INTRODUCTION

Worldwide, an estimated 644,000 new cases of H&NC are diagnosed each year, with two-thirds of these cases occurring in developing countries (1). In the United States, H&NC accounts for 3.2% (39,750) of all new cancers and 2.2% (12,460) of all cancer deaths (2). Malnutrition is common in patients with H&NC. Nutritional deficits have a significant impact on mortality, morbidity and quality of life in patients with H&NC (3).

Methods or tools designed to measure and monitor nutritional status can play a dynamic role in the recovery and quality of life for this patient population. Bioelectrical impedance analysis (BIA) detect changes in tissue electrical properties. The study was conducted to evaluate soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by bioelectrical impedance vector analysis in patients with head and neck cancer. Whole-body measurements were made with ImpediMed bioimpedance analysis in 56 adult, white, male subjects 42 to 79 years old: 28 patients with head and neck squamous cell carcinoma (H&NC) and 28 healthy volunteers matched by sex, age and BMI as a control group. All patients were previously untreated and without active nutritional interventions. Mean vectors of H&NC group vs. the control group were characterized by an increased normalized resistance component with a reduced reactance component (separate 95% confidence limits, P<0.05), indicating a decreased ionic conduction (dehydration) with loss of dielectric mass (cell membranes and tissue interfaces) of soft tissue. Monitoring vector displacement trajectory toward the reference target vector position may represent useful feedback in support therapy planning of individual patients before surgery in patients with head and neck cancer in order to reduce post-operational complications.

Key words: bioelectrical impedance analysis, bioelectrical impedance vector analysis, body composition analysis, cancer, squamous cell carcinoma

INTRODUCTION

BIOIMPEDANCE VECTOR PATTERN IN HEAD AND NECK SQUAMOUS CELL CARCINOMA

Direct bioimpedance measures (resistance, reactance, phase angle (PA)) determined by bioelectrical impedance analysis (BIA) detect changes in tissue electrical properties. The study was conducted to evaluate soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by bioelectrical impedance vector analysis in patients with head and neck cancer. Whole-body measurements were made with ImpediMed bioimpedance analysis in 56 adult, white, male subjects 42 to 79 years old: 28 patients with head and neck squamous cell carcinoma (H&NC) and 28 healthy volunteers matched by sex, age and BMI as a control group. All patients were previously untreated and without active nutritional interventions. Mean vectors of H&NC group vs. the control group were characterized by an increased normalized resistance component with a reduced reactance component (separate 95% confidence limits, P<0.05), indicating a decreased ionic conduction (dehydration) with loss of dielectric mass (cell membranes and tissue interfaces) of soft tissue. Monitoring vector displacement trajectory toward the reference target vector position may represent useful feedback in support therapy planning of individual patients before surgery in patients with head and neck cancer in order to reduce post-operational complications.

Key words: bioelectrical impedance analysis, bioelectrical impedance vector analysis, body composition analysis, cancer, squamous cell carcinoma
impedance vectors from adult male patients with H&NC differed from healthy male age- and BMI-matched control subjects.

MATERIALS AND METHODS

Study design

This study investigated whether the position on the R-Xc plane of impedance vectors from adult male patients with H&NC differed from healthy male age- and BMI-matched control subjects. No interventions were made based on the impedance data of patients.

This study was conducted according to the guidelines set forth in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by the Research Ethics Committee of the Medical University of Lublin, Poland. All patients gave their written informed consent as a precondition of participation in the study.

Study population

Between October 2009 and May 2010 56 subjects underwent examination of tissue electrical properties. Twenty-eight pre-surgical male patients with H&NC were examined between the ages of 42 and 79 years old. The histological diagnosis of these patients was squamous cell carcinoma (SCC). This study included 12 patients with laryngeal SCC, 9 patients with oropharyngeal SCC, 6 patients with oral cavity SCC, 2 patients with hypopharyngeal SCC and 1 patient with nasal cavity SCC. All patients were treated at the Otolaryngology Department, Head and Neck Oncology, of the Medical University of Lublin. Twenty-eight healthy male subjects from the same region matched by age and BMI were selected as the control group for this study. The group of patients with H&NC underwent a baseline nutritional assessment, which included laboratory measurements of serum albumin, transferrin and total protein, subjective global assessment (SGA) and BIA. The control group underwent a baseline nutritional assessment, which included SGA and BIA.

Bioimpedance

BIA was performed by a medical doctor using ImpediMed bioimpedance analysis SFB7 BioImp v1.55 (Pinkenba Qld 4008, Australia). BIA was performed after a 10 minute rest period while the patients were lying supine on a bed, with their legs apart and their arms not touching their torso. All evaluations were conducted on the patients' right side by using the 4 surface standard electrode (tetra polar) technique on the hand and foot. R and Xc were measured directly in ohms at 5, 50, 100, 200 kHz. R and Xc values were measured three times in each patient, and the mean values were used. PA was obtained from the arctangent ratio Xc/R. To transform the result from radians to degrees, the result that was obtained was multiplied by 180°/π.

Bioelectrical impedance vector analysis

According to the RXc graph method (27) measurements of R and Xc were standardized by the H subjects (i.e., R/H and Xc/H) and expressed in ohms per meter. By using the bivariate normal distribution of R/H and Xc/H, we calculated the bivariate 95% confidence limits for mean impedance vectors of cancer patients and healthy subjects (i.e., the limit containing the magnitude and the phase angle of the mean vectors with 95% probability). Two mean vectors, from two independent groups of subjects, were compared with the two-sample Hotelling’s T² test. Separate 95% confidence limits indicate a statistically significant difference between mean vector positions on the R-Xc plane, i.e., in their R/H, Xc/H, or both components or in their magnitude, phase angle or both (P<0.05, which is equivalent to a significant Hotelling T² test) (27).

Statistical methods

Our results are expressed as mean±S.D. The Shapiro-Wilk (S-W) test was used to assess the distribution conformity of examined parameters with a normal distribution; the Fisher (F) test was used to assess variance homogeneity. For group comparisons of metric data we used the Mann-Whitney-U-test. A p value <0.05 was considered statistically significant. The

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (H&amp;NC patients)</th>
<th>Value (control group)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (y)</td>
<td>57.0±7.26</td>
<td>56.5±13.62</td>
<td>NS</td>
</tr>
<tr>
<td>Subjective Global Assessment (SGA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well-nourished:</td>
<td>17 (61)</td>
<td>31 (100)</td>
<td></td>
</tr>
<tr>
<td>Moderately malnourished:</td>
<td>9 (32)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Severely malnourished:</td>
<td>2 (7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>22.8±5.0</td>
<td>23.4±2.26</td>
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<tr>
<td>Height (cm)</td>
<td>172.6±7.02</td>
<td>171.5±6.18</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.96±14.89</td>
<td>69.32±8.81</td>
<td>NS</td>
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<tr>
<td>Serum albumin (g/dL)</td>
<td>4.0±0.37</td>
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<tr>
<td>Total protein (mg/dL)</td>
<td>6.97±0.63</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Serum transferrin (mg/dL)</td>
<td>201.39±40.01</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>R at 50 kHz (ohm)</td>
<td>590.1±98.81</td>
<td>538.5±51.77</td>
<td>0.04</td>
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<tr>
<td>R/H (ohm/m)</td>
<td>342.54±59.96</td>
<td>314.52±33.26</td>
<td>NS</td>
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<td>Xc at 50 kHz (ohm)</td>
<td>47.54±7.32</td>
<td>51.75±7.9</td>
<td>0.03</td>
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<tr>
<td>Xc/H (ohm/m)</td>
<td>27.62±4.72</td>
<td>30.19±4.59</td>
<td>0.02</td>
</tr>
<tr>
<td>Phase angle at 50 kHz (°)</td>
<td>4.67±0.74</td>
<td>5.49±0.71</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table 1. Baseline characteristics of the H&NC patient and control group; n=28.
The observed impedance pattern indicated altered electrical properties of tissue, presumably of the body cell mass, because the Xc component of the impedance vector is determined mainly by dielectric properties of cell membranes of soft tissue (21-25). In our group of patients a pure disorder of soft tissue hydration can not be ruled out because the R component of the impedance vector was increased in comparison with the control group. Indeed, as documented in the literature, impedance vectors were longer and steeper in dehydration (e.g., after fluid removal by hemodialysis) (26-28). In our small study population of H&NC patients, we observed that there was a smaller distribution of water between the extra and intra cellular compartments, and that there was a greater resistance of electric current due to the smaller distribution of water in these patients. The hypothesis of altered tissue structure due to alterations induced by cancer is also consistent with findings by Kadar and colleagues (29).

The clinical usefulness of early detection of cancer metabolic activity independent of tumor mass would be determined by an increased precision of prognosis and the identification of subjects at risk for malnutrition and subsequent cancer cachexia, which can be useful in the tailoring of therapy. Our SGA results indicated that 61% of this group was well-nourished, 32% was moderately malnourished and only 7% was severely malnourished. When one considers all available information from BIA, real malnutrition may be obscured by the subjectivity of SGA, and BIA may be a more sensitive measure of the nutritional status of cancer patients.

To the best of our knowledge, this is the first study to evaluate soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by bioelectric impedance vector analysis among pre-surgical H&NC patients. Our study was largely restricted to newly diagnosed patients (only 4 patients had previous treatment history). The results observed in our study provide valuable information on the nutritional status of the patient prior to surgery. Other methods of assessing nutritional status in this patient population, such as SGA, may not be sensitive enough to determine a deficiency. In our opinion, further research with a larger sample size could support our results, provide an avenue for early nutritional intervention and corrective nutritional replacement, ultimately combined with oncology intervention leading to increased survival in this patient population (30). Previous studies, such as a study by De Luis DA. et al. (31) were conducted on a population of Spanish ambulatory post-surgical male patients. However, there was not an evaluation of soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by BIVA. Their study did not indicate how long after the surgical procedure the BIA measurements were taken. The difference in the time period of performing BIA measurement is significant as post-operative patients may experience a rapid improvement in nutritional status.

Evaluating soft tissue hydration and mass through pattern analysis of vector plots as height, normalized resistance, and reactance measurements by bioelectric impedance vector analysis among pre-surgical H&NC patients can provide a quick, simple and reproducible means to determine nutritional status. This quick assessment of the nutritional status of the patient can allow for early corrective intervention.

CONCLUSION

Pre-surgical patients diagnosed with H&NC have altered tissue electrical properties. Prospective outcome prediction and volume status assessment are difficult tasks. Rapidly available, non-invasive, bioelectric impedance vector analysis may offer objective measures to improve clinical decision-making and predict...
outcomes. Monitoring vector displacement trajectory toward the reference target vector position may represent useful feedback in support therapy planning of individual patients before surgery in patients with H&NC patients in order to reduce post-operational complications due to malnutrition. Further observations of a larger patient group would be valuable to monitor nutritional and therapeutic interventions in this patient population.

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REFERENCES

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