Effect of Systemic Inflammatory Response Index on Cardiovascular Disease Risk in Patients with Chronic Kidney Disease

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Abstract: Objective: To investigate the effect of systemic inflammatory response index on cardiovascular disease in patients with chronic kidney disease.Methods: In this prospective cohort study, 12417 patients with chronic kidney disease (CKD) with complete data and no previous history of cardiovascular disease who participated in the health examination for the first time in Kailuan Group from 2006 to 2007 were selected as the observation objects, with new-onset cardiovascular disease as the endpoint event, and followed up until the end of 2021. Patients were grouped according to the SIRI quartile, Kaplan-Meier method was used to calculate the cumulative incidence of cardiovascular diseases and subtypes in different groups, and multivariate Cox proportional risk regression model was used to analyze the impact of different groups on cardiovascular diseases.Result: A total of 12417 participants were included in the study, 75.8% of whom were male. The mean age of the subjects was 57.6±13.5 years. During the mean follow-up period of (11.81±3.84) years, The incidence densities of CVD in each group were 11.79/1000, 13.86/1000, 14.84/1000 and 16.73/1000, respectively. After adjusting for confounding factors such as age and sex, Cox regression analysis showed that compared with group Q1, the HR (95%CI) of CVD in groups Q2, Q3 and Q4 were 1.14 (1.00,1.30), 1.17 (1.03,1.33) and 1.25 (1.10,1.42), respectively, $P < 0.05$.Conclusion: SIRI is an independent risk factor for cardiovascular disease in patients with chronic kidney disease.

***Keywords*:** Systemic inflammatory response index; Chronic kidney disease; Cardiovascular diseases; Cohort study

1. Introduction

Chronic Kidney Disease (CKD) is a growing global public health problem, affecting approximately 13.4% of the global population [1]. Data show that the number of CKD patients in China reached 151 million in 2019, and the prevalence rate is increasing year by year [2], which brings huge medical and economic burden to the society. Cardiovascular Disease (CVD) is one of the important complications in patients with CKD and the main cause of death in patients with CKD [3]. Therefore, it is of great importance to prevent the occurrence of CVD in patients with CKD [4]. However, controlling traditional cardiovascular risk factors does not completely reduce the risk of cardiovascular disease associated with CKD, and further study of other risk factors is needed.

Current studies believe that compared with the general population, the accumulation of toxins, oxidative stress and the imbalance of intestinal microbiota in CKD patients promote the activation of inflammatory pathways, resulting in increased systemic inflammation [5], accelerating the development of atherosclerosis, and thus increasing the risk of CVD. The Systemic Inflammatory Response Index (SIRI) is an inflammatory index proposed in recent years by combining peripheral blood neutrophils, monocytes and lymphocytes, and comprehensively reflects the inflammatory and immune states of the body [6]. Previous studies have shown that the increased level of SIRI is positively correlated with the severity of coronary artery disease and the incidence of acute coronary syndrome [7]. A meta-analysis indicated that SIRI is a marker of inflammation for evaluating the clinical outcome of various types of stroke [8]. Kong et al. found that increased SIRI in obese people was associated with increased risk of cardiovascular disease death and all-cause death [9]. However, the relationship between SIRI and cardiovascular disease risk in patients with CKD is unclear.

In this context, relying on the Kailuan study cohort, this study aims to explore the relationship between SIRI and cardiovascular disease risk in CKD population, promote the identification and management of cardiovascular disease in CKD patients, and reduce the risk of cardiovascular disease in CKD population.

2. Data and methods

2.1 Research objects

The Kailuan Study is a large prospective cohort study based on a northern population. From 2006 to 2007, Kailuan

General Hospital and its affiliated hospitals conducted the first physical examination of employees of Kailuan Group and collected relevant data, and then conducted a physical examination every two years. Data including questionnaire survey, physical examination and laboratory examination were collected. Cardiovascular events were followed up annually during the follow-up period. All subjects agreed to participate in the Kailuan study and signed informed consent. This study was approved by the Ethics Committee of Kailuan General Hospital ([2006] Yilun Zi No. 5).

The study included 14,548 participants with CKD who participated in a health checkup in 2006-2007. CKD is defined as glomerular filtration rate (eGFR) < 60mL/min/1.73m^2 and/or positive albuminuria (> 30mg/g). eGFR was calculated according to the formula of the Chronic Kidney Disease Epidemiology Cooperative Group [10]. After excluding 1557 patients who had a history of cardiovascular disease during physical examination, and 574 patients with neutrophil count, monocyte count, and lymphocyte count, a total of 12417 patients with CKD were included in the study.

2.2 Data Collection

General information: Demographic data, personal lifestyle, personal disease history, and drug use were collected through a unified questionnaire.

Anthropometric indicators: Height and body mass are measured by calibrated RGZ-120 body mass scale, accurate to 0.1cm height and 0.1kg body mass. Body mass index (BMI) = body mass (kg)/height (m^2). Blood pressure measurement: The subject is not allowed to smoke or drink tea or coffee within 30 minutes before the measurement, sit back for 15 minutes, and the right brachial artery blood pressure is measured by qualified medical personnel.

Biochemical index detection: Venous blood was collected after fasting for more than 8h, and creatinine, fasting blood glucose, triglyceride, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, high sensitivity C-reactive protein and other indicators were detected by Hitachi 7600 automatic biochemical analyzer. Blood routine index detection: neutrophil count, lymphocyte count and monocyte count were detected by SysmexXT-1800i automatic blood cell analyzer. Urine routine testing: Urine samples were analyzed using the Dirui N-600 semi-automatic urine analyzer, and the test results for proteinuria were classified as negative, small, 1+, 2+, 3+ and 4+.

2.3 Relevant definitions

SIRI: (Neutrophil count x monocyte count)/lymphocyte count. Hypertension: more than 3 times in different days, SBP≥140mmHg (1mmHg= 0.133kPa) and/or DBP≥90mmHg, or although SBP < 140mmHg and DBP < 90mmHg, use antihypertensive drugs or have a history of hypertension. Diabetes: Fasting blood glucose ≥7.0mmol or fasting blood glucose < 7.0mmol but using hypoglycemic drugs or have a history of diabetes. Smoking: defined as a history or current smoker. Alcohol consumption: defined as a history or current consumption of alcohol. Physical exercise: defined as the number of exercises ≥3 times/week, each duration ≥30min.

2.4 Grouping and follow-up

Patients were grouped according to the SIRI quartile (group Q1: SIRI≤0.45; Group Q2:0.45 < SIRI≤0.67; Q3 group: 0.67 < SIRI≤1.01; Q4 group: SIRI > 1.01). The time when the first physical examination was completed was the starting point of follow-up, and the occurrence of CVD was the end event, which was defined as myocardial infarction, atrial fibrillation, heart failure, coronary stent implantation and stroke. Stroke includes ischemic stroke and hemorrhagic stroke. If more than one event occurs, the time and event at which the final event occurs first are the ending points. If no CVD occurred, the last follow-up was December 31, 2021. These events were all confirmed by professional physicians in the inpatient records. The diagnosis of myocardial infarction is based on the 2018 global definition of myocardial infarction [11]. The diagnosis of heart failure and atrial fibrillation is based on the guidelines of the European Society of Cardiology [12]. The diagnosis of stroke is based on the definition of stroke by the World Health Organization [13].

2.5 Statistical Methods

All data were analyzed using SAS 9.4 statistical software. The measurement data conforming to normal distribution were represented by mean ± standard deviation, the comparison between groups was represented by ANOVA, the measurement data of skew distribution was represented by median (P25, P75), and the comparison between groups was performed by non-parametric test (Kruskal-Wallis). Counting data were expressed as frequency and percentage, and the X2 test was used for comparison between groups. Cox proportional hazard regression model was used to calculate hazard ratio (HR) and 95% confidence interval (CI) to analyze the effects of different SIRI levels on the risk of CVD, heart failure, myocardial infarction, and stroke. The grouping variables were substituted into Cox proportional risk regression model as continuous variables for trend test. Kaplan-Meier method was used to calculate the cumulative incidence of CVD and subtypes in different groups, and comparison between groups was performed by log-rank. To further explore the effect of SIRI on CVD

events, we stratified the included population by sex (male or female), age (< 60 years or ≥60 years), BMI (< 24 or ≥24kg/m^2), hypertension (yes or no), diabetes (yes or no), and modeled the same covariates and interactions in the above analyses. Analyze multiplicative interactions with SIRI. See Figure 1.

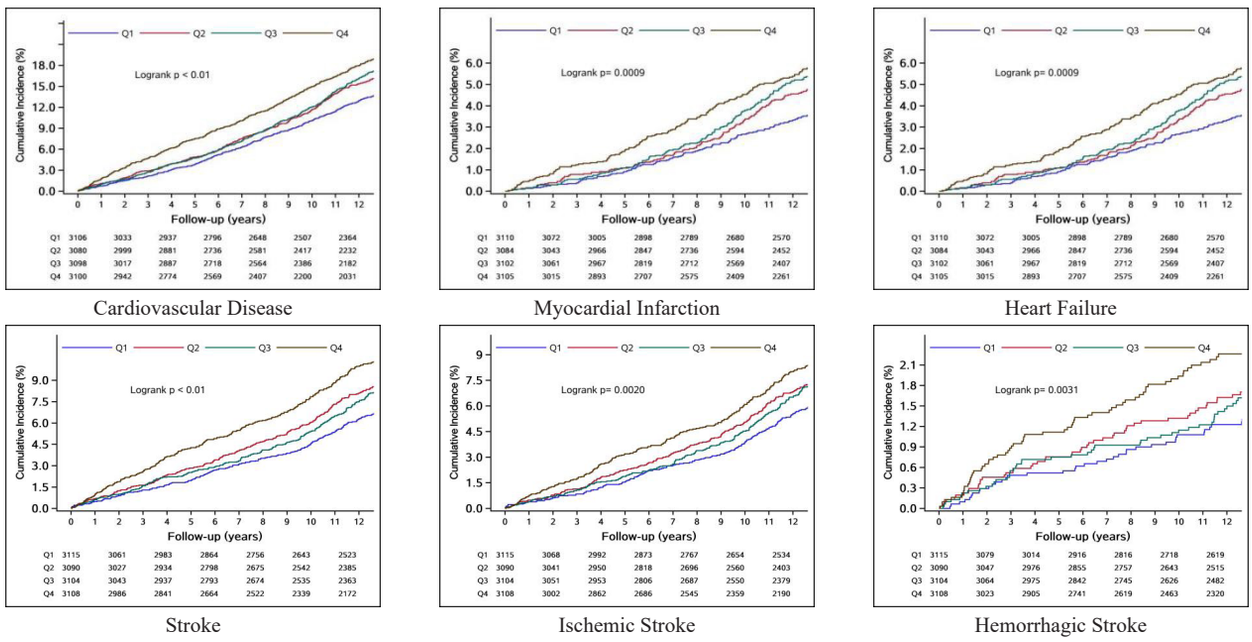

Figure 1. Cumulative incidence of SIRI and CVD and subtypes in the chronic kidney disease population

3. Results

3.1 Baseline characteristics of research objects in different groups

A total of 12417 patients with CKD were included in this study, including 11242 patients with eGFR < 60mL/min/1.73m^2 and normal urine protein, 818 patients with positive urine protein but normal eGFR, 357 patients with eGFR < 60mL/min/1.73m^2 and positive urine protein. The mean age of the subjects was 57.6±13.5 years, and 75.8% of them were male. The patients were divided into four groups (Q1-Q4) according to the SIRI quartile. The average age of the participants in the Q4 group was older, and the proportion of people who smoked and were overweight was higher. In addition, the levels of systolic blood pressure, diastolic blood pressure, fasting blood glucose, total cholesterol and hypersensitive C-reactive protein were also higher, with statistically significant differences ($p < 0.05$). (See Table 1).

Table 1. Baseline characteristics of subjects in different groups [example (%)]

item	General population	SIRIQuartile grouping				p-value
	(n=12417)	Q1(n=31)	Q2(n=30)	Q3(n=310)	Q(n=3108)	
Age (years)	57.6±13.5	57.5±13.9	56.9±13.4	57.5±13.4	58.4±13.3	<0.001
male	9410(75.8)	2046(65.3)	2337(75.6)	2448(78.9)	2579(83.5)	<0.001
drinking	3546(28.6)	938(29.9)	891(28.8)	843(27.7)	874(28.3)	<0.001
smoking	3693(29.7)	868(27.7)	892(28.9)	937(30.2)	996(32.2)	<0.001
overweight	2673(21.5)	531(16.9)	667(21.6)	678(21.8)	797(25.8)	<0.001
SBP(mmHg)	138.7±22.3	134.5±21.8	137.8±21.1	139.7±22.1	140.0±23.4	<0.001
DBP(mmHg)	86.3±12.2	84.0±11.6	86.1±11.5	87.0±12.2	88.2±13.0	<0.001
FBG(mmol/L)	5.7±2.1	5.5±1.8	5.7±2.1	5.8±2.2	5.9±2.3	<0.001
TG(mmol/L)	2.0±1.6	2.0±1.6	2.0±1.6	2.0±1.6	2.0±1.6	<0.001
TC(mmol/L)	4.9±1.4	4.8±1.4	4.8±1.4	4.9±1.4	5.0±1.3	<0.001
LDL-C(mmol/L)	2.6±0.8	2.5±0.8	2.5±0.7	2.6±0.8	2.6±0.9	<0.001
HDL-C(mmol/L)	1.6±0.4	1.6±0.4	1.6±0.4	1.6±0.4	1.6±0.4	<0.001
hs-CRP(mg/L)	0.9(0.4,2.5)	0.8(0.3,2.0)	0.8(0.3,2.1)	0.9(0.4,2.4)	1.3(0.5,3.6)	<0.001

item	General population	SIRIQuartile grouping				p-value
	(n=12417)	Q1(n=31)	Q2(n=30)	Q3(n=310)	Q(n=3108)	
MON(10^9/L)	0.4±0.3	0.3±0.4	0.4±0.1	0.5±0.2	0.7±0.3	<0.001
NEUT(10^9/L)	4.1±1.4	3.0±0.8	3.7±0.8	4.2±0.9	5.3±1.6	<0.001
LYM(10^9/L)	2.4±0.8	2.4±1.0	2.4±0.7	2.4±0.7	2.3±0.8	<0.001
eGFR(mL/ min/1.73m^2)	53.1±14.0	52.8±13.2	52.9±13.2	53.1±15.7	53.7±13.6	<0.001
Take lipid-lowering drugs	138(1.1)	38(1.2)	27(0.9)	40(1.3)	33(1.1)	0.420
Take blood pressure medication	1705(13.7)	388(12.4)	408(13.2)	413(13.3)	496(16.1)	<0.001
Take hypoglycemic drugs	431(2.0)	97(3.1)	105(3.4)	115(3.7)	114(3.7)	0.508
Take diuretics	158(1.3)	39(1.3)	42(1.4)	36(1.2)	41(1.3)	0.905

Note: Data are expressed as mean ± standard deviation, median (p25, p75), or n (percent). LDL-C: Low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; hs-CRP: highly sensitive C-reactive protein; MON: Monocyte; Neutrophils; LY: Lymphocyte; eGFR: Estimation of glomerular filtration rate.

3.2 Influence of SIRI level on CVD risk of different groups of subjects

During a mean follow-up of (11.81±3.84) years, there were 2089 new CVD events, including 347 myocardial infarction, 594 heart failure, and 1033 stroke. The number of CVD cases in each group was 448, 512, 545 and 584, respectively. The incidence densities of CVD in each group were 11.79/1000, 13.86/1000, 14.84/1000 and 16.73/1000, respectively. The Log-rank test showed that the cumulative incidence was significantly different among different groups ($P < 0.05$). After correction, Cox regression analysis showed that compared with group Q1, the HR (95%CI) of CVD in group Q2, Q3 and Q4 were 1.14 (1.00,1.30), 1.17 (1.03,1.33) and 1.25 (1.10,1.42), respectively. The HR (95%CI) of heart failure, myocardial infarction and stroke in Q4 group were 1.49 (1.16,1.90), 1.29 (1.01,1.78) and 1.38 (1.15,1.65), respectively, all $P < 0.05$ (see Table 2).

Table 2. Cox regression analysis of the effect of SIRI on CVD risk in CKD population (n=12417)

	Number of cases(%)	Incidence density(/Per thousand years)	model1	model2	model3	model4
			HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)
Cardiovascular disease						
Q1	448(14.38)	11.79	1.00	1.00	1.00	1.00
Q2	512(16.57)	13.88	1.18(1.04,1.34)	1.15(1.01,1.31)	1.14(1.01,1.30)	1.14(1.00,1.30)
Q3	545(17.56)	14.84	1.22(1.08,1.39)	1.19(1.04,1.35)	1.17(1.03,1.33)	1.17(1.03,1.33)
Q4	584(18.79)	16.73	1.34(1.18,1.52)	1.28(1.13,1.45)	1.26(1.11,1.43)	1.25(1.10,1.42)
$P_{trend\ value}$			<0.001	<0.001	<0.001	<0.001
Heart failure						
Q1	115(3.69)	2.90	1.00	1.00	1.00	1.00
Q2	151(4.88)	3.90	1.02(0.83,1.25)	1.39(1.08,1.74)	1.39(1.08,1.78)	1.39(1.08,1.78)
Q3	162(5.22)	4.20	1.41(1.11,1.82)	1.47(1.15,1.87)	1.46(1.14,1.86)	1.45(1.14,1.86)
Q4	166(5.34)	4.48	1.51(1.18,1.92)	1.51(1.18,1.93)	1.49(1.16,1.91)	1.49(1.16,1.90)
P trend value			<0.001	<0.001	<0.001	<0.001
Myocardial infarction						
Q1	74(2.38)	1.86	1.00	1.00	1.00	1.00
Q2	85(2.75)	2.18	1.19(0.87,1.62)	1.15(0.83,1.57)	1.13(0.82,1.56)	1.13(0.82,1.56)
Q3	83(2.75)	2.13	1.12(0.82,1.55)	1.07(0.77,1.47)	1.04(0.75,1.43)	1.04(0.75,1.43)
Q4	105(3.38)	2.81	1.452(1.07,1.97)	1.37(1.03,1.85)	1.31(1.01,1.78)	1.31(1.01,1.78)
$P_{trend\ value}$			0.026	0.072	0.139	0.152
Cerebral apoplexy						
Q1	211(6.77)	5.37	1.00	1.00	1.00	1.00
Q2	264(8.54)	6.93	1.27(1.06,1.52)	1.24(1.04,1.49)	1.24(1.04,1.49)	1.24(1.03,1.49)

	Number of cases(%)	Incidence density(/Per thousand years)	model1	model2	model3	model4
			HR(95%CI)	HR(95%CI)	HR(95%CI)	HR(95%CI)
Q3	247(7.96)	6.48	1.14(0.95,1.37)	1.11(0.92,1.34)	1.10(0.92,1.33)	1.10(0.91,1.32)
Q4	311(10.01)	8.57	1.48(1.23,1.75)	1.41(1.18,1.68)	1.39(1.16,1.66)	1.38(1.15,1.65)
P trend value			<0.001	0.001	0.002	0.004
Ischemic stroke						
Q1	187(6.00)	4.75	1.00	1.00	1.00	1.00
Q2	226(7.31)	5.89	1.22(1.01,1.49)	1.20(0.99,1.46)	1.20(0.99,1.46)	1.20(0.99,1.46)
Q3	215(6.92)	5.61	1.12(0.92,1.37)	1.10(0.90,1.34)	1.09(0.85,1.33)	1.09(0.89,1.33)
Q4	248(7.98)	6.79	1.32(1.09,1.60)	1.27(1.05,1.54)	1.26(1.04,1.53)	1.26(1.03,1.52)
P trend value			<0.001	0.045	0.058	0.067
Hemorrhagic apoplexy						
Q1	43(1.38)	1.07	1.00	1.00	1.00	1.00
Q2	51(1.65)	1.30	1.17(0.78,1.76)	1.15(0.77,1.73)	1.14(0.76,1.72)	1.15(0.76,1.73)
Q3	51(1.64)	1.31	1.45(0.76,1.72)	1.10(0.73,1.65)	1.09(0.72,1.65)	1.10(0.73,1.65)
Q4	76(2.45)	2.03	1.71(1.17,2.49)	1.64(1.20,2.39)	1.60(1.09,2.34)	1,60(1.09,2.34)
$P_{\text{trend value}}$			0.006	0.013	0.019	0.022

Note: Model 1: corrected for age and sex; Model 2: On the basis of model 1, smoking, alcohol consumption, physical exercise, education level, and body mass index were adjusted; Model 3: Low density lipoprotein cholesterol, high density lipoprotein cholesterol, high sensitivity C-reactive protein, proteinuria, hypertension, diabetes mellitus were corrected on the basis of model 2. Model 4: eGFR is corrected based on Model 3.

3.3 Hierarchical analysis of the influence of SIRI level on CVD risk of different research groups

In patients < 60 years of age, men and women, BMI < 24 and ≥24, with hypertension, and without diabetes, increased risk of CVD was associated with increased SIRI levels, while no interaction was observed in stratified factors (P interaction > 0.05), suggesting that SIRI was an independent risk factor for increased risk of CVD. (See Table 3)

Table 3. Stratified analysis of SIRI's influence on CVD risk in CKD population (n=12417)

item	Number of cases(%)	SIRIQuartile grouping［HR(95%CI)］				$P_{\text{interaction}}$ value
		Q1	Q2	Q3	Q4	
age						0.054
<60(n=7448)	965(12.96)	1.00	1.25(1.02,1.52)	1.39(1.15,1.69)	1.50(1.24,1.82)	
≥60(n=4969)	1124(22.62)	1.00	1.06(0.89,1.26)	1.01(0.85,1.94)	1.07(0.90,1.27)	
sex						0.190
male(n=9410)	1744(18.53)	1.00	1.09(0.94,1.26)	1.11(0.96,1.28)	1.17(1.02,1.35)	
female(n=3007)	345(11.47)	1.00	1.32(0.98,1.78)	1.39(1.04,1.87)	1.66(1.22,2.26)	
BMI						0.529
<24(n=4172)	596(14.29)	1.00	1.20(0.95,1.51)	1.27(1.01,1.60)	1.26(0.99,1.60)	
≥24(n=8405)	1493(17.76)	1.00	1.12(0.96,1.31)	1.13(0.97,1.31)	1.25(1.07,1.45)	
hypertension						0.974
have(n=7299)	1632(22.36)	1.00	1.11(0.95,1.28)	1.12(0.97,1.29)	1.22(1.05,1.41)	
no(n=4578)	457(9.98)	1.00	1.12(0.86,1.45)	1.17(0.91,1.52)	1.11(0.84,1.46)	
diabetes						0.443
have(n=2001)	519(25.94)	1.00	1.15(0.88,1.51)	1.14(0.88,1.49)	1.11(0.85,1.43)	
no(n=10416)	1570(15.07)	1.00	1.13(0.97,1.30)	1.16(1.01,1.34)	1.26(1.08,1.46)	
eGFR						0.831
<45ml/(min·1.73m^2)	397(17.98)	1.00	1.19(0.89,1.62)	1.38(1.03,1.84)	1.54(1.14,2.09)	
≥45ml/(min·1.73m^2)	1692(16.57)	1.00	1.13(0.98,1.35)	1.23(0.98,1.30)	1.22(1.06,1.40)	

Note: The model adjusted for age, sex, smoking, alcohol consumption, physical activity, education level, body mass index, LDL cholesterol, HDL cholesterol, hypersensitive C-reactive protein, proteinuria, hypertension, diabetes, eGFR.

4. Discussion

Our analysis of 12,417 patients with CKD showed that high levels of SIRI were strongly associated with an increased risk of CVD in the CKD population, independent of eGFR, and in patients < 60 years of age, women, and eGFR < 45mL/min/1.73m^2. SIRI was more significantly associated with CVD risk.

SIRI is a complex inflammatory index, which was originally proposed as a prognostic indicator of adverse outcomes in cancer patients [14]. A prospective study showed that SIRI level was significantly increased in patients with poor prognosis such as non-fatal myocardial infarction and non-fatal stroke [15]. Zhao S et al. found that a high level of SIRI was an independent predictor of cardiovascular death and all-cause death in hypertensive patients [16]. This study extends these findings to the CKD population, demonstrating an increased risk of cardiovascular disease in CKD patients with higher levels of SIRI. This suggests that management of CKD patients should pay attention not only to renal function, but also to systemic inflammation.

Our results suggest that SIRI levels are positively associated with CVD risk in patients with CKD (P trend < 0.05). After adjusting for multiple confounders, the multifactor Cox risk scale model showed that SIRI was an independent risk factor for cardiovascular disease risk in patients with persistent CKD. In addition, we found differences in the effect of high SIRI proficiency on different outcome events, with increased SIRI proficiency increasing the risk of heart failure by 49% compared to myocardial infarction, compared to 31% for myocardial infarction. We also found that Q4 participants had a 26% and 60% increased risk of ischemic stroke and hemorrhagic stroke, respectively, compared to Q1 participants, and we speculate that SIRI may be more reflective of the inflammatory status of hemorrhagic stroke in CKD patients than ischemic stroke.

Although no interaction was found in subgroup analysis, the Q4 group had a 66% increased risk of CVD in female participants and a 17% increased risk of CVD in male participants compared with Q1 group, suggesting that the effect of elevated SIRI on CVD is greater in female CKD patients, and this gender difference may be due to the cross-action of hormones and the immune system. There was no association between SIRI and CVD risk in subjects aged ≥60 years, while SIRI was significantly associated with CVD risk in subjects aged < 60 years. Previous studies also found that the younger the age of onset of hypertension and diabetes, the higher the risk of adverse outcomes [17-18]. This suggests that early or younger exposure to high levels of chronic inflammatory states has a higher long-term prognostic risk. In addition, we found that SIRI elevation increased the risk of CVD by 22% in patients with eGFR≥45mL/min/1.73m^2 and 54% in patients with eGFR < 45mL/min/1.73m^2, suggesting that SIRI elevation increased the risk of CVD in patients with end-stage renal disease. Barreto DV et al. also found that inflammatory activities in stages IV and V of CKD may be more obvious than those in stages I to III [19], which may be attributed to the fact that eGFR reduction leads to abnormal lipid metabolism, mineral and bone metabolism disorders and promotes the activation of inflammatory pathways [20], thereby increasing the risk of cardiovascular disease.

Current studies consider that CKD is an inflammatory disease [21]. Inflammation triggers abnormal activation of the neutrophil and mononuclear macrophage systems and subsequently induces the release of inflammatory factors, which lead to vascular endothelial damage and platelet aggregation [22]. On the contrary, lymphocytes have a regulatory function in inflammation and may play an inhibitory role in atherosclerosis [23]. A retrospective multicenter cohort study observed that individuals with high levels of SIRI tended to have elevated levels of neutrophils and monocytes and low levels of lymphocytes [24]. A large number of studies consistently support these findings, suggesting that increased monocyte and neutrophilic levels and decreased lymphocyte levels are positively associated with increased risk of cardiovascular disease [25], which may provide a plausible explanation for the increased risk of CVD associated with increased SIRI levels in CKD patients.

SIRI, which can be obtained by complete blood count, holds great promise and significant economic benefits in clinical Settings. By demonstrating the relationship between SIRI and CVD risk, our study suggests that SIRI could be an important marker for clinicians to assess CVD risk in patients with CKD.

The advantages of this study are prospective cohort design, large sample size, and long follow-up time. There are limitations to this study: First, our diagnosis of CKD was based on a single eGFR measurement and one-time strip test without follow-up assessment after 3 months, which may have led to overdiagnosis of CKD. Second, although we consider as many covariates as possible, there may be confounding factors that are not adjusted for. Third, more than 75% of the participants in this study were Chinese men from the Kailuan community, which may limit the generalizability of our results across gender-specific and geographically diverse populations.

5. Conclusion

SIRI was positively associated with CVD risk in patients with CKD. Monitoring SIRI can help identify high-risk patients early, enabling timely and targeted interventions.

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