse and Alcoholism.
Table 2. Hazard ratios of incident hypertension by parental hypertension and cardiorespiratory fitness

<table>
<thead>
<tr>
<th>Category</th>
<th>Number at risk</th>
<th>Number of cases</th>
<th>Model 1*</th>
<th>Model 2†</th>
<th>Model 3‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Parental hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4194</td>
<td>995</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Yes</td>
<td>2084</td>
<td>550</td>
<td>1.28 (1.15, 1.42)</td>
<td>1.19 (1.08, 1.33)</td>
<td>1.20 (1.08, 1.33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.42</td>
<td>1.33</td>
<td>1.33</td>
</tr>
<tr>
<td>Cardiorespiratory fitness§</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>268</td>
<td>77</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Moderate</td>
<td>1858</td>
<td>481</td>
<td>0.74 (0.58, 0.94)</td>
<td>0.84 (0.66, 1.07)</td>
<td>0.84 (0.66, 1.07)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.94</td>
<td>1.07</td>
<td>1.07</td>
</tr>
<tr>
<td>High</td>
<td>4152</td>
<td>987</td>
<td>0.58 (0.46, 0.73)</td>
<td>0.75 (0.58, 0.96)</td>
<td>0.75 (0.58, 0.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.73</td>
<td>0.96</td>
<td>0.96</td>
</tr>
</tbody>
</table>

HR, hazard ratio; CI, confidence interval.

*Adjusted for age (single year), gender, and examination year. †Adjusted for variables in model 1 plus smoking status (never, former, current), alcohol intake (heavy drinking, yes or no), resting systolic and diastolic blood pressure, hypercholesterolemia (present or not), BMI, and physical inactivity (yes or no). ‡Adjusted for variables in model 2 plus each of the other variables
in the table. Participants were categorized into three groups based on age- and sex-specific quintiles of maximal treadmill time in the overall ACLS population: low as the lowest 20%, moderate as the middle 40%, and high as the upper 40%.
Parental HTN Hazard Ratio

- REF: 1.0
- Yes: 1.16*, 1.36*
- Yes: 1.7*

High Fitness
Moderate Fitness
Low Fitness

Hazard Ratio

No: 1.1
Yes: 1.26
Yes: 1.7

Parental HTN