



Is malnutrition a determining factor of health-related quality of life in hemodialysis patients? A cross-sectional design examining relationships with a comprehensive assessment of nutritional status

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Abstract

Purpose To identify relationships between health-related quality of life (HRQOL) and nutritional status in hemodialysis (HD) patients.

Method Secondary data from a cross-sectional survey was utilized. HRQOL was assessed for 379 HD patients using the generic Short Form 36 (SF-36) and disease-specific Kidney-Disease Quality of Life-36 (KDQOL-36). Malnutrition was indicated by malnutrition inflammation score (MIS) ≥ 5 , and presence of protein-energy wasting (PEW). The individual nutritional parameters included the domains of physical status, serum biomarkers, and dietary intake. Multivariate associations were assessed using the general linear model.

Results MIS ≥ 5 was negatively associated with SF-36 scores of *physical functioning* (MIS $< 5 = 73.4 \pm 8.0$ SE vs MIS $\geq 5 = 64.6 \pm 7.7$ SE, $P < 0.001$), *role-limitation-physical* (MIS $< 5 = 65.3 \pm 14.3$ SE vs MIS $\geq 5 = 52.9 \pm 14.0$ SE, $P = 0.006$), *general health* (MIS $< 5 = 53.7 \pm 7.5$ SE vs MIS $\geq 5 = 47.0 \pm 7.1$ SE, $P = 0.003$), and *PCS-36* (MIS $< 5 = 40.5 \pm 3.3$ SE vs MIS $\geq 5 = 35.9 \pm 3.1$ SE, $P < 0.001$); and KDQOL-36 score of *symptoms/problems* (MIS $< 5 = 78.9 \pm 5.6$ SE vs MIS $\geq 5 = 74.8 \pm 5.4$ SE, $P = 0.022$), but not with PEW by any tool. Of individual nutritional parameters, underweight (68.1 ± 5.4 SE, $P = 0.031$), normal weight (63.8 ± 2.8 SE, $P = 0.023$), and overweight (64.3 ± 2.9 SE, $P = 0.003$) patients had significantly higher *physical functioning* scores compared to obese patients (44.8 ± 5.5 SE). Serum albumin levels were positively associated with *physical functioning* ($P = 0.041$) score. HGS was also positively associated with *physical functioning* ($P = 0.036$), and *vitality* ($P = 0.041$) scores. Greater dietary phosphorus intakes were significantly associated with lower scores for *role limitation-physical* ($P = 0.008$), *bodily pain* ($P = 0.043$), and *PCS-36* ($P = 0.024$).

Conclusion Malnutrition diagnosis by MIS, but not PEW, indicated associations with HRQOL in HD patients. Individual nutritional parameters that related to higher HRQOL were BMI < 30 kg/m², better dietary phosphorus control, greater muscle strength and higher visceral protein pool.

Keywords Health-related quality of life · SF-36 · KDQOL-36 · Malnutrition diagnosis · Nutritional status

Plain English summary

Hemodialysis (HD) patients commonly express poor health-related quality of life (HRQOL). The relationship of nutritional status to HRQOL is unclear on the basis of malnutrition diagnosis considering inflammation or presence of

protein energy wasting (PEW). As well, nutritional parameters representative of multiple domains as recommended by experts need to be included in the statistical model. These aspects were studied in a Malaysian HD population using two commonly used HRQOL tools, namely the generic short-form 36 (SF-36) and disease-specific kidney disease quality of life-36 (KDQOL-36). The main finding was patients diagnosed with inflammation-related malnutrition (MIS ≥ 5) had poorer physical-related dimensions of HRQOL, whereas PEW did not relate to HRQOL. HRQOL was higher if patients were not obese, and had higher muscle

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strength, higher visceral protein status, and better dietary phosphorus control. This suggests that HRQOL monitoring of these nutritional parameters is critical when strategizing nutritional repletion to overcome malnutrition.

Introduction

The health-related quality of life (HRQOL) of end-stage kidney disease (ESKD) patients in relation to physical, mental, and social domains are well researched with reference to morbidity and mortality [1–4]. The dialysis patient group, in particular, is established to have the worst HRQOL compared to geriatric patients and patients with other chronic diseases such as rheumatoid arthritis, osteoarthritis, and diabetes mellitus [5]. Suboptimal HRQOL reflects the high disability burden from chronic kidney disease (CKD) [6] as dialysis patients majorly face disrupted lifestyles from the impact and side effects of the dialysis treatment including fatigue, inability to work, anxiety/stress, time constraints, and family burden [7–9]. Suboptimal HRQOL reported by the hemodialysis (HD) patient group is consistently associated with the physical dimension criteria, whilst the association with the mental dimension criteria is inconclusive [10–17].

Malnutrition greatly impacts the physical status of patients on dialysis [18–20] leading to frailty, sarcopenia, and impaired muscle function [19], which accounts for the pronounced poorer physical [21–23], mental [23], and burden of kidney disease [23] dimensions of HRQOL. Being highly prevalent in HD patients [24], malnutrition increases risks for hospitalization and mortality [25–27]. Its etiology in HD patients is multifactorial but centered on chronic inflammation and suboptimal dietary intakes [20, 28]. The dialysis diet is perceived as restrictive as it calls for both energy and protein optimization to prevent malnutrition, alongside several nutrient restrictions to prevent toxicities related to mineral disturbances such as hyperkalemia and hyperphosphatemia [29–31]. Indeed, dietary monotony practices prevail in this population [32], contributing to poor diet quality [33]. Psychosocial behaviors such as depression and lack of social support are also factors associated with malnutrition in HD patients [20], suggesting the possible relationship between mental status and malnutrition in dialysis patients.

Malnutrition-focused HRQOL reporting on individual assessment parameters such as BMI [1, 11, 34, 35], serum albumin [11, 12, 36, 37], and serum creatinine [11, 12, 36, 37] observe the physical component summary (*PCS*) but not the mental component summary (*MCS*) being significantly influenced. Dietary protein and energy intakes have been evaluated by limited studies [11, 13, 34, 38–41] which report inconclusive associations with both *PCS* and *MCS*. Other

studies have shown subjective global assessment (SGA) [1, 42] or the 7-points SGA [12, 14, 43, 44] being associated with poorer *PCS*, whilst associations with *MCS* remain inconsistent. Whereas, the Malnutrition Inflammation Score (MIS) [40, 42, 43, 45, 46] appears to be negatively correlated with both *PCS* and *MCS*. One study using the International Renal Nutrition and Metabolism (ISRN) criteria for diagnosis of protein-energy wasting (PEW) associated PEW with poorer *PCS* but not *MCS* [43]. Notably, these studies applied MIS or PEW criteria as continuous scores rather than comparing patients with and without malnutrition.

Nutritional status assessment for ESKD patients should ideally incorporate parameters inclusive of anthropometry, body composition, nutritional biomarkers, and dietary intake domains, as individual parameters will not conclusively identify which domain/s are causative of poor nutritional status [47, 48]. Such comprehensive nutritional assessment facilitates nutrition diagnosis for malnutrition in order to strategize nutritional interventions as required by the nutrition care process [49, 50]. Another limitation of these studies is to only report HRQOL summary scores whilst omitting the specific individual criteria components that makeup *PCS* and *MCS* [1, 11–13, 39].

Taking account of these gaps, the present study aimed to determine the associations of malnutrition as facilitated by the nutritional domains necessary for nutrition diagnosis with HRQOL. HRQOL assessment was performed with individual components along with summaries of SF-36 [51] and KDQOL-36 [52] in HD patients. These two HRQOL tools are commonly applied to the dialysis population [53].

Methods

Study design and patient recruitment

This cross-sectional study was conducted as a secondary analysis of primary data from the screening of patients being recruited for the Palm Tocotrienols in Chronic Haemodialysis (PaTCH) study. The PaTCH screening was conducted from October 2015 to November 2018 at four governmental, six non-governmental organization, and three private dialysis units in Klang Valley, Malaysia. Exclusion criteria were pregnant and lactating female patients, or patients with cognitive impairment or terminal illnesses. Patients with incidence of hospitalization > 2 times in the past 90 days or once in the past 30 days prior to enrolment were also excluded as recurring illness affects nutritional or HRQOL status. Cutoffs of energy intake: basal metabolic rate (EI:BMR) ratios of < 1.2, 1.2–2.4, and > 2.4 guided identification of under-, acceptable, and over-reported dietary data respectively [54]. Mis-reporting patients with either under-reporting or over-reporting of dietary intakes were excluded from the analysis.

All patients signed written consent. This study received ethical approval from the Medical Research Ethics Committee of the Ministry of Health, Malaysia (NMRR-15-865-25260). A sample size of $n = 365$ was estimated using Krejcie and Morgan formula [55] in the main screening study.

Primary data: HRQOL assessment

Both SF-36 [56] and KDQOL-36 [57] have been validated for use in Malaysia. Validated Malay, Chinese, and English language versions of these tools [56–58] were administered by multilingual interviewers during the HD session.

- (i) Short-Form 36 (SF-36): The 36-item SF-36 is a generic questionnaire [59] applied to the preceding 4 weeks of the patient interview uses a Likert-scale to assess eight general health components of HRQOL, namely *physical functioning*, *role limitation-physical*, *bodily pain*, *general health*, *vitality*, *social functioning*, *role limitation-emotional*, and *mental health*. Each component score ranges from 0 to 100, with higher scores indicating greater HRQOL. These components yield two summary scores, namely physical component summary-36 (*PCS-36*) and mental component summary-36 (*MCS-36*) as measures of overall physical HRQOL and mental HRQOL respectively. Standard scoring algorithms are used to compute components [59] and summary scores [60]. A norm-standard of 50 ± 10 SD for both *PCS-36* and *MCS-36* scores is the standard reference for a general population and may also be applied to this study population [60]. Suboptimal component scores are identified as falling < 50 [14].
- (ii) Kidney Disease Quality of Life-36 (KDQOL-36): KDQOL-36 is also a 36-item questionnaire inclusive of a generic core of *SF-12* and three kidney disease-specific components, namely *symptoms/problems*, *effects of kidney disease*, and *burden of kidney disease*, [52]. A scoring system in Microsoft Excel format, available online by RAND (https://www.rand.org/health-care/surveys_tools/kdqol.html), was used to derive scores for generic summary score of kidney disease-specific component scores of *symptoms/problems*, *effects of kidney disease*, and *burden of kidney disease* with greater scores indicating lesser bothersome caused by symptoms/problems, effects, and burden of kidney disease respectively. Additionally, *KDQOL-36 Summary Score* is computed from the average scores of all items from kidney disease-specific components [61]. Suboptimal summary [62] and component scores were defined as falling < 50 [14].

Secondary data

Sociodemographic, medical history, dietary, and blood investigations data were obtained from the primary analyses [33, 63] to fulfill this study's objectives.

- (i) Malnutrition diagnosis:

Malnutrition-Inflammation Score—The Malnutrition-Inflammation Score (MIS) was administered to assess the severity of the malnutrition-inflammation complex syndrome (MICS) in HD patients [64]. Comprised of ten components, each is scored from 0 to 3 denoting normal to the severe nutritional deficit. A cumulative score of 0–30 from all ten components denotes the ascending severity level of MICS. So far there was only a small study ($n = 100$) from Thailand [65] proposing a MIS cut-off ≥ 7.5 for HD patients. Given the paucity of studies to determine a consensus on the MIS cut-off for Southeast Asian patients, we elected to adopt the MIS ≥ 5 as criteria for malnutrition based on receiver operating characteristic curve analysis of three large studies [24].

Protein-energy wasting—The PEW status was assessed according to the ISRNM criteria as previously described [33]. In brief, PEW was diagnosed in the presence of at least one criteria in three out of four categories inclusive of serum chemistry, body mass, muscle mass, and dietary intake [19]. The criteria adopted for this study were (i) serum albumin < 38 g/dL, (ii) BMI < 23 kg/m², (iii) reduction $> 10\%$ in mid-arm muscle circumference (MAMC) in relation to 50th percentile of reference population [66], and (iv) dietary energy intake < 25 kcal/kg ideal body weight (IBW) as criteria from each category to diagnose PEW.

- (ii) Individual nutritional parameters:

Anthropometric Assessment—Post-dialysis weight and height were measured using a SECA digital scale (Model 220, SECA, Germany) to derive BMI (kg/m²).

Bio-impedance Analysis (BIA)—A portable whole-body bio-impedance spectroscopy device (Body Composition Monitor, Fresenius Medical Care, Bad Homburg, Germany) was used to assess body composition before the HD session, with patients resting about 15 min in supine position before the measurement. Two electrodes were positioned on the wrist of the non-fistula arm and on the ipsilateral ankle respectively before connecting to the device. Lean tissue index (LTI), and fat tissue index (FTI) were recorded.

Handgrip Strength Assessment—Handgrip strength (HGS) was measured using a digital hand

dynamometer (Jamar BK-7498; Fred Sammons, Inc., Burr Ridge, IL) before the HD session, with patients standing and squeezing the dynamometer upright as hard as possible using the non-fistula arm with elbow flexion of 90°. The measurement was repeated three times at 10–20 s intervals, and the median value was used.

Serum Biochemical Markers—Data was retrieved from patient medical records for serum creatinine (Jaffe method), hemoglobin (colorimetric method), phosphorus (ammonium molybdate method), and potassium (enzymatic method). These parameters were analyzed in-house as per standard operating procedures accredited by the Ministry of Health, Malaysia, using automated clinical chemistry (Roche/Hitachi 912 System, Roche Diagnostics, Tokyo, Japan). Whereas, serum albumin (bromocresol green method) and serum high-sensitivity C-reactive protein (hs-CRP) (immunoturbidimetric assay method) were measured at an independent laboratory.

Dietary Intake Assessment—Three days of 24-h dietary recalls (3DDR) of patients inclusive of a dialysis day, a non-dialysis day and 1 weekend day [67], were collected by trained dietitians through face-to-face interviews. These were analyzed using the Nutritionist Pro™ 2.2.16 software (Axxya Systems LLC, Stafford, TX, USA) which carried the nutritional composition of ethnic-specific Malaysian foods [68, 69]. Average daily energy, protein intake, phosphorus, potassium, sodium, and fluid were derived from these records, and dietary energy (DEI), and dietary protein (DPI) intakes per IBW were computed.

Statistical analysis

Data collected were analyzed using IBM Statistical Package for Social Sciences (SPSS) version 25.0 (IBM SPSS Statistics Inc, Chicago, IL, USA). Normality test was performed for continuous data, whilst non-normally distributed data were transformed using natural logarithm (ln). Missing data for body composition variables from the same seven datasets inclusive of both FTI (1.8%) and LTI (1.8%) were imputed using multiple imputation method with chained equation. General linear model was used to describe both the univariate and multivariate relationships of nutritional parameters with HRQOL components and summary scores. In multivariate analyses, separate models of MIS, PEW, and individual nutritional parameters (anthropometric, BIA, serum biochemical markers, and dietary intakes) with individual HRQOL components and summaries were performed respectively. In the analyses, we tested the linearity of all pairs of associations and BMI was only found to have

non-linear relationships with HRQOL. Therefore, BMI was categorized according to the WHO classification [70] for the analyses with HRQOL components and summaries scores. These models were controlled for demographic (age, gender, ethnicity, education, monthly income, working status, marital status, dialysis sector), and clinical characteristics (comorbidities of DM, HPT and CVD; *Kt/V* and dialysis vintage). Variance inflation factor (VIF) < 5 [71] for independent variables were used as an acceptable level to avoid multicollinearity in these models. Statistical significance was set at $P < 0.05$.

Result

The final analysis included 379 HD patients after excluding dietary mis-reporters as represented in the Consort diagram (Fig. 1). Patient characteristics are presented in Table 1. The prevalence of malnutrition as per MIS ≥ 5 and PEW was 43.5% and 23%, respectively.

SF-36 (Table 2) generic summaries indicated a greater proportion of patients with poorer *PCS-36* than *MCS-36*. For the components of SF-36 (Table 2), patients scored the highest for *social functioning*, but the lowest for *general health*. As regards the KDQOL-36 (Table 3), *burden of kidney disease* was assigned the lowest score by the patients.

Associations of sociodemographic and clinical characteristics with HRQOL

Significant associations with HRQOL components and summary scores are reported for age, gender, ethnicity, educational status, monthly incomes, working status, marital status, dialysis sector, comorbidities of HPT, DM, CVD, and dialysis vintage in relation to SF-36 (Table 2) and KDQOL-36 (Table 3). Therefore, these variables were adjusted in the multivariate model.

Associations of nutritional status with HRQOL

Data for all univariate analyses are available as supplementary information (Online Resources 1, 2, 4, 5). Results discussed here pertain only to the multivariate model. The results pertaining to SF-12 are also provided as supplementary information (Online Resources 6, 7).

Malnutrition diagnosis

For multivariate analysis as per the SF-36 assessment, malnourished patients identified with MIS ≥ 5 compared

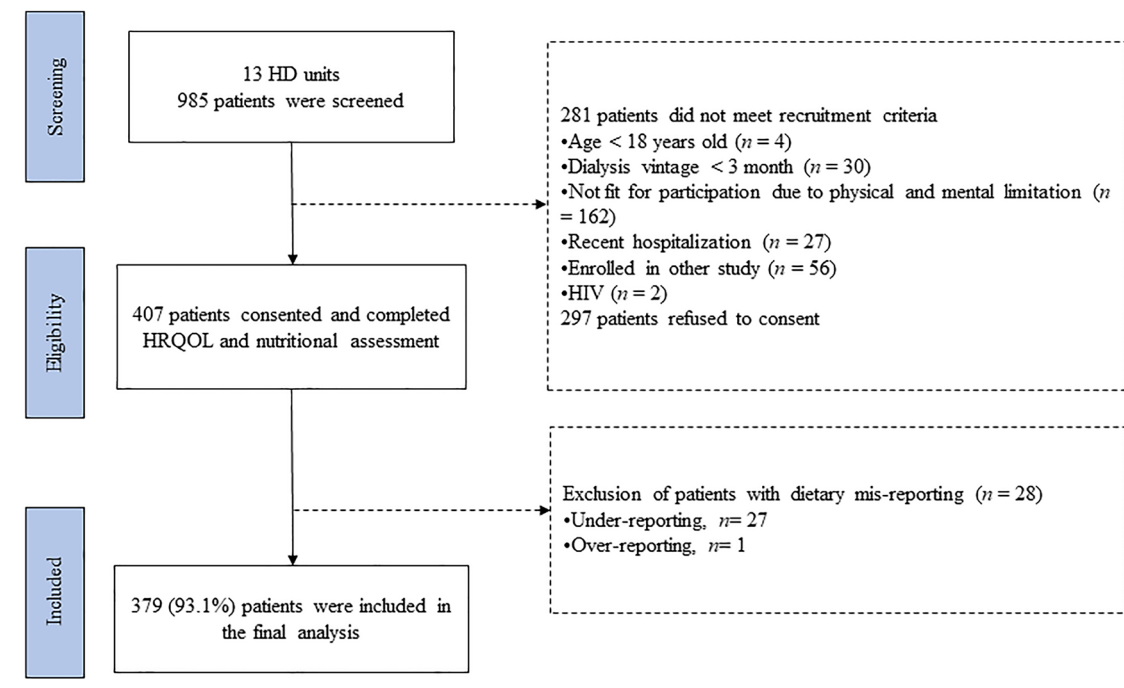


Fig. 1 Stock flow of patients' recruitment

to well-nourished patients ($MIS < 5$) (Fig. 2) had significantly lower *physical functioning* ($MIS < 5 = 73.4 \pm 8.0$ SE vs $MIS \geq 5 = 64.6 \pm 7.7$ SE, $P < 0.001$), *role-limitation-physical* ($MIS < 5 = 65.3 \pm 14.3$ SE vs $MIS \geq 5 = 52.9 \pm 14.0$ SE, $P = 0.006$), *general health* ($MIS < 5 = 53.7 \pm 7.5$ SE vs $MIS \geq 5 = 47.0 \pm 7.1$ SE, $P = 0.003$) and *PCS-36* ($MIS < 5 = 40.5 \pm 3.3$ SE vs $MIS \geq 5 = 35.9 \pm 3.1$ SE, $P < 0.001$) scores. In contrast, with KDQOL-36 assessment malnourished compared to well-nourished patients scored significantly lower *symptoms/problems* ($MIS < 5 = 78.9 \pm 5.6$ SE vs $MIS \geq 5 = 74.8 \pm 5.4$ SE, $P = 0.022$) score. In addition, across the MIS quartiles (Online Resources 3), we observed significantly decreasing trend scores for *physical functioning* ($P < 0.001$), *role limitation-physical* ($P = 0.008$), *general health* ($P = 0.011$), and *PCS-36* ($P < 0.001$) of SF-36; and *symptoms/problems* ($P = 0.013$) of KDQOL-36.

As regards PEW and non-PEW patients, both SF-36 and KDQOL-36 components and summary scores were not significantly different between groups (Fig. 3).

Other nutritional parameters

Measures of BMI, HGS and serum albumin appear to be associated with SF-36 but not KDQOL-36. As regards associations of BMI (Table 4), underweight (68.1 ± 5.4 SE, $P = 0.031$), normal weight (63.8 ± 2.8 SE, $P = 0.023$), and overweight (64.3 ± 2.9 SE, $P = 0.003$) patients had significantly higher *physical functioning* scores compared to

obese patients (44.8 ± 5.5 SE). Scores for *physical functioning* were also associated with HGS ($\beta = 0.36$, $P = 0.036$) and serum albumin levels ($\beta = 0.61$, $P = 0.041$). HGS was also positively associated with the *vitality* ($\beta = 0.33$, $P = 0.041$) component.

Whereas hs-CRP as an indicator of inflammatory status was only associated with KDQOL-36. The log-transformed hs-CRP ($\beta = -0.16$, $P = 0.032$) was negatively associated with the *KDQOL-36 Summary Score* (Table 5).

Both SF-36 and KDQOL appeared to be inversely associated with serum phosphorus and dietary phosphorus. With SF-36, higher serum phosphorus levels were significantly associated with lower scores for *bodily pain* ($\beta = -0.76$, $P = 0.045$), *general health* ($\beta = -0.50$, $P = 0.032$) and *PCS-36* ($\beta = -0.19$, $P = 0.037$), while greater dietary phosphorus intakes were significantly associated with lower scores for *role limitation-physical* ($\beta = -3.51$, $P = 0.008$), *bodily pain* ($\beta = -1.95$, $P = 0.043$), and *PCS-36* ($\beta = -0.77$, $P = 0.024$). With KDQOL-36, higher serum phosphorus levels were significantly associated with lower *symptoms/problems* ($\beta = -0.38$, $P = 0.020$) scores (Table 5).

Serum creatinine level was positively associated with SF-36 for *physical functioning* ($\beta = 0.14$, $P = 0.007$), and *PCS-36* ($\beta = 0.06$, $P = 0.026$).

The generic SF-36 components had the most number of associations with nutritional parameters in multivariate analyses (9 pairs) which were > 3 pairs for SF-36 generic summaries, > 1 pair for KDQOL-36 disease-specific

Table 1 Patient characteristics stratified with nutritional status ($n=379$)

| Variables | Overall | MIS < 5 n (%) = 214 (56.5) | MIS \geq 5 n (%) = 165 (43.5) | P value | Non-PEW n (%) = 292 (77.0) | PEW n (%) = 87 (23.0) | P value |
|---|-----------------|---------------------------------|--------------------------------------|------------------|---------------------------------|----------------------------|------------------|
| Age (years), mean \pm SE | 55.1 \pm 0.7 | 53.9 \pm 1.2 | 56.6 \pm 0.9 | 0.064 | 55.9 \pm 0.8 | 54.1 \pm 1.8 | 0.334 |
| Gender, n (%) | | | | | | | |
| Males | 182 (48.0) | 104 (27.4) | 78 (20.6) | 0.019 | 124 (32.7) | 58 (15.3) | 0.009 |
| Females | 197 (52.0) | 110 (29.0) | 87 (23.0) | | 168 (44.3) | 29 (7.7) | |
| Ethnicity, n (%) | | | | | | | |
| Malay | 140 (36.9) | 95 (25.0) | 45 (11.9) | 0.382 | 115 (30.3) | 25 (6.6) | 0.418 |
| Chinese | 181 (47.8) | 89 (23.5) | 92 (24.3) | | 140 (36.9) | 41 (10.8) | |
| Indians | 58 (15.3) | 30 (7.9) | 28 (7.4) | | 37 (9.8) | 21 (5.5) | |
| Education, n (%) | | | | | | | |
| No formal education | 25 (6.6) | 11 (2.9) | 14 (3.7) | 0.250 | 18 (4.7) | 7 (1.9) | 0.220 |
| Primary | 93 (24.5) | 41 (10.8) | 52 (13.7) | | 77 (20.3) | 16 (4.2) | |
| Secondary | 177 (46.7) | 106 (28.0) | 71 (18.7) | | 134 (35.4) | 43 (11.3) | |
| Tertiary | 84 (22.2) | 56 (14.8) | 28 (7.4) | | 63 (16.6) | 21 (5.6) | |
| Monthly income, n (%) | | | | | | | |
| \leq MYR 1000 | 220 (58.0) | 104 (27.4) | 116 (30.6) | 0.104 | 166 (43.8) | 54 (14.2) | 0.920 |
| $>$ MYR 1000 | 159 (42.0) | 110 (29.0) | 49 (12.9) | | 126 (33.2) | 33 (8.7) | |
| Working status, n (%) | | | | | | | |
| Yes | 96 (25.3) | 70 (18.5) | 26 (6.9) | 0.352 | 73 (19.3) | 23 (6.0) | 0.652 |
| No | 283 (74.7) | 151 (39.8) | 132 (34.8) | | 219 (57.8) | 64 (16.9) | |
| Marital status, n (%) | | | | | | | |
| Married | 298 (78.6) | 170 (44.9) | 128 (33.8) | 0.472 | 234 (61.7) | 64 (16.9) | 0.784 |
| Single/widow(er)/separated | 81 (21.4) | 44 (11.6) | 37 (9.8) | | 58 (15.3) | 23 (6.1) | |
| Dialysis sector, n (%) | | | | | | | |
| Governmental | 122 (32.2) | 65 (17.2) | 57 (15.0) | 0.544 | 92 (24.3) | 30 (7.9) | 0.337 |
| Non-governmental organization | 214 (56.5) | 113 (29.8) | 101 (26.6) | | 167 (44.1) | 47 (12.4) | |
| Private | 43 (11.3) | 36 (9.5) | 7 (1.8) | | 33 (8.7) | 10 (2.6) | |
| Comorbidities, n (%) | | | | | | | |
| Hypertension, yes | 302 (79.7) | 177 (46.7) | 125 (33.0) | 0.183 | 239 (63.1) | 63 (16.6) | 0.117 |
| Hypertension, no | 77 (20.3) | 37 (9.8) | 40 (10.6) | | 53 (14.0) | 24 (6.3) | |
| Diabetes mellitus, yes | 156 (41.2) | 89 (23.5) | 67 (17.7) | 0.616 | 128 (33.8) | 28 (7.4) | 0.030 |
| Diabetes mellitus, no | 223 (58.8) | 125 (33.0) | 98 (25.9) | | 164 (43.0) | 59 (15.6) | |
| Cardiovascular disease, yes | 58 (15.3) | 27 (7.1) | 31 (8.2) | 0.357 | 44 (11.6) | 14 (3.7) | 0.840 |
| Cardiovascular disease, no | 321 (84.7) | 187 (49.3) | 134 (35.4) | | 248 (65.4) | 73 (19.3) | |
| Dialysis vintage (years), median (IQR) | 5.0 (6.4) | 3.1 (5.3) | 6.6 (7.3) | <0.001 | 5.4 (6.4) | 4.3 (8.7) | 0.477 |
| Kt/V , mean \pm SE | 1.66 \pm 0.02 | 1.58 \pm 0.03 | 1.72 \pm 0.03 | 0.001 | 1.64 \pm 0.02 | 1.74 \pm 0.05 | 0.047 |
| Anthropometry | | | | | | | |
| BMI (kg/m^2), mean \pm SE | 24.7 \pm 0.3 | 26.2 \pm 0.4 | 23.5 \pm 0.4 | <0.001 | 25.8 \pm 0.3 | 20.5 \pm 0.3 | <0.001 |
| $<$ 18.5, underweight, n (%) | 29 (7.7) | 6 (1.6) | 23 (6.1) | <0.001 | 8 (2.1) | 21 (5.5) | <0.001 |
| 18.5–24.9, normal weight, n (%) | 184 (48.5) | 91 (24.0) | 93 (24.5) | | 125 (33.0) | 59 (15.6) | |
| 25.0–29.9, overweight, n (%) | 122 (32.2) | 85 (22.4) | 37 (9.8) | | 116 (30.6) | 6 (1.6) | |
| \geq 30.0, obese, n (%) | 44 (11.6) | 32 (8.4) | 12 (3.2) | | 43 (11.3) | 1 (0.3) | |
| Bio-impedance analysis | | | | | | | |
| FTI (kg/m^2), mean \pm SE | 11.7 \pm 0.3 | 12.5 \pm 0.4 | 10.9 \pm 0.4 | 0.005 | 12.6 \pm 0.3 | 7.8 \pm 0.4 | <0.001 |
| LTI (kg/m^2), mean \pm SE | 13.0 \pm 0.1 | 13.8 \pm 0.2 | 12.5 \pm 0.4 | <0.001 | 13.2 \pm 0.2 | 12.5 \pm 0.3 | 0.030 |
| Handgrip strength (kg), mean \pm SE | 19.5 \pm 0.4 | 21.0 \pm 0.7 | 18.0 \pm 0.5 | <0.001 | 19.3 \pm 0.5 | 19.0 \pm 1.02 | 0.726 |

Table 1 (continued)

| Variables | Overall | MIS < 5 n (%) = 214 (56.5) | MIS ≥ 5 n (%) = 165 (43.5) | P value | Non-PEW n (%) = 292 (77.0) | PEW n (%) = 87 (23.0) | P value |
|----------------------------------|---------------|-------------------------------|-------------------------------|----------------|-------------------------------|--------------------------|----------------|
| Biochemical markers | | | | | | | |
| Albumin (g/L), mean ± SE | 39.2 ± 0.2 | 40.7 ± 0.2 | 38.0 ± 0.3 | < 0.001 | 39.6 ± 0.2 | 37.2 ± 0.6 | < 0.001 |
| Creatinine (μmol/L), mean ± SE | 831.7 ± 10.6 | 868.9 ± 17.5 | 788.7 ± 13.7 | < 0.001 | 841.3 ± 12.1 | 748.8 ± 24.3 | < 0.001 |
| Phosphorus (mmol/L), mean ± SE | 1.76 ± 0.03 | 1.88 ± 0.04 | 1.71 ± 0.03 | 0.002 | 1.84 ± 0.06 | 1.55 ± 0.06 | < 0.001 |
| Potassium (mmol/L), mean ± SE | 5.18 ± 0.19 | 5.05 ± 0.06 | 4.95 ± 0.06 | 0.239 | 5.03 ± 0.05 | 4.8 ± 0.1 | 0.099 |
| hs-CRP (mg/dL), median (IQR) | 3.68 (6.87) | 3.09 (5.04) | 4.10 (7.14) | 0.045 | 3.65 (6.61) | 3.82 (6.20) | 0.798 |
| Dietary intake | | | | | | | |
| DEI (kcal/kg IBW/day), mean ± SE | 22.4 ± 0.4 | 25.4 ± 0.5 | 25.0 ± 0.4 | 0.480 | 25.7 ± 0.5 | 23.4 ± 0.5 | 0.002 |
| DPI (g/kg IBW/day), mean ± SE | 0.84 ± 0.02 | 0.93 ± 0.03 | 0.89 ± 0.02 | < 0.001 | 0.93 ± 0.02 | 0.88 ± 0.03 | 0.200 |
| Phosphorus (mg/day), mean ± SE | 626.1 ± 12.8 | 683.9 ± 23.3 | 628.4 ± 16.1 | 0.043 | 667.3 ± 16.1 | 596.4 ± 22.6 | 0.029 |
| Potassium (mg/day), mean ± SE | 1097.6 ± 25.9 | 1270.7 ± 51.3 | 1085.3 ± 77.7 | < 0.001 | 1166.5 ± 29.6 | 1079.7 ± 67.2 | 0.187 |
| Sodium (mg/day), mean ± SE | 2580.0 ± 59.1 | 2850.5 ± 103.7 | 2591.9 ± 77.7 | 0.047 | 2759.4 ± 69.8 | 2491.8 ± 140.5 | 0.075 |
| Fluid (mL/day), mean ± SE | 1064.2 ± 17.5 | 1133.1 ± 30.5 | 1061.2 ± 22.0 | 0.057 | 1110.9 ± 20.9 | 1022.2 ± 35.31 | 0.051 |

BMI body mass index; *DEI* dietary energy intake; *DPI* dietary protein intake; *ESKD* end-stage kidney disease; *FTI* fat-tissue index; *hs-CRP* high sensitivity-C-reactive protein; *LTI* lean tissue index; *MIS* malnutrition-inflammation score; *PEW* protein-energy wasting

Bold values indicate statistical significance with $P < 0.05$

components, and 1 pair for KDQOL-36 disease-specific summaries.

Discussion

Assessing malnutrition in ESKD is challenging as it includes multiple aetiologies [20, 28]. Although BMI [1, 11, 34, 35], serum albumin [11, 12, 36, 37], and serum creatinine [11, 12, 36, 37] have been shown to associate negatively with poor physical HRQOL, these individual nutritional parameters may not reflect the overall status of malnutrition and may be affected by other factors such as overhydration, and inflammation [47]. In contrast, the use of composite nutrition scores such as MIS and PEW facilitate the diagnosis of malnutrition. In the present study, we elucidated the relationship of nutritional status and HRQOL among HD patients with the primary objective to determine whether the diagnosis of malnutrition determined by MIS ≥ 5 or the presence of PEW was associated with the HRQOL status. Importantly, we added individual nutritional parameters representative of domains required to satisfy malnutrition diagnosis [47, 48, 72] into the multivariate models, to determine the critical variables associated with the HRQOL outcomes,

and therefore could be applied to strategize treatment of malnutrition.

Our study showed for the first time that the presence of malnutrition defined by MIS ≥ 5 compared to its absence (MIS < 5) differentiated HRQOL status between groups, with the former scoring poorer compared to the latter. Although previous studies have reported an inverse relationship exists between MIS and HRQOL status of HD patients, the model adopted by these studies applied MIS as a continuous variable [40, 42, 43, 45, 46] to establish a linear relationship. Our findings indicated clearly that malnourished patients scored not just a poorer *PCS-36* summary but also for physical-related components as assessed by SF-36. Although the KDQOL-36 assessment also differentiated malnutrition status defined by the MIS category, negative associations were only limited to the *symptoms/problems* of the kidney-specific component.

In contrast, applying the ISRNM criteria to identify PEW could not differentiate HRQOL status between PEW and non-PEW patients for both SF-36 and KDQOL-36. This finding suggests that MIS, rather than PEW is an important factor associated with HRQOL in HD patients. This closely concurs with a Dutch study [43] involving 489 HD patients where HRQOL showed stronger positive associations with

Table 2 Associations of sociodemographic and clinical characteristics with SF-36 components and summary scores

| Variables | Health-Related Quality of Life Score, mean \pm SE or β (SE) | | | | | | | | | |
|-------------------------------|---|--------------------------|-----------------|-----------------------------|-------------------------------|-----------------------------|---------------------------|-----------------|-----------------------------|-----------------------------|
| | Physical functioning | Role limitation-physical | Bodily pain | General health | Vitality | Social functioning | Role limitation-emotional | Mental health | PCS-36 | MCS-36 |
| Overall score | 66.6 \pm 24.8 | 69.9 \pm 39.8 | 71.4 \pm 32.9 | 54.8 \pm 21.4 | 61.0 \pm 18.0 | 88.5 \pm 20.5 | 83.3 \pm 33.4 | 79.1 \pm 17.1 | 42.1 \pm 9.9 | 54.5 \pm 8.5 |
| Suboptimal: < 50, n (%) | 82 (21.6) | 94 (24.8) | 109 (28.8) | 144 (38.0) | 83 (21.9) | 17 (4.5) | 62 (16.4) | 29 (7.7) | 282 (74.4) | 88 (23.2) |
| Age (years) | -0.73 (0.09)* | 0.06 (0.15) | 0.05 (0.13) | -0.003 (0.08) | -0.17 (0.07)* | 0.30 (0.08)* | 0.10 (0.13) | 0.08 (0.07) | -0.14 (0.04)* | 0.12 (0.03)* |
| Gender | | | | | | | | | | |
| Females | 63.6 \pm 1.8 ^a | 66.7 \pm 3.0 | 69.3 \pm 2.4 | 54.5 \pm 1.6 | 62.0 \pm 1.3 | 87.6 \pm 1.6 | 81.6 \pm 2.6 | 77.4 \pm 1.3 | 41.2 \pm 0.7 | 54.4 \pm 0.7 |
| Males | 69.9 \pm 1.7 ^a | 73.2 \pm 2.8 | 73.6 \pm 2.4 | 55.1 \pm 1.5 | 60.0 \pm 1.3 | 89.5 \pm 1.4 | 85.1 \pm 2.3 | 80.8 \pm 1.1 | 43.1 \pm 0.7 | 54.7 \pm 0.5 |
| Ethnicity | | | | | | | | | | |
| Malay | 72.7 \pm 2.0 ^c | 69.6 \pm 3.4 | 74.1 \pm 2.7 | 56.8 \pm 1.6 | 64.7 \pm 1.4 ^c | 84.9 \pm 2.0 ^a | 84.7 \pm 2.7 | 81.7 \pm 1.2 | 43.5 \pm 0.8 | 54.7 \pm 0.7 |
| Chinese | 61.2 \pm 1.9 ^c | 70.7 \pm 3.0 | 71.9 \pm 2.5 | 51.5 \pm 1.7 ^a | 57.0 \pm 1.4 ^{b,c} | 91.4 \pm 1.3 ^a | 84.3 \pm 2.5 | 78.0 \pm 1.4 | 40.9 \pm 0.7 | 54.8 \pm 0.6 |
| Indians | 68.8 \pm 2.6 | 67.7 \pm 5.1 | 63.1 \pm 4.3 | 60.0 \pm 2.6 ^a | 64.6 \pm 2.2 ^b | 88.1 \pm 2.7 | 76.4 \pm 5.0 | 75.9 \pm 2.3 | 42.7 \pm 1.0 | 53.3 \pm 1.2 |
| Education | | | | | | | | | | |
| No formal education | 55.0 \pm 5.5 ^{a,b} | 72.0 \pm 7.8 | 66.4 \pm 6.8 | 47.2 \pm 3.9 | 58.4 \pm 4.2 | 99.0 \pm 0.7 ^a | 89.3 \pm 6.0 | 77.0 \pm 3.9 | 38.5 \pm 2.2 ^a | 57.0 \pm 1.7 |
| Primary | 57.4 \pm 2.6 ^{c,f} | 65.9 \pm 4.4 | 70.8 \pm 3.6 | 56.1 \pm 2.6 | 58.4 \pm 2.0 | 87.8 \pm 2.1 | 77.4 \pm 3.9 | 76.1 \pm 2.1 | 40.8 \pm 1.1 | 53.6 \pm 1.0 |
| Secondary | 69.7 \pm 1.8 ^{a,c} | 70.9 \pm 3.0 | 70.3 \pm 3.5 | 54.0 \pm 1.6 | 62.1 \pm 1.4 | 89.8 \pm 1.4 | 85.7 \pm 2.3 | 79.5 \pm 1.2 | 42.4 \pm 0.7 | 54.9 \pm 0.6 |
| Tertiary | 73.9 \pm 2.4 ^{b,f} | 71.4 \pm 4.2 | 75.7 \pm 3.2 | 57.1 \pm 1.9 | 62.3 \pm 1.7 | 83.6 \pm 2.9 ^a | 82.9 \pm 3.7 | 82.0 \pm 1.5 | 44.2 \pm 1.0 ^a | 53.8 \pm 0.9 |
| Monthly income | | | | | | | | | | |
| \leq RM 1000 | 64.5 \pm 1.7 ^a | 71.3 \pm 2.7 | 70.4 \pm 2.3 | 54.8 \pm 1.5 | 59.8 \pm 1.3 | 89.7 \pm 1.3 | 83.3 \pm 2.3 | 78.2 \pm 1.2 | 41.8 \pm 0.7 | 54.5 \pm 0.6 |
| > RM 1000 | 69.6 \pm 1.9 ^a | 67.9 \pm 3.2 | 72.7 \pm 2.5 | 54.8 \pm 1.6 | 62.8 \pm 1.3 | 86.9 \pm 1.7 | 83.2 \pm 2.6 | 80.1 \pm 1.3 | 42.6 \pm 0.8 | 54.5 \pm 0.7 |
| Working status | | | | | | | | | | |
| Yes | 78.8 \pm 1.9 ^c | 74.2 \pm 3.7 | 69.9 \pm 3.4 | 57.1 \pm 1.9 | 65.2 \pm 1.5 ^b | 85.4 \pm 2.4 | 83.3 \pm 3.2 | 80.9 \pm 1.4 | 44.8 \pm 1.0 ^b | 52.6 \pm 0.7 |
| No | 62.5 \pm 1.5 ^c | 68.4 \pm 2.4 | 71.9 \pm 2.0 | 54.0 \pm 1.3 | 59.6 \pm 1.1 ^b | 89.6 \pm 1.1 | 83.3 \pm 2.0 | 78.4 \pm 1.1 | 41.3 \pm 0.6 ^b | 53.7 \pm 0.5 |
| Marital status | | | | | | | | | | |
| Married | 64.2 \pm 1.5 ^c | 71.0 \pm 2.3 | 72.6 \pm 1.9 | 56.2 \pm 1.2 ^b | 60.8 \pm 1.1 | 89.6 \pm 1.1 | 84.8 \pm 1.9 | 79.7 \pm 1.0 | 42.0 \pm 0.6 | 55.1 \pm 0.6 ^b |
| Single/widow/separated | 75.4 \pm 2.2 ^c | 65.7 \pm 4.6 | 67.1 \pm 3.8 | 49.4 \pm 2.3 ^b | 61.7 \pm 1.9 | 84.4 \pm 2.5 | 77.8 \pm 4.0 | 76.8 \pm 1.7 | 42.7 \pm 1.1 | 51.7 \pm 0.9 ^b |
| Dialysis sector | | | | | | | | | | |
| Government | 69.4 \pm 2.1 | 693.3 \pm 3.7 | 73.0 \pm 2.5 | 55.7 \pm 1.8 | 63.3 \pm 1.5 | 83.6 \pm 2.1 ^b | 78.7 \pm 3.1 | 77.9 \pm 1.6 | 43.6 \pm 0.9 | 54.2 \pm 1.3 |
| Non-governmental organization | 63.6 \pm 1.6 | 71.5 \pm 2.6 | 76.4 \pm 1.8 | 54.5 \pm 1.5 | 60.4 \pm 1.2 | 91.3 \pm 1.1 ^b | 84.0 \pm 2.2 | 78.2 \pm 1.1 | 43.9 \pm 0.7 | 52.0 \pm 0.8 ^a |
| Private | 70.5 \pm 4.0 | 77.9 \pm 5.8 | 78.7 \pm 4.7 | 56.0 \pm 3.2 | 65.9 \pm 2.6 | 84.3 \pm 4.7 | 83.1 \pm 1.7 | 80.4 \pm 2.5 | 43.8 \pm 1.6 | 56.0 \pm 1.3 ^a |
| Comorbidities | | | | | | | | | | |
| Hypertension | | | | | | | | | | |

Table 2 (continued)

| Variables | Health-Related Quality of Life Score, mean \pm SE or β (SE) | | | | | | | | | |
|--------------------------|---|--|--|--|--|--------------------|--|----------------|--|----------------|
| | Physical functioning | Role limitation-physical | Bodily pain | General health | Vitality | Social functioning | Role limitation-emotional | Mental health | PCS-36 | MCS-36 |
| Yes | 66.6 \pm 1.4 | 72.4 \pm 2.3^a | 73.7 \pm 1.8^a | 55.9 \pm 1.2^a | 60.7 \pm 1.0 | 89.5 \pm 1.1 | 85.2 \pm 1.9^a | 79.0 \pm 1.0 | 42.8 \pm 0.5^a | 54.6 \pm 0.5 |
| No | 66.7 \pm 3.1 | 59.7 \pm 4.6^a | 62.2 \pm 4.1^a | 50.2 \pm 2.6^b | 62.3 \pm 2.0 | 84.6 \pm 2.8 | 75.8 \pm 4.0^a | 79.4 \pm 1.7 | 39.7 \pm 1.3^a | 54.1 \pm 1.0 |
| Diabetes mellitus | | | | | | | | | | |
| Yes | 57.8 \pm 2.0^c | 73.4 \pm 3.1 | 68.0 \pm 2.3^a | 56.7 \pm 1.7 | 58.3 \pm 1.5^a | 90.2 \pm 1.5 | 85.3 \pm 2.6 | 79.9 \pm 1.5 | 41.5 \pm 0.7 | 55.4 \pm 0.7 |
| No | 72.8 \pm 1.5^c | 67.4 \pm 2.7 | 76.2 \pm 2.5^a | 53.4 \pm 1.5 | 62.9 \pm 1.2^a | 87.3 \pm 1.5 | 81.9 \pm 2.3 | 78.4 \pm 1.1 | 42.6 \pm 0.7 | 53.8 \pm 0.6 |
| Cardiovascular disease | | | | | | | | | | |
| Yes | 57.2 \pm 3.3^b | 70.7 \pm 4.7 | 70.4 \pm 4.5 | 47.5 \pm 2.6^b | 57.3 \pm 2.7 | 90.0 \pm 2.6 | 83.3 \pm 4.3 | 79.1 \pm 2.4 | 39.4 \pm 1.2^a | 55.3 \pm 1.2 |
| No | 68.3 \pm 1.4^b | 69.7 \pm 2.3 | 71.6 \pm 1.8 | 56.1 \pm 1.2^b | 61.7 \pm 1.0 | 88.2 \pm 1.2 | 83.3 \pm 1.9 | 79.0 \pm 0.9 | 42.6 \pm 0.6^a | 54.4 \pm 0.5 |
| Dialysis vintage (years) | -0.01 (0.22) | -0.53 (0.35) | -0.92 (0.29)* | -0.53 (0.19)* | -0.06 (0.16) | 0.004 (0.18) | -0.37 (0.29) | -0.06 (0.15) | -0.22 (0.09)* | -0.01 (0.07) |
| Kr/V (per 0.1 unit) | 0.11 (0.31) | -0.16 (0.50) | -0.37 (0.41) | -0.43 (-0.27) | 0.10 (0.23) | 0.09 (0.26) | -0.66 (0.42) | -0.51 (0.21) | 0.003 (0.12) | -0.19 (0.11) |

MCS mental component summary; PCS physical component summary; SF-36 short-form 36

*Bold values indicate statistical significance with $P < 0.05$

Pairs of same superscripts ^{a,d} indicate statistical significance $P < 0.05$, ^{b,e} indicate statistical significance with $P < 0.01$, ^{e,f} indicate statistical significance with $P < 0.001$ in groups comparison

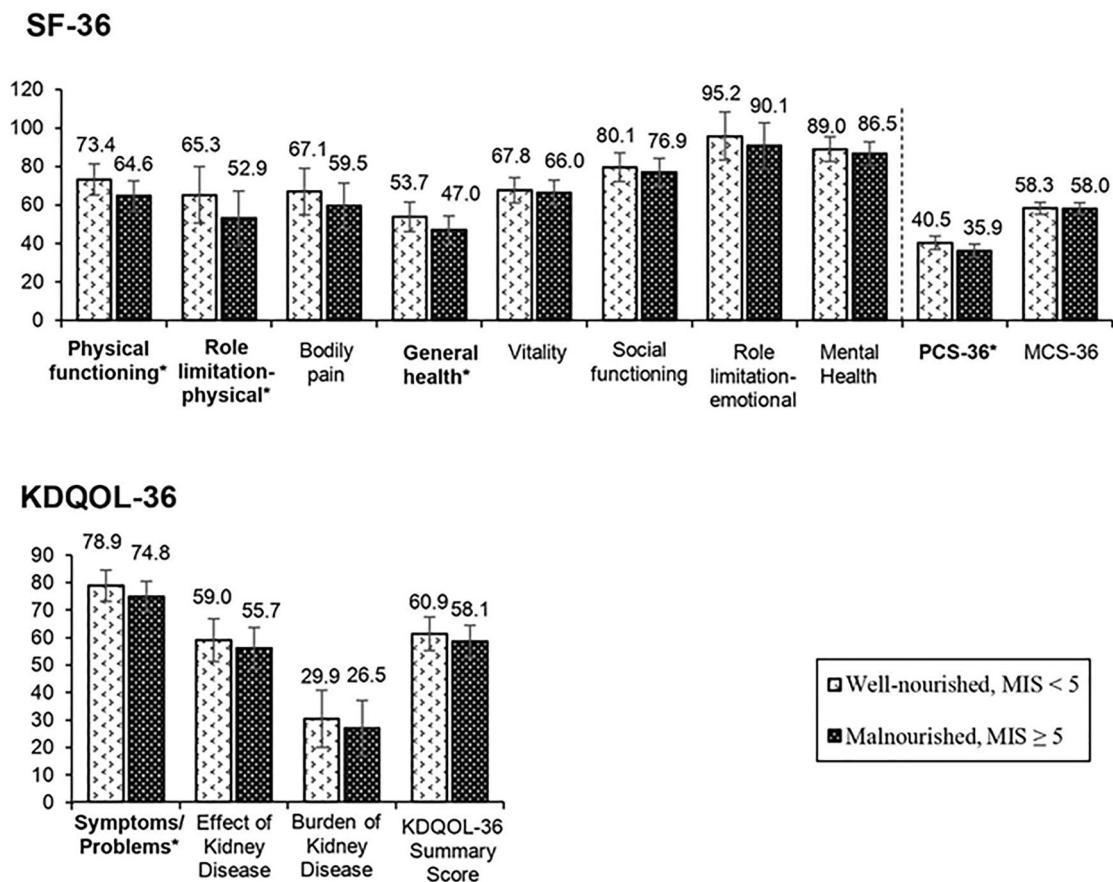
Table 3 Associations of sociodemographic and clinical characteristics with KDQOL-36 components and summary scores

| Variables | Health-Related Quality of Life Score, mean \pm SE or β (SE) | | | |
|-------------------------------|---|--|--------------------------|--|
| | Symptoms/Problems | Effect of kidney disease | Burden of kidney disease | KDQOL-36 Summary Score |
| Overall score | 84.4 \pm 15.5 | 75.4 \pm 22.3 | 44.2 \pm 28.0 | 73.8 \pm 17.0 |
| Suboptimal: <50, <i>n</i> (%) | 9 (2.4) | 53 (14.0) | 203 (53.6) | 35 (9.5) |
| Age (years) | 0.02 (0.06) | 0.52 (0.08)* | 0.12 (0.11) | 0.20 (0.06)* |
| Gender | | | | |
| Females | 82.8 \pm 1.1^a | 73.8 \pm 1.6 | 43.2 \pm 2.0 | 71.4 \pm 1.2^c |
| Males | 86.2 \pm 1.1^a | 77.1 \pm 2.3 | 45.3 \pm 2.0 | 76.3 \pm 1.2^c |
| Ethnicity | | | | |
| Malay | 84.6 \pm 1.3^a | 70.5 \pm 2.0^c | 45.2 \pm 2.4 | 71.0 \pm 1.5^b |
| Chinese | 86.2 \pm 1.0^b | 81.1 \pm 1.5^{b,c} | 45.4 \pm 2.0 | 77.7 \pm 1.1^{b,d} |
| Indians & others | 78.5 \pm 2.4^{a,b} | 69.5 \pm 3.0^b | 38.3 \pm 3.9 | 68.3 \pm 2.3^d |
| Education | | | | |
| No formal education | 81.8 \pm 3.9 | 83.9 \pm 3.5^a | 49.3 \pm 5.2 | 76.8 \pm 2.5 |
| Primary | 84.0 \pm 1.4 | 79.5 \pm 2.3^b | 44.4 \pm 2.9 | 75.5 \pm 1.6 |
| Secondary | 84.2 \pm 1.3 | 75.1 \pm 1.7 | 43.4 \pm 2.2 | 73.2 \pm 1.4 |
| Tertiary | 86.1 \pm 1.4 | 68.9 \pm 2.5^{a,b} | 44.3 \pm 3.0 | 72.2 \pm 1.8 |
| Monthly income | | | | |
| \leq RM 1000 | 84.2 \pm 1.1 | 77.8 \pm 1.4^a | 42.0 \pm 1.9 | 74.4 \pm 1.1 |
| > RM 1000 | 84.6 \pm 1.2 | 72.1 \pm 1.8^a | 47.4 \pm 2.2 | 72.9 \pm 1.4 |
| Working status | | | | |
| Yes | 85.2 \pm 1.5 | 70.2 \pm 2.3^b | 48.1 \pm 2.6 | 73.4 \pm 1.7 |
| No | 84.1 \pm 0.9 | 77.1 \pm 1.3^b | 42.9 \pm 1.7 | 73.9 \pm 1.0 |
| Marital status | | | | |
| Married | 84.8 \pm 0.9 | 76.7 \pm 1.3^a | 43.6 \pm 1.7 | 74.1 \pm 1.0 |
| Single/widow/separated | 82.9 \pm 1.7 | 70.6 \pm 2.3^a | 46.7 \pm 2.9 | 72.6 \pm 1.7 |
| Dialysis sector | | | | |
| Government | 84.1 \pm 1.3 | 72.7 \pm 2.0^a | 47.8 \pm 2.5 | 71.2 \pm 1.6 |
| Non-governmental organization | 85.4 \pm 1.0 | 79.2 \pm 1.4^{a,b} | 43.9 \pm 1.8 | 72.5 \pm 1.1 |
| Private | 80.0 \pm 2.7 | 74.2 \pm 4.0^b | 43.3 \pm 1.3 | 69.5 \pm 3.1 |
| Comorbidities | | | | |
| Hypertension | | | | |
| Yes | 84.6 \pm 0.9 | 75.8 \pm 1.3 | 44.7 \pm 1.6 | 74.0 \pm 1.0 |
| No | 83.8 \pm 1.7 | 73.6 \pm 2.5 | 42.5 \pm 3.1 | 72.8 \pm 1.8 |
| Diabetes mellitus | | | | |
| Yes | 83.8 \pm 1.3 | 77.0 \pm 1.8 | 43.8 \pm 2.4 | 73.7 \pm 1.4 |
| No | 84.8 \pm 1.0 | 74.2 \pm 1.5 | 44.6 \pm 1.8 | 73.8 \pm 1.1 |
| Cardiovascular disease | | | | |
| Yes | 83.1 \pm 2.2 | 79.5 \pm 2.5 | 45.2 \pm 3.4 | 74.9 \pm 1.9 |
| No | 84.7 \pm 0.9 | 74.6 \pm 1.3 | 44.1 \pm 1.6 | 73.6 \pm 1.0 |
| Dialysis vintage (years) | 0.23 (0.14) | 0.55 (0.19)* | 0.33 (0.25) | 0.40 (0.15)* |
| <i>Kt/V</i> (per 0.1 unit) | -0.13 (0.19) | 0.18 (0.28) | 0.16 (0.35) | 0.02 (0.21) |

KDQOL-36 kidney disease quality of life-36

*Bold values indicate statistical significance with $P < 0.05$

Pairs of same superscripts ^{a,d} indicate statistical significance with $P < 0.05$, ^{b,e} indicate statistical significance with $P < 0.01$, ^{c,f} indicate statistical significance with $P < 0.001$ in groups comparison



Abbreviations: KDQOL-36, Kidney Disease Quality of Life -36; MCS, mental components summary; MIS, Malnutrition-Inflammation Score; PCS, physical component summary; SF-36, Short-Form 36
 *Bold at category name indicate statistical significance at $P < 0.05$

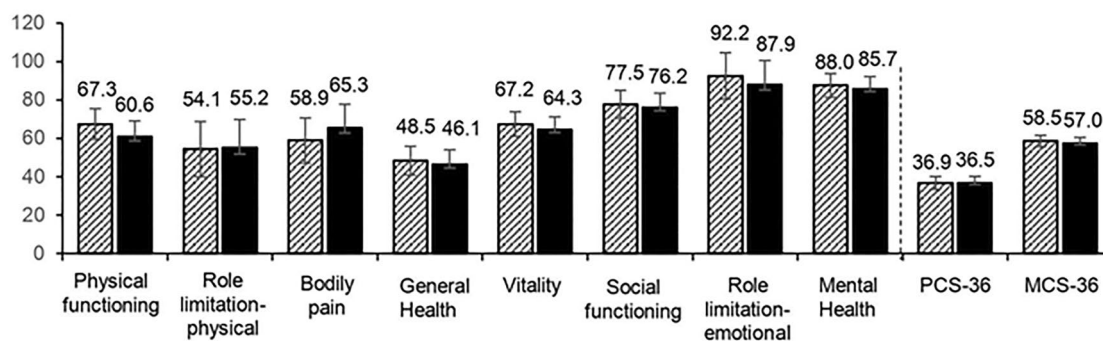
Fig. 2 Multivariate associations of MIS categorizations with SF-36 and KDQOL-36

MIS but weaker correlation for all PEW diagnostic criteria included in the analyses. MIS allows the severity of malnutrition to be accessed on a continuous scale, and it comprehensively covers physiology, body composition, weight status, biochemical markers, and comorbidities [26]. Whereas the ISRNM-PEW diagnostic criteria identify the binary status of malnutrition with either presence or absence of PEW based on three out of four criteria. Further, PEW favors the identification of only a cachexic form of malnutrition [73], possibly excluding patients with lesser severity of malnutrition (fulfilling only one or two PEW criteria) compared to MIS assessment. It must be observed that the application of PEW nutritional status on mortality outcome is inconclusive [74–77] while the MIS has been consistently shown to predict mortality in HD patients [25, 46, 78, 79].

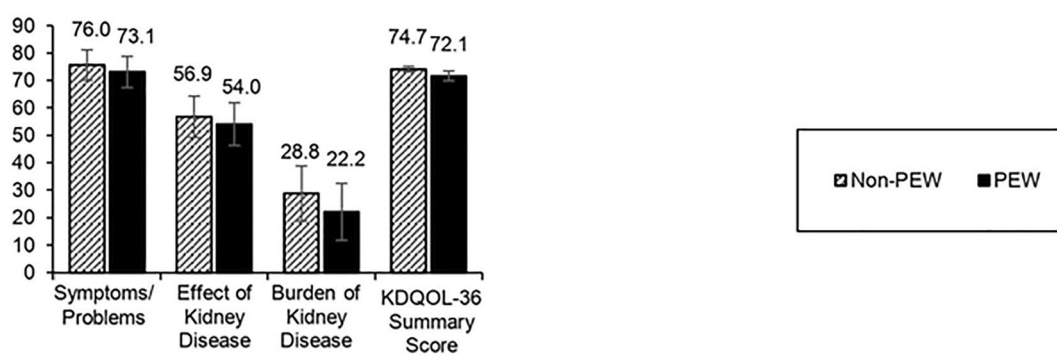
We observed a non-linear association of BMI categorizations with *physical functioning* scores being homogenous from underweight to overweight but significantly lower for obese patients. In contrast, with another study also using

multivariate models, an inverted U-shaped relationship was reported for BMI categories and *physical functioning* for a larger dialysis population ($n = 2467$) [80]. But this study used limited nutritional parameters. Excessive weight may explain reduced mobility in terms of difficulty in posture control with loss of balance, slower walking speed, chronic weight strain on weight-bearing joints, as well as joints and hip pain [81]. However, we did not observe poorer *physical functioning* of underweight patients, which may due to a smaller number ($n = 29$) of underweight patients in this study population. The paradox of obesity with poorer physical functioning was noted by us although greater survival may be mediated by this adiposity [80]. This additional fat store could be protective against the catabolism and inflammation associated with ESKD [80]. In fact, mortality was perceived as the one of core priorities by healthcare professionals, patients, and caregivers, followed by mobility as one of secondary priorities [82, 83]. Therefore, weight

SF-36



KDQOL-36



Abbreviations: KDQOL-36, Kidney Disease Quality of Life -36; MCS, mental components summary; PCS, physical component summary; PEW, protein-energy wasting; SF-36, Short-Form 36
 *Bold at category names indicate statistical significance at $P < 0.05$

Fig. 3 Multivariate associations of PEW with SF-36 and KDQOL-36

management for greater physical functioning in HD patients may be subject to clinicians' priority and justification.

As regards measurement of muscle strength, reporting HGS with continuous variables in the multivariate model positively associated only with *physical functioning* and *vitality* component scores in SF-36 but not with any component of KDQOL-36. This finding is expected as muscle strength is intuitively important for mobility. In contrast, Giglio et al. [21] showed with univariate analyses that low HGS (HGS < 30 kg for males and < 20 for females) compared to normal HGS in HD patients associated with significantly lower scores in more components and summaries of KDQOL-SF. Poor HGS has been consistently reported to associate with poor HRQOL for physical-related domains in kidney transplant recipients [84], healthy population [85–87], chronic liver disease [88], DM [89], and hospitalized patients [90]. Reduced HGS, suggested as a more sensitive indicator of muscle depletion [18], is associated with malnutrition, development of comorbidities, and a greater

risk of mortality in ESKD patients [91]. In fact, nutrition intervention with a combination of oral nutrition supplementation (ONS) and resistance exercise in HD patients has shown the greatest improvement in HGS and the number of KDQOL-SF components compared to ONS alone or with a combination of ONS and aerobic exercise [92].

The relationship of serum albumin, which is an indicator of visceral protein stores, is consistent positively with *PCS* but not *MCS* in many studies [11, 12, 35–37, 80, 93], without including inflammatory markers in their assessment models. Serum albumin is sensitive to inflammation in the uremic state [94, 95]. With our model which considered hs-CRP as an inflammatory marker, we showed that serum albumin as a biomarker of malnutrition was only positively associated with *physical functioning* but with neither *PCS* nor *MCS* as assessed by SF-36 or KDQOL-36. Specific to inflammation, we report for the first time an inverse association between log-transformed hs-CRP and *KDQOL-36 Summary Score*. This association was not observed with SF-36 components

Table 4 Multivariate associations of nutritional parameters with SF-36 components and summary scores

| Variables | Health-Related Quality of Life Score, mean ± SE or β (SE) | | | | | | | | | |
|----------------------------------|---|---------------------------------|---------------------------------|---------------------------------|--------------------------------|--------------------|---------------------------|---------------|---------------------------------|--------------|
| | Physical functioning | Role-limitation-physical | Bodily pain | General health | Vitality | Social functioning | Role limitation-emotional | Mental health | PCS-36 | MCS-36 |
| <i>Physical status</i> | | | | | | | | | | |
| BMI (kg/m ²) | | | | | | | | | | |
| < 18.5, underweight | 68.1 ± 5.4^a | 66.8 ± 10.4 | 63.4 ± 8.7 | 46.1 ± 5.7 | 68.8 ± 5.2 | 93.4 ± 5.1 | 75.3 ± 8.5 | 78.2 ± 4.6 | 40.7 ± 2.5 | 55.2 ± 2.4 |
| 18.5–24.9, normal weight | 63.8 ± 2.8^d | 65.7 ± 5.1 | 62.5 ± 4.2 | 47.9 ± 2.6 | 62.9 ± 2.5 | 89.3 ± 2.5 | 82.4 ± 4.8 | 78.5 ± 2.4 | 39.2 ± 1.3 | 55.7 ± 1.3 |
| 25.0–29.9, overweight | 64.3 ± 2.9^b | 69.0 ± 5.5 | 63.2 ± 4.9 | 50.7 ± 3.2 | 60.9 ± 2.7 | 86.6 ± 2.7 | 74.1 ± 4.5 | 80.3 ± 2.1 | 40.1 ± 1.4 | 54.2 ± 1.5 |
| ≥ 30, obese | 44.8 ± 5.5^{a,b,d} | 49.2 ± 10.6 | 63.5 ± 8.9 | 51.2 ± 5.5 | 49.5 ± 4.6 | 74.2 ± 5.6 | 67.9 ± 9.5 | 77.1 ± 4.8 | 35.7 ± 2.6 | 52.5 ± 2.1 |
| FTI (kg/m ²) | 0.14 (0.37) | 0.43 (0.79) | -0.41 (0.73) | -0.23 (0.47) | 0.74 (0.37) | 0.71 (0.42) | 0.83 (0.70) | 0.06 (0.34) | -0.06 (0.19) | 0.29 (0.16) |
| LTI (kg/m ²) | -0.04 (0.52) | -1.69 (1.10) | -1.11 (0.91) | -0.44 (0.61) | -0.22 (0.51) | 0.60 (0.54) | -0.45 (0.91) | -0.36 (0.45) | -0.35 (0.22) | 0.01 (0.23) |
| HGS (kg) | 0.36 (0.17)^c | 0.16 (0.37) | 0.18 (0.31) | 0.05 (0.17) | 0.34 (0.17)^c | 0.17 (0.16) | 0.51 (0.33) | 0.23 (0.15) | 0.08 (0.06) | 0.15 (0.07) |
| <i>Serum biochemical markers</i> | | | | | | | | | | |
| Albumin (g/L) | 0.61 (0.28)^a | 0.33 (0.54) | 0.24 (0.44) | 0.18 (0.32) | -0.03 (0.28) | -0.34 (0.27) | 0.15 (0.47) | -0.09 (0.28) | 0.22 (0.13) | -0.16 (0.13) |
| Creatinine (per 10 μmol/L) | 0.14 (0.06)^a | 0.44 (0.15) | 0.13 (0.09) | 0.02 (0.06) | -0.05 (0.07) | 0.05 (0.09) | 0.03 (0.11) | 0.07 (0.09) | 0.06 (0.03)^a | -0.06 (0.02) |
| Phosphorus (per 0.1 mmol/L) | -0.03 (0.30) | -0.75 (0.50) | -0.76 (0.40)^a | -0.50 (0.27)^a | -0.00 (0.25) | -0.14 (0.21) | -0.35 (0.39) | 0.01 (0.23) | -0.19 (0.11)^a | 0.01 (0.14) |
| Potassium (mmol/L) | 0.07 (0.28) | -0.29 (0.55) | 0.51 (0.45) | 0.05 (0.31) | -0.08 (0.24) | -0.23 (0.25) | -0.48 (0.45) | -0.03 (0.27) | 0.09 (0.12) | -0.14 (0.15) |
| In hs-CRP (per 0.1 unit) | -0.12 (0.11) | 0.06 (0.23) | -0.01 (0.15) | -0.08 (0.12) | 0.05 (0.08) | -0.17 (0.13) | -0.09 (0.14) | 0.10 (0.08) | -0.27 (0.44) | 0.09 (0.03) |
| <i>Dietary intake</i> | | | | | | | | | | |
| DEI (kcal/kg IBW/day) | 0.14 (0.33) | 0.61 (0.53) | 0.08 (0.47) | -0.18 (0.34) | 0.14 (0.26) | 0.12 (0.32) | 0.38 (0.49) | -0.04 (0.25) | 0.09 (0.15) | 0.04 (0.13) |
| DPI (per 0.1 g/kg IBW/day) | -1.18 (0.73) | -1.20 (1.37) | -0.13 (1.14) | 0.25 (0.73) | -0.12 (0.61) | -0.74 (0.70) | -0.43 (1.19) | 0.13 (0.63) | -0.29 (0.32) | 0.03 (0.29) |
| Phosphorus (per 100 mg/day) | -0.80 (0.66) | -3.51 (1.29)^a | -1.95 (1.04)^a | -0.17 (0.69) | 0.27 (0.55) | -0.39 (0.68) | -0.75 (1.01) | -0.23 (0.55) | -0.77 (0.28)^a | 0.10 (0.25) |
| Potassium (per 100 mg/day) | 0.47 (0.33) | 0.77 (0.64) | 0.36 (0.55) | -0.16 (0.32) | -0.35 (0.27) | 0.10 (0.33) | 0.25 (0.57) | 0.18 (0.25) | 0.19 (0.18) | -0.13 (0.15) |
| Sodium (per 100 mg/day) | -0.07 (0.13) | 0.08 (0.21) | 0.32 (0.20) | 0.12 (0.11) | 0.04 (0.12) | 0.02 (0.12) | 0.15 (0.17) | -0.08 (0.09) | 0.07 (0.04) | -0.02 (0.06) |
| Fluid (per 100 mL/day) | 0.78 (0.41) | -0.67 (0.79) | -0.20 (0.65) | 0.17 (0.45) | 0.29 (0.34) | -0.07 (0.39) | -0.90 (0.68) | 0.27 (0.34) | 0.09 (0.19) | -0.07 (0.18) |

Multivariate analysis adjusted for sociodemographic factors (age, gender, ethnicity, education, monthly income, working status, marital status, dialysis sector), and clinical characteristic (comorbidities, Kt/V, dialysis vintage). The highest variance inflation factor value of independent variables in the model was 4.61
BMI body mass index; *DEI* dietary energy intake; *DPI* dietary protein intake; *FTI* fat-tissue index; *HGS* handgrip strength; *hs-CRP* high sensitivity-C-reactive protein; *LTI* lean tissue index; *MCS* mental component summary; *PCS* physical component summary

*Bold values indicate statistical significance with *P* < 0.05

In multiple comparisons using Bonferroni's *Post hoc* test, pairs of same superscripts ^{a,d} indicate statistical significance with *P* < 0.05, ^{b,c} indicate statistical significance with *P* < 0.01, ^{c,f} indicate statistical significance with *P* < 0.001

Table 5 Multivariate associations of nutritional parameters with KDQOL-36 components and summary scores

| Variables | Health-Related Quality of Life Score, mean \pm SE or β (SE) | | | |
|----------------------------------|---|--------------------------|--------------------------|------------------------|
| | Symptoms/Problems | Effect of kidney disease | Burden of kidney disease | KDQOL-36 Summary Score |
| <i>Physical status</i> | | | | |
| BMI (kg/m ²) | | | | |
| < 18.5, underweight | 80.2 \pm 4.1 | 66.1 \pm 5.9 | 52.2 \pm 7.6 | 70.2 \pm 4.4 |
| 18.5–24.9, normal weight | 80.7 \pm 1.9 | 71.7 \pm 2.8 | 47.6 \pm 3.5 | 71.3 \pm 2.1 |
| 25.0–29.9, overweight | 82.3 \pm 2.1 | 78.1 \pm 3.2 | 50.1 \pm 4.3 | 75.0 \pm 2.3 |
| \geq 30, obese | 75.0 \pm 4.1 | 79.5 \pm 5.9 | 37.2 \pm 7.7 | 69.2 \pm 4.3 |
| FTI (kg/m ²) | 0.22 (0.32) | −0.50 (0.41) | 0.83 (0.57) | 0.07 (0.36) |
| LTI (kg/m ²) | −0.16 (0.45) | −0.90 (0.57) | 0.31 (0.79) | −0.45 (0.43) |
| HGS (kg) | −0.002 (0.13) | −0.01 (0.20) | −0.23 (0.26) | −0.09 (0.18) |
| <i>Serum biochemical markers</i> | | | | |
| Albumin (g/L) | −0.03 (0.20) | −0.07 (0.29) | 0.23 (0.39) | −0.10 (0.25) |
| Creatinine (per 10 μ mol/L) | 0.03 (0.07) | −0.002 (0.06) | −0.03 (0.11) | −0.001 (0.06) |
| Phosphorus (per 0.1 mmol/L) | −0.38 (0.20)* | −0.41 (0.24) | −0.25 (0.33) | −0.32 (0.21) |
| Potassium (mmol/L) | 0.22 (0.22) | −0.34 (0.27) | −0.45 (0.41) | −0.09 (0.23) |
| ln hsCRP (per 0.1 unit) | −0.15 (0.78) | −0.12 (0.11) | −0.22 (0.14) | −0.16 (0.79)* |
| <i>Dietary intake</i> | | | | |
| DEI (kcal/kg IBW/day) | −0.25 (0.23) | 0.14 (0.31) | 0.28 (0.39) | 0.06 (0.22) |
| DPI (per 0.1 g/kg IBW/day) | −0.36 (0.57) | −0.69 (0.78) | −1.27 (1.03) | −0.75 (0.60) |
| Phosphorus (per 100 mg/day) | −0.14 (0.50) | −0.32 (0.68) | 0.71 (0.89) | 0.05 (0.53) |
| Potassium (per 100 mg/day) | −0.08 (0.24) | −0.02 (0.35) | 0.32 (0.46) | 0.05 (0.28) |
| Sodium (per 100 mg/day) | 0.10 (0.10) | 0.02 (0.13) | 0.05 (0.17) | 0.09 (0.10) |
| Fluid (per 100 mL/day) | 0.28 (0.33) | 0.27 (0.42) | 0.37 (0.56) | 0.34 (0.35) |

Multivariate analysis adjusted for sociodemographic factors (age, gender, ethnicity, education, monthly income, working status, marital status, dialysis sector), and clinical characteristic (comorbidities, *Kt/V*, dialysis vintage). The highest variance inflation factor value of independent variables in the model was 4.61

BMI body mass index; *DEI* dietary energy intake; *DPI* dietary protein intake; *FTI* fat-tissue index; *HGS* handgrip strength; *hs-CRP* high sensitivity-C-reactive protein; *LTI* lean tissue index

*Bold values indicate statistical significance with $P < 0.05$

In multiple comparisons using Bonferroni's *Post hoc* test, pairs of same superscripts ^{a,d} indicate statistical significance with $P < 0.05$, ^{b,e} indicate statistical significance with $P < 0.01$, ^{c,f} indicate statistical significance with $P < 0.001$

or summaries. As regards SF-36, either no [34, 96] or negative associations of hsCRP with *PCS-36* [35, 97] and *MCS-36* [97] have been reported. Notably, inflammation mediates malnutrition, CKD-MBD, and anemia in HD patients [98], which potentially explains the greater sensitivity of disease-specific domains of KDQOL as per symptoms/problems, effects, and burden of HD treatment to associate with hsCRP, rather than the SF-36.

The detrimental effects of hyperphosphatemia in dialysis patients are soft tissue necrosis, proximal myopathy, osteoporosis, and osteomalacia [99], which explain the poor HRQOL outcomes specific to physical-related dimensions. As expected, greater serum phosphorus levels in study patients were associated with lower scores of *general health*, and *PCS-36* in SF-36, as well as *symptoms/problems* of KDQOL-36. Serum phosphorus levels > 1.78 compared to

within target of 1.13–1.78 mmol/L in 33,879 HD patients in the United States negatively associated with the SF-36 components of *bodily pain*, *general health*, *vitality*, and *mental health* [100]. However, hyperphosphatemia in dialysis is also attributed to the accumulation of phosphorus as the result of excessive dietary phosphorus intake. For the first time, our study showed that greater dietary phosphorus intake in our patients appeared to associate negatively with *role-limitation-physical* and *PCS-36*. This finding emphasizes the importance of phosphorus control for patients' towards achieving better HRQOL beyond clinical comorbidities' management.

Our study findings on obesity, serum albumin, and HGS associations with generic component scores but not with summary scores, suggest interpretations of the former are more sensitive and relevant in assessing the subtle difference

in HRQOL in relation to nutritional status. Furthermore, generic SF-36 had 12 pairs of associations with nutritional parameters in multivariate analyses which were greater than 2 pairs for KDQOL-36. This suggests that the application of SF-36 with generic components and summaries in relation to nutritional status may be more relevant than KDQOL-36 for the HRQOL assessment of dialysis patients. In the clinical context, it appears that the SF-36 is an appropriate assessment and monitoring tool to be adopted for nutritional interventions to address malnutrition in dialysis patients in line with the nutrition care process.

A limitation to consider is the cross-sectional nature of this study which does not allow inference of causal-effect relationships of nutritional parameters with HRQOL. Additionally, as this study only recruited HD patients from urban dialysis centers, findings should not be generalized to rural areas. We have used SF-36 and KDQOL-36 versions derived for the US population [101] to facilitate cross-country comparisons. We note that the standard algorithms have been widely applied to non-US HD populations [43, 101–103]. As individual nutritional parameters are affected by non-nutritional factors, these findings should be interpreted with caution and not be interpreted in isolation with single nutritional parameters.

Conclusion

Malnutrition diagnosis by MIS, but not PEW, indicated associations with HRQOL in HD patients. The multivariate model identified specific nutritional parameters that related to higher HRQOL which were BMI < 30, better dietary phosphorus control, lower inflammation, greater muscle strength and higher visceral protein pool. Future research is warranted to confirm if the SF-36 with generic components and summaries is more reflective of nutritional status than KDQOL-36 and therefore is more relevant for the HRQOL assessment of dialysis patients.

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