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Original article

Major liver resection reduces nonprotein respiratory quotient and increases nonesterified fatty acid at postoperative day 14 in patients with hepatocellular carcinoma

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SUMMARY

Background & aims: We reported decreased nonprotein respiratory quotient (npRQ) after liver resection in patients with hepatocellular carcinoma (HCC); however, whether liver resection volume affects energy metabolism in these patients is unclear. We aimed to examine the relationship between liver resection and energy metabolism indices.
Methods: NpRQ was measured in 53 patients with HCC and seven with at the pre- and postoperative days. Patients were classified into four groups: Minor-lowICG group (n = 17): minor (subsegment or less) resection and low indocyanine green retention rate at 15 min (ICGR15) (<15%); Minor-highICG group (n = 18): minor resection and high ICGR15 (≥15%) and Major-lowICG group (n = 18): major (lobe) resection and low ICGR15 (<15%). We investigated dietary intake and blood biochemistry at energy measurement. The difference in npRQ and nonesterified fatty acid (NEFA) pre- and post-hepatectomy was shown as ΔnpRQ and ΔNEFA, respectively.
Results: Compared with the preoperative values, npRQ significantly decreased in the Minor-highICG and Major-lowICG groups and NEFA significantly increased in the Major-lowICG group at postoperative day 14. In single regression analysis, ΔnpRQ significantly correlated with HCV infection and ΔNEFA with resection volume, HCV infection, and ICGR15. In multiple regression analysis, ΔNEFA significantly correlated with resection volume after adjusting for age, etiology, and ICGR15.
Conclusions: These results suggest that postoperative nutritional recovery is slower in major resection than in minor resection patients. Hence, nutritional care to prevent starvation is needed in major resection patients.

1. Introduction

Hepatocellular carcinoma (HCC) is one of the most common malignancies worldwide, accounting for 750,000 new cases and causing approximately 700,000 deaths each year [1,2]. Liver resection is the main treatment modality for liver cancer [3–5]. However, this treatment is invasive, it leads to deterioration of liver function easily. Hence perioperative nutritional therapy is crucial for these patients. Malnutrition leads to increased complications in liver disease patients [6], resulting in poor prognosis of liver disease [7,8]. Nutritional assessment is important for nutritional therapy, and the Harris–Benedict equation is the gold standard for estimating energy requirements [9]. It has been recommended for normal-weight patients with liver cirrhosis [10]. Perioperative nutritional treatment of a patient undergoing hepatectomy prevents malnutrition and affects postoperative complications [11]. The nonprotein respiratory quotient (npRQ), as an individual assessment index of nutritional condition, is extremely important

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in patients with liver disease. Due to metabolic disturbances, npRQ decreased after overnight fasting [12,13]. NPRQ has a negative correlation with nonesterified fatty acid (NEFA) [12]. Following liver resection, npRQ is influenced by decreased glycogen accumulation because of decreased liver volume and the worsening of the existing metabolic abnormalities. Therefore, severe patients cannot undergo a major liver resection. Additionally, npRQ decreases with the progression of liver disease, and patients with a low npRQ (<0.85) have poorer prognosis [14].

In our previous study, we reported that decreased npRQ and increased NEFA were observed at post-operative days in patients who underwent liver resection [15]. NPRQ decreases due to inadequate energy intake. In patients with insufficient oral intake, adequate nutritional support in the form of enteral nutrition or parenteral nutrition is required. Thus, identification of factors complicating nutritional status is very important while administering nutritional treatment to patients with liver disease. Richter et al. reported that patients undergoing major hepatectomy (e.g., lobectomy and extended lobectomy) predominately benefited from parenteral nutrition and that those undergoing minor hepatectomy (subsegmentectomy) benefited from enteral nutrition [16]. Moreover, Fan et al. reported that perioperative nutritional support can decrease complications after major hepatectomy in patients with HCC [17]. These studies suggest that nutritional management should be changed based on resection volume. Post-hepatectomy patients reached a state of starvation following surgery at a fasting state. Resection volume of liver would affect the level of starvation after operation, but there was little information about relationship between resection volume and postoperative nutritional state. Therefore, we investigated factors that affect energy metabolism in hepatectomy patients.

2. Methods

2.1. Participants

This study was conducted at the Tokushima University Hospital; 53 hospitalized patients with HCC who underwent liver resection were enrolled. These patients were classified into three groups depending on the resection volume: 1) minor resection (less segment or partial resection), indocyanine green retention rate at 15 min (ICGR15) <15% (Minor-lowICG group); 2) minor resection, ICGR15 ≥ 15% (Minor-highICG group); 3) major resection (resection ≥ one lobe), ICGR15 < 15% (Major-lowICG group). No applicant satisfied major resection (resection ≥ one lobe), ICGR15 ≥ 15% (Major-highICG group). In addition, we measured the nutritional index the day before the operation (Pre) and POD 14. The purpose of the study was explained in detail to all subjects, and informed consent was obtained. The study design was approved by the ethical committee of Tokushima University Hospital (No 810). The study conformed to the principles of the 1975 Helsinki Declaration.

2.2. Measurement of energy metabolism

Body weight and body mass index were measured using the DC-320 body composition meter (Tanita Corp., Tokyo, Japan) under fasting conditions.

Indirect calorimetric measurements were performed at Pre and POD 14. Patients were instructed to abstain from eating and drinking any fluids except noncaloric water or tea from 19:00 the day before indirect calorimetric measurements. Dietitians recorded the amount of intake of food (meals + snacks) and conducted food investigation on the day previous to the day of energy metabolism measurement. We calculated the energy intake on the basis of standard tables of food composition in Japan (fifth revised and enlarged edition). All patients were fed a standard daily hospital diet containing 30–35 kcal/kg (60% carbohydrate, <25% fat, and 15–20% protein) before operation and at POD 14. Patients with inadequate food intake who received supplemental enteral nutrients were excluded from the study. Additionally, 24-h urine samples were collected, and urinary urea nitrogen was measured. Energy metabolism was measured at 8:00 h after overnight fasting using the AE-300S respiratory gas analyzer (Minato Medical Science Corp., Ltd., Osaka, Japan). Following overnight fasting, patients were instructed to remain in bed for 30 min before indirect calorimetric measurement and to maintain a supine position throughout the measurement period. Oxygen consumption and carbon dioxide production rates were measured for 15 min, and the mean values for the final 10 min were used for analysis. Resting energy expenditure (REE) and npRQ for each patient were then calculated using measured oxygen consumption rates. Carbon dioxide was estimated according to the Harris–Benedict equation, and the ratio of REE to basal energy expenditure was expressed as % REE.

2.3. Blood biochemistry

Blood samples were collected when energy metabolism was measured and were analyzed to determine the following parameters: platelet count and levels of cholinesterase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (T-Bil), albumin (Alb), blood glucose, and NEFA (Tables 1 and 2).

2.4. Statistical analysis

All data were expressed as mean ± SEM. Statistical analyses were performed using SPSS for Windows, release 21.0 (SPSS Inc, Chicago, IL, USA). Clinical data on Pre and POD 14 were compared using Student's *t*-test, and npRQ and NEFA values were compared using one-way analysis of variance. The difference in npRQ and nonesterified fatty acid (NEFA) pre- and post-hepatectomy was shown as ΔnpRQ and ΔNEFA, respectively. Furthermore, predictive variables of ΔnpRQ and ΔNEFA in a single and multiple linear regression analysis were age, ICGR15, resection volume, and HBV and HCV infection in HCC. The significance threshold was $P < 0.05$.

Table 1
Clinical profiles of hepatectomy patients.

	Minor resection						Major resection		
	HCC (ICGR15 < 15.0)			HCC (ICGR15 ≥ 15.0)			HCC (ICGR15 < 15.0)		
	Minor-lowICG			Minor-highICG			Major-lowICG		
	n = 17			n = 18			n = 18		
Male/Female	14/3			14/4			13/5		
Etiology									
HBV	4			5			8		
HCV	8			6			3		
HBV/HCV	0			1			0		
Alcohol	0			1			3		
Other	5			5			4		
Child-Pugh									
A/B	17/0			14/3			18/0		
ICGR15 (%)	8.6	±	0.9	23.4	±	1.6	9.5	±	0.7
ChE (IU/L)	248	±	17	180	±	17	262	±	17
Age (y)	66.6	±	2.1	63.5	±	2.2	65.1	±	2
Hospital days (d)	14.7	±	1.1	29.1	±	6.3	20	±	2.1

HCC, hepatocellular carcinoma; HBV, hepatitis B virus; HCV, hepatitis C virus; ICGR15, retention rate of indocyanine green in 15 min; ChE, cholinesterase.