Greater Odds for Angina in Uranium Miners Than Nonuranium Miners in New Mexico

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Objective: The aim of this study was to test the hypothesis that uranium miners in New Mexico (NM) have a greater prevalence of cardiovascular disease than miners who extracted the nonuranium ore. **Methods:** NM-based current and former uranium miners were compared with nonuranium miners by using cross-sectional standardized questionnaire data from the Mining Dust in the United States (MiDUS) study from 1989 to 2016. **Results:** Of the 7215 eligible miners, most were men (96.3%). Uranium miners ($n = 3151$, 43.7%) were older and diabetic, but less likely to currently smoke or use snuff ($P \leq 0.001$ for all). After adjustment for covariates, uranium miners were more likely to report angina (odds ratio 1.51, 95% confidence interval 1.23 to 1.85) than nonuranium miners. **Conclusion:** Our data suggest that along with screening for pulmonary diseases, uranium industry workers should be screened for cardiovascular diseases.

Learning Objectives

- Become familiar with the occupational health risks associated with uranium mining, and with emerging research on cardiovascular risks associated with radiation exposure.
- Summarize the new findings on the risks of cardiovascular outcomes in uranium miners in New Mexico, compared to non-uranium miners.
- Discuss the implications for health screening and follow-up in this occupational group.

Cardiovascular disease is the leading cause of death in both men and women in the United States (U.S.), amounting to 610,000 deaths in 2015.[1,2] It is the leading cause of death among blacks, Hispanics, and non-Hispanic whites, but is second to cancer among American Indians or Alaska natives as well as Asians or Pacific Islanders.[1] The estimated cost of heart disease in the U.S. is $200 billion annually, which includes the cost of health care services, medications, and lost productivity.[1] Obtaining a history of patients' medical problems and lifestyle habits can help decipher what preventive measures are needed to reduce risk factors for cardiovascular diseases. Risk factors such as tobacco use, diabetes mellitus, dyslipidemia, and obesity are the most universally known and well-studied causes of cardiovascular diseases.[1] One important risk factor that has not been highlighted in the public arena is radiation exposure.

Radiation exposure has been studied extensively as a cause for pulmonary fibrosis, hematological disorders, and certain cancers.[3–7] There is also a growing number of studies showing that high-dose ionizing radiation exposure in environmental and therapeutic settings increases the risk for cardiovascular diseases.[8–10] Among Japanese atomic bomb survivors, acute whole-body irradiation was associated with an increased risk for cardiovascular diseases with a linear dose response and a latency of approximately 10 years.[11–15] Similarly, therapeutic chest irradiation, which involves high-dose ionizing radiation, among patients with lymphoma or different solid tumor cancers, also increases the risk for cardiovascular diseases.[16–18] Occupational exposures to radiation, which are generally at lower doses but over longer durations than atomic bomb and therapeutic radiation exposure, have been inconsistently associated with cardiovascular diseases.[19–22] Mining, processing, and transporting uranium ore, associated with occupational exposure to radiation, have been investigated as a risk factor for cardiovascular disease, but current literature is inconclusive, constituting a critical gap in this field.[21,23–28]

One of the richest uranium ore deposits in the U.S. is located in northwestern New Mexico (NM), an area that was extensively mined between 1949 and 1989, produced more than 225 million tons of ore during that period. Although much lower in amount, the U.S. continues to produce uranium amounting to 1125 tons in 2016.[29] Uranium workers, due to the long latency period involved, continue to suffer from malignant and nonmalignant respiratory health effects: the latter including chronic obstructive pulmonary disease (COPD), pneumoconiosis/silicosis, and pulmonary fibrosis.[25,30] American Indians are disproportionately affected with an elevated standardized mortality ratio of 2.6 found in Navajo uranium workers for nonmalignant respiratory diseases.[31] Our objective was to examine the risk for cardiovascular diseases in uranium workers. We hypothesized that NM uranium workers have a higher prevalence of cardiovascular diseases relative to workers who extracted other minerals from the ground and were able to assess this in screening data from NM miners.

METHODS

Study Design

In this cross-sectional study, we used data obtained from the NM-based Mining Dust in the United States (MiDUS) study from 1989 to 2016. The MiDUS study recruits current or former workers employed in the NM mining industry who voluntarily undergo medical surveillance. These surveillance activities are performed using a mobile outreach clinic, organized by rotation in each of the 20 rural NM communities with a high concentration of miners. This surveillance program is jointly run by Miners' Colfax Medical Center (MCMC) at Raton, NM, and the University of New Mexico

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(UNM) School of Medicine at Albuquerque, NM, and is supported by the New Mexico Black Lung Clinics Grant funded by the Health Resources and Services Administration. Data collected at baseline evaluation were examined.

Inclusion Criteria

The study included all those employed in the mining industry for at least 1 year who also participated in the above-mentioned clinical surveillance initiative.

Study Methods

Upcoming mobile clinics are advertised in the target rural communities through print, media, and radio, as well as by working with community/church leaders and mine safety officers. Patients can also self-refer themselves for screening evaluations. Participants are not charged out-of-pocket expenses for their screening clinic visit, which takes approximately 1 hour to complete. At each mobile screening clinic, miners are assessed for respiratory, hearing, and musculoskeletal disorders associated with mining-related exposures. Assessment also includes common health conditions such as lung diseases and exposures such as tobacco use.

The mobile screening clinic is held in a specially outfitted trailer, which is 53 feet long with a diesel generator to supply power. The clinic consists of five separate areas, including a patient reception area, a digital chest x-ray unit, sound-proof audiometry booth, spirometry room, and an examination room. The staffing model in the mobile screening clinic consists of a mid-level provider (ie, a physician assistant or nurse practitioner), a radiology/audiometry technician, and a medical assistant/nursing technician who is certified by the National Institute of Occupational Safety and Health (NIOSH) for performing spirometry. Race and ethnicity-specific predicted values were used for non-Hispanic whites and Hispanics. Crapo American Indian reference standards was used for American Indians.[32,33]

Before the screening examination, patients complete a comprehensive occupational and clinical history intake form, based on the adult American Thoracic Society Diffuse Lung Disease 1978 (ATS DLD-78) Questionnaire.[34] The questionnaire responses are reviewed and confirmed by the mid-level clinical provider. The screening visit includes a vital sign assessment, including a blood pressure assessment at rest and measurement of standing height and weight without shoes, pre-bronchodilator spirometry using ATS guidelines, audiometry, and a standard posterior-anterior chest radiograph. A complete history and physical examination is performed by a mid-level provider who develops a treatment and care plan for the patient depending on the primary diagnosis. The records are reviewed for quality by a UNM-based preventive medicine and pulmonary medicine specialist.

Exposure

Exposure status was classified as those who were ever employed with the uranium mining industry (termed uranium miners in this study) versus those who were never similarly employed, but instead worked with extracting and processing other minerals such as coal, metal, and nonmetals (termed nonuranium miners).

Outcomes

Study outcomes included self-reported history of physician diagnosed angina, myocardial infarction, cerebrovascular events and hypertension, as well as measured systolic or diastolic hypertension. For self-reported angina, myocardial infarction, cerebrovascular events, and hypertension, the subjects were asked the following questions:

(1) Has a doctor ever told you that you have angina or chest pain from your heart?
(2) Has a doctor ever told you that you had a heart attack?
(3) Have you ever had a cerebrovascular accident?
(4) Have you ever had high blood pressure/hypertension?

Measured hypertension was defined as either systolic blood pressure at least 140 mm Hg or diastolic blood pressure at least 90 mm Hg, measured by either a manual blood pressure cuff (sphygmomanometer) or automatic blood pressure cuff, in a resting sitting position. Severe hypertension or hypertensive urgency, a subset of measured hypertension, was defined as either systolic blood pressure at least 180 mm Hg or diastolic blood pressure at least 110 mm Hg.

Covariates

Selection of covariates was based upon known biological and/or mechanistic plausibility of each variable's role as a potential confounder in evaluating the risk for cardiovascular disease. Covariates in multivariable analysis model 1 included age, sex, race/ethnicity, body mass index (BMI), self-reported diabetes mellitus, current cigarette smoking status, current snuff use status, current alcohol use status, and total mining tenure. Current snuff user was defined as a subject who reported having ever used snuff or chewing tobacco for at least a week or more and had used it within the prior 6 months. Current alcohol user was defined as a subject who reported having consumed alcohol within the prior 24 hours. Total mining tenure was used as a continuous variable. The correlation between age and total mining tenure was modest at 0.33. The variance inflation factors for miners' age and total mining tenure was 1.24 and 1.19 respectively, which was small. It is therefore reasonable to include both variables in the multivariable analysis. In addition, statistical model 2 included prebronchodilator forced expiratory volume in 1 second (FEV_1) as a covariate. Reliable information on lipid disorders was not available and therefore not used as a covariate. The multivariable analysis of cardiovascular outcomes also included self-reported hypertension or measured hypertension as an additional covariate.

Statistical Analysis and IRB Approval

Chi-square and Student *t* test were utilized for univariate analysis of categorical and continuous outcomes respectively. For the Chi-square test, a 2 by 2 test for each variable was created with the two categories of (uranium vs nonuranium) miners. Logistic regression (PROC LOGISTIC function) was used for multivariable analysis. Formal two-way tests of interaction were separately performed between uranium mining exposure and underground mining/mining tenure/smoking variables on the outcome "angina." Data were analyzed using Statistical Analysis Software (SAS) 9.4 version (Cary, North Carolina) with two-tailed *P* values less than 0.05 considered significant.

This study was approved by the University's Human Research Protection Office Institutional Review Board (HRPO 14–058) that also approved a waiver of consent from participants.

RESULTS

Table 1 demonstrates the distribution of select characteristics, many known to be associated with risk for cardiovascular disease, among all eligible uranium ($n = 3151$ or 43.7%) and nonuranium miners ($n = 4064$ or 56.3%). The two groups of miners had a similar gender distribution, which both were predominantly male. Relative to nonuranium miners, uranium miners were older, less educated, and more likely to be American Indian; however, reported lower pack years of smoking. They were also less likely to be current miners and current smokers or snuff or alcohol users ($P \leq 0.001$ for all). Uranium miners had fewer years of mining tenure and were more likely to be employed in underground mining activities than nonuranium miners ($P < 0.001$). Despite a lower

TABLE 1. Comparison of Characteristics Between Uranium and Nonuranium Miners, $N = 7{,}215$, 1989–2016; MiDUS Cohort

Characteristic	All Miners $N = 7{,}215$ N (%) or Mean ± SD	Nonuranium Miners $N = 4{,}064$ N (%) or Mean ± SD	Uranium Miners $N = 3{,}151$ N (%) or Mean ± SD	P
Male sex	6,946 (96.3%)	3,897 (95.9%)	3,049 (96.8%)	0.05
Age, years	55.0 ± 14.3	51.9 ± 15.7	59.0 ± 11.1	<0.001
BMI, kg/m^2	28.8 ± 5.0	29.2 ± 5.2	28.3 ± 4.7	<0.001
≥ High school education	3,090 (42.8%)	2,100 (51.7%)	990 (31.4%)	<0.001
Race/ethnicity				
(missing)	134 (1.9%)	87 (2.1%)	47 (1.5%)	
Non-Hispanic white	2,071 (28.7%)	1,586 (39.0%)	485 (15.4%)	
Hispanic	2,627 (36.4%)	1,742 (42.9%)	885 (28.1%)	<0.001
Black	39 (0.5%)	23 (0.6%)	16 (0.5%)	
American Indian	2,342 (32.5%)	624 (15.4%)	1,718 (54.5%)	
Other	2 (0.0)	2 (0.0)	0 (0)	
Smoking status				
(missing)	85 (1.2%)	25 (0.6%)	60 (1.9%)	
Never	3,424 (47.5%)	1,832 (45.1%)	1,592 (50.5%)	<0.001
Former	2,406 (33.3%)	1,383 (34.0%)	1,023 (32.5%)	
Current	1,300 (18.0%)	824 (20.3%)	476 (15.1%)	
Pack-years of smoking (for current and former smokers)	10.2 ± 19.5	11.2 ± 19.9	8.7 ± 18.8	<0.001
Snuff user				
(missing)	619 (8.6%)	47 (1.2%)	572 (18.2%)	
Never	4,713 (65.3%)	2,806 (69.0%)	1,907 (60.5%)	
Former	1,148 (15.9%)	676 (16.6%)	472 (15.0%)	<0.001
Current	735 (10.2%)	535 (13.2%)	200 (6.3%)	
Alcohol intake				
(missing)	630 (8.7%)	53 (1.3%)	577 (18.3%)	
Never	779 (10.8%)	392 (9.6%)	387 (12.3%)	<0.001
Former	4,922 (68.2%)	3,035 (74.7%)	1,887 (59.9%)	
Current	884 (12.3%)	584 (14.4%)	300 (9.5%)	
Current miner status	2,046 (28.4%)	1,895 (46.6)	151 (4.8%)	<0.001
Mining location				
(missing)	1,731 (24.0%)	1,546 (38.0%)	185 (5.9%)	
Below ground mining	2,629 (36.4%)	724 (17.8%)	1,905 (60.5%)	
Above ground/open pit mining	1,812 (25.1%)	1,296 (31.9%)	516 (16.4%)	<0.001
Both below and above ground mining	1,043 (14.5%)	498 (12.3%)	545 (17.3%)	
Total mining tenure, years	15.0 ± 11.9	16.7 ± 12.6	13.5 ± 11.0	<0.001
Uranium mining tenure				
Unknown/no exposure	4,187 (58.0%)		123 (3.9%)	
1–4 years	926 (12.8%)		926 (29.4%)	
5–9 years	780 (10.8%)		780 (24.8%)	NA
≥10 years	1,322 (18.3%)		1,322 (42.0%)	
Total mining tenure category				
(missing)	1,540 (21.3%)	1,415 (34.8%)	125 (4.0%)	
1–4 years	1,173 (16.3%)	497 (12.2%)	676 (21.5%)	<0.001
5–9 years	1,057 (14.7%)	388 (9.5%)	669 (21.2%)	
≥10 years	3,445 (47.7%)	1,764 (43.4%)	1,681 (53.3%)	
FEV_1, L	3.2 ± 0.9	3.4 ± 0.9	3.1 ± 0.8	<0.001
FEV_1% predicted	97.0 ± 20.0	97.6 ± 19.7	96.3 ± 20.2	0.0037
Self-reported COPD/chronic bronchitis/emphysema	873 (12.1%)	472 (11.6%)	401 (12.7%)	<0.001
Self-reported COPD/chronic bronchitis/emphysema (missing)	629 (8.7%)	50 (1.2%)	579 (18.4%)	
Self-reported asthma	663 (9.2%)	405 (10.0%)	258 (8.2%)	0.95
Self-reported asthma (missing)	643 (8.9%)	57 (1.4%)	586 (18.6%)	
Self-reported diabetes mellitus	992 (13.7%)	507 (12.5%)	485 (15.4%)	<0.001
Self-reported diabetes mellitus (missing)	940 (13.0%)	287 (7.1%)	653 (20.7%)	

Missing data were noted among the 7,215 miners for the following continuous variables: age ($n = 20$ or 0.3%); BMI ($n = 87$ or 1.2%); pack-years of smoking ($n = 357$ or 4.9%); FEV_1 ($n = 448$ or 6.2%); and FEV1 percent predicted ($n = 476$ or 6.6%). Missing data for total mining tenure (continuous variable) are provided in the row for the categorical variable total mining tenure.

mean BMI, uranium miners had a significantly higher prevalence of self-reported diabetes mellitus than nonuranium miners ($P < 0.001$). Absolute and percent predicted FEV_1 values were also lower and self-reported prevalence of COPD was higher in uranium miners than in nonuranium miners ($P < 0.001$).

Uranium miners were significantly more likely than nonuranium miners to self-report hypertension, even after adjustment for covariates (Models 1 and 2, Table 2). Uranium miners were significantly more likely to have measured hypertension in the unadjusted model, but this association was reversed, when

TABLE 2. Association Between Uranium Mining Exposure and Hypertension, $N = 7{,}215$; 1989–2016; MiDUS Cohort

Cardiovascular Outcomes	Uranium Miners $N = 3{,}151$ N (%)	Nonuranium Miners $N = 4{,}064$ N (%)	Unadjusted Model OR (95% CI)	Multivariable Model 1* OR (95% CI)	Multivariable Model 2* OR (95% CI)
Self-reported hypertension	1,099 (44.4%)	1,254 (33.6%)	1.58 (1.42–1.75)	1.43 (1.24–1.66)	1.42 (1.22–1.65)
Measured hypertension	1,339 (43.3%)	1,329 (33.5%)	1.51 (1.37–1.67)	0.85 (0.74–0.97)	0.88 (0.77–1.02)
Hypertensive urgency	17 (0.5%)	21 (0.5%)	1.04 (0.55–1.97)	0.53 (0.20–1.38)	0.51 (0.19–1.37)

CI, confidence interval; OR, odds ratio.
*Multivariable analysis model 1 was adjusted for age, sex, race/ethnicity, diabetes mellitus, BMI, current smoking status, current snuff use status, current alcohol use status, and duration of total mining tenure. Model 2 additionally adjusted for absolute FEV_1 as a covariate. The missing data for total mining tenure are included in order to keep sample size among analyses consistent.

adjustment was made for covariates, indicating that this association was explained by confounding variables.

Uranium miners were also more likely to self-report angina, myocardial infarction, and cerebrovascular event. In the multivariable model adjusting for self-reported hypertension, only the association with angina remained consistently significant (Table 3). In the multivariable model adjusting for measured hypertension, the association with angina and myocardial infarction remained significant (Table 4).

In unadjusted interaction analyses, underground mining and longer mining tenure were disproportionately associated with higher odds of self-reported angina in nonuranium miners than in uranium miners (interaction $P = 0.004$ and $P < 0.001$, respectively). As compared to never smoking, former smoking was disproportionately associated with self-reported angina among nonuranium miners than uranium miners (interaction $P = 0.002$). The adjusted interaction analyses confirmed differential angina association for nonuranium miners with smoking status ($P = 0.04$) but not with mining location ($P = 0.89$) or mining tenure ($P = 0.50$).

DISCUSSION

Our cross-sectional study indicates that exposure to uranium mining is associated with greater odds for angina than exposure to nonuranium mining. This association is not fully explained by the older age and higher prevalence of diabetes mellitus in uranium miners, who also had lower BMI, lower nicotine use, and lower duration of mining tenure than nonuranium miners.

Kreuzer et al[21] utilized the German Wismut cohort, the largest cohort of uranium miners in the world, in assessing the risk for cardiovascular and cerebrovascular death in uranium miners. The results of their 2006 study showed that there was no significant increase in cardiovascular mortality among uranium miners.[21] A Canadian group headed by Villeneuve et al[23] reviewed the Newfoundland fluorspar mining cohort in order to validate the previous study by Kruezer et al,[21] with results being consistent with a nonsignificant excess risk for cardiovascular mortality. Drubay et al[24] studied French uranium miners in assessing the exposure risk of external gamma rays and radon on cardiovascular and cerebrovascular disease mortality by the use of the French National Vital Statistics Registry. These results again showed that there was no significant increase in cardiovascular death rates among uranium miners; there was however a significantly higher risk of cerebrovascular mortality. On the contrary, a study of nonwhite uranium miners, predominantly Navajo, in the Colorado Plateau Study group, found that the standardized mortality rate from cardiovascular causes was significantly lower than the mortality rates for nonwhites.[31] In a 1991 cross-sectional study, Samet et al[35] examined a relatively young group of NM underground uranium miners and noted that their observed death rate from circulatory causes, as identified on death certificate, was significantly lower than that expected for the general population, with a standardized mortality ratio of 0.6 [95% confidence interval (95% CI) 0.4 to 0.8]. These studies, like our own, did not directly measure occupational uranium exposure or even the exposure to particulate matter that they were studying but estimated cumulative radiation exposure. Another weakness of these studies is the unreliability of death certificates in helping to define the cardiovascular cause of death outside the hospital.[36] Data indicate that clinical diagnoses certified in death certificate, and later found to disagree with autopsy findings were most frequent for cerebrovascular and cardiovascular disease.[37] Our approach of documenting self-reported questionnaire-based physician diagnosis of cardiovascular diseases and measured hypertension among living miners may be more accurate than data abstracted from death certificates. Most studies compared uranium miners with the general population, an approach that is limited by the healthy worker effect, whereby workers may exhibit lower overall morbidity and mortality rates than the general population because the severely ill and chronically disabled are ordinarily excluded from taxing jobs or suffer attrition from the work force.[38] By comparing uranium miners to miners involved in other extractive industries, our

TABLE 3. Association Between Uranium Mining Exposure and Vascular Diseases, $N = 7{,}215$; 1989–2016; MiDUS Cohort

Cardiovascular Outcomes	Uranium Miners $N = 3{,}151$ N (%)	Nonuranium Miners $N = 4{,}064$ N (%)	Unadjusted Model OR (95% CI)	Multivariable Model 1* OR (95% CI)	Multivariable Model 2* OR (95% CI)
Self-reported angina	655 (21.3%)	390 (10.2%)	2.40 (2.10–2.75)	1.61 (1.32–1.97)	1.51 (1.23–1.85)
Self-reported myocardial infarction	378 (13.5%)	274 (7.2%)	2.02 (1.72–2.38)	1.35 (1.05–1.73)	1.25 (0.98–1.61)
Self-reported cerebrovascular event	141 (5.9%)	113 (3.8%)	1.58 (1.23–2.04)	1.10 (0.79–1.53)	1.06 (0.76–1.49)

Covariates include self-reported hypertension.
CI, confidence interval; OR, odds ratio.
*Multivariable analysis model 1 was adjusted for age, sex, race/ethnicity, diabetes mellitus, BMI, self-reported hypertension, current smoking status, current snuff use status, current alcohol use status, and duration of total mining tenure. Model 2 additionally adjusted for absolute FEV_1 as a covariate. The missing data for total mining tenure are included in order to keep sample size among analyses consistent.

TABLE 4. Association Between Uranium Mining Exposure and Vascular Diseases, $N = 7{,}215$; 1989–2016; MiDUS Cohort

Cardiovascular Outcomes	Uranium Miners N = 3,151 N (%)	Nonuranium Miners N = 4,064 N (%)	Unadjusted Model OR (95% CI)	Multivariable Model 1* OR (95% CI)	Multivariable Model 2* OR (95% CI)
Self-reported angina	655 (21.3%)	390 (10.2%)	2.40 (2.10–2.75)	1.68 (1.37–2.06)	1.57 (1.28–1.93)
Self-reported myocardial infarction	378 (13.5%)	274 (7.2%)	2.02 (1.72–2.38)	1.42 (1.11–1.82)	1.33 (1.04–1.71)
Self-reported cerebrovascular event	141 (5.9%)	113 (3.8%)	1.58 (1.23–2.04)	1.08 (0.78–1.51)	1.05 (0.75–1.48)

Covariates include measured hypertension.
CI, confidence interval; OR, odds ratio.
*Multivariable analysis model 1 was adjusted for age, sex, race/ethnicity, diabetes mellitus, BMI, measured hypertension, current smoking status, current snuff use status, current alcohol use status, and duration of total mining tenure. Model 2 additionally adjusted for absolute FEV_1 as a covariate. The missing data for total mining tenure are included in order to keep sample size among analyses consistent.

study minimizes the healthy worker effect. Depending on the mean miner age in individual studies, cardiovascular morbidity may be a more sensitive measure than mortality, even if there will be an eventual cardiovascular cause of death. Given that excess mortality from cancers has clearly been demonstrated for uranium miners, excess cardiovascular morbidity may not lead to significant excess cardiovascular mortality.[35]

A limited cross-sectional analysis of disease morbidity among 2835 NM miners screened during 2004 to 2014 in the MiDUS study has been previously published by Shumate et al.[39] As compared to the study by Shumate et al[39] that compared across various sectors of miners, our current analysis includes a larger number of miners accrued over a longer timeframe in a binary categorical analysis, and therefore has greater power. Similar to our current analysis, Shumate et al[39] showed a significantly higher prevalence of self-reported hypertension among uranium miners than other miners. Although the odds for having angina and heart attack in the study by Shumate et al[39] was higher in uranium miners, these associations did not reach statistical significance after adjusting for covariates including self-reported hypertension.[39] A potential weakness of previously published studies of miners, including that by Shumate et al,[39] is inadequate adjustment for the confounding effect of low FEV_1 value. It has been previously reported that low FEV_1 ranks second to smoking and above blood pressure and cholesterol as a predictor of cardiovascular mortality.[40] Our study however demonstrated that the pattern of significant outcomes did not differ much with and without adjustment for FEV_1 in Tables 2 and 3, except in the case of self-reported myocardial infarction where the association lost statistical significance after additional adjustment for FEV_1.

Studies linking nonoccupational uranium exposure to cardiovascular disease provide supportive evidence for our findings without establishing causality.[41] A recent study highlighted the effects of inhalational environmental uranium exposure on cardiovascular disease outcomes among Navajo community members who live in close proximity to abandoned uranium mines in NM.[41] Primary human coronary artery endothelial cells treated for 4 hours with serum provided by Navajo study participants revealed that proximity to abandoned uranium mine strongly predicted endothelial transcriptional responses to serum cell adhesion molecules and chemokines (including CCL2, VCAM-1, and ICAM-1), suggesting inflammatory potential associated with residential proximity to abandoned uranium mines.[41] The upregulation of these cell adhesion molecules and chemokines by endothelial cells has been shown to play a role in the multistep process leading to cardiovascular diseases.[42] Although our study does not demonstrate causation, it is possible that uranium miners exhibit similar inflammatory endothelial responses and this possibility needs further research.

Most studies pertaining to the radiation effect on the cardiovascular system involve doses above 2 Gy. Radiation-specific mechanisms at low doses of exposure are as yet unclear, although there is evidence pointing to vascular structures and tissues of the heart as possible initiating targets.[22] Basic research has shown that exposure to particulate matter during mining causes endothelial inflammation and dysfunction in both myocardial tissues and peripheral blood vessels, thus a mechanism to explain the increased of risk of hypertension and cardiovascular diseases in miners.[41] An increased thickness of the intima in irradiated arteries and an increase in proteoglycan deposition in the media has been demonstrated.[43] Radiation also induces functional changes in the endothelium by increasing production of inflammatory eicosanoids and von Willebrand factor and decreased production in thrombomodulin and adenosine diphosphatase.[44]

The strengths of our study include its large sample size and the use of a control population that was occupationally exposed to similar agents except radiation, reducing the possibility of healthy worker effect.[38] Our study included a significant proportion of American Indian and Hispanic miners, thus increasing the generalizability of this study to minority populations. Additional strength includes community-based recruitment of study subjects without charge to them. As compared to hospital-based recruitment, our recruitment strategy allows for greater geographic and socioeconomic inclusion as well as avoidance of Berkson bias.

The limitations of our study include absence of occupational radiation and silica exposure measurements; absence of direct measurement of uranium concentrations via urine sampling; possible confounding from environmental radiation exposure from uranium tailings in and near homes; and information bias based upon self-report of vascular outcomes. Some studies have utilized a job-exposure matrix to obtain estimates on exposure without direct measurement. However, that would be difficult in the present study due to the history of remote uranium mining and associated recall bias. Urine samples for uranium testing were not collected, as the mobile screening clinic lacks this capability, and the study lacks the resources for the same.[45] Several of our study outcomes rested largely on self-report of previously physician-diagnosed health outcomes. Our study assumes that all miners are equally likely to have received a physician diagnosis. However, some health hazards associated with uranium mining are well known, and uranium miners may receive significantly more medical scrutiny than do other miners, such as through the Radiation Exposure Screening and Education Program (RESEP). This might increase the likelihood that uranium miners receive a physician diagnosis of cardiovascular disease or hypertension. This is however unlikely, as our screening activity was funded by the New Mexico Black Lung and not the RESEP program, and therefore, a reverse bias against uranium miners might be possible. Further, due to the greater awareness of the risks of uranium mining, it is possible that uranium miners themselves sought health care with primary care providers to a greater extent, were more likely to recall diagnoses, or had greater familiarity with the medical terms used in the question. This is less likely, as uranium miners in our study were significantly less educated than other miners (Table 1). Nevertheless, molecular and imaging studies looking at biomarkers of cardiovascular disease in occupational cohorts will be helpful. Uranium miners are disproportionately American Indian, a group known to have a high prevalence of chronic health conditions including cardiovascular diseases.[46] It is however unlikely that race and ethnicity explains away our findings, as this was included as a covariate in our multivariable statistical model. Our study did not have data on and therefore could not adjust for dyslipidemia, an important risk factor for cardiovascular disease. There are many ways in which an opt-in community clinic screening can lead to selection bias based on who chooses to report for screening evaluations. For instance, retired miners are more likely to report for screening than current miners. Given the drop off in uranium mining in NM, uranium miners of the same age are more likely to be retired or underemployed and have more time to report than nonuranium miners. Sicker workers are often assumed to be more likely to report to such a clinic, further contributing to selection bias.

Low lung function is a risk factor for cardiovascular diseases.[40] Although uranium miners had a lower FEV_1 than nonuranium miners, the inclusion of FEV_1 in the multivariable analysis model in Table 2 did not significantly change the results for angina. Miners are typically screened for pulmonary diseases such as COPD and pneumoconiosis, due to significant data on the association of these diseases with mining and recent reports of increasing prevalence of pneumoconiosis among miners.[47] Due to limited data on cardiovascular risk in miners, monitoring for cardiovascular disease has not been enforced during surveillance. However, our study provides evidence for further research on cardiovascular disease monitoring in uranium miners.

CONCLUSION

Our data conclude that NM uranium miners are more likely to demonstrate angina than nonuranium miners, after adjustment for covariates. This is the first study that we are aware of to demonstrate an association between cardiovascular disease and occupational radiation exposure. In conclusion, our data suggest that while screening for pulmonary diseases in uranium miners is well established, further research on cardiovascular disease monitoring is needed.

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