Critical Limb Ischemia Related to Toxic Metal Levels in the Strong Heart Study

COLUMBIA | VAGELOS COLLEGE OF PHYSICIANS & SURGEONS
PROGRAM FOR EDUCATION IN GLOBAL AND POPULATION HEALTH

Kishan Bhatt, MPA – Columbia University, VP&S, Class of 2025
Filippo Ravalli; Marta Galvez-Fernandez, MD; Ana Navas-Acien, MD, PhD

Research Question: What is the association between toxic metal exposure and amputation status among American Indian communities in the Strong Heart Study?

BACKGROUND

- Toxic metal exposure has been associated with peripheral artery disease (PAD) and diabetes among American Indian (AI) communities in the Strong Heart Study.
- The most advanced stage of PAD is critical limb ischemia (CLI) of the lower limbs, and its poor long-term prognosis can require amputation in severe cases.
- PAD rates among AIs are significantly higher than among other populations.

DESCRIPTION OF ORGANIZATION

- The Strong Heart Study (SHS) is a community-based participatory cohort study.
- According to its website, there were three components to the study:
  - “The first was a survey to determine cardiovascular disease mortality rates from 1984 to 1994 among tribal members aged 35-74 years of age residing in the 3 study areas (the community mortality study).
  - The second was the clinical examination of 4,500 eligible tribal members.
  - The third component is the morbidity and mortality (M&M) surveillance of these 4,500 participants."

TABLES AND FIGURES

	Sample size	OR(95%CI)–Unadjusted model	p.value	OR(95%CI)–Model with Demographic and Lifestyle Adjustments	p.value	OR(95%CI)–Model with Demographic, Lifestyle, and Physiological Adjustments model	p.value
Age, 45–55 years	1327	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Age, 55–65 years	895	2.46 (1.15, 5.23)	0.02	2.49 (1.07, 5.8)	0.034	1.98 (0.86, 4.56)	0.111
Age, ≥65 years	502	1.45 (0.53, 3.94)	0.469	1.28 (0.42, 3.92)	0.671	1 (0.33, 3.04)	0.996
Arizona	353	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Oklahoma	1200	0.16 (0.07, 0.39)	<0.001	0.15 (0.06, 0.39)	<0.001	0.23 (0.09, 0.57)	0.002
South Dakota	1171	0.27 (0.13, 0.58)	0.001	0.22 (0.09, 0.51)	<0.001	0.33 (0.14, 0.78)	0.011
BMI<25 kg/m2	478	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
BMI 25–30 kg/m2	632	0.91 (0.39, 2.12)	0.819	1.02 (0.42, 2.48)	0.974	1.16 (0.47, 2.87)	0.745
BMI ≥30 kg/m2	1614	0.38 (0.17, 0.87)	0.023	0.48 (0.2, 1.19)	0.112	0.58 (0.24, 1.45)	0.246
No High School	458	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Some High School	964	0.52 (0.21, 1.3)	0.162	0.45 (0.17, 1.14)	0.092	0.42 (0.16, 1.07)	0.068
Completed High School	1302	0.62 (0.27, 1.42)	0.257	0.49 (0.2, 1.2)	0.118	0.4 (0.16, 0.99)	0.048
Never Smoker	803	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Former Smoker	897	1.5 (0.65, 3.45)	0.34	1.55 (0.64, 3.78)	0.335	1.39 (0.57, 3.36)	0.47
Current Smoker	1024	0.96 (0.39, 2.32)	0.924	1.1 (0.41, 2.94)	0.854	1.07 (0.41, 2.79)	0.896
Male	1131	1.75 (1.08, 2.83)	0.022	1.78 (1.07, 2.95)	0.026	1.87 (1.11, 3.17)	0.02
Diabetes	1143	5.66 (3.13, 10.23)	<0.001	6.38 (3.45, 11.8)	<0.001	5.62 (2.95, 10.72)	<0.001
Hypertension	990	1.53 (0.95, 2.48)	0.082	1.6 (0.95, 2.67)	0.075	1.28 (0.76, 2.17)	0.354
Peripheral Artery Disease	279	4.37 (2.59, 7.37)	<0.001	3.39 (2, 5.75)	<0.001	2.86 (1.62, 5.05)	<0.001

Table 2. OR (95%CI) of Amputation by Participant Characteristics

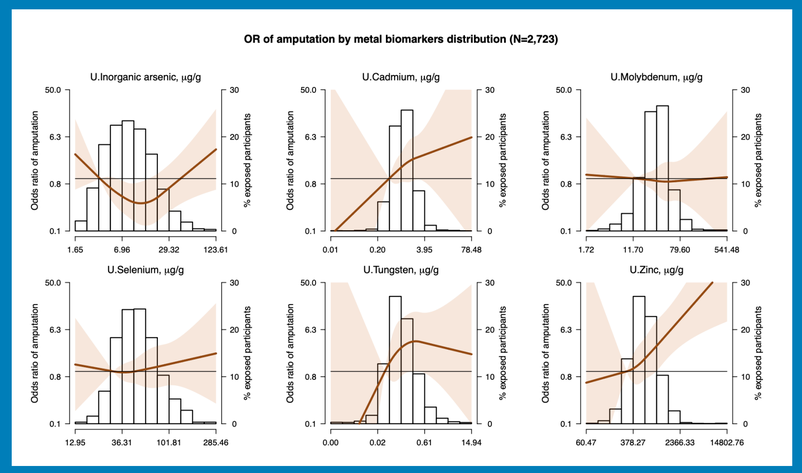

Figure 1. OR(95CI) of amputation by metal biomarkers distribution

METHODS

- We included 2,723 participants from 13 AI communities who were examined at baseline at three centers between 1989 and 1991.
- Among this group, there were 35 participants with amputations related to PAD and/or diabetes.
- We used logistic regression models comparing the prevalence of amputation with tertile urinary metal levels in the Strong Heart Study population.

- Higher urinary zinc levels are associated with significant increased odds of amputation.
- Other metals such as arsenic, cadmium, and tungsten showed non-significant increased odds of amputation.

DISCUSSION

- The strong association between zinc levels and amputation status, which was robust to various model specifications, might involve diabetes, which was also consistently associated with elevated odds of amputation.
- Because insulin secretion requires zinc, excess urinary zinc levels could reflect metabolic irregularities from more severe diabetes, which in turn would elevate odds of amputation.

REFERENCES

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Funded by: Columbia University Vagelos College of Physicians and Surgeons, Program for Education in Global and Population Health

Acknowledgments: Thank you to the staff and participants of the SHS, without whom this analysis would not be possible.

Contact Information:

Kishan Bhatt, MD Candidate
Columbia University Vagelos College of Physicians and Surgeons,
kab2294@cumc.columbia.edu