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Research article

Associations between Life's Essential 8 and risks of all-cause and cardiovascular mortality in cancer survivors: A prospective cohort study from NHANES

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ABSTRACT

Background: Life's Essential 8 (LE8), an indicator of cardiovascular health (CVH), can predict overall and cardiovascular mortality in the general population. Considering that cancer survivors have a higher risk of cardiovascular disease (CVD), our study aimed to investigate the association between LE8 and the prognosis of cancer survivors.

Methods: A total of 2191 cancer survivors were included from the National Health and Nutrition Examination Survey (2005–2018). LE8 scores, derived from eight individual metrics, were categorized into three groups: low (0–49), moderate (50–79), and high (80–100). Cox regression analysis, nonlinear analysis, sensitivity analysis, and subgroup analysis were conducted to explore the association between LE8 scores and mortality risks, adjusting for potential confounders.

Results: During a median follow-up of six years, 479 deaths were recorded, including 118 CVD events and 156 cancer events. LE8 scores showed an inverse linear relationship with all-cause and cardiovascular mortality. A 10-point increase in LE8 scores was associated with a 25 % reduction in all-cause mortality (hazard ratio [HR], 0.75; 95 % CI, 0.66–0.85) and a 29 % reduction in cardiovascular mortality (HR, 0.71; 95 % CI, 0.57–0.89). Additionally, moderate CVH was linked to a lower risk of all-cause mortality (HR, 0.55; 95 % CI, 0.37–0.81), while high CVH was associated with an even lower risk (HR, 0.35; 95 % CI, 0.19–0.68). Similarly, moderate CVH demonstrated a decreased risk of cardiovascular mortality (HR, 0.31; 95 % CI, 0.15–0.63), with high CVH showing an even lower risk (HR, 0.23; 95 % CI, 0.09–0.58). However, LE8 scores was not associated with cancer-specific mortality.

Conclusions: A higher LE8 score was independently associated with a decreased risk of both all-cause and cardiovascular mortality in cancer survivors, underscoring the significance of optimizing CVH during the survivorship phase of cancer care.

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1. Introduction

Recent advancements in cancer screening, diagnosis, and treatment have led to a growing number of cancer survivors, exceeding 18 million in the United States [1]. The primary determinant of cancer patients' survival is receiving treatment from professional healthcare providers. However, it is crucial to recognize that complications arising from cancer and its therapies can negatively impact physical functioning, lifestyle, and mental well-being, ultimately reducing life expectancy [2]. Additionally, cancer survivors often face comorbidities such as obesity, hypertension, and diabetes, which significantly affect their quality of life and prognosis [3]. Therefore, managing cancer patients requires a comprehensive consideration of multiple factors, including adopting a healthy lifestyle and effectively controlling chronic diseases.

Cancer survivors are at a greater risk of cardiovascular diseases (CVD) and related mortality compared to individuals without cancer [4–7]. Thus, focusing on the cardiovascular health (CVH) of cancer survivors is important for their overall prognosis. The concept of Cardio-Oncology Rehabilitation also highlights the significance of addressing CVD risk in cancer patients and implementing effective management strategies [8]. Recently, the American Heart Association (AHA) introduced an updated definition of CVH known as Life's Essential 8 (LE8), which incorporates sleep and revises the scoring algorithm for its components [9]. LE8 includes four health behaviors (diet, physical activity, nicotine exposure, and sleep duration) and four health factors (body mass index [BMI], non-high-density lipoprotein [HDL] cholesterol, blood glucose, and blood pressure) [9]. Research studies have demonstrated that modifying these risk factors, such as physical activity, diet, smoking, and BMI, can improve the prognosis of cancer patients [2,10–12]. Additionally, several studies have identified that higher CVH scores based on LE8 are independently associated with lower risks of all-cause and cardiovascular mortality in the general population [13–16]. However, the utility of LE8 in cancer survivors remains unknown. Therefore, this study aimed to investigate the association between LE8 scores and mortality rates, encompassing all-cause, cardiovascular, and cancer mortality, within a nationally representative sample of US cancer survivors.

2. Materials and methods

2.1. Study population and design

Data for this study were obtained from the NHANES 2005–2018, a nationally representative survey designed to assess the health and nutrition status of individuals in the US. The survey employed a combination of health interviews conducted at participants' homes and health measurements conducted at mobile exam centers. To ensure the reliability and quality of the data, modern equipment was utilized. The National Center for Health Statistics Ethics Review Board approved the protocol. Written informed consent was obtained from all participants.

Seven NHANES cycles spanning from 2005 to 2018 were included. Initially, 70,190 participants were in the study, with 66,408 participants without self-reported cancer history being eliminated. Moreover, 273 participants who were within the first year since

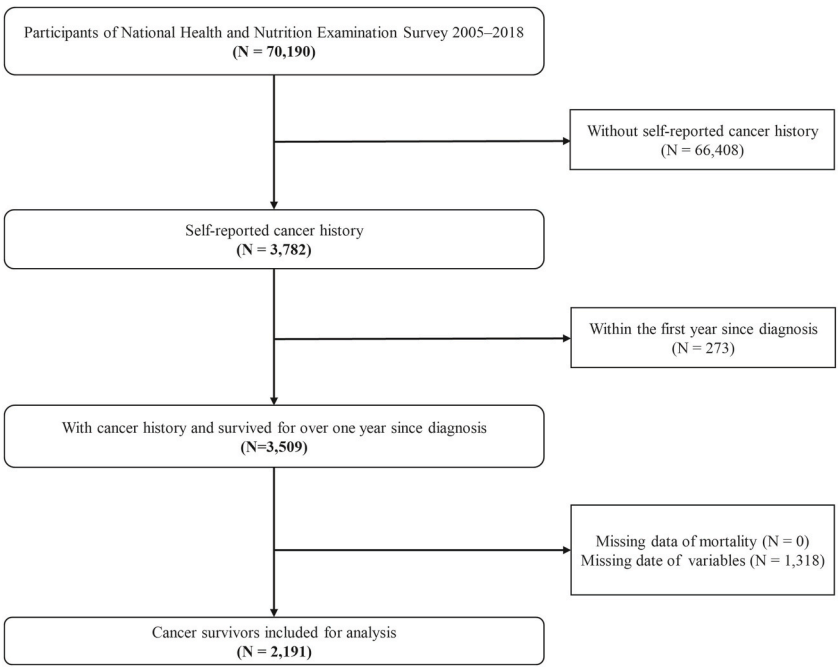

Fig. 1. Study flowchart. Of 3782 participants with self-reported cancer history in the 2005–2018 National Health and Nutrition Examination Survey (NHANES), 2191 remained after fulfilling inclusion and exclusion criteria.

their cancer diagnosis and 1318 participants with incomplete data on variables of interest were also excluded. Finally, a total of 2191 participants (1137 females and 1054 males) were included in the analyses. The filtering process is shown in Fig. 1.

2.2. Measurement of LE8

LE8 scoring algorithm consists of four health behaviors (diet, physical activity, nicotine exposure, and sleep duration) and four health factors (BMI, non-HDL cholesterol, blood glucose, and blood pressure). The detailed algorithms for calculating the LE8 scores for each of the metrics to NHANES data have been previously published [9,17] and can be found in Supplementary Table 1. In brief, each of the eight CVH metrics is scored ranging from 0 to 100 points. The overall LE8 score is calculated as the arithmetic average of these eight metrics. Participants with LE8 scores of 80–100 are classified as having high CVH, scores of 50–79 indicate moderate CVH, and scores of 0–49 represent low CVH(9).

The diet metric was evaluated using the Healthy Eating Index (HEI) 2015 [18]. The components and scoring standards HEI–2015 are summarized in Supplementary Table 2. Dietary intake data obtained from two 24-h dietary recalls are combined with United States Department of Agriculture (USDA) food patterns equivalents data to calculate the HEI-2015 scores [19]. The HEI-2015 scores are computed using the simple HEI scoring algorithm method (by person) with an official SAS code provided by the National Cancer Institute [20]. Self-report questionnaires collected physical activity, smoking, sleeping information, diabetes history, and medication history. Measurements of blood pressure, height, and weights were measured during the physical examination. BMI was calculated as the weight in kilograms divided by the height in meters squared. Blood samples were collected and sent to central laboratories for analysis of blood lipids, plasma glucose, and hemoglobin A1c [18].

2.3. Assessment of mortality

The NCHS provided the Public-Use Linked Mortality Files, which were utilized to determine the mortality outcomes in this study. To establish the mortality status, the unique study identification was linked to the National Death Index, with the last follow-up conducted on December 31, 2019, and updated in 2022. The causes of death were identified based on the International Statistical Classification of Diseases, 10th Revision (ICD-10) codes. The main findings of this study focused on mortality rates related to all-cause, cardiovascular diseases (including codes I00-I09, I11, I13, I20-I25, I26-I51, and I60-I69), and cancer (codes C00-C97).

2.4. Ascertainment of covariates

The following variables served as covariates in the statistical model: age, gender, race/ethnicity, education level (grades 0–12, high school graduate/GED, or some college or above), marital status, family income to poverty ratio, alcohol intake, the number of cancer types, and age at the first cancer diagnosis. Alcohol intake was defined as having an intake greater than 0 g per day (within the past 24 h). The cancer types and age of cancer survivors at each diagnosis were further asked, by “What kind of cancer was it?” and “How old were you when this cancer was first diagnosed?”

2.5. Statistical analyses

All statistical analyses adhered to the NHANES analysis and reporting criteria, taking into account sample weights, stratification, and clustering. Baseline characteristics were assessed using T-tests for continuous variables, presented as mean ± standard error (SE), and chi-square tests for categorical variables, presented as percentages. To evaluate multicollinearity, the variance inflation factor (VIF) was applied. A VIF exceeding 10 indicated high multicollinearity [21]. No obvious multicollinearity was observed in the study (Supplementary Table 3).

Person-years were measured from the enrollment date to the earlier date of death or censoring. The 95 % confidence interval (*CI*) and hazard ratio (*HR*) for statistical indicators were reported. Four weighted Cox regression models were constructed to investigate the relationship between LE8 scores and mortality, and all variables met the proportional hazards assumption [22]. The prognostic variations in several LE8 scores groups were assessed using Kaplan-Meier survival analysis and log-rank test. Restricted cubic splines with three knots at the 5th, 50th, and 95th centiles were employed to evaluate potential non-linear relationships between LE8 scores and mortality. A likelihood ratio test was conducted to compare the model with linear and cubic spline terms against the model with only a linear term. Furthermore, four sensitivity analyses were performed. Firstly, deaths with less than two years of follow-up were excluded. Secondly, the CVD histories were additionally adjusted to mitigate their effects. Thirdly, the main analyses were repeated according to tertiles of LE8 scores. Fourthly, we applied Fine & Gray Cox proportional hazard models to investigate the potential competing risks of cancer-related and other-cause mortality as potential risks for cardiovascular deaths [23]. Subgroup analyses were performed to explore whether the relationship of LE8 scores with mortality varied based on age, gender, race/ethnicity, education level, marital status, family income to poverty ratio, and alcohol intake. Wald tests were used to assess potential effect modifiers through multiplicative interactions. All statistical tests were two-sided and a P value < 0.05 was considered statistically significant. The analyses were conducted using R 4.2.2 software.

3. Results

3.1. Population characteristics

Table 1 presents the study population's baseline characteristics by three categories of total CVH scores. The weighted mean age of the study population was 62.91 years (95 % CI, 62.42–63.40 years), and 1137 participants were female (weighted percentage [WP], 55.04 %). The weighted mean (standard error) value of the LE8 scores was 65.27 (0.41) for all participants. Among the participants, 12.99 %, 70.45 %, and 16.56 % had low (LE8 scores <50), moderate (LE8 scores ≥50 but <80), and high (LE8 scores ≥80) CVH levels, respectively. Individuals with higher CVH levels were more likely to be younger, non-Hispanic White, married, and had higher levels of education, family income, and alcohol consumption.

3.2. Survival analysis

During a medain follow-up of 6 years, a total of 479 deaths were documented (WP, 16.56 %; 95 % CI, 13.93–19.19 %), including 118 incident CVD events (WP, 4.59 %; 95 % CI, 2.97–6.21 %) and 156 incident cancer events (WP, 5.13 %; 95 % CI, 3.57–6.69 %). The weighted death rates of all-cause mortality were 25.32 %, 16.23 %, and 9.31 % in the low, moderate, and high CVH groups,

Table 1
Characteristics of US adults by three categories of total CVH scores. NHANES 2005–2018[a].

Characteristics	Overall (N = 2191)	Total CVH scores			*P* value
		0–49 (N = 358)	50–79 (N = 1566)	80–100 (N = 267)	
Age, years, mean (SE)	62.91(0.49)	63.48(0.94)	63.58(0.51)	59.61(1.24)	**0.010**
Gender, n (%)					
Female	1137(55.04)	215(58.76)	773(53.36)	149(59.30)	0.326
Male	1054(44.96)	143(41.24)	793(46.64)	118(40.70)	
Race/ethnicity, n (%)					**< 0.001**
Non-Hispanic White	1531(83.94)	230(83.29)	1083(86.02)	218(93.70)	
Other	660(13.06)	128(16.71)	483(13.98)	49(6.30)	
Education, n (%)					**< 0.001**
Grades 0–12	406(10.17)	108(21.13)	277(9.36)	21(4.98)	
High school graduate/GED	490(19.67)	89(25.63)	367(21.32)	34(8.00)	
Some colleges or above	1295(70.16)	161(53.24)	922(69.32)	212(87.02)	
Family in come to poverty ratio†, n (%)					**< 0.001**
<1.3	507(13.90)	136(29.89)	338(12.78)	33(6.12)	
1.3–3.49	884(35.63)	153(42.80)	657(38.31)	74(18.58)	
≥3.5	800(50.47)	69(27.31)	571(48.90)	160(75.31)	
Marital status, n (%)					**< 0.001**
Coupled	1276(64.03)	185(52.91)	909(63.62)	182(74.47)	
Single or separated	915(35.97)	173(47.09)	657(36.38)	85(25.53)	
Alcohol consumption, n (%)					**< 0.001**
Yes	629(33.83)	51(15.44)	458(33.33)	120(50.38)	
No	1562(66.17)	307(84.56)	1108(66.67)	147(49.62)	
Breast cancer, n (%)					0.374
Yes	333(14.34)	54(14.64)	229(13.44)	50(17.94)	
No	1858(85.66)	304(85.36)	1337(86.56)	217(82.06)	
Prostate cancer, n (%)					0.662
Yes	364(11.11)	47(10.11)	273(11.62)	44(9.74)	
No	1827(88.89)	311(89.89)	1293(88.38)	223(90.26)	
Number of cancer types, n (%)					0.937
1	1973(89.67)	319(89.98)	1412(89.29)	242(91.01)	
2	197(9.25)	35(9.19)	139(9.58)	23(7.89)	
≥3	21(1.08)	4(0.83)	15(1.12)	2(1.10)	
Age at cancer first diagnosed, years, mean (SE)	51.05(0.59)	51.75(1.33)	51.40(0.69)	48.97(1.16)	0.166
Life's Essential 8 scores (out of 100 possible points), mean (SE)					
Total score	65.27(0.41)	42.89(0.64)	64.68(0.30)	85.33(0.43)	**< 0.001**
Diet score	39.84(1.13)	19.54(1.84)	37.74(1.30)	64.66(2.43)	**< 0.001**
Physical activity score	69.54(1.10)	23.88(3.03)	71.15(1.34)	98.47(0.46)	**< 0.001**
Nicotine exposure score	74.33(1.11)	53.73(2.90)	74.05(1.43)	91.69(1.26)	**< 0.001**
Sleep health score	85.04(0.69)	70.49(1.91)	85.83(0.73)	93.07(1.15)	**< 0.001**
Body mass index score	59.95(1.08)	34.58(2.46)	57.99(1.19)	88.16(1.85)	**< 0.001**
Blood lipids score	60.41(1.06)	43.90(2.38)	60.26(1.13)	73.99(2.76)	**< 0.001**
Blood glucose score	70.22(0.87)	53.19(1.94)	69.10(0.91)	88.39(1.91)	**< 0.001**
Blood pressure score	62.85(1.02)	43.83(2.91)	61.34(1.07)	84.22(1.44)	**< 0.001**

Abbreviations: CVH, cardiovascular health; NHANES, National Health and Nutrition Examination Survey; SE, standard error; GED, general equivalency diploma.

†Family income to poverty ratio represents family income to the poverty threshold, adjusted for household size.

[a] Means and percentages were adjusted for survey weights of NHANES.

respectively. In the fully adjusted model (model 2), compared to participants with low CVH, those with moderate CVH had a lower risk of all-cause mortality (HR, 0.55; 95 % CI, 0.37–0.81), and those with high CVH had an even lower risk (HR, 0.35; 95 % CI, 0.19–0.68). Furthermore, for every 10-point increase in LE8 scores, the multivariate-adjusted HR for all-cause mortality was 0.75 (95 % CI, 0.66–0.85; Table 2). Similar trends toward reduced risk of all-cause mortality were observed for higher individual CVH scores of diet, physical activity, nicotine exposure, sleep duration, and blood glucose (all P values < 0.05; Supplementary Table 4).

The weighted death rates of cardiovascular mortality were 8.90 %, 4.22 %, and 2.81 % for the low, moderate, and high CVH groups, respectively. In model 2, compared to participants with low CVH, those with moderate CVH had a lower risk of cardiovascular mortality (HR, 0.31; 95 % CI, 0.15–0.63), and those with high CVH had an even lower risk (HR, 0.23; 95 % CI, 0.09–0.58). Additionally, for every 10-point increase in LE8 scores, the multivariate-adjusted HR for cardiovascular mortality was 0.71 (95 % CI, 0.57–0.89; Table 2). Similar trends toward reduced risk of cardiovascular mortality were observed for higher individual CVH scores of blood glucose and blood pressure (all P values < 0.05; Supplementary Table 5).

The weighted death rates for cancer mortality were 5.06 %, 5.63 %, and 3.04 % in the low, moderate, and high CVH groups, respectively. However, in all models, neither the LE8 scores nor the individual metrics of LE8 were found to be significantly associated with the risk of cancer mortality (Table 2 and Supplementary Table 6).

Furthermore, Kaplan-Meier curves showed that participants who achieved higher CVH scores had a significantly lower cumulative incidence rate of all-cause and cardiovascular mortality ($P < 0.05$ for all log-rank tests, Fig. 2A–C).

3.3. Dose-response relationships between LE8 scores and mortality

According to the restricted cubic spline analyses, an approximately linear relationship was observed between LE8 scores and both all-cause and cardiovascular mortality (all *P* for overall <0.05, all *P* for non-linearity >0.05; Fig. 3A–C), indicating that as LE8 scores increased, the risk of all-cause and cardiovascular mortality decreased in a linear fashion.

3.4. Subgroup analysis

Subgroup analyses revealed that the inverse association between LE8 scores and all-cause mortality remained consistent across subgroups of age, sex, education, family income to poverty, marital status, and alcohol consumption. However, a higher LE8 score was only significantly associated with a reduced all-cause mortality in non-Hispanic White (*HR* for every 10-scores increase, 0.73; 95 % *CI*, 0.63–0.83; Table 3). Furthermore, the significant inverse association between LE8 scores and cardiovascular mortality was found in older age (≥70 years, *HR*, 0.75; 95 % *CI*, 0.61–0.93), females (*HR*, 0.65; 95 % *CI*, 0.48–0.88), non-Hispanic White (*HR*, 0.68; 95 % *CI*, 0.54–0.87), those with college graduate or above education background (*HR*, 0.62; 95 % *CI*, 0.45–0.86), married individuals (*HR*, 0.68; 95 % *CI*, 0.50–0.93), and participants without alcohol consumption (*HR*, 0.69; 95 % *CI*, 0.54–0.87; Supplementary Table 7). Additionally, the inverse association between LE8 scores and cancer mortality was only significant in participants who reported alcohol consumption (*HR*, 0.67; 95 % *CI*, 0.50–0.90; Supplementary Table 8). Significant interactions were observed between LE8 scores and race/ethnicity for all-cause mortality, between LE8 scores and education level for cardiovascular mortality, and between LE8 scores and alcohol consumption for cancer mortality (all $P < 0.05$ for interaction).

Table 2
Survey-weighted association of LE8 scores with all-cause, cardiovascular, and cancer mortality.

	Death, n	Weighted death (%)	Univariable model		Model 1		Model 2	
			HR (*95%CI*)	*P* value	*HR* (*95%CI*)	*P* value	*HR* (*95%CI*)	*P* value
All-cause mortality								
Low (0–49)	94	25.32	1[Reference]	/	1[Reference]	/	1[Reference]	/
Moderate (50–79)	344	16.23	**0.57(0.38,0.84)**	**0.005**	**0.54(0.36,0.81)**	**0.003**	**0.55(0.37,0.81)**	**0.002**
High (80–100)	41	9.31	**0.29(0.15,0.54)**	**< 0.001**	**0.35(0.18,0.67)**	**0.001**	**0.35(0.19,0.68)**	**0.002**
Per 10 points increase	/	/	**0.74(0.67,0.82)**	**< 0.001**	**0.75(0.66,0.85)**	**< 0.001**	**0.75(0.66,0.85)**	**< 0.001**
Cardiovascular mortality								
Low (0–49)	27	8.90	1[Reference]	/	1[Reference]	/	1[Reference]	/
Moderate (50–79)	78	4.22	**0.41(0.20,0.85)**	**0.016**	**0.30(0.15,0.63)**	**0.001**	**0.31(0.15,0.63)**	**0.001**
High (80–100)	13	2.81	**0.24(0.09,0.63)**	**0.004**	**0.20(0.08,0.53)**	**0.001**	**0.23(0.09,0.58)**	**0.002**
Per 10 points increase	/	/	**0.74(0.62,0.88)**	**< 0.001**	**0.69(0.55,0.87)**	**0.001**	**0.71(0.57,0.89)**	**0.003**
Cancer mortality								
Low (0–49)	25	5.06	1[Reference]	/	1[Reference]	/	1[Reference]	/
Moderate (50–79)	120	5.63	1.00(0.53,1.91)	0.995	1.12(0.56,2.20)	0.754	1.12(0.58, 2.18)	0.731
High (80–100)	11	3.04	0.48(0.17,1.34)	0.164	0.73(0.26,2.07)	0.558	0.73(0.26, 2.09)	0.559
Per 10 points increase	/	/	**0.79(0.66,0.93)**	**0.006**	0.85(0.69,1.05)	0.124	0.85(0.67, 1.06)	0.150

Abbreviations: LE8, Life's Essential 8; *HR*, hazard ratio; *CI*, confidence interval. Model 1 was adjusted for age, gender, race/ethnicity, education level, marital status, and family income to poverty ratio; Model 2 was additionally adjusted for alcohol consumption, the number of cancer types, and age at the first cancer diagnosis.

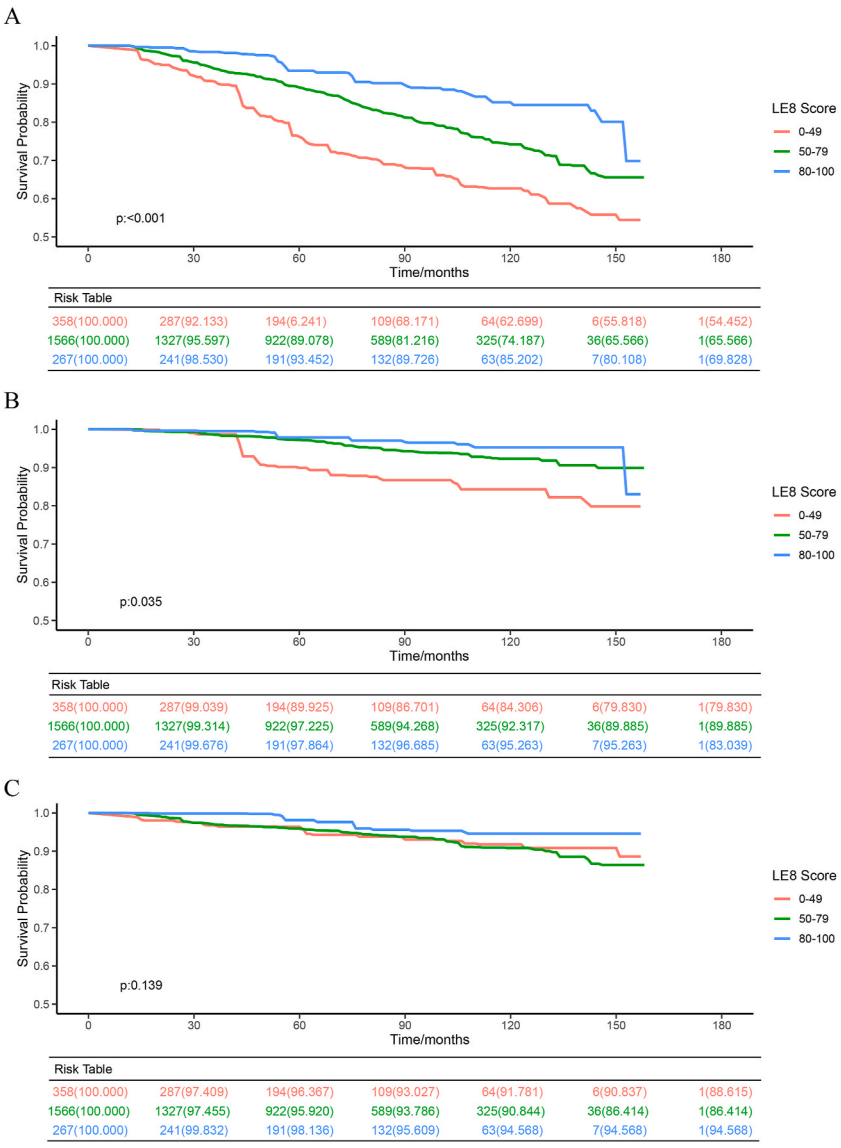

Fig. 2. Kaplan-Meier survival curve of all-cause mortality (A), cardiovascular mortality (B), and cancer mortality (C) by LE8 scores.

3.5. Sensitivity analysis

In four sensitivity analyses, the results remained robust. Firstly, when deaths with a follow-up period of fewer than two years were excluded, the findings were not influenced (Supplementary Table 9). Secondly, after adjusting for the CVD histories, the associations of LE8 scores with all-cause and cardiovascular mortality were still significant (Supplementary Table 10). Thirdly, when the main analyses were repeated using tertiles of LE8 scores, the results did not change obviously (Supplementary Table 11). Fourthly, after correcting for covariates, the Fine and Gray Cox Proportional Hazard models revealed that LE8, whether presented as a continuous or categorical variable, was still significantly associated with cardiovascular deaths ($P = 0.023$ and 0.010, respectively).

4. Discussion

In this large prospective cohort study utilizing NHANES data from 2005 to 2018, we found a significant and dose-dependent relationship between a high CVH level, as indicated by the LE8 score, and a reduced risk of all-cause and cardiovascular mortality among cancer survivors. Remarkably, for each additional 10 points on the CVH scale, we observed a substantial 25 % and 29 % reduction in the risk of all-cause and cardiovascular mortality, respectively, among cancer survivors. However, we did not find a significant association between the CVH level and cancer mortality. These findings emphasize the importance of maintaining a high CVH level for enhancing overall and cardiovascular health outcomes in individuals who have experienced cancer.

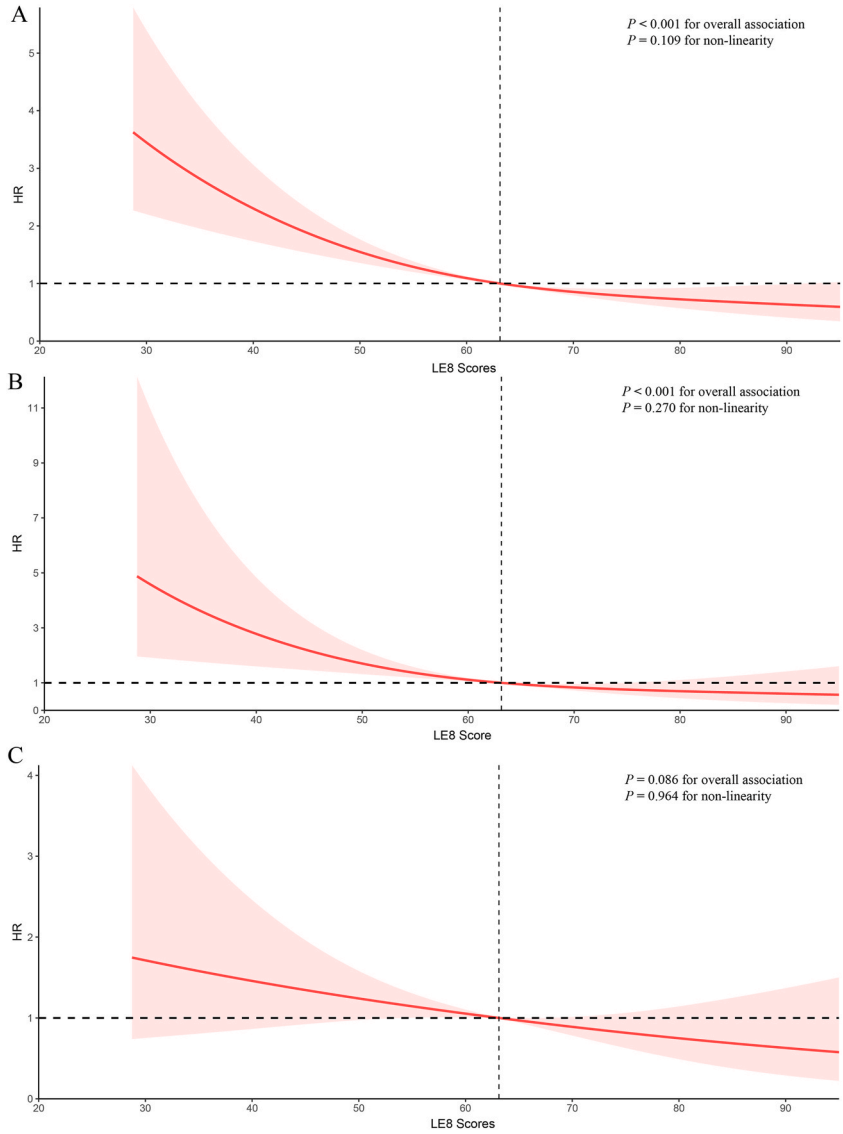

Fig. 3. Dose-response relationships between LE8 scores and all-cause mortality (A), cardiovascular mortality (B), and cancer mortality (C). All are adjusted for age, gender, race/ethnicity, education level, marital status, family income to poverty ratio, alcohol consumption, the number of cancer types, and age at the first cancer diagnosis. The shaded part represents the 95 % CI.

To our knowledge, this study represents the first investigation into the association of AHA's LE8 metrics with the prognosis of cancer survivors. The convergence of cancer and CVD is evident, as they frequently share common risk factors and underlying pathophysiologic mechanisms, rendering individuals more susceptible to the occurrence of both conditions [24]. Furthermore, cancer patients often undergo treatments such as radiation and chemotherapy, which can have side effects on CVH [25,26]. For example, androgen deprivation therapy in prostate cancer has been associated with an elevated risk of CVD [27], and the administration of anthracyclines and HER-2-targeted drugs can induce cardiomyopathy and congestive heart failure in breast cancer [26,28]. This highlights the importance of the emerging discipline of Cardio-Oncology, which focuses on understanding the intricate interplay between cancer and CVD(25). Moreover, a large-scale prospective cohort study conducted by Florido et al. revealed that adult cancer survivors face an increased risk of CVD, particularly heart failure, compared to individuals without cancer [6]. Another study utilizing the Surveillance, Epidemiology, and End Results (SEER) database found an elevated risk of cardiovascular mortality among cancer survivors [4]. These compelling findings highlight the significance of considering CVH during the long-term follow-up of cancer survivors, rather than solely concentrating on the cancer itself.

Research investigations have elucidated that Life's Simple 7 (LS7), endorsed by the AHA in 2010 as a CVH metric, serves as an effective tool for evaluating the CVD risk among cancer survivors, underscoring the important role of CVH in preventing CVD development [29]. Recently, the AHA introduced the LE8 metric, which not only encompasses a sleep metric in addition to LS7, but

Table 3
Subgroup analysis of the association of LE8 scores with all-cause mortality.

Subgroups	Death, n	Weighted death (%)	Univariable model		Model 1		Model 2		*P* for interaction*
			HR (*95%CI*)	*P* value	*HR* (*95%CI*)	*P* value	*HR* (*95%CI*)	*P* value	
Age									0.596
<70 years	116	7.99	0.64 (0.55,0.75)	<0.001	0.75 (0.58,0.96)	0.021	0.77 (0.60,0.99)	0.042	
≥70 years	363	29.41	0.78 (0.70,0.88)	<0.001	0.78 (0.69,0.89)	<0.001	0.79 (0.69,0.90)	<0.001	
Gender									0.252
Female	178	11.56	0.68 (0.60,0.77)	<0.001	0.73 (0.63,0.85)	<0.001	0.72 (0.62,0.83)	<0.001	
Male	301	22.04	0.78 (0.66,0.92)	0.003	0.77 (0.64,0.93)	0.006	0.78 (0.64,0.94)	0.009	
Race/ethnicity									0.035
Non-Hispanic White	387	17.21	0.73 (0.65,0.81)	<0.001	0.73 (0.63,0.83)	<0.001	0.73 (0.63,0.83)	<0.001	
Other	92	9.98	0.81 (0.65,1.00)	0.047	0.98 (0.79,1.22)	0.876	1.01 (0.81,1.26)	0.928	
Education									0.087
Grades 0–12	128	26.58	0.91 (0.79,1.05)	0.193	0.84 (0.72,0.99)	0.040	0.81 (0.67,0.97)	0.024	
High school graduate/GED	130	23.74	0.94 (0.76,1.16)	0.568	0.82 (0.64,1.06)	0.127	0.84 (0.66,1.08)	0.170	
Some colleges or above	221	12.68	0.65 (0.54,0.77)	<0.001	0.70 (0.58,0.85)	<0.001	0.69 (0.56,0.84)	<0.001	
Family income to poverty ratio									0.111
<1.3	125	23.84	0.93 (0.74,1.16)	0.516	0.83 (0.66,1.04)	0.102	0.83 (0.66,1.03)	0.090	
1.3–3.49	237	22.83	0.88 (0.76,1.03)	0.113	0.81 (0.69,0.95)	0.008	0.80 (0.69,0.94)	0.007	
≥3.5	117	9.55	0.61 (0.49,0.76)	<0.001	0.65 (0.50,0.86)	0.002	0.64 (0.49,0.84)	0.001	
Marital status									0.208
Coupled	230	20.66	0.68 (0.57,0.80)	<0.001	0.71 (0.59,0.86)	<0.001	0.71 (0.59,0.86)	<0.001	
Single or separated	249	13.80	0.84 (0.73,0.96)	0.011	0.81 (0.68,0.97)	0.019	0.81 (0.67,0.97)	0.024	
Alcohol consumption									0.546
Yes	358	16.90	0.68 (0.53,0.87)	0.002	0.71 (0.57,0.89)	0.003	0.71 (0.56,0.90)	0.004	
No	121	15.02	0.76 (0.69,0.85)	<0.001	0.77 (0.67,0.89)	<0.001	0.78 (0.67,0.89)	<0.001	

Abbreviations: LE8, Life's Essential 8; *HR*, hazard ratio; *CI*, confidence interval. **P* for interaction of Model 2. Model 1 was adjusted for age, gender, race/ethnicity, education level, marital status, and family income to poverty ratio, if not already stratified; Model 2 was additionally adjusted for alcohol consumption, the number of cancer types, and age at the first cancer diagnosis, if not already stratified.

also provides a more detailed evaluation of CVH on a scale from 0 to 100. Several studies conducted across different cohorts have substantiated the efficacy of LE8 in predicting the risk of both all-cause and cardiovascular mortality within the general population [13–16,30]. Thus, our aim was to investigate whether the degree of CVH, as measured by LE8, was associated with the prognosis of individuals who have survived cancer. Our findings revealed an inverse gradient relationship between LE8 scores and the risk of all-cause and cardiovascular mortality among cancer survivors. Intriguingly, for every 10-point increment in LE8 scores, the decline in cardiovascular mortality risk surpassed that of all-cause mortality risk (29 % vs. 25 %). Furthermore, drawing upon the NHANES database, Yi et al. [31] found that a 10-point elevation in LE8 scores corresponded to a 14 % reduction in all-cause mortality and a 19 % reduction in cardiovascular mortality within the general population, while the effect size observed in cancer survivors proved more substantial in our study. This observation implies that elevating CVH assumes particular significance in enhancing the prognostic outlook for cancer survivors. Nevertheless, our study did not ascertain any discernible correlation between an increase in LE8 scores and cancer-specific survival among cancer survivors. Plausible explanations encompass the augmented impact of CVH on cardiovascular mortality, thereby obfuscating any latent association between LE8 and cancer-related mortality due to the presence of competing causes of death. Additionally, the majority of cancer survivors included in our study had undergone cancer therapies, which may diminish the influence of modifiable factors on tumor outcomes.

Numerous studies have extensively investigated the shared mechanisms between CVD and cancer. Firstly, inflammatory pathways are important in the development, progression, and complications of both cancer and atherosclerotic plaques. Modulating these pathways has exhibited promising advancements in cancer treatment and emerged as potential strategies to reduce cardiovascular events [32]. Secondly, the excessive generation of reactive oxygen species, surpassing the cellular antioxidant defense mechanisms, leads to cellular damage and death in both CVD and cancer [33]. Additionally, influential factors such as hormones, cytokines, and

metabolic pathways may influence the interconnected biology of CVD and cancer [24]. Moreover, common health behaviors and factors including smoking, physical activity, obesity, diabetes, and hypertension are associated with inflammation and oxidative stress within the body [34–38], thereby elucidating the shared risk factors between CVD and cancer. Therefore, regulating these modifiable factors not only reduces the risk of cancer but also decreases the risk of CVD. This partially explains the stronger association observed between the increase in LE8 scores and the improved prognosis in cancer survivors, surpassing the effects observed in the general population.

We investigated the association between individual health behaviors and factors and the risk of mortality. Our findings were consistent with NHANES studies conducted on the general population [13], demonstrating that poor diet, physical inactivity, smoking, insufficient sleep duration, and diabetes significantly contribute to an increased risk of all-cause mortality. Additionally, diabetes and high blood pressure were identified as significant risk factors for cardiovascular mortality. We also observed a favorable trend suggesting a lower risk of cardiovascular mortality with higher levels of physical activity, lower smoking rates, and appropriate sleep duration (HR < 1). However, we did not find a significant relationship between BMI and mortality risk in cancer survivors, while low levels of non-HDL cholesterol were associated with an increased risk of death, consistent with previous findings [13,31,39]. Previous studies have reported a U-shaped association between BMI and non-HDL cholesterol with mortality [39,40]. Considering that the highest score in the LE8 metric is assigned to the lowest level of BMI or non-HDL cholesterol, further refinement may be necessary to accurately assess obesity and blood lipid levels within the LE8 framework. Furthermore, LE8 assigns the highest score to a sleep duration of 7–9 h, indicating that the impact on CVH increases as sleep duration deviates from this range. The U-shaped relationship between sleep duration and mortality has been confirmed by multiple studies [41,42]. Consistent with these findings, our results demonstrate that appropriate sleep duration significantly improves overall survival in cancer survivors and has a suggestive effect on CVH (model 1). However, we did not observe a significant relationship between sleep duration and cancer-specific mortality. This discrepancy may be attributed to the fact that only long sleep duration, rather than short sleep duration, is linked to an increased risk of cancer mortality [43], and the influence of sleep on different types of tumors can vary [44].

Subgroup analysis revealed an interaction between races, particularly among non-Hispanic whites, where LE8 was associated with a reduced risk of all-cause mortality. However, this association was not observed in other races. This may be due to the fact that non-Hispanic whites in the United States have better socioeconomic status and healthcare systems [45–47], which makes the role of maintaining cardiovascular health in extending lifespan even more prominent. Furthermore, Zhang et al. found a correlation between frailty and increased mortality risk in elderly cancer survivors [48]. Cao et al., analyzing the UK Biobank database, identified an association between frailty and the incidence of cardiovascular disease and type 2 diabetes mellitus in cancer survivors [49]. Preserving ideal cardiovascular health has the potential to reduce frailty risk in the elderly [50], consequently lowering the likelihood of mortality.

Our study, based on a nationally representative sample of the US population, uncovers a novel association between LE8 scores and the prognosis of cancer survivors, emphasizing the important role of improving CVH in enhancing their prognosis. Furthermore, sensitivity analysis confirmed the robustness of this relationship, and subgroup analysis demonstrated the effectiveness of LE8 in reflecting all-cause mortality across different demographic and lifestyle subgroups, including age, sex, education level, income, marital status, and alcohol consumption. However, it is important to consider several limitations of our study. Firstly, the eight CVH metrics we employed only captured baseline data and did not account for dynamic changes during the follow-up period. Secondly, previous research has demonstrated variations in the risk of CVD among different types of cancer [6], which can be influenced by the specific characteristics of tumors and the corresponding treatment modalities. However, due to the limited number of patients included in our study, we were unable to investigate the relationship between LE8 and prognosis in distinct cancer subgroups. Thirdly, as cancer treatment itself can contribute to CVD, the lack of information on medication use prevented us from adjusting for the impact of different therapies on the prognosis of cancer survivors. Nevertheless, our results revealed a significant association between LE8 and overall as well as cardiovascular mortality, indicating that enhancing CVH can be beneficial for the prognosis of cancer survivors. Moreover, efforts to better manage the cardiotoxic effects of cancer treatment could further mitigate the risk of CVD in this population. Fourthly, the information on dietary intake, physical activity, nicotine exposure, and sleep health in the NHANES database relied on self-reported questionnaires, potentially introducing recall bias. Finally, our study was conducted using the US NHANES database, and further research is needed to determine the generalizability of our findings to other populations.

5. Conclusions

In conclusion, our study revealed that the LE8 score, a novel CVH metric, was independently associated with the risk of all-cause and cardiovascular mortality in cancer survivors. The inverse linear relationship between the LE8 score and mortality risk enables effective risk stratification in this specific population. Furthermore, these findings highlight the clinical significance of optimizing modifiable risk factors related to the LE8 score to improve the prognosis of cancer survivors. Importantly, implementing such interventions holds substantial implications for public health.

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Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical review and approval for the research involving human participants were obtained from the Ethics Review Board of the National Center for Health Statistics (NCHS) (Protocol #98-12). The current analysis, which is based on publicly available data, did not necessitate any further ethics approval. Written informed consent was obtained from all patients or participants who were part of the study.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be downloaded here: https://www.cdc.gov/nchs/nhanes/ (NHANES 2005–2018).

CRediT authorship contribution statement

Wen Liu: Writing – original draft, Visualization, Validation, Software, Methodology, Formal analysis, Conceptualization. **Jia Wang:** Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. **Miaomiao Wang:** Writing – original draft, Software, Methodology, Formal analysis. **Huimin Hou:** Validation, Methodology, Formal analysis. **Xin Ding:** Software, Formal analysis. **Miao Wang:** Writing – review & editing, Visualization, Validation, Funding acquisition, Formal analysis, Conceptualization. **Ming Liu:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36954.

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