



Case Control Study

Resting energy expenditure in cirrhotic patients with and without hepatocellular carcinoma

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Abstract

BACKGROUND

The diagnosis of malnutrition in patients with independent hepatocellular carcinoma (HCC) varies from 20% to 50%, is related to important complications and has a direct impact on the prognosis. Determination of the resting energy expenditure (REE) has become an important parameter in this population, as it allows therapeutic adjustments to recover their nutritional status. The REE in cirrhosis, with and without HCC, is not clearly defined, and requires the identification and definition of the best nutritional approach.

AIM

To evaluate the REE of patients with cirrhosis, with and without HCC.

METHODS

This is a prospective observational study evaluating the REE of 118 patients, 33 with cirrhosis and hepatocellular carcinoma and a control group of 85 patients

writing and revision of the scientific article.

Institutional review board

statement: This project was approved by the Research Ethics Committee of Irmandade Santa Casa de Misericórdia de Porto Alegre (number 2.387.800).

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with cirrhosis without HCC, using indirect calorimetry (IC), bioimpedance, and predictive formulas.

RESULTS

The REE determined by IC in cirrhotic patients with HCC was 1643 ± 364 and in those without HCC was 1526 ± 277 ($P = 0.064$). The REE value as assessed by bioimpedance was 1529 ± 501 for those with HCC and 1660 ± 385 for those without HCC ($P = 0.136$). When comparing the values of REE determined by IC and predictive formulas in cirrhotics with HCC, it was observed that only the formulas of the Food and Agriculture Organization (FAO)/World Health Organization (WHO) (1985) and Cunningham (1980) presented values similar to those determined by IC. When comparing the REE values determined by IC and predictive formulas in cirrhotics without HCC, it was observed that the formulas of Schofield (1985), FAO/WHO (1985), WHO (2000), Institute of Medicine (IOM) (2005) and Katch and McArdie (1996) presented values similar to those determined by IC.

CONCLUSION

The FAO/WHO formula (1985) could be used for cirrhotic patients with or without HCC; as it is the one with the values closest to those obtained by IC in these cirrhotic patients.

Key Words: Carcinoma; Hepatocellular; Liver cirrhosis; Calorimetry; Indirect; Rest energy expenditure

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Core Tip: This prospective study was conducted to evaluate the resting energy expenditure in 118 patients with and without hepatocellular carcinoma. Indirect calorimetry is considered the golden standard for determining resting energy expenditure; however, when this is impossible, use of the FAO/WHO formula (1985) in this population is indicated.

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INTRODUCTION

The main causes of liver cirrhosis worldwide are alcoholic liver disease and chronic hepatitis B virus and/or hepatitis C virus infections. Over a period of 15 to 30 years, chronic liver diseases can lead to liver cirrhosis and its complications. The prognosis is highly variable and influenced by several factors, such as etiology, severity of liver disease, presence of complications and comorbidities^[1].

The prevalence of sarcopenia in patients with hepatocellular carcinoma (HCC) varies from 27.5%^[2] to 78.2%^[3] and malnutrition affects 20% to 50% of patients with cirrhosis, and both are related to important complications and have a direct impact on prognosis.

Early nutritional diagnosis has significant relevance in cirrhotics, as it reflects positively on their recovery, enables specific therapeutic interventions and prevents the appearance of complications^[4-8].

Daily intake should be sufficient to meet the body's demands^[9] and can be measured directly or indirectly^[10]. Resting energy expenditure (REE) is the energy needed to maintain physiological processes; during indirect measurement, an interval of 4 h is necessary since the last meal, and a rest of 30 min before the examination^[11].

Indirect calorimetry (IC) is the gold standard for measuring REE^[11-13], it is non-

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invasive and safe, it uses the calorimeter to measure REE through gas exchange and, in a formula, using the Weir Equation ($QR = 0.83$) evaluates the volume of oxygen consumed, the volume of carbon dioxide produced and the nitrogen excreted, since each calorie consumed requires a certain amount of oxygen to be converted into energy, which are good predictors of REE changes^[14].

Other methods, such as electrical bioimpedance (BIA) and predictive formulas, commonly used in clinical practice, can also be used to predict REE.

The aim of this study is to evaluate the REE of patients with cirrhosis, with and without HCC, measured by IC and to compare the results with those obtained by BIA and predictive formulas, in order to identify which is the best method of evaluation^[15].

MATERIALS AND METHODS

The study included 118 patients, aged ≥ 18 years, of both sexes, divided into two groups. One group consisted of 33 patients with cirrhosis and HCC and a control group of 85 patients with cirrhosis but without HCC, who attended the Department of Gastroenterology and Liver Transplantation of Irmandade da Santa Casa de Misericórdia de Porto Alegre, RS, Brazil, from March 2017 to August 2018.

Hospitalized cirrhotics or those participating in dietary or physical activity programs for weight gain, and/or in a rehabilitation program were excluded; patients with neoplasms other than HCC and those who did not have physical and motor conditions for anthropometric and functional evaluation were also excluded.

All participants agreed to participate in the research by reading and signing the informed consent form. This research protocol was approved by the Research Ethics Committee of Irmandade Santa Casa de Misericórdia de Porto Alegre (number 2387800).

Data from the electronic medical records of the patients, related to the diagnosis, staging by the Child-Pugh score, age and sex of the participants were collected. The diagnosis of cirrhosis and/or HCC was made by clinical, laboratory, imaging and/or, eventually, liver biopsy. The classification of patients with HCC was carried out using the Barcelona Clinic Liver Cancer Group (BCLC) staging system^[16].

Current body weight was measured using a Filizola® anthropometric scale with 0.1 kg precision, previously calibrated. Height was measured with a stadiometer fixed to the wall, with the patient in an upright position and barefoot. Body mass index (BMI) was calculated by dividing the weight by height squared $\{BMI = \text{Weight (kg)} / [\text{Height (cm)}]^2\}$ and classification according to the Food and Agriculture Organization (FAO)/World Health Organization (WHO)^[17].

The IC was measured by the Korr® MetaCheck calorimeter, with the patient fasting for 4 h and resting for 30 min before starting the assessment. The measurement was made under conditions of absolute rest for 10 to 30 min, with the patient sitting and using a rigid breathing mask, in a stable condition, and the calculation of energy expenditure was based on the consumption of O_2 (VO_2), CO_2 production (VCO_2) and urinary urea nitrogen, using the formula $REE = \{3.9 (VO_2) + [1.1 (VCO_2)]\}$, described by WEIR, 1949^[18,19].

The BIA evaluation used the Biodynamics device model 450, with an electric current intensity of 800 μA , frequency of 50 kHz and disposable electrodes of the HeartBeat® brand. The patient was in the dorsal decubitus, comfortable and relaxed position, without shoes, socks, watch, bracelets and necklaces, with legs spread, hands open and supported on the stretcher. A distal electrode was placed at the base of the middle toe of the right foot and the proximal electrode just above the line of the right ankle joint, between the medial and lateral malleolus. Another set of electrodes were also placed, the distal electrode at the base of the middle finger of the right hand and the proximal electrode just above the line of the right wrist joint, coinciding with the styloid process^[20].

The predictive formulas for calculating the energy expenditure used in this study are listed in Table 1^[21-27].

Sample size calculation

The sample size for patients with HCC was by convenience sample, and the sample from the control group with cirrhosis was based on the study by Teramoto *et al*^[28], comparing the measured and predicted energy expenditure in patients with liver cirrhosis, considering an 80% power and significance level of 5%, thus obtaining the sample number of 85 patients.

Table 1 Predictive formulas for calculating energy expenditure^[8]

Ref.	Age range	Gender	Equation
Harris and Benedict ^[21]	Non-specified	Male	$66.437 + [5.0033 \times H \text{ (cm)}] + [13.7516 \times W \text{ (kg)}] - [6.755 \times Y \text{ (yr)}]$
	Non-specified	Female	$655.0955 + [1.8496 \times H \text{ (cm)}] + [9.5634 \times W \text{ (kg)}] - [4.6756 \times Y \text{ (yr)}]$
Schofield ^[22] in kcal/day	10-17	Male	$[0.074 \times W \text{ (kg)} + 2.754] \times 239$
		Female	$[0.056 \times W \text{ (kg)} + 2.898] \times 239$
	18-29	Male	$[0.063 \times W \text{ (kg)} + 2.896] \times 239$
		Female	$[0.062 \times W \text{ (kg)} + 2.036] \times 239$
	30-59	Male	$[0.048 \times W \text{ (kg)} + 3.653] \times 239$
		Female	$[0.034 \times W \text{ (kg)} + 3.538] \times 239$
	From 60 yr	Male	$[0.049 \times W \text{ (kg)} + 2.459] \times 239$
		Female	$[0.038 \times W \text{ (kg)} + 2.755] \times 239$
WHO ^[23] in kcal/day	10-17	Male	$17.5 \times W + 651$
		Female	$12.2 \times W + 746$
	18-29	Male	$15.3 \times W + 679$
		Female	$14.7 \times W + 496$
	30-59	Male	$11.6 \times W + 879$
		Female	$8.7 \times W + 829$
	From 60 yr	Male	$13.5 \times W + 487$
		Female	$10.5 \times W + 596$
Mifflin <i>et al</i> ^[24] in kcal/day	19-78	Male	$10 \times W \text{ (kg)} + 6.25 \times H \text{ (cm)} - 5 \times Y \text{ (yr)} + 5$
	19-78	Female	$10 \times W \text{ (kg)} + 6.25 \times H \text{ (cm)} - 5 \times Y \text{ (yr)} - 161$
FAO/WHO ^[17]	10-17	Male	$(16.6 \times W) + [77 \times H \text{ (m)}] + 572$
		Female	$(7.4 \times W) + [482 \times H \text{ (m)}] + 217$
	18-30	Male	$(15.4 \times W) - [27 \times H \text{ (m)}] + 717$
		Female	$(13.3 \times W) + [334 \times H \text{ (m)}] + 35$
	31-60	Male	$(11.3 \times W) + [16 \times H \text{ (m)}] + 901$
		Female	$(8.7 \times W) - [25 \times H \text{ (m)}] + 865$
	From 60 yr	Male	$(8.8 \times W) + [1128 \times H \text{ (m)}] - 1071$
		Female	$(9.2 \times W) + [637 \times H \text{ (m)}] - 302$
IOM ^[25]	Non-specified	Male	$293 - (3.8 \times \text{age}) + (401.5 \times \text{height}) + (8.6 \times \text{weight})$
	Non-specified	Female	$247 - (2.67 \times \text{age}) + (456.4 \times \text{height}) + (10.12 \times \text{weight})$
Cunningham ^[26]	Non-specified	Male, Female	$500 \text{ kcal} + (\text{lean mass in kg} \times 22)$
McArdle <i>et al</i> ^[27]	Non-specified	Male, Female	$(\text{lean mass in kg} \times 21.6) + 370$

W: Weight; H: Height; Y: Years.

Statistical analysis

Quantitative variables were described by mean and standard deviation and categorical variables by absolute and relative frequencies.

To compare means between genders, the Student *t*-test for independent samples was applied. Population estimates were performed using the 95% confidence interval.

To compare groups, the Student *t*-test for independent samples (quantitative variables) and Pearson's Chi-square (categorical variables) were applied.

To compare means between the estimated energy expenditure formulas with indirect calorimetry, the Student *t*-test for paired samples was used.

To assess the association between anthropometric variables and indirect

calorimetry, Pearson's correlation coefficient was used.

The level of significance adopted was 5% ($P < 0.05$) and the analyses were performed using the Statistical Package for Social Sciences 21.0 software for Windows.

RESULTS

The mean age of cirrhotic patients with HCC was 62.8 ± 8.1 years and in those without HCC was 56.7 ± 9.4 years ($P = 0.001$); 78.8% of those with HCC were male and 56.5% of those without HCC were female ($P = 0.001$). The clinical characterization of cirrhotic patients was performed using the Child-Pugh score, which identified similarities between the two groups ($P = 0.224$). According to the BCLC staging in our study, most patients with HCC were classified as 0, A and B, as shown on [Table 2](#).

The REE determined by IC in cirrhotics with HCC was 1643 ± 364 and in those without HCC was 1526 ± 277 ($P = 0.064$), as shown on [Table 3](#).

The REE value assessed by BIA was 1529 ± 501 for those with HCC and was 1660 ± 385 for those without HCC ($P = 0.136$). In the comparison between the REE determined by the IC, the group with HCC did not show a significant difference and the group without HCC did show a significant difference ($P = 0.001$), as shown on [Table 4](#).

The estimated REE values of cirrhotics with and without HCC, using the predictive formulas of Harris and Benedict^[21], Schofield^[22], WHO^[23], Mifflin *et al*^[24], FAO/WHO^[17], IOM^[25], Cunningham^[26] and McArdle *et al*^[27] showed that only the Harris and Benedict^[21] formula ($P < 0.001$) and the IOM formula^[25] ($P = 0.001$) demonstrated a difference between the two groups, as shown on [Table 5](#).

When comparing the REE values determined by the IC and the predictive formulas in cirrhotics with HCC, it was observed that only the formulas of the FAO/WHO^[17] and Cunningham^[26] presented values similar to those determined by the IC, the others underestimated these values, as shown on [Table 6](#).

When comparing the REE values determined by the IC and the predictive formulas in cirrhotics without HCC, it was observed that the formulas of Schofield^[22], WHO^[23], FAO/WHO^[17], IOM^[25] and McArdle *et al*^[27] presented similar but erratic values to those determined by the IC, as shown on [Table 7](#).

DISCUSSION

Cirrhotic patients have an imbalance in energy metabolism, which contributes to protein-calorie malnutrition and a worse prognosis^[5,27-32]. When HCC is associated with cirrhosis, clinical conditions and additional needs may worsen such as dietary restrictions. To date, there is no established standard and significant evidence to justify increased REE in these patients. Several studies, with different methodologies, such as IC, BIA and predictive formulas, have evaluated REE in cirrhotics with and without HCC^[13,14,27,30,33-36].

In the present study, 118 cirrhotic patients were evaluated, 33 with HCC (62.8 ± 8.1 years and 78.8% male), and 85 without HCC (56.7 ± 9.4 years and 56.5% female) ($P = 0.001$) which is in accordance with the findings of the literature, where more older men present with HCC^[30,32,37,38].

Anthropometry showed that the BMI in those with HCC was 27 kg/m^2 (± 4.0) similar to that of the control group, and in cirrhotics without HCC, BMI was 28.7 kg/m^2 (± 5.7). We identified a low prevalence of malnutrition, with overweight, but we must consider that the BMI underestimates the prevalence of malnutrition in cirrhotic patients, as body weight can represent significant changes due to frequent hydroelectrolytic disorders (edema and ascites), and these findings are concordant with previous studies carried out in cirrhotic^[23,39-41] and cancer patients^[42,43]. These results are also in line with studies carried out in cirrhotic patients, with and without HCC^[14,30,31,34,37]. A publication by Fernandes *et al*^[31], did not identify BMI as a safe method of assessing nutritional status in this population, due to inherent changes in body weight.

Considered as the gold standard for measuring REE, IC is a safe and non-invasive method, capable of determining nutritional needs through gas exchange^[11,44,45].

In our study, the average REE calculated by IC in cirrhotic patients with HCC was 1643 ± 364 calories and that of cirrhotics without HCC was 1526 ± 277 calories ($P = 0.064$). These results are similar to those found by Segadilha *et al*^[45], where REE was 1568 ± 374 calories in a population of 97 elderly cirrhotic patients hospitalized in Rio de Janeiro, and similar to those found by Pinto *et al*^[44], of 1534 ± 300 calories, who

Table 2 Sample characterization - cirrhotics with and without hepatocellular carcinoma (n = 118)

Variables	HCC (n = 33)	Without HCC (n = 85)	¹ P value
	mean ± SD	mean ± SD	
Age (yr)	62.8 ± 8.1	56.7 ± 9.4	0.001
Male gender	26 (78.8%)	37 (43.5%)	0.001 ²
Weight (kg)	73.9 ± 12.9	78.2 ± 17.2	0.206
Height (m)	1.65 ± 0.09	1.65 ± 0.09	0.810
BMI (kg/m ²)	27.0 ± 4.0	28.7 ± 5.7	0.115
Lean mass (kg)	51.3 ± 10.6	53.4 ± 12.3	0.396
Child Pugh			0.224 ²
A	13 (39.4%)	32 (37.6%)	
B	17 (51.5%)	34 (40.0%)	
C	3 (9.1%)	19 (22.4%)	
BCLC			-
0	4 (12.1%)	-	
A	12 (36.4%)	-	
B	10 (30.3%)	-	
C	4 (12.1%)	-	
D	3 (9.1%)	-	

¹Student *t*-test for independent samples; ²Pearson's chi-square test. HCC: Hepatocellular carcinoma; SD: Standard deviation; BCLC: Barcelona Clinic Liver Cancer Group.

Table 3 Energy expenditure at rest by indirect calorimetry in cirrhotics with and without hepatocellular carcinoma (n = 118)

Variables	HCC (n = 33)		Without HCC (n = 85)		¹ P value
	mean ± SD	IC 95%	mean ± SD	IC 95%	
Calorimetry	1643 ± 364	1514–1772	1526 ± 277	1466–1586	0.064

¹Student *t*-test for independent samples. HCC: Hepatocellular carcinoma; SD: Standard deviation; IC: Indirect calorimetry.

Table 4 Resting energy expenditure by electrical bioimpedance in cirrhotics with and without hepatocellular carcinoma, compared with indirect calorimetry (n = 118)

Variables	HCC (n = 33)		Without HCC (n = 85)		¹ P value
	mean ± SD	IC 95%	mean ± SD	IC 95%	
BIA	1529 ± 501	1352–1707	1660 ± 385	1577–1743	0.133
Calorimetry	1643 ± 364	1606–1907	1526 ± 277	1356–1623	0.064
P value	0.136		0.001		

¹Student *t*-test for independent samples. HCC: Hepatocellular carcinoma; BIA: Electrical bioimpedance; SD: Standard deviation; IC: Indirect calorimetry.

studied a population of 45 cirrhotic patients listed for liver transplantation, which corroborates the expectation of correct caloric prediction by the method used^[44].

Our REE findings, determined by BIA, in cirrhotics with HCC were 1529 ± 501 calories and 1660 ± 385 calories in those without HCC (*P* = 0.136). These values differ from those of Pinto *et al*^[44], in their study with 53 cirrhotic patients with HCC in the

Table 5 Resting energy expenditure calculated using predictive formulas in cirrhotics with and without hepatocellular carcinoma (n = 118)

Variables	HCC (n = 33)		Without HCC (n = 85)		¹ P value
	mean ± SD	IC 95%	mean ± SD	IC 95%	
Harris and Benedict ^[20] formula	1466 ± 224	1387–1546	2138 ± 499	2030–2246	< 0.001
Schofield ^[22] formula	1489 ± 203	1417–1561	1539 ± 218	1491–1586	0.265
WHO ^[23] formula	1518 ± 208	1444–1592	1536 ± 282	1475–1597	0.744
Mifflin <i>et al</i> ^[24]	1433 ± 196	1363–1503	1439 ± 212	1393–1485	0.883
FAO/WHO formula ^[17]	1522 ± 208	1449–1596	1566 ± 223	1518–1614	0.333
IOM ^[25] formula	1402 ± 168	1342–1462	1544 ± 242	1491–1596	0.001
Cunningham ^[26] formula	1629 ± 233	1546–1712	1674 ± 271	1616–1733	0.396
McArdle <i>et al</i> ^[27] formula, 1996	1478 ± 229	1397–1559	1523 ± 266	1466–1581	0.396

¹Student *t*-test for independent samples. HCC: Hepatocellular carcinoma; SD: Standard deviation.

Table 6 Differences between resting energy expenditure calculated using predictive formulas in cirrhotic patients with hepatocellular carcinoma, compared with indirect calorimetry (n = 118)

	Mean difference	IC 95%	¹ P value
Calorimetry X Harris Benedict formula ^[21]	177	59.8 a 293	0.004
Calorimetry X Schofield formula ^[22]	154	36.9 a 270	0.011
Calorimetry X WHO formula ^[23]	125	9.1 a 240	0.035
Calorimetry X Mifflin <i>et al</i> ^[24] formula	210	98.5 a 321	0.001
Calorimetry X FAO/WHO formula ^[17]	120	-2.3 a 243	0.054
Calorimetry x IOM formula ^[25]	241	116 a 366	< 0.001
Calorimetry x Cunningham formula ^[26]	14	-101 a 129	0.806
Calorimetry x McArdle <i>et al</i> ^[27] formula	165	49.5 a 279	0.006

¹Student *t*-test for paired samples.

liver pre-transplant, who found the average REE calculated by the BIA was 1817 calories, while that calculated by IC was 1651 calories, similar to our findings.

When comparing the REE determined by BIA with the IC value, we found that the group with HCC did not show a significant difference ($P = 0.136$), and the group without HCC did show a significant difference ($P = 0.001$).

Table 1 shows the predictive formulas used to calculate the REE, with their peculiarities.

Table 6 shows the estimated REE values in cirrhotics with and without HCC, and it can be seen that, with the exception of the Harris Benedict (1919)^[22] and IOM (2005)^[25] formulas, which show significant differences between the two groups ($P < 0.001$), the others show similar values.

A comparison of the REE data from the IC with those estimated by the predictive formulas, in relation to cirrhotics with HCC, shows that only the FAO/WHO^[17] ($P = 0.054$) and Cunningham^[26] ($P = 0.806$) formulas have similarity, and the other six were different ($P < 0.05$); in cirrhotics without HCC the inverse was noted, where five values were similar ($P > 0.05$) and three were different ($P < 0.05$). These findings prevent the determination of a uniform rule. The disparities in our data are consistent with numerous findings in the literature that demonstrate different values for the various methods^[14,28,34–36,46].

The applicability of predictive formulas, even with their practicality and low cost, is controversial because they are very erratic, and underestimate or overestimate the REE^[35,23], and are thus unreliable.

Table 7 Differences between resting energy expenditure calculated using predictive formulas in cirrhotics without hepatocellular carcinoma, compared with indirect calorimetry ($n = 118$)

	Mean difference	IC 95%	¹ P value
Calorimetry X Harris Benedict formula ^[21]	-611	-691 a -531	< 0.001
Calorimetry X Schofield formula ^[22]	-12.3	-67.2 a 42.6	0.658
Calorimetry X WHO formula ^[23]	-9.5	-73.1 a 54.2	0.768
Calorimetry X Mifflin-St Jeo formula ^[24]	87.2	49.5 a 125	< 0.001
Calorimetry X FAO/WHO formula ^[17]	-39.8	-93.2 a 13.6	0.142
Calorimetry x IOM formula ^[25]	-17.5	-41.5 a 6.6	0.153
Calorimetry x Cunningham formula ^[26]	-148	-172 a -123	< 0.001
Calorimetry x McArdle <i>et al</i> ^[27] formula	3.2	-20.9 a 27.3	0.792

¹Student *t*-test for paired samples.

Our results suggest that the predictive formulas do not provide precise REE values because when using the body weight of cirrhotics, they may incur an intrinsic error, due to water retention (ascites and edema) that directly affects the calculation of REE^[38,39].

Studies on other diseases, such as that by Zanella *et al*^[11], who compared the calculation of REE by IC with predictive formulas and BIA, in patients with pulmonary hypertension, showed that IC obtained values were different to all the other methods, which underestimated the predicted REE by more than 200 kcal, except that of the Cunningham's formula^[26], and the formula by McArdle *et al*^[27] showed the greatest difference in the REE estimate in the studied population^[15].

The use of IC for determining the REE in routine clinical practice has some difficulties, related to difficulty in buying the device, which has a high cost, the time needed to perform the test and the possible lack of cooperation in patients^[35].

Thus, based on the data from our study, we suggest the use of BIA values for cases with HCC or those of the FAO/WHO formula^[17] for those with or without HCC; the Cunningham formula^[26] could be used in cases without HCC and the formula by McArdle *et al*^[27] for those with HCC, as they are the ones closest to those obtained by IC in these cirrhotic patients^[23].

The choice of these formulas in the present study is not in line with the recommendation by Plauth *et al*^[47] in the guidelines of the European Society for Parenteral and Enteral Nutrition of 1997 for nutrition in liver diseases and transplants, where it was suggested that the Harris and Benedict predictive formula^[21] should be applied to estimate REE in patients with cirrhosis when IC is not available in a clinical setting^[47].

Our results demonstrate that the formulas of Harris and Benedict^[21] and IOM^[25] were the ones that showed the greatest differences when compared to the determination of REE by IC, which is why we do not recommend these predictive formulas.

The determination of REE by IC, BIA or by any recommended predictive formula, in cirrhotics with or without HCC, is essential for the nutritional diagnosis. Individualized treatment and specific nutritional interventions can delay the emergence of malnutrition and poor clinical evolution^[48].

Thus, we emphasize that the same method of evaluation in different populations can present different correlations with the available predictive formulas.

CONCLUSION

The REE by IC in cirrhotic patients with and without HCC was similar. When comparing the IC values with those of the BIA, we found that in patients with HCC, the values were similar. The values estimated by the predictive formulas are very erratic and disparate, when compared to IC. The FAO/WHO formula^[17] could be used for those with or without HCC; Cunningham formula^[26] in those without HCC and the McArdle *et al*^[27] in those with HCC, as they are the ones with the closest values to those

obtained by IC in these cirrhotic patients^[23,49]. Apparently, the presence of HCC in cirrhotics does not appear to significantly alter the REE.

ARTICLE HIGHLIGHTS

Research background

The diagnosis of malnutrition in patients with hepatocellular carcinoma (HCC) varies from 20% to 50%, as it is related to important complications and has a direct impact on prognosis. Determination of the resting energy expenditure (REE) has become an important parameter in this population, as it allows therapeutic adjustments to recover their nutritional status. The REE in HCC is not clearly defined, and requires the identification and definition of the best nutritional approach.

Research motivation

The diagnosis of malnutrition in patients with HCC varies from 20% to 50%, is related to important complications and has a direct impact on prognosis. Determination of the REE has become an important parameter in this population, as it allows therapeutic adjustments to recover their nutritional status. The REE in HCC is not clearly defined, and the identification and definition of the best nutritional approach is necessary.

Research objectives

The aim of this study is to evaluate the REE of patients with cirrhosis, with and without HCC, measured by IC and to compare these values with those obtained by bioimpedance (BIA) and predictive formulas, in order to identify which is the best method of evaluation.

Research methods

This prospective observational study included 118 patients, aged ≥ 18 years, of both sexes, divided into two groups. One group consisted of 33 cirrhotic patients with HCC and a control group of 85 cirrhotics without HCC, attending the Department of Gastroenterology and Liver Transplantation of Irmandade da Santa Casa de Misericórdia de Porto Alegre, RS, Brazil, from March 2017 to August 2018. Quantitative variables were described by mean and standard deviation and categorical variables by absolute and relative frequencies.

Research results

The REE determined by indirect calorimetry (IC) in cirrhotic patients with HCC was 1643 ± 364 and in those without HCC was 1526 ± 277 ($P = 0.064$). The REE value as assessed by BIA was 1529 ± 501 for those with HCC and was 1660 ± 385 for those without HCC ($P = 0.136$). When comparing the values of REE determined by IC and predictive formulas in cirrhotics with HCC, it was observed that only the formulas of FAO/WHO (1985) and Cunningham (1980) presented values similar to those determined by IC. When comparing the REE values determined by the IC and predictive formulas in cirrhotics without HCC, it was observed that the formulas of Schofield (1985), FAO/WHO (1985), WHO (2000), IOM (2005) and Katch and McArdie (1996) presented values similar to those determined by IC.

Research conclusions

The REE determined by IC in cirrhotic patients with HCC was 1643 ± 364 and in those without HCC was 1526 ± 277 ($P = 0.064$). The REE value assessed by BIA was 1529 ± 501 for those with HCC and 1660 ± 385 for those without HCC ($P = 0.136$). When comparing the values of REE determined by IC and predictive formulas in cirrhotics with HCC, it was observed that only the formulas of FAO/WHO (1985) and Cunningham (1980) presented values similar to those determined by IC. When comparing the REE values determined by the IC and predictive formulas in cirrhotics without HCC, it was observed that the formulas of Schofield (1985), FAO/WHO (1985), WHO (2000), IOM (2005) and Katch and McArdie (1996) presented values similar to those determined by IC.

Research perspectives

The REE as assessed by IC in cirrhotics with and without HCC was similar. When comparing the IC values with those of the BIA, we found that in patients with HCC, the values were similar. The values estimated by the predictive formulas were very

erratic and disparate, when compared to IC. The FAO/WHO formula could be used for those with or without HCC; the Cunningham formula in those without HCC and the McArdle in those with HCC, as they are the ones with the closest values to those obtained by IC in these cirrhotic patients. Apparently, the presence of HCC in cirrhotics does not appear to significantly alter the REE.

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