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Association of Life's Essential 8 with risk of incident cardiovascular disease and mortality among adults with chronic kidney disease

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ABSTRACT

Background: The American Heart Association recently released an updated algorithm for evaluating cardiovascular health (CVH), Life's Essential 8 (LE8). However, few studies have examined the association of LE8 with risk of cardiovascular disease (CVD) and mortality among individuals with chronic kidney disease (CKD). We investigated whether LE8 was associated with subsequent risk of CVD and mortality in the Chinese population of adults with CKD.

Methods: This prospective study included 18,716 adults (55.4 ± 14.0 years, 77.9 % men) with CKD free of CVD at baseline from the Kailuan study. A LE8 score (range 0–100 points) was constructed based on diet, physical activity, smoking, sleep duration, body mass index, blood lipids, blood glucose, and blood pressure. Incident CVD and mortality were identified by electronic health records and registers. Multivariable Cox regression models were used to compute hazard ratios (HRs) and 95 % confidence intervals (CIs).

Results: During a median follow-up of 14.0 and 14.4 years, 2117 cases of CVD and 4190 deaths were documented. After adjusting for potential confounders, comparing the high LE8 score (80–100 points) to the low LE8 score (<50 points), the multivariable HRs (95 % CIs) were 0.28 (0.20, 0.40) for CVD, 0.14 (0.06, 0.34) for myocardial infarction, 0.35 (0.25, 0.50) for total stroke, and 0.68 (0.56, 0.83) for all-cause mortality, respectively.

Conclusions: Among patients with CKD, greater adherence to CVH, as defined by LE8, was significantly associated with a lower risk of CVD and all-cause mortality.

1. Introduction

Chronic kidney disease (CKD) is a significant public health challenge with a global prevalence ranging from 8 % to 16 % [1–3]. In China, a nationally representative cross-sectional study showed that the prevalence of CKD was 8.2% from 2018 to 2019 [4]. CKD is associated with an increased risk of cardiovascular disease (CVD) and mortality [5–7]. In particular, individuals with CKD face a five to ten-fold higher likelihood

Abbreviations: AHA, American Heart Association; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; CVH, cardiovascular health; eGFR, estimated glomerular filtration rate; LE8, Life's Essential 8; LS7, Life's Simple 7; MI, myocardial infarction; NHANES, National Health and Nutrition Examination Survey; PAR, population attributable risk; SD, standard deviation; VIF, variance inflation factor.

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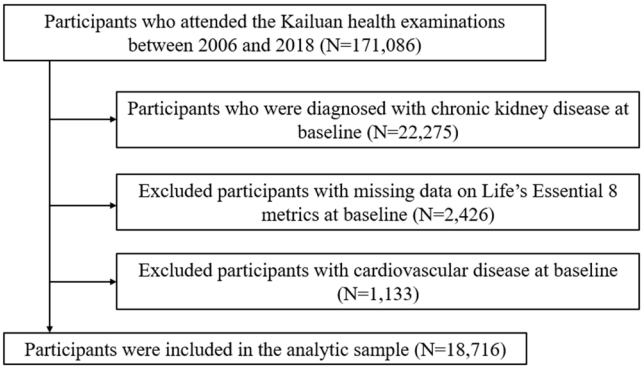


Fig. 1. Flowchart showing participant selection for the study.

of premature death compared to progressing to end-stage kidney disease [8]. Therefore, it is crucial to identify modifiable risk factors in relation to CVD and mortality among patients with CKD.

The main pathophysiological mechanisms of progression from CKD to CVD and mortality include shared risk factors between CKD and CVD. These include unhealthy lifestyle factors (unhealthy diet, physical inactivity, overweight, and smoking), as well as conditions like hypertension, dyslipidemia, and diabetes [7]. Besides these well-identified risk factors, mounting evidence shows that sleep health was associated with the development and progression of CKD [9,10]. Thus, managing these risk factors is essential for maintaining cardiovascular health (CVH) in people with CKD. In this context, the American Heart Association (AHA) recently updated its algorithm for assessing CVH, known as Life's Essential 8 (LE8), with the aim of enhancing CVH in the general population [11]. Compared with previous Life's Simple 7 (LS7), which included diet, physical activity, smoking, blood lipids, blood glucose, blood pressure (BP), and body mass index (BMI), the LE8 newly introduced sleep duration as a novel component [11]. Furthermore, the scoring algorithm of the LE8 was updated. Although several previous studies have indicated an inverse association between LE8 score and risks of CVD and mortality in the general population [12–15], few studies have investigated the association in patients with CKD. Given that CKD patients exhibit distinct metabolic characteristics compared to the general population [16], findings from studies on the general adults may be not directly applied to adults with CKD.

To date, only one cohort study conducted in the US National Health and Nutrition Examination Survey (NHANES) showed that higher adherence to LE8 score among patients with CKD was associated with a lower risk of all-cause and cause-specific mortality [17]. However, these findings might not be generalizable to Chinese adults with different lifestyles and genetic predispositions in relation to diseases. Moreover, the association between LE8 and risk of CVD remains unclear in CKD patients.

To fill this knowledge gap, we prospectively investigated whether LE8 was associated with subsequent risk of CVD and mortality in the Chinese population of adults with CKD. We hypothesized that greater adherence to the LE8 would be associated with a lower risk of subsequent CVD events and total mortality among patients with CKD.

2. Methods

2.1. Study population

This study utilized data from the Kailuan Study, a large ongoing prospective cohort of participants aged 18 years and older in Tangshan, China. The detailed study design and procedures have been described in previous studies [18–20]. In brief, 101,510 participants from the Kailuan community received health checkups and filled in questionnaires in the Kailuan General Hospital and other 10 affiliated hospitals between 2006 and 2007. The study continued to enroll new participants in subsequent years: 2008 ($n = 24,540$), 2010 ($n = 9118$), 2012 ($n = 17,981$), 2014 ($n = 9088$), 2016 ($n = 4112$), and 2018 ($n = 4737$). As of December 2018, a total of 171,086 individuals had been enrolled in the Kailuan Cohort. Detailed information on lifestyle factors and medical history was collected at baseline and updated biennially through validated questionnaires. The study was approved by the Ethics Committee of the Kailuan Medical Group, and all participants provided written informed consent.

In the current study, we included participants with prevalent CKD at their first health examination between 2006 and 2018 ($n = 22,275$). CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min per 1.73 m^2 and/or proteinuria ≥1+ (>30 mg/g) [21,22]. A total of 18,716 CKD patients were included after excluding patients with missing information on LE8 ($n = 2426$) or who had prevalent CVD at baseline ($n = 1133$). Fig. 1 shows the flowchart of the study sample selection.

2.2. Assessment of LE8

Based on the AHA updated algorithm for evaluating CVH [11], we developed a LE8 score [13,15,23]. The LE8 score included 8 components: diet, physical activity, smoking, sleep, BMI, blood lipids, blood glucose, and BP. Information on diet, physical activity, smoking, and sleep was collected through a standardized questionnaire at baseline [20]. Height and body weight were measured by trained staff following a standard protocol. BMI was calculated as the body weight (kg) divided by the height squared (m^2). Fasting blood lipids (including total cholesterol, low-density lipoprotein-cholesterol, and high-density lipoprotein-cholesterol) and blood glucose were measured by Hitachi 7600 autoanalyzer (Tokyo, Japan) at the central laboratory of Kailuan General Hospital. BP was measured at least twice by an automated device or manual sphygmometer under standard protocols by trained nurses, and averaged values were used for analyses. The criterion for the creation of the LE8 score is provided in **Table S1** and our recent work [20]. Each of the 8 components was scored on a scale of 0 to 100, and the aggregate score was also scaled from 0 to 100 points with higher scores indicating better adherence to CVH. Adherence was categorized into three groups: low (0–49 points), moderate (50–79 points), and high (80–100 points) according to the AHA advisory [11,20]. **Figure S1** shows the distribution of the LE8 score and each component of the LE8.

2.3. Ascertainment of outcomes

The primary outcomes were the first occurrence of CVD and all-cause mortality. The subtypes of CVD included myocardial infarction (MI) and total stroke (including ischemic stroke and hemorrhagic stroke). Information on incident CVD and all-cause mortality was obtained from the Municipal Social Insurance Institution and the Discharge Register of all 11 Kailuan affiliated hospitals, which was updated annually during the follow-up period and covered all the Kailuan study participants [15]. Potential CVD events were identified based on the ICD-10. An expert panel reviewed the annual discharge records from the 11 hospitals to identify patients with suspected CVD. As with our previous work [24], MI events were ascertained by patients' clinical symptoms, electrocardiography findings, and dynamic changes in myocardial enzymes according to the World Health Organization's Multinational Monitoring of Trends and Determinants in CVD criteria. Stroke was determined according to neurological signs and symptoms and imaging examinations, including brain computed tomography or magnetic resonance, and it was divided into ischemic and hemorrhagic stroke [24].

2.4. Assessment of covariates

Information on covariates such as age, sex, alcohol intake (current or non-current drinkers), education levels (high school or above, or

Table 1
Baseline characteristics of study participants by the Life's Essential 8 score (n = 18,716) [a].

Characteristics	Total	Life's Essential 8 score			P for trend [b]
		Low (0–49 points)	Moderate (50–79 points)	High (80–100 points)	
Number of participants	18,716	2618	15,143	955	<0.001
Life's Essential 8 score	63.5 (13.5, 100.0)	44.8 (13.5, 49.8)	64.8 (50.0, 79.8)	82.5 (80.0, 100.0)	<0.001
Age, years	55.4 ± 14.0	54.5 ± 11.4	56.0 ± 14.0	49.4 ± 17.2	<0.001
Men, n (%)	14,581 (77.9)	2422 (92.5)	11,724 (77.4)	435 (45.6)	<0.001
BMI, (kg/m2)	24.8 ± 5.1	26.7 ± 5.5	24.7 ± 5.0	20.8 ± 4.7	<0.001
Current drinker, n (%)	5281 (28.2)	1528 (58.4)	3624 (23.9)	129 (13.5)	<0.001
Current smoker, n (%)	5208 (27.8)	1955 (74.7)	3235 (21.4)	18 (1.9)	<0.001
Senior high school or above, n (%)	3124 (16.7)	450 (17.2)	2340 (15.5)	334 (35.0)	<0.001
SBP (mmHg)	138±23	148±22	138±22	111±14	<0.001
DBP (mmHg)	87±13	94±12	86±12	71±8	<0.001
FBG (mmol/L)	5.83 ±2.34	7.41 ±3.56	5.61±2.01	4.85 ±0.56	<0.001
TC (mmol/L)	4.93 ±1.45	5.72 ±2.08	4.83±1.28	4.38 ±0.84	<0.001
TG (mmol/L)	1.94 ±1.58	2.70 ±2.21	1.85±1.44	1.16 ±0.75	<0.001
HDL-C (mmol/L)	1.56 ±0.47	1.50 ±0.43	1.57±0.49	1.57 ±0.41	<0.001
LDL-C (mmol/L)	2.57 ±0.83	2.91 ±1.03	2.53±0.79	2.36 ±0.64	<0.001
Marital status (married), n (%)	18,459 (98.6)	2595 (99.1)	14,956 (98.8)	908 (95.1)	<0.001
Family history of CVD, n (%)	811 (4.3)	219 (8.4)	546 (3.6)	46 (4.8)	<0.001
eGFR (ml/min/ 1.73 m2)	60.1 ± 21.9	63.7 ± 24.1	59.3 ± 20.6	62.4 ± 32.0	<0.001
Proteinuria (dipstick ≥+) [c]	5759 (32.2)	1179 (46.7)	4325 (29.8)	255 (29.0)	<0.001

[a] Continuous variables are expressed as means (standard deviations) or medians (interquartile range) and categorical variables are expressed as numbers (percentages). BMI, body mass index; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.
[b] Continuous variables were compared using analysis of variance or the Kruskal-Wallis test according to distribution, and categorical variables were compared with the chi-square test.
[c] 807 participants had missing data on proteinuria.

others), marital status (married or never), and family history of CVD was collected using a structured questionnaire [18,20].

2.5. Statistical analysis

Baseline characteristics of the study participants were presented as means ± standard deviations (SD) or medians (P25, P75) for continuous variables and numbers (percentages) for categorical variables. Continuous variables were compared using analysis of variance or the Kruskal-Wallis test according to distribution, and categorical variables were compared with the chi-square test.

Person-years of follow-up for each participant were calculated from the date of the first survey to the date of CVD occurrence, all-cause mortality, or the end of follow-up (December 31, 2021), whichever occurred first. Associations between the LE8 score and the risk of CVD

Table 2
Associations of Life's Essential 8 score with risk of cardiovascular disease and all-cause mortality among participants with chronic kidney disease (n = 18,716)[a].

	Life's Essential 8 score			P for trend [b]	Per 10-point increase
	Low (0–49 points) (n = 2618)	Moderate (50–79 points) (n = 15,143)	High (80–100 points) (n = 9,55)		
Cardiovascular disease					
Number of cases/ person-years	439/ 30,445	1640/ 185,637	38/ 12,193	–	–
Incidence per 1000 person-years	14.42	8.83	3.11	–	–
Model 1	1.00 (reference)	0.61 (0.55, 0.68)	0.28 (0.20, 0.39)	<0.001	0.74 (0.71, 0.76)
Model 2	1.00 (reference)	0.61 (0.54, 0.68)	0.28 (0.20, 0.40)	<0.001	0.72 (0.69, 0.75)
Model 3	1.00 (reference)	0.61 (0.55, 0.68)	0.28 (0.20, 0.40)	<0.001	0.72 (0.70, 0.75)
Myocardial infarction					
Number of cases/ person-years	112/ 32,165	379/ 191,980	5/12,332	–	–
Incidence per 1000 person-years	3.48	1.97	0.41	–	–
Model 1	1.00 (reference)	0.56 (0.45, 0.69)	0.15 (0.06, 0.36)	<0.001	0.71 (0.65, 0.76)
Model 2	1.00 (reference)	0.52 (0.41, 0.65)	0.14 (0.06, 0.34)	<0.001	0.68 (0.62, 0.73)
Model 3	1.00 (reference)	0.51 (0.41, 0.64)	0.14 (0.06, 0.34)	<0.001	0.67 (0.62, 0.73)
Total stroke					
Number of cases/ person-years	340/ 31,032	1314/ 187,455	35/ 12,226	–	–
Incidence per 1000 person-years	10.96	7.01	2.86	–	–
Model 1	1.00 (reference)	0.65 (0.57, 0.73)	0.34 (0.24, 0.48)	<0.001	0.75 (0.72, 0.78)
Model 2	1.00 (reference)	0.65 (0.57, 0.73)	0.35 (0.25, 0.50)	<0.001	0.74 (0.71, 0.77)
Model 3	1.00 (reference)	0.65 (0.57, 0.74)	0.35 (0.25, 0.50)	<0.001	0.74 (0.71, 0.78)
Ischemic stroke					
Number of cases/ person-years	304/ 31,240	1131/ 188,506	31/ 12,243	–	–
Incidence per 1000 person-years	9.73	6.00	2.53	–	–
Model 1	1.00 (reference)	0.62 (0.55, 0.71)	0.34 (0.23, 0.49)	<0.001	0.74 (0.70, 0.77)
Model 2	1.00 (reference)	0.62 (0.54, 0.71)	0.35 (0.24, 0.51)	<0.001	0.73 (0.69, 0.76)
Model 3	1.00 (reference)	0.63 (0.55, 0.72)	0.35 (0.24, 0.50)	<0.001	0.73 (0.70, 0.76)
Hemorrhagic stroke					
Number of cases/ person-years	47/32,584	231/ 192,756	5/12,347	–	–

(continued on next page)

Table 2 (*continued*)

	Life's Essential 8 score			*P* for trend [b]	Per 10-point increase
	Low (0–49 points) (*n* = 2618)	Moderate (50–79 points) (*n* = 15,143)	High (80–100 points) (*n* = 9,55)		
Incidence per 1000 person-years	1.44	1.20	0.40	–	–
Model 1	1.00 (reference)	0.85 (0.62, 1.17)	0.38 (0.15, 0.95)	0.06	0.86 (0.77, 0.95)
Model 2	1.00 (reference)	0.83 (0.60, 1.15)	0.38 (0.15, 0.96)	0.05	0.84 (0.76, 0.94)
Model 3	1.00 (reference)	0.83 (0.60, 1.15)	0.38 (0.15, 0.96)	0.05	0.84 (0.76, 0.94)
All-cause mortality					
Number of cases/ person-years	621/ 32,821	3446/ 193,971	123/ 12,365	–	–
Incidence per 1000 person-years	18.92	17.77	9.95	–	–
Model 1	1.00 (reference)	0.91 (0.84, 0.99)	0.74 (0.61, 0.90)	0.002	0.92 (0.89, 0.94)
Model 2	1.00 (reference)	0.82 (0.75, 0.90)	0.68 (0.56, 0.83)	<0.001	0.88 (0.86, 0.91)
Model 3	1.00 (reference)	0.82 (0.75, 0.90)	0.68 (0.56, 0.83)	<0.001	0.88 (0.86, 0.91)

Model 1: adjusted for age and sex.
Model 2: adjusted for variables in model 1 plus alcohol drinking status, education level, marital status, and family history of cardiovascular disease.
Model 3: adjusted for variables in model 2 plus estimated glomerular filtration rate.
[a] Values are given as hazard ratios and 95 % confidence intervals within parentheses.
[b] *P* for trend was computed by assigning the categories of the Life's Essential 8 score as an ordinal variable.

and all-cause mortality were assessed using Cox proportional hazards models. The proportionality of the hazards assumption was tested by including an interaction term between the LE8 score and the duration of follow-up in the Cox proportional hazards model [25], and no violation of the assumption was detected ($P > 0.05$ for all models).

Three multivariable models were fitted. Model 1 adjusted for age and sex. Model 2 adjusted for age, sex, alcohol drinking status, education level, marital status, and family history of CVD. Model 3 further adjusted for eGFR. The selection of covariates for the multivariable models was based on a directed acyclic graph (**Figure S2**) [26,27]. In addition, multicollinearity among these covariates was examined by variance inflation factors (VIFs) with acceptable collinearity observed (all VIF values <3.0). The *P* for trend was computed by assigning the categories of the LE8 score as an ordinal variable. To estimate the proportion of CVD and all-cause mortality that theoretically would be prevented if all CKD patients adhered to high CVH, we computed the population attributable risk (PAR) [28,29].

We performed stratified analyses by sex (men or women), age (<65 or ≥65 years), education (high school or above/others), alcohol intake (current or non-current drinkers), baseline eGFR (<45 or ≥45 ml/min/1.73 m^2). Interaction between the LE8 score and these stratified variables was assessed by adding the interaction terms in the Cox models.

Furthermore, we performed several sensitivity analyses to test the robustness of the results. First, we additionally adjusted for urinary protein. Second, we defined CKD only using eGFR. Second, to assess the influence of individual components on the association between the overall LE8 score and outcomes, we recomputed the scores, without each component and evaluated the association between the recomputed score and risk of outcomes. Finally, we excluded events that occurred within the first four years of follow-up to address reverse causation.

All analyses were conducted using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at a 2-tailed $P < 0.05$.

3. Results

3.1. Baseline characteristics

The final analytical sample consisted of 18,716 adults with CKD (mean ± SD age: 55.4 ± 14.0 years; 77.9 % men). Among them, 2618 (13.9 %) had low CVH, 15,143 (80.9 %) had moderate CVH, and 955 (5.1 %) had high CVH. Table 1 shows the distributions of baseline characteristics according to the CVH status. Compared with participants with a lower LE8 score, those with a higher LE8 score were more likely to be younger, women, and well-educated, but were less likely to be current drinkers and current smokers. In addition, participants with a higher LE8 score had better metabolic characteristics (e.g., lower BMI, BP, and blood glucose).

3.2. Associations of LE8 with risk of CVD and all-cause mortality

During a median follow-up of 14.4 (interquartile range: 10.5–15.1) and 14.6 (interquartile range: 12.2–15.1) years, we identified 2117 (11.3 %) CVD cases (including 496 MI cases, 1689 total stroke cases, 1466 ischemic stroke cases, and 283 hemorrhagic stroke cases) and 4190 (22.4 %) deaths. Table 2 displays the associations between the LE8 score and the risks of CVD and all-cause mortality. The age- and sex-adjusted hazard ratios (HRs) and 95 % confidence intervals (CIs) for an increase of 10 points were 0.74 (0.71, 0.76) for CVD, 0.71 (0.65, 0.76) for MI, 0.75 (0.72, 0.78) for total stroke, 0.74 (0.70, 0.77) for ischemic stroke, 0.86 (0.77, 0.95) for hemorrhagic stroke, 0.92 (0.89, 0.94) for all-cause mortality, respectively. The results did not materially change after additional adjustment for alcohol drinking status, education level, marital status, family history of CVD, and eGFR; the corresponding HRs (95 % CIs) for an increase of 10 points were 0.72 (0.70, 0.75) for CVD, 0.67 (0.62, 0.73) for MI, 0.74 (0.71, 0.78) for total stroke, 0.73 (0.70, 0.76) for ischemic stroke, 0.84 (0.76, 0.94) for hemorrhagic stroke, 0.88 (0.86, 0.91) for all-cause mortality, respectively. Furthermore, the PAR % for CVD and all-cause mortality was 54.0 % (95 % CI: 38.5 %, 65.3 %) and 54.8 % (95 % CI: 39.6 %, 65.9 %).

3.3. Subgroup analysis

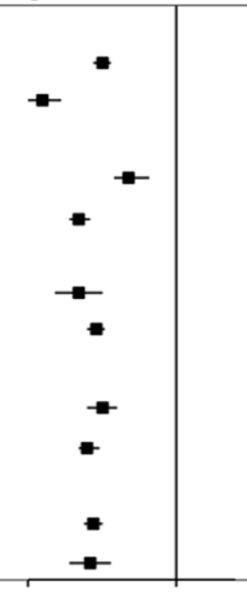
The inverse associations between LE8 score and risk of CVD and all-cause mortality were stronger among women than men (*P* for interaction <0.001). In addition, the inverse association of the LE8 score with risk of all-cause mortality was stronger among younger adults than older adults (*P* for interaction <0.001) and more pronounced among current drinkers than non-current drinkers (*P* for interaction <0.001). Furthermore, the association between LE8 score and risk of all-cause mortality was more pronounced among CKD patients with lower baseline eGFR (*P* for interaction <0.001). The association between LE8 score and risk of CVD was more pronounced among non-current drinkers than current drinkers (*P* for interaction = 0.03, Fig. 2).

3.4. Sensitivity analysis

In sensitivity analyses, the results did not substantially change when we further adjusted for proteinuria or re-defined CKD only using baseline eGFR (**Table S2** and **Table S3**). Likewise, the significant association remained when iteratively removing each CVH component from the total score (**Table S4**). Finally, similar results were yielded when

A

Subgroups	Cardiovascular disease cases/Total	HR (95% CI) per 10 points increment	*P* for interaction
Sex			
Men	1,823/14,581	0.75 (0.72, 0.78)	<0.001
Women	294/4,135	0.55 (0.49, 0.61)	
Age (years)			
≥65	706/4,654	0.84 (0.79, 0.91)	0.33
<65	1,411/14,041	0.67 (0.64, 0.71)	
Education			
High school or above	237/3,124	0.67 (0.59, 0.75)	0.18
Others	1,880/15,592	0.73 (0.70, 0.76)	
Alcohol intake			
Current drinker	647/5,281	0.75 (0.70, 0.80)	0.03
Non-current drinker	1,470/13,435	0.70 (0.67, 0.74)	
eGFR (ml/min/1.73 m^2)			
≥45	1,800/16,173	0.72 (0.69, 0.75)	0.52
<45	317/2,543	0.71 (0.64, 0.78)	



B

Subgroups	All-cause mortality cases/Total	HR (95% CI) per 10 points increment	*P* for interaction
Sex			
Men	3,707/14,581	0.90 (0.87, 0.93)	<0.001
Women	483/4,135	0.60 (0.55, 0.66)	
Age (years)			
≥65	1,650/4,654	0.94 (0.90, 0.97)	<0.001
<65	2,540/14,041	0.75 (0.72, 0.79)	
Education			
High school or above	365/3,124	0.82 (0.75, 0.90)	0.93
Others	3,825/15,592	0.89 (0.86, 0.91)	
Alcohol intake			
Current drinker	1,014/5,281	0.85 (0.81, 0.90)	<0.001
Non-current drinker	3,176/13,435	0.85 (0.83, 0.88)	
eGFR (ml/min/1.73 m^2)			
≥45	3,457/16,173	0.88 (0.85, 0.91)	<0.001
<45	733/2,543	0.85 (0.79, 0.91)	

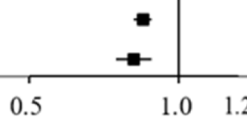


Fig. 2. Subgroup analyses of Life's Essential 8 score in relation to the risk of cardiovascular disease and all-cause mortality in patients with chronic kidney disease. HRs were adjusted for age, sex, alcohol drinking status, education level, marital status, family history of cardiovascular disease, and estimated glomerular filtration rate, except for the stratified factors.

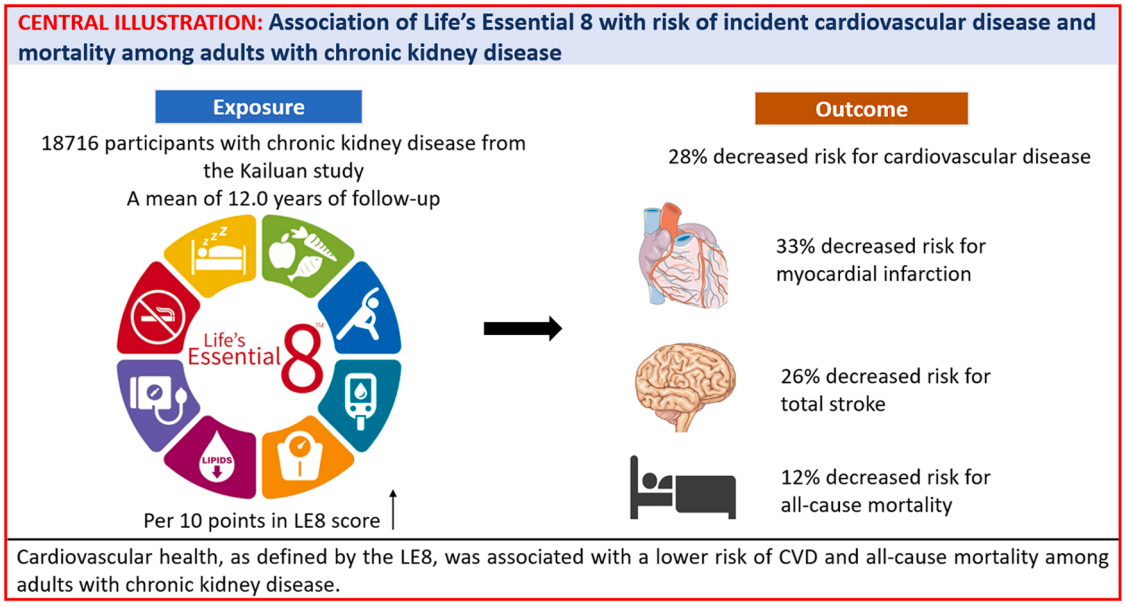
excluding the CVD or all-cause mortality events that occurred within the first four years of follow-up (**Table S5**).

4. Discussion

In this large prospective cohort of Chinese adults with CKD followed up for a median of 14.0 years, we observed that a higher LE8 score was associated with a lower risk of CVD (including MI, total stroke, ischemic stroke, and hemorrhagic stroke) and all-cause mortality. The results were robust in a series of sensitivity and subgroup analyses.

4.1. Comparison with other studies and possible explanations

To our knowledge, the associations of CVH, defined by LE8, with risks of CVD and all-cause mortality have been less explored among adults with CKD. Our study showed that a higher LE8 score was



Central Illustration.

significantly associated with a lower risk of CVD and all-cause mortality in CKD patients. Our findings were supported by the results from several previous studies conducted in the general adult population. For example, our previous studies observed that a higher LE8 score was associated with lower risks of premature CVD and all-cause mortality in Chinese young adults [15]. Meanwhile, the CVH score as assessed by the LE8 metrics significantly predicted future stroke risk [13]. Similarly, a Finnish study showed that LE8 was inversely associated with the risk of CVD death and all-cause mortality among aging men [30]. In addition, a prospective study from the UK Biobank showed that a high LE8 score was associated with a 64 % decrease in the risk of CVD in the general population [12]. Likewise, another study in the UK Biobank documented that ideal CVH was associated with lower risks of CVD and all-cause mortality [31]. Furthermore, a study from the US NHANES indicated that a high LE8 score was related to a considerably increased life expectancy in US adults [14]. Another US NHANES study showed that a higher LE8 score was associated with a reduced risk of all-cause and CVD-specific mortality [32]. However, these previous studies were conducted in the general population. Of note, CKD patients have different metabolic characteristics from the general population [16]. In addition, CKD patients were at increased risk of developing CVD [33]. Therefore, evidence regarding LE8 and cardiovascular health from CKD patients is needed.

To date, only one study using the US NHANES data showed that a higher LE8 score was associated with a lower risk of all-cause and cause-specific mortality [17]. In addition, a UK Biobank study indicated that a higher LS7 score (not including sleep compared with LE8) was associated with a lower risk of CVD events and mortality among patients with CKD [34]. However, due to the differences in lifestyle, and disease susceptibility between Chinese and Western populations, evidence from the Western population may not be entirely applicable to Chinese CKD patients. Our current study provides novel insights, highlighting the potential benefits of higher CVH scores in reducing the burden of CVD and mortality among Chinese adults with CKD. Importantly, our data suggested that strictly adhering to LE8 recommendations could provide great health benefits, though only a small proportion of CKD patients achieved high CVH (LE8 score: 80–100 points) in our study population.

Interestingly, we observed that among CKD patients, the inverse associations of LE8 score with risk of CVD and all-cause mortality were stronger among women. Such interaction was observed in studies in the general population [12]. This is partly explained by that women had a healthier lifestyle than men [12,35,36]. In addition, the inverse association of the LE8 score with risk of all-cause mortality was stronger among younger adults. Furthermore, this association between LE8 score and risk of CVD was more pronounced among non-current drinkers, while the association between LE8 score and risk of all-cause mortality was more pronounced among current drinkers. Also, the association between LE8 score and risk of all-cause mortality was more pronounced among those with lower baseline eGFR.

Because various factors (diet, physical activity, smoking, sleep duration, BMI, blood lipids, blood glucose, and BP) are usually correlated and may affect the disease risk in concert [11], we did not analyze the associations of single LE8 components with the risk of CVD and all-cause mortality. As an alternative, we re-calculated the CVH score by removing each metric from the LE8 score and analyzing the association of the re-calculated CVH score and risk of CVD and all-cause mortality. Such an approach can provide a deeper insight into the influence of individual components on the association between the overall LE8 score and health outcomes [37]. The results indicated that the protective associations of the LE8 score with risks of CVD and all-cause mortality were only slightly influenced by the individual components.

4.2. *Strengths and limitations*

The strengths of the current study include the prospective design, large sample size, long-term follow-up (maximum 15.5 years), and detailed measurements of lifestyle variables. In addition, information on the study outcomes including CVD and total mortality was reliable, minimizing potential misclassification bias of the outcomes. Moreover, the consistency of the associations observed in the study over sensitivity and subgroup analyses indicates the robustness of the findings.

The present study also has several potential limitations. First, lifestyle data were self-reported and only baseline data were used in the main analysis, which raises concerns about exposure misclassification. Second, although we adjusted for a number of covariates identified by the directed acyclic graph, residual confounding from unknown or unmeasured factors might still exist. Third, reverse causality is a potential concern. To reduce potential reverse causality bias, we introduced a 4-year lag analysis, and the results were not materially altered. Finally, the study participants were recruited from a relatively fixed geographic region, Tangshan, China, and exhibited relatively homogeneous genetic risk, geographic environment, and lifestyle factors. This homogeneity

may limit the generalizability of the findings to populations from other countries and ethnic groups.

5. Conclusions

In conclusion, our findings indicate that CVH, as defined by the LE8, was associated with a lower risk of CVD and all-cause mortality among adults with CKD. Since CKD is highly correlated with CVD, this study underscores the importance of an early-adopted LE8 strategy to reduce CVD and all-cause mortality. Clinicians would be strongly advised to expand their knowledge and offerings to patients with CKD.

CRediT authorship contribution statement

Zhenyu Huo: Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Jinfeng Li:** Writing – original draft, Methodology, Formal analysis, Data curation. **Shunming Zhang:** Writing – original draft, Validation, Methodology. **Liuxin Li:** Validation, Conceptualization. **Jingdi Zhang:** Formal analysis. **Yiran Xu:** Formal analysis. **Aitian Wang:** Writing – review & editing, Data curation. **Shuohua Chen:** Validation, Supervision, Project administration, Data curation. **Jun Feng:** Validation, Data curation. **Zhangling Chen:** Validation, Formal analysis. **Shouling Wu:** Writing – review & editing, Validation, Data curation, Conceptualization. **Tingting Geng:** Writing – review & editing, Visualization, Conceptualization. **Zhe Huang:** Writing – review & editing, Conceptualization. **Jingli Gao:** Writing – review & editing, Data curation, 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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Data sharing

Data described in the manuscript can be made available upon request pending application and approval by the chair of the steering committee for the cohort.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2025.100994.

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