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Original Article

Bioelectrical impedance analysis-derived phase angle as a pragmatic screening tool for assessing sarcopenia in multi-ethnic peritoneal dialysis patients

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SUMMARY

Objective: Sarcopenia, characterized by the loss of muscle mass and function, is prevalent in peritoneal dialysis (PD) patients. Early diagnosis is crucial, but universal screening is often hindered by the complexity of diagnostic algorithms and limited clinical resources. Therefore, this study aims to investigate the ability of bioelectrical impedance analysis-derived phase angle (PhA), a convenient and cost-effective technique, in detecting sarcopenia among PD patients.

Methods: A single-center cross-sectional study was conducted on 130 multi-ethnic PD patients in Malaysia. Sarcopenia was assessed using Asian Working Group for Sarcopenia (AWGS) 2019 diagnostic algorithm. PhA was measured by a multi-frequency bioelectrical impedance analysis device at 50kHz. Multivariable logistic regression was used to determine predictability of PhA on sarcopenia. Receiver operating characteristics analysis was used to evaluate the discriminative performance of PhA in detecting sarcopenia. Optimal gender-specific PhA cut-off values for sarcopenia

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detection were determined based on desired sensitivity and specificity.

Results: Sarcopenia was identified in 25.4% of the PD patients. PhA emerged as an independent predictor of sarcopenia (adjOR= 0.147; 95%CI =0.042–0.516; P =0.003), exhibiting excellent discriminative power in identifying sarcopenia (adjAUC$_{overall}$= 0.818±0.041; bootstrapped 95%CI =0.734–0.899, P *<0.001*). The optimal PhA cut-off values for sarcopenia detection were ≤4.05° (92.9% sensitivity and 53.8% specificity) and ≤3.75° (78.9% sensitivity and 51.1% specificity) for male and female patients, respectively.

Conclusion: PhA serves as a pragmatic screening tool for identifying multi-ethnic Malaysian PD patients at risk of sarcopenia, facilitating early diagnosis and intervention to improve patient outcomes.

Introduction

Sarcopenia is a progressive and generalized musculoskeletal disorder, characterized by the gradual loss of skeletal muscle mass, strength and functionality. [1] Since the introduction of International Classification of Disease, Tenth Revision, Clinical Modification (ICD-10-CM) Code, sarcopenia has gained recognition as a distinct medical condition necessitating prompt diagnosis and timely intervention. [2] It is pervasive in patients undergoing peritoneal dialysis (PD) due to a multiplicity of factors, including chronic inflammation, hormone derangement, dialysate nutrient loss, and nutrition insufficiency resulting from dietary restriction and anorexia. [3] Sarcopenia leads to extensive negative consequences, including depression, reduced functionality, lower quality of life, increased hospitalization, morbidity, mortality, and escalated healthcare costs due to a loss of autonomy and frequent hospitalization. [3,4].

Early identification and intervention are imperative to mitigate these effects. [5] However, the detection of sarcopenia can be challenging, as its manifestation is not always discernible from physical appearance or laboratory findings, potentially leading to underdiagnosis by clinicians. [6] While the Asian Working Group for Sarcopenia (AWGS) 2019 Consensus provides a diagnostic protocol for sarcopenia in Asians, its practicality is constrained by the complexity of its diagnostic algorithm and the requirement for additional manpower, equipment and set-up. With the growing adoption of PD-preferred policy in many countries, [7] the need for a convenient and cost-effective marker for sarcopenia detection becomes particularly important, especially for healthcare centers with limited resources for universal screening.

Bioelectrical impedance analysis (BIA) is a non-invasive and reliable technology for body composition assessment. A key BIA parameter, phase angle (PhA), calculated as the arctangent of the ratio of capacitive reactance to resistance at 50 kHz, has gained attention as a prognostic indicator for nutritional status and clinical outcomes. [8,9] PhA is independent of empirical equations and constant hydration status assumption, making it more accurate than other BIA parameters. [9] PhA provides valuable insights into cellular mass, function, and integrity, rendering it a useful surrogate for muscle mass and strength. [10] Notably, the European Working Group on Sarcopenia in Older People (EWGSOP) Consensus has identified PhA as a potential marker for sarcopenia, with implications for future intervention strategies. [5].

While there is a growing body of evidence supporting PhA as a sarcopenia indicator in diverse populations, [11] its validation in PD patients is limited and outdated. Employing contemporary consensus diagnostic criteria for accurate sarcopenia detection is crucial. [12] However, existing evidence from PD populations relies on incomplete diagnostic criteria and is based on the older version of

the diagnostic algorithm for sarcopenia diagnosis. [13,14] Additionally, there is a lack of evidence from Southeast Asian countries, characterized by diverse ethnicities. Malaysia, in particular, possesses a unique ethnic composition and lifestyle patterns that may influence the performance of PhA in assessing muscle mass and function. [8,15,16] To address these research gaps, our study aims to investigate the diagnostic performance of PhA as a pragmatic biomarker for detecting sarcopenia and to establish an optimal PhA cut-off value specifically tailored to multi-ethnic Malaysian PD patients.

Methods

Study design and subject recruitment

This cross-sectional study was conducted between January and April 2022, in the PD clinic of a tertiary government hospital in the Klang Valley, Malaysia. Adult Malaysian outpatients who have been undergoing regular PD treatment for at least 6 months were consecutively recruited. Patients with communication barriers, contraindications for BIA, Parkinson's Disease, stroke, limb amputation, arthritis, acquired immunodeficiency syndrome (AIDS), malignancy, and history of peritonitis, infections, trauma or surgical procedure in past 3 months were excluded.

Sample size was calculated using MedCalc version 19.2.0 (MedCalc Software Ltd, Ostend, Belgium) statistical software for area under receiver operating characteristic (ROC) curve, with alpha level of 0.05, beta level of 0.2, area under ROC curve of 0.7, and negative/positive group ratio of 4.62 based on weighted rate of previous studies. The calculated sample size after accounting for 20% non-response rate was 142 subjects (supplementary document 1). The research activities were explained to subjects and written consent was obtained prior data collection. All research procedures were performed in accordance with the World Medical Association Declaration of Helsinki. This study was approved by Ethics Committee of the National Medical Research Register (NMRR-21-790-59396).

Sociodemographic, clinical and biochemical data

Sociodemographic data (i.e., age, gender ethnicity, marital status, education background, employment status and monthly household income) were gathered through face-to-face interviews, whereas clinical data (i.e., history of dialysis modality, dialysis vintage, presence of comorbidity and dialysis adequacy) and biochemical data (i.e., renal function test, liver function test, lipid profile and full blood count) were retrieved from latest electronic-based medical records (i.e., within 1 month).

Anthropometry measurement

Body weight, height, mid-arm circumference (MAC) and calf circumference (CC) were measured in accordance with International Society of Advancement in Kinanthropometry (ISAK) protocol. Subjects were measured for their height using a portable stadiometer (Model 213, Seca, Hamburg, Germany) and for their weight using a digital weighing scale (Model HD-319, Tanita, Tokyo, Japan) in light clothing. MAC and CC were measured using a non-stretchable Lufkin® metal measuring tape (Apex Tool Group, LLC, NC, USA), on the right side of the body. Every measurement was made twice, with the mean value being recorded.

Body composition analysis

BIA measurement was performed using a portable direct segmental multifrequency (1–1000kHz) BIA machine (Inbody S10, InBody Co., Ltd, Seoul, Korea), which complies with the AWGS 2019 recommendation. [1] BIA measurements were performed in lying position using tetrapolar 8-points touch-type electrodes attached to corresponding body parts as per the manufacturer's measurement protocol. [17] For subjects with dialysate-instilled during the BIA measurement, the weight of instilled dialysate was deducted from the measured weight, in order to reflect subjects' actual body weight. This

approach has been validated in our previous study, where it effectively minimized dialysate-induced bias in BIA measurements. [18] Specifically, this approach did not introduce statistically or clinically significant measurement bias in the parameters under investigation in the current study, namely PhA and appendicular skeletal muscle mass index (ASMI).

PhA was measured at a frequency of 50 kHz. ASMI, expressed in kg/m^2, was calculated as appendicular muscle mass divided by squared height. [19] Other BIA-derived measurements reported in this study included body fat percentage (BFP), skeletal muscle mass (SMM) and extracellular water/total body water (ECW/TBW) ratio.

Muscle strength assessment

Muscle strength was evaluated using handgrip strength (HGS) measured with Jamar Plus Digital hand dynamometer (Paterson Medical, Green Bay, WI, USA), following the protocol recommended by AWGS 2019. HGS was assessed on the dominant arm of subjects while in a seated position with a 90° elbow flexion. Three measurements of HGS were taken, and the highest value was recorded.

Physical performance assessment

Physical performance was assessed by the five-time chair stand test (5TCST). Subjects were instructed to fold their arms across their chest and perform sit-to-stand movements for five times at their fastest speed, on a chair with a straight back and seat height of 43cm. Demonstration was provided by the researcher prior to the test. The test was conducted twice with a five-minute interval, and the average reading was recorded. [1,20] For safety reasons, subjects who were physically unable to complete the 5TCST were not compelled to continue; instead, their incapacity to finish the test was considered indicative of test failure.

Sarcopenia diagnosis

Sarcopenia diagnosis was determined based on AWGS 2019 consensus. Subjects exhibiting low muscle mass, along with low muscle strength and/or low physical performance, were classified as sarcopenia. Specifically, (a) low muscle mass was defined as ASMI <7.0kg/m^2 for male and <5.7kg/m^2 for female; (b) low muscle strength was defined as HGS <28kg for male and <18kg for female; (c) low physical performance was defined as completion time of 5TCST $\geq$12 seconds.

Statistical analysis

The data processing and statistical analysis were conducted using Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM, Chicago, IL, USA) and R statistical computing software version 4.2.2 (R Core Team 2022). A significance threshold of *P*-value <0.05 was applied for all analyses. The association between variables and sarcopenia was evaluated using independent t-test, Chi-square test and Mann-Whitney test (for skewed continuous data). The predictive power of PhA in sarcopenia identification was determined via multivariable logistic regression analysis after adjusting for patients' characteristics. Sarcopenia diagnostic criteria were dichotomized based on the cut-off suggested by AWGS 2019. Subjects with outliers (n=4) were excluded from analysis and dialysis vintage data was logit-transformed to fulfill the requirements of logistic regression.

The discriminative performance of PhA in detecting sarcopenia among PD patients was examined using receiver operating characteristic (ROC) curve analysis with the “ROCR” package in R software. Covariates were adjusted to prevent their contribution to discrimination performance. [21] Internal validation for robustness check was performed using bootstrapping with 1000 resamples through the “fbroc” package in R software. Data visualization was accomplished using the “ggplot2” package in R software. The discriminative power of PhA was evaluated based on the area under the curve (AUC), where an AUC between 0.7 and <0.8 was considered acceptable, between 0.8 and <0.9 was excellent and $\geq$0.9 was outstanding. [22] The optimal PhA cut-off value for sarcopenia identification was

determined based on ideal sensitivity and specificity in unadjusted ROC model. Sensitivity was prioritized over specificity in this study to minimize false negative cases.

Results

Subjects' recruitment

Out of the initial pool of 317 PD patients, 222 met the study's eligibility criteria. Employing a consecutive sampling method, we approached 142 patients for participation. Among them, 130 patients consented and were successfully recruited into the study. Only 12 patients chose not to participate, resulting in a response rate of 91.5% (130/142). The subject recruitment flow is depicted in Figure 1.

Subjects' characteristics

The sociodemographic and clinical characteristics of the study participants are summarized in Table 1. The mean age of subjects was 53.1±13.3 years old. The gender distribution was nearly equal, with male subjects comprising 50.8% and female subjects representing 49.2%. The ethnic distribution was

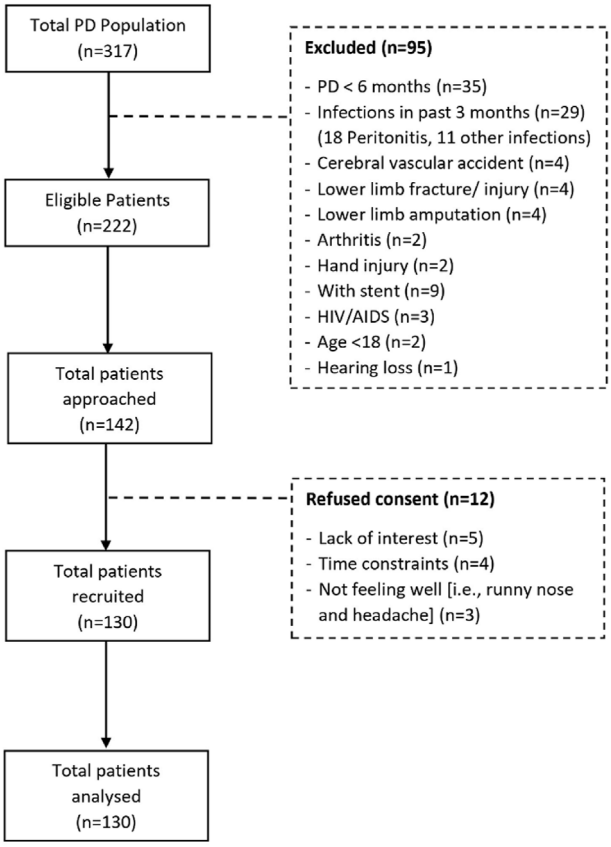

Figure 1. Flowchart of Subjects Screening and Recruitment. Abbreviation: AIDS: acquired immunodeficiency syndrome; HIV: human immunodeficiency virus; PD: peritoneal dialysis.

Table 1
Subjects' characteristics

Variables	All subjects (n=130)	Sarcopenia (n=33)	Non-sarcopenia (n=97)	χ^2 or *t*-/*U*-value	*P*
Gender					
Male	66 (50.8)	14 (42.4)	52 (53.6)	1.232	0.267
Age	53.1 ± 13.3	59.1 ± 10.6	51.0 ± 13.5	-3.529	**0.001**
Ethnicity					
Malay	89 (68.5)	20 (60.6)	69 (71.1)	1.264	0.26[a]
Chinese	34 (26.2)	11 (33.3)	23 (23.7)		
Indian	7 (5.4)	2 (6.1)	5 (5.2)		
Marital Status					
Married	107 (82.3)	29 (87.9)	78 (80.4)	0.943	0.332
Education Level					
≤ Secondary	83 (63.8)	28 (84.8)	55 (56.7)	8.451	**0.004**
Employment Status					
Employed	32 (24.6)	5 (15.2)	27 (27.8)	2.135	0.144
Household Income					
B40 (<RM4850)	88 (67.7)	25 (75.8)	63 (64.9)	1.315	0.251
No. of Comorbidities	2.7 ± 1.0	2.8 ± 1.1	2.7 ± 1.0	-0.464	0.643
Dialysis Vintage (mos)	26.5 (34.3)	27.0 (47.5)	26.0 (34.0)	1458.500	0.447[b]
Modality of PD					
Manual[d]	84 (64.6)	20 (60.6)	64 (66.0)	NA	0.737[c]
Automated[d]	44 (33.8)	13 (39.4)	31 (32.0)		
Combined[d]	2 (1.5)	0 (0.0)	2 (2.1)		
Kt/V	1.9 (0.5)	1.9 (0.6)	1.9 (0.5)	1511.500	0.634[b]
ECW/TBW Ratio	0.408 ± 0.013	0.413 ± 0.010	0.407 ± 0.014	-3.014	**0.003**
PhA (∘)	3.85 ± 0.97	3.28 ± 0.80	4.05 ± 0.94	4.237	**<0.001**
Dry Weight (kg)	60.5 ± 11.6	53.8 ± 9.0	62.8 ± 11.5	4.090	**<0.001**
BMI (kg/m^2)	23.8 ± 3.7	22.0 ± 3.2	24.4 ± 3.6	3.455	**0.001**
BFP (%)	31.1 ± 9.6	33.1 ± 9.6	30.4 ± 9.5	-1.368	0.174
SMM (kg)	22.4 ± 4.6	18.4 ± 3.0	23.8 ± 4.3	7.819	**<0.001**
MAC (cm)	27.9 ± 3.9	26.0 ± 3.6	28.5 ± 3.9	3.261	**0.001**
CC (cm)	33.6 ± 3.7	30.7 ± 3.0	34.6 ± 3.4	-5.830	**<0.001**
Male-specific	34.5 ± 3.4	31.4 ± 2.7	35.4 ± 3.1	-4.383	**<0.001**
Female-specific	32.7 ± 3.7	30.3 ± 3.2	33.7 ± 3.5	-3.697	**<0.001**
Albumin (g/L)	29.8 ± 5.1	28.0 ± 5.7	30.4 ± 4.7	2.439	**0.016**
Creatinine(umol/L)	1002.3 ± 317.3	872.6 ± 282.6	1046.5 ± 317.7	2.789	**0.006**
TC (mmol/L)	5.0 ± 1.3	4.8 ± 1.4	5.1 ± 1.3	1.013	0.313
TIBC (ug/dL)	196.6 ± 36.4	185.4 ± 45.4	200.4 ± 32.1	1.763	0.085
Hb (g/dL)	10.8 ± 1.9	10.8 ± 1.8	10.7 ± 2.0	-0.055	0.956
ASMI (kg/m^2)	6.8 ± 1.2	5.6 ± 0.8	7.2 ± 1.1	-7.967	**<0.001**
Male-specific	7.5 ± 1.0	6.3 ± 0.6	7.8 ± 0.8	-6.659	**<0.001**
Female-specific	6.1 ± 1.0	5.1 ± 0.5	6.6 ± 0.9	-7.893	**<0.001**
Failed test	45 (34.6)	33 (100.0)	12 (12.4)	83.540	**<0.001**
HGS (kg)	24.2 ± 8.5	17.1 ± 6.2	26.6 ± 7.8	-6.307	**<0.001**
Male-specific	28.8 ± 7.6	20.8 ± 7.0	31.0 ± 6.2	-5.322	**<0.001**
Female-specific	19.4 ± 6.6	14.4 ± 3.8	21.5 ± 6.4	-5.532	**<0.001**
Failed test	60 (46.2)	28 (84.8)	32 (33.0)	26.646	**<0.001**
5TCST (s)	NA	NA	NA	NA	NA
Failed test	65 (50.0)	28 (84.8)	37 (38.1)	21.484	**<0.001**

Categorical data was presented as n (% column); normally-distributed continuous data was presented as mean ± SD, whereas skewed data was presented as median (interquartile range); categorical data was analyzed by Pearson χ^2 test; normally-distributed continuous data was analyzed with independent t-test, whereas skewed data was analyzed with Mann-Whitney test.

[a] Data was analyzed by Malay versus non-Malay.

[b] Data was analyzed with Mann-Whitney test.

[c] Data was analyzed with Fisher's exact test.

[d] Manual: continuous ambulatory peritoneal dialysis (2L dialysate per exchange, 4 exchanges per day); Automated: nocturnal intermittent peritoneal dialysis (10L dialysate, run 10 hours per day); Combined: automated PD at night (10L dialysate, run 10 hours per day) and manual PD in the morning (2L dialysate, 1 exchange per day). NA: unbiased analysis was unattainable as a considerable proportion (20.8%) of subjects failed to complete the test due to physical weakness. Abbreviations: ASMI, appendicular skeletal muscle mass index; B40, bottom 40% of household income in Malaysia; BFP; body fat percentage; BMI, body mass index; CC, calf circumference; ECW/TBW, extracellular water/total body water; Hb, hemoglobin; HGS, handgrip strength; MAC, mid-arm circumference; mos, months; PhA, phase angle; SMM, skeletal muscle mass; TC, total cholesterol; TIBC; total iron-binding capacity; 5TCST, five-time chair stand test.

predominantly Malays (68.5%), followed by Chinese (26.2%) and Indians (5.4%), aligning with the national composition of ethnicities. The majority of subjects were married (82.3%), held secondary-level education (45.4%), were unemployed (75.4%) and belonged to the bottom 40% household income category (67.7%). The median dialysis vintage was 26.5 months (IQR:34.3), and the median Kt/V was 1.9 (IQR:0.5). The mean ECW/TBW ratio was 0.408 ± 0.013, whereas the mean PhA was 3.85±0.97°.

Factors associated with sarcopenia

Out of the total study population of 130 subjects, approximately 25.4% (33/130) were diagnosed with sarcopenia based on AWGS 2019 definition. A univariate analysis (Table 1) revealed several significant associations. Sarcopenic patients were notably older and tended to have a lower educational attainment. Additionally, they exhibited significantly higher ECW/TBW ratio and lower values of dry weight, body mass index (BMI), serum albumin, SMM, MAC, CC, serum creatinine and PhA. On the other hand, multivariable logistic regression analysis (Table 2) revealed that PhA remained an independent factor associated with sarcopenia, after adjusting for various sociodemographic and clinical factors.

Predictive ability of PhA for sarcopenia detection

Figure 2 provides a visualization of PhA's predictive ability for both the overall diagnosis of sarcopenia and individual diagnostic criteria according to AWGS 2019. Even after adjusting for subjects' characteristics, PhA remained to be a significant predictor of sarcopenia (adjOR=0.147; 95% CI =0.042–0.516; P =0.003). Specifically, for every one-unit decrease in PhA, the odds of being diagnosed with sarcopenia increased by 6.8 times. Concerning individual AWGS diagnostic criteria, PhA could only significantly predict one out of three AWGS diagnostic criteria, specifically low ASMI (adjOR=0.131; 95% CI =0.039–0.441; P =0.001). In other words, the odds of being diagnosed with low ASMI was increased by 7.6 times for every one-unit decrease in PhA. On the other hand, no significant association was observed between PhA and the other two diagnostic criteria for sarcopenia, namely

Table 2
Logistic regression analysis for sarcopenia according to variables

	Univariate		Multivariable	
	Crude OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age (per 1 year increase)	1.056 (1.019–1.095)	**0.003**	1.048 (0.991–1.109)	0.099
Gender				
Female (ref: male)	1.511 (0.678–3.368)	0.312	0.863 (0.271–2.747)	0.804
Ethnicity				
Chinese (ref: Malay)	1.755 (0.725–4.248)	0.213	1.840 (0.573–5.914)	0.306
Indian (ref: Malay)	1.340 (0.241–7.440)	0.738	1.347 (0.134–13.557)	0.800
Education level				
Secondary (ref: ≤primary)	0.792 (0.294–2.132)	0.644	0.744 (0.199–2.782)	0.661
Tertiary (ref: ≤primary)	0.219 (0.063–0.762)	**0.017**	0.526 (0.087–3.183)	0.484
Marital status				
Married (ref: single)	1.740 (0.543–5.579)	0.351	1.024 (0.203–5.155)	0.977
Employment status				
Unemployed (ref: employed)	2.173 (0.758–6.234)	0.149	0.407 (0.084–1.974)	0.264
Monthly household income				
>RM 4850 (ref: ≤RM4850)	0.610 (0.247–1.506)	0.284	0.676 (0.208–2.204)	0.517
No. of comorbidities (per 1 disease increase)	1.122 (0.761–1.655)	0.560	0.880 (0.512–1.513)	0.644
Kt/V (per 1 unit increase)	1.713 (0.501–5.851)	0.391	1.188 (0.243–5.810)	0.832
Log dialysis vintage (per 1 unit increase)	1.229 (0.785–1.924)	0.367	1.171 (0.665–2.065)	0.584
ECW/TBW Ratio (per 0.001 increase)	1.042 (1.008–1.078)	**0.017**	0.921 (0.844–1.004)	0.061
PhA (per 1 degree increase)	0.371 (0.219–0.630)	**<0.001**	0.147 (0.042–0.516)	**0.003**

Multi-variables logistic regression was adjusted for age, gender, ethnicity, education level, marital status, employment status, monthly household income, number of comorbidities, kt/V, log dialysis vintage, ECW/TBW ratio and PhA; n= 126 (4 sets data with outliers was excluded).

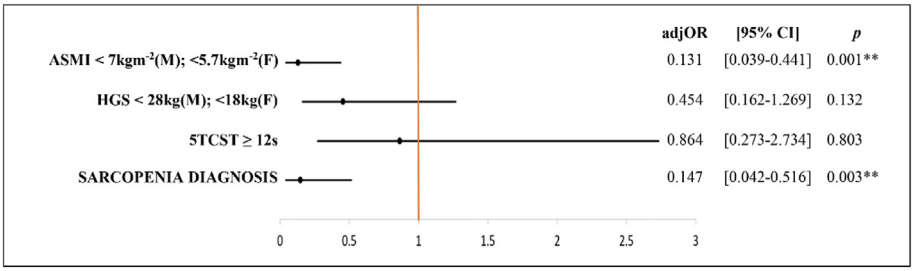

Figure 2. Forest plot for adjusted odds ratio of PhA for overall sarcopenia diagnosis and individual diagnostic criteria of AWGS 2019. Abbreviation: adjOR: adjusted odds ratio; ASMI: appendicular skeletal muscle mass index; HGS: handgrip strength; 5TCST: 5-time chair stand test. OR was adjusted for age, gender, ethnicity, education level, marital status, employment status, monthly household income, no. of comorbidities, Kt/V, log-transformed dialysis vintage and ECW ratio. n= 126 (4 sets data with outliers were excluded). $^{**}P<0.01$.

HGS (adjOR=0.454; 95% CI =0.162–1.269; P =0.132) and 5TCST (adjOR=0.864; 95% CI =0.273–2.734; P =0.803).

Discriminative performance of PhA for sarcopenia detection

Figure 3 illustrates the discriminative performance of PhA in detecting sarcopenia among Malaysian PD patients. The unadjusted ROC (green line) demonstrated an AUC of 0.737±0.048 (bootstrapped 95% CI =0.644–0.827, P =0.009), significantly outperforming the random classifier (AUC = 0.5). This indicates the acceptable discriminative ability of the raw model in distinguishing between sarcopenia and non-sarcopenia cases. Notably, after adjusting to sociodemographic and clinical characteristics, the AUC of PhA improved to 0.818±0.041 (bootstrapped 95% CI =0.734–0.899, P <0.001), indicating an excellent discriminative performance in identifying sarcopenia among PD patients.

Similar trends were also observed in gender-specific ROC curve analysis. For male, the AUC was 0.755±0.069 (bootstrapped 95% CI =0.617–0.866, P =0.010) and improved to 0.845±0.068 (bootstrapped 95% CI =0.696–0.957, P <0.001) after adjustment for covariates. For female, the AUC was 0.722±0.072 (bootstrapped 95% CI =0.566–0.854, P =0.026) and improved to 0.868±0.051 (bootstrapped 95% CI =0.747–0.952, P <0.001) after the adjustment.

Table 3 depicts discriminative performance of optimal PhA cut-off for sarcopenia detection. Based on unadjusted ROC analysis, the optimal PhA cut-off for sarcopenia detection in PD patients was ≤3.95° (81.8% sensitivity and 52.6% specificity). Meanwhile, the optimal gender-specific PhA cut-off for sarcopenia detection was ≤4.05° (corresponding to the threshold of 0.182 in Figure 3B) for males (92.9% sensitivity and 53.8% specificity) and ≤3.75° (corresponding to the threshold of 0.256 in Figure 3C) for female (78.9% sensitivity and 51.1% specificity).

Discussion

The current study contributes significant insights into the role of PhA as an independent predictor of sarcopenia among PD patients. While some studies have shown mixed results, our findings align with the prevailing consensus in the literature. [13,14,23] The variation in results across studies may, in part, be attributed to differences in diagnostic criteria employed in each study. For instance, Bae *et al.* [24] reported a non-significant association between PhA and sarcopenia in hemodialysis patients. This outcome could be linked to their utilization of non-Asian-specific diagnostic criteria for sarcopenia, despite their study population predominantly consisting of Asian subjects.

In addition, the AUC of unadjusted ROC in our study is consistent with the findings of two previous studies conducted in PD patients. [13,14] However, it is essential to acknowledge that confounding could potentially impact the validity of the present cross-sectional study. Therefore, we made a strategic decision to employ an adjusted model that incorporates common demographic and clinical

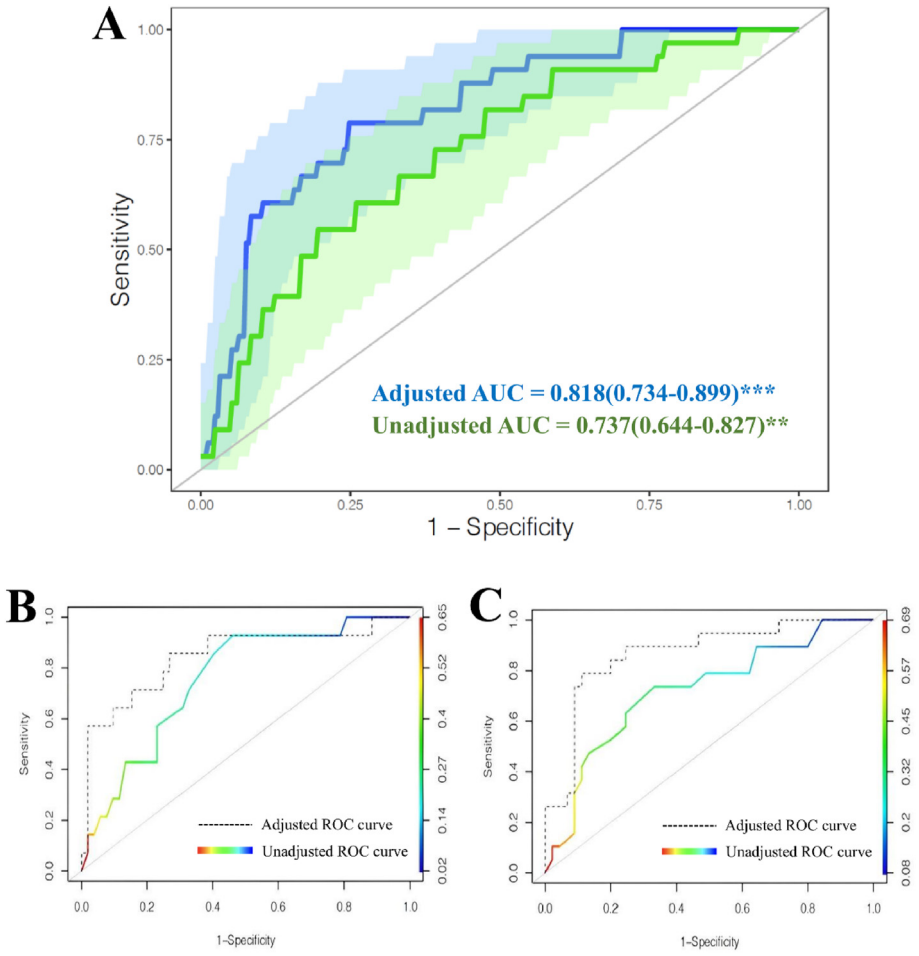

Figure 3. ROC analyses for phase angle to detect sarcopenia among peritoneal dialysis patients. (A) Unadjusted and adjusted bootstrapped overall ROC analyses. The shaded regions represent the 95% CI around the ROC curves; the diagonal line represents the ROC curve for a model with no discrimination power, corresponding to an AUC = 0.5. Adjusted AUC was adjusted for gender, age, ethnicity, education level, marital status, employment status, monthly household income, no. of comorbidities, Kt/V, log-transformed dialysis vintage and ECW/TBW ratio. (B) Unadjusted and adjusted bootstrapped male-specific ROC analyses; (C) Unadjusted and adjusted bootstrapped female-specific ROC analyses. Rainbow ROCs are illustrated for visualizing the decision threshold. Adjusted ROC curve was adjusted for age, ethnicity, education level, marital status, employment status, monthly household income, no. of comorbidities, Kt/V, log-transformed dialysis vintage and ECW/TBW ratio.

variables. The adjusted ROC model resulted in an improved discriminative performance of PhA in identifying sarcopenia, enhancing the internal validity and robustness of our study findings.

PhA represents the relationship between resistance (R) and reactance (Xc) of an electrical signal as it passes through biological tissues, calculated as arctan (Xc/R). [10] Muscle cells are good conductors of electricity due to their high water and electrolyte content, and they have high capacitive properties due to their cell membranes. As such, increased muscle cell mass would lead to increased reactance and reduced resistance, which consequently be reflected in higher PhA. [25] Thus, it is not unexpected that current study identified PhA as an independent predictor of ASMI status, with higher PhA values indicative of better ASMI status. A similar finding was reported in a study of chronic kidney disease and PD patients, which found that the lean mass index was independently associated with PhA. [26].

Table 3
Discriminative performance of optimal PhA cut-off for sarcopenia detection

	PhA Cut-Off (°)	Sensitivity (%)	Specificity (%)	AUC	95% CI	*P*-value
Overall (n=130)	≤ 3.95°	81.8	52.6	0.737	0.644–0.827	0.009
Male (n=66)	≤ 4.05°	92.9	53.8	0.755	0.617–0.866	0.010
Female (n=64)	≤ 3.75°	78.9	51.1	0.722	0.566–0.854	0.026

Data was analyzed with ROC analysis. Abbreviations: AUC, area under curve.

Interestingly, despite the predictive ability of PhA for overall sarcopenia diagnosis and ASMI criterion, we did not find a significant association between PhA with another two AWGS 2019 diagnostic criteria, namely HGS (i.e., muscle strength) and 5TCST (i.e., physical performance). This outcome resonates with prior research, including studies involving physically active elderly women [27] and post-kidney transplantation patients, even when a different measure of physical performance (i.e., gait speed) was used. [28] This intriguing finding challenges the conventional expectation that higher muscle mass, and subsequently higher PhA, should inherently coincide with greater muscle strength and physical performance. The complexity of this relationship becomes evident when considering factors beyond skeletal muscle mass, such as anemia, electrolyte imbalance, joint pain, heart problems, neurological problems, depression and mental states. [29,30] This is supported by the observed difference in decline rates between muscle mass and strength, where the annual decline in strength was found to be 3–5 times higher than the rate of muscle loss, [3,31] indicating the multifactorial nature of muscle strength. This holistic perspective highlights the intricate interplay of factors influencing muscle strength and physical performance, underscoring the importance of considering these multifaceted dynamics when assessing sarcopenia.

In our study, the decision to employ unadjusted ROC model to identify the optimal PhA cut-off values for sarcopenia detection stemmed from a strategic aim to establish robust and generalizable cut-off values for real-world clinical settings. Consistent with previous studies, [14,23,32] current study prioritized sensitivity over specificity when deciding on the PhA cut-off value for sarcopenia detection, given the serious health consequences of false negativity, including compromised quality of life, prognosis and survival rates. Moreover, late detection and intervention can significantly impair treatment efficacy. [3].

Notably, the optimal PhA cut-off values identified in our study were relatively lower when compared to two previous studies conducted on PD patients in China and South Korea. The discrepancy could be attributed to variations in subject characteristics. For instance, Chen *et al.* [13] reported a much higher PhA cut-off value (≤5.3°) for sarcopenia detection in Chinese PD patients, likely influenced by the exclusion of patients with broader medical conditions that predispose them to low PhA, as well as the relatively younger age and lower prevalence of edema within the study population. Similarly, the study by Do *et al.* [14] had a more well-nourished (with higher BMI and serum albumin) and less oedematous population, and a higher proportion of male participants, which could explain the higher PhA cut-off value (≤4.4°) for sarcopenia detection in that study. Furthermore, we acknowledge that differences in recommended PhA cut-off values for sarcopenia detection between studies could be attributed to variations in sarcopenia definition, muscle mass estimation approach, BIA device, ethnicity and lifestyle. [29,33,34] Notably, ethnicity and lifestyle are associated with both PhA and sarcopenia, [35–38] suggesting the need for region-specific PhA cut-offs for sarcopenia identification.

The study stands as one of the pioneering investigations into the predictive ability of PhA in the context of sarcopenia among PD patients, with full adherence to the AWGS 2019 consensus, the state-of-the-art Asian-specific sarcopenia diagnostic protocol, hence providing more accurate evidence. In addition, this research is the first study to provide evidence regarding the ability of PhA in detecting sarcopenia among PD patients in a multi-ethnic Southeast Asian country, adding valuable insights to the existing body of knowledge. Furthermore, the use of bootstrapping method in our analysis enhances the internal validity of our findings.

However, this study has several limitations that should be acknowledged. Firstly, despite the subjects' characteristics mirroring national data, [39] the study was confined to a single center, which may introduce limitations in the generalizability of the findings to a broader and more diverse population. Secondly, the estimation of muscle mass relied on a multi-frequency BIA (MFBIA) device, which is

generally considered to be less accurate compared to the gold-standard dual-energy x-ray absorptiometry (DXA). In spite of this, the MFBIA model (InBody S10) utilized in the current study demonstrated good agreement with DXA in a validation analysis conducted within a dialysis population. [40] While these limitations should be recognized, they do not diminish the significance of the insights gained from this study, and they underscore areas for potential refinement and expansion in future studies. Future studies aiming to improve accuracy and generalizability should consider a multicentre design with a probability sampling method, and the use of DXA in body composition assessment. To further enhance the accuracy of PhA in detecting sarcopenia, consideration should be given to establishing ethnicity-specific, hydration status-specific and even age-decade-specific cut-offs.

In conclusion, this study provides compelling evidence that BIA-derived PhA emerges as an independent predictor of sarcopenia in Malaysian PD patients. Given the inherent challenges of universal screening for sarcopenia in clinical settings, PhA, which is readily available in routine hydration or body composition BIA tests, holds promise as a pragmatic screening tool. Its utilization can effectively identify PD patients at risk of sarcopenia, streamlining the diagnostic process and enabling early intervention aimed at improving patient outcomes.

Author contribution

Shi-Wah Lee: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Visualization, Writing—original draft. **Zulfitri Azuan Mat Daud**: Conceptualization, Methodology, Funding acquisition, Supervision, Validation, Writing—review & editing. **Jun-Hao Lim**: Methodology, Formal analysis, Visualization, Writing—review & editing. **Cordelia-Kheng-May Lim**: Methodology, Investigation, Formal analysis, Writing—review & editing. **Imliya Ibrahim**: Methodology, Investigation, Formal analysis, Writing—review & editing. **Yoke-Mun Chan**: Methodology, Supervision, Writing—review & editing. **Nor Fadhlina Zakaria**: Methodology, Resources, Supervision, Writing—review & editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

[1] Chen LK, Woo J, Assantachai P, Auyeu TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. J Am Med Dir Assoc 2020;21(3):300–307.e2. https://doi.org/10.1016/j.jamda.2019.12.012.

[2] Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. J Cachexia Sarcopenia Muscle 2016;7(5). https://doi.org/10.1002/jcsm.12147.
[3] Sabatino A, Cuppari L, Stenvinkel P, Lindholm B, Avesani CM. Sarcopenia in chronic kidney disease: what have we learned so far? J Nephrol 2020;(123456789). https://doi.org/10.1007/s40620-020-00840-y.
[4] Lo Y-TC, Wahlqvist ML, Huang Y-C, Chuang S-Y, Wang C-F, Lee M-S. Medical costs of a low skeletal muscle mass are modulated by dietary diversity and physical activity in community-dwelling older Taiwanese: a longitudinal study. Int J Behav Nutr Phys Act 2017;14:1–12. https://doi.org/10.1186/s12966-017-0487-x.
[5] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Revised European consensus on definition and diagnosis. Age Ageing 2019;48(1):16–31. https://doi.org/10.1093/ageing/afy169.
[6] Cruz-Jentoft AJ, Sayer AA. Sarcopenia. Lancet. 2019;393(10191):2636–46. https://doi.org/10.1016/S0140-6736(19)31138-9.
[7] Moura-Neto JA, Divino-Filho JC, Ronco C. Nephrology worldwide. 1st ed. Springer; 2021.
[8] Lim C-K-M, Lim J-H, Ibrahim I, Chan YM, Zakaria NF, Yahya R, et al. Bioelectrical impedance analysis derived-phase angle as a pragmatic tool to detect protein energy wasting among multi-ethnic hemodialysis patients. Diagnostics 2021;11(10):1745. https://doi.org/10.3390/diagnostics11101745.
[9] Norman K, Stobäus N, Pirlich M, Bosy-Westphal A. Bioelectrical phase angle and impedance vector analysis - Clinical relevance and applicability of impedance parameters. Clin Nutr 2012;31(6):854–61. https://doi.org/10.1016/j.clnu.2012.05.008.
[10] Sardinha LB. Physiology of exercise and phase angle: Another look at BIA. Eur J Clin Nutr 2018;72(9):1323–7.
[11] Di Vincenzo O, Marra M, Di Gregorio A, Pasanisi F, Scalfi L. Bioelectrical impedance analysis (BIA)-derived phase angle in sarcopenia: A systematic review. Clin Nutr 2021;40(5):3052–61. https://doi.org/10.1016/j.clnu.2020.10.048.
[12] da Silva MZC, Vogt BP, Reis NS do C, Caramori JCT. Update of the European consensus on sarcopenia: what has changed in diagnosis and prevalence in peritoneal dialysis? Eur J Clin Nutr 2019;73(8):1209–11. https://doi.org/10.1038/s41430-019-0468-z.
[13] Chen Y, Wu J, Ran L, Yu D, Chen X, Liu M. The combination of phase angle and age has a good diagnostic value for sarcopenia in continuous ambulatory peritoneal dialysis patients. Front Nutr 2022;9:1036796. https://doi.org/10.3389/fnut.2022.1036796.
[14] Do JY, Kim AY, Kang SH. Association between phase angle and sarcopenia in patients undergoing peritoneal dialysis. Front Nutr 2021;8:742081. https://doi.org/10.3389/fnut.2021.742081.
[15] Mundstock E, Amaral MA, Baptista RR, Sarria EE, Dos Santos RRG, Detoni Filho A, et al. Association between phase angle from bioelectrical impedance analysis and level of physical activity: systematic review and meta-analysis. Clin Nutr 2019;38(4):1504–10.
[16] Wang T-D, Goto S, Bhatt DL, Steg PG, Chan JCN, Richard AJ, et al. Ethnic differences in the relationships of anthropometric measures to metabolic risk factors in Asian patients at risk of atherothrombosis: results from the REduction of Atherothrombosis for Continued Health (REACH) Registry. Metabolism 2010;59(3):400–8. https://doi.org/10.1016/j.metabol.2009.08.009.
[17] InBody Co. Ltd. Inbody S10: User's Manual. Published 2019. Accessed April 12, 2023. https://nl.inbody.com/wp-content/uploads/2019/01/InBodyS10_CDmanual_Eng_E.pdf.
[18] Lee SW, Daud ZAM, Lim JH, Lim CKM, Ibrahim I, Chan YM, et al. A pragmatic approach to derogate dialysate-induced body composition bias in peritoneal dialysis patients: insight from a single center study. Turkish J Nephrol 2024;33(1):68–75. https://doi.org/10.5152/turkjnephrol.2023.23626.
[19] InBody Co. Ltd. The Professional's Guide to The InBody Result Sheet. Published 2018. Accessed April 12, 2023. https://uk.inbody.com/wp-content/uploads/2018/08/The_Professional_s_Guide_to_the_InBody_Result_Sheet.pdf.
[20] Nishimura T, Arima K, Okabe T, Mizukami S, Tomita Y, Kanagae M, et al. Usefulness of chair stand time as a surrogate of gait speed in diagnosing sarcopenia. Geriatr Gerontol Int 2017;17(4):659–61.
[21] Janes H, Pepe MS. Adjusting for covariates in studies of diagnostic, screening, or prognostic markers: an old concept in a new setting. Am J Epidemiol 2008;168(1):89–97.
[22] Hosmer DW, Lemeshow S, Sturdivant RX. Applied logistic regression. 3rd ed. Wiley; 2013. https://doi.org/10.1002/9781118548387.
[23] Ding Y, Chang L, Zhang H, Wang S. Predictive value of phase angle in sarcopenia in patients on maintenance hemodialysis. Nutrition 2022;94:111527. https://doi.org/10.1016/j.nut.2021.111527.
[24] Bae E, Lee TW, Bae W, Kim S, Choi J, Jang HN, et al. Impact of phase angle and sarcopenia estimated by bioimpedance analysis on clinical prognosis in patients undergoing hemodialysis: a retrospective study. Medicine (Baltimore) 2022;101(25):e29375.
[25] López-Gómez JM. Evolution and applications of bioimpedance in managing chronic kidney disease. Nefrol (English Ed. 2011;31(6):630–4. https://doi.org/10.3265/Nefrologia.pre2011.Oct.11015.
[26] Han B-G, Lee JY, Kim J-S, Yang J-W. Clinical significance of phase angle in non-dialysis CKD stage 5 and peritoneal dialysis patients. Nutrients 2018;10(9):1331. https://doi.org/10.3390/nu10091331.
[27] Pessoa DF, de Branco FMS, Dos Reis AS, Limirio LS, Borges L de P, Barbosa CD, et al. Association of phase angle with sarcopenia and its components in physically active older women. Aging Clin Exp Res 2020;32:1469–75. https://doi.org/10.1007/s40520-019-01325-0.
[28] Dos Reis AS, Santos HO, Limirio LS, de Oliveira EP. Phase angle is associated with handgrip strength but not with sarcopenia in kidney transplantation patients. J Ren Nutr 2019;29(3):196–204. https://doi.org/10.1053/j.jrn.2018.10.005.
[29] Yoowannakul S, Tangvoraphonkchai K, Davenport A. The prevalence of muscle wasting (sarcopenia) in peritoneal dialysis patients varies with ethnicity due to differences in muscle mass measured by bioimpedance. Eur J Clin Nutr 2018;72(3):381–7. https://doi.org/10.1038/s41430-017-0033-6.
[30] Larsen LH, Z'Graggen WJ, Bostock H, Tan SV, Buus NH, Tankisi H. The role of potassium in muscle membrane dysfunction in end-stage renal disease. Clin Neurophysiol 2021;132(12):3125–35.
[31] Distefano G, Goodpaster BH. Effects of exercise and aging on skeletal muscle. Cold Spring Harb Perspect Med 2018;8(3):a029785. https://doi.org/10.1101/cshperspect.a029785.

[32] Ruiz-Margáin A, Xie JJ, Román-Calleja BM, Pauly M, White MG, Chapa-Ibarguengoitia M, et al. Phase angle from bioelectrical impedance for the assessment of sarcopenia in cirrhosis with or without ascites. Clin Gastroenterol Hepatol 2021;19(9):1941–1949.e2. https://doi.org/10.1016/j.cgh.2020.08.066.
[33] Abro A, Delicata LA, Vongsanim S, Davenport A. Differences in the prevalence of sarcopenia in peritoneal dialysis patients using hand grip strength and appendicular lean mass: Depends upon guideline definitions. Eur J Clin Nutr 2018;72(7): 993–9. https://doi.org/10.1038/s41430-018-0238-3.
[34] Hew-Butler T, Holexa BT, Fogard K, Stuempfle KJ, Hoffman MD. Comparison of body composition techniques before and after a 161-km ultramarathon using DXA, BIS and BIA. Int J Sports Med 2015;36(2):169–74.
[35] Kuchnia AJ, Teigen LM, Cole AJ, Mulasi U, Gonzalez MC, Heymfield SB, et al. Phase angle and impedance ratio: reference cut-points from the United States National Health and nutrition examination survey 1999–2004 from bioimpedance spectroscopy data. J Parenter Enter Nutr 2017;41(8):1310–5. https://doi.org/10.1177/0148607116670378.
[36] Yoowannakul S, Tangvoraphonkchai K, Vongsanim S, Mohamed A, Davenport A. Differences in the prevalence of sarcopenia in haemodialysis patients: the effects of gender and ethnicity. J Hum Nutr Diet 2018;31(5):689–96. https://doi.org/10.1111/jhn.12555.
[37] Jaremków A, Markiewicz-Górka I, Hajdusianek W, Gać P. Relationships between Body Composition Parameters and Phase Angle as Related to Lifestyle among Young People. J Clin Med 2021;11(1):80. https://doi.org/10.3390/jcm11010080.
[38] Bigman G, Ryan AS. Implications of race and ethnicity in sarcopenia US National prevalence of sarcopenia by muscle mass, strength, and function indices. Gerontol Geriatr Res 2021;4(1).
[39] Ong L. Concise Summary of Essential Statistics for Year 2020. https://msn.org.my/nrr/wp-content/uploads/2022/12/Concise-Summary-of-Essential-Statistics-for-year-2020-dated-19th-Oct-2022.pdf. [Accessed 11 April 2023].
[40] Jayanama K, Putadechakun S, Srisuwarn P, Vallibhakara SAO, Chattranukulchai Shantavasinkul P, Sritara C, et al. Evaluation of body composition in hemodialysis Thai patients: comparison between two models of bioelectrical impedance analyzer and dual-energy X-ray absorptiometry. J Nutr Metab 2018. https://doi.org/10.1155/2018/4537623.