CREB Centre de Recerca en Enginyeria Biomèdica
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PhD Thesis

SEGMENTAL AND WHOLE BODY ELECTRICAL IMPEDANCE MEASUREMENTS IN DIALYSIS PATIENTS

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Lexa D. Nescolarde Selva
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To my husband, Paco

To my daughter, Ana

To my brother, Josué

How can you come to know yourself? Never by thinking, always by doing. Try to do your duty, and you'll know right away what you amount to.

Johann Wolfgang von Goethe

Contents

Acronyms

AHD: After hemodialysis.
APD: After peritoneal dialysis.
BHD: Before hemodialysis.
BIA: Body Impedance analysis
BIVA: Bioelectrical Impedance Vector Analysis.
BMI: Body mass index.
BPD: Before peritoneal dialysis.
BP_{mean}: Mean blood pressure.
BSR: Blood sedimentation rate.
CAPD: Continuous ambulatory peritoneal dialysis.
CRI: Chronic renal insufficiency.
CRP: C-reactive protein.
CVD: Cardiovascular disease.
DBP: Distolic blood pressure.
DEXA: X-ray absorptiometry.
DM: Mahalanobis distance.
ECF: Extracellular fluid.
ECW: Extracellular water.
FAT: Fat mass.
FFM: Fat free mass.
HD: Hemodialysis.
HDL-C: High density lipoprotein cholesterol.
ICW: Intracellular water.
iPTH: Intac parthyroid hormone.
LDL-L: Low density lipoprotein cholesterol.
PD: Peritoneal dialysis.
SBIS: Segmental impedance spectroscopy.
SBP: Systolic blood pressure.
TBW: Total body water
Tprot: Total protein.
WBIS: Whole-body impedance spectroscopy.

Summary

The main objective of this thesis is to improve the diagnostic methods based on electrical impedance in dialysis patients. The thesis is structured in three fundamental parts with the following objectives: 1) to establish reference data for Cuban healthy population, 2) to improve the diagnostic based on impedance methods in Cuban hemodialysis patients and 3) to improve the impedance methods for continuous ambulatory peritoneal dialysis patients (CAPD).

For healthy and hemodialysis groups we have used the Bioelectrical Impedance Vector Analysis (BIVA) with measurements of impedance between the wrist and the ankle, also called right-side or whole-body measurements. For peritoneal dialysis patients we have used new indicators based on whole-body measurements and also based on segmental measurements.

Healthy population

The objective of this part of the thesis is to establish bivariate reference intervals for the BIVA method in Cuban population, which is a mixture of several race-ethnicities. We analyzed the impedance vector distribution for the three more representative race-ethnicities in Cuba. Single frequency (50 kHz), tetrapolar (hand-foot), impedance measurements (resistance, R, and reactance, Xc, vector components) were obtained. The impedance components were standardized by the height H of the subjects, (R/H and Xc/H) to obtain de impedance vector Z/H, which is represented in the RXc-graph (abscise R/H, ordinate Xc/H). We measured 1196 healthy adult subjects living in Santiago de Cuba (689 men, 507 women, 18-70 yr, BMI 19-30 kg/m^2) with a BioScan (model BL-960141, Spain). The 95% confidence ellipses were drawn using specific BIVA software for mean vectors of different races according to the RXc-graph. This pattern allows the construction of one set of sex and race specific tolerance ellipses (e.g. 50%, 75%, and 95%) to be used in the clinical setting for the evaluation of body composition of individual subject's vectors. Due to the close distribution of mean vectors, we found for the three race-ethnicities, that only one set of sex-specific tolerance ellipses can be used at the bedside, which simplifies the analysis.

Hemodialysis patients

In this part of the work, the Bioelectrical Impedance Vector Analysis (BIVA) method is used in a sample of hemodialysis patients in stable, (without edema) and critical, (hyper-hydrated and malnutrition) states, in order to establish the relation between hyperhydration (oedema) and mortality. Measurements were performed on a sample of 74 patients (30 men and 44 women, 18-70 year, Body Mass Index (BMI), 19-30 kg/m^2) at the Saturnino Lora University Hospital in Santiago de Cuba. The 74 patients were classified in 46 stables (28 men and 18 women) and 28 critical (16 men and 12 women). We used the reference population measured previously. Student's t test and Hotelling's T^2 test were used to analyse the separation of groups obtained by means of clinical diagnosis and those obtained by BIVA. We obtained a significant difference ($P < 0.05$) in R/H, Xc/H and phase angle (PA) in men as in women between the location of Z/H vectors in the RXc-graph and the separation made by the doctors between stable and critical patients. Critical (hyper-hydrated and malnutrition) patients were located below the inferior pole of the 75% tolerance ellipse, whereas stable patients were within the tolerance ellipses. Some cases classified as stable by the clinic were classified as hyper-hydrated by BIVA with 100% sensitivity and 48% specificity. In conclusion, the BIVA method could be used to detect hyper-hydration state before edema appears, and to predict survival through PA. Advantages of the method are its simplicity, objectivity and that it does not require the definition of a patient dry weight.

Continuous Ambulatory Peritoneal Dialysis patients (CAPD)

The whole-body bioimpedance technique holds promise as a non-invasive, fast and inexpensive bed-side method to monitor hydration status. Using segmental bioimpedance measurement we can get information about the fluid change in each body segment. In this pilot study we have measured 25 male patients (30-65 yr, BMI 20-32 kg/m^2) undergoing continuous ambulatory peritoneal dialysis (CAPD). Tetrapolar segmental (longitudinal and transversal) impedance measurements were obtained using 9 configurations (7 longitudinal and 2 transversal). Measurements were taken in the morning, before a fluid exchange, and after complete drainage of the abdominal cavity in all male patients undergoing CAPD at the Service of Nephrology of the Fundaciò Puigvert (Barcelona, Spain). For the

fist study we analyzed Z, Z/H and ZBMI index. 23 male patients were classified according to the hydration state as normo-hydrated (group 0) or hyper-hydrated (group 1). Group 0 includes 10 patients (55.6 ± 10.5 yr, BMI 24.0 ± 1.9 kg/m2). Group 1 includes 13 patients (56.6 ± 9.0 yr, BMI 29.5 ± 1.7 kg/m2). Wilcoxon test was used to analyze the change in impedance (longitudinal and transversal) produced by a session of peritoneal dialysis (APD-BPD). Mann-Whitney U test was used to analyse the separation between groups obtained by means of clinical diagnosis and those obtained by Z, Z/H or ZBMI. Statistical significance was set at $P < 0.05$. Spearman correlation was used to study the correlation between Z, Z/H, ZBMI vectors in each segment, with clinical assessment. This study show that the term Z is more sensible to detect changes APD-BPD that if we used other terms such as Z/H or ZBMI. The use of ZBMI is not a good index for the detection of fluid changes because it gives information about the specific resistivity of tissues and not to fluid and fat mass changes; this is only true for a cylindrical geometry. The transversal measurements in the leg region and in the thorax region could be useful to corroborate the hydration and nutritional state in CAPD patients. We confirm that the BIVA method (Z/H, righ-side measurements) in CAPD patients could be useful to separate hyper-hydrated patient (in whole-body) and normo-hydrated patients. To apply at the same time BIVA and transversal measures, could be an alternative method to know the hydric and nutritional state in CAPD patients.

In the second study we incorporated two new male patients. A new classification was performed. Group 0 has normo-hydrated patients and group 1 has varying degrees of hypertension, overhydration, and high score on cardiovascular risk factors (e.g. increased left ventricular mass LVM, increased cholesterol, homocysteine levels, etc). Group 0 includes 10 normo-hydrated patients (52.8 ± 9.6 yr, BMI 24.5 ± 1.9 kg/m^2). Group 1 includes 15 hyper-hydrated leading to hypertesion patients (55.3 ± 9.8 yr, BMI 29.1 ± 3.7 kg/m^2). The Mahalanobis Distance (dM^2) was calculated for the mean blood pressure (BP_{mean}) and the impedance parameter R normalized by body height H for the right-side (R_{RS}/H) and the thorax segment (R_{TH}/H). Hotelling's T^2 test was used to analyzed difference between groups (0 and 1) through (R_{TH}/H, BP_{mean}) and (R_{RS}/H, BP_{mean}) vectors. We obtained a significant difference ($P < 0.05$) in both vectors. Mann-Whitney U-test was used to compare the differences in clinical measurements, laboratory test,

and bioimpedance measurements (Right-Side (R_{RS}/H) and thorax (R_{TH}/H)) between groups (0 and 1). Statistical significance was set at $P<0.05$. Differences between groups were significant ($P<0.0001$) for R_{TH}/H and for BP_{mean} and less significant ($P=0.016$) for R_{RS}/H. Group 1 patients showed a small dM^2 with respect to a reference patient (a critical patient with acute lung oedema) with high BP_{mean} and low values of R_{TH}/H and R_{RS}/H. Moreover, Group 0 patients showed a larger dM^2 with respect to the reference patient with lower BP_{mean} and higher values of R_{TH}/H and R_{RS}/H. All patients classified as hyper-hydrated leading to hypettension by clinical assessment were correctly classified using R_{TH}/H in conjunction with BP_{mean} *using* dM^2. In conclusion, segmental-monofrequency non-invasive bioimpedance of the thoracic region could be a simple, objective, non-invasive method of support to facilitate the clinical assessment of CAPD patients.