Research paper

Inflammation response index (SIRI) is associated with all-cause and cardiovascular mortality in maintenance hemodialysis patients

Keywords
Systemic inflammatory response index (SIRI), motality, maintenance hemodialysis

Abstract

Introduction
The aim of this study was to investigate the association between inflammation response index (SIRI) on all-cause and cardiovascular (CVD) mortality in maintenance hemodialysis (MHD) patients.

Material and methods
371 MHD patients were included in this retrospective study. Time-dependent receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive value of SIRI. Patients were categorized into two groups based on the median value of SIRI. Kaplan-Meier survival analysis was used to compare the difference in survival rate. Cox regression analysis was used to analyze all-cause and CVD mortality risk factors, and nomograms were established.

Results
The average age of the patients was (60.71±15.34), and the median follow-up was 42 months. 157 patients died. SIRI had a predictive value for all-cause and CVD mortality. The AUC of the SIRI to predict the all-cause mortality was 0.698, 0.664, 0.713, and 0.900 at 1, 3, 5, and 10 years, respectively. For CVD mortality, the AUC of the SIRI was 0.678, 0.667, 0.717, and 0.906 at 1, 3, 5, and 10 years, respectively. Kaplan-Meier survival analysis showed that patients with high SIRI levels show a significantly lower survival rate. Multivariate Cox regression analysis showed that SIRI > 1.88 was an independent risk factor for all-cause and CVD mortality.

Conclusions
SIRI can independently predict all-cause and CVD mortality in MHD patients, which has important value for prognosis.

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Introduction

Maintenance hemodialysis (MHD) patients have higher mortality compared to the general population. The morbidity of cardiovascular complications is high, and cardiovascular disease (CVD) is the major cause of mortality in MHD patients [1]. Traditional risk factors may not fully explain the high incidence of CVD in MHD patients because these patients also suffer from uremic toxins and dialysis-related risk factors, such as microinflammatory state [2]. Microinflammatory state is common in MHD patients and is an important reason for poor prognosis.

Systemic inflammation response index (SIRI) is a novel marker of microinflammation, which is calculated as neutrophil count × monocyte/lymphocyte count [3, 4, 5]. SIRI might better reflect the host immune and inflammation balance, but the pathophysiology remains incompletely understood. It is widely known that immune cells play an important role in triggering inflammation responses and modulating inflammation. Former research has confirmed that during the early period of inflammation, neutrophil could release cytokines and chemokines, induce apoptosis of endothelial cells, and cause vascular damage. This promoted the development and progression of CVD [6]. Due to the increase of monocyte, the number of macrophage differentiated from monocyte also rise. The macrophage can be transformed into foamy cells, which are closely correlated with vascular endothelial dysfunction, thus accelerating the progression of atherosclerotic lesions [7]. Previous studies have also shown that blood monocyte count predicted total and cardiovascular mortality in HD patients [8]. Lymphocyte plays a vital role in the immune response of human. Fei J et al. [9] found that lymphopenia at an early stage could aggravate the severity and elevate the death risk of COVID-19 patients. Previous research has

shown that significant lymphocyte apoptosis was observed in the vascular endothelial with atherosclerosis. A lower lymphocyte level was associated with adverse CVD outcomes [10]. However, neutrophil, monocyte, and lymphocyte are easily affected by dehydration, exercise, etc, so the specificity is unsatisfactory. C-reactive protein (CRP) has been confirmed to be a predictor of mortality in HD patients [11]. However, CRP is an acute phase protein, which can be easily affected by weight change, smoking, diabetes, and other factors. Hence its specificity is also not high [12]. In recent years, research has also found that the neutrophil-lymphocyte ratio (NLR) was a short-term predictor of all-cause mortality in patients with diabetic nephropathy [13] A higher NLR was associated with frequent congestive heart failure decompensation and long-term mortality [10]. Besides, the monocyte-to-lymphocyte ratio (MLR) has been shown to be a predictor of cardiovascular and all-cause mortality in hemodialysis patients [14]. By comparison, the measurement method on the SIRI is simple and stable. SIRI is supposed to integrate the three different mechanisms of inflammatory and immunological responses for neutrophil, monocyte, and lymphocyte. So it is more comprehensive and easily accessible. The increase in SIRI can indicate the immune system disorder is becoming more apparent, and the inflammatory response is more powerful. This may be the potential mechanism that would influence outcomes for patients.

SIRI has been widely studied in predicting terminal events in many diseases and has a good predictive effect and clinical guidance value. Studies have shown that SIRI can predict the prognosis of patients with stroke and cancer [3,4,5]. Another study found that SIRI was associated with increased all-cause and cardiovascular mortality among patients with hypertension [15]. However, there are currently fewer studies on the effect of SIRI on the prognosis of MHD. In this study, we aimed to explore the association between inflammation reflected by SIRI and all-cause and CVD mortality in

MHD patients.

Material and methods

In this retrospective study, patients who initiated MHD in the hemodialysis center of the Second Affiliated Hospital of Soochow University in China were enrolled from September 2010 to September 2022. The inclusion criteria were as follows: (1) age > 18 years; (2) on hemodialysis for at least 3 months. The exclusion criteria were as follows: (1) complicated by severe infection at baseline; (2) during the active stages of autoimmune diseases at baseline; (3) hematological system diseases; (4) malignant tumors; (5) received peritoneal dialysis (PD) or kidney transplants during the follow-up period; (6) changed hemodialysis center or lost to follow-up. The end of follow-up time was 31 December 2022. This study was approved by the Clinical Research Ethics Committee of The Second Hospital Affiliated of Soochow University

Baseline data were collected, including age, gender, and smoking history. Body mass index (BMI) was calculated according to height and weight. We recorded the history of hypertension and diabetes, the history of CVD, and the pathogenesis of end-stage renal disease (ESRD). Laboratory parameters including neutrophil count, monocyte count, lymphocyte count, hemoglobin, CRP, serum creatinine, serum urea nitrogen, serum uric acid, serum albumin, serum calcium, serum phosphorus, serum potassium, blood cholesterol, triglyceride, parathyroid hormone (PTH), and total Kt/V (Kt/V is the fractional urea clearance, defined as urea clearance (K) multiplied by the dialysis session length (t) divided by the urea distribution volume V). The Kt/V results were obtained using the special HD formula of Kt/V. The glomerular filtration rate (eGFR) was estimated using the CKD-EPI formula. The SIRI was calculated as neutrophil count × monocyte/lymphocyte count [3,4,5]. The NLR and MLR were also calculated. All data were obtained within 1 month after the patient's regular HD reached dry

body mass. We recorded the causes of death. Patients who died of coronary artery disease, valvular heart disease, myocardial disease, arrhythmia, cerebrovascular disease, and peripheral vascular disease were defined as CVD mortality.

Statistical Analysis

The statistical analysis was performed using SPSS 26.0 (IBM SPSS, Somers, NY, USA) and R software (version 4.3.0, Vienna, Austria). Continuous variables followed the normal distribution with mean and standard deviation. Parameters with skewed distribution were presented as (median, interquartile). The t-test was used for normal distribution data to compare the differences between two groups. Nonparametric statistical methods, the Mann-Whitney test, were used for data with skewed distribution. Categorical data were expressed as the count (percentage) and compared using a $\chi 2$ test. The time-dependent ROC curve and area under the curve (AUC) were used to compare the predictive performance of SIRI, NLR, and MLR at 1, 3, 5, and 10 years for all-cause and CVD mortality. Kaplan-Meier methods were used to compute the survival analysis, and the significance test was done using the log-rank method. Univariate and multivariate Cox regression analyses were performed to assess the risk factors of all-cause and CVD mortality. Univariate Cox regression analysis was first performed, and the multivariate Cox regression analysis included factors with a p value less than 0.10. Two nomograms were developed to predict all-cause and CVD mortality at 1, 3, 5, and 10 years. All p values were two-sided, and $p < 0.05$ was taken as statistically significant.

Results

Baseline characteristics

A total of 578 patients were enrolled, and 207 of whom were excluded. 371 patients were finally included in the study. The median value of SIRI was 1.88. According to the median value, these

patients were categorized into low group (SIRI ≤ 1.88) and high group (SIRI > 1.88) (Figure 1). The average age was (60.71±15.34), and the median follow-up was 42 (20-66) months. 121 patients had a history of CVD. 157 (42.3%) patients passed away during follow-up. The causes of death in these patients include CVD in 98 cases, infections in 25 cases, multiple organ failure in 14 cases, gastrointestinal hemorrhage in 7 cases, and other or unknown causes in 13 cases.

ROC curve analysis

The time-dependent ROC curve analysis was used to evaluate the predictive ability of SIRI, NLR, and MLR. Compared to NLR and MLR, SIRI showed a stronger ability in predicting all-cause and CVD mortality. The AUC of the SIRI to predict the all-cause mortality was 0.698 (95%CI: 0.610-0.786), 0.664 (95%CI: 0.602-0.726), 0.713 (95%CI: 0.648-0.779), and 0.900 (95%CI: 0.782-1.000) at 1, 3, 5, and 10 years, respectively (Figure 2). For CVD mortality, the AUC of the SIRI was 0.678 (95%CI: 0.571-0.784), 0.667 (95%CI: 0.590-0.743), 0.717 (95%CI: 0.646-0.789), and 0.906 (95%CI: 0.788-1.000) at 1, 3, 5, and 10 years, respectively (Figure 3).

Comparison of SIRI ≤ 1.88 group and SIRI > 1.88 group

The results of the two groups were compared at baseline. The high SIRI group showed significantly older age and a higher proportion of previous CVD, and the CRP level was higher. However, serum creatinine, serum albumin, and serum potassium were significantly lower (all $p < 0.05$) (Table 1).

Survival analysis

The medium survival time of the low SIRI group and high SIRI group was 48 months and 36 months, respectively. The parameters significantly differed ($Z = -3.902$, $p < 0.001$). In the low SIRI group, 50 patients died, and the all-cause mortality rate was 26.74%. The number of CVD deaths was 28, and CVD accounted for 14.97% of all deaths. 107 patients died in the high group, and the all-cause

mortality rate was 58.15%. In this group, the number of CVD deaths was 70, and CVD accounted for 38.04% of all deaths. It demonstrated that all-cause and CVD mortality was higher in the SIRI > 1.88 group (all $p < 0.001$). The Kaplan-Meier survival curves indicated that there were significant statistical differences in all-cause ($\chi2 = 41.31$, $p < 0.001$) (Figure 4) and CVD mortality ($\chi2 = 34.82$, $p < 0.001$) between the two groups (Figure 5).

Cox regression analysis and nomogram

Variables with $p < 0.10$ in the univariate regression were included in the model for multivariate regression. SIRI, NLR, and MLR were all divided into two groups according to their median value. Our results showed that age (HR = 1.030; 95%CI: 1.016-1.044; $p < 0.001$), diabetes (HR = 1.909; 95%CI: 1.326-2.750; $p = 0.001$), history of CVD (HR = 2.172; 95%CI: 1.524-3.097; $p < 0.001$), SIRI > 1.88 (HR = 2.254; 95%CI: 1.362-3.729; $p = 0.002$), serum phosphorus (HR = 1.541; 95%CI: 1.013-2.340; $p = 0.043$) were independent risk factors for all-cause mortality (Table 2). The concordance index was 0.753 (95%CI: 0.716-0.790). For CVD mortality, age (HR = 1.017; 95%CI: 1.001-1.034; $p = 0.044$), diabetes (HR = 2.516; 95%CI: 1.560-4.058; $p < 0.001$), history of CVD (HR = 2.123; 95%CI: 1.348-3.344; $p = 0.001$), SIRI > 1.88(HR = 3.838; 95%CI: 2.022-7.285; $p < 0.001$) were independent risk factors (Table 3). The concordance index was 0.771 (95%CI: 0.728-0.814). Both models showed good performance.

The predictive models were visualized as nomograms. Based on these predictors from the Cox regression model, we developed two nomograms to predict all-cause and CVD mortality at 1, 3, 5, and 10 years in MHD patients. For all-cause mortality, variables included age, hypertension, diabetes, history of CVD, eGFR, SIRI > 1.88, NLR > 3.91, MLR > 0.45, CRP, serum creatinine, serum urea nitrogen, serum albumin, and serum phosphorus (Figure 6). For CVD mortality, variables included age,

hypertension, diabetes, history of CVD, eGFR, SIRI > 1.88, NLR > 3.91, MLR > 0.45, CRP, serum creatinine, serum urea nitrogen, and serum phosphorus (Figure 7).

Discussion

Our study confirmed that the baseline SIRI > 1.88 was independently associated with all-cause and CVD mortality in MHD patients, and SIRI had advantages in predicting the prognosis over other parameters, including NLR and MLR. Microinflammation is universal and uncontrolled both in MHD and PD patients. A study showed that higher SIRI levels were predictive of an increased incidence of all-cause and CVD deaths in PD patients, and SIRI had a prognostic value comparable to the NLR and MLR [16]. Their results were similar to ours. However, using the time-dependent ROC curve analysis, we further demonstrated that SIRI had a stronger ability to predict all-cause and CVD mortality in different lifetimes for MHD patients. Recently, Yan Z et al. [17] also found that the SIRI was an accurate prediction value for diabetic MHD, and the SIRI had a higher risk of all-cause death. Our study involved both diabetic and non-diabetic MHD patients and had a longer follow-up time. We demonstrated that SIRI was an independent risk factor not only for all-cause mortality but also for CVD mortality.

Previous studies have reported that persistent microinflammatory state contributed pivotally to cardiovascular disease and were the leading causes of death [18]. Microinflammation could accelerate the progression of atherosclerotic, exacerbate myocardial ischemia and damage, and finally cause adverse cardiovascular outcomes [19]. In addition, Paraskevaidis et al. found that inflammation could excessively activate of intracellular mitochondria, endoplasmic reticulum, and other organelles, releasing a variety of proteases, lipids, and inflammatory cytokines, thereby inducing myocardial cell damage [20]. Persistent microinflammatory status is a signature feature of chronic kidney disease

(CKD). Studies have confirmed that MHD patients' microinflammatory state was more apparent [21]. The development of microinflammation in MHD patients is of multifactorial reasons, including uremic toxin, fluid retention, heart failure, and metabolic acidosis [22]. Other reasons related to hemodialysis treatment include vascular access infection, blood exposure to exogenous substances such as dialysis membranes, and endotoxin in dialysate during HD, which stimulate inflammation response [23]. It has also been found that hemodialysis could alter hepatic blood flow and diminish liver function, leading to endotoxemia and, thus, increased inflammation [24]. The incidence of CVD in two groups was compared at baseline. We found that the high SIRI group had a higher rate of CVD. This may suggest that before receiving dialysis, the damage to the cardiovascular system caused by microinflammation in CKD patients has already existed. Similarly, all-cause and cardiovascular mortality was higher in the SIRI > 1.88 group. We believed that during the treatment of hemodialysis, MHD patients were still long-term exposed to microinflammation, which would increase the risk of adverse cardiovascular outcomes and death.

In our study, the average age of patients in the high SIRI group was significantly higher. It is common believed that aged people are physically weak, and always with decreased multi-organ functions and declined immunity function. Research has shown that SIRI was associated with aging [25]. In this study, we also found serum albumin, serum creatinine, and serum potassium were significantly lower in the high SIRI group. The reason may be that although the blood creatinine level was relatively lower in this group, these patients tend to have more significant symptoms of uremia and need to start hemodialysis at the time. It is well-accepted that the existence of inflammation will worsen protein catabolism. Also, uremic toxins can result in decreased appetite and inadequate nutrient intake. Serum albumin, serum creatinine, and serum potassium could also reflect the nutritional status

of MHD patients, and lower levels of the above parameters indicated a poorer nutritional status. Research has shown that poor nutritional status would lead to decreased immunity function and disorder of immunity regulation and exacerbate the inflammatory reaction [26]. That is, nutrition and inflammation are interrelated and mutually influenced. In our study, we found that increased age, diabetes, and history of CVD were independent risk factors for all-cause and CVD mortality in MHD patients. These conclusions are consistent with clinical practice and previous studies. Besides, elevated serum phosphorus is strongly associated with adverse outcomes in CKD patients. For example, Zhu et al. demonstrated that higher serum phosphate level could increase all-cause mortality and the incidence of adverse cardiovascular events [27]. Our result also showed that elevated serum phosphorus was an independent risk factor for all-cause mortality in MHD patients. However, for CVD mortality, Cox multivariate analysis showed no statistical difference. This may be due to the limited amounts of samples in the study.

The strengths of this study include a long follow-up period, and we confirmed that when patients began to undergo hemodialysis, SIRI could independently predict all-cause and CVD mortality in different lifetimes. However, this study also has some limitations. First, the SIRI had not been monitored dynamically, so the changing situation of SIRI with time was unknown. Second, this study is a single-center study with a small sample size. Multicenter studies with a large sample size are needed to verify our results.

Conclusion

The inflammation index SIRI is associated with all-cause and CVD mortality and can be used as an effective independent predictive indicator among MHD patients. Therefore, monitoring the SIRI level was useful to identify high-risk MHD patients.

Authors' Contributions

Qiuhong Shi and Bo Lv designed the study, analyzed the data, and wrote the initial draft of the manuscript. Shan Jiang and Ying Zeng analyzed the data and managed the dataset. Sheng Feng and Kai Song revised the article critically for important intellectual content. Each author contributed important intellectual content to the content of this manuscript.

Disclosure

Qiuhong Shi and Bo Lv contributed equally to this article. The authors declare no conflict of interest.

Ethical approval

This study was approved by the Clinical Research Ethics Committee of The Second Hospital Affiliated of Soochow University, approval number JD-HG-2024-008.

Data Availability Statement:

The data used in this study are available from the corresponding author upon request.

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References

[1] Saran R, Robinson B, Abbott KC, Bragg-Gresham J, Chen X, Gipson D, et al. US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2020;75(1 Suppl 1):A6-A7.

[2] Wang Y, Gao L. Inflammation and Cardiovascular Disease Associated With Hemodialysis for End-Stage Renal Disease. Front Pharmacol. 2022;13:800950.

[3] Li S, Lan X, Gao H, Li Z, Chen L, Wang W, et al. Systemic Inflammation Response Index (SIRI), cancer stem cells and survival of localised gastric adenocarcinoma after curative

resection. J Cancer Res Clin Oncol. 2017;143(12):2455-2468..

[4] Qi Q, Zhuang L, Shen Y, Geng Y, Yu S, Chen H, et al. A novel systemic inflammation response index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy. Cancer. 2016;122(14):2158-2167.

[5] Zhang Y, Xing Z, Zhou K, Jiang S. The Predictive Role of Systemic Inflammation Response Index (SIRI) in the Prognosis of Stroke Patients. Clin Interv Aging. 2021;16:1997-2007.

[6] Li J, He D, Yu J, Chen S, Chen S, Wu Q, Cheng Z, et al. Dynamic Status of SII and SIRI Alters the Risk of Cardiovascular Diseases: Evidence from Kailuan Cohort Study. J Inflamm Res. 2022;15:5945-5957.

[7] Adamsson Eryd S, Smith JG, Melander O, Hedblad B, Engstrom, G. Incidence of coronary events and case fatality rate in relation to blood lymphocyte and neutrophil counts. Arterioscler Thromb Vasc Biol. 2012;32(2):533-539.

[8] Kato A, Takita T, Furuhashi M, Maruyama Y, Kumagai H, Hishida A. Blood monocyte count is a predictor of total and cardiovascular mortality in hemodialysis patients. Nephron Clin Pract. 2008;110(4):c235-243.

[9] Fei J, Fu L, Li Y, Xiang HX, Xiang Y, Li MD, et al. Reduction of lymphocyte count at early stage elevates severity and death risk of COVID-19 patients: a hospital-based case-cohort study. Arch Med Sci 2023, 19(5):1303-1313.

[10] Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. Expert Rev Cardiovasc Ther. 2016;14(5):573-577.

[11] Zsom L, Faludi M, Fulop T, Dossabhoy NR, Rosivall L, Tapolyai MB. The association of overhydration with chronic inflammation in chronic maintenance hemodiafiltration patients.

Hemodial Int. 2019;23(3):384-391.

[12] Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO, Criqui M, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation. 2003;107(3):499-511.

[13] Sato H, Takeuchi Y, Matsuda K, Kagaya S, Saito A, Fukami H, et al. Pre-Dialysis Neutrophil-Lymphocyte Ratio, a Novel and Strong Short-Term Predictor of All-Cause Mortality in Patients With Diabetic Nephropathy: Results From a Single-Center Study. Ther Apher Dial 2017, 21(4):370-377

[14] Xiang F, Chen R, Cao X, Shen B, Liu Z, Tan X, et al. Monocyte/lymphocyte ratio as a better predictor of cardiovascular and all-cause mortality in hemodialysis patients: A prospective cohort study. Hemodial Int 2018, 22(1):82-92.

[15] Zhao S, Dong S, Qin Y, Wang Y, Zhang B, Liu A. Inflammation index SIRI is associated with increased all-cause and cardiovascular mortality among patients with hypertension. Front Cardiovasc Med. 2022;9:1066219.

[16] Li J, Li Y, Zou Y, Chen Y, He L, Wang Y, et al. Use of the systemic inflammation response index (SIRI) as a novel prognostic marker for patients on peritoneal dialysis [J]. Ren Fail, 2022, 44(1): 1227-1235.

[17] Yan Z, Li L. Prognostic Value of Systemic Inflammatory Response Index for the Prognosis of Diabetic Maintenance Hemodialysis Patients: A Retrospective Observational Study. Int J Gen Med 2023, 16:3613-3622

[18] Liberale L, Badimon L, Montecucco F, Luscher TF, Libby P, Camici GG. Inflammation,

Aging, and Cardiovascular Disease: JACC Review Topic of the Week. J Am Coll Cardiol. 2022;79(8):837-847.

[19] Soysal P, Arik F, Smith L, Jackson SE, Isik AT. Inflammation, Frailty and Cardiovascular Disease. Adv Exp Med Biol. 2020;1216:55-664.

[20] Paraskevaidis I, Farmakis D, Papingiotis G, Tsougos E. Inflammation and Heart Failure: Searching for the Enemy-Reaching the Entelechy. J Cardiovasc Dev Dis. 2023;10(1):19.

[21] Wu J, Guo N, Chen X, Xing C. Coexistence of micro-inflammatory and macrophage phenotype abnormalities in chronic kidney disease. Int J Clin Exp Pathol. 2020;13(2):317-323.

[22] Friedrich B, Alexander D, Janessa A, Haring HU, Lang F, Risler T. Acute effects of hemodialysis on cytokine transcription profiles: evidence for C-reactive protein-dependency of mediator induction. Kidney Int. 2006;70(12):2124-2130.

[23] Mandic A, Cavar I, Skoro I, Tomic I, Ljubic k, Coric S, et al. Body Composition and Inflammation in Hemodialysis Patients. Ther Apher Dial. 2017;21(6):556-564.

[24] Marants R, Qirjazi E, Lai KB, Szeto CC, Li PKT, Li F, et al. Exploring the Link Between Hepatic Perfusion and Endotoxemia in Hemodialysis. Kidney Int Rep. 2021;6(5):1336-1345.

[25] Pawelec G, Goldeck D, Derhovanessian E. Inflammation, ageing and chronic disease. Curr Opin Immunol. 2014;29:23-28.

[26] Kanda E, Kato A, Masakane I, Kanno, Y. A new nutritional risk index for predicting mortality in hemodialysis patients: Nationwide cohort study. PLoS One. 2019;14(3):e0214524.

[27] Zhu M, Dou L, Zhu M, Liu, S, Zhan Y, Lu J, et al. Variability of serum phosphorus and its association with mortality among hemodialysis patients. Clin Nephrol. 2018 Aug;90(2):79-86.

SIRI is associated with the prognosis of MHD patients

Retrospective study

n = 371

60.71±15.34
average age

2010.09 - 2022.09
median follow-up was 42 months

157 died
CVD in 98 cases

Grouping based on the median value of SIRI

SIRI ≤ 1.88 | **SIRI > 1.88**

SIRI = neutrophil count × monocyte/lymphocyte count

Outcome

SIRI had a stronger ability in predicting all-cause and CVD mortality at 1, 3, 5, and 10 years, respectively (Compared to NLR and MLR)

All-cause mortalily: SIRI > 1.88 (HR = 2.254; 95%CI: 1.362-3.729; p = 0.002)

CVD motality:SIRI > 1.88 (HR = 3.838; 95%CI: 2.022-7.285; p < 0.001)

*SIRI: systemic inflammation response index;MHD: maintenance hemodialysis; CVD: cardiovascular disease; NLR: neutrophil count/monocyte count; MLR: monocyte count/lymphocyte

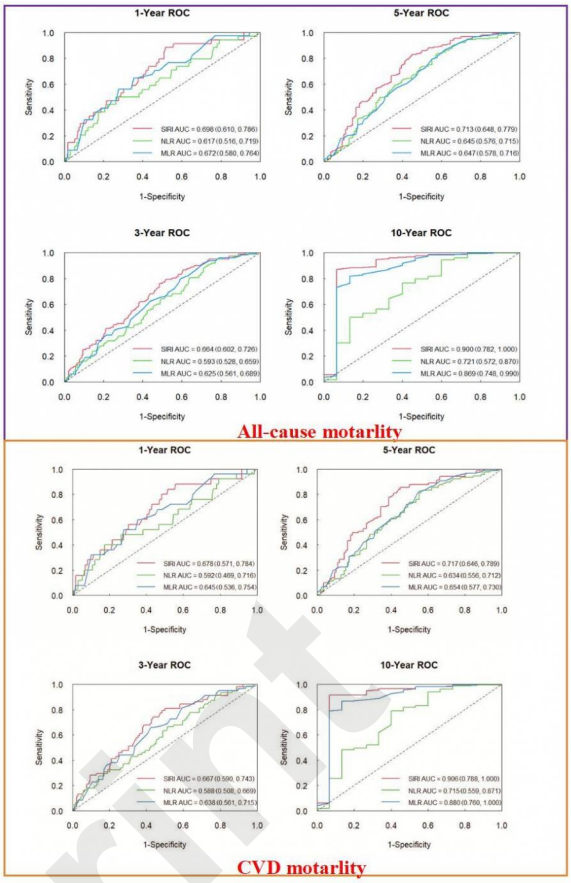

Table 1. Baseline characteristics of the SIRI ≤ 1.88 group and SIRI > 1.88 group

Characteristic	SIRI ≤ 1.88 (*n* = 187)	SIRI > 1.88 (*n* = 184)	*p* value
Age, year	57.64 ± 16.85	63.84 ± 13.42	< 0.001
Gender (male), *n* (%)	136 (72.73)	133 (72.28)	0.924
Smokers, *n* (%)	24 (12.83)	26 (14.13)	0.715
BMI (kg/m^2)	21.95 ± 3.12	21.57 ± 3.53	0.274
Hypertension, *n* (%)	169 (90.37)	169 (91.85)	0.618
Diabetes, *n* (%)	72 (38.50)	78 (42.39)	0.445
History of CVD	45 (24.06)	76 (41.30)	< 0.001
Cause of (ESRD)			
Glomerulonephritis, *n* (%)	100 (53.48)	81 (44.02)	0.069
Diabetic nephropathy, *n* (%)	58 (31.02)	67 (36.41)	0.271
Polycystic kidney, *n* (%)	14 (7.49)	14 (7.61)	0.965
Hypertensive nephrosclerosis, *n* (%)	5 (2.67)	9 (4.89)	0.262
Others, *n* (%)	10 (5.35)	13 (7.07)	0.493
Kt/V	1.26 ± 0.21	1.25 ± 0.25	0.522
eGFR (ml/min/1.73 m^2)	6.91 ± 4.45	7.55 ± 5.16	0.206
Hemoglobin (g/L)	91.56 ± 20.38	90.70 ± 20.57	0.686
CRP(mg/L)	5.90 (5.30, 7.00)	7.40 (5.80, 24.93)	< 0.001
Serum creatinine (umol/L)	817.75 ± 379.90	714.68 ± 300.59	0.004
Serum urea nitrogen (mmol/L)	25.16 ± 12.17	23.91 ± 10.77	0.296
Serum uric acid (mmol/L)	435.93 ± 146.45	437.88 ± 152.92	0.900
Serum albumin (g/L)	34.08 ± 6.52	31.86 ± 6.14	0.001
Serum calcium (mmol/L)	2.03 ± 0.26	2.03 ± 0.35	0.903
Serum phosphorus (mmol/L)	1.83 ± 0.63	1.77 ± 0.56	0.332
Serum potassium (mmol/L)	4.49 ± 0.81	4.27 ± 0.77	0.009
Blood cholesterol (mmol/L)	4.36 ± 1.36	4.24 ± 1.21	0.355
Triglyceride (mmol/L)	1.50 ± 1.09	1.46 ± 0.92	0.662
PTH (pg/mL)	278.90 (137.10, 435.39)	232.02 (131.80, 389.40)	0.187

BMI: body mass index; CVD: cardiovascular disease; eGFR: glomerular filtration rate; SIRI: systemic inflammation response index; CRP: C-reactive protein; PTH: parathyroid hormone.

Table 2. Cox regression analysis of risk factors for all-cause mortality

Characteristic	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age	1.041	1.030 - 1.052	< 0.001	1.030	1.016 - 1.044	< 0.001
Male	0.789	0.562 - 1.108	0.789			
Smoker	1.006	0.615 - 1.645	0.982			
BMI	1.026	0.979 - 1.076	0.285			
Hypertension	3.570	1.463 - 8.712	0.005	2.269	0.899 - 5.724	0.083
Diabetes	2.347	1.708 - 3.227	< 0.001	1.909	1.326 - 2.750	0.001
History of CVD	3.644	2.652 - 5.007	< 0.001	2.172	1.524 - 3.097	< 0.001
Kt/V	0.912	0.476 - 1.748	0.782			
eGFR	1.033	1.004 - 1.063	0.023	0.966	0.914 - 1.021	0.225
SIRI > 1.88	1.082	1.042 - 1.124	< 0.001	2.254	1.362 - 3.729	0.002
NLR > 3.91	1.962	1.418 - 2.715	< 0.001	1.062	0.666 - 1.693	0.800
MLR > 0.45	1.927	1.393 - 2.665	< 0.001	0.890	0.573 - 1.381	0.603
Hemoglobin	0.995	0.988 - 1.003	0.200			
CRP	1.016	1.008 - 1.024	< 0.001	1.003	0.994 - 1.012	0.560
Serum creatinine	0.999	0.998 - 0.999	< 0.001	0.999	0.998 - 1.000	0.170
Serum urea nitrogen	0.981	0.967 - 0.996	0.011	0.981	0.959 - 1.004	0.113
Serum uric acid	1.000	0.999 - 1.001	0.738			
Serum albumin	0.979	0.956 - 1.003	0.081	1.007	0.979 - 1.035	0.632
Serum calcium	0.977	0.560 - 1.704	0.935			
Serum phosphorus	0.777	0.595 - 1.014	0.064	1.541	1.013 - 2.340	0.043
Serum potassium	0.923	0.757 - 1.127	0.433			
Blood cholesterol	1.017	0.904 - 1.144	0.777			
Triglyceride	0.936	0.799 - 1.097	0.414			
PTH	1.000	0.999 - 1.000	0.161			

BMI: body mass index; CVD: cardiovascular disease; eGFR: glomerular filtration rate; SIRI: systemic inflammation response index; NLR: neutrophil count/monocyte count; MLR: monocyte count/lymphocyte count; CRP: C-reactive protein; PTH: parathyroid hormone.

Table 3. Cox regression analysis of risk factors for CVD mortality

Characteristic	Univariate analysis			Multivariate analysis		
	HR	95% CI	*p* value	HR	95% CI	*p* value
Age	1.034	1.020 - 1.048	< 0.001	1.017	1.001 - 1.034	0.044
Male	1.284	0.792 - 2.080	0.311			
Smoker	1.185	0.660 - 2.127	0.570			
BMI	1.049	0.989 - 1.113	0.111			
Hypertension	2.243	0.910 - 5.531	0.079	1.290	0.501 - 3.325	0.598
Diabetes	2.754	1.834 - 4.136	< 0.001	2.516	1.560 - 4.058	< 0.001
History of CVD	3.697	2.471 - 5.532	< 0.001	2.123	1.348 - 3.344	0.001
Kt/V	0.706	0.311 - 1.600	0.404			
eGFR	1.044	1.010 - 1.079	0.012	0.962	0.901 - 1.026	0.237
SIRI > 1.88	3.542	2.265 - 5.542	< 0.001	3.838	2.022 - 7.285	< 0.001
NLR > 3.91	1.748	1.166 - 1.748	0.007	0.563	0.311 – 1.019	0.058
MLR > 0.45	2.160	1.423 - 3.328	< 0.001	1.021	0.588 - 1.775	0.941
Hemoglobin	0.995	0.986 - 1.004	0.298			
CRP	1.019	1.009 - 1.029	< 0.001	1.007	0.996 - 1.017	0.238
Serum creatinine	0.999	0.998 - 0.999	< 0.001	0.999	0.998 - 1.001	0.268
Serum urea nitrogen	0.974	0.955 - 0.992	0.006	0.979	0.950 - 1.009	0.169
Serum uric acid	1.000	0.998 - 1.001	0.475			
Serum albumin	0.982	0.953 - 1.011	0.226			
Serum calcium	0.933	0.457 - 1.906	0.849			
Serum phosphorus	0.676	0.477 - 0.958	0.028	1.406	0.827 - 2.389	0.208
Serum potassium	0.911	0.708 - 1.172	0.468			
Blood cholesterol	0.947	0.805 - 1.113	0.508			
Triglyceride	0.941	0.771 - 1.147	0.545			
PTH	1.000	0.999 - 1.001	0.996			

BMI: body mass index; CVD: cardiovascular disease; eGFR: glomerular filtration rate; SIRI: systemic inflammation response index; NLR: neutrophil count/monocyte count; MLR: monocyte count/lymphocyte count; CRP: C-reactive protein; PTH: parathyroid hormone.

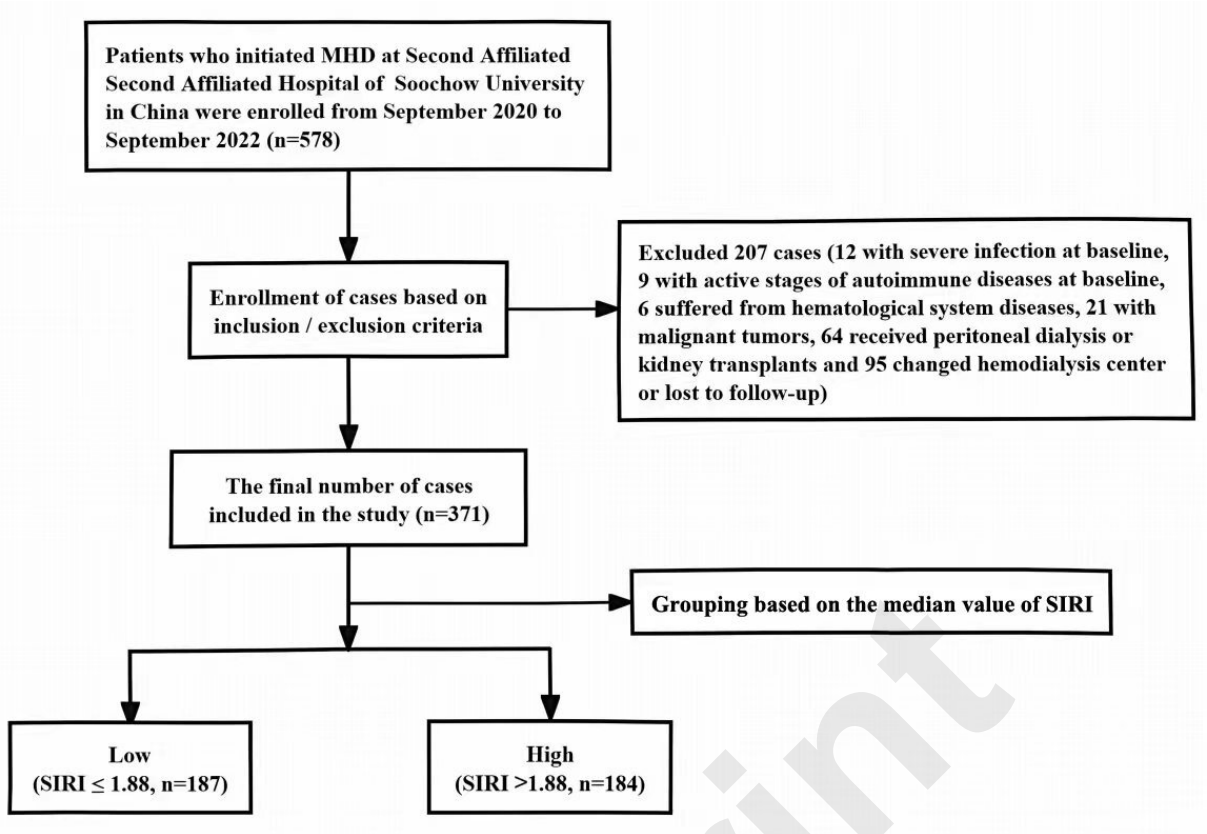

Figure 1. Flowchart of sample collection.

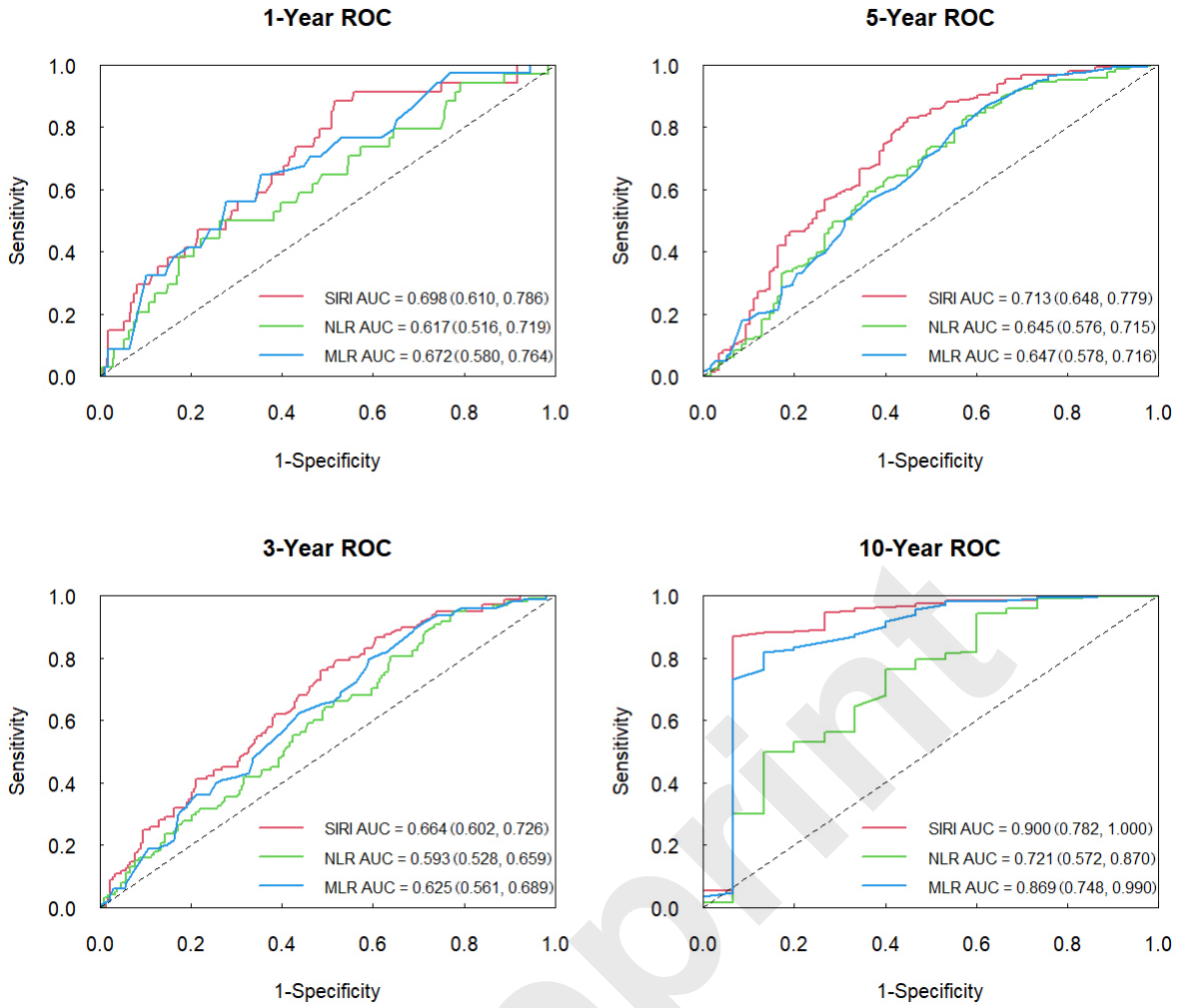

Figure 2. The time-dependent ROC curve and area under the curve (AUC) were used to compare the predictive performance of SIRI, NLR, and MLR at 1, 3, 5, and 10 years for all-cause mortality in MHD patients.

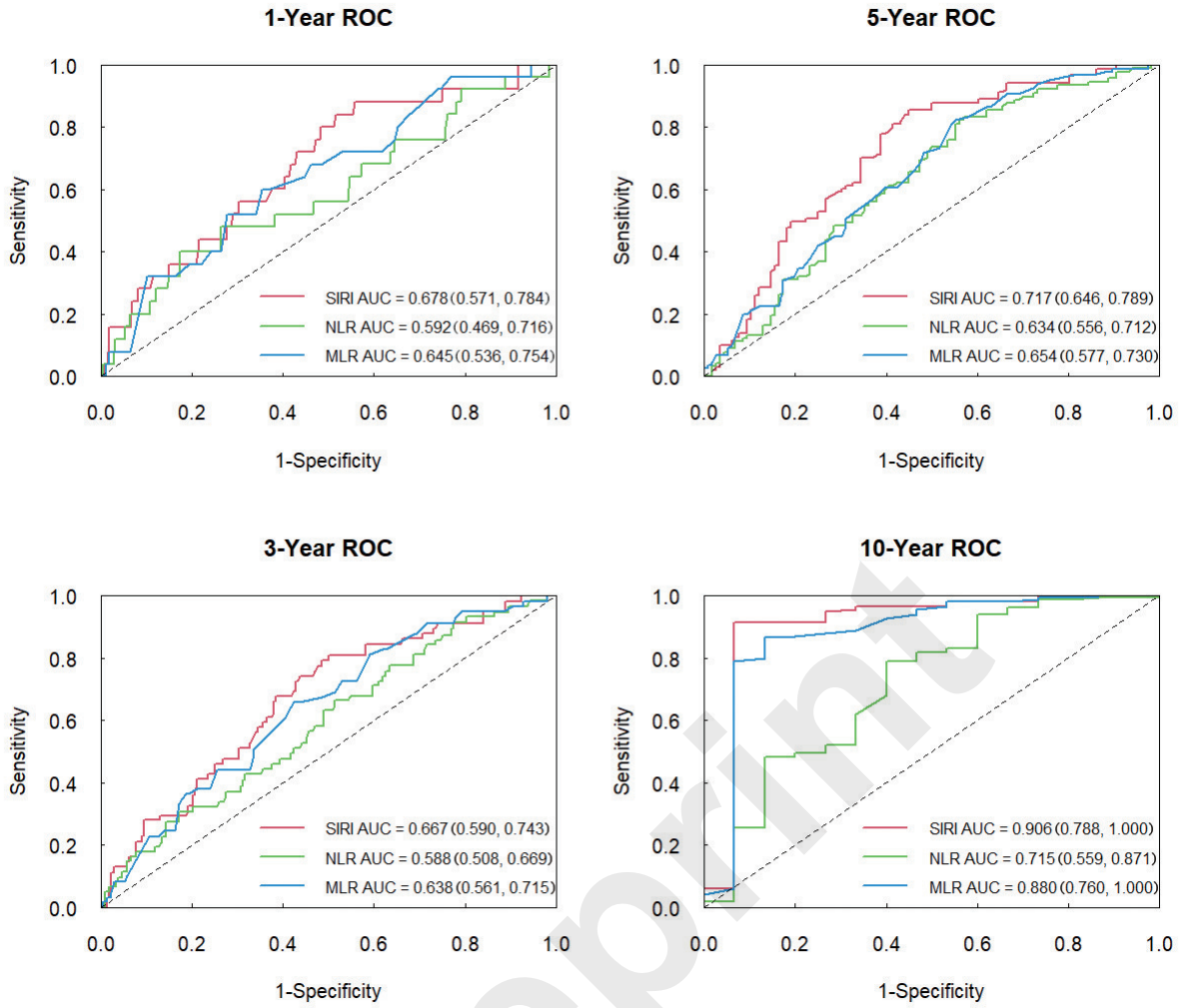

Figure 3. The time-dependent ROC curve and area under the curve (AUC) were used to compare the predictive performance of SIRI, NLR, and MLR at 1, 3, 5, and 10 years for CVD mortality in MHD patients.

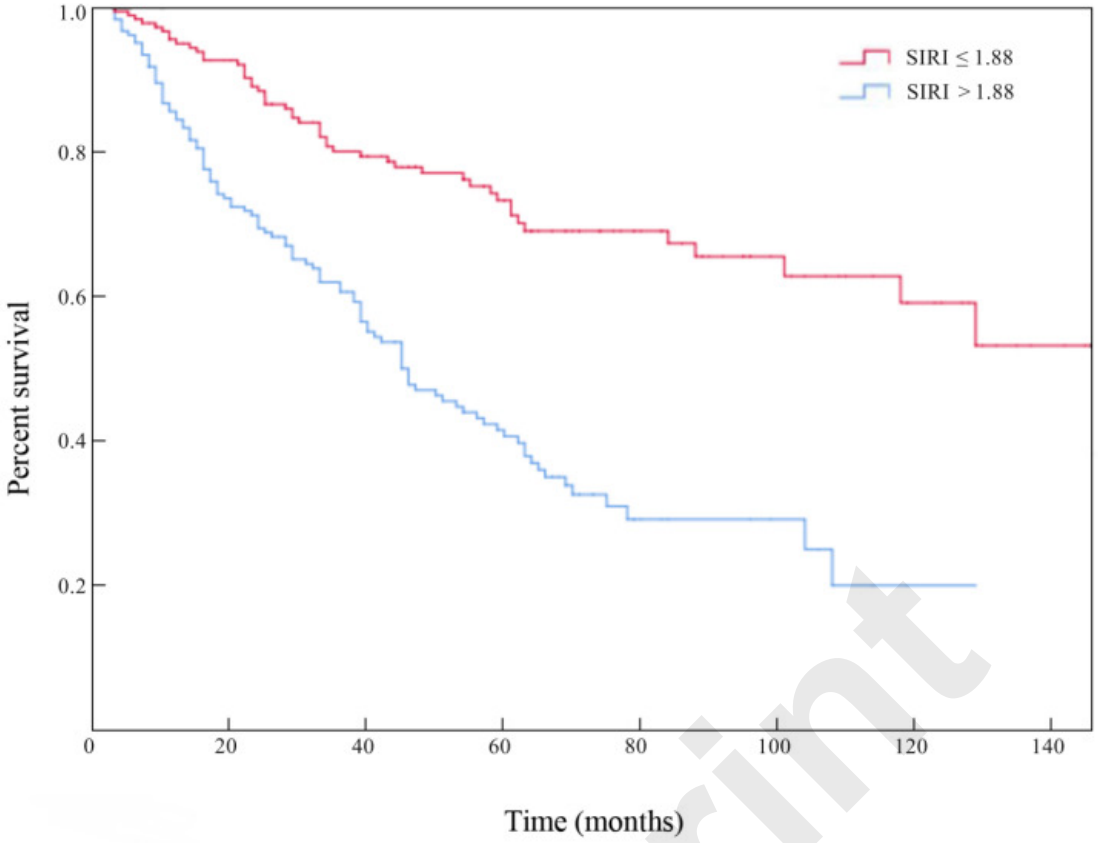

Figure 4. The Kaplan–Meier curve for survival probabilities from all-cause motality of MHD patients.

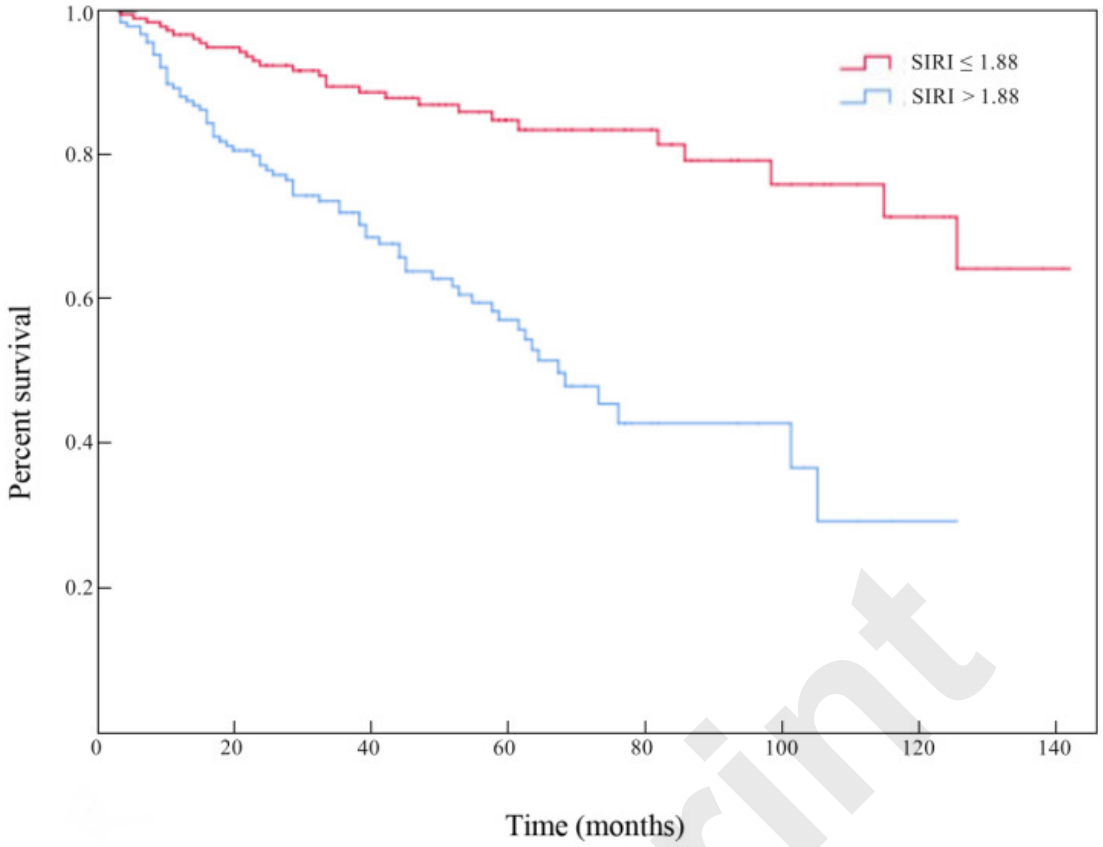

Figure 5. The Kaplan–Meier curve for survival probabilities from CVD motality of MHD patients.

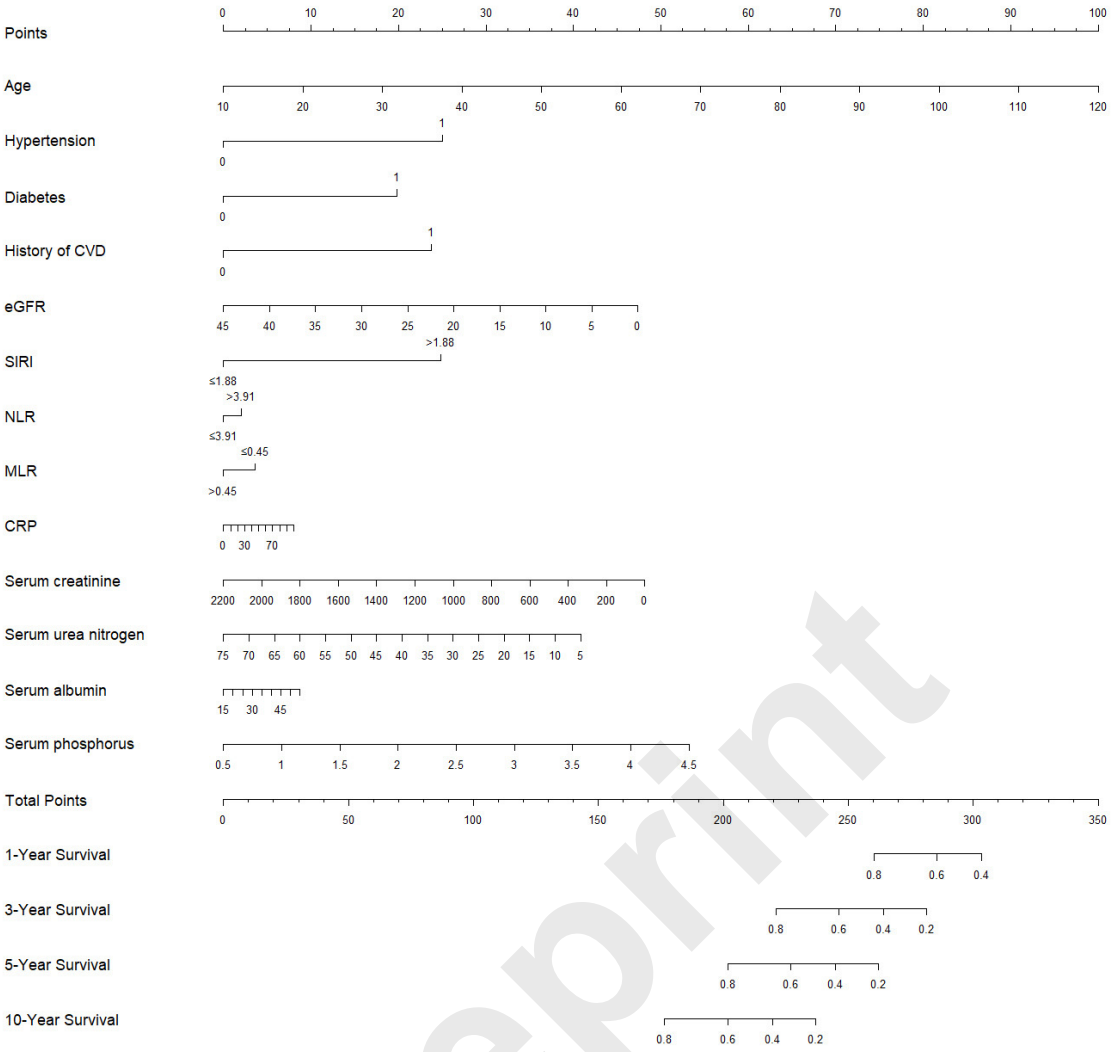

Figure 6. Nomogram to predict risk of all-cause mortality in MHD patients. The value of each predictor was given a score on the point scale axis. A total score could be easily obtained by adding each single score. By projecting a line straight down on the total points scale, the probability of all-cause mortality at 1, 3, 5, and 10 years could be estimated.

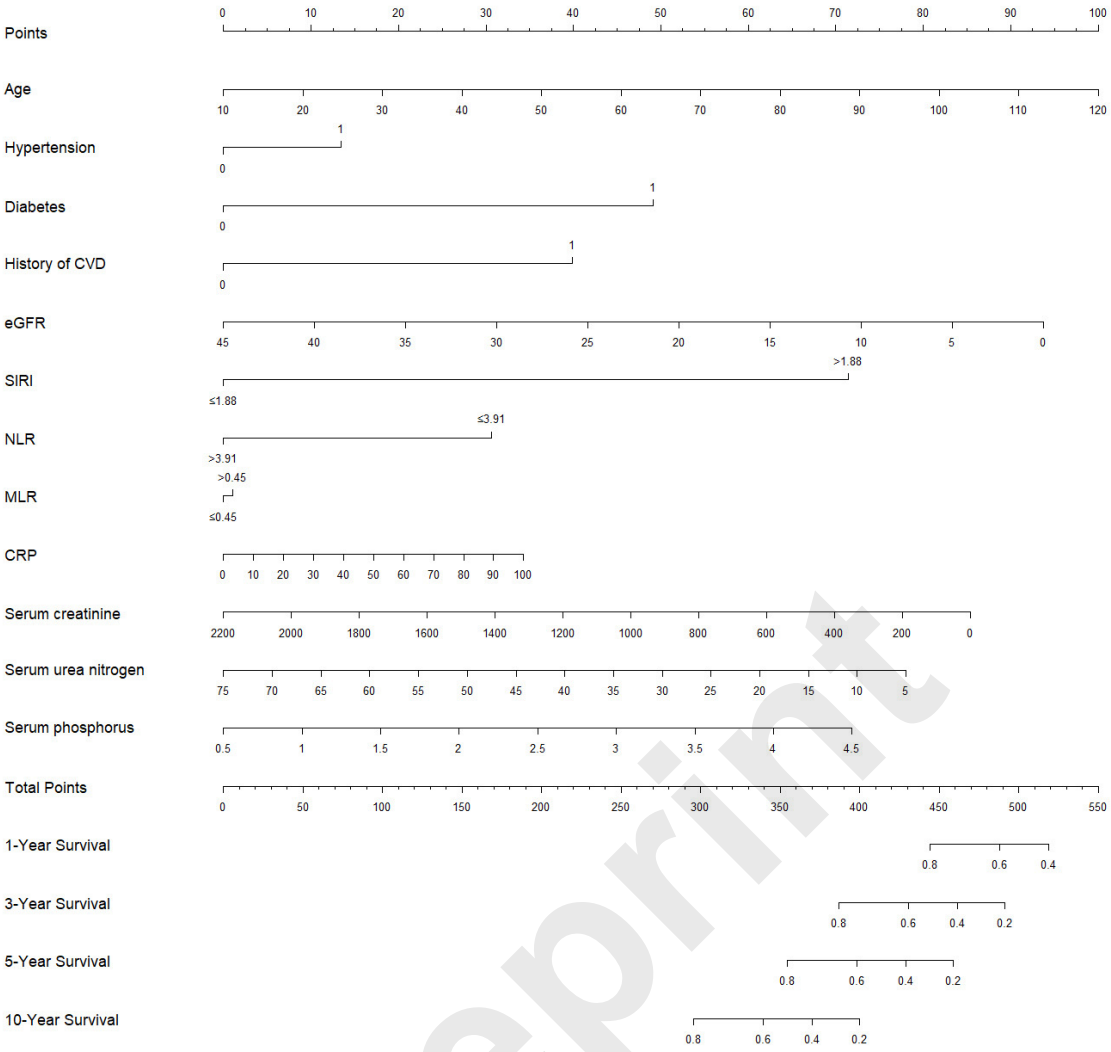

Figure 7. Nomogram to predict risk of CVD mortality in MHD patients. The value of each predictor was given a score on the point scale axis. A total score could be easily obtained by adding each single score. By projecting a line straight down on the total points scale, the probability of CVD mortality at 1, 3, 5, and 10 years could be estimated.