## RESEARCH



# Association between TMSE/MoCA and MIS/NAF in ESKD patients undergoing hemodialysis: a cross-sectional study



Taksaporn Lertritdecha<sup>1</sup>, Pichaya Tantiyavarong<sup>1,2</sup> and Aphichat Chatkrailert<sup>1,3\*</sup>

## Abstract

**Background** Both cognitive impairment and malnutrition are common in hemodialysis (HD) patients and are associated with increased hospitalization rates, infection, poor clinical outcomes, and mortality. The study investigated the association between cognitive and nutrition status among end-stage kidney disease (ESKD) patients undergoing hemodialysis.

**Methods** In this cross-sectional study, we enrolled 115 patients with ESKD who underwent regular hemodialysis (HD). Data collection included the use of screening tools for mild cognitive impairment (MCI), specifically Thai Mental State Examination (TMSE) and Montreal Cognitive Assessment (MoCA). In addition, we collected data using nutritional screening tools including Malnutrition Inflammation Score (MIS) and Nutrition Alert Form (NAF). Our primary outcome was to demonstrate whether there was a relationship between TMSE/MoCA and MIS/NAF scores in this population. Secondary outcomes were a prevalence of MCI and malnutrition status in ESKD patients, an association between TMSE and MoCA with other surrogate nutritional markers, and factors affecting MCI in such patients.

**Results** A total of 109 patients undergoing HD completed our protocol. Their mean age was 63.42 ( $\pm$  15.82) years, and 51.38% were male. Mean TMSE and MoCA were 23.98 ( $\pm$  5.06) points and 18.3 ( $\pm$  6.40) points, respectively. The prevalence of TMSE  $\leq$  23 and MoCA  $\leq$  24 were 39.45% and 83.49%, respectively. TMSE had a statistically significant negative correlation with MIS (R<sup>2</sup> = 0.16, *p* < 0.001) and NAF. MoCA also negatively correlated with MIS and NAF. The age, total educational year, the status of whether having a caregiver, serum albumin, serum phosphorus level, hand-grip strength, and lean mass tissue were correlated with TMSE.

**Conclusion** Nutritional parameters, including MIS score, NAF score, serum albumin, lean tissue mass, and lean tissue index, significantly correlate with TMSE and MoCA.

Keywords ESKD, Mild cognitive impairment, Malnutrition, MoCA, TMSE, NAF and MIS

\*Correspondence:

Aphichat Chatkrailert

tengaphi@gmail.com

<sup>1</sup> Division of Nephrology, Department of Internal Medicine, Faculty

of Medicine, Thammasat University, Pathumthani, Thailand

<sup>2</sup> Department of Clinical Epidemiology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand

<sup>3</sup> 60th Anniversary HRH Maha Chakri Sirindhorn Hemodialysis Center, Thammasat University Hospital, Pathumthani, Thailand

## Introduction

Chronic kidney disease (CKD) is one of the most common chronic diseases worldwide [1]; moreover, end-stage kidney disease (ESKD) prevalence is increasing [2]. One of the most common problems of such patients is protein-energy wasting (PEW), which is caused by plenty of factors encompassing inadequate nutrients, hormonal dysregulation, uremic toxins, systemic inflammation, metabolic acidosis, and other comorbidities. Approximately 50–70% of ESKD patients experience PEW, which



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is also associated with frailty and cachexia. These conditions contribute to high healthcare costs, as well as increased morbidity and mortality rates [3, 4]. Therefore, regarding Kidney Disease Outcomes Quality Initiative (KDOGI) guidelines, patients with CKD should be evaluated for nutritional status for PEW at least biannually by combining several tools and measurements, including dietary routine physical examination, body composition measurements, laboratory measurements, the amount of protein and calorie intake, and composite nutritional indices [5]. In order to screen malnutrition in CKD patients, various composite nutritional indices have been established as screening tools. One of the most popular and recommended worldwide is the Malnutrition Inflammation Score (MIS) [6]. In Thailand, the Nutrition Alert Form (NAF) is also encouraged to use in such patients to identify high-risk malnutrition [7]. The most essential purpose of nutritional screening is to identify high risk patients and apply an appropriate nutritional intervention to prevent miserable outcomes.

Also commonly found around 16-38% of ESKD patients [8], mild cognitive impairment (MCI) is a condition characterized by problems with cognitive function that do not significantly impair daily living activities; however, patients with MCI experience greater memory or thinking problems compared to others of the same age. MCI can impact a person's ability to make judgments, eat, and take medications properly [9]. Patients with MCI have an elevated risk of progression to dementia in a later stage [10]. Although it is a complicated process to diagnose MCI, several tests have been developed to screen MCI, including Montreal Cognitive Assessment (MoCA) [11] and Thai Mental State Examination (TMSE) [12], adapted from Mini-Mental State Examination (MMSE), and applied for screening dementia in Thailand since 1993 [13]. According to a previous study, estimated glomerular filtration rate (eGFR) decline in CKD, supported by both vascular and metabolic factors, was associated with increased cognitive decline, leading to adverse outcomes encompassing reduced functional capacity, poor quality of life and increased mortality [14]. Moreover, after the commencement of hemodialysis, cognition swiftly declines [15].

The prevalence of PEW and MCI in ESKD patients is altogether high. In addition, MCI might affect malnutrition in HD patients, and vice versa, via several mechanisms. However, only a few previous studies explored an association between cognitive status and malnutrition in CKD patients. Moreover, the data exploring the association between malnutrition and MCI among ESKD patients could be more comprehensive, especially in hemodialysis patients. This study investigated the association between cognitive and nutrition status among such populations. In addition, risk factors for cognitive impairment in ESKD receiving HD were also examined.

## Materials and methods Study Design and Setting

The study was a cross-sectional study, enrolling and collecting the data from 115 ESKD patients proceeding with regular HD between January 1, 2022, and March 31, 2022, at the 60th anniversary HRH Princess Maha Chakri Sirindhorn Dialysis Center, Thammasat University Hospital, Pathum Thani, Thailand.

#### Participants

ESKD patients aged  $\geq$  18 years, outpatient regular HD for at least three months, and capable of reading, listening, and writing Thai were included in this study after they were informed and signed consent forms. Dementia, delirium, and psychiatric patients were excluded. Disability patients, such as bilateral blindness, dysarthria, and weakness from any causes which might affect an evaluation process (such as drawing pictures or connecting dots) of MoCA or TMSE, were also excluded due to problems participating in the program.

## Variables and Data Source/Measurement

Demographic data, including sex, age, educational year, caregiver existence, comorbidities, and duration of HD, were collected. Laboratory results, encompassing complete blood count (CBC), pre-dialytic blood urea nitrogen (BUN), serum creatinine (Cr), calcium (Ca), phosphorus (P), parathyroid hormone (PTH), vitamin D (vitD), albumin, c-reactive protein (CRP), lipid profile and total iron binding capacity (TIBC), normalized protein catabolic rate (nPCR) were collected. Data involving screening tools for MCI, including TMSE and MoCA were obtained by well-trained medical scientists. In addition, well-trained nurses gathered information regarding nutritional status using anthropometric measurement and nutritional screening tools including MIS and NAF. Weight was measured by scale (SECA 674) after the HD session. Mid-arm circumference was measured by tapeline. Triceps skinfold thickness was measured by the skinfold caliper (Sequoia TrimCal400). The handgrip strength was measured by a handgrip dynamometer (CAMRY EH101) using a higher 2-time measurement value evaluated from the dominant hand. Bio-impedance analysis (BIA) results were obtained for lean tissue index, lean tissue mass, fat tissue index and fat mass by The Fresenius Body Composition Monitor (BCM) machine.

The primary outcome was to demonstrate whether there was a relationship between cognitive represented by TMSE and MoCA and nutritional status represented by MIS and NAF. Secondary outcomes were an

## **Study Size**

The sample size was calculated based on the previous data, which demonstrated that the prevalence of cognitive impairment in ESKD patients was 25% (16 – 38%); additionally, assume that the margin of error was 10% and type I error ( $\alpha$ ) as 0.05. Thus, the estimated number of ESKD patients with MCI was approximately 75. Moreover, regarding the previous study, the prevalence of malnutrition in ESKD patients was around 70% (50–75%). As a result, the sample size number was around 107.

#### Bias

The data were collected from ESKD patients on the 60th anniversary of HRH Princess Maha Chakri Sirindhorn Dialysis Center, which comprised 118 patients at recruitment. All patients in the HD centre were invited to the study to prevent selection bias.

#### TMSE/MoCA and NAF/MIS scores assessment

TMSE and MoCA have been developed for cognitive impairment screening. TMSE has six evaluation domains, including orientation, registration, attention, calculation, language, and recall, which totals 30 points. The cut-off of TMSE for high-risk MCI is  $\leq 23$  from 30. MoCA has eight evaluation domains encompassing visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. The cut-off of MoCA for high-risk MCI is  $\leq 24$  from 30; the score is plus one if people's education years are less than six years. NAF and MIS were applied for nutritional screening. Both have a total score of 30. The more scores the patient has, the higher the malnutrition risk. To assess NAF and MIS, all patients were interviewed regarding food swallowing and chewing problems, other abnormal eating symptoms (such as nausea and vomiting), the characteristics and the quantity of food content, the ability to access meals, the daily activity, underlying diseases, and current weight change history are obtained. Several investigations such as serum albumin, TIBC, and total lymphocyte count were examined. Physical examinations regarding fat storage (below eyes, triceps, or biceps) and signs of muscle wasting (such as the clavicle, scapular, or knee) were performed to determine MIS. MIS is classified into three groups: A (1-2) low risk for malnutrition, B (3–5) moderate risk for malnutrition, and C ( $\geq 6$ ) high risk for malnutrition. NAF was classified into three groups: A (0-5) normal-mild malnutrition, B (6-10) moderate malnutrition and  $C (\geq 11)$  severe malnutrition. Participants with incomplete data were rejected from the analyses.

## Ethics

The study was approved by The Human Research Ethics Committee of Thammasat University (Medicine) (MTU-EC-IM-0–096/64). All participants were informed and signed consent forms prior to the study. The study was conducted according to the Declaration of Helsinki.

## **Statistical Methods**

The STATA program version 16 was used for statistical analysis. Regarding baseline demographic data, noncontinuous data were demonstrated as frequency and percentage, normal-distributed continuous data were demonstrated as mean and standard deviation, and non-normal-distributed continuous data were demonstrated as median and interguartile range. MIS and NAF classified patients into A, B, or C and were reported as frequency and percentage. TMSE  $\leq$  23 or MoCA  $\leq$  24 patients were also reported as frequency and percentage. Regression analyses were performed to identify the relationship between TMSE/MoCA and MIS/NAF scores; additionally, TMSE/MoCA and baseline characteristics, anthropometric parameters and handgrip strength were also conducted to explore risk factors of MCI. According to non-normal distribution of TMSE and MoCA, multivariable analyses of 1/TMSE and 1/ MoCA were conducted with MIS/NAF and other variables to explore whether there were associations. Results demonstrated by the coefficient of determination with the *p*-value. The *P*-value < 0.05 was considered as statistically significant.

## Results

During the recruitment period, there were 118 ESKD patients receiving HD in the centre. One had bilateral blindness, four had dementia, and four of them had incomplete laboratory data; as a result, a total of 109 patients undergoing HD were complete data collected following protocol. Baseline characteristics of patients are shown in Table 1. Mean age was  $63.42 \pm 15.82$  years, and 51.38% were male. The mean education year was  $10.17 \pm 5.32$  years. Most of them had no caregiver. The principal underlying diseases were hypertension, hyperlipidemia, and diabetes. Mean serum albumin was  $3.78 \pm 0.34$  g/dl, and mean nPCR was  $1.11 \pm 0.30$  g/kg/day, respectively.

Table 2 shows anthropometric measurement parameters sorted by sex. The mean weight of male and female patients was  $67.22 \pm 14.59$  kg and  $57.25 \pm 13.67$ 

## Table 1 Baseline demographic of study

| Baseline characteristics                                    | Result           |
|---|------------------|
| Sex   |                  |
| Male, n (%)   | 56 (51.38%)      |
| Female, <i>n</i> (%)  | 53 (48.62%)      |
| Age, years, mean±SD   | 63.42±15.82      |
| Education year, years, mean $\pm$ SD                        | 10.17±5.32       |
| Caregiver existence   |                  |
| Yes, n (%)  | 48 (44.04%)      |
| No, n (%)   | 61 (55.96%)      |
| Comorbidity   |                  |
| Diabetes mellitus, n (%)                                    | 65 (59.63%)      |
| Hypertension, n (%)   | 101 (92.66%)     |
| Dyslipidemia, n (%)   | 90 (82.57%)      |
| Old cerebrovascular accident (CVA), n (%)                   | 15 (13.76%)      |
| Coronary arterial disease (CAD), n (%)                      | 28 (25.69%)      |
| Cancer, <i>n</i> (%)  | 5 (4.59%)        |
| Hemodialysis vintage, months, median (IQR)                  | 47 (54)          |
| Laboratory results  |                  |
| Hemoglobin (Hb), g/dl, mean ± SD                            | $10.27 \pm 1.42$ |
| Total lymphocyte count (TLC), 10 <sup>3</sup> /mcl, mean±SD | $1.30 \pm 0.46$  |
| Blood urea nitrogen, mg/dl, mean $\pm$ SD                   | 61.19±18.06      |
| Serum creatinine, mg/dl, mean $\pm$ SD                      | $9.33 \pm 2.61$  |
| Calcium, mg/dl, mean±SD                                     | $9.04 \pm 0.88$  |
| Phosphorus, mg/dl, mean ± SD                                | $4.24 \pm 1.32$  |
| Parathyroid hormone, pg/ml, median (IQR)                    | 398 (359)        |
| 25-OH Vitamin D (25-OH vit D), ng/ml, mean $\pm$ SD         | 38.73±14.43      |
| Albumin, g/dl, mean±SD                                      | $3.78 \pm 0.34$  |
| nPCR, g/kg/day, mean ± SD                                   | $1.11 \pm 0.30$  |
| C-reactive protein (CRP), mg/l, median (IQR)                | 2.2 (5.67)       |
| TIBC, mcg/dl, mean ± SD                                     | $200 \pm 36.49$  |
| Cholesterol, mg/dl, mean $\pm$ SD                           | 147.57±44.59     |
| Triglyceride, mg/dl, median (IQR)                           | 110 (72)         |
| Low density lipoprotein (LDL), mg/dl, mean $\pm$ SD         | 84.65±32.31      |

 Table 2
 Anthropometric measurement parameters assorted by sex

| Parameters   | Male<br>56 (51.38%) | Female<br>53 (48.62%) |
|--|---------------------|-----------------------|
| Weight, kg, mean±SD                                  | 67.22±14.59         | 57.25±13.67           |
| Height, cm, mean ± SD                                | $167.54 \pm 7.65$   | $155.30 \pm 4.82$     |
| BMI, kg/m <sup>2</sup> , mean $\pm$ SD               | $24.74 \pm 4.38$    | $24.53 \pm 5.46$      |
| Mid arm muscle circumference, cm, mean $\pm$ SD      | $26.12 \pm 3.06$    | 25.67±4.30            |
| Triceps skinfold thickness, cm, mean $\pm$ SD        | $12.59 \pm 6.19$    | 15.47±6.40            |
| Handgrip, kg, mean±SD                                | $19.14 \pm 8.95$    | $17.30 \pm 9.07$      |
| Lean tissue index, kg/m <sup>2</sup> , mean $\pm$ SD | $12.44 \pm 2.91$    | $10.22 \pm 2.53$      |
| Lean tissue mass, kg, mean $\pm$ SD                  | $35.06 \pm 9.02$    | $24.76 \pm 6.72$      |
| Fat tissue index, kg/m <sup>2</sup> , mean $\pm$ SD  | $11.12 \pm 4.87$    | 13.39±6.49            |
| Fat mass, kg, mean±SD                                | $23.07 \pm 10.54$   | 23.67±11.31           |

## Table 3 MIS and NAF

| Nutritional assessment | Result      |  |  |  |  |
|------------------------|-------------|--|--|--|--|
| MIS                    |             |  |  |  |  |
| A, n (%)               | 12 (11.01%) |  |  |  |  |
| B, n (%)               | 43 (39.45%) |  |  |  |  |
| C, n (%)               | 54 (49.54%) |  |  |  |  |
| NAF                    |             |  |  |  |  |
| A, n (%)               | 19 (17.43%) |  |  |  |  |
| B, n (%)               | 76 (69.72%) |  |  |  |  |
| C, n (%)               | 14 (12.84%) |  |  |  |  |

#### Table 4 TMSE and MoCA

| Cognitive test             | Result         |  |  |
|----------------------------|----------------|--|--|
| TMSE, point, mean ± SD     | 24.0±5.1       |  |  |
| TMSE≤23, n (%)             | 43 (39.45%)    |  |  |
| MoCA, point, mean $\pm$ SD | $18.3 \pm 6.4$ |  |  |
| MoCA≤24, n (%)             | 91 (83.49%)    |  |  |

kg. Males had higher anthropometric parameter values, except for triceps skinfold thickness, fat tissue index, and fat mass.

Patients were assessed nutritional status by applying MIS and NAF and classified into three groups. Regarding MIS, the prevalence of MIS groups A, B, and C were 11.01%, 39.45%, and 49.54%, respectively. By using NAF, NAF A, B, and C were 17.43%, 69.72%, and 12.84%, orderly (Table 3).

TMSE and MoCA data were collected for cognitive testing in the study. Mean TMSE and MoCA were  $23.98 \pm 5.06$  points and  $18.3 \pm 6.40$  points, respectively. The prevalence of TMSE  $\leq 23$  and MoCA  $\leq 24$  were 39.45% and 83.49%, respectively (Table 4).

TMSE had a statistically significant negative correlation with MIS ( $R^2=0.16$ , p<0.001) (Fig. 1: The Relationship between TMSE and MIS) and NAF ( $R^2=0.06$ , p=0.013) (Fig. 2: The Relationship between TMSE and NAF). In addition, MoCA negatively correlated with MIS ( $R^2=0.18$ , p<0.001) (Fig. 3: The Relationship between MoCA and MIS) and NAF ( $R^2=0.08$ , p=0.003) (Fig. 4: The Relationship between MoCA and NAF) as well.

Male sex, age, total educational year, status of whether having a caregiver, serum albumin, serum phosphorus level, serum creatinine and TIBC were significantly related to both TMSE and MoCA (Table 5). Regarding anthropometric parameters, lean mass tissue and index were significantly associated with TMSE and MoCA. Handgrip strength also tended to correlate with TMSE and MoCA (Table 6).

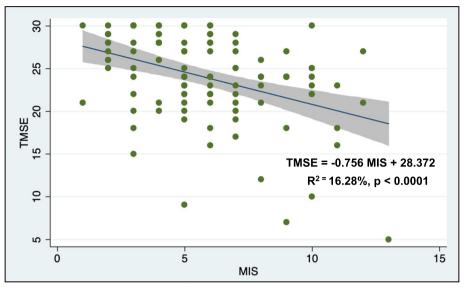


Fig. 1 The Relationship between TMSE and MIS

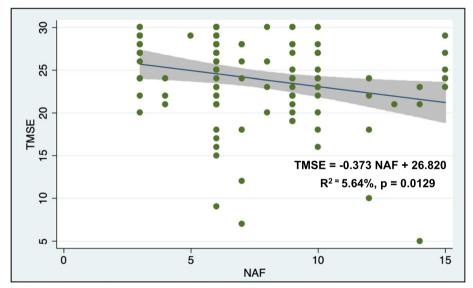


Fig. 2 The Relationship between TMSE and NAF

Multivariable analyses (Table 7) showed a significant association between MIS and cognitive function, measured by TMSE and MoCA, even after adjusting for various variables. The unadjusted MIS positively correlated with 1/TMSE (P<0.001) and 1/MoCA (P<0.001). Adjustments for age, education, and caregiver existence slightly reduced the strength of this association but remained significant for most models. In the fully adjusted model, the correlation between MIS and 1/TMSE was marginal (P=0.063), while the correlation with 1/MoCA remained significant (P=0.022). These findings emphasize the

strong link between malnutrition and cognitive impairment in hemodialysis patients.

## Discussion

This study is one of the first to investigate the association between the cognitive demonstrated by TMSE/MoCA and nutritional status represented by MIS/NAF among ESKD patients undergoing HD. Moreover, anthropometric parameters were also assessed to determine whether there was a relationship between such parameters and TMSE/MoCA representing MCI. The prevalence of

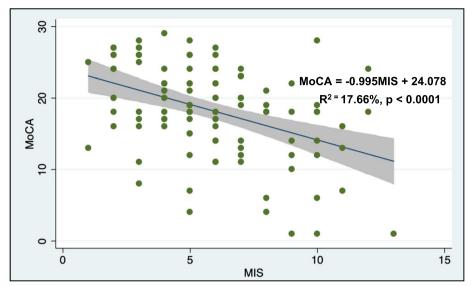


Fig. 3 The Relationship between MoCA and MIS

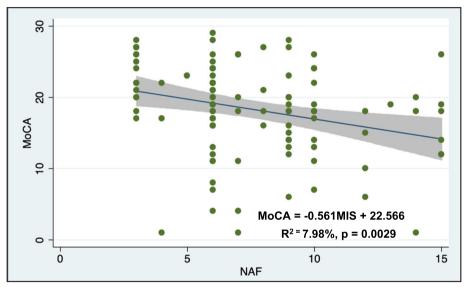


Fig. 4 The Relationship between MoCA and NAF

TMSE  $\leq$  23 and MoCA  $\leq$  24 were found to be 39.45% and 83.49%, respectively, which were relatively high; however, clinical symptoms were required for MCI and dementia diagnosis by neurologist evaluations and cognitive tests for diagnosis. In addition, it was also found that 49.54% of patients were MIS C and 82.56% were NAF B and C, which reflected malnutrition status in such patients and may require intervention. Regarding our population, it might be implied that malnutrition and MCI are generally common in ESKD patients. According to our population, elderly age, high MIS score, high NAF score, male sex, low total educational year, lack of a caregiver, low serum albumin, low serum phosphorus, low serum creatinine, and low TIBC were associated with low TMSE/ MoCA score. Poor lean tissue mass, index, and handgrip strength also increased cognitive impairment risk. Furthermore, the multivariable analyses, which aimed to account for other significant factors, showed a robust link between malnutrition in ESKD and MCI. This finding underscores the importance of nutritional management for ESKD patients to improve their quality of life. Additionally, regular nutritional screenings are vigorously

| Variables                  | TMSE        |                |         | MoCA        |                |         |
|----------------------------|-------------|----------------|---------|-------------|----------------|---------|
|                            | Coefficient | 95% CI         | P-value | Coefficient | 95% CI         | P-value |
| Male sex                   | 2.13        | 0.24 - 4.02    | 0.027   | 2.46        | 0.07—4.86      | 0.044   |
| Age (years)                | -0.20       | -0.25          | < 0.001 | -0.20       | -0.250.15      | < 0.001 |
| Educational year (years)   | 0.52        | 0.37 – 0.68    | < 0.001 | 0.72        | 0.54 - 0.90    | < 0.001 |
| Existence of caregiver     | -4.40       | -6.15          | < 0.001 | -7.31       | -9.34          | < 0.001 |
| Comorbidity                |             |                |         |             |                |         |
| Diabetes                   | -0.75       | -2.72 - 1.21   | 0.448   | -2.08       | -4.54 - 0.37   | 0.095   |
| Hypertension               | -2.18       | -5.86 - 1.50   | 0.243   | -1.43       | -6.10 - 3.24   | 0.546   |
| Dyslipidemia               | -2.38       | -4.89 - 0.12   | 0.062   | -3.65       | -6.79—-0.51    | 0.023   |
| Old CVA                    | -2.53       | -5.29 - 0.23   | 0.072   | -3.52       | -7.00 - 0.43   | 0.047   |
| CAD                        | -0.12       | -2.33 - 2.09   | 0.915   | -0.65       | -3.44 - 2.14   | 0.646   |
| Cancer                     | 0.19        | -4.60 - 4.64   | 0.993   | -4.93       | -10.68 - 0.83  | 0.092   |
| Laboratory Investigation   |             |                |         |             |                |         |
| Hb (g/dl)                  | 0.21        | -0.66 - 0.71   | 0.950   | 0.09        | -0.78 - 0.95   | 0.845   |
| TLC (10 <sup>3</sup> /mcl) | 0.60        | -1.53 - 2.72   | 0.580   | 1.53        | -1.14 - 4.20   | 0.257   |
| BUN (mg/dl)                | 0.04        | -0.01 - 0.10   | 0.117   | 0.05        | -0.02 - 0.12   | 0.145   |
| Cr (mg/dl)                 | 0.83        | 0.49 - 1.17    | < 0.001 | 1.13        | 0.71 – 1.55    | < 0.001 |
| Ca (mg/dl)                 | -0.81       | -1.91 - 0.28   | 0.144   | -0.38       | -1.77 - 1.02   | 0.592   |
| P (mg/dl)                  | 1.29        | 0.60 – 1.99    | < 0.001 | 1.82        | 0.96 – 2.68    | < 0.001 |
| PTH (pg/ml)                | 0.001       | -0.002 - 0.004 | 0.458   | 0.002       | -0.002 - 0.005 | 0.406   |
| 25-OH vitD (ng/ml)         | 0.01        | -0.06 - 0.07   | 0.852   | 0.05        | -0.04 - 0.13   | 0.263   |
| Albumin (g/dl)             | 4.00        | 1.27 – 6.71    | 0.004   | 7.17        | 3.87 – 10.47   | < 0.001 |
| nPCR (g/kg/day)            | 2.92        | -0.30 - 6.14   | 0.075   | 3.33        | -0.75 - 7.40   | 0.109   |
| CRP (mg/l)                 | 0.002       | -0.042 - 0.047 | 0.921   | -0.016      | -0.072 - 0.040 | 0.563   |
| TIBC (mcg/dl)              | 0.03        | 0.01 - 0.06    | 0.017   | 0.05        | 0.02 - 0.08    | 0.003   |
| Cholesterol (mg/dl)        | -0.01       | -0.03 - 0.02   | 0.609   | -0.01       | -0.03 - 0.02   | 0.617   |
| Triglyceride (mg/dl)       | 0.002       | -0.010 - 0.013 | 0.790   | 0.002       | -0.013 - 0.017 | 0.786   |
| LDL (mg/dl)                | <-0.001     | -0.030 - 0.030 | 0.988   | 0.004       | -0.042 - 0.034 | 0.835   |

| Table 5 | Regression | analyses | of baseline | characteristic | and TMSE and MoCA |
|---------|------------|----------|-------------|----------------|-------------------|
|         |            |          |             |                |                   |

recommended to abstain unfavorable outcomes for these patients.

In terms of cognitive impairment in CKD patients, there are both non-CKD-related and CKD-related factors. Generally, non-CKD-related risk factors for cognitive impairment include diabetes, hypertension, and dyslipidemia. On the other hand, CKD-related risk factors encompass uremic toxins causing inflammation, hemodialysis-related factors such as intradialytic hypotension, and other underlying conditions [16]. According to previous studies, various factors, including age, low educational year, underlying diseases (cardiovascular and cerebrovascular disease, anaemia, and depression) [14], and hemodialysis-related risks (poor hemodialysis adequacy and unstable hemodynamic status), were associated with cognitive impairment. Compared to various studies, this study demonstrated that some risk factors, including age and low educational year, correlate with cognitive impairment [17]. Additionally, this study confirmed the close relationship between malnutrition and cognitive impairment by showing that low serum albumin, low serum phosphorus, low serum creatinine, low TIBC, low lean tissue mass, low lean tissue index, and poor handgrip strength performance were significantly associated with low TMSE/MoCA score. Several previous studies also explored the correlation between malnutrition and cognitive status in advanced CKD and ESKD patients. Regarding HD patients, a cross-sectional study from a dialysis centre in north-eastern Romania showed that malnutrition scores (Subjective Global Assessment; SGA and Mini Nutritional Assessment; MNA) correlated to cognitive impairment (MMSE) in HD patients [18]. Another study from Croatia also found that HD patients with poorer Dialysis Malnutrition Scores (DMS) performed worse on cognitive tests assessed by Trail Making Test (TMT) A and Symbol Digit Mortalities Test (SDMT) [19]. Moreover, the study in Italy also explored the association between MoCA and MIS in HD patients [20].

Malnutrition, common in HD patients, occurs due to various determinants encompassing chronic

| Variables        | TMSE        |               |         | MoCA        |              |         |
|------------------|-------------|---------------|---------|-------------|--------------|---------|
|                  | Coefficient | 95% CI        | P-value | Coefficient | 95% CI       | P-value |
| Weight           |             |               |         |             |              |         |
| Male             | 0.05        | -0.03 - 0.12  | 0.236   | 0.07        | 0.02 - 0.17  | 0.114   |
| Female           | 0.11        | <-0.01 - 0.23 | 0.052   | 0.13        | -0.16 - 0.27 | 0.079   |
| Height           |             |               |         |             |              |         |
| Male             | 0.16        | 0.02 - 0.30   | 0.022   | 0.16        | -0.02 - 0.33 | 0.081   |
| Female           | 0.27        | -0.06 - 0.60  | 0.103   | 0.45        | 0.04 - 0.86  | 0.032   |
| BMI              |             |               |         |             |              |         |
| Male             | 0.04        | -0.21 - 0.30  | 0.733   | 0.18        | -0.13 - 0.50 | 0.255   |
| Female           | 0.23        | -0.05 - 0.52  | 0.110   | 0.23        | -0.14 - 0.61 | 0.212   |
| Mid arm Circum   | ference     |               |         |             |              |         |
| Male             | 0.14        | -0.22 - 0.50  | 0.451   | 0.20        | -0.25 - 0.65 | 0.381   |
| Female           | 0.18        | -0.13 - 0.50  | 0.255   | 0.54        | 0.08 - 0.99  | 0.022   |
| Triceps skinfold | thickness   |               |         |             |              |         |
| Male             | 0.05        | -0.13 - 0.23  | 0.593   | 0.08        | -0.14 - 0.30 | 0.473   |
| Female           | 0.35        | 0.12 – 0.58   | 0.004   | 0.39        | 0.09 - 0.69  | 0.013   |
| Handgrip         |             |               |         |             |              |         |
| Male             | 0.14        | 0.20 – 0.26   | 0.023   | 0.13        | -0.02 - 0.28 | 0.087   |
| Female           | 0.25        | 0.09 - 0.41   | 0.003   | 0.38        | 0.18 – 0.58  | < 0.001 |
| Lean tissue inde | х           |               |         |             |              |         |
| Male             | 0.66        | 0.32 - 1.00   | < 0,001 | 0.93        | 0.52 – 1.34  | < 0.001 |
| Female           | 0.71        | 0.10 - 1.31   | 0.023   | 0.94        | 0.17 – 1.71  | 0.018   |
| Lean tissue mas  | S           |               |         |             |              |         |
| Male             | 0.23        | 0.13 – 0.34   | < 0.001 | 0.31        | 0.18 - 0.44  | < 0.001 |
| Female           | 0.30        | 0.07 – 0.52   | 0.011   | 0.40        | 0.12 - 0.69  | 0.007   |
| Fat tissue index |             |               |         |             |              |         |
| Male             | -0.17       | -0.40 - 0.50  | 0.127   | -0.16       | -0.44 - 0.12 | 0.270   |
| Female           | 0.08        | -0.17 - 0.33  | 0.513   | 0.05        | -0.27 - 0.37 | 0.749   |
| Fat mass         |             |               |         |             |              |         |
| Male             | -0.05       | -0.16 - 0.52  | 0.322   | -0.05       | -0.18 - 0.09 | 0.479   |
| Female           | 0.06        | -0.08 - 0.20  | 0.405   | 0.06        | -0.13 - 0.24 | 0.546   |

 Table 7
 Multivariable analyses of TMSE and MOCA with MIS adjusted by various variables

| MIS            | 1/TMSE      |                  |         | 1/MOCA      |                 |                 |
|----------------|-------------|------------------|---------|-------------|-----------------|-----------------|
|                | Coefficient | 95% CI           | P-value | Coefficient | 95% CI          | <i>P</i> -value |
| Unadjusted MIS | 0.0029      | 0.0015—0.0043    | < 0.001 | 0.0204      | 0.0099 – 0.0309 | < 0.001         |
| Model 1        | 0.0015      | 0.00003 -0.0030  | 0.046   | 0.0144      | 0.0027 - 0.0260 | 0.016           |
| Model 2        | 0.0022      | 0.0008 -0.0036   | 0.003   | 0.0169      | 0.0060 - 0.0278 | 0.003           |
| Model 3        | 0.0023      | 0.0009 - 0.0038  | 0.002   | 0.0169      | 0.0060 - 0.0278 | 0.003           |
| Model 4        | 0.0014      | -0.0001 - 0.0029 | 0.063   | 0.0137      | 0.0020 - 0.0254 | 0.022           |

Model 1: MIS adjusted by age, Model 2: MIS adjusted by academic year, Model 3: MIS adjusted by an existence of caregiver, and Model 4: MIS adjusted by age, academic year, and an existence of caregiver

inflammation, acidosis, hypercatabolic state and loss of nutrients via dialysis. Risk factors include age, hemodialysis duration, socioeconomic status, comorbidity, and educational level [21]. Compared to cognitive impairment in ESKD, malnutrition in ESKD has several similar risk factors. Thus, this is the reason that our study demonstrated a strong correlation between these two conditions. In addition, one of the unique pathophysiology of dementia in ESKD includes vascular disease and vascular abnormality [14, 17] such as vascular calcification, a significant component of metabolic bone disease in CKD (MBD-CKD), which takes place due to plenty of reasons; for example, uremic toxin causing systemic inflammation, positive calcium balance from dialysate calcium and oral calcium as phosphate binders, secondary hyperparathyroidism, and inadequate hemodialysis [22, 23]. It is widely accepted that malnutrition inflammation in CKD and ESKD patients also increases atherosclerosis and adverse premature cardiovascular outcomes; thus, malnutrition in ESKD would lead to atherosclerosis [24-27] which is also responsible for vascular calcification, and cognitive impairment. Therefore, it is reasonable to recognize malnutrition in HD patients and improve their nutritional status to not only alleviate MCI and dementia, but also improve quality of life and decrease morbidity and mortality in such patients [8]. According to the study results, we should pay attention to patients with risk factors such as elderly age, low educational year, and non-existence of a caregiver. Several combined nutritional assessments such as NAF and MIS scores using simple questions and available laboratory investigation are helpful and easy to apply to screen malnutritional status. Furthermore, BIA, an adaptable machine conducted to explore body components, combined with another functional capacity assessment such as hand grip strength, are also beneficial for exploring malnutrition, which leads to cognitive impairment and dementia in such patients.

Although vivid and exciting study results, some limitations of the study should also be acknowledged. Firstly, this is a cross-sectional study with mixed populations that could not directly determine the cause-and-effect relationship between malnutrition and cognitive impairment. Instead, the study was only able to inform the relationship between both issues. To ensure the results, a longitudinal cohort study for further testing should be conducted. Secondly, some patients were prescribed nutrient supplements before or during the study, which made their MIS and NAF scores better than they should have been. In addition, the diagnosis of MCI or dementia in the study protocol was not definite, according to no confirmation by a neurologist. Although TMSE or MoCA are helpful screening tools, it was not adequate for diagnosing both dementia and MCI. Also, this study applied NAF and TMSE, which were widely used in the Thai population; however, applying such methods might be rare in other settings. Finally, both TMSE and MoCA comprise several domains; however, we analyzed and considered the data as a total score and did not analyze each domain to other variables.

## Conclusion

Nutritional parameters, including MIS score, NAF score, serum albumin, lean tissue mass, and lean tissue index, significantly correlate with TMSE and MoCA.

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#### Authors' contributions

All authors contributed to the work, as well as reading and approving the final manuscript. TL was responsible for data acquisition, asking for informed consent, drafting of work, and writing manuscript. PT was responsible for the design of the study, drafting of work, data interpretation and statistical analysis. AC was responsible for design of the study, drafting of work, data interpretation, statistical analysis, writing manuscript, and primary corresponding author.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Data availability

No datasets were generated or analysed during the current study.

#### Declarations

#### Ethics approval and consent to participate

Ethics approval by The Human Research Ethics Committee of Thammasat University (Medicine) (MTU-EC-IM-0–096/64) was obtained before the commencement of data collection. All participants either signed or put a thumbprint on an informed consent form to support their verbal consent before they were interviewed.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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