BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Association of the modified creatinine index with quality of life in haemodialysis patients

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Abstract

Aims/Background The evaluation of health-related quality of life in patients undergoing maintenance haemodialysis has garnered increasing attention. The modified creatinine index, a surrogate marker for muscle mass, has been linked to various clinical outcomes. However, the relationship between modified creatinine index and health-related quality of life in maintenance haemodialysis patients remains unclear. This study aims to elucidate the association between modified creatinine index and health-related quality of life in individuals receiving maintenance haemodialysis.

Methods This cross-sectional study included 217 maintenance haemodialysis patients. Health-related quality of life was assessed using the Kidney Disease Quality of Life Instrument. Collected data included general patient information, laboratory results, and haemodialysis-related parameters. The modified creatinine index was calculated based on gender, age, single-pool Kt/V (spKt/V), and pre-dialysis serum creatinine levels. Multiple linear regression models and smooth curve fitting were used to investigate the relationship between modified creatinine index and health-related quality of life. Subgroup analyses and interaction tests were performed to identify potential effect modifiers.

Results The 217 maintenance haemodialysis patients had a mean age of 53.66±13.15 years and a median dialysis vintage of 39 (25–84) months; 120 (55.30%) were male. The mean health-related quality of life score was 55.76±10.33, and the mean modified creatinine index was 22.72±2.95 mg/kg/day. After adjusting for confounding factors, an increase in modified creatinine index was associated with an improvement in health-related quality of life (β=0.55, 95% CI: 0.04, 1.06, p = 0.033). No nonlinear relationship was identified between modified creatinine index and health-related quality of life by smooth curve fitting. Subgroup and interaction analyses indicated that the relationship between modified creatinine index and health-related quality of life was stable and not significantly influenced by age, gender, dialysis vintage, diabetes status, or body mass index (p > 0.05).

Conclusion Modified creatinine index is positively correlated with health-related quality of life in maintenance haemodialysis patients, suggesting its potential utility in evaluating patient quality of life. Modified creatinine index could be clinically useful to improve the predictability of health-related quality of life in maintenance haemodialysis patients.

Key words: Haemodialysis; Health-related quality of life; Modified creatinine index; Sarcopenia

Submitted: 29 May 2024; **Revised:** 20 June 2024; **Accepted:** 11 July 2024

How to cite this article:
Zeng J, Wang Y, Li H, Wen H. Association of the modified creatinine index with quality of life in haemodialysis patients. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0298

Introduction

Chronic kidney disease (CKD) has become a global public health issue, with a prevalence rate of 10.8% in China (Wang et al, 2023). When CKD progresses to end-stage renal disease (ESRD), renal replacement therapy is required, with maintenance haemodialysis (MHD) being one of the primary treatment modalities (Evans et al, 2022). With the promotion of the bio-psycho-social medical model, Health-related quality of life (HRQOL) is as important as traditional clinical outcomes in assessing patient health status (Chesnaye et al, 2022). Although MHD can effectively prolong patients' lives, it also induces various complications, leading to a further decline in patients' HRQOL (Brown et al, 2021). Therefore, evaluating HRQOL in MHD patients, actively identifying its influencing factors, and exploring potential intervention targets have become crucial tasks in clinical and nursing practice.

Due to protein-energy wasting, metabolic acidosis, and reduced physical activity, MHD patients often suffer from sarcopenia, characterised by decreased muscle mass, strength, and function (Shu et al, 2022). One study has shown that sarcopenia is associated with reduced HRQOL in MHD patients, making early monitoring and intervention crucial for improving their HRQOL (Inaba et al, 2021). However, measuring muscle mass requires specialised equipment, and assessing muscle function can be complex, hindering the clinical application of sarcopenia screening (Dent et al, 2018).

The modified creatinine index (mCI), calculated based on routine indicators such as gender, age, pre-dialysis serum creatinine levels, and single-pool Kt/V (spKt/V), is a convenient and reliable tool for assessing muscle mass, muscle function, and nutritional status in MHD patients (Yamamoto et al, 2021). Studies have shown that mCI is closely associated with adverse clinical outcomes such as cardiovascular events (Arase et al, 2018), fractures (Yamada et al, 2017), and increased mortality risk (Arase et al, 2020).

Currently, no reports exist on the use of mCI to evaluate HRQOL in MHD patients, and the relationship between mCI and HRQOL in these patients needs further investigation. We hypothesise that mCI can predict HRQOL in MHD patients. This study aims to explore the relationship between mCI and HRQOL in MHD patients, providing more evidence for the clinical application of mCI.

Methods

Study settings and participants

A cross-sectional study was conducted at the Blood Purification Centre of the Affiliated Hospital of North Sichuan Medical College from June 2023 to February 2024. Inclusion criteria consisted of: (1) Age ≥18 years; (2) Meeting the diagnostic criteria for CKD (Chen et al, 2019); (3) Regular haemodialysis treatment for more than 3 months. Exclusion criteria were: (1) Patients with severe infections or severe damage to vital organs such as the heart and lungs; (2) Patients with cognitive impairment, psychological disorders, and/or a history of mental illness; (3) Patients with incomplete data. The study was approved by the Medical Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (no. 2023ER220-1). The protocol adhered to the principles of the Declaration of Helsinki, and informed consent was obtained from all participants.

Clinical, biological, and haemodialysis parameters

The following data were recorded: age, sex, dialysis vintage, dialysis vascular access, diabetes status, and height. Post-dialysis weight, pre-dialysis systolic blood pressure, and pre-dialysis diastolic blood pressure were measured as the average values of the most recent week. Fasting blood samples were obtained via the arteriovenous fistula or central venous catheter immediately preceding dialysis. Biochemical parameters, including haemoglobin, high-sensitivity C-reactive protein (hs-CRP), phosphorus, intact parathyroid hormone (iPTH), serum iron, serum ferritin, serum creatinine (Scr), blood urea nitrogen (BUN), and serum albumin, were measured using a fully automatic biochemical analyser (Mindray BS2000M, Shenzhen, China). Haemodialysis parameters were recorded simultaneously. spKt/V and urea reduction ratio (URR) were measured according to relevant equations (Kopple, 2001). The mCI was calculated using the following formula (Canaud et al, 2014):

Modified creatinine index (mg/kg/d)=16.21 + 1.12 × (male=1; female=0) – 0.03 × age (years) – 0.08 × spKt/V + 0.009 × pre-dialysis Scr (umol/L).

Health-related quality of life assessment

The Chinese version of the Kidney Disease Quality of Life-Short Form (KDQOL™-36) was utilised to assess HRQOL. This instrument comprises the Physical Component Summary (PCS) and Mental Component Summary (MCS) from the SF-12, along with kidney disease-specific domains such as the burden of kidney disease (BKD), effects of kidney disease (EKD), and symptom/problem list of kidney disease (SPLKD). Scores range from 0 to 100, with higher scores indicating better quality of life (Tao et al, 2014). In this study, the Cronbach's α coefficient of the scale was 0.842.

Statistical analysis

This cross-sectional study utilised the formula method to calculate the sample size, with $N=(U_{1-\alpha/2\sigma}/\delta)^2$, where α for a two-sided test is set at 0.05, giving $U_{1-\alpha/2}=1.96$ from the table. Taking MHD patients' HRQOL scores as the outcome indicator, the overall standard deviation σ was set at 20 based on pre-experiment results and previous study (Tao et al, 2014), with a permissible error δ of 3. Including a 20% sample loss rate, the minimum sample size required was 203 patients.

All data underwent testing for normal distribution using the Shapiro-Wilk test and for homogeneity of variances using Levene's test. Normally distributed continuous variables were expressed as mean and standard deviation, while non-normally distributed continuous variables were expressed as median and interquartile range. Categorical data were described using frequencies and percentages.

Univariate linear regression analysis was utilised to evaluate the correlation between clinical, biological, and haemodialysis parameters with HRQOL. The mCI was divided into quartiles: Q1 (16.68–20.51) mg/kg/d, Q2 (20.51–22.46) mg/kg/d, Q3 (22.46–22.49) mg/kg/d, Q4 (22.49–30.83) mg/kg/d. Data comparisons were performed using one-way ANOVA or Kruskal-Wallis test among the four subgroups. When significant differences were observed, multiple comparison analysis was conducted using the Dunnett *t*-test or Steel-Dwass test, with group 1 designated as the control.

Multiple linear regression was used for multivariate analysis of the relationship between mCI and HRQOL. Subjects were categorised based on KDQOL™-36 scores summary (KSS) into two groups: high HRQOL (KSS <50) and low HRQOL (KSS ≥50). Two independent sample *t*-tests were used for continuous variables with normal distribution and homogeneous variances. The Kolmogorov-Smirnov test was employed for continuous variables with non-normal distribution. Chi-square tests were utilised for categorical variables. Additionally, multivariable logistic regression analysis was carried out to examine the relationship between mCI and HRQOL groups. Confounders were selected based on their association with the outcome of interest ($p < 0.1$) or a 10% change in effect estimate.

Subgroup analysis was conducted to explore the stability of the relationship between mCI and HRQOL. A smooth curve fitting was conducted to investigate the linear or nonlinear relationship between mCI and HRQOL, and log-likelihood ratio tests were performed to measure p values. Subgroup analyses included stratification by sex, age (<60 years and ≥60 years), dialysis vintage (<18 months and ≥18 months), arteriovenous fistula (yes and no), diabetes status (yes and no), and body mass index (<23 kg/m^2 and ≥23 kg/m^2) (Fouque et al, 2008). A likelihood ratio test was used to calculate p for interaction.

The data were analysed using the statistical packages R (The R Foundation; http://www.r-project.org; version 4.2.0) and EmpowerStats (www.empowerstats.net, XandY Solutions, Inc., Boston, MA, USA). All tests were 2-tailed, and a significance level of $p < 0.05$ was considered statistically significant.

Results

Univariate analysis of quality of life in maintenance haemodialysis patients

A total of 217 MHD patients were included in this study, comprising 120 males (55.30%) and 97 females (44.70%). The mean age was 53.66±13.15 years, with a median dialysis vintage of 39 (25–84) months. The overall quality of life score was 55.76±10.33 points. Univariate analysis revealed statistically significant differences in terms of sex, body mass index, Scr, and mCI ($p < 0.05$), as detailed in Table 1. Additionally, statistically significant differences in age, sex, Scr, albumin, phosphorus, and mCI were observed between the high HRQOL group and low HRQOL group ($p < 0.05$), as detailed in Supplementary Table 1.

Furthermore, mCI was found to be significantly associated with age, sex, arteriovenous fistula, diabetic status, diastolic blood pressure, iPTH, blood urea nitrogen, Scr, albumin, spKt/V, and URR ($p < 0.05$), as detailed in Supplementary Table 2.

Table 1. The results of univariate analysis (n=217)				
Characteristics	**Statistics (n=217)**	**SE**	**β (95% CI)**	***p***
Age, years	53.66±13.15	0.05	–0.09 (–0.20,0.01)	0.083
Sex, *n* (%)				
Male	120 (55.30)		Reference	Reference
Female	97 (44.70)	1.40	–2.99 (–5.75, –0.23)	0.034
Dialysis vintage, months	39.00 (25.00–84.00)	0.02	0.02 (–0.01,0.05)	0.163
Arteriovenous fistula, *n* (%)				
Yes	195 (89.86)		Reference	Reference
No	22 (10.14)	2.31	–4.11 (–8.66,0.45)	0.077
Diabetic status, *n* (%)				
Yes	49 (22.58)		Reference	Reference
No	168 (77.42)	1.68	1.63 (–1.66,4.94)	0.332
Body mass index, kg/m²	22.35±3.27	0.21	0.56 (0.15,0.98)	0.009
Systolic blood pressure, mmHg	138.39±18.43	0.04	–0.06 (–0.14,0.01)	0.110
Diastolic blood pressure, mmHg	78.96±9.42	0.07	–0.10 (–0.25,0.04)	0.169
Haemoglobin, g/L	107.89±13.39	0.05	0.05 (–0.06,0.15)	0.367
NLR	3.85 (3.08–4.95)	0.34	–0.18 (–0.84,0.49)	0.601
Hs-CRP, mg/L	2.10 (0.93–5.49)	0.03	–0.01 (–0.07,0.06)	0.792
iPTH/10, ng/L	24.28 (16.10–38.26)	0.03	–0.02 (–0.08,0.03)	0.382
Phosphorus, mmol/L	2.03±0.61	1.15	1.80 (–0.46,4.06)	0.118
Serum iron, mmol/L	11.60 (8.90–15.00)	0.13	0.17 (–0.09,0.42)	0.198
Ferritin/10, µg/L	9.20 (5.40–15.10)	0.09	–0.01 (–0.18,0.16)	0.921
BUN, mmol/L	25.25±6.95	0.10	0.10 (–0.10,0.30)	0.327
Scr/10, µmol/L	100.64 (83.89–117.64)	0.03	0.07 (0.02,0.12)	0.011
Albumin, g/L	38.08±3.46	0.20	0.31 (–0.09,0.71)	0.133
spKt/V for urea	1.49±0.37	1.90	–2.81 (–6.56,0.95)	0.142
URR	70.51±8.75	0.08	–0.16 (–0.31,0.00)	0.053
mCI, mg/kg/d	22.72±2.95	0.23	0.69 (0.23,1.15)	0.004
Q1, *n* (%)	55 (25.35)		Reference	Reference
Q2, *n* (%)	54 (24.88)	1.94	3.33 (–0.50,7.15)	0.088
Q3, *n* (%)	54 (24.88)	1.94	4.44 (0.61,8.26)	0.023
Q4, *n* (%)	54 (24.88)	7.94	6.52 (2.70,10.34)	0.001

Values for continuous variables are presented as means±standard deviations or medians and interquartile ranges. Categorical variables are expressed as numbers (%).

Abbreviations: SE: standard error; NLR: Neutrophil-to-Lymphocyte Ratio; hs-CRP: high-sensitivity C-reactive protein; iPTH: intact parathyroid hormone; iPTH/10: 10ng/L per change in iPTH; Ferritin/10: 10µg/L per change in ferritin; BUN: blood urea nitrogen; Scr: serum creatinine; mCI: modified creatinine index; spKt/V: single-pool Kt/V; URR: urea reduction ratio.

Comparison of health-related quality of life among maintenance haemodialysis patients with different modified creatinine index values

Differences were observed in the KSS, SPLKD, and PCS among different groups ($p < 0.05$). However, there were no statistically significant differences in EKD, BKD, or MCS among different groups ($p > 0.05$), as shown in Table 2.

Multifactorial analysis of the relationship between modified creatinine index and health-related quality of life in maintenance haemodialysis patients

Multifactorial analysis revealed that with an increase in mCI, HRQOL in MHD patients gradually improved. After adjusting for confounding factors, an increase in mCI was associated with an improvement in HRQOL (β=0.55, 95% CI: 0.04, 1.06, $p = 0.033$). Patients in the Q4 group had a 2.08-point higher HRQOL compared to the Q1 group (95% CI: 1.77, 9.97), as shown in Table 3. Logistic regression analysis revealed that with each unit increase in mCI, the likelihood of experiencing low HRQOL decreased by 18%. Additionally, the risk of low HRQOL was found to decrease by 80% in the Q4 group compared to the Q1 group, as shown in Supplementary Table 3**.**

Smooth curve fitting analysis of the relationship between modified creatinine index and health-related quality of life

Adjusted for arteriovenous fistula, diabetic nephropathy, body mass index, and iPTH, no nonlinear relationship was identified by smooth fitting curve between mCI and HRQOL ($p = 0.141$), as shown in Figure 1.

Table 2. Comparative analysis of health-related quality of life in maintenance haemodialysis patients with different modified creatinine index

	Q1	Q2	Q3	Q4	F/H statistic	*p*
PCS	41.12±9.72	44.34±9.31	46.49±8.16*	46.89±7.32*	5.05	0.002
MCS	49.49±9.83	47.60±11.13	50.80±9.18	50.92±7.5	2.52	0.472
BKD	25.00 (18.75–50.00)	31.25 (12.50–62.50)	34.38 (25.00–50.00)	40.62 (25.00–56.25)	3.20	0.362
SPLKD	79.24±14.68	81.87±12.76	85.88±10.16*	88.62±7.32*	16.56	<0.001
EKD	57.22±20.46	63.83±19.80	65.22±16.95	64.64±15.26	2.27	0.081
KSS	52.21±10.52	55.54±12.35	56.65±7.62*	58.73±9.42*	9.66	0.022

*Values for continuous variables are presented as means±standard deviations or medians and interquartile ranges. For comparison of PCS and EKD between groups, we used one-way ANOVA, and for other variables, we used the Kruskal-Wallis rank sum test. *p < 0.05 vs. Q1.*

Abbreviations: PCS: Physical Component Summary; MCS: Mental Component Summary; BKD: burden of kidney disease; EKD: effects of kidney disease; SPLKD: symptom/problem list of kidney disease; KSS: Kidney Disease Quality of Life-Short Form (KDQOL™-36) scores summary.

Table 3. The results of multivariate analysis

Variables	SE	β (95% CI)	*p*
mCI (mg/kg/d)	0.26	0.55 (0.04,1.06)	0.033
Q1	Reference	Reference	Reference
Q2	1.96	3.34 (–0.53,7.20)	0.090
Q3	2.02	4.00 (–0.00,8.00)	0.050
Q4	2.08	5.87 (1.77,9.97)	0.005

The model was adjusted for arteriovenous fistula, diabetic nephropathy, body mass index, and iPTH. mCI: modified creatinine index.

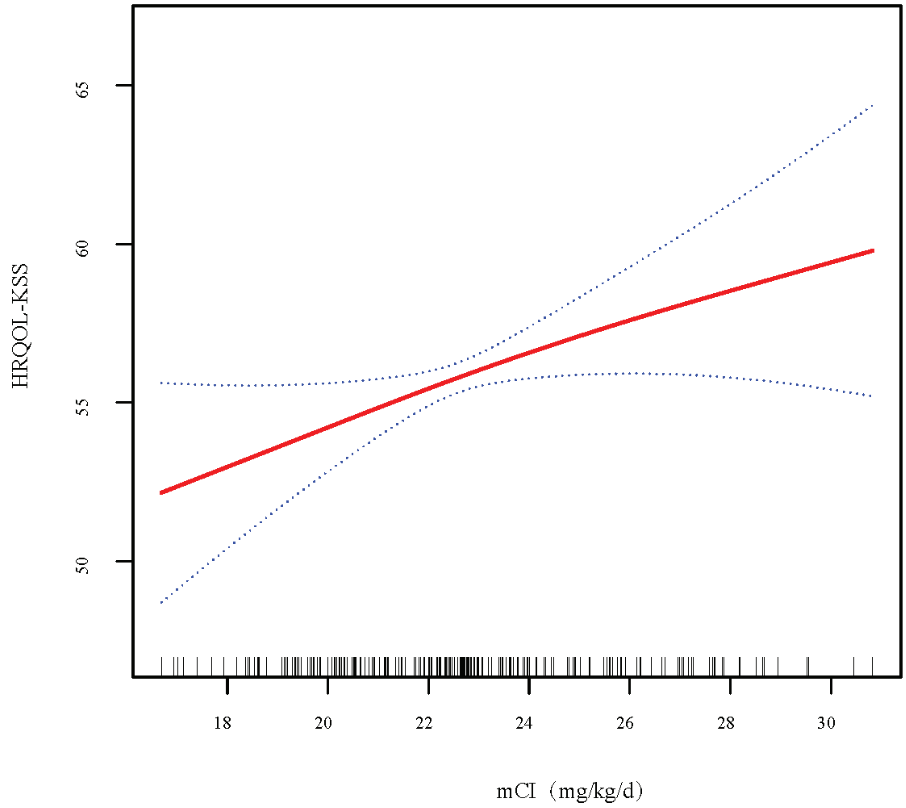

Figure 1. Smooth curve fitting of modified creatinine index and health-related quality of life.

Subgroup analysis of the relationship between modified creatinine index and health-related quality of life

Subgroup analysis was conducted to assess the consistency of the relationship between mCI and HRQOL across various patient groups, while also examining the interaction effects of age, sex, dialysis vintage, diabetes status, and body mass index. Adjusted for arteriovenous fistula and iPTH, the findings revealed a stable relationship between mCI and HRQOL, unaffected by age, gender, dialysis vintage, diabetes status, or body mass index ($p > 0.05$), as depicted in Figure 2.

Discussion

The evaluation of HRQOL in MHD patients is gaining increasing attention, with mCI emerging as an alternative indicator of muscle mass linked to various clinical outcomes. However, the relationship between mCI and HRQOL in MHD patients remains unclear. Our study uncovered a positive correlation between mCI and HRQOL in MHD patients, revealing that HRQOL increased by 0.55 points for each 1 mg/kg/d increase in mCI. Patients with an mCI in the range of 22.49–30.83 mg/kg/d (Q4) showed a 2.08-point higher HRQOL compared to those with an mCI in the range of 16.68–20.51 mg/kg/d (Q1).

Modified creatinine index is a composite index that integrates gender, age, spKt/V, and pre-dialysis Scr levels to assess muscle mass (Canaud et al, 2020), muscle function (Tian et al, 2022), and nutritional status (Tsai et al, 2021) in MHD patients. Sarcopenia, characterised by decreased muscle mass and function, is prevalent in MHD patients due to chronic metabolic disorders, malnutrition, and persistent inflammation (Shu et al, 2022), and is closely linked to HRQOL (Reis et al, 2022). Protein-energy wasting (PEW) is also common among MHD patients, characterised by concurrent loss of body protein and energy, resulting in reduced muscle and fat mass and ultimately cachexia, which is associated with

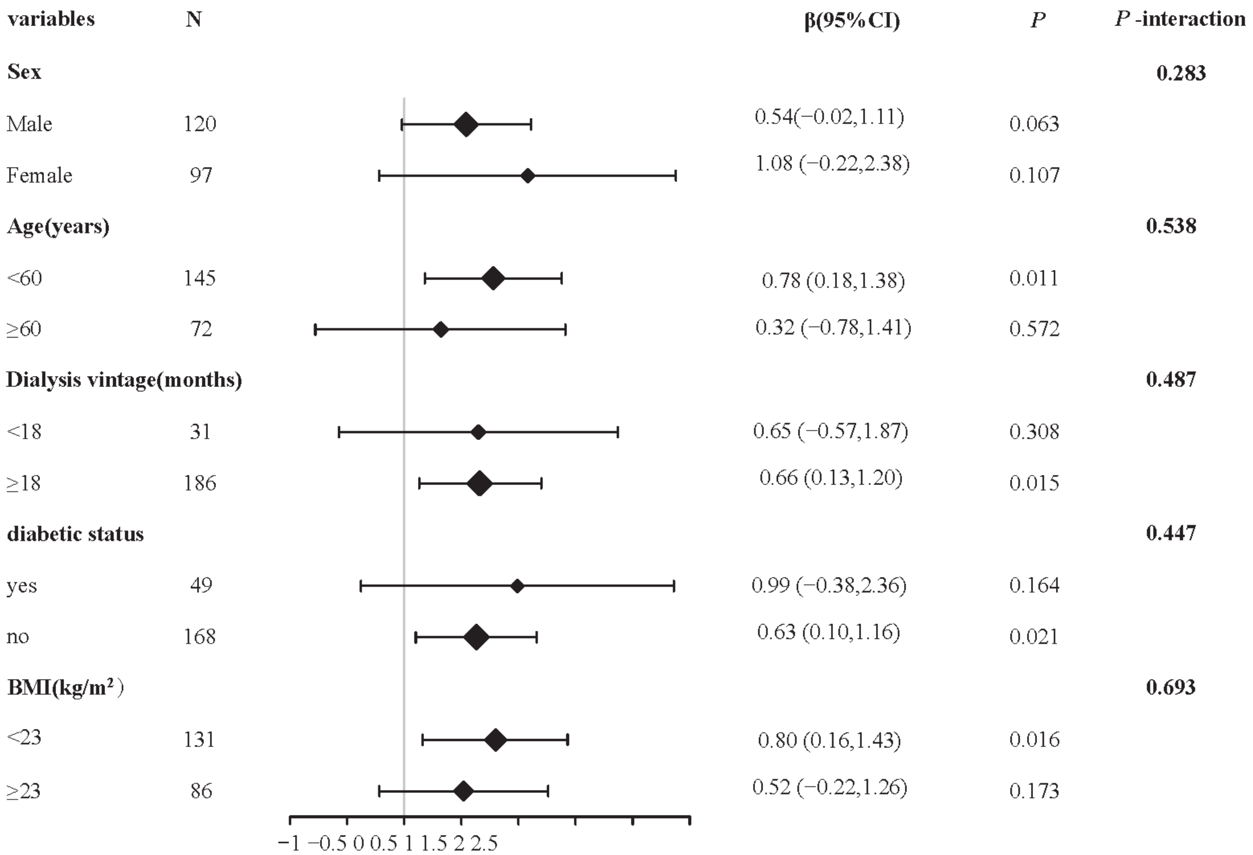

Figure 2. Subgroup analysis of the relationship between modified creatinine index and health-related quality of life.

decreased HRQOL (de Roij van Zuijdewijn et al, 2016). Currently, effective and simple assessment methods for sarcopenia or PEW are lacking. Therefore, the mCI, calculated using routine monitoring parameters, may serve as an ideal surrogate marker for assessing HRQOL in MHD patients. Our findings support this hypothesis, demonstrating a positive correlation between mCI and HRQOL in MHD patients.

Furthermore, the residual renal function might influence mCI levels, potentially indicating better residual renal function with higher mCI (Canaud et al, 2020). This function is crucial for maintaining metabolic balance and reducing toxin accumulation. Study suggests that patients with better residual renal function generally exhibit higher HRQOL (Elgendy et al, 2022). Canaud et al (2020) categorised patients into two subgroups based on dialysis vintage (less than 12 months and more than 18 months), with the former likely having a better residual renal function. They found consistent relationships between mCI and clinical outcomes in both groups. Our subgroup analysis similarly indicated a positive correlation between mCI and HRQOL in patients with a dialysis vintage exceeding 18 months, although no significant interaction effect of dialysis vintage was observed. Hence, while the relationship between mCI and HRQOL in MHD patients may not be influenced by residual renal function, further research is warranted to clarify this association, as residual renal function was not assessed in our study.

Health-related quality of life serves as a predictor of mortality risk in MHD patients, with some countries incorporating regular HRQOL assessments into quality control indicators (Hall et al, 2020). Our study utilised the Kidney Disease Quality of Life-Short Form (KDQOL™-36) to evaluate HRQOL in MHD patients, yielding an overall score of 55.76±10.33, indicative of a relatively low level of quality of life. This finding aligns with domestic and international studies (Chow and Tam, 2014; Peipert et al, 2019). The

KDQOL™-36 encompasses five dimensions, and our preliminary findings suggest that mCI may be related to PCS and SPLKD but does not significantly impact MCS, EKD, or BKD. As a surrogate indicator for sarcopenia and malnutrition, mCI may have a more pronounced effect on physical aspects (Reis et al, 2022). Nagy et al (2021) found that protein malnutrition correlated with symptom impact, energy, and physical strength in MHD patients. Similarly, Poppe et al (2020) measured creatinine synthesis rate (CSR) and HRQOL in MHD patients, highlighting that CSR is primarily associated with physical function. Both CSR and mCI are derived from creatinine kinetics models and reflect muscle function and nutritional status. While mCI is simpler and more accessible, further research is warranted to compare their predictive capabilities for clinical outcomes.

Several limitations should be acknowledged in this study. Firstly, the cross-sectional design constrains our ability to infer causality between mCI and HRQOL. Longitudinal studies are warranted to establish causality and track changes over time. Secondly, residual renal function, a potential confounding factor, was not assessed in this study. Future research should incorporate residual renal function assessments for a more comprehensive analysis. Thirdly, while the sample size was adequate, it may not fully represent the diverse population of MHD patients, particularly those with varied comorbidities and demographics. Larger, multicenter studies are essential to enhance generalizability. Lastly, while the KDQOL™-36 is a robust tool for assessing quality of life, additional instruments may be necessary to capture all relevant dimensions for MHD patients.

Conclusion

In summary, our study uncovers a positive correlation between mCI and HRQOL in MHD patients. Higher mCI within a specific range is linked to improved quality of life, likely attributed to better muscle mass, nutritional status, and residual renal function. This underscores the importance of integrating mCI alongside other factors to enhance the quality of life in haemodialysis patients. mCI may serve as an alternative indicator for monitoring HRQOL in MHD patients and play a crucial role in enhancing patients' clinical outcomes.

Key points

- Evaluating the HRQOL in MHD patients is crucial, given the substantial burden of CKD and its treatment.
- While the mCI serves as an indicator of muscle mass and nutritional status and has shown associations with various clinical outcomes such as cardiovascular events, fractures, and increased mortality risk, its relationship with HRQOL in MHD patients remains understudied.
- This study reveals a positive correlation between mCI and HRQOL in MHD patients.
- Furthermore, the relationship between mCI and HRQOL remains consistent across various subgroups, including age, gender, dialysis vintage, diabetes status, and body mass index, indicating no significant interaction effects.
- These findings underscore the utility of mCI as a valuable tool for assessing HRQOL in MHD patients. mCI offers a simple, easily obtainable, and clinically relevant surrogate marker in clinical settings.

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Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Author contributions

HYW and JZ conceived and designed the research study. JZ and YJW performed data acquisition. HL analysed and interpreted the data. JZ wrote the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Affiliated Hospital of North Sichuan Medical College (no. 2023ER220-1). The entire experimental procedure adhered to the principles of informed consent, with patients or their family members being provided with information about the study.

Acknowledgement

Not applicable.

Funding

This study was funded by Nanchong City School Science and Technology Strategic Cooperation Project (22SXQT0179).

Conflict of interest

The authors declare no conflict of interest.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at https://www.magonlinelibrary.com/doi/suppl/10.12968/hmed.2024.0298.

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