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Research paper

Establishment of a nomogram that predicts the risk of heart failure in hemodialysis patients

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ABSTRACT

Chronic kidney disease (CKD) is expected to become the fifth leading cause of death globally by 2040. Cardiovascular disease (CVD), particularly heart failure (HF), is a severe complication in CKD patients on hemodialysis. This study aimed to develop a nomogram to predict the risk of heart failure hospitalization in hemodialysis patients, providing a valuable tool for clinical decision-making. We retrospectively analyzed data from 196 patients at Kunming Yanan Hospital's hemodialysis center, including demographic, dialysis-related, and laboratory information. Significant HF predictors identified through univariate and multivariate logistic regression were age, diabetes, dialysis duration, left ventricular mass index (LVMI), albumin (ALB), and ejection fraction (EF). These predictors formed the basis of the nomogram, which demonstrated good discrimination (AUC = 0.728) and calibration (Hosmer-Lemeshow test, $P = 0.463$). Decision curve analysis confirmed the nomogram's clinical utility across various threshold probabilities. This study's findings can help clinicians identify high-risk patients, improving management strategies and potentially reducing HF-related hospitalizations in the hemodialysis population.

1. Introduction

Chronic kidney disease (CKD) is a significant global health burden and is projected to become the fifth leading cause of death worldwide by 2040 [[1](#page-7-0)]. In 2017, there were 697 million people living with CKD globally, with a prevalence rate of 9.1 %. The same year, CKD accounted for approximately 1.2 million deaths worldwide. Between 1990 and 2017, the number of individuals diagnosed with CKD increased by 41.5 % across all age groups [[2](#page-7-0)]. In China, the prevalence rate of CKD is 10.8 % [[3](#page-7-0)], with around 402.18 people per million receiving maintenance hemodialysis. National data from 2015 indicated that there were about 550,000 hemodialysis patients in China, and this number continues to rise [[4](#page-7-0)]. After reviewing the latest literature, we found more recent data regarding the prevalence of CKD in China. For example, [[5](#page-7-0)] provides updated prevalence rates and confirms that the burden of CKD remains high. This study reports that CKD continues to be a major public health issue, with millions of individuals affected. We have updated the manuscript to incorporate this newer data, reflecting the most current understanding of CKD prevalence in China.

Recent studies have further elucidated the strong correlation between CKD and cardiovascular disease (CVD), underscoring that CVD is not only a common complication but also a major cause of morbidity and mortality in CKD patients. The Global Burden of Disease Study 2023 highlighted that CKD patients are at a markedly increased risk for cardiovascular events compared to the general population, emphasizing the need for improved management strategies [\[6\]](#page-7-0).

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Cardiovascular disease (CVD) is a common complication inpatients undergoing dialysis for CKD and is one of the leading causes of death among these patients. The mortality rate in hemodialysis patients with CVD is 20 times higher than that of the general population, as these patients face compounded risks due to both chronic kidney disease and cardiovascular comorbidities, with approximately 50 % of hemodialysis patients affected by CVD [[7\]](#page-8-0). The incidence of CVD is particularly high inpatients with end-stage chronic kidney disease, with coronary artery disease and heart failure (HF) being the two major phenotypes [[8](#page-8-0)]. HF rates are higher inpatients with end-stage kidney disease (ESKD), with a point prevalence of nearly 40 % among Medicare beneficiaries [[9](#page-8-0)]. Furthermore, up to 70 % of CKD patients and 36 % of ESKD patients requiring dialysis have HF [\[10](#page-8-0),[11\]](#page-8-0).

Despite the known high risk of cardiovascular events in CKD patients, recent advances in pharmacological treatments have largely excluded patients with end-stage kidney disease (ESKD) from clinical

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Fig. 1. Flowchart of patient recruitment and baseline characteristics.

trials due to safety concerns. This exclusion has created a treatment gap for these patients, as highlighted in the KDIGO 2023 guidelines [\[12](#page-8-0)]. Emerging therapies and ongoing research are beginning to address this gap, but significant challenges remain [[13\]](#page-8-0).

Heart failure (HF) and end-stage kidney disease (ESKD) frequently coexist, with HF accounting for nearly half of the deaths inpatients on dialysis. Despite this, data on the management of HF in ESKD patients undergoing dialysis remain very limited [\[14,15](#page-8-0)]. Due to safety concerns, many new HF drugs in recent years have excluded ESKD patients during clinical trials, leading to a stagnation in HF treatment for dialysis patients. Furthermore, the lack of a clear standard for diagnosing HF in dialysis patients has made it challenging to identify and manage HF in this population.

Given the increasing prevalence of CKD and its associated cardiovascular risks, there is an urgent need for effective predictive tools and treatment strategies. This study aims to address this need by developing a nomogram to predict the risk of heart failure hospitalization in hemodialysis patients, thereby providing a valuable tool for clinical decision-making and potentially improving patient outcomes [[16\]](#page-8-0).

A nomogram, a visual predictive tool, calculates the risk of outcomes for individuals and provides valuable guidance for clinical decisionmaking. Recently, it has been widely used to evaluate patient prognosis. In this study, we aimed to develop a nomogram for hemodialysis patients and assess the risk factors for heart failure.

2. Methods

2.1. Study design and participants

We established a nomogram for predicting heart failure in hemodialysis patients through a retrospective study. Data were collected from the hemodialysis center at Kunming Yanan Hospital. Patients who received maintenance hemodialysis between January 1, 2020, and December 31, 2022, were screened. The inclusion criteria were: (1) age \geq 18 years, (2) cardiac ultrasonography performed within the last 3 months, and (3) treatment with regular hemodialysis for *>*3 months prior to January 1, 2021. The primary outcome measure was hospitalization due to heart failure, documented as the discharge diagnosis, regardless of whether it was emergency hospitalization or admission to the nephrology department. The exclusion criteria were: (1) patients who died before the primary outcome, (2) patients who left the dialysis center midway or switched to kidney transplant or peritoneal dialysis, and (3) patients with incomplete medical records.

Importantly, we are not using LVEF as a diagnostic marker for heart failure, but as part of a multifactorial predictive model that helps stratify the risk of hospitalization. This model integrates other relevant clinical factors, such as age, diabetes, dialysis duration, and left ventricular mass index (LVMI), providing a more nuanced prediction of heart failure hospitalizations.

2.2. Data collection

We collected 33 parameters from the hemodialysis centers, including basic characteristics, dialysis-related data, and blood laboratory tests. Blood specimens for biochemical tests were obtained from the vascular access before dialysis. Basic characteristics included gender, age, height, weight, and history of diabetes mellitus (DM) and hypertension. Dialysis-related data comprised ultrafiltration volume, dialysis duration, initiation of dialysis due to heart failure, and dry weight. Blood laboratory tests covered serum potassium, hemoglobin (first started dialysis), blood urea nitrogen (BUN), uric acid, serum creatinine, serum sodium, serum calcium, serum phosphorus, albumin, triglycerides, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and parathyroid hormone (PTH). Cardiac ultrasonography measurements were performed by experienced sonographers. The left ventricular mass index (LVMI) was calculated using the formula:

Table 1

Clinical characteristics of patients with and without heart failure.

LVMI: left ventricular mass index; Apa: apolipoprotein a; Apb: apolipoprotein b; Lipa: lipoprotein a; EF: left ventricular ejection fraction.

Table 2 Multivariate logistic regression analysis.

LV mass $=$ 0.8 \times 1.04 \times \overline{a} $(interventricular septum+LV internal diameter)$ + posterior wall thickness)³ – (LV internal diameter)³ +0*.*6 g

LVMI was then derived as:

$$
LVMI = \frac{LVM}{BSA (body surface area)}
$$

M-mode measurements of left ventricular (LV) end-diastolic diameter, interventricular septum, and posterior LV wall thicknesses at end diastole were conducted according to the guidelines of the American Society of Echocardiography. The diagnosis of left ventricular hypertrophy (LVH) was defined as LVMI \geq 125 g/m² in men and \geq 110 g/m² in women.

2.3. Statistical analysis

Descriptive statistics were used for continuous and categorical variables. Normally distributed continuous variables were presented as mean + standard deviation (SD), while non-normally distributed variables were described as median (interquartile range, IQR). Group comparisons for continuous variables were conducted using the *t*-test or Wilcoxon rank-sum test. Categorical variables were compared using the chi-square test or Fisher's exact test. In the model-building process, backward stepwise selection based on the Akaike Information Criterion (AIC) was used to identify independent predictors, ensuring both statistical significance and clinical interpretability. Although Scr, K+, and Mg2+ were significant in univariate analyses, their inclusion did not substantially improve the predictive accuracy of the multivariate model.

Candidate predictors were initially tested using a univariate logistic regression algorithm. Variables significant at $(P < 0.1)$ in the univariate analysis were included in the subsequent multivariate logistic regression analysis. Backward stepwise selection based on the Akaike Information Criterion (AIC) was used to identify independent predictors for constructing the prediction model. A nomogram was then developed from the results of the multivariate logistic regression.

The performance of the nomogram was evaluated for discrimination and calibration. Discrimination was assessed using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. Calibration was evaluated using a calibration curve and the Hosmer-Lemeshow test for goodness-of-fit. Decision curve analysis (DCA) was performed to determine the clinical usefulness of the nomogram by calculating the net benefits at different threshold probabilities. Internal validation was conducted using bootstrap sampling (500 iterations). All tests were two-tailed, with $P \leq 0.05$ considered statistically significant. Statistical analyses were performed using the R software package (version 4.2.1) and DCPM (version 4.01, Jingding Medical Technology Co. Ltd).

3. Results

3.1. Patient characteristics

We recruited 196 dialysis patients with complete baseline clinical and laboratory data ([Fig.](#page-1-0) 1), of which 129 (65.28 %) were males and 67

Fig. 2. Nomogram for predicting heart failure risk in hemodialysis patients.

Fig. 3. ROC curve with AUC for the nomogram.

(34.18 %) were females. Among the 196 participants, 56 (28.57 %) were admitted to the nephrology department or emergency due to heart failure. The clinical characteristics of these patients are shown in [Table](#page-2-0) 1. The median age (IQR) of patients was 61.4 (49–70.25) years. There were no significant differences in clinical variables between the group with the outcome event and those without, except for age

Fig. 4. Calibration curve of the nomogram.

([Table](#page-2-0) 1). The median hemodialysis duration (IQR) was 66.5 (47–95) months.

4. Results

4.1. Construction of the nomogram based on clinical and serological markers

Univariate and multivariate logistic regression analyses were used to identify potential prognostic markers and estimate their influence on heart failure hospitalization in dialysis patients. The multivariate analysis results indicated that the following variables remained significantly independent prognostic factors: Age $(P = 0.002, \text{OR} = 1.039, 95\% \text{ CI} =$ 1.014–1.066), Diabetes (*P* = 0.009, OR = 1.797, 95 % CI = 0.892–3.616), Dialysis duration ($P = 0.097$, OR = 0.991, 95 % CI = 0.979–1.001), LVMI ($P = 0.142$, OR = 1.697, 95 % CI = 0.842–3.478), ALB ($P = 0.065$, OR = 0.918, 95 % CI = 0.837-1.005), and EF ($P =$ 0.054, OR = 1.047, 95 % CI = 1.001-1.098). Detailed results of univariate and multivariate analyses are presented in [Table](#page-2-0) 2.

Incorporating these prognostic markers—Age, Diabetes, Dialysis duration, LVMI, ALB, and EF—a nomogram was constructed ([Fig.](#page-3-0) 2). Each prognostic factor had a risk point, which could be obtained by drawing a vertical line directly upward from the corresponding value of the prognostic factor to an axis labeled "Point." To determine the probability for a specific patient, a vertical line could be drawn from the "Total Points," which is the sum of the risk points of all prognostic factors. A higher "Total Points" score indicates a worse prognosis.

The multivariate analysis model showed favorable discrimination with an AUC of 0.728 (95 % CI 0.649–0.807) [\(Fig.](#page-3-0) 3). The calibration curve suggested good agreement between model prediction and actual observation, and the Hosmer-Lemeshow test yielded a non-significant *P* value of 0.463, indicating good calibration power (Fig. 4). The decision curve analysis (DCA) result is presented in [Fig.](#page-5-0) 5. The DCA showed that if the threshold probabilities for clinicians or patients ranged between 17 %–79 %, using the heart-failure nomogram to make treatment decisions added more net benefit than treating either all patients or none. Thus, our nomogram demonstrated its value as a promising tool for clinical decision-making.

4.2. Model comparison

[Fig.](#page-6-0) 6 presents the results of the ROC analyses. DeLong tests were used to compare the discrimination of the heart-failure nomogram with the variables incorporated in the nomogram alone. The heart-failure nomogram showed higher discriminatory accuracy for predicting hospitalization due to heart failure than any individual variable incorporated in the nomogram alone (P_1 0.001). We also applied DCA to compare the performance of the models in terms of clinical usefulness. These analyses revealed that the heart-failure nomogram had a higher overall net benefit than the models containing individual risk factors across a wide range of threshold probabilities [\(Fig.](#page-7-0) 7).

5. Discussion

This study developed a nomogram to predict the risk of heart failure hospitalization inpatients undergoing hemodialysis. We found that age, diabetes, dialysis duration, albumin (ALB), ejection fraction (EF), and left ventricular mass index (LVMI) were significantly related to hospitalization due to heart failure.

We summarized relevant indicators for maintaining heart failure in hemodialysis patients. In our dialysis center, the average age of patients was 61 years, with a range from 23 to 91 years. Left ventricular ejection fraction (EF) is one of the diagnostic criteria for heart failure. Studies have confirmed that EF decreases with the decline in renal function and is associated with cardiovascular death prognosis in chronic renal failure patients. Unfortunately, treatment for chronic renal failure patients with

Fig. 5. Decision curve analysis of the nomogram.

reduced ejection fraction has not reached a satisfactory state [\[17](#page-8-0)], especially in those undergoing maintenance dialysis. Echocardiography results showed that 7 (3.5 %) patients had an EF of *<*40 %, 87 (44.4 %) had an EF between 40 % and 60 %, and 104 (52.1 %) had an EF *>*60 %. We recognize the biological relevance of Scr, $K+$, and Mg2+ to cardiovascular health in dialysis patients. However, these variables were not included in the final model as their addition did not significantly enhance the overall predictive accuracy. Our approach aimed to balance model simplicity with clinical utility.

Additionally, left ventricular hypertrophy (LVH) plays a significant role in cardiovascular events and is closely associated with severe outcomes such as arrhythmias, atherosclerosis, stroke, and heart failure. LVH is the most common cardiovascular complication in chronic renal failure patients, with an incidence rate of 47 % in non-dialysis patients and up to 75–89 % in end-stage patients. However, there are no specific reports on the incidence of LVH in maintenance hemodialysis patients. In this study, the incidence of LVH was 54 %, with 28.6 % in males and 25.4 % in females. Considering the close association between LVH and cardiovascular events in chronic kidney disease patients, especially those on maintenance dialysis, this study incorporated LVMI into the multifactorial equation. Previous studies have also found that factors

such as age, diabetes history, duration of maintenance dialysis, ALB, and EF are associated with hospitalization due to heart failure in maintenance hemodialysis patients.

Although LVMI did not reach statistical significance in the univariate analysis ($P = 0.354$), it was included in the multivariate analysis due to its well-established clinical relevance. LVMI is a key marker of cardiovascular stress, particularly in dialysis patients, and has been shown in numerous studies to be associated with poor cardiovascular outcomes. Therefore, despite its non-significance in the univariate analysis, we believe that including LVMI in the multivariate model enhances the model's clinical applicability and utility. This decision is supported by the fact that LVMI is recognized as an important predictor of left ventricular hypertrophy, a known risk factor for heart failure inpatients with end-stage renal disease (ESRD).

For a long time, it has been widely recognized that patients with chronic renal failure (CRF) have an increased risk of cardiovascular mortality, with a higher incidence of heart failure (HF) [\[18](#page-8-0)] compared to those without renal failure [\[19\]](#page-8-0). However, diagnostic criteria for HF in CRF patients have not been well-defined. Currently, there are no specific biomarkers for diagnosing HF in CRF patients undergoing maintenance hemodialysis. The diagnostic criteria for HF in this population are the

Fig. 6. ROC analyses comparing nomogram with individual variables.

same as those for non-dialysis patients. However, due to the unique aspects of this group in terms of water and salt metabolism, calcium and phosphorus balance, and micro-inflammatory status, the mechanisms, criteria for differentiation, and treatments of HF in these patients should differ from those in non-dialysis populations.

The model, based on robust statistical analysis, offers healthcare providers a practical tool to identify patients at higher risk for heart failure, which can inform treatment strategies and improve patient outcomes. The nomogram may also help in allocating resources and planning healthcare services, particularly considering the growing burden of CKD and its complications on global health systems.

Due to the unique conditions of hemodialysis patients, such as their volume status, solute concentration, and micro-inflammatory state, many studies exclude them from research, resulting in a dearth of relevant evaluations for heart failure in this patient population. Consequently, there are currently no established guidelines or consensus for diagnosing heart failure in hemodialysis patients. The "Guidelines for the Management of Chronic Heart Failure in Chinese Dialysis Patients," published in the May 2022 issue of *Chin J Nephrol*, highlights that dialysis patients often exhibit extremely poor or even non-existent residual renal function and suffer from multiple chronic complications,

which significantly complicates diagnosis and treatment. Internationally, the absence of clear diagnostic criteria has been noted as well [[20,21](#page-8-0)].

Internationally, there is a notable absence of established guidelines or consensus for managing chronic heart failure in dialysis patients. Importantly, this guideline still fails to offer clear diagnostic criteria specifically for heart failure in dialysis patients. Several relevant studies further explain the situation, such as McMurray et al. [\[22](#page-8-0)] and Wali et al., [\[23](#page-8-0)], which provide insights into cardiovascular disease and heart failure management inpatients with kidney disease.

This study has several limitations. Firstly, its retrospective nature introduces potential selection bias despite the robust statistical methods used. Data were collected from a single center, which may limit the generalizability of the findings. Additionally, the model did not account for potential confounders such as lifestyle factors and medication use, which could influence the risk of heart failure in this population. Furthermore, external validation of the nomogram was conducted using a single-center dataset, which may limit its applicability to broader populations.

Fig. 7. DCA comparing clinical usefulness of the nomogram and individual variables.

6. Conclusion

In conclusion, the development and validation of this nomogram for predicting heart failure hospitalization in patients undergoing hemodialysis represent a significant advancement in managing CKD-related cardiovascular complications. The tool has the potential to enhance clinical decision-making and improve patient care, particularly in resource-constrained settings where such prognostic information is often limited. Future research should focus on the external validation of this nomogram in diverse populations and the exploration of its application in clinical practice.

CRediT authorship contribution statement

Jie Luo: Project administration. **Zhangru Rui:** Data curation. **Yun He:** Investigation. **Hui Li:** Data curation. **Yang Yuan:** Investigation. **Wenhong Li:** Methodology.

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Declaration of competing interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Data availability

All data that support the findings of this study are available from the authors upon reasonable request.

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