The Cardiovascular Impact of Household Air Pollution in Semi-Urban and Rural Communities in Puno, Peru
by
Melissa Burroughs Peña

Duke Global Health Institute
Duke University

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Thesis submitted in partial fulfillment of
the requirements for the degree of
Master of Science in the Duke Global Health Institute
in the Graduate School of Duke University

2015
ABSTRACT

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Abstract

Background: The Global Burden of Disease Study estimated the global cardiovascular disease burden attributed to household air pollution from biomass fuel combustion based on data from ambient air pollution exposure. The effect of biomass fuel use on cardiac geometry and function has not been well described. Our objective was to determine the association between air pollution from biomass fuel use with cardiac structure and function by transthoracic echocardiography.

Methods: We identified a random sample of residents living in the high-altitude region of Puno, Peru. Daily biomass fuel use was self-reported in a questionnaire. Each participant underwent transthoracic echocardiography. Multivariable linear regression analyses were used to examine the relationship between biomass fuel use with each echocardiographic variable, adjusting for age, sex, height, body mass index, diabetes, physical activity, and tobacco use.

Results: 187 participants were included in this analysis; 80 biomass fuel users and 107 nonusers. Fifty-eight percent of the participants were women. After adjusting for multiple variables, daily exposure to biomass fuel smoke was associated with increased left ventricular internal diastolic diameter, left atrial diameter, left atrial area (4-chamber and 2-chamber), septal E’, and lateral E’. There was no relationship between biomass fuel use with left ventricular systolic function or right ventricular size or function.
Conclusion: Daily biomass fuel use was associated with increased left ventricular and left atrial size in a population-based sample of individuals living at high-altitude in Puno, Peru. This difference in cardiac structure potentially increases the risk for multiple adverse cardiovascular outcomes in biomass fuel users. Additional studies are needed to better describe the relationship between household air pollution from biomass fuel use and cardiovascular outcomes.
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1. Introduction

Paradoxically, while high-income countries have a greater prevalence of cardiovascular risk factors, low- and middle-income have a higher rate of major cardiovascular events, including cardiovascular-related death, myocardial infarction and stroke. Additionally, within middle-income countries a similar paradox exists between rural and urban dwellers in which rural residents have fewer cardiovascular risk factors but a higher major cardiovascular event rate. While differential access to medical care and pharmacological therapy for risk factor control likely contribute to the disproportionate burden of cardiovascular events in rural communities in middle-income countries, many policymakers including the World Health Organization have advocated for improved public health interventions to decrease cardiovascular risk.

Intervenable elements of the built environment that increase cardiovascular risk, such as air pollution, provide an opportunity for cardiovascular risk reduction at the population level.

Fossil fuel combustion from vehicular emissions and industrial sources releases gases and particular matter of varying sizes, which become suspended in the air and cause ambient air pollution. Exposure to the individual components of ambient air pollution, including fine particulate matter and NO₂, has been associated with atherosclerosis, left ventricular hypertrophy, myocardial infarction, cerebrovascular events, heart failure hospitalization, atrial fibrillation, sudden cardiac death and
cardiovascular mortality.\textsuperscript{3-16} Systemic inflammation, endothelial dysfunction, increased platelet aggregation, upregulation of coagulation factors, increased vascular tone and autonomic dysfunction are potential mechanisms that link air pollution exposure to cardiovascular disease.\textsuperscript{17-22} However, the data supporting the association between exposure to household air pollution and cardiovascular disease outcomes are fewer and less robust. In contrast to ambient air pollution, household air pollution is largely derived from biomass fuel combustion in which wood, animal dung and other organic debris are burned for cooking and heating. Household air pollution exposure from biomass fuel use is associated with increased systolic and diastolic blood pressure, hypertension prevalence, pro-inflammatory and pro-thrombotic biomarkers, increased carotid intimal-medial thickness and ST changes on electrocardiogram.\textsuperscript{23-28} However, in a large cohort study in Bangladesh, there was no association between household air pollution from biomass fuel use and cardiovascular-related mortality after 10 years of follow-up.\textsuperscript{29}

Despite the lack of evidence that links household air pollution exposure to cardiovascular outcomes, the Global Burden of Disease Study estimated the cardiovascular and cerebrovascular impact of household air pollution exposure and determined that household air pollution is the third greatest risk factor for death worldwide.\textsuperscript{30} However, the global cardiovascular impact of household air pollution exposure was based on the estimated concentration of fine particulate matter (PM$_{2.5}$)
released in biomass fuel combustion and data from ambient air pollution studies on the cardiovascular risk associated with PM$_{2.5}$ exposure. The analysis of the Global Burden of Disease Study did not take into consideration the inherent differences in smoke from biomass fuel combustion in comparison to pollutants released from fossil fuel combustion, including the chemical composition of the particulate matter and differences in the relative concentrations of noxious gases, including NO$_2$, CO, SO$_2$, all of which can affect cardiovascular outcomes differently. Therefore, the association between household air pollution and cardiovascular disease and the magnitude of the public health impact has yet to be determined.

In the absence of large-scale, prospective studies on the effect of household air pollution exposure from biomass fuel use on cardiovascular disease outcomes and mortality, it is possible to detect subclinical alterations in cardiac function in order to determine the ways in which household air pollution exposure could lead to adverse cardiovascular outcomes. Similar to prior studies of the association between biomass fuel use and subclinical atherosclerosis, it is possible to evaluate alterations in cardiac function and geometry by transthoracic echocardiography in order to examine the relationship between biomass fuel use and cardiovascular disease. A greater description of the physiologic changes associated with household air pollution exposure not only has the potential to further the understanding of the negative cardiovascular impact of
household air pollution exposure, but also reveal the mechanisms by which adverse cardiovascular outcomes might occur.

The objective of this study is to determine the association between exposure to smoke from daily biomass fuel use and cardiac structure and function measured by transthoracic echocardiography in population-based cohort in Puno, Peru.
2. Methods

Study setting

The CRONICAS study is a longitudinal cohort study designed to characterize the prevalence of and risk factors for chronic disease in three geographically distinct settings in Peru. This study was conducted in a sample of CRONICAS participants at the Puno site and uses data from the baseline round of data collection and echocardiographic data that were collected during the 5-year follow-up. Located near the Bolivian border at 3,825 meters above sea level, Puno consists of a small, urban provincial capital and several rural villages where biomass fuel is widely used for cooking and heating. Puno primarily consists of indigenous, Andean people with both Quechua and Aymara speaking populations.

Study design

Individuals aged ≥35 years, full-time residents in the area, that provided informed consent were invited to participate in the study. We identified a sex- and age-stratified (35-44, 45-54, 55-64 and ≥65 years) and location-stratified (urban vs. rural) sample, and only one participant per household was enrolled. Maintaining age- and sex-stratification, we used a random number generator to select 200 urban CRONICAS participants and 200 rural CRONICAS participants for a total of 400 participants that were eligible to participate in this sub-study. The study was approved by the
Study procedures

Participants responded to a questionnaire on sociodemographic information, cardiopulmonary risk factors, and history of cardiopulmonary symptoms during the baseline round of data collection. During the follow-up visit for this sub-study in the 5th year of the cohort, nurse fieldworkers measured weight, height, heart rate and blood pressure. Systolic and diastolic blood pressures were measured in using a digital sphygmomanometer (OMRON HEM-780, Osaka, Japan). We used the right arm for all measurements using an appropriately fitted cuff size.

Participants underwent transthoracic echocardiography performed by either a senior sonographer or a senior cardiology fellow. The transthoracic echocardiography protocol was created specifically for this study and was adapted from the Duke Cardiac Diagnostic Unit protocol (unpublished) with permission from the director. Parasternal long axis, parasternal short axis, apical four-chamber, apical two-chamber, apical three-chamber and subcostal views were obtained. Using 2D imaging, continuous wave spectral Doppler, pulse wave spectral Doppler and M-mode imaging, the following echocardiographic measurements were performed: left ventricular internal diameter in
diastole, left ventricular internal diameter in systole, left ventricular mass, left ventricular ejection fraction, left atrial anterior-posterior diameter, left atrial area (4-chamber and 2-chamber), E/A ratio, lateral and septal E’ velocity, lateral and septal A’ velocity, lateral and septal S’ velocity, right ventricular width at the base, right ventricular width at the mid-cavity, right ventricular length, right ventricular systolic pressure (RVSP), tricuspid annular plane systolic excursion (TAPSE), and right ventricular outflow tract time to peak velocity. Left ventricular ejection fraction was calculated using the method of discs (Simpson’s rule), which is calculated using planimetry of the left ventricle in the apical four chamber and apical two-chamber views in end-systole and end-diastole. Left atrial area was calculated by planimetry of the left atrium in both the apical four-chamber and two-chamber views. Right ventricular systolic pressure (RVSP) was estimated from the tricuspid regurgitant jet velocity with the equation \( \text{RVSP} = 4(\text{TR jet velocity})^2 + \text{estimated right atrial pressure} \). Right atrial pressure was estimated using the maximum and minimum inferior vena cava (IVC) diameter 1 inch from the hepatic vein in the subcostal view before and after inspiration using the following criteria: 3 mmHg if the maximum IVC diameter is less than 2 cm and collapses >50% with inspiration; 8 mmHg if the maximum IVC diameter is greater than 2 cm and collapses >50% with inspiration or the maximum IVC diameter is less than 2 cm and does not collapse >50% with inspiration; 15 mmHg if the maximum IVC diameter is greater than 2 cm and does not collapse >50% with inspiration. Left
ventricular mass was determined based on 2D measurements using the American Society of Echocardiography Equation: Left ventricular mass = 0.8 x (1.04 x (left ventricular internal diameter in diastole + posterior wall thickness + septal wall thickness)^3 − (left ventricular internal diameter in diastole))^3) + 0.6.35

Definitions

The following variables were determined by self-report in a structured questionnaire: Daily biomass fuel use, prior diabetes diagnosis, physical activity and pack-years of tobacco smoking. Daily biomass fuel use was defined as self-reported daily burning of wood or dung for cooking or heating for more than six months at any time during the participant’s lifetime. Physical activity was determined based on leisure time and transport time domains of International Physical Activity Questionnaire as recommended for Latin American populations.36 Alcohol abuse was measured using the Alcohol Use Disorders Identification Test.37 Education was categorized by schooling years (<6 years, 7-11 years and 12 or more years). Socioeconomic status was defined as wealth index based on household income, assets and household facilities as previously described.38
Biostatistical methods

The primary aim was to compare measures of left heart and right heart structure and function in participants with and without daily exposure to biomass fuel smoke. The baseline characteristics of daily biomass fuel users and nonusers were compared using t-test for continuous variables and Chi-squared test for categorical variables. Using histograms, Q-Q plots and the skewness test, each echocardiographic variable was evaluated for normality. Variables without a normal distribution were log transformed and normality was re-assessed in the transformed variable. Multivariable linear regression analyses were used to model the association between daily biomass fuels use with each echocardiographic variable. In the fully-adjusted model, we controlled for age, sex, BMI, height, diabetes, pack-years of smoking, and low physical activity. Statistical analyses were conducted in STATA 13 (STATA Corp, College Station, USA).
3. Results

3.1 Participant Characteristics

A total of 187 participants were included in this study, including 80 daily biomass fuel users and 107 nonusers (Table 1). While there were no statistically significant differences in age or sex, daily biomass fuel users had lower body mass indices, lower diabetes prevalence, less education and lower wealth index.
Table 1. Characteristics of Daily Biomass Fuel Users and Non-Users in Puno, Peru

<table>
<thead>
<tr>
<th>Participant Characteristics</th>
<th>Biomass Fuel Non-Users (N=107)</th>
<th>Daily Biomass Fuel Users (N=80)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>58</td>
<td>60</td>
<td>0.201</td>
</tr>
<tr>
<td>Male</td>
<td>46 (43.0%)</td>
<td>33 (41.3%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Body mass index, kg/m² (mean)</td>
<td>27.6</td>
<td>25.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Heart rate, beats per minute (mean)</td>
<td>76.2</td>
<td>73.6</td>
<td>0.11</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9 (8.6%)</td>
<td>5 (7.0%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4 (3.9%)</td>
<td>10 (14.3%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Pack-years of tobacco use (mean)</td>
<td>0.79</td>
<td>0.33</td>
<td>0.37</td>
</tr>
<tr>
<td>Hazardous alcohol use</td>
<td>15 (14.3%)</td>
<td>10 (14.1%)</td>
<td>0.97</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>83 (79.8%)</td>
<td>50 (69.4%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Less than primary education</td>
<td>9 (8.6%)</td>
<td>45 (62.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lowest tertile of wealth index</td>
<td>19 (18.1%)</td>
<td>50 (70.4%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
3.2 Bivariate and Multivariable Analysis of Left Heart Structure and Function

In the unadjusted analysis, none of the echocardiographic measures of left atrial size or left ventricular structure and function were associated daily biomass fuel use except for the A’ velocity of the septal aspect of the mitral valve annulus (0.50 m/s, 95% Confidence Interval (CI) 0.04, 1.12) (Table 2). After adjusting for multiple covariates, daily biomass fuel use was associated with increased left atrial and left ventricular size. Biomass mass fuel use was associated with a 0.23 cm (95% CI 0.08, 0.38) increase in left ventricular internal diameter at the end of diastole (Figure 1). Left atrial anterior-posterior diameter (0.18 cm; 95% CI 0.02, 0.33) and left atrial area in the apical 4-chamber view (1.80 cm²; 95% CI 0.57, 3.03) and apical 2-chamber view (1.67 cm²; 0.34, 3.01) were also greater in daily biomass fuel users compared to nonusers.

Daily biomass fuel use was associated with changes in diastolic function. E/A ratio was increased in daily biomass fuel users by 1.03 (95% CI 1.20, 1.17). Additionally, both lateral and septal peak E’ velocities were increased in daily biomass fuel users when compared to nonusers (0.71 cm/s: 95% CI 0.04, 1.38; 1.10 cm/s: 95% CI 1.03, 1.19, respectively). There was no association between daily biomass fuel use and left ventricular systolic function as measured by the left ventricular ejection fraction.
Table 2. Bivariate and Multivariable Linear Regression Analysis Comparing Left Atrial and Ventricular Echocardiographic Parameters in Daily Biomass Fuel Users and Nonusers Adjusting for Age, Sex, Body Mass Index, Height, Physical Activity, Pack-years of Tobacco Use and Diabetes in Puno, Peru

<table>
<thead>
<tr>
<th>Echocardiographic Parameters</th>
<th>Bivariate Model (95% CI)</th>
<th>p-value</th>
<th>Multivariable Model (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular internal diameter, diastole, cm</td>
<td>0.10 (-.06, 0.26)</td>
<td>0.20</td>
<td>0.23 (0.08, 0.38)</td>
<td>0.004</td>
</tr>
<tr>
<td>Left ventricular internal diameter, systole, cm</td>
<td>0.08 (-0.9, 0.25)</td>
<td>0.37</td>
<td>0.14 (-0.03, 0.32)</td>
<td>0.12</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>-0.89 (-2.57, 0.78)</td>
<td>0.29</td>
<td>-0.95 (-2.79, 0.88)</td>
<td>0.31</td>
</tr>
<tr>
<td>Left ventricular mass, g</td>
<td>0.96 (0.88, 1.04)</td>
<td>0.29</td>
<td>1.02 (0.95, 1.10)</td>
<td>0.57</td>
</tr>
<tr>
<td>Left atrial diameter, cm</td>
<td>0.03 (-0.13, 0.19)</td>
<td>0.70</td>
<td>0.18 (0.02, 0.33)</td>
<td>0.03</td>
</tr>
<tr>
<td>Left atrial area, 4-chamber, cm²</td>
<td>0.58 (-0.67, 1.84)</td>
<td>0.36</td>
<td>1.80 (0.57, 3.03)</td>
<td>0.004</td>
</tr>
<tr>
<td>Left atrial area, 2-chamber, cm²</td>
<td>0.46 (-0.96, 1.89)</td>
<td>0.52</td>
<td>1.67 (0.34, 3.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.04 (0.96, 1.13)</td>
<td>0.28</td>
<td>1.03 (1.02, 1.17)</td>
<td>0.01</td>
</tr>
<tr>
<td>Lateral E’, cm/s</td>
<td>0.43 (-0.20, 1.50)</td>
<td>0.13</td>
<td>0.71 (0.04, 1.38)</td>
<td>0.04</td>
</tr>
<tr>
<td>Lateral A’, cm/s</td>
<td>-0.26 (-0.92, 0.40)</td>
<td>0.44</td>
<td>-0.20 (-0.87, 0.48)</td>
<td>0.57</td>
</tr>
<tr>
<td>Lateral S’, cm/s</td>
<td>-0.10 (-0.68, 0.73)</td>
<td>0.73</td>
<td>-0.10 (-0.71, 0.74)</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>Value 1</td>
<td>Value 2</td>
<td>Value 3</td>
<td></td>
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<td>-------------</td>
<td>-------------</td>
<td>-------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>Sepal E', cm/s</td>
<td>1.08 (1.00, 1.18)</td>
<td>0.05</td>
<td>1.10 (1.03, 1.19)</td>
<td>0.006</td>
</tr>
<tr>
<td>Septal A', cm/s</td>
<td>0.58 (0.04, 1.12)</td>
<td>0.04</td>
<td>0.37 (-0.17, 0.91)</td>
<td>0.18</td>
</tr>
<tr>
<td>Sepal S', cm/s</td>
<td>0.29 (0.17, 0.74)</td>
<td>0.22</td>
<td>0.25 (-0.21, 0.70)</td>
<td>0.29</td>
</tr>
</tbody>
</table>
Figure 1. Left Ventricular Internal Diameter at End Diastole, Left Ventricular Diameter at End Systole and Left Atrial Area (4-Chamber and 2-Chamber) in Biomass Fuel Users and Nonusers
3.3 Bivariate and Multivariable Analysis of Right Heart Structure and Function

There was no association between daily biomass fuel use and measures of right ventricular size and function (Table 3). Of note, there was a trend towards increased right ventricular width at the base and length in daily biomass fuel users in the fully adjusted analysis, but the increase was not statistically significant (0.18 cm, 95% CI -0.01, 0.36; 0.25 cm, 95% CI -0.01, 0.51, respectively).
Table 3. Bivariate and Multivariable Linear Regression Analysis Comparing Right Atrial and Ventricular Echocardiographic Parameters in Daily Biomass Fuel Users and Nonusers Adjusting for Age, Sex, Body Mass Index, Height, Physical Activity, Pack-years of Tobacco Use and Diabetes in Puno, Peru

<table>
<thead>
<tr>
<th>Echocardiographic Parameters</th>
<th>Bivariate Model (95% CI)</th>
<th>p-value</th>
<th>Multivariable Model (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricular diameter, base, cm</td>
<td>0.10 (-0.09, 0.28)</td>
<td>0.32</td>
<td>0.18 (-0.01, 0.36)</td>
<td>0.058</td>
</tr>
<tr>
<td>Right ventricular diameter, mid-cavity, cm</td>
<td>-0.02 (-0.19, 0.16)</td>
<td>0.86</td>
<td>0.11 (-0.06, 0.27)</td>
<td>0.20</td>
</tr>
<tr>
<td>Right ventricular length</td>
<td>-0.002 (0.27, 0.27)</td>
<td>0.99</td>
<td>0.25 (-0.01, 0.51)</td>
<td>0.06</td>
</tr>
<tr>
<td>RVSP</td>
<td>0.77 (-3.28, 1.74)</td>
<td>0.55</td>
<td>0.16 (-2.48, 2.80)</td>
<td>0.91</td>
</tr>
<tr>
<td>TAPSE</td>
<td>-0.04 (-0.14, 0.07)</td>
<td>0.52</td>
<td>0.05 (-0.06, 0.17)</td>
<td>0.37</td>
</tr>
<tr>
<td>Right ventricular outflow tract time to peak velocity, ms</td>
<td>3.50 (-4.97, 11.98)</td>
<td>0.42</td>
<td>6.25 (-3.20, 15.71)</td>
<td>0.19</td>
</tr>
</tbody>
</table>
4. Discussion

In a sample from a population-based cohort in Peru there was an association between daily biomass fuel use with increased left ventricular diameter in diastole and increased left atrial size by transthoracic echocardiography. No statistically significant association was found between daily biomass fuel use and echocardiographic measures of right heart size or function.

While there are other ongoing echocardiographic studies of household air pollution, there are very few published studies that examine the changes in right and left cardiac structure and function that are associated with biomass fuel use. Previous studies from our group have examined the relationship between RVSP by transthoracic echocardiography and serum NT-pro-BNP levels in a sample of 153 participants in Puno\textsuperscript{39}. This study found no relationship between biomass fuel use with either RVSP or NT-pro-BNP, which is consistent with the findings of this study. However, Kargin et al. examined the relationship between chronic biomass fuel use with pulmonary artery systolic pressure and myocardial performance indices of the right and left ventricles by transthoracic echocardiography in 77 women in Turkey.\textsuperscript{40} This study found an increase in pulmonary artery systolic pressure and increases in right ventricular and left ventricular myocardial performance indices in the biomass fuel use group in comparison to the nonuser group, indicating worse right and left ventricular function in biomass fuel users. While our study did not measure the myocardial performance index
(also known as the Tei index), we did not see the differences in conventional measures of right ventricular function, including TAPSE and pulmonary artery systolic pressure, in contrast to the Turkish study. However, the sample used by Kargin et al. was subject to selection bias as it was derived from a medical center patient population and not the general population. Additionally, the small sample size in that study might explain other differences in the findings of our study and Kargin et al.

The increase in left atrial size in daily biomass fuel users in comparison to nonusers represents a remodeling in cardiac structure that is associated with future adverse cardiovascular outcomes. While often a subclinical finding in the absence of mitral valve disease, left atrial enlargement is often an early sign of increased left ventricular end diastolic pressure, signifying changes in left ventricular compliance. In multiple populations left atrial enlargement is associated with increased risk of fatal and nonfatal cardiovascular events and cardiovascular mortality.\textsuperscript{41-46} An analysis from the Framingham Heart Study found that incremental left atrial enlargement was associated with increased risk of stroke in men and increased risk of all-cause mortality in men and women.\textsuperscript{41} Data from another population-based cohort in Italy found that individuals with left atrial enlargement and no other echocardiographic findings had increased risk of fatal and nonfatal cardiovascular events, including myocardial infarction, stroke and heart failure.\textsuperscript{44} Moreover in a population-based cohort of Native Americans, left atrial enlargement was associated with increased risk of first cardiovascular event, fatal and
nonfatal coronary heart disease and any cardiovascular death. In our study in Peru, the mean left atrial size of daily biomass fuels users remains within the normal range, yet a rightward shift in the population distribution curve of left atrial size could translate into increased risk for cardiovascular events in a greater number daily biomass fuel users in comparison to nonusers.

The results of this study have implications for both public health policy and energy policy. Due to the widespread use of biomass fuels for cooking and heating in low-income communities throughout the developing world, there has been increased interest in clean cook-stove interventions on a global scale. Yet, despite large-scale investment improving cook-stoves and cultural adaptation, the totality of the health impact of household air pollution from biomass fuels use remains unknown. This uncertainty is important to highlight, because there are no clear guidelines for what constitutes a successful cook-stove intervention, both in terms of reduction in the exposure to airborne pollutants and the health impact of any given reduction in the exposure. Better understanding of the way in which household air pollution increases risk for cardiovascular disease not only provides greater justification for investing in clean cook-stove technology, but also provides benchmarks with which we can evaluate the efficacy of clean cook-stove interventions to improve health outcomes in low-income communities.
This study is an observational study and thus cannot determine causation. Daily biomass fuel users are more likely than nonusers to live in rural communities, and therefore unmeasured confounders potentially exist. Moreover, while both groups in our sample lived at similar altitudes, it remains unclear whether extreme altitude affects the relationship between biomass fuel use and cardiac structure and function. This study is also limited by the relatively small sample size and may be underpowered to detect differences in left ventricular systolic function or right ventricular systolic function. Additionally, we used daily biomass fuel use as proxy for household air pollution exposure and did not measure the individual particulate matter and gaseous components of biomass fuel combustion smoke to better determine which pollutant is more greatly associated with changes in cardiac structure and function.
5. Conclusion

Daily biomass fuel use is associated with increased left ventricular and left atrial size in a population-based sample of individuals living at high-altitude in Puno, Peru. This difference in cardiac structure potentially increases the risk for multiple adverse cardiovascular outcomes in biomass fuel users. Additional studies are needed to better understand the relationship between biomass fuel use, cardiac remodeling and cardiovascular outcomes. Clean cook-stove interventions should be evaluated according to the ability of the intervention to reduce adverse cardiac remodeling and hard cardiovascular events.
**References Cited**


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