available. Third, although the pathology was examined by two experienced thoracic pathologists, the slides were reviewed by both pathologists concurrently; therefore, we cannot provide data on interobserver variability. Finally, as only limited follow-up is available, we cannot comment on the clinical outcomes associated with ILA or specific histopathologic findings within this cohort.

In conclusion, this study provides evidence that ILA—in particular, ILA with subpleural radiologic features—is most strongly associated with histopathologic findings of subpleural fibrosis as well as other histopathologic findings that are present in UIP. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Ezra R. Miller, M.D.*
Rachel K. Putman, M.D., M.P.H.*
Marina Vivero, M.D.
Yin Hung, M.D. Ph.D.
Tetsuro Araki, M.D., Ph.D.
Mizuki Nishino, M.D., M.P.H.
George R. Washko, M.D.
Ivan O. Rosas, M.D.
Hiroto Hatabu, M.D., Ph.D.
Lynette M. Sholl, M.D.
Gary M. Hunninghake, M.D., M.P.H.
*Brigham and Women's Hospital
Boston, Massachusetts*

*These authors contributed equally to this article.

ORCID ID: 0000-0002-8027-7450 (R.K.P.).

References

1. Raghu G, Collard HR, Egan JJ, Martinez FJ, Behr J, Brown KK, *et al.*; ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011;183:788–824.
2. Washko GR, Hunninghake GM, Fernandez IE, Nishino M, Okajima Y, Yamashiro T, *et al.*; COPDGene Investigators. Lung volumes and emphysema in smokers with interstitial lung abnormalities. *N Engl J Med* 2011;364:897–906.
3. Hunninghake GM, Hatabu H, Okajima Y, Gao W, Dupuis J, Latourelle JC, *et al.* MUC5B promoter polymorphism and interstitial lung abnormalities. *N Engl J Med* 2013;368:2192–2200.
4. Lederer DJ, Enright PL, Kawut SM, Hoffman EA, Hunninghake G, van Beek EJ, *et al.* Cigarette smoking is associated with subclinical parenchymal lung disease: the Multi-Ethnic Study of Atherosclerosis (MESA)-lung study. *Am J Respir Crit Care Med* 2009;180:407–414.
5. Podolanczuk AJ, Oelsner EC, Barr RG, Hoffman EA, Armstrong HF, Austin JH, *et al.* High attenuation areas on chest computed tomography in community-dwelling adults: the MESA study. *Eur Respir J* 2016;48:1442–1452.
6. Araki T, Putman RK, Hatabu H, Gao W, Dupuis J, Latourelle JC, *et al.* Development and progression of interstitial lung abnormalities in the Framingham Heart Study. *Am J Respir Crit Care Med* 2016;194:1514–1522.
7. Putman RK, Hatabu H, Araki T, Gudmundsson G, Gao W, Nishino M, *et al.*; Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators; COPDGene Investigators. Association between interstitial lung abnormalities and all-cause mortality. *JAMA* 2016;315:672–681.
8. Doyle TJ, Washko GR, Fernandez IE, Nishino M, Okajima Y, Yamashiro T, *et al.*; COPDGene Investigators. Interstitial lung abnormalities and reduced exercise capacity. *Am J Respir Crit Care Med* 2012;185:756–762.
9. Katzenstein AL. Smoking-related interstitial fibrosis (SRIF): pathologic findings and distinction from other chronic fibrosing lung diseases. *J Clin Pathol* 2013;66:882–887.
10. Araya J, Kawabata Y, Jinho P, Uchiyama T, Ogata H, Sugita Y. Clinically occult subpleural fibrosis and acute interstitial pneumonia a precursor to idiopathic pulmonary fibrosis? *Respirology* 2008;13:408–412.

Copyright © 2018 by the American Thoracic Society

Household Air Pollution Is Associated with Altered Cardiac Function among Women in Kenya

To the Editor:

Exposure to household air pollution from burning biomass fuels is a major environmental risk factor contributing to the global disease burden (1). The greatest number of deaths attributable to air pollution are related to cardiovascular disease (2, 3). Household air pollution exposure is particularly dire in sub-Saharan Africa, where the majority of homes burn solid fuel indoors for both cooking and heating purposes (4). We describe the cross-sectional association between household air pollution measures of carbon monoxide (CO) and fine particulate matter (particulate matter less than or equal to 2.5 μm in aerodynamic diameter, $\text{PM}_{2.5}$) and echocardiographic characteristics of cardiac structure and function among women in western Kenya; an earlier version was presented as an oral abstract (5).

Methods

We present a cross-sectional analysis of baseline data collected between December 2013 and November 2014 from 44 women enrolled in a prospective cook stove replacement study in Turbo subdivision, a rural agricultural community in western Kenya. Houses are constructed with mud, and the kitchen is generally a poorly ventilated, separate structure. Women cook indoors using a traditional open fire cook stove using locally acquired wood as fuel. Women at least 18 years of age spending a minimum of 4 hours per day in the kitchen, residing in the community for at least 6 months, and willing to allow household air pollution assessment in their home were included in the study. Active smokers and women with chest deformities prohibiting performance of an echocardiogram were excluded. The Institutional Review Boards of Duke, Stanford, and Moi universities approved the study, and all participants provided written informed consent.

Trained study staff collected baseline demographic, medical, and physical exam data on all participants. A research echocardiographer performed transthoracic echocardiograms using a Philips CX-50 ultrasound machine (Philips Healthcare) on

This study was supported by the Duke Global Health Institute, Doris Duke International Clinical Research Scholarship, Stanford University Medical Scholars Award, and the NHLBI (contract HHSN268200900031C).

Author Contributions: All authors contributed to this manuscript. Conception and design: A.A., D.M., S.S.M., E.J.V., R.V., and G.S.B.; analysis and interpretation: A.A., K.K., M.N.E., F.A., R.V., G.A.W., and G.S.B.; and drafting and editing the manuscript: A.A., K.K., F.A., S.S.M., E.J.V., R.V., G.A.W., and G.S.B.

Originally Published in Press as DOI: 10.1164/rccm.201704-0832LE on September 19, 2017.

participants after household air pollution measurements were collected. Cardiac chamber structure and function were assessed using dimensions, estimated pressure, ejection fraction, and myocardial speckle tracking imaging according to guidelines of the American Society of Echocardiography (6). Household air pollution measures included household CO, measured in parts per million, using the EasyLog USB CO Monitor (Lascar Electronics); and PM_{2.5}, measured in micrograms per cubic meter, using a nephelometric device (Personal Data Ram, 1000AN; Thermo Scientific) hung from the ceiling in the center of the kitchen by trained study staff. The equipment measures and records CO and PM_{2.5} levels in intervals of 1 minute. The median value of air pollution levels in the kitchen across at least 20 hours of recording time was used as a proxy for individual participant exposure specifically from their home cook stove. For each participant, we calculated the 24-hour median levels of CO and PM_{2.5} from these 1-minute averages to reduce the influence of transient high levels and outlier values.

We used linear regression models to assess the cross-sectional association between median 24-hour levels of CO and PM_{2.5} with baseline echocardiographic measures, adjusting for age, body mass index, and years of education (7). We assessed trends across tertiles of pollutants by assigning each tertile the median pollutant level within that tertile and including the term as a continuous variable in a regression model. Categorizing the exposure variable in tertiles facilitates clinical interpretation of the outcome echocardiographic variables and avoids assumptions about linearity of the concentration–response relationship. We

also modeled each natural log–transformed pollutant as a linear continuous variable. Analyses were performed in Revolution R Enterprise version 7.3 (Revolution Analytics).

Results

The mean age was 34.5 (SD, 6.4; range, 21–49) years with a mean body mass index of 25.1 (SD, 5.5; range, 16.4–40.4) kg/m². Participants reported using a traditional cook stove for a mean of 20.2 (SD, 7.4) years, and all used wood as the primary fuel. The median levels of CO and PM_{2.5} were 13.8 (interquartile range, 7.0–26.9) ppm and 57.0 (interquartile range, 32.0–83.1) µg/m³, respectively. Log median CO had a linear association with log median PM_{2.5} with a Pearson correlation coefficient of 0.61.

The majority of participants across all three tertiles of CO had a normal estimated right atrial pressure (Table 1). The mean tricuspid annular plane excursion and right ventricular systolic pressure were numerically higher in those in the highest tertile of CO but remained in clinically normal ranges. Mean left ventricular ejection fraction shifted progressively lower from 64.3% (SD, 4.6%) to 59.3% (SD, 7.8%) with higher levels of CO, and this difference was statistically significant in adjusted models (Figure 1). Results were similar in adjusted linear regression analyses considering log-CO as a linear continuous variable. Mean pulmonary arterial diastolic pressure was 9.1 (SD, 4.8) versus 6.3 (SD, 2.1) mm Hg in the highest versus

Table 1. Echocardiographic Characteristics of Participants, Overall and across Tertiles of CO

Echocardiographic Measure	Overall Mean ± SD or n (%)	Mean ± SD or n (%) within Tertiles of CO				Per IQR Increase in log CO [†]	
		Tertile 1 (N = 15) (3.0–8.7 ppm)	Tertile 2 (N = 14) (>8.7–18.8 ppm)	Tertile 3 (N = 15) (>18.8–89.0 ppm)	P _{Trend} *	Change (95% CI)	P Value
Right atrial minor axis, cm	4.0 ± 0.6	4.0 ± 0.6	4.1 ± 0.6	4.1 ± 0.7	0.50	0.06 (–0.24 to 0.35)	0.71
Right atrial pressure [‡]							
3 mm Hg	37 (84.1)	14 (93.3)	12 (85.7)	11 (73.3)	—	—	—
8 mm Hg	4 (9.1)	1 (6.7)	2 (14.3)	8 (6.7)	—	—	—
15 mm Hg	3 (6.8)	0 (0.0)	0 (0.0)	3 (20.0)	—	—	—
Right ventricular basal diameter, cm	3.0 ± 0.7	3.1 ± 0.8	3.1 ± 0.6	2.9 ± 0.7	0.31	–0.21 (–0.53 to 0.12)	0.21
Tricuspid annular plane excursion, cm	2.4 ± 0.5	2.3 ± 0.5	2.4 ± 0.4	2.5 ± 0.6	0.66	0.11 (–0.11 to 0.33)	0.32
Right ventricular systolic pressure, mm Hg	26.4 ± 7.0	22.5 ± 3.2	28.2 ± 8.8	28.3 ± 7.2	0.21	0.27 (–3.39 to 3.92)	0.89
Pulmonary arterial diastolic pressure, mm Hg	7.4 ± 3.6	6.3 ± 2.1	6.7 ± 2.7	9.1 ± 4.8	0.047	1.16 (0.55 to 2.87)	0.19
Mean pulmonary arterial pressure, mm Hg	14.1 ± 4.5	11.7 ± 2.0	14.2 ± 3.4	15.9 ± 5.5	0.084	0.92 (–1.53 to 3.36)	0.47
Left ventricular ejection fraction, %	62.3 ± 6.0	64.3 ± 4.6	63.2 ± 3.7	59.3 ± 7.8	0.002	–2.82 (–5.23 to –0.42)	0.027
Left ventricular global longitudinal strain, %	–21.0 ± 3.3	–21.4 ± 1.9	–21.6 ± 4.2	–20.3 ± 3.5	0.48	0.08 (–1.44 to 1.61)	0.92
Right ventricular global longitudinal strain, %	–22.5 ± 4.6	–23.8 ± 4.7	–22.4 ± 5.5	–21.4 ± 3.3	0.19	0.27 (–2.01 to 2.55)	0.82

Definition of abbreviations: CI = confidence interval; CO = carbon monoxide; IQR = interquartile range; ppm = parts per million.

*P value from the test for linear trend across tertiles of CO from linear regression models adjusted for age, body mass index, and education.

[†]Change in outcome comparing the upper versus lower quartiles of CO in linear regression models adjusted for age, body mass index, and education.

[‡]Three discrete categories of right atrial pressure are 3, 8, and 15 mm Hg (7).

Figure 1. Association between tertile of pollutant exposure and left ventricular ejection fraction. Higher levels of exposure to both carbon monoxide (CO) and particulate matter less than or equal to 2.5 μm in aerodynamic diameter (PM_{2.5}) are associated with reduced left ventricular ejection fraction (LVEF). Data are presented as mean (95% confidence interval).

lowest tertile of CO, with a statistically significant linear trend from the adjusted linear regression model ($P < 0.05$). No other statistically significant findings were observed. Results for PM_{2.5} were qualitatively similar, but the associations tended to be weaker.

Discussion

This study demonstrates that CO and PM_{2.5} levels are high inside homes using traditional cook stoves in western Kenya, and that higher CO levels are associated with both right and left heart abnormalities. The association between higher levels of household air pollution and echocardiographic abnormalities is stronger for CO compared with PM_{2.5}. This pilot study provides a novel and unique assessment of intermediate cardiovascular disease endpoints using echocardiography in rural sub-Saharan Africa.

The results of this study suggest that inhabitants of western Kenya may be at increased risk for cardiac dysfunction with increased cumulative exposure to household air pollution (8–10). CO itself at the observed levels may not be directly cardiotoxic but may serve as a useful indicator of a complex mixture of particles, gases, and volatile organic compounds from unvented burning of biomass fuels, which cumulatively have deleterious effects on cardiovascular health (11).

Echocardiographic measures of cardiac function reveal greater dysfunction among participants with the highest household air pollution. The increased pulmonary artery pressures in women with high household air pollution are possible harbingers of subsequent right heart failure, a major public health problem in sub-Saharan Africa (12). Higher levels of household air pollution were associated with reduced left ventricular ejection fraction, suggesting myocardial function may also be affected.

This study has several limitations. First, it may be challenging to detect an association between household air pollution levels and cardiac dysfunction because of the small sample size of this pilot study in women with no apparent clinical disease. Second, we

use kitchen pollutant levels as proxies for individual exposures to household air pollution (13). This may overestimate individual exposure, as the participant is not restricted to the kitchen for the entire duration of household air pollution level measurements. There may also be intrahousehold and seasonal variation in household air pollution levels in this region, which our study did not capture. Lastly, younger participants are less likely to manifest cardiovascular disease compared with older participants as a result of less cumulative exposure to household air pollution.

Traditional cooking practices continue to expose women in impoverished regions of the world to a high risk for cardiopulmonary disease (14). This study reveals an association between greater household air pollution levels and both right- and left-sided cardiac dysfunction, using echocardiography as a critical imaging biomarker of subclinical cardiovascular disease. This study fills an important gap in the current literature on the relationship between household air pollution and cardiopulmonary disease in low- and middle-income countries and suggests future areas of research inquiry. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Anubha Agarwal, M.D.
Duke University
Durham, North Carolina

Kipruto Kirwa, Ph.D.
Tufts University
Medford, Massachusetts

Melissa N. Eliot, Ph.D.
Brown University School of Public Health
Providence, Rhode Island

Fawaz Alenezi, M.D., M.Sc.
Duke University
Durham, North Carolina

Diana Menya, M.B. Ch.B., M.Sc.
Moi University
Eldoret, Kenya

Sumeet S. Mitter, M.D.
Icahn School of Medicine at Mount Sinai
New York, New York

Eric J. Velazquez, M.D.
Duke University
Durham, North Carolina

Rajesh Vedanthan, M.D., M.P.H.
Icahn School of Medicine at Mount Sinai
New York, New York

Gregory A. Wellenius, Sc.D.
Brown University School of Public Health
Providence, Rhode Island

Gerald S. Bloomfield, M.D., M.P.H.
Duke University
Durham, North Carolina

References

1. GBD 2015 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;388:1659-1724.
2. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017;389:1907-1918.
3. McCracken JP, Wellenius GA, Bloomfield GS, Brook RD, Tolunay HE, Dockery DW, et al. Household air pollution from solid fuel use: evidence for links to CVD. *Glob Heart* 2012;7:223-234.
4. Fullerton DG, Semple S, Kalambo F, Suseno A, Malamba R, Henderson G, et al. Biomass fuel use and indoor air pollution in homes in Malawi. *Occup Environ Med* 2009;66:777-783.
5. Kirwa K, Agarwal A, Bloomfield GS, Alenezi F, Eliot MN, Carter EJ, et al. Household air pollution from burning wood is associated with altered cardiac hemodynamics and function among women in western Kenya: results from the Kenya HAP study. Herndon, VA: International Society for Environmental Epidemiology; 2015 [accessed 2017 May 1]. Available from: <https://ehp.niehs.nih.gov/isee/2015-2522/>.
6. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;23:685-713.
7. Burroughs Peña MS, Velazquez EJ, Rivera JD, Alenezi F, Wong C, Grigsby M, et al. Biomass fuel smoke exposure was associated with adverse cardiac remodeling and left ventricular dysfunction in Peru. *Indoor Air* 2017;27:737-745.
8. Penney D, Benignus V, Kephelopoulous S, Kotzias D, Kleinman M, Verrier A. WHO guidelines for indoor air quality: selected pollutants. Geneva: World Health Organization; 2010;55-89 [accessed 2017 May 1]. Available from: http://www.euro.who.int/_data/assets/pdf_file/0009/128169/e94535.pdf
9. Mitter SS, Vedanthan R, Islami F, Pourshams A, Khademi H, Kamangar F, et al. Household fuel use and cardiovascular disease mortality: Golestan Cohort Study. *Circulation* 2016;133:2360-2369.
10. Klasen EM, Wills B, Naithani N, Gilman RH, Tielsch JM, Chiang M, et al; COCINAS Trial Working Group. Low correlation between household carbon monoxide and particulate matter concentrations from

biomass-related pollution in three resource-poor settings. *Environ Res* 2015;142:424-431.

11. Allred EN, Bleecker ER, Chaitman BR, Dahms TE, Gottlieb SO, Hackney JD, et al. Short-term effects of carbon monoxide exposure on the exercise performance of subjects with coronary artery disease. *N Engl J Med* 1989;321:1426-1432.
12. Stewart S, Wilkinson D, Hansen C, Vaghela V, Mvungi R, McMurray J, et al. Predominance of heart failure in the Heart of Soweto Study cohort: emerging challenges for urban African communities. *Circulation* 2008;118:2360-2367.
13. Carter E, Norris C, Dionisio KL, Balakrishnan K, Checkley W, Clark ML, et al. Assessing exposure to household air pollution: a systematic review and pooled analysis of carbon monoxide as a surrogate measure of particulate matter. *Environ Health Perspect* 2017; 125:076002.
14. Alexander D, Northcross A, Wilson N, Dutta A, Pandya R, Ibigbami T, et al. Randomized controlled ethanol cookstove intervention and blood pressure in pregnant Nigerian women. *Am J Respir Crit Care Med* 2017;195:1629-1639.

Copyright © 2018 by the American Thoracic Society

The Epworth Sleepiness Scale: Minimum Clinically Important Difference in Obstructive Sleep Apnea

To the Editor:

The Epworth Sleepiness Scale (ESS) is a self-administered questionnaire that quantifies daytime sleepiness, with higher scores indicating increased daytime hypersomnolence (1). Although it is frequently used as an endpoint in intervention trials of patients with obstructive sleep apnea syndrome (2, 3), the minimum clinically important difference (MCID) of the ESS has not been established.

In a prospective service evaluation of 125 consecutive patients with obstructive sleep apnea syndrome (apnea-hypopnea index [4], or $\geq 4\%$ oxygen desaturation index, >7.5 events/h, and symptoms of daytime tiredness and hypersomnolence) offered continuous positive airway pressure (CPAP), ESS was measured at baseline and follow-up (3-months post-CPAP initiation). At follow-up, patients were asked, "Compared with your last visit (before treatment), how would you describe the change in your daytime sleepiness?" Responses were recorded using a seven-point Likert global rating of change in sleepiness questionnaire ("1: Much less sleepy" to "7: Much more sleepy," with "4: No change") (5).

Distribution- and anchor-based methods were used to estimate the MCID of the ESS. For distribution-based methods, we calculated half the SD (0.5SD) (6) and the SE of measurement (7), using the equation:

This work was supported by the National Institute for Health Research (NIHR) Respiratory Biomedical Research Unit at the Royal Brompton and Harefield NHS Foundation Trust and Imperial College, London, United Kingdom, who fund or part fund S.P., R.E.B., and A.K.S. C.M.N. is supported by an NIHR Doctoral Fellowship. W.D.-C.M. was supported by an NIHR Clinician Scientist Award, Medical Research Council (UK) New Investigator Research Grant, NIHR Clinical Trials Fellowship, and the NIHR Collaboration for Leadership in Applied Health Research and Care Northwest London (CLAHRC) for Northwest London. The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR, or the Department of Health.

Originally Published in Press as DOI: 10.1164/rccm.201704-0672LE on September 29, 2017.