Bioelectrical impedance analysis as a marker of nutritional status in chronically ill patients

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KEYWORDS

nutritional risk, albumin, phase angle, chronic disease.

ABSTRACT

Objective
The aim of the study was to evaluate different methods of nutritional status analysis like basic anthropometric data, laboratory data and bioelectrical impedance analysis (BIA) with phase angle (PA) in patients with chronic diseases.

Setting
Clinic for Internal Medicine, Department of Nephrology, University Clinical Centre Maribor, a tertiary referral centre in Slovenia, Europe.

Subjects
Patients with chronic disease and increased nutritional risk (≥1 fulfilled NRS 2002 criterion) at the time of inclusion in the study.

Results
Patients had chronic kidney disease (93%), arterial hypertension (80%), active infection (33.3%), heart failure (23.3%), diabetes mellitus (20%), active malignancy (10%), autoimmune disease (6.6%), history of stroke (6.6%), chronic obstructive pulmonary disease (3.3%) and/or liver cirrhosis (3.3%). Mean serum albumin was 33.6±5.7 g/L, mean BMI 25.6±4.4 kg/m2 and mean PA 4.4±1.2°. No correlation between serum albumin and BMI was found. Lower PA was associated with lower serum albumin (p=0.045) and advanced age (p=0.043). The department nurses conducted nutritional education for all patients included in the study. Study was performed in accordance with the Strengthening the reporting of observational studies in epidemiology.

Conclusion
Results of the study show the importance of nutritional risk assessment in all chronically ill patients. BIA is a promising method of determining nutritional status. PA values have important diagnostic, therapeutic and prognostic implications as they are a marker of body cell mass, membrane function and metabolic health. A multifaceted approach to assess malnutrition in patients with chronic diseases is important, followed by a prompt nutritional intervention.

INTRODUCTION

Malnutrition is a general term indicating a state of nutrition in which a deficiency, excess or imbalance of energy, protein and other nutrients causes adverse effects on body composition, function and clinical outcome (Poulia et al 2012). It can be the result of poor nutritional intake, impaired utilisation or loss of nutrients, or may stem from several acute or chronic diseases. Malnutrition affects 7-16% of patients out of hospital (Leistra et al 2009) and is even more common in hospitalised patients (Leistra et al 2013). Additionally, nutritional status often deteriorates during a hospital stay (Allard et al 2016), which leads to higher rates of complications, increased morbidity and mortality (Kyle et al 2013; Poulia et al 2012).

The first step to successfully treat malnutrition is the appropriate diagnosis. To recognise patients at risk, several screening tools have been proposed. The Nutritional Risk Screening 2002 (NRS-2002) is the tool proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN). It includes four questions about the following parameters: body mass index (BMI) <20.5 kg/m2, presence of weight loss in the past three months, presence of low dietary intake in the past week and the severity of illness. A positive response to any of these questions warrants further nutritional assessment (Poulia et al 2012).

Nutritional status can be assessed by several different methods. Most clinicians currently rely on global clinical assessment and anthropometric parameters, such as body weight, height, waist circumference, and BMI. There are several laboratory parameters which can be used to assess nutritional status, most commonly serum albumin level (Bharadwaj et al 2016). These parameters give us no information on body composition and have therefore several limitations to their application. More advanced modalities on nutritional status assessment and body composition analysis include imaging techniques, such as density assessment, anthropometry, dual energy X-ray absorptiometry (DEXA), computed tomography (CT), magnetic resonance imaging (MRI), nuclear magnetic resonance (NMR) spectroscopy or the use of isotopes. These are, however, expensive, time consuming, and in most hospitals, unavailable for routine use (Jones et al 2009).

Body impedance analysis (BIA) is the most commonly used method to calculate body composition due to its high accuracy, safety, portability and low cost. It provides information on fat mass, muscle mass and hydration status, which is especially useful in chronic kidney disease (CKD) and heart failure patients. It is based on the principle of bioelectrical impedance (the vector sum of resistance and reactance). Although monofrequency BIA (50 kHz) has been the most used method to date, multi-frequency BIA (5-100 kHz) has arisen as a method with more developed and complex theoretical bases, giving us better information on the distribution of water between intra- and extracellular spaces (Caravaca et al 2011).

Phase angle (PA) value determined by BIA is an indicator of cell membrane damage and body cell mass (Varan et al 2016). Higher values represent higher cellularity, cell membrane integrity and better cell function (Norman et al 2012). In healthy subjects, age and gender are the major determinants of PA (Zhang et al 2014). Since it is based on body cell mass, it can be used as an excellent reference for several physiological processes, including energy expenditure and proteolysis. Recent studies have shown that lower levels of PA are associated with increased nutritional risk, higher morbidity and mortality in chronic diseases, cancer and surgical patients (Varan et al 2016; Mushnick et al 2003).

The aim of this study was to use different methods of nutritional status analysis, including basic anthropometric data, laboratory data and BIA with PA in patients with different chronic diseases, who were at risk for malnutrition according to the NRS 2002 screening tool.

STUDY DESIGN AND METHODS

Thirty patients that were hospitalised in the Department of Nephrology, Clinic for Internal Medicine of University Clinical Centre Maribor, in a three-month period (November 1 2016 - January 31 2017), were included in the study.

Patients were mostly admitted from the internal medicine emergency department, some were transferred from other departments and hospitals. The inclusion criteria were increased nutritional risk (≥1 fulfilled NRS 2002 criterion) at the time of admission to the hospital and the presence of at least one chronic disease prior to the hospital admission. Institutional electronic information system was used to check patients' previous chronic diseases. The most common comorbidity was CKD (stages 1-5), including those on renal replacement therapy. Other observed chronic diseases were arterial hypertension, diabetes mellitus, heart failure, chronic obstructive pulmonary disease, liver cirrhosis, malignant disease, autoimmune disease, a history of stroke and/or the presence of an active infection. All patients were given written informed consent before inclusion in the study.

The study was performed in accordance to the STROBE guidelines (STrengthening the Reporting of OBservational studies in Epidemiology). The study was approved by the University Clinical Centre Maribor ethics committee. Informed consent was obtained from each patient.

BMI and BIA parameters, such as muscle mass, fat mass and PA, were used in the nutritional assessment of included patients. To perform bioelectrical impedance, multi-frequency segmental body composition analyser *Tanita, MC780*® (Croatia) was used. The apparatus has a measuring platform which requires standing position of the subject for correct measurement. Patients unable to walk or stand were therefore excluded from the study due to their inability to stand on the measuring platform. The measurements were made on an empty stomach, between 8-12 AM, by the department nurses.

Glomerular filtration rate (GFR) was estimated by using the Chronic Kidney Disease Epidemiology Collaboration equation. By drawing peripheral venous blood, standard laboratory data, such as serum creatinine, haemoglobin, albumin and C-reactive protein (CRP) levels were measured.

Statistical analysis was performed using the SPSS Statistics 22 for Windows. The data was expressed as means ± standard deviations or percentages. Associations between different methods of nutritional status analysis data were tested by the Spearman's correlation coefficient. A p-value < 0.05 was considered statistically significant.

RESULTS

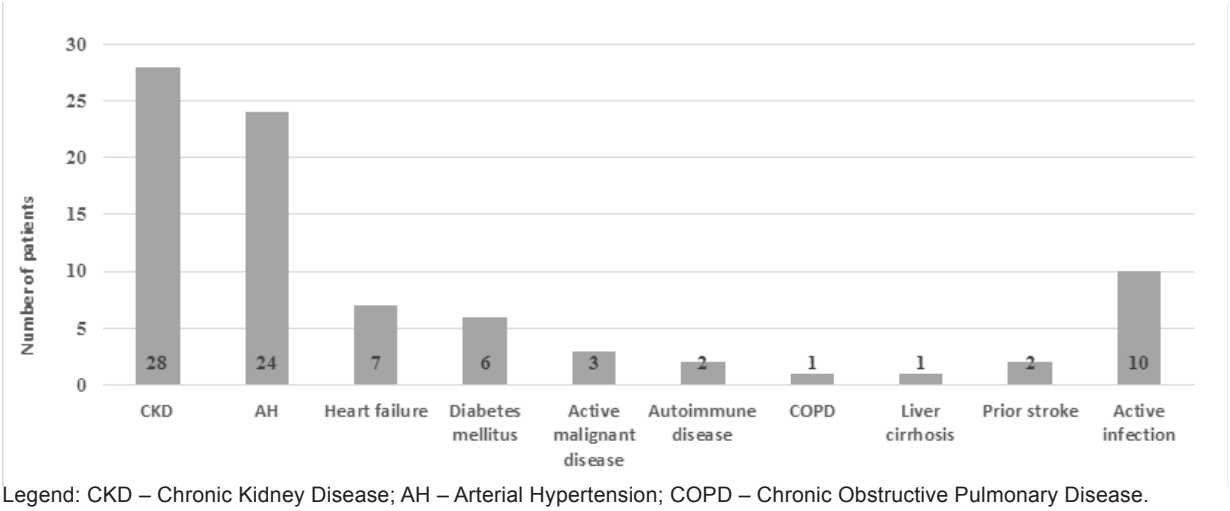
Thirty patients were included in the study, most of them were male (20/30, 66.7%). Their average age was 70.8±17.2 years. Nearly all of them had one fulfilled NRS-2002 criterion (28/30; 93.3%), two patients (6.7%) had two or three fulfilled NRS-2002 criteria, respectively.

All of them had at least one concomitant chronic illness, most commonly CKD (28/30; 93.3%). Mean serum creatinine was 172.1±85.7 μmol/L, mean estimated GFR was 53.4±26 ml/min/1.73 m2. One patient was on haemodialysis for seven years prior to the study (1/30; 3.3%). The second most common concomitant chronic disease was arterial hypertension (24/30; 80%), followed by heart failure (7/30; 23.3%) and diabetes mellitus (6/30; 20%). Active malignant disease was present in three patients (10%), two of them had colorectal adenocarcinoma, and one had a prostate adenocarcinoma. One patient with colorectal carcinoma was in-between cycles of chemotherapy; none of the other patients were receiving radiotherapy or other oncological treatment regimens at the time of the study. Autoimmune disease was present in two patients (6.6%), both

had systemic lupus erythematosus. Chronic obstructive pulmonary disease and liver cirrhosis were observed in one patient (3.3%). Two patients had a history of a cerebrovascular event prior to the inclusion in the study (6.6%). Most of the patients had no active infection at the time of the study (20/30; 66.7%). Those with an infection had an inflammation of the biliary tract (5/10; 50%), a respiratory tract infection (4/10; 40%) or an upper urinary tract infection (1/10; 10%).

Most common comorbidities of included patients and basic descriptive statistics are shown in tables 1 and 2.

Table 1: Comorbidities of included patients.



Legend: CKD – Chronic Kidney Disease; AH – Arterial Hypertension; COPD – Chronic Obstructive Pulmonary Disease.

Table 2: Basic descriptive statistics of included patients.

Parameter	Minimum value	Maximum value	Mean value ± SD
Age (years)	31	94	70.8 ± 17.2
NRS 2002	1	3	1,1 ± 0.4
Serum creatinine (µmol/L)	62	763	172.1 ± 185.7
eGFR (CKD-EPI equation; ml/ min/1.73 m2)	6	90	53.4 ± 26
Serum haemoglobin (g/L)	82	152	115 ± 19.4
CRP (mg/L)	3	359	52.2 ± 83.6
Albumin level (g/L)	17.8	44.4	33.7 ± 5.7
BMI (kg/m2)	18	35	25.6 ± 4.4
Fat mass (kg)	3	29	16.9 ± 7.7
Muscle mass (kg)	34	72	53.5 ± 10.4
Phase angle (°)	3	7	4.4 ± 1.2

Legend: SD – standard deviation; NRS – nutritional risk screening; eGFR – estimated glomerular filtration rate; CKD-EPI equation - Chronic Kidney Disease Epidemiology equation; CRP – C-reactive protein; BMI – Body Mass Index.

Mean serum albumin was 33.7±5.7 g/L, mean BMI was 25.6±4.4 kg/m2, mean fat mass was 16.9±7.7 kg, mean muscle mass was 53.5±10.4 kg and mean PA was 4.4±1.2° (table 2). No correlation between serum albumin and BMI was found. There was also no significant correlation between muscle mass, fat mass and serum albumin. Higher fat mass and muscle mass were associated with higher BMI ($p<0.0001$). Lower PA was associated with lower serum albumin ($p=0.045$) and advanced age ($p=0.043$), however, no correlation was found between muscle mass, fat mass, BMI and phase angle values.

All the patients in the study, and their relatives where possible, received nutritional education by the department nurses.

DISCUSSION

Chronic illnesses and advanced age are the most important risk factors for malnutrition (Correia et al 2014). Several studies have shown correlation between malnutrition and CKD (Muscaritoli et al 2009), severe heart failure (Rahman et al 2016; Amare et al 2015) and liver disease (Purnak and Yilmaz 2013). It is estimated that nearly half of patients with malignant disease develop a syndrome of cachexia, with anorexia, progressive loss of adipose tissue and skeletal muscle mass (Aoyagi et al 2015). Several autoimmune diseases are linked to progressive wasting, especially autoimmune thyroid disease (Kawicka and Regulska-Ilow 2015). Patients with advanced chronic obstructive pulmonary disease are in a state of undernutrition, referred to as pulmonary cachexia (Itoh et al 2013). Patients who suffered stroke are likely to develop malnutrition during the acute phase of the stroke, and later during the rehabilitation stage of the disease (Bouziana and Tziomalos 2011). Muscle mass wasting is a hallmark of diabetes mellitus as well (Chevalier and Farsijani 2014). Protein-energy malnutrition is an independent risk factor predicting decreased length of overall survival and survival at home in geriatric patients (Correia et al 2014). Studies have repeatedly shown that clinical malnutrition is generally associated with increased morbidity and mortality both in acute and chronic illnesses. Longer length of hospital stay and higher treatment costs are reported in malnutrition. Since it has been demonstrated that proper nutritional care can reduce the prevalence of hospital malnutrition and costs, nutritional assessment is mandatory to recognise malnutrition early and initiate timely nutritional therapy (Norman et al 2008).

The BIA is one of the newer techniques for determining body composition and nutritional status. It is especially useful in patients with disturbed hydration and/or altered distribution of extra - and intracellular water, which is the case in many chronic illnesses (for example CKD, liver cirrhosis, heart failure and obesity). The most clinically established impedance parameter is the PA. The PA differs across categories of sex and age. In patients over 70 years old, the normal PA is approximately 5.5° in women (5.6±1.0°) and 6° in men (6.2±1.0°) (Barbosa-Silva et al 2005). Included patients were older adults (average age 70.8 years) and had several comorbidities. The study was performed at the Nephrology department were the most common concomitant illness was CKD. All patients were at increased nutritional risk (≥1 fulfilled NRS criterion). Their lower PA values (average 4.4, range from 3°, to 7°) are therefore understandable.

Lower PA values are associated with adverse prognosis in several diseases. Gupta et al (2004a) evaluated 52 patients (aged 29-79 years) with colorectal carcinoma and concluded that PA values were better at predicting survival than nutrition assessment methods commonly used in clinical practice. In another study, Gupta et al (2004b) confirmed the importance of PA as a prognostic indicator in patients with pancreatic cancer. Abad et al (2011) evaluated 164 dialysis patients (127 on hemodialysis and 37 on peritoneal dialysis) and found that PA is a good predictor of long-term survival in dialysis patients.

According to Araujo Antunes et al (2012), higher values of PA were prognostically favourable in HIV positive patients. In patients with liver cirrhosis, low PA values were associated with shorter survival times, according to a study by Belarmino et al (2017).

Authors, Varan et al (2016), performed a cross sectional study on 120 older adults (average age 75±7.27 years; mean PA 4.2±1.8°) and found statistically significant correlation between lower PA and higher malnutrition risk. According to their data, PA correlated with serum albumin and advanced age, which is similar to this study, where statistically significant correlation between PA and albumin level and between lower PA and advanced age was found.

Since PA and albumin level is influenced by the intracellular to extracellular water ratio, the lower values seen in older patients and in those with several chronic illnesses are thought to reflect a reduction in skeletal mass and hence intracellular water which may be compounded by oedema/extracellular accumulation with aging and poor health (Kyle et al 2012). According to Perna et al (2014), lower PA is linked to reduced relative muscle mass in the elderly. The results of the presented study did not confirm this, as no statistically significant correlation between PA and muscle mass was found. This is most likely due to a small sample size and different measuring technique used in their study (BIA vs Dual Energy X-Ray Absorptiometry - DXA).

No statistically significant correlation between serum albumin and muscle mass was found. Serum albumin is a potential marker of nutritional risk, but it is non-specific and can be reduced in several other conditions, such as in response to physiological stress, in CKD, liver disease and inflammation. Limited longitudinal research available on this topic questions the use of serum albumin measures for this purpose (Snyder et al 2012).

BIA is a promising method of determining fluid balance, nutrition status and it can also be used as a prognostic tool in patients with several chronic illnesses. By providing us with information on body composition it by-passes several weaknesses of other commonly used tools, such as BMI. In the future, more work should be done on detecting patients at risk for malnutrition. Patients at risk should be monitored more closely and they should also undergo nutritional education and if indicated, receive dietary supplements. Studies have shown that prompt intervention can decrease the rate of protein-energy wasting and have favourable prognostic implications (Ocepek et al 2017). There are not enough dietitians and nutritionists available to serve the entire healthcare industry. Nurses therefore play a very important role in nutritional risk assessment, education and in a potential intervention. They are an integral part of patient care, including nutritional assessment and should be properly educated in this field of practice (Henning 2009).

The presented study has several limitations. It is a small, single centre, cohort study, which was performed in only one out of several internal medicine departments in University Clinical Centre, Maribor. The study was performed in a Nephrology department, patients with CKD were therefore over-represented in the sample of included patients.

Patients unable to walk or stand, who are especially at risk for muscle wasting, were not included in the study due to the BIA measurement requirements. The study, however, also has some important advantages. It is one of the first studies researching the role of BIA in this part of Europe and it highlights the importance of nutritional status assessment by using different diagnostic modalities. All the patients in the study received nutritional education, performed by trained nurses. Due to the importance of social support, patients' relatives were also part of the nutritional education. Further monitoring, additional nutritional risk assessment and potential therapeutic interventions of the patients will be done through outpatient clinics.

CONCLUSION

Nutritional risk assessment should be made on all patients with chronic diseases. Currently, the best way is a multifaceted approach, including measuring body weight, height, BMI, serum albumin and performing a body composition analysis. PA values have important diagnostic, therapeutic and prognostic implications. Patients at risk and their relatives if possible should undergo nutritional education by trained professionals. Common reassessments of the nutritional status and prompt intervention in case of increased nutritional risk are important in all chronically ill patients.

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