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Original Article

Energy expenditure measured using indirect calorimetry after elective cardiac surgery in ventilated postoperative patients: A prospective observational study

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S U M M A R Y

Background & aims: Resting energy expenditure (REE) following cardiac surgery is not determined. We conducted this prospective observational study to clarify this, comparing REE to basal energy expenditure (BEE) estimated using the Harris-Benedict equation (HBE).

Methods: Consecutive patients who underwent cardiac surgery (coronary artery bypass graft sursgery, valve surgery, and total arch replacement) in our hospital from September 2013 to March 2015 were included. Patients who were <18 years of age, undergoing hemodialysis, or had undergone emergency surgery were excluded. REE was measured using indirect calorimetry during intubation, or at 9 a.m. on postoperative day 1 in the intensive care unit. BEE was estimated using the HBE and compared with REE. Patients were divided into 2 groups: patients who received cardiac surgery with cardiopulmonary bypass (CPB) (on-pump group; n = 34) and without CPB (off-pump group; n = 13).

Results: We enrolled 47 patients. Mean age, body weight, and height were 73 ± 10 years (mean ± standard deviation), 55 ± 10 kg, and 155 ± 10 cm, respectively. BEE was 1147 ± 148 kcal/day. The average REE during ventilation was 1314 ± 148 kcal/day (23.9 ± 6.8 kcal/kg/day), significantly higher than estimated BEE (114 ± 35% BEE, $p < 0.0001$). The average REE was not significantly different between the 2 groups (24 ± 7 vs. 24 ± 6 kcal/kg/day, $p = 0.87$).

Conclusions: REE was 1314 ± 148 kcal/day (23.9 ± 6.8 kcal/kg/day), or 1.14 times higher than the estimated BEE, in postoperative

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cardiac surgery patients. The average REE was not significantly different between the on-pump and off-pump groups.

1. Introduction

Individual nutrition therapy is important for patients in the intensive care unit (ICU), as their energy requirements are influenced by several factors, such as inflammation, age, fever, sedation, and catecholamine levels [1,2]. Although nutrition management plays an important therapeutic role in patients in the ICU, it is difficult for intensivists to estimate the optimal caloric target in ICU patients. Several guidelines recommend indirect calorimetry (IC) to determine energy requirements [3,4]. In addition, recent guidelines suggest that a published predictive equation, such as the Harris-Benedict equation (HBE), or a simplistic weight-based equation (25–30 kcal/kg/day) be used in the absence of IC [3]. However, many predictive equations of energy expenditure have been proved to imprecisely predict REE and lead to under- or overfeeding in ICU patients [5]. In fact, we previously reported that resting energy expenditure (REE), as measured by IC in the early postoperative stage after minimally invasive esophagectomy, was significantly lower than the basal energy expenditure (BEE) estimated using the HBE [6]. Therefore, we consider the measurement of EE using IC for each surgical procedure to be important, because estimating EE is difficult, even for patients undergoing scheduled surgery.

Further to this point, the postoperative REE in patients undergoing cardiac surgery remains unclear. Thus, we conducted this prospective, observational study to evaluate the optimal REE in patients undergoing cardiac surgery and compared the obtained value with the BEE estimated using the HBE. Furthermore, we hypothesized that cardiopulmonary bypass (CPB) might affect the REE after surgery, because CPB is known to activate inflammatory responses [7] and myocardial ischemia/reperfusion [8]. Therefore, we compared the REE of patients who underwent cardiac surgery with and without CPB as a secondary analysis.

2. Methods

The study protocol complied with the Helsinki Declaration of 1975 and its subsequent revisions, and with the Australian National Health and Medical Research Council guidelines or other national guidelines of an equivalent standard. The ethics committee of our hospital approved this study (IRB #25–64), and we obtained written informed consent from all participants. This manuscript adheres to the applicable CONSORT guidelines.

This study included consecutive patients who underwent cardiac surgery (coronary artery bypass graft surgery, valve surgery, and total arch replacement) in our hospital from September 2013 to March 2015. Patients who were <18 years of age, undergoing hemodialysis, or had undergone emergency surgery were excluded from the study.

We measured REE after patients undergoing cardiac surgery had been admitted to the ICU with the Engström Carestation (GE Healthcare Japan, Tokyo, Japan), an indirect calorimeter module on the ventilator. This indirect calorimeter calculates REE breath-by-breath, and REE records were taken every 15 min. IC calculates REE by measuring oxygen consumption and carbon dioxide production at every respiratory cycle, in addition to the respiratory quotient (RQ). The device calculates REE using Weir's equation: $REE = (3.94 \times VO_2 + 1.11 \times VCO_2) \times 1.44$, where VO_2 is the oxygen consumption and VCO_2 is the carbon dioxide production [9]. We measured the REE from the time of ICU admission to extubation, or to 9 a.m. on postoperative day (POD) 1, if the patient was still intubated at the time. BEE was estimated using the HBE. We didn't use the equation of HB with or without disease factor multiplication, but we checked diseases such as diabetes, dyslipidemia.

All patients achieved the stable conditions suitable for IC measurement; that is, they received mechanical ventilation in the pressure-controlled ventilation mode (tidal volume: 6–10 mL kg^{-1}) in the ICU, under propofol and dexmedetomidine sedation. Each physician adjusted the ventilation setting and the doses of these sedative agents in accordance with the patients' respiratory condition, data from the arterial blood gas analysis, and their Richmond Agitation-Sedation Scale (RASS) score. The patients received an infusion of 10% glucose solution at a rate of 192 kcal day^{-1} after ICU admission. The blood glucose levels were maintained between 110 and 180 mg dL^{-1} using STG-55 artificial pancreas (Nikkiso, Tokyo, Japan). This device ensures continuous blood glucose levels and controls the blood glucose levels automatically using an original algorithm [10]. We catheterized the pulmonary artery using Swan-Ganz™ continuous end diastolic volume and continuous cardiac output thermodilution catheters (Edwards Lifesciences, Irvine, California, USA) via the right internal jugular vein and continuously monitored the patients' temperature using a Vigilance monitor (Edwards Lifesciences). The RASS score and temperature were recorded each hour during ventilation.

The primary outcome measure was the REE, as measured by IC. We present the REEs from the start of measurement, 3 and 6 h after the start of measurement, 1 h before extubation or 8 a.m. on POD 1, and at extubation or 9 a.m. on POD 1. We also calculated the average REE during the study period. For the secondary analysis, we divided all patients into 2 groups: those who underwent cardiac surgery with CPB (on-pump group) and those who underwent cardiac surgery without CPB (off-pump group). The timing of the measurements of the REE was the same as those for the primary analysis.

3. Statistical analysis

The data are expressed as the means ± standard deviations. The REE and BEE were compared using one-way repeated ANOVA. If a significant difference was detected, post-hoc test with Bonferroni was used to determine where the difference existed. For the secondary analysis, we used the chi-squared test and the unpaired t-test, as appropriate. All statistical analyses were performed using JMP 9.0 software (SAS Institute Japan, Tokyo, Japan) and EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria), and $p < 0.05$ was considered statistically significant.

4. Results

We enrolled 47 patients (23 women and 24 men) in this study (Fig. 1 and Table 1). The patients' mean age, body weight, and height were 73 ± 10 years, 55 ± 10 kg, and 155 ± 10 cm, respectively. Sixty percent of patients underwent valve surgery, followed by off-pump coronary artery bypass grafting (CABG) (28%), vascular surgery (11%), and on-pump CABG (2%). The mean pH and base excess on ICU admission were 7.35 ± 0.06 and −1.28 ± 2.89, respectively. The respiratory data during the study period are shown in Table 2. The average FiO_2, tidal volume, and respiratory rate were 0.49 ± 0.09, 6.7 ± 1.6 mL kg^{-1}, and 15 ± 3 min^{-1}, respectively. The mean BEE estimated using the HBE was 1147 ± 148 kcal day^{-1}.

5. Primary analysis

The results of the IC and patients' data during the study period are shown in Table 3, Fig. 2. The mean REE at the start of measurement was 1421 ± 539 kcal day^{-1} (25.9 ± 8.4 kcal kg day^{-1}), which was significantly higher than the estimated BEE (123 ± 42% of the BEE, $p < 0.0001$). The REE just before extubation or at 9 a.m. on POD 1 was 1377 ± 645 kcal day^{-1} (25.1 ± 9.5 kcal kg^{-1} day^{-1}), which was also significantly higher than the estimated BEE (120 ± 50% of the BEE, $p < 0.0001$). The average REE during ventilation was 1314 ± 148 kcal day^{-1} (23.9 ± 6.8 kcal kg^{-1} day^{-1}), which was significantly higher than the BEE (114 ± 35% of the BEE, $p = 0.01$). The average body temperature and RASS score were 38.2 ± 3.3 °C and −3 ± 1, respectively (see Table 4).

In addition, we perform a Bland Altman evaluation between REE measured by indirect calorimetry and calculated by the harris benedict equation to evaluate the accuracy of the predictive equation

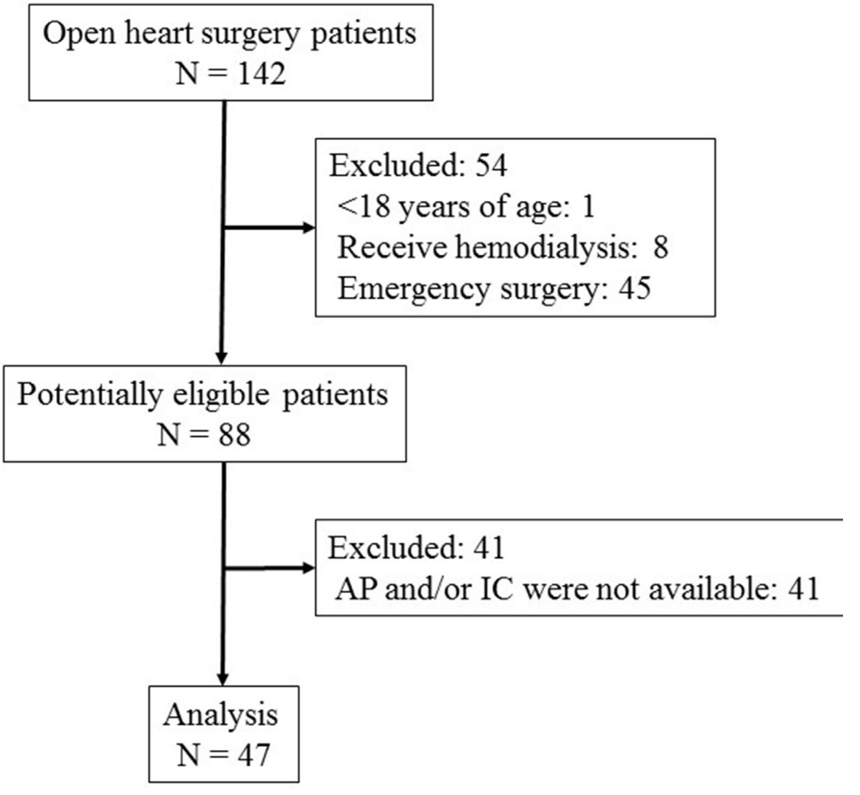


Fig. 1. Flow diagram of patient selection in this study. IC: Indirect calorimetry, AP: Artificial pancreas.

(Fig. 3). The mean of difference is 116.6 kcal/day, upper agreement limits is 292 kcal/day, lower agreement limits is 41.0 kcal/day.

6. Secondary analysis

We performed the secondary analysis after dividing the patients into 2 groups. The on-pump and off-pump groups included 34 and 13 patients, respectively. There were no significant differences between these groups in terms of age, height, body weight, anesthesia time, bleeding during surgery, temperature in the ICU, and RASS score. In the on-pump group, there were significantly more female patients and a significantly higher volume of urine during anesthesia than in the off-pump group (Table 3). Further, the BEE was not significantly different between the 2 groups (1138 ± 181 kcal day^{-1} vs. 1174 ± 146 kcal day^{-1}, $p = 0.52$). Although the REE at the start of measurement in the off-pump group was significantly higher than that in the on-pump group (31 ± 11 vs. 24 ± 7 kcal kg^{-1} day^{-1}, $p = 0.02$), the average REE did not significantly differ between the 2 groups (24 ± 7 vs. 24 ± 6 kcal kg^{-1} day^{-1}, $p = 0.87$). The RQ at the start of measurement was not significantly different between the 2 groups (0.77 ± 0.14 vs. 0.71 ± 0.11, $p = 0.18$). However, the RQs at 3 and 6 h after the start of measurement in the on-pump group were significantly higher compared to those in the off-pump group (0.75 ± 0.10 vs. 0.69 ± 0.06, $p = 0.04$; 0.76 ± 0.10 vs. 0.69 ± 0.06, $p = 0.03$, respectively). In addition, the average RQ in the on-pump group was significantly higher than in the off-pump group (0.75 ± 0.08 vs. 0.70 ± 0.05, $p = 0.03$).

Table 1
Characteristics of the study patients.

	N = 47
Age (years)	73 ± 10
Height (cm)	155 ± 10
Weight (kg)	55 ± 10
Female, n (%)	23 (49)
Body mass index (kg/m^2)	22.6 ± 3.8
Basal energy expenditure (kcal/day)	1147 ± 148
Preoperative comorbid conditions	
Hypertension, n (%)	31 (67)
Diabetes, n (%)	14 (30)
Hyperlipidemia, n (%)	22 (47)
History of smoking, n (%)	26 (55)
Surgical procedure, n (%)	
Off-pump coronary artery bypass grafting	13 (28)
On-pump coronary artery bypass grafting	1 (2)
Valve surgery	28 (60)
Vascular surgery	5 (11)
Duration of anesthesia (min)	514 ± 132
Duration of surgery (min)	456 ± 128
Use of cardiopulmonary bypass (CPB), n (%)	34 (72)
Duration of CPB (min)	226 ± 84
Total amount of intraoperative fluid (ml)	4819 ± 1712
Total amount of intraoperative bleeding (ml)	2350 ± 1523
Total amount of intraoperative urine (ml)	1171 ± 775
Intraoperative fluid balance (ml)	1124 ± 1626
pH on ICU admission	7.35 ± 0.06
Base excess on ICU admission	−1.3 ± 2.9

Data are expressed as mean ± standard deviation.
Basal energy expenditure: estimated using the Harris-Benedict equation.
ICU: intensive care unit.

7. Discussion

We conducted this prospective observational study to evaluate the standard REE in elective cardiac surgery patients and to compare this value with the BEE estimated using the HBE. Our study shows that the average REE during ventilation was 1314 ± 148 kcal day^{-1} (23.9 ± 6.8 kcal kg^{-1} day^{-1}), which was 1.14 times higher than the BEE, estimated by the HBE in patients after cardiac surgery. In addition, our secondary analysis revealed that although the average REE was not significantly different between the on-pump and off-pump groups, the average RQ in the on-pump group was significantly higher than in the off-pump group.

Recent guidelines suggest that a published predictive equation, such as the HBE, or a simplistic weight-based equation (25–30 kcal/kg/day) be used in the absence of IC [3]. A previous study reported that the mean lower and upper limits of agreement between IC-derived measurements and the HBE calculated values were −589.48 and 691.97 kcal/day, respectively, although the mean difference

Table 2
Average respiratory data during the study period.

FiO_2	0.49 ± 0.09
Tidal volume (mL/kg)	6.7 ± 1.6
Respiratory rate (/min)	15 ± 3
PEEP (cmH_2O)	6 ± 2
Peak pressure (cmH_2O)	17 ± 3

Data are expressed as mean ± standard deviation.
PEEP: positive end-expiratory pressure.

Table 3
The comparison between REE and BEE during the study period.

	REE (kcal/day)	% HBE
At 0 h	1421 ± 539	123 ± 42
At 3 h	1294 ± 418	112 ± 31
At 6 h	1218 ± 425	106 ± 32
At last 1 h	1377 ± 690	121 ± 61
Final	1377 ± 645	120 ± 50
Average	1314 ± 476	114 ± 35

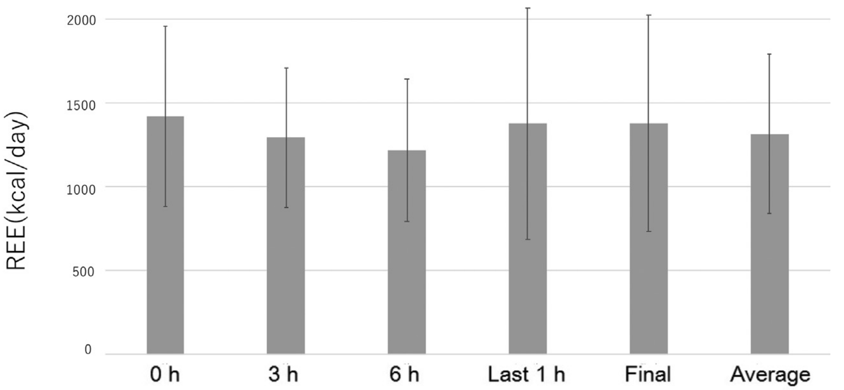
Data are expressed as mean ± standard deviation.
0 h: data at the start of measurement, 3 h: 3 h after the start of measurement, 6 h: 6 h after the start of measurement, Last 1 h: 1 h before the final measurement, Final: final measurement, just before extubation or at 9 a.m. on postoperative day 1.
BEE: basal energy expenditure estimated using the Harris-Benedict equation; REE: resting energy expenditure measured by indirect calorimetry; %HBE: (REE/BEE)*100.

between the methods was small (51.2 kcal/day) in critically ill patients [11]. Another study reported that there was a 10% or greater difference in resting metabolic rate between IC and the Penn State equation in 89% of cardiothoracic surgical patients [12]. These studies concluded that the calculated REE was poorly correlated with IC. In our study, the REE was significantly higher than the BEE

Table 4
Characteristics of patients in the on-pump and off-pump groups.

	On-pump (N = 34)	Off-pump (N = 13)	*P* value
Age (years)	72 ± 11	74 ± 6	0.54
Height (cm)	154 ± 10	159 ± 8	0.13
Weight (kg)	54 ± 10	57 ± 9	0.33
Female, n (%)	20 (58)	3 (23)	**0.03**
Body mass index (kg/m^2)	22.6 ± 2.6	22.7 ± 4.2	0.93
Basal energy expenditure (kcal/day)	1138 ± 181	1174 ± 14 6	0.52
Preoperative comorbid conditions			
Hypertension, n (%)	23 (68)	8 (62)	0.69
Diabetes, n (%)	7 (21)	7 (54)	**0.03**
Hyperlipidemia, n (%)	12 (35)	10 (77)	**0.01**
History of smoking, n (%)	15 (44)	11 (85)	**0.01**
Duration of anesthesia (min)	529 ± 142	475 ± 78	0.23
Duration of surgery (min)	473 ± 138	411 ± 83	0.14
Total amount of intraoperative fluid (ml)	4736 ± 1901	5037 ± 1101	0.60
Total amount of intraoperative bleeding (ml)	2560 ± 1665	1802 ± 902	0.13
Total amount of intraoperative urine (ml)	1421 ± 749	520 ± 351	**<0.001**
Intraoperative fluid balance (ml)	516 ± 1464	2715 ± 675	**<0.001**
REE (kcal/kg/day)			
At 0 h	24 ± 7	31 ± 11	**0.02**
At 3 h	23 ± 7	24 ± 6	0.67
At 6 h	23 ± 7	22 ± 5	0.82
At last 1 h	27 ± 15	23 ± 8	0.36
Final	26 ± 10	24 ± 9	0.51
Average	24 ± 7	24 ± 6	0.87
RQ			
At 0 h	0.77 ± 0.14	0.71 ± 0.11	0.18
At 3 h	0.75 ± 0.10	0.69 ± 0.06	**0.04**
At 6 h	0.76 ± 0.10	0.69 ± 0.06	**0.03**
At last 1 h	0.75 ± 0.10	0.71 ± 0.07	0.18
Final	0.77 ± 0.11	0.72 ± 0.10	0.19
Average	0.75 ± 0.08	0.70 ± 0.05	**0.03**

0 h: data at the start of measurement, 3 h: 3 h after the start of measurement, 6 h: 6 h after the start of measurement, Last 1 h: 1 h before the final measurement, Final: final measurement, just before extubation or at 9 a.m. on postoperative day 1.
BEE: basal energy expenditure estimated using the Harris-Benedict equation; ICU: intensive care unit, RASS: Richmond Agitation-Sedation Scale; REE: resting energy expenditure measured by indirect calorimetry, RQ: respiratory quotient.



	0 h	3 h	6 h	Last 1 h	Final	Average
REE (kcal/day)	1421 ± 539	1294 ± 418	1218 ± 425	1377 ± 690	1377 ± 645	1314 ± 476
REE (kcal/kg/day)	25.9 ± 8.4	23.6 ± 6.2	22.5 ± 6.6	25.4 ±13.0	25.1 ± 9.5	23.9 ±6.8
RQ	0.75 ±0.13	0.74 ± 0.10	0.74 ± 0.10	0.74 ± 0.10	0.74 ± 0.10	0.74 ± 0.08
BT (°C)	37.1 ± 0.9	37.4 ± 0.9	37.4 ± 0.9	38.2 ± 0.8	38.1 ± 0.8	38.2 ± 3.3
RASS	-4 ± 2	-4 ± 1	-4 ± 2	-3 ± 2	-3 ± 2	-3 ± 1

Fig. 2. Results of the indirect calorimetry and the patients' data during the study period. Data are expressed as mean ± standard deviation. 0 h: data at the start of measurement, 3 h: 3 h after the start of measurement, 6 h: 6 h after the start of measurement, Last 1 h: 1 h before the final measurement, Final: final measurement, just before extubation or at 9 a.m. on postoperative day 1. BEE: basal energy expenditure; RASS: Richmond Agitation-Sedation Scale; REE: resting energy expenditure measured by indirect calorimetry; %HBE: (REE/BEE)*100; RQ: respiratory quotient.

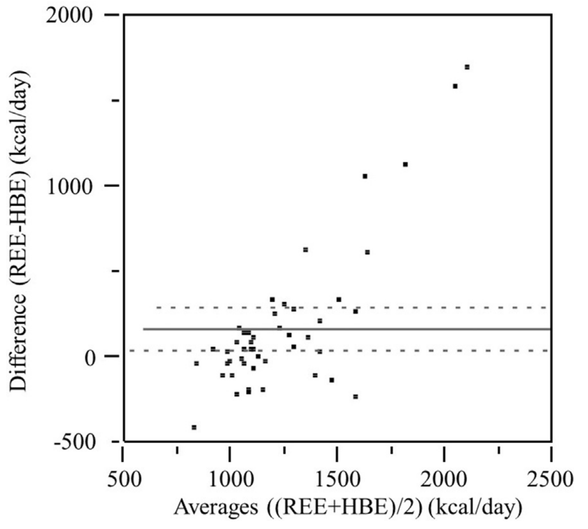


Fig. 3. Results of Bland-Altman plot of between REE measured by indirect calorimetry and calculated by the harris benedict equation. Large dashed line denotes bias (mean of difference) and small dashed line denotes 95% limits of agreement.

estimated by the HBE, and the average REE during the study period was 1.14 times higher than the estimated BEE. Our result is similar to that of previous studies in Europe and the United States [11,12]. Thus, there might be a 10% or greater difference in resting metabolic rate between IC and calculated values in these populations, regardless of body mass index. On the other hand, a recent review reported that cardiac surgery patients in the ICU did not receive adequate calories in the acute phase [13]. Therefore, a 10% difference in the real EE compared to estimated values may not have a clinical impact. In other words, the BEE estimated with the HBE might be useful in the absence of IC.

The influence of CPB on postoperative REE also remains unclear. Therefore, we compared the REE between the on-pump and off-pump groups. Our study revealed that although the REE at the start of measurement in the off-pump group was significantly higher than in the on-pump group (31 ± 11 vs. 24 ± 7 kcal kg^{-1} day^{-1}, $p = 0.02$), the average REE was not significantly different between the 2 groups (24 ± 7 vs. 24 ± 6 kcal kg^{-1} day^{-1}, $p = 0.87$). Off-pump CABG have been shown to be significantly less invasive than their CPB counterparts, and have shown a consistent trend toward reducing morbidity and mortality generally, and in high-risk subsets [14,15]. A previous review described that CPB provokes the development of systemic inflammatory response syndrome, which has important clinical implications [7]. Our study suggested that use of CPB might not affect postoperative REE because the average REE was similar in both groups.

Our study has some limitations. First, the REE measurements were only recorded until POD 1 because, in our hospital, IC is used to measure REE only in intubated patients, and almost all the patients were extubated on POD 1. Therefore, we could not determine the REE after this period. Accordingly, the timing of our study might not be optimal, because the patient's metabolism may have changed dynamically from the postoperative state in which the effects of anesthesia may remain, through periods of arousal and weaning from the ventilator for extubation. Further investigations of REE after extubation are required using different equipment. Second, there was a significant difference in urine volume during anesthesia between the on-pump and off-pump groups. This could have influenced the postoperative RQ, because the majority of nitrogen is excreted as urea in the urine [16]. Third, our study showed that the RQ in the off-pump group was significantly lower than in the on-pump group. It is possible that the steroid administration in the on-pump group might have affected the RQ. However, no research has been conducted on the relationship between RQ and steroid administration in the acute phase of surgical recovery. Fourth, the majority of patients in this study were low risk cardiac surgery patients because we only included elective surgery. Therefore, this significantly reduces the overall generalizability of the findings to all patients. Fifth, there was a significant difference in female distribution between the on-pump and off-pump groups. This could have influenced the REE at the start of measurement, because REE in female was generally lower than male [Ishikawa-Tanaka K, rt al. Physical activity level in healthy free-living Japanese estimated by doubly labelled water method and internal Physical Activity Questionnaire. Eur J Clin Nutr 62: 885–891,2008]. Sixth, there was a significant difference in number of diabetic patients between the on-pump and off-pump groups. This could have some effects on the RQ because the RQ in diabetes mellitus was reported to be low [Nakaya Y, Ohnaka M, Sakamoto S, Niwa Y, Okada K, Nomura M, Hara T, Kusonoki M. Respiratory quotient in patients with non-insulin-dependent diabetes mellitus treated with insulin and oral hypoglycemic agents. Ann Nutr Metab. 1998;42 (6):333–40]. Finally, comparison between the on-pump group and the off-pump group should be performed in on-pump and off-pump CABG patients. We could not compare between off-pump CABG and on-pump CABG because we included only 1 patient who received on-pump CABG. There were significant differences in preoperative comorbid conditions and gender in both groups which might have affected our results.

In conclusion, our prospective observational study showed that, after elective cardiac surgery, the mean REE measured by IC was 1314 ± 148 kcal day^{-1} (23.9 ± 6.8 kcal kg^{-1} day^{-1}), which was 1.14 times higher than the BEE estimated by the HBE. In addition, our secondary analysis revealed that the average REE was not significantly different between the on-pump and off-pump groups.

Statement of authorship

Takahiko Tamura (T.T.) and Tomoaki Yatabe (T.Y.) equally contributed to the conception and design of the research; T.Y. contributed to the design of the research; T.T. and T.Y. contributed to the acquisition and analysis of the data; T.T. contributed to the interpretation of the data; and T.T. drafted the manuscript. T.Y. and Masataka Yokoyama (M.Y.) critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Conflicts of interest

None.

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