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BRIEF REPORT

Social Determinants of Health and Mortality in Cardiovascular-Kidney-Metabolic Syndrome

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Cardiovascular disease (CVD), chronic kidney disease (CKD), and type 2 diabetes are leading causes of morbidity and mortality in the United States.[1,2] To enhance prevention and management of these interrelated conditions, the American Heart Association introduced a novel staging framework, termed cardiovascular-kidney-metabolic (CKM) syndrome,[1] with 4 stages: 1 (excess/dysfunctional adiposity); 2 (additional metabolic risk factors and/or CKD); 3 (subclinical CVD or high predicted CVD risk); and 4 (clinical CVD). Stage 0 is defined as the absence of CKM syndrome.

CKM syndrome is highly prevalent in the United States and disproportionately impacts individuals facing multiple adverse social determinants of health (SDOH).[3,4] However, the extent to which cumulative social burden influences mortality risk in CKM syndrome has not been rigorously assessed, despite their established effects on both CVD and CKD progression.[1] As such, exploring the impact of SDOH on CKM syndrome could enhance screening, risk stratification, individualized management, and policy interventions.

Using nationally representative data from the National Health Interview Survey (NHIS), we assessed adverse SDOH burden among U.S. adults with CKM syndrome and examined the association between CKM syndrome and all-cause mortality.

What is the clinical question being addressed?
How does mortality vary by cumulative social burden in U.S. adults with CKM syndrome?

What is the main finding?
Greater cumulative social burden was associated with worse CKM health and higher mortality risk across all CKM syndrome stages, particularly among adults at more advanced stages of CKM syndrome.

METHODS

This study used data from the 2013-2018 NHIS, a series of annual cross-sectional national surveys to provide representative estimates of the noninstitutionalized U.S. population.[5] NHIS data were merged with the National Death Index (NDI) through 2019, representing the latest available linkage with the NDI. We included all participants ≥18 years of age with available death record data and information on individual CKM components. Participants with unavailable

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ABBREVIATIONS AND ACRONYMS

CKD = chronic kidney disease

CKM = cardiovascular-kidney-metabolic

CVD = cardiovascular disease

NDI = National Death Index

NHIS = National Health Interview Survey

SDOH = social determinants of health

death status information or insufficient identifying data (<2%) were excluded from the study population. Missing values for individual study variables were ≤6.5%; thus, no imputation was performed. This study used publicly available, deidentified data, and was exempt from Institutional Board Review.

As per American Heart Association criteria, CKM syndrome was determined by the presence of overweight/obesity (body mass index ≥25 kg/m^2), risk factors (CKD, diabetes, hypertension, or high cholesterol), and clinical CVD (myocardial infarction, angina/coronary heart disease, or stroke) using self-reported survey responses. CKM syndrome stages 2 and 3 were combined due to the absence of subclinical CVD data in NHIS.

SDOH index was created using 37 equally weighted SDOH variables from 5 domains: economic stability, education, health care access, neighborhood and community context, and food insecurity. Each variable was classified as either favorable or unfavorable and assigned a value of 0 or 1, respectively, before aggregation. The range of values of the resulting index was divided into quartiles, with the most favorable (ie, lowest) SDOH scores in the first quartile (Q1), and the most unfavorable (ie, highest) scores in the fourth quartile (Q4). All-cause mortality was defined as a participant being recorded as "deceased" in the NDI during the study follow-up period.

Ordinal regression was used to estimate age-adjusted mortality rates (AAMR) and 95% CI per 100,000 person-years (PY) for each CKM stage, overall and by subgroups of interest, including sex, race/ethnicity, and SDOH burden, as well as OR for CKM syndrome by SDOH burden. Cox proportional hazards regression was performed to calculate the HRs for mortality by SDOH burden, adjusting for age, sex, race/ethnicity, and comorbidities (lung and liver disease, cancer, and arthritis). Analyses were performed with STATA MP 17.0 (StataCorp, LLC).

RESULTS

The final sample comprised 125,385 U.S. adults, with a nationally weighted CKM syndrome prevalence of 76.6%. Of those with CKM syndrome, most had stages 2 to 3 (36.8%), followed by stage 1 (32.1%) and stage 4 (7.6%). CKM stage 4 was more prevalent among older adults (23.1%) compared to younger adults (0.9%) and was more common among non-Hispanic Black (7.9%) and White (8.6%) adults than Hispanic (4.1%) adults. Individuals with CKM stage 4 were more often men (55.8%) than women (44.2%).

Individuals in SDOH-Q4 experienced higher prevalence of CKM stages 1 (28.9%) and 4 (9.6%) compared to those in SDOH-Q1 (27.9% and 3.4%). After covariate adjustment, higher cumulative SDOH burden was associated with an increased prevalence of CKM syndrome. Relative to those with the most favorable SDOH profile (SDOH-Q1), the odds of experiencing CKM syndrome increased progressively across increasing SDOH burden (quartiles): Q2 (OR: 1.09; 95% CI: 1.04-1.13), Q3 (OR: 1.17; 95% CI: 1.12-1.22), and Q4 (OR: 1.42; 95% CI: 1.36-1.48).

More advanced CKM syndrome was also associated with higher all-cause mortality rate. Namely, U.S. adults with CKM stages 2 to 3 (AAMR, 593.4 [95% CI: 548.4-638.4] per 100,000 PY) and 4 (1,356.1 [95% CI: 1,222.6-1,489.6] per 100,000 PY) had significantly higher AAMRs compared to stage 0 (456.3 [95% CI: 369.0-543.7] per 100,000 PY). Adults with CKM stages 0 and 1 had similar AAMRs (**Figure 1A**). Adverse SDOH burden was also associated with larger increases in mortality risk among participants with more advanced CKM stages, indicating a stronger impact of adverse SDOH on mortality in those with higher CKM burden (**Figure 1A**).

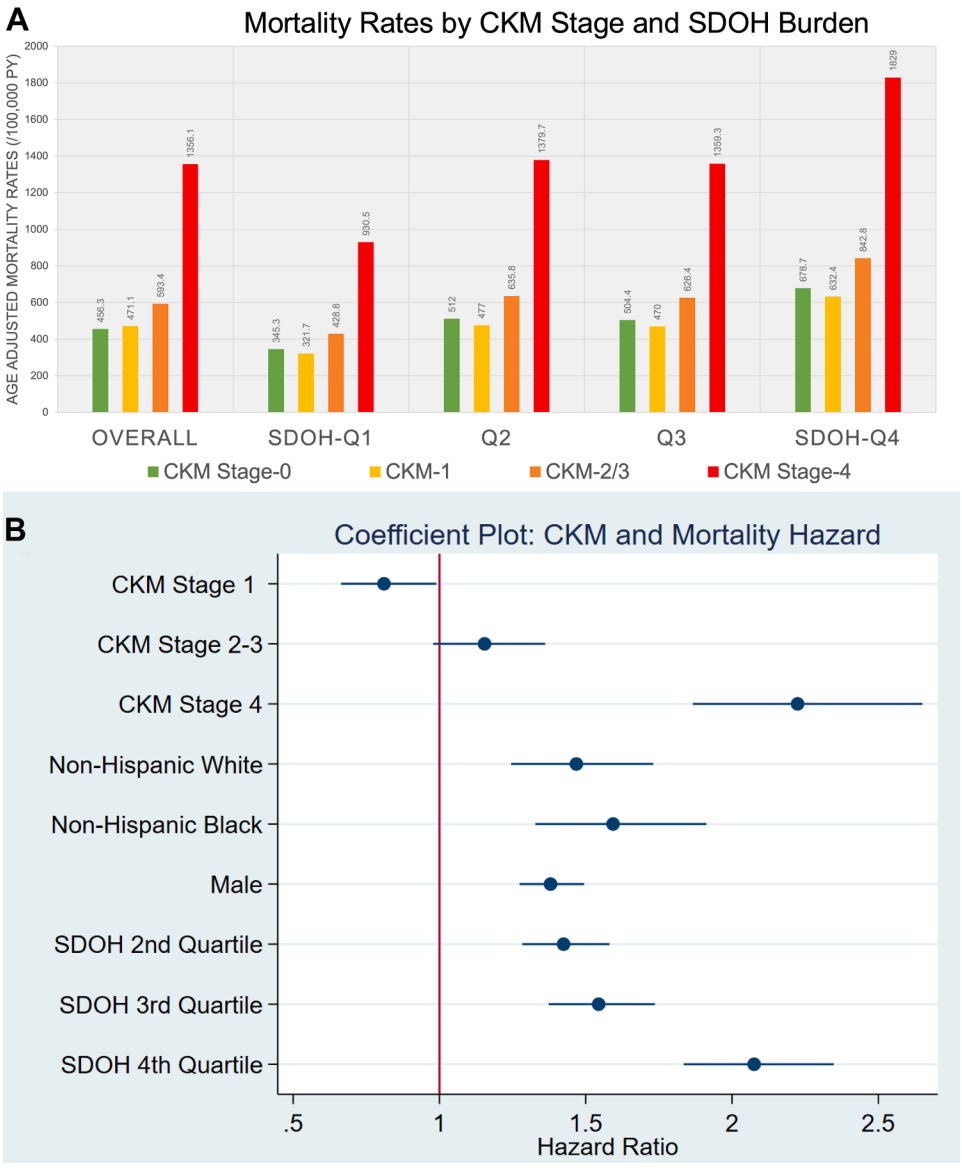
Irrespective of CKM stage, mortality HR increased by at least 2-fold from SDOH-Q1 to SDOH-Q4 (**Figure 1B**). There were no significant differences in mortality HR between non-Hispanic Black and White adults, while SDOH-Q4 was associated with greater increases in risk compared to SDOH-Q2 and Q3, which had comparable HRs (**Figure 1B**).

DISCUSSION

This nationally representative study found that higher adverse SDOH burden was associated with higher prevalence of CKM syndrome. Moreover, greater cumulative social burden was associated with a significantly greater risk of all-cause mortality in all CKM syndrome stages, with this risk more pronounced among individuals with worse CKM health. This disparity suggests that interventions targeting SDOH may be especially effective among individuals with worse CKM health. The higher prevalence of CKM syndrome among adults with greater social burden also highlights the importance of comprehensively assessing SDOH to better inform CKM risk stratification and prevent disease progression.

Some limitations should be noted. NHIS data are self-reported and cross-sectional, which may

FIGURE 1 CKM Syndrome Prevalence and Mortality by SDOH Burden



(A) Age-adjusted mortality rates (AAMR) in 100,000 person-years (PY), overall and stratified by SDOH quartile. (B) HRs for all-cause mortality by CKM stage (reference: stage 0), race (reference: Hispanic adults), and SDOH quartile (reference: Q1). CKM = cardiovascular-kidney-metabolic; SDOH = social determinants of health.

introduce bias and limit the ability to establish causal relationships between SDOH and CKM syndrome. We were also unable to distinguish CKM stages 2 and 3 due to lack of available data on subclinical CVD.

Overall, our findings highlight disparities in CKM syndrome outcomes and support the need for robust SDOH screening to mitigate mortality risk in CKM syndrome patients. Future research should prospectively explore the impact of polysocial risk scores and other SDOH-oriented interventions to improve CKM health.

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