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Basal Energy Expenditure measured by indirect calorimetry in patients with squamous cell carcinoma of the esophagus

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Abstract

Background: Determination of Basal Energy Expenditure (BEE) is essential for planning nutritional therapy in patients with esophageal cancer. Aims: The objective of this study was to determine BEE through indirect calorimetry (IC) in patients with squamous cell carcinoma of the esophagus (SCC).

Methods: Cross-sectional study involving 30 patients admitted with a diagnosis of SCC who underwent IC before starting cancer therapy. The BEE was evaluated using IC and also estimated by means of the Harris-Benedict Equation (HBE). Nutritional assessment was conducted using anthropometric parameters (body mass index, arm circumference, triceps skinfold thickness, arm muscle circumference, and weight loss), biochemical parameters (albumin, transferrin and C-reactive protein) and tetrapolar bioimpedance to assess body composition (fat free mass). Additionally, lung capacity was measured and clinical staging of the cancer established by the TNM method.

Results: The mean of the BEE for IC and Harris-Benedict Equation were 1421.8 ± 348.2 kcal/day and 1310.6 ± 215.1 kcal/day, respectively. No association was found between BEE measured by IC and clinical staging (p=0.255) or the Tiffeneau Index (p=0.946). There were no significant associations between BEE measured by IC and altered dosages of transferrin, albumin and C-reactive protein (p=0.364, 0.309 and 0.780 respectively). The factors most associated with BEE were BMI and fat free mass.

Conclusion: The BEE of patients with SCC was underestimated when using the HBE, and the result overestimated when incorporating an injury factor with the HBE. Therefore, despite the practical difficulties of implementing IC, its use should be considered.

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Key words: Esophageal cancer. Indirect calorimetry. Basal energy expenditure.

Resumen

Antecedentes: La determinación del gasto energético basal (GEB) es esencial para la planificación de la terapia nutricional en pacientes con cáncer de esófago.

Objetivos: El objetivo de este estudio fue determinar GEB por calorimetría indirecta (CI) en pacientes con carcinoma de células escamosas del esófago (CCS).

Métodos: Estudio transversal con 30 pacientes ingresados con el diagnóstico de CCS que se sometieron CI antes de iniciar la terapia contra el cáncer. La abeja se evaluó con CI y estimó por medio de la ecuación de Harris-Benedict (EHB). La evaluación nutricional se realizó utilizando los parámetros antropométricos (índice de masa corporal, circunferencia del brazo, el pliegue del triceps, circunferencia muscular del brazo y pérdida de peso), parámetros bioquímicos (albúmina, transferrina y la proteína C reactiva) y bioimpedancia tetrapolar para evaluar la composición corporal (grasa masa). Además, la capacidad pulmonar se midió y la estadificación clínica del cáncer establecido por el método TNM.

Resultados: La media de la abeja para la ecuación CI y Harris-Benedict Equation fueron 1421.8 ± 348.2 kcal/día y 1310.6 ± 215.1 kcal/día, respectivamente. No se encontró asociación entre GEB medido por CI y la estadificación clínica (p=0.255) o el Índice Tiffeneau (p=0.946). No se encontraron asociaciones significativas entre GEB medidos por CI y alteración de la transferrina, albúmina y proteína C reactiva (p=0.364, 0.309 y 0.780, respectivamente). Los factores más asociados con GEB fueron el IMC y la masa libre de grasa.

Conclusion: La abeja de los pacientes con CCS fue subestimada cuando se utiliza el EHB, y el resultado sobreestimado cuando se incorpora un factor de daño con el EHB. Por lo tanto, a pesar de las dificultades de aplicación práctica de CI, su uso debe ser considerado.

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Palabras clave: Cáncer de esófago. Calorimetría indirecta. El gasto energético basal.
Abbreviations

BEE: Basal Energy expenditure.
IC: Indirect Calorimetry.
HBE: Equação de Harris-Benedict.
SCC: Squamous cell carcinoma.
BMI: Body Mass Index.
CRP: C-reactive protein.
FFM: Fat Free Mass.

Introduction

Basal Energy Expenditure (BEE) is the main contributor to total energy expenditure (60% to 75%) and corresponds to the energy expenditure over a 24 hour period used for the maintenance of vital bodily processes such as respiration, circulation, and biochemical reactions involved in the maintenance of the metabolism.

Indirect calorimetry (IC) is a noninvasive method for determining energy needs from the gas exchanges that take place between the body and the environment, namely, the volume of oxygen consumed (VO2), a major component of BEE, and the volume of carbon dioxide produced (VCO2). This is obtained by analysis of air inhaled and exhaled by the lungs.

Prediction equations are used to establish a standard that will serve as a benchmark for the comparison of BEE in sick individuals. The Harris-Benedict Equation (HBE) is the most commonly used method to calculate BEE in clinical practice.

Basal Energy Expenditure

BEE was measured in a thermoneutral environment by indirect calorimetry (CORTEX Biophysik Met-Lyzer® 3B, Germany), after a fasting period of at least 6 hours. Patients were at rest for 30 minutes before data collection commenced. The system was calibrated in accordance with the instruction manual before each measurement. Oxygen consumption and carbon dioxide production were measured with the patient being in a supine position over a period of 25 minutes (including the initial time of 5 minutes). Measurement of the Basal Metabolic Rate (kcal/min) was obtained through the Weir equation:

\[ \text{Kcal/min} = \left( \frac{3.9(\text{VO}_2)}{1000} + \frac{1.1(\text{VCO}_2)}{1000} \right) \times 1.440 \]

Body Composition

Fat free mass (FFM) was ascertained by means of bioelectrical impedance analysis using a body composition analyzer (model Bodystat® 1500). Participants were instructed to fast for 8 hours prior to the procedure, and in addition, to take no part in physical activity from the day before the exam until the procedure was completed.

Prediction Equation

The expected BEE was estimated using the Harris-Benedict Equation (HBE):

Women: BEE: 655+(9.6xW)+(1.8xH)-(4.7xA)
Men: BEE: 66.5+(13.8xW)+(5xH)-(6.8xA)
Where \( W \) represents weight, \( H \) is height, and \( A \) is age.

An additional method for prediction was included based on recommendations for the use of an injury factor for cancer of 1.3 in combination with the HBE\(^{12} \).

Patients with a measured BEE of less than 90% of the predicted value were classified as hypometabolic, those between 90 and 110% as being normal metabolic, and those in excess of 110% as being hypermetabolic, as conforming with Boothby et al\(^{13} \).

**Statistical Analysis**

Data analysis was performed using SPSS software (Statistical Package for the Social Sciences) version 18.0.

Quantitative variables were described through mean and standard deviation, except for measurement of CRP for which the median and range of variation were used. Categorical variables were described using absolute and relative frequencies.

Student’s t-test for independent samples was used to compare continuous variables according to group.

Energy expenditure measured by IC was compared to values gained through estimation methods using Student’s t-test for paired samples. When adjusted for FFM the analysis of covariance was applied. The Bland-Altman method was used for assessing agreement between the findings.

Pearson’s chi-square test was applied to assess associations between categorical variables, and Pearson’s correlation analysis when assessing associations between continuous variables.

The multiple linear regression model with backward elimination was used to control confounding factors. The criterion for entering a variable in the model was that it presented a \( p < 0.10 \) in the bivariate analysis.

The Cochran test was used to compare methods of nutritional assessment. In the case of statistical significance, the McNemar test was applied to locate the difference.

The level of statistical significance considered was 5\% (\( p \leq 0.05 \)).

**Results**

Thirty patients with SCC were studied, this being 21 men (70\%) and 9 women (30\%) with an average age of 61.4 (± 8.6) years.

In relation to BMI, 8 patients (26.7\%) were malnourished, 14 (46.7\%) were of a normal weight and 8 (26.7\%) were overweight.

Twenty-seven individuals (90\%) lost weight and of these, 25 (83\%) had a significant weight loss, resulting in a mean percentage weight loss of 13.2\% (± 8.8). Anorexia was reported by 7 (23.3\%) patients.

The percentage of FFM (%FFM) among individuals was 69.6\% (± 7.7) and body fat 30.4\% (± 7.7). Dysphagia related to solid and soft foods was present in 23 (85.2\%) patients and in four (14.8\%) patients for liquids. Patient characteristics are described in table I.

The mean for BEE measured by IC was 1421.8 (± 348.2) kcal/day; estimated by HBE was 1310.6 (± 215.1) kcal/day (\( p = 0.014 \)); estimated by HBE with inclusion of injury factor of 1.3 for cancer was 1703.8 (± 279.7) kcal/day (\( p < 0.001 \)).

Figure 1 demonstrates the association between %FFM and BEE measured by IC. It can be seen that the higher the %FFM, the higher the BEE.

Table II shows the mean differences, limits of agreement, and the population proportion that is included in the acceptable limits of ± 10\%.

According to the classification of Boothby et al\(^{13} \), 6 (20\%) patients were considered hypometabolic, 7 (23.3\%) normal metabolic, and 17 (56.7\%) hypermetabolic.

Nutritional status determined by BMI and % weight loss was linked with BEE measured by IC. A significant difference was found in the BEE between malnourished (1181.7 ± 278.1 kcal/day) and well nourished patients (1509.1 ± 334.1 kcal/day) by BMI (\( p = 0.020 \)), whereas no significant differences were found using % weight loss, 1403.4 ± 369.0 kcal/day and 1514.0 ± 222.0 kcal/day respectively (\( p = 0.526 \)). The BEE for patients with a lower than expected %FFM was 1408.9 ± 364.3 kcal/day, as compared to 1538.4 ± 97.5 kcal/day for patients with an adequate %FFM (\( p = 0.550 \)).

Associations between BEE and demographic and clinical characteristics of patients are shown in table I.

### Table I

**Demographic & Anthropometric Characteristics of study (\( n = 30 \))**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender - n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21 (70%)</td>
</tr>
<tr>
<td>Female</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Age (years) - Mean ± SD</td>
<td>61.4 ± 8.6</td>
</tr>
<tr>
<td>Weight (kg) - Mean ± SD</td>
<td>60.9 ± 13.6</td>
</tr>
<tr>
<td>Height (m) - Mean ± SD</td>
<td>1.65 ± 0.10</td>
</tr>
<tr>
<td>BMI (kg/m(^2)) - Mean ± SD</td>
<td>22.4 ± 4.2</td>
</tr>
<tr>
<td>% FFM – Mean ± SD</td>
<td>69.6 ± 7.7</td>
</tr>
<tr>
<td>Staging - n (%)</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>II</td>
<td>10 (33.3)</td>
</tr>
<tr>
<td>III</td>
<td>12 (40.0)</td>
</tr>
<tr>
<td>IV</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>Dysphagia - n (%)</td>
<td>27 (90.0)</td>
</tr>
<tr>
<td>Diet - n (%)</td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td>10 (33.3)</td>
</tr>
<tr>
<td>NFT*</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Oral+NFT</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>Weight Loss (%) - Mean ± SD</td>
<td>13.2 ± 8.8</td>
</tr>
</tbody>
</table>

*Nasoenteral Feeding Tube.*
III. No association with BEE measured by IC was found between age (p=0.267), clinical staging (p=0.255) and the Tiffeneau Index (p=0.946). There was a significant association of BEE measured by IC with BMI (p=0.001) and %FFM (p=0.019).

No significant associations were found between BEE measured by IC and the pathology tests. In relation to transferrin in malnourished patients the BEE was 1504.9 ± 273.1 kcal/day and 1380.3 ± 379.8 kcal/day for the others (p=0.364); for albumin the figures were 1667.7 ± 119.2 kcal/day and 1404.3 ± 353.4 kcal/day respectively (p=0.309). In relation to CRP in patients with altered values the BEE measured by IC was 1403.6 ± 296.8 kcal/day and 1440.1 ± 402.8 kcal/day for the others (p=0.780). The mean for albumin was 4.1 ± 0.39 g/dL and for transferrin 218.1 ± 34.9 mg/dL. The median for the 16 patients who presented alterations in CRP was 10.2 mg/L (6.6 mg/L to 123 mg/L).

A multiple linear regression analysis was performed to evaluate independent factors associated with BEE measured by IC. The variables %FFM (p=0.002) and BMI (p<0.001) showed that the two factors together contributed 52.9% to BEE.

Discussion

Many studies in recent decades have investigated energy expenditure in cancer patients with some maintaining the idea that these patients have a high BEE which significantly contributes to the development of malnutrition14, while others have found no change15.

Our study found the mean BEE measured by IC of patients with SCC to be 1421.8 ± 348.2 kcal/day. Research by Reeves16, which looked at post-radiotherapy patients with lung and gastrointestinal tract cancers found the mean BEE measured by IC to be 1589.4 ± 89.7 kcal/day. A further study by Thomson17 involving only black patients with esophageal cancer found the mean BEE measured by IC was 1484.6 ± 200.7 kcal/day.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Predicted value Mean ± SD</th>
<th>Difference Mean ± SD</th>
<th>Limits of agreement</th>
<th>Proportion within ±10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBE</td>
<td>1310.6 ± 215.1</td>
<td>-111 ± 234</td>
<td>-45.1 to 27</td>
<td>26.7%</td>
</tr>
<tr>
<td>HBE x 1.3</td>
<td>1703.8 ± 279.7</td>
<td>282 ± 230</td>
<td>-4.6 to 88.6</td>
<td>26.7%</td>
</tr>
</tbody>
</table>

Table II
Predicted BEE, mean of differences, and limits and agreement for the differences between the predicted and measured BEE of patients with SCC
In conclusion, when comparing the BEE measured by IC of patients with SCC, it was found that the HBE with no injury factor underestimated BEE whereas the
HBE with injury factor of 1.3 overestimated the figure. The factors that contributed most to the increase of BEE measured by IC were BMI and FFM. The use of IC should always be considered since it is the «gold standard» method for determining BEE. However, even today the use of IC is not routine and thus further studies involving larger numbers of patients with SCC are necessary in order to identify the ideal injury factor to be used with the HBE, for those occasions when IC is not available.

Acknowledgements

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