Do not ignore environmental contaminants as risk factors for PAD, CLTI, and lower extremity amputations

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The timely American Heart Association (AHA) policy statement ‘Reducing nontraumatic lower-extremity amputation by 20% by 2030: Time to get to our feet’ proposes a multi-pronged approach to identify and prevent progression of peripheral artery disease (PAD). This statement, however, misses the opportunity to highlight the growing understanding of environmental risk factors in cardiovascular disease, including PAD.

There are 2 modifiable environmental risk factors that, if intervened upon, might lead to a reduction of PAD, and potentially reduce lower extremity vascular events: fine particulate air pollution (PM$_{2.5}$) and contaminant metals.

Particulate air pollutants consist of a complex mixture classified by its size in microns. PM$_{2.5}$, corresponding to particles 2.5 microns and smaller, is a complex mixture of carbon species, sulfates, nitrates, and variable proportions of metal contaminants such as cadmium, lead, arsenic, aluminum, nickel, vanadium, zinc, and iron. A recent review in the Journal of the American College of Cardiology highlights PM$_{2.5}$ as a leading risk factor for global morbidity and mortality, with cardiovascular events being the largest contributor. Numerous studies support the association between ambient air PM$_{2.5}$ and cardiovascular disease, including PAD.

In a population-based community study in northeastern United States, every 10 µg/m$^3$ increase in average daily PM$_{2.5}$ levels between 2000-2008 was associated with a significant 4.4% (95% CI: 3.5-5.35%) increase in PAD hospitalizations; while a 10 µg/m$^3$ increase in daily PM$_{2.5}$ levels was associated with an increase of 0.26% (95% CI: 0.08-0.45%) of PAD hospitalization over the following 24h.

Contaminant metals have been identified by the AHA as cardiovascular risk factors in American Indians and Alaska Natives and as non-conventional risk factors for PAD. In NHANES 1999-2000 (N=2,125), the odds ratio for PAD comparing the highest to the lowest
quartile of blood cadmium levels was 2.42 (95% CI 1.13-5.15). For blood lead, although the odds ratio comparing the highest to lowest quartile was not significant (2.88, 95% CI 0.87, 9.47), there was a positive trend across all quartiles (p for linear trend 0.01). In the Strong Heart study, a prospective cohort study in American Indian communities ongoing since 1989-91, the hazard ratio (95% CI) for incident PAD comparing the highest to the lowest tertile of urinary cadmium was 1.96 (1.32, 2.81), after adjustment for smoking status and pack-years. In a small study of patients with PAD (N=22), higher urine cadmium was associated with an increase in PAD severity, with the highest urine cadmium levels found in patients with critical limb threatening ischemia. An environment-wide association study evaluating 417 risk factors with PAD in NHANES 1999-2004 identified blood cadmium as one of the four key predictors of PAD. Despite this evidence, most cohort studies of PAD do not include information on contaminant metal levels or air pollution exposures.

Thus, we propose that to meet the 20% reduction of lower extremity amputation by 2030, recognition, measurement, and reduction of environmental pollutants must be part of the formula.

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References


