The Association between Bioimpedance Analysis and Quality of Life in Pre-Dialysis Stage 5 Chronic Kidney Disease, Hemodialysis and Peritoneal Dialysis Patients

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Background: Protein-energy wasting is a significant problem in End stage renal disease (ESRD) patients. Furthermore, it compromises the patient's Quality of life (QOL). Multifrequency Bioimpedance Spectroscopy (BIS) is a validated method to assess body composition in dialysis patients. There has been no data on the relationship between body composition and QOL in ESRD patients who were treated with different modalities.

Objective: To explore the association between body composition as assessed by BIS and QOL in ESRD patients who received different treatment modalities.

Material and Method: The present study is a cross sectional, descriptive analytic study of the association between QOL and BIS in ESRD patients in Burapha University, Chonburi, Thailand. QOL was assessed by WHOQOL-BREF questionnaire, body composition was measured by BIS technique. The difference between groups was tested by one-way ANOVA test, relationship between groups was tested with Pearson correlation test.

Results: Eighteen predialysis-CKD5, 26 peritoneal dialysis (PD), and 34 hemodialysis (HD) patients were included in the present study. All PD patients had weekly Kt/V ≥1.7 per week and all HD patients had weekly Kt/V ≥3.6 per week. There were no statistically difference in baseline characteristics including Charlson comorbidity index, dietary intake, BMI, and blood pressure between groups. Mean QOL scores in each group were in the middle range and not significantly difference. PD patients had more over hydration when compare to HD patients (16.18±11.24 vs. 2.36±11.07 %OH/ECW p<0.0001). There were inversed correlation between overhydration and physical health in HD patients (r = -0.372, p = 0.033) but not in PD and CKD5 patients. CKD5 patients had more lean tissue index (LTI) than PD and HD patients (LTI = 14.34±3.13, 12.26±3.65, 11.48±3.48 kg/m² respectively, p = 0.023). There were correlation between LTI and overall QOL in CKD5 (r = 0.690, p = 0.002) and PD patients (r = 0.498, p = 0.010). In HD patients, LTI was associated with better physical health (r = 0.464, p = 0.007).

Conclusion: QOL in predialysis-CKD5, PD and HD patients were not statistically different. HD patients had better volume control than PD patients. Higher LTI were associated with better QOL in ESRD patients.

Keywords: Nutritional status, Body composition, Quality of life, End stage renal disease, Bioimpedance spectroscopy

The incidence and prevalence of End Stage Renal Disease (ESRD) in Thailand is rising along with a higher cost of treatment[1]. The "PD First" policy in Thailand was implemented on January 1, 2008 to promote Continuous Ambulatory Peritoneal Dialysis (CAPD) as the treatment of choice for Thai ESRD patients. Since then, the number of CAPD patients in

Thailand increased more than 10 folds[1]. Previous studies showed comparable mortality and morbidity outcomes in peritoneal dialysis (PD) and hemodialysis (HD) patients[2,3] but comparison of the treatment outcome in ESRD patients by body composition measurement has not been well studied across PD and HD patients. Multifrequency Bioimpedance Spectroscopy (BIS) with a body composition model is a validated method to assess hydration and nutritional status in pre-dialysis and dialysis patients[4-6]. In the current study, we examined the association between body composition as measured by BIS with quality of life (QOL) as measured by WHO-QOL BREF in a

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cohort of 78 adult ESRD patients receiving different treatment modalities. We hypothesized that better nutritional parameters are associated with better QOL and there should be no difference in QOL in each treatment modality.

Material and Method
Patients
The present study is a cross-sectional, descriptive analytic study in Burapha University, Chonburi, Thailand. Seventy-eight ESRD patients in the Renal Unit, Burapha University Hospital, Thailand were recruited. Inclusion criteria were (1) dialysis patients who had been undergoing HD or CAPD for at least three months, (2) pre-dialysis CDK-5 patients (glomerular filtration rate measured by MDRD formula less than 15 ml/min/1.73 m^2) had been followed in CKD clinic for more than three months. Exclusion criteria were (1) patients who had limb amputation or metallic prosthesis in their body, (2) those who were not able to sign the consent form. The assessment of nutritional status by multifrequency bioimpedance spectroscopy (BIS) was performed after midweek HD session in HD patients. CAPD patients were measured with 2L dwelling peritoneal fluid. All HD patients had total weekly Kt/V of 3.6 or more and CAPD patients had total weekly Kt/V of 1.7 or more. Calories, protein and salt intake were assessed and calculated by food record form, Nephrology Society of Thailand. The protocol for this research project has been approved by the Ethics Committee of Burapha University, Thailand and conforms to the provisions of the Declaration of Helsinki. All subjects were informed about the study protocol and consents were signed, all information was kept anonymously.

Multifrequency bioelectrical spectroscopy (BIS) assessment
The BIS was measured by Body Composition Monitor (BCM®; Fresenius Medical Care, Bad Homburg, Germany)[7,8] by the same operator. This machine measured resistance, reactance, and phase angle from frequencies oscillating between 5 kHz and 1,000 kHz. The main results were expressed as body mass index (BMI, kg/m^2), lean tissue mass (LTM, kg), lean tissue index (LTI, kg/m^2), fat tissue mass (FTM, kg), fat tissue index (FTI, kg/m^2), body cell mass (BCM, kg), over hydration (OH, L), extracellular fluid volume (ECF, L), intracellular fluid volume (ICF, L), and intracellular to extracellular fluid volume ratio (E/I ratio)

Quality of life measurement
Quality of life measurement was evaluated by WHOQOL-BREF instrument comprising of 26 items, which measured the following broad domains, physical health, psychological health, social relationship, and environment. The total score was then re-calculated to a maximum of five score scale. The WHOQOL-BREF is a shorter version of the original instrument that may be more convenient for use in clinical trials.

Data collection and ethical aspects
Baseline data and laboratory parameters were collected from the patient's medical records with their permission (from patient's informed consent). Charlson comorbidity index was recorded according to the protocol[9]. The present study protocol was approved by the Ethics Committee of Burapha University. All patients gave their informed consent to the study protocol before data collection and BIS measurement.

Dialysis adequacy assessment
Dialysis adequacy in HD patients was measured by urea kinetic model using midweek pre and post dialysis urea concentration. Dialysis adequacy in PD patients was measured by the sum of weekly Kt/V of residual renal function and collection of 24 hours dialysate to measure dialysate urea concentration and the same day blood sampling to measure serum urea concentration to calculate weekly Kt/V urea.

Statistical analysis
Data was presented as mean ± SD or number and percentage when appropriate. The one-way ANOVA test for independent samples was used to compare means between CKD-5, HD, and PD groups. Bonferroni's test was used for multiple comparisons. Correlation between quality of life and nutritional status were tested by Pearson's correlation coefficient. A $p < 0.05$ was considered as statistically significant. Statistical analyses were carried out with the statistical software program R version 3.0.1 (Free software foundation's GNU project, Boston, MA, USA).

Results
Demographic data
Seventy-eight ESRD patients were evaluated. Characteristics of the patients are listed in Table 1. The baseline characteristic, Charlson comorbidity index and food intake were not significantly different between

groups. Mean Comorbidity index in this population was higher than in the previous studies[9], indicating a higher severity and poorer prognosis. Mean caloric intake and protein intake in these patients was less than the recommended value with a good salt restriction of less than 3 grams per day.

Quality of life
The overall quality of life scores in the three groups were not significantly different. Our patients had overall quality of life in the middle range with psychological health and environmental health perspectives in the good range as shown in Table 2.

Multifrequency bioimpedance spectroscopy
The results of BIS measurement are shown in Table 3. The three groups had comparable BMI, systolic blood pressure, FTI. They had lower LTI when compared to the normal population (as shown by LTI difference). CKD patients had more LTI than HD and PD patients. CAPD patients had more fluid overload than HD patients and this was mostly located in the extracellular space since the intracellular fluid volume

was not significantly different between groups. They had comparable volume of urea distribution with trend toward lower total body water and extracellular fluid water in HD patients. Extracellular fluid volume expansion was more pronounced in PD patients when compared to HD and CKD patients.

Correlation between quality of life and BIS parameters
LTI, BCM and ICF were modestly correlated with overall QOL in all ESRD patients (r = 0.402, p<0.001; r = 0.361, p = 0.001; r = 0.318, p = 0.005 respectively). E/I ratio, Volume of urea distribution, percent fat mass and TBW were weakly correlated with QOL, but not hydration status, BMI or systolic blood pressure. The strongest correlation between LTI and QOL was found in the physical domain and social relationship (r = 0.500, p<0.001; r = 0.476, p<0.001 respectively). Subgroup analysis found positive correlation between LTI, BCM and overall QOL in PD (r = 0.498, p = 0.010; r = 0.468, p = 0.016 respectively) and pre-dialysis CKD5 groups (r = 0.690, p = 0.002; r = 0.608, p = 0.010 respectively) but not HD group. In HD group, there was positive correlation between

Table 1. Characteristics of the study population

Patient characteristics	CKD-5 (n = 18)		HD (n = 34)		PD (n = 26)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age (years)	59.11	11.72	61.12	15.46	52.96	14.42	0.081
Age range	29-82		29-85		87-22		-
Sex (percent male patients)	38.9%		47.1%		53.8%		-
Charlson comorbidity index	9.75	2.77	9.50	2.39	8.50	2.387	0.192
Calorie intake (kcal/kg/d)	21.50	8.20	26.94	8.68	24.44	7.55	0.364
Protein intake (gm/kg/d)	0.81	0.29	0.96	0.36	0.87	0.26	0.481
Sodium intake (gm/d)	2.66	1.30	2.86	0.96	2.98	0.92	0.635

CKD-5 = chronic kidney disease stage 5; HD = hemodialysis; PD = continuous ambulatory peritoneal dialysis

Table 2. Quality of life in ESRD patients

Perspective	CKD-5 (n = 18)		HD (n = 34)		PD (n = 26)		p-value
	Mean	SD	Mean	SD	Mean	SD	
Overall QOL	3.00	0.74	3.06	0.587	3.46	0.735	0.052
Physical health	2.96	0.91	2.94	0.808	3.04	0.854	0.904
Psychological health	3.70	0.90	3.73	0.621	3.68	0.670	0.961
Social relations	3.52	0.77	3.10	0.835	3.37	0.655	0.150
Environment	3.70	0.59	3.81	0.598	3.64	0.608	0.548
Total score	3.43	0.60	3.42	0.475	3.45	0.566	0.950

ESRD = end stage renal disease; QOL = quality of life; CKD-5 = chronic kidney disease stage 5; HD = hemodialysis; PD = continuous ambulatory peritoneal dialysis

Table 3. Nutritional and hydration status assessed by BIS

Variables	CKD-5 (n = 18)		HD (n = 34)		PD (n = 26)		p-value
	Mean	SD	Mean	SD	Mean	SD	
BMI (kg/m^2)	23.98	3.52	22.29	4.532	24.23	4.460	0.186
sBP (mmHg)	147.29	15.85	136.88	19.01	139.12	24.60	0.237
LTI (kg/m^2)	14.34*	3.13	11.48	3.48	12.26	3.65	0.023
LTI different	2.25*	2.46	-0.84	2.37	-0.70	2.936	<0.0001
BCM (kg)	20.47	6.87	15.67	7.41	17.35	7.28	0.86
FTI (kg/m^2)	8.63	4.15	10.52	4.67	10.79	5.84	0.327
V urea (L)	30.81	6.16	26.46	7.23	29.64	6.25	0.058
ECF volume (L)	15.52	3.06	12.59*	2.84	15.89	3.46	<0.0001
ICF volume (L)	16.98	3.87	14.65	4.64	15.88	3.85	0.165
%OH	12.57	11.27	2.36*	11.07	16.18	11.24	<0.0001
E/I ratio	0.93	0.16	0.89*	0.18	1.02	0.21	0.035

* p<0.05, comparison were estimated using Bonferroni's test
BIS = bioimpedance spectroscopy; CKD-5 = chronic kidney disease stage 5; HD = hemodialysis; PD = continuous ambulatory peritoneal dialysis; BMI = body mass index; sBP = systolic blood pressure; LTI = lean tissue index; BCM = body cell mass; FTI = fat tissue index; V urea = volume distribution of urea; ECF = extracellular fluid; ICF = intracellular fluid; OH = over hydration; E/I ratio = ratio of extracellular fluid to intracellular fluid

LTI and physical health (r = 0.464, p = 0.007). Over hydration and hypertension were correlated with lower physical health in HD group (r = -0.372, p = 0.033; r = -0.428, p = 0.013 respectively). Correlation between BIS parameters and QOL domain is shown in Fig. 1.

Discussion

Outcome measurement in dialysis patients such as all-cause mortality and cause specific mortality ratio are hard endpoints that need long term follow-up. For the cross sectional study, suggested endpoints such as quality of life and nutritional status are recommended[10]. Dialysis patients usually have multiple co-morbidities that affect their outcome, Charlson co-morbidity index is an established tool to classify the patient's severity of disease and predict treatment outcome[9,11]. The authors examined and compared the BIS parameters to QOL of ESRD patients on dialysis and pre-dialysis period. Our patients in three groups had comparable base line characteristics and Charlson co-morbidity index. Mean caloric intake (25.01 cal/kg/d) was lower than the recommended value[12] but not significantly different between groups. The overall quality of life of these patients was in the middle range and not statistically different between groups. This finding is different from previous studies that found higher quality of life in PD patients than HD patients[13]. Pre-dialysis

CKD-5 group had same QOL score as dialysis groups probably due to the effect of pre-dialysis clinic attendance program[14] and the higher LTI.

Multifrequency bioelectrical impedance spectroscopy found comparable LTI in both dialysis groups but lower than pre-dialysis CKD-5 group and the normal population. The cause of lower LTI than the normal population in dialysis groups could be explained by protein-energy wasting state in ESRD patients[15,16]. LTI and BCM were modestly correlated to overall QOL in all ESRD patients (r = 0.408, p<0.0001 for LTI; r = 0.361, p = 0.001 for BCM). Other studies also found correlation between QOL and nutritional status measured by mid arm circumference, lean body mass and fat mass in dialysis patients[17,18]. Therefore, to improve outcomes in ESRD patients, physician must pay attention to their nutritional status and follow the nutritional parameters closely[19]. The finding of better fluid control in HD group can be partly explained by our protocol that measured BIS during post dialysis period. In HD group, the higher fluid overload impaired physical health. It was felt, according to this finding, they might have strong benefit from active fluid management to improve nutritional status and prevent long-term complications[20]. Some limitations should be considered from the present study. Firstly, there was selection bias since this is a single study and our patients may be more severe than
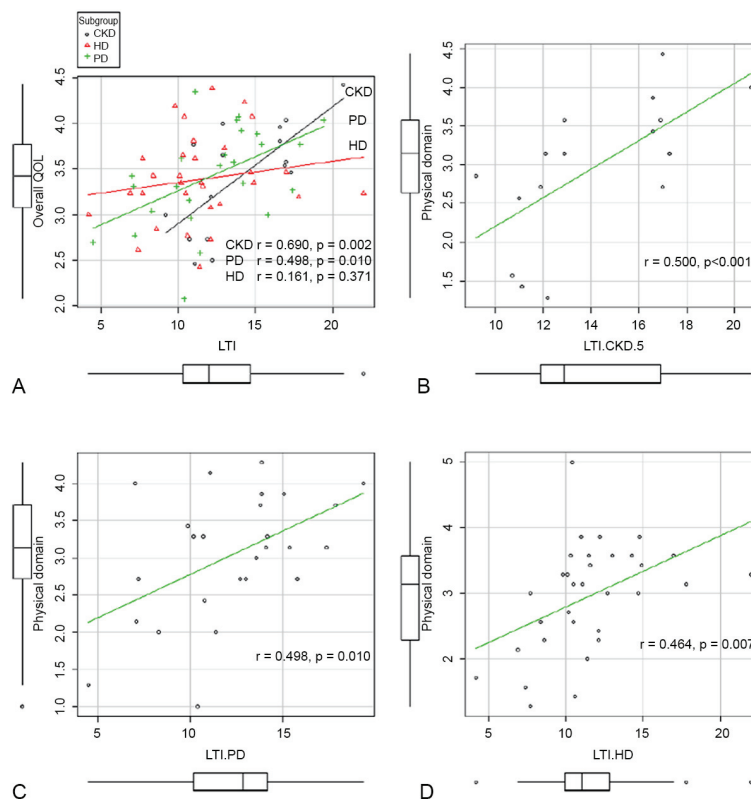
Fig. 1 Correlation between BIS parameters and QOL in ESRD patients.
Panel A show correlation between LTI and overall QOL in all ESRD patients.
Panel B, C and D show correlation between LTI and physical health in CKD-5, PD and HD patients respectively.
CKD-5 = chronic kidney disease stage 5; HD = hemodialysis; PD = continuous ambulatory peritoneal dialysis;
LTI = lean tissue index; QOL = quality of life

general ESRD population as shown by high Charlson comorbidity index. Secondly, as in any observational study, there might be some other unmeasured confounding.

Conclusion

QOL is not different between pre-dialysis CKD-5, PD, and HD patients. Moreover, higher LTI is significantly correlated with better QOL in all ESRD subgroups. Over hydration is associated with lower physical health in HD patients. We suggest that BIS can be used as a tool to evaluate nutritional and fluid status in ESRD patients.

What is already known on this topic?

Malnutrition in ESRD patient is common and it has impact on patient outcome. The number of PD patients in Thailand is increasing but there was no data on nutritional status and QOL in ESRD patients receiving PD or HD.

What this study adds?

Nutritional status and QOL in PD patients were comparable to those of HD and pre-dialysis CKD-5 patients. Health care provider should pay attention to nutritional parameter especially LTI since it is correlated with better QOL in all patient subgroups.

Potential conflicts of interest

None.

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ภาวะโภชนาการกับคุณภาพชีวิตในผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่ได้รับการรักษาก่อนการบำบัดทดแทนไต ล้างไตทางช่องท้อง และฟอกเลือดด้วยเครื่องไตเทียม

สมชาย ยงศิริ, จิรนุช ธรรมคำภีร์, สุริยา โปร่งน้ำใจ, ผกาพรรณ ดินซูไท, รัชนีพร ชื่นสุวรรณ, ศิริพร ตั้งจาตุรนต์รัศมี, เพ็ชรงาม ไชยวาณิช

ภูมิหลัง: ภาวะทุพโภชนาการในผู้ป่วยไตวายเรื้อรังทำให้คุณภาพชีวิตและผลการรักษาแย่ลง การตรวจวัด *body composition model (BCM)* ด้วยเครื่องมือ *bioimpedance spectroscopy (BIS)* สามารถบอกถึงภาวะโภชนาการและสารน้ำในร่างกายได้ดี ยังไม่มีข้อมูลความสัมพันธ์ระหว่าง *BCM* กับคุณภาพชีวิตในกลุ่มผู้ป่วยไตวายเรื้อรังระยะสุดท้าย *(CKD5)* ผู้ป่วยที่ได้รับการบำบัด ทดแทนไตด้วยวิธีฟอกเลือด *(HD)* และล้างไตทางช่องท้อง *(CAPD)*

วัตถุประสงค์: เพื่อเปรียบเทียบภาวะโภชนาการจากการวัดด้วย *BIS* กับคุณภาพชีวิตในผู้ป่วยไตวายเรื้อรังกลุ่มต่างๆ

วัสดุและวิธีการ: ทำการศึกษาภาคตัดขวางผู้ป่วยไตวายเรื้อรังระยะสุดท้ายในโรงพยาบาลมหาวิทยาลัยบูรพา วัด *BCM* ด้วยเครื่องมือ *BCM-Fresenius medical care,* วัดคุณภาพชีวิตด้วย *WHO-QOL-BREF,* เก็บข้อมูลเกี่ยวกับผู้ป่วยจากแฟ้มเวชระเบียน คำนวณหาความแตกต่างระหว่างกลุ่มด้วย *one way ANOVA test* คำนวณหาความสัมพันธ์ระหว่างตัวแปรต่างๆ ด้วย *Pearson correlation test*

ผลการศึกษา: กลุ่มตัวอย่างประกอบด้วยผู้ป่วย *CKD5* 18 ราย *PD* 26 ราย *HD* 34 ราย ทุกกลุ่มมีระดับความรุนแรงของโรค ร่วมวัดด้วย *Charlson's comorbidity index,* การรับประทานอาหาร, ดัชนีมวลกาย, ความดันโลหิต และคุณภาพชีวิตไม่ต่างกัน ผู้ป่วย *HD* ทุกรายมี *weekly Kt/V* ≥3.6 ผู้ป่วย *PD* ทุกรายมี *weekly Kt/V* ≥1.7 ผู้ป่วยกลุ่ม *PD* มีภาวะน้ำเกินมากกว่ากลุ่ม *HD (16.18±11.24 vs. 2.36±11.07 %OH/ECW p<0.0001)* ภาวะน้ำเกินมีผลทำให้คุณภาพชีวิตในกลุ่มผู้ป่วย *HD* แย่ลง *(r = -0.372, p = 0.033)* ผู้ป่วยกลุ่ม *CKD5* มี *lean tissue index (LTI 14.34±3.13 kg/m²)* มากกว่าผู้ป่วยกลุ่ม *PD* *(12.26±3.65 kg/m²)* และ *HD (11.48±3.48 kg/m²) p = 0.023 LTI* ที่สูงขึ้นมีความสัมพันธ์กับคุณภาพชีวิตที่ดีขึ้นอย่าง มีนัยสำคัญในกลุ่ม *CKD5 (r = 0.690, p = 0.002)* และกลุ่ม *PD (r = 0.498, p = 0.010)* ในกลุ่ม *HD* พบว่า *LTI* สัมพันธ์กับ สุขภาพกายที่ดีขึ้นอย่างมีนัยสำคัญ *(r = 0.464, p = 0.007)*

สรุป: ผู้ป่วยไตวายเรื้อรังระยะสุดท้ายทั้ง 3 กลุ่ม มีคุณภาพชีวิตไม่แตกต่างกัน ผู้ป่วย *CKD5* มี *lean tissue index* มากกว่า ผู้ป่วย *PD* และ *HD* ผู้ป่วย *PD* มีภาวะน้ำเกินมากกว่า *CKD5* และ *HD LTI* ที่สูงขึ้นในผู้ป่วยไตวายเรื้อรังมีความสัมพันธ์กับ คุณภาพชีวิตที่ดีขึ้นอย่างมีนัยสำคัญ