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Chronic exposure to biomass fuel is associated with increased carotid artery intima-media thickness and a higher prevalence of atherosclerotic plaque

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Abstract

Background—Biomass fuels are used for cooking in the majority of rural households worldwide. While their use is associated with an increased risk of lung diseases and all-cause mortality, the effects on cardiovascular disease (CVD) are not well characterised. Exposure to biomass fuel smoke has been associated with lung-mediated inflammation and oxidative stress, which may increase the risk of atherosclerosis as evaluated by carotid intima-media thickness (CIMT), carotid atherosclerotic plaque prevalence and blood pressure.

Methods—A cross-sectional study was performed in 266 adults aged ≥35 years in Puno, Peru (3825 m above sea level). We stratified participants by their long-term history of exposure to clean

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Contributors MSP and WC conceived, designed and conducted the study; RHG, ADV-V, JJM, RAW and VGD-R assisted in design, conception and conduct of the study; SLP conducted the environmental assessment. All authors participated in interpretation of analysis and writing of the manuscript. WC is ultimately responsible for the study conduct, analysis and interpretation of results.

Competing interests None.

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fuel (n=112) or biomass fuel (n=154) and measured 24 h indoor particulate matter ($PM_{2.5}$) in a random subset (n=84). Participants completed questionnaires and underwent a clinical assessment, laboratory analyses and carotid artery ultrasound. The main outcome measures were CIMT, carotid plaque and blood pressure.

Results—The groups were similar in age and gender. The biomass fuel group had greater unadjusted mean CIMT (0.66 vs 0.60 mm; p<0.001), carotid plaque prevalence (26% vs 14%; p=0.03), systolic blood pressure (118 vs 111 mm Hg; p<0.001) and median household $PM_{2.5}$ (280 vs 14 μg/m^3; p<0.001). In multivariable regression, the biomass fuel group had greater mean CIMT (mean difference=0.03 mm, 95% CI 0.01 to 0.06; p=0.02), a higher prevalence of carotid plaques (OR=2.6, 95% CI 1.1 to 6.0; p=0.03) and higher systolic blood pressure (mean difference=9.2 mm Hg, 95% CI 5.4 to 13.0; p<0.001).

Conclusions—Chronic exposure to biomass fuel was associated with increased CIMT, increased prevalence of atherosclerotic plaques and higher blood pressure. These findings identify biomass fuel use as a risk factor for CVD, which may have important global health implications.

INTRODUCTION

Exposure to biomass fuel smoke is an important cause of morbidity and mortality in low- and middle-income countries (LMIC). Biomass fuels (which include wood, animal dung and crop residues) are used for cooking and heating the home by approximately 90% of rural households worldwide.[1] Chronic exposure to biomass fuel smoke is associated with an increased risk of lower respiratory infections,[2] tuberculosis,[3] chronic obstructive pulmonary disease and all-cause mortality.[4] Interventions replacing traditional open-fire stoves with improved cooking stoves have shown decreased air pollution exposures and improved lung function.[5] It is estimated that indoor air pollution is the fourth overall cause of disability-adjusted life years lost worldwide and is estimated to be attributable for up to 18% of the global burden of ischaemic heart disease.[6] Few studies, however, have examined the link between exposure to biomass fuel smoke and cardiovascular disease (CVD).[7–11]

Worldwide, CVD is responsible for more than 15 million deaths annually,[12] and 80% of the CVD burden occurs in LMIC.[13] Although the increasing prevalence of CVD in LMIC has been linked to traditional risk factors such as hypertension, obesity and tobacco, biomass fuel smoke exposure may represent an under-recognised population-attributable risk factor. Notably, recent studies have found an association between biomass fuel smoke exposure and both elevated blood pressure[79] and self-reported heart disease.[10] Biomass smoke is associated with markedly elevated particulate matter (PM) exposure[14] which may increase the risk of atherosclerosis and CVD via similar mechanisms to outdoor air pollution—namely, lung-mediated inflammation, autonomic dysfunction and oxidative stress.[15–17] Long-term prospective cohort studies of outdoor air pollution have shown an association between elevated PM concentrations and an increased risk of atherosclerosis and death from CVD.[18–21]

Population-based studies have found that CVD is strongly associated with increased carotid artery intima-media thickness (CIMT), which is a robust intermediate phenotype of atherosclerosis,[22–27] and carotid atherosclerotic plaques. We therefore used carotid artery

ultrasound to test our primary hypothesis that biomass fuel smoke exposure is associated with increased CIMT and increased prevalence of carotid artery atherosclerotic plaques, and measured blood pressure to evaluate our secondary hypothesis that biomass fuel exposure is associated with higher blood pressure.

METHODS

Study setting

The study population consisted of adults ≥35 years of age living in the city of Puno, Peru (population of approximately 100 000) and surrounding rural communities, at an elevation of 3825 m above sea level. City dwellers work chiefly in commerce and education and cook predominantly with clean fuels including liquid propane gas, kerosene and electricity. Rural dwellers live as subsistence farmers and cook indoors almost exclusively with traditional open-fire stoves and use combinations of wood, animal dung and crop residue as fuel.

Study design

In preparation for study activities for the CRONICAS cohort study, we conducted a door-to-door household census of 18 500 people in the study area from which a large age-, sex- and site-stratified population-based cohort was derived.[28] We then selected a random subset of 266 participants from the larger CRONICAS study for inclusion into this ancillary study in which we measured CIMT and examined for carotid plaque by utrasound.[28] Between February and October 2011, trained field workers conducted a standardised questionnaire to assess cooking patterns, traditional cardiovascular risk factors, socioeconomic status, education, past medical history and tobacco use, followed by a clinical assessment, including blood pressure, as described previously.[2829] Certified phlebotomists collected blood for processing in a centralised testing facility for serum lipids, fasting glucose, fasting insulin, haemoglobin A1c and high sensitivity C-reactive protein (hsCRP).[28]

Definitions

We stratified participants by their history of long-term household cooking with clean fuel or biomass fuel (ie, urban vs rural households). We used dwelling locale as a proxy for chronic exposure biomass to fuel use. Specifically, environmental exposure data in our study population has shown that the majority of rural houses have heavy indoor $PM_{2.5}$ and carbon monoxide exposures while cooking (median >250 μg/m^3 and >2 ppm, respectively), whereas the majority of urban households have low indoor environmental exposures throughout the entire day (<25 μg/m^3 and <1 ppm).

We defined the presence of CVD as a self-reported history or current medication use for one or more of the following: arrhythmias, angina, myocardial infarction, heart failure, hyper-lipidaemia or stroke. We defined a history of hypertension and diabetes as a self-reported history or current medication use for each, respectively. We defined poverty, according to official 2010 Peruvian government guidelines, as a monthly income of less than US$100 per capita.[30] We used the standard definition for Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR)—that is, the product of fasting glucose (mmol/l) and fasting insulin (μU/ml)/22.5.[31]

Measurement of PM

We carried out direct-reading passive measurements of indoor kitchen $PM_{2.5}$ concentrations using the pDR-1000 (Thermo Fisher Scientific, Waltham, Massachusetts, USA) in a random subset of 84 households in our study population. Our random sample consisted of 27 homes in the urban city centre of Puno and 59 homes in the surrounding rural communities. We placed particle monitors 1.5–2.0 m off the ground and 0.5–1.0 m from the kitchen stove. We recorded $PM_{2.5}$ data in 1 min intervals for 24 h. We also recorded relative humidity concurrently using the HOBO U10 data-logger (Onset Corporation, Bourne, Massachusetts, USA), and $PM_{2.5}$ data were adjusted accordingly as previously described.[32] Empirical evidence suggests that the pDR-1000 detects particles in the size range 0.3–2 μm more efficiently than those of 2–10 μm, and these measurements have been shown to correlate closely with $PM_{2.5}$ measurements.[33]

Carotid artery ultrasound

We performed carotid ultrasound using a 9 MHz linear array transducer with the portable MicroMaxx (Sonosite, Bothell, Washington, USA). Two trained operators acquired images of both carotid arteries. We exported the images for offiine digital analysis using SonoCalc V.4.1 (Sonosite semi-automatic edge detection software). The mean CIMT measurements were expressed as the average of the far wall intima-media thickness from both right and left common carotid arteries during peak R wave.[34] Each reported measurement represents the average of three separate measurements obtained by a single observer of the 1 cm proximal to the carotid bulb. We defined an atherosclerotic plaque as a focal intima-media thickness >1.5 mm or focal wall thickening that protruded into the lumen >0.5 mm or >50% of the surrounding CIMT.[34] The primary reader and secondary reader assessed the reproducibility of the measurements by evaluating 20% of the original studies randomly; both readers were blinded to all other measurements. Intra- and inter-observer intraclass correlation coefficients for repeated measures of CIMT were 0.99 and 0.84, respectively. For plaque reproducibility, two independent blinded observers reviewed all plaques. There was complete agreement for 81% of cases and only these were considered indicative of plaque for the final analysis. For those without plaque, both observers reviewed 10% of the cases; there was 100% agreement for the absence of atherosclerotic plaques.

Biostatistical methods

Primary outcomes were CIMT and the presence of carotid artery atherosclerotic plaque. Secondary outcomes were systolic (SBP) and diastolic blood pressure (DBP). The primary risk factor of interest was chronic exposure to biomass fuel smoke. We used t tests to compare continuous variables between groups if normally distributed and Mann–Whitney U tests if non-normally distributed. We used χ^2 or Fisher exact tests whenever appropriate, if categorical variables. We used multivariable linear regression to evaluate the association between chronic exposure to biomass fuel smoke and CIMT (mean and maximum), adjusted for age, SBP, gender, low-density lipoprotein (LDL), high-density lipoprotein (HDL), body mass index (BMI), HOMA-IR and antihypertensive medication use. Multivariable logistic regression was used to evaluate the association between chronic biomass fuel smoke exposure and presence of atherosclerotic plaques adjusted for the same variables. We used

multivariable linear regression to evaluate the association between chronic exposure to biomass fuel smoke and blood pressure (SBP and DBP), adjusted for age, gender, LDL, HDL, BMI and HOMA-IR. Statistical analyses were conducted in R (http://www.r-project.org).

RESULTS

Baseline characteristics

The study population consisted of 266 long-term high altitude residents. One participant from the clean fuel group did not fully complete the questionnaire and was excluded from the multivariable analysis. Thirteen participants did not give a blood sample (five participants in the clean fuel group and eight in the biomass fuel group). The mean±SD age was 57±12 years. The clean fuel and biomass fuel groups consisted of 112 (55±12 years, 47% women) and 154 subjects (58±12 years, 59% women), respectively (table 1). Participants in the biomass fuel group had a significantly longer history of exposure to biomass fuels than those in the clean fuel group (median 48 years vs 15 years; $p<0.001$). More than 98% of participants in the clean fuel group used liquid propane gas for cooking while the remainder used either kerosene or electricity. As expected, the clean fuel group was predominantly urban for their entire life, better educated and of a higher socioeconomic status. The clean fuel group had a higher self-reported history of hypertension and CVD, smoking history, BMI, total cholesterol, triglycerides, fasting glucose, hsCRP levels and more insulin resistance (HOMA-IR).[31] Medical history of type 2 diabetes and serum haemoglobin A1c levels were similar in the two groups. Use of CVD-related medications was low in both groups, but was significantly higher in the clean fuel group. No participants reported use of calcium channel blockers or diuretics in either group. Median 24 h concentrations of indoor $PM_{2.5}$ were 14 $\mu g/m^3$ (IQR 8–21) in the clean fuel homes versus 280 $\mu g/m^3$ (IQR 107–574) in the biomass fuel homes ($p<0.001$).

Carotid intima-media thickness

The association between mean CIMT and age, SBP, LDL, HDL, gender, BMI, HOMA-IR and antihypertensive medication use is shown in figure 1. Unadjusted mean CIMT (0.66 vs 0.60 mm; $p<0.001$) and maximum CIMT (0.76 vs 0.71 mm; $p<0.01$) were significantly higher in the biomass fuel group than in the clean fuel group (table 2). Mean CIMT (mean difference 0.03 mm, 95% CI 0.01 to 0.06; $p=0.02$; figure 2) and maximum CIMT (0.03 mm, 95% CI 0.01 to 0.06; $p=0.04$) remained significantly larger after adjustment for age, gender, HDL, LDL, SBP, BMI, HOMA-IR and antihypertensive medication use (table 3). Multivariable regression modelling also showed that both mean and maximum CIMT were directly associated with increasing age.

Carotid artery atherosclerotic plaque

Atherosclerotic plaques in the carotid artery were significantly more prevalent in the biomass fuel group than in the clean fuel group (26% vs 14%; OR=2.1, 95% CI 1.1 to 4.3; $p=0.03$; table 2). This difference remained after adjusting for age, gender, HDL, LDL, SBP, BMI, HOMA-IR and antihypertensive medication use (OR=2.6, 95% CI 1.1 to 6.0; $p=0.03$;

table 3). Multivariable logistic regression also showed that plaque presence was directly associated with increasing age.

Blood pressure

SBP (median 118 vs 111 mm Hg) and DBP (75 vs 71 mm Hg) were both higher in the biomass fuel than in the clean fuel group ($p<0.001$, table 1). In multivariable linear regression, both SBP (mean difference 9.2 mm Hg, 95% CI 5.4 to 13.0) and DBP (mean difference=6.5, 95% CI 4.1 to 8.9) remained higher in the biomass fuel group after adjusting for age, gender, LDL, HDL, HOMA-IR, BMI and antihypertensive medication use ($p<0.001$, table 3). Multivariable regression modelling also showed that both SBP and DBP were directly associated with increasing age, being male and greater BMI.

DISCUSSION

In this prospective population-based study, we evaluated 266 long-term residents of Puno, Peru, grouped according to long-term history of exposure to household biomass fuel use to test the hypothesis that chronic exposure to biomass fuel smoke was associated with higher blood pressure and increased atherosclerotic burden. Our study shows that exposure to biomass fuels from cooking is associated with increased CIMT and higher prevalence of carotid artery atherosclerotic plaques, as well as higher blood pressure. Multivariable regression analysis showed that, even after controlling for age, gender, SBP, BMI, insulin resistance, HDL, LDL and antihypertensive medication use, chronic exposure to biomass fuel smoke remained significantly associated with increased CIMT and with an increased prevalence of carotid artery atherosclerotic plaques, similar in magnitude to that reported in tobacco smokers.[35–37] We acknowledge that traditional risk factors such as hypertension may be under-reported in the biomass fuel group and potentially undertreated due to lack of access to medical care; however, use of CVD-related medications was low in both groups. Although the two groups were similar in many ways including ethnicity, long-term residence at high altitude and a low prevalence of daily smoking, the results are even more striking in that the clean fuel group had a significantly higher CVD risk factor burden, previously associated with increased CIMT and carotid plaque.[2734] Since CIMT and carotid atherosclerotic plaques are well-characterised surrogate markers for CVD, and blood pressure is an important risk factor for CVD morbidity and mortality, the findings of the present study suggest that there is an important association between chronic exposure to biomass fuel smoke and increased risk for CVD.

We used carotid artery ultrasound to assess both CIMT and atherosclerotic plaques because this is a well-validated, inexpensive, non-invasive surrogate marker of both current and future coronary artery disease and atherosclerosis.[26] After adjusting for age and Framingham risk factors, the highest quartile of CIMT (risk ratio 1.5–4.9) and of carotid artery plaque (risk ratio 1.8–4.1) have been associated with an increased risk for myocardial infarction, stroke or death over follow-up periods of 3–10 years.[34] CIMT has been shown to be associated with a number of other CVD risk factors,[21232735] but its association with biomass fuel exposure has not been well characterised.

Recent studies have suggested an association between chronic biomass fuel use and CVD risk. Higher blood pressure in women exposed to biomass fuel smoke has been reported in a number of studies[79–11] and has supported a dose-response relationship.[38] Our data also show elevated SBP and DBP among participants chronically exposed to biomass fuels, even after controlling for many potentially confounding variables. PM from other sources, environmental air pollution and passive tobacco have been associated with an increased prevalence of hypertension[39]; hypertension is a known risk factor for increased CIMT.[2326] These findings are suggestive of an important, potentially causative, factor for the increase in CIMT and atherosclerotic plaques seen in this study. Previous studies have also shown an association between biomass fuel smoke exposure and both increased ST segment depression[8] and self-reported CVD history.[10] This study was not designed to evaluate these outcomes, but nevertheless contributes to the growing body of literature suggesting a strong link between chronic exposure to biomass fuels and CVD.

The mechanistic pathways linking both tobacco smoke and ambient air pollution to increased prevalence of atherosclerosis have been well described,[213539] and it is hypothesised that biomass fuels affect CVD risk through similar biochemical pathways. Combustion in each of these scenarios releases PM, polycyclic aromatic hydrocarbons and free radicals, each of which has been associated with an increased risk of atherosclerosis.[10] Principally, the mechanisms involve increases in oxidative stress, lung-mediated inflammation and stimulation of the autonomic nervous system.[40] Despite a paucity of controlled studies in the field of biomass fuel smoke exposure in humans, recent studies have demonstrated that exposure is associated with increased airway inflammation,[16] serum amyloid A,[15] inflammatory cytokines, circulating neutrophils,[17] oxidised LDL particles and reactive oxygen species,[11] all of which are associated with the development of atherosclerosis. Intriguingly, however, the biomass fuel group in our study actually demonstrated less inflammation (lower hsCRP) than those in the clean fuel group. This is consistent with other observed increases in traditional CVD risk factors (higher LDL, lower HDL, higher insulin resistance) in the clean fuel group commonly seen in more urbanised settings. Specific markers of endothelial dysfunction were not measured and merit future study.

PM is the most well-characterised measure of ambient environmental CVD risk.[14] Epidemiological studies of the effects of $PM_{2.5}$ show a significant link with both chronic atherosclerosis and acute ischaemic coronary syndromes. Long-term studies have demonstrated a 10% increase in all-cause mortality and a greater increase in cardiovascular mortality per 10 $\mu g/m^3$ increase in chronic $PM_{2.5}$ exposure.[18–2039] Studies have also shown increases in coronary artery calcium,[41] CIMT,[21] myocardial infarction,[39] stroke and all-cause mortality[2039] in association with chronic $PM_{2.5}$ exposure. The evidence for short-term exposure suggests a 0.4–1.0% increase in daily all-cause and CVD mortality per 10 $\mu g/m^3$ elevation in $PM_{2.5}$ in the preceding 1–5 days.[3942] In our population, 24 h $PM_{2.5}$ was significantly higher in biomass fuel households. Although mechanisms were not assessed in this study, we suspect that increased levels of PM probably represent an important mechanism by which biomass fuel exposure increases CIMT and carotid atherosclerotic plaque prevalence in this population.[43]

Our study has some potential shortcomings. First, little is known regarding CVD morbidity and mortality in this population. Although BMI and diabetes were more prevalent in the clean fuel group, it is likely that at least some of the differences in CVD risk factors and blood pressure in this study are due to decreased access to healthcare in the biomass fuel group and that this may confound our results. In addition, although the normal CIMT values for the region are variable[44] our CIMT values were similar to those from a nearby population in Arequipa, Peru.[36] Population-based and intervention studies have shown that CIMT is a well-validated surrogate measure of coronary atherosclerosis and is a significant predictor of coronary events and stroke; CIMT correlates well with traditional CVD risk factors in the general population.[232526] In addition, there is evidence that PM from biomass fuel smoke results in activation of circulating platelets that produce high levels of leucocyte-platelet aggregates,[45] factor VIII and fibrinogen levels,[15] enhancing blood coagulation and increasing the risk of acute cardiovascular events. Future studies should better define the relationship between biomass fuel exposure, both acutely and chronically, and cardiovascular events. Second, previous studies on the effects of biomass fuels have concentrated on women. We did not power our study to examine gender interactions, but accounted for this limitation by controlling for gender in our regression models. However, it is also possible that the differences are not as striking in our study population as both men and women spend a considerable amount of time indoors during cooking and for heating. Further studies are needed to better define both exposure and outcome differences between genders across different geographical settings. Third, our sample size is small; however, despite this shortcoming, we were still able to detect important differences in CIMT, plaque prevalence and blood pressure between participants with and without chronic exposure to biomass fuel smoke in both single variable and multivariable analyses. Fourth, different types of biomass fuels (wood vs dung vs agricultural crop waste) may have differential adverse effects on health; however, we were not able to test this hypothesis in our study population because all participants who cooked with biomass fuels used combinations of biomass fuel types. Finally, we did not control for socioeconomic differences in our models; the strong collinearity between socioeconomic status and type of fuel use makes separation of the effects sizes of these coexistent sociological factors difficult to tease apart in our study population. Further studies are needed to associate individual CIMT measurement with PM exposure as well as hard CVD endpoints in this population, and to study interventions in rural communities with heavy biomass fuel use to determine whether a reduction in exposure to biomass fuel smoke leads to a slower progression of atherosclerosis as assessed by CIMT.

In summary, compared with clean fuel stoves, chronic exposure to biomass fuel smoke was associated with increased CIMT and a higher prevalence of atherosclerotic plaques, both of which are risk factors for CVD, as well as higher blood pressure. As evidence continues to mount on the negative health consequences of biomass fuel use, future studies must evaluate the role of interventions aimed at reducing CVD risk. Non-invasive markers based on carotid ultrasound assessment may provide a valuable surrogate endpoint in improved cooking stove intervention trials.

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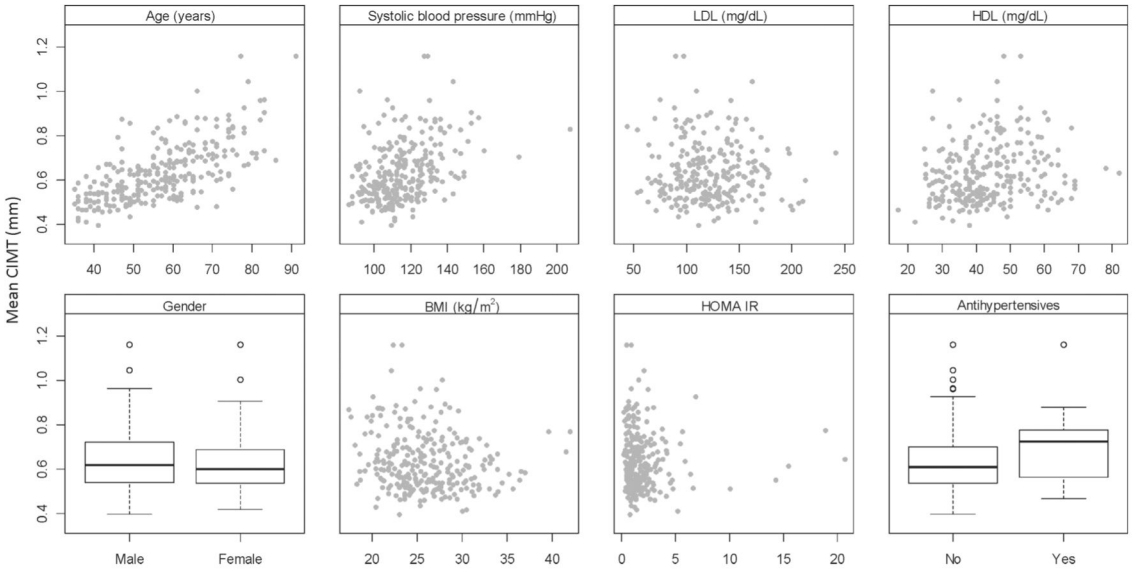

Figure 1.

Mean carotid intima-media thickness (CIMT) distribution by age, systolic blood pressure, low-density lipoprotein (LDL), high-density lipoprotein (HDL), gender, body mass index (BMI), Homeostasis Model of Assessment-Insulin Resistance (HOMA-IR) and antihypertensive medication use.

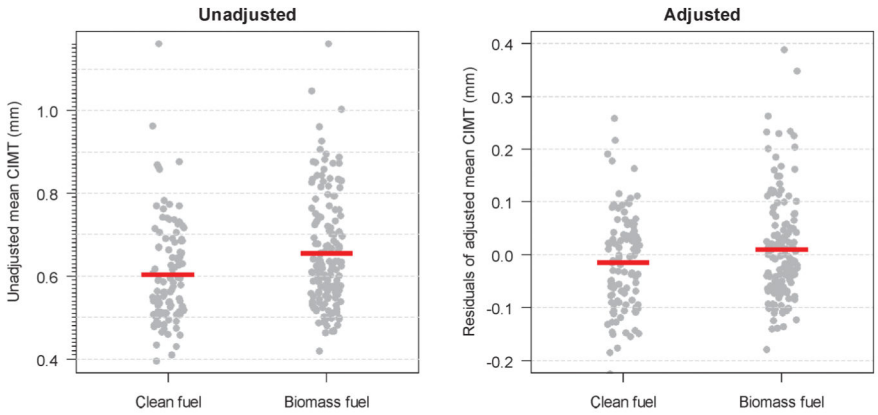

Figure 2.

Distribution of unadjusted and adjusted mean carotid intima-media thickness (CIMT) values by group (clean fuel vs biomass fuel).

Table 1

Baseline characteristics of the participants according to cooking fuel, clean fuel versus biomass fuel

Characteristic	Total (n=266)	Clean fuel (n=112)	Biomass fuel (n=154)	p Value
Demographics				
Age (years)				
35–44	49 (18%)	27 (24%)	22 (14%)	0.20
45–54	67 (25%)	29 (26%)	38 (25%)	
55–64	80 (30%)	29 (26%)	51 (33%)	
65+	70 (26%)	27 (24%)	43 (28%)	
Men, n (%)	123 (46%)	60 (53%)	63 (41%)	0.07
Body mass index, median (IQR), kg/m^2	25 (23–29)	27 (23–30)	24 (22–27)	<0.001
Born in rural household, n (%)	165 (62%)	12 (11%)	153 (99%)	<0.001
Living in same community as birth, n (%)	213 (80%)	67 (60%)	146 (95%)	<0.001
Living below the poverty line, n (%)	213 (80%)	61 (55%)	152 (99%)	<0.001
Completed primary school, n (%)	142 (53%)	102 (91%)	40 (26%)	<0.001
Cooking characteristics				
Years exposed to biomass fuels, median (IQR)	40 (18–52)	15 (6–20)	48 (38–58)	<0.001
Number of participants who cook, n (%)	208 (78%)	76 (68%)	132 (86%)	<0.001
Time cooking, median (IQR), years	34 (29–46)	29 (18–35)	40 (30–50)	<0.001
Haemodynamics				
Heart rate, median (IQR), beats/min	67 (61–74)	69 (61–76)	63 (60–71)	<0.001
Systolic blood pressure, mean (SD), mm Hg	115 (16)	111 (14)	118 (17)	<0.001
Diastolic blood pressure, mean (SD), mm Hg	73 (9)	71 (8)	75 (9)	<0.001
Past medical history, n (%)				
Hypertension	28 (11%)	23 (21%)	5 (3%)	<0.001
Diabetes	3 (1%)	2 (2%)	1 (1%)	0.58
Cardiovascular disease	22 (8%)	20 (18%)	2 (1%)	<0.001
Smoking history, n (%)				
Never	190 (72%)	64 (57%)	126 (82%)	<0.001
Previous	60 (22%)	36 (32%)	24 (16%)	
Current	16 (6%)	12 (11%)	4 (3%)	
Laboratory values				
Total cholesterol, mean (SD), mg/dl	192 (37)	199 (39)	187 (35)	0.01
LDL, median (IQR), mg/dl	117 (98–140)	122 (98–144)	114 (98–140)	0.19
HDL, median (IQR), mg/dl	41 (35–50)	40 (34–50)	43 (37–52)	0.16
Triglycerides, median (IQR), mg/dl	123 (91–172)	142 (110–194)	111 (82–147)	<0.001
Haemoglobin A1c, median (IQR), %	5.8 (5.5–6.1)	5.9 (5.6–6.1)	5.8 (5.5–6.0)	0.12
Fasting glucose, median (IQR), mg/dl	88 (81–95)	90 (82–99)	87 (80–93)	0.002
HOMA-IR mmol/l×μU/ml, median (IQR)	1.3 (0.8–2.1)	1.5 (1.0–2.8)	1.1 (0.6–1.9)	<0.001
hsCRP, median (IQR), μg/ml	0.9 (0.4–2.3)	1.6 (0.8–2.8)	0.6 (0.4–1.3)	<0.001
Medications, n (%)				
β-Blockers	3 (1%)	3 (3%)	0 (0%)	0.07

Characteristic	Total (n=266)	Clean fuel (n=112)	Biomass fuel (n=154)	p Value
ACE inhibitor or angiotensin receptor blocker	11 (4%)	10 (9%)	1 (1%)	<0.001
Aspirin	6 (2%)	6 (5%)	0 (0%)	0.005
Statin	5 (2%)	5 (4%)	0 (0%)	0.01
Insulin or metformin	3 (1%)	2 (2%)	1 (1%)	0.58
Bronchodilators	1 (<1%)	1 (1%)	0 (0%)	0.42

Data are presented as mean (SD) if normally distributed, median (IQR) if non-normally distributed and percentage if categorical variables.

HDL, high-density lipoprotein; HOMA-IR, Homeostasis model of assessment-insulin resistance; hsCRP, high sensitivity C-reactive protein; LDL, low-density lipoprotein.

Table 2

Unadjusted mean and maximum carotid intima-media thickness (CIMT) values and prevalence of atherosclerotic plaques by study group (clean vs biomass fuel)

	Unadjusted values, mean (SD) or %			
	Total (n=266)	**Clean fuel (n=112)**	**Biomass fuel (n=154)**	**p Value**
Mean CIMT, mm	0.63 (0.13)	0.60 (0.12)	0.66 (0.13)	<0.001
Maximum CIMT, mm	0.74 (0.14)	0.71 (0.14)	0.76 (0.14)	0.003
Prevalence of carotid artery atherosclerotic plaques (%)	21.1	14.3	26.1	0.03

Table 3

Multivariable linear regression models of mean carotid intima-media thickness (CIMT), maximum CIMT, systolic blood pressure and diastolic blood pressure and multivariable logistic regression of carotid artery plaque

	Coefficient	95% CI	p Value
Mean CIMT (mm)			
Age, years	0.006	0.005 to 0.007	<0.001
Gender, woman	0.01	−0.02 to 0.04	0.70
Systolic blood pressure, mm Hg	0.001	−0.001 to 0.002	0.10
LDL, mg/dl	0.0002	−0.001 to 0.001	0.39
HDL, mg/dl	0.001	−0.001 to 0.002	0.43
Body mass index, kg/m^2	−0.002	−0.005 to 0.001	0.25
HOMA-IR, mmol/l×μU/ml	0.002	−0.003 to 0.007	0.49
Antihypertensive medication use	0.04	−0.02 to 0.10	0.15
Chronic exposure to biomass fuels	0.03	0.01 to 0.06	0.02
Maximum CIMT (mm)			
Age, years	0.007	0.006 to 0.008	<0.001
Gender, woman	0.01	−0.02 to 0.04	0.58
Systolic blood pressure, mm Hg	0.001	−0.001 to 0.002	0.07
LDL, mg/dl	0.0002	−0.001 to 0.001	0.27
HDL, mg/dl	0.001	−0.001 to 0.002	0.39
Body mass index, kg/m^2	−0.002	−0.004 to 0.001	0.45
HOMA-IR, mmol/l×μU/ml	0.003	−0.01 to 0.01	0.37
Antihypertensive medication use	0.05	−0.01 to 0.11	0.16
Chronic exposure to biomass fuels	0.03	0.01 to 0.06	0.04
Systolic blood pressure (mm Hg)			
Age, years	0.52	0.37 to 0.67	<0.001
Gender, woman	−8.1	−11.6 to −4.6	<0.001
LDL, mg/dl	0.04	−0.01 to 0.09	0.11
HDL, mg/dl	0.04	−0.13 to 0.21	0.67
Body mass index, kg/m^2	0.59	0.10 to 1.08	0.02
HOMA-IR, mmol/l×μU/ml	0.64	−0.14 to 1.42	0.11
Antihypertensive medication use	6.6	−1.8 to 15.0	0.12
Chronic exposure to biomass fuels	9.2	5.4 to 13.0	<0.001
Diastolic blood pressure (mm Hg)			
Age, years	0.10	0.01 to 0.19	0.04
Gender, woman	−4.0	−6.2 to −1.8	<0.001
LDL, mg/dl	0.03	−0.01 to 0.06	0.11
HDL, mg/dl	0.01	−0.99 to 1.01	0.86
Body mass index, kg/m^2	0.62	0.31 to 0.93	<0.001
HOMA-IR, mmol/l×μU/ml	0.26	−0.23 to 0.75	0.29
Antihypertensive medication use	3.1	−2.1 to 8.3	0.25

	Coefficient	95% CI	p Value
Chronic exposure to biomass fuels	6.5	4.1 to 8.9	<0.001
	OR	95% CI	p Value
Carotid artery atherosclerotic plaque			
Age, years	1.08	1.05 to 1.12	<0.001
Gender, woman	0.55	0.27 to 1.11	0.10
Systolic blood pressure, mm Hg	1.00	0.97 to 1.02	0.80
LDL, mg/dl	1.01	1.00 to 1.02	0.08
HDL, mg/dl	0.97	0.94 to 1.00	0.08
Body mass index, kg/m^2	1.02	0.92 to 1.13	0.68
HOMA-IR, mmol/l×μU/ml	1.01	0.88 to 1.17	0.84
Antihypertensive medication use	1.66	0.40 to 6.8	0.48
Chronic exposure to biomass fuels	2.55	1.08 to 5.98	0.03

HDL, high-density lipoprotein; HOMA-IR, Homeostasis model of assessment-insulin resistance; LDL, low-density lipoprotein.