Original Article

Respiratory quotient as an early predictor of length of stay after cardiac surgery: A prospective observational study

Huijuan Ruan PhD[1†], Qi Yang MD[2†], Xuelin Zhao MD[1], Qingya Tang MD[1], Yi Feng PhD[1]

[1]*Department of Clinical Nutrition, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China*
[2]*Department of Cardiothoracic Surgery, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China*
[†]*Both authors contributed equally to this manuscript*

Background and Objectives: This study aimed to investigate the respiratory quotient (RQ) levels and its trend in the early postoperative period of patients with heart disease. Additionally, we explored factors influencing RQ and evaluated the predictive capabilities of RQ and lactic acid for various outcomes. **Methods and Study Design:** In this prospective observational study, participants included were heart disease patients aged 18-80 years who underwent elective open-heart surgery and were subsequently admitted to the cardiothoracic surgery ICU post-operation. Indirect calorimetry (IC) measurements were conducted on patients during the first three days after surgery to assess their RQ levels. Clinical data, including personal information, postoperative characteristics, and duration of surgery, were documented based on the patient's medical history. **Results:** In this study, 135 patients, of whom 57.04% were male, underwent a total of 247 IC measurements following cardiac surgery. On the first, second, and third days of admission to the ICU, the RQ values were 0.77±0.09, 0.80±0.07, and 0.78±0.05, respectively. The ROC curve analysis showed that on the first day of admission to the ICU, RQ was a better predictor of prolonged mechanical ventilation, LOS in ICU, and LOS in hospital compared to lactate level. However, on the second day of ICU admission, neither RQ nor lactate level could predict longer durations of mechanical ventilation, LOS in ICU, and LOS in hospital. **Conclusions:** RQ may serve as a potential predictor for LOS in patients after cardiac surgery.

Key Words: respiratory quotient, indirect calorimetry, length of stay, serum lactate, cardiac surgery

INTRODUCTION

Resting energy expenditure (REE) is frequently used as a standard index to study human metabolic rate, aiding in guiding clinical nutrition and dietary supply.[1,2] Besides REE, another crucial parameter, the respiratory quotient (RQ), can be determined using indirect calorimetry (IC). While prior research has examined REE after cardiac surgery, the relationship between heart disease and the metabolic indicator RQ remains largely unexplored.[3]

RQ is a commonly used indicator in the evaluation for evaluating energy substrate utilization. The continuous, non-invasive measurement of expired gas through indirect calorimetry (IC) has been used to detect anaerobic metabolism.[4] IC showed increases in both oxygen uptake (VO_2) and carbon dioxide production (VCO_2), with a notable dominance of VCO_2 under anaerobic conditions. This led to an increase in the respiratory quotient ($RQ = VCO_2 / VO_2$).[5] In animal models, elevations in RQ have also been observed in tissue hypoperfusion. Elevated RQ values (close to 1.0) are indicative of carbohydrate oxidation, while lower values (near 0.7) suggest triacylglycerol oxidation. Values in between these extremes point to a mixture of fuels or protein oxidation, with the latter

often considered negligible.[5,6] If a combination of substrates is oxidized, the overall RQ is typically 0.8.[5] Previous studies have shown that the RQ, as measured by IC, correlates with the prognosis of patients suffering from liver fibrosis.[7] In patients with hepatocellular carcinoma, the normalization of RQ following liver resection takes longer to improve compared to blood biochemical markers.[8] Another study revealed that cardiovascular surgery in pediatric patients does not significantly alter resting energy expenditure but does affect substrate utilization.[9]

Corresponding Author: Dr Yi Feng, Department of Clinical Nutrition, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200092, China
Tel: 0086021-25078671
Email: fengyi@xinhuamed.com.cn
Dr Huijuan Ruan, Department of Clinical Nutrition, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200092, China
Tel: 0086021-25078672
Email: ruanhuijuan@xinhuamed.com.cn

A clinical study suggested that a nutritional support strategy using IC could enhance the prognosis of patients with severe traumatic brain injury by improving substrate utilization.[10] Additionally, it was found that pre-operative RQ levels are associated with post-operative weight loss in patients undergoing bariatric surgery.[11]

In clinical practice, lactate serves as the foremost biomarker of tissue hypoxia.[12] Hyperlactatemia is relatively common in cardiac surgical patients and is usually regarded as a marker of illness severity. The prevalence of hyperlactatemia in cardiac surgical patients is approximately 10–20%.[12] The metabolic state of the heart can undergo significant alterations in conditions such as the post-operative phase of cardiac surgery involving extracorporeal circulation, characterized by shifts in oxygen consumption (VO_2) and lactate metabolism.[13] In patients undergoing cardiac surgery, serum lactate level and its dynamic fluctuations are metrics that necessitate monitoring. Anaerobic metabolism may occur due to a discrepancy between O_2 demand and supply, a phenomenon frequently observed in pediatric patients following cardiopulmonary bypass (CPB). This can lead to hyperlactatemia, which is linked to adverse events in the early post-operative period.[14] Reducing oxygen supply to the tissue elevates serum lactate levels. However, since lactate is a normal byproduct of glucose metabolism, its increase may not be solely attributed to hypoxia. In addition, serum lactate levels, a standard marker of anaerobic metabolism, are influenced by lactate production, conversion and clearance and may lag behind the anaerobic response.[15] Although several studies have confirmed the correlation between elevated lactate levels and adverse outcomes after cardiac surgery,[12,16] the reliability of this indicator remains questionable. It has also been noted that an increased RQ predicts patient mortality after cardiac surgery; however, the study did not discuss the trend of postoperative RQ in patients, the factors affecting its level, or the relationship between RQ and the hospital stay of surviving patients after surgery.[17]

In this study, we explored the RQ level and its trend in the early post-operative period of cardiac patients through prospective observational analysis. We compared the RQ differences between patients who did and did not undergo CPB. Additionally, we analyzed the factors influencing RQ among these patients and assessed the capabilities of RQ and lactate level to predict the duration of mechanical ventilation, the length of stay (LOS) in ICU, and the overall LOS in hospital. The findings from this study can aid in understanding the physiological and metabolic shifts in patients after surgery, thereby assisting in the development of more suitable nutritional intervention programs.

METHODS
Study protocol
This study is a single-center, prospective, observational research. The participants were heart disease patients, aged 18 to 80, from the Department of Cardiothoracic Surgery in Shanghai Xinhua Hospital who had undergone elective open-heart surgery and were admitted to the cardiothoracic surgery ICU post-operation between January 2017 and January 2018. IC was conducted 1 to 3 days following surgery to assess RQ. All patients received mechanical ventilation using the SIMV model (Evita 4; Drägerwerk AG & Co., Lübeck, Germany). As interruptions results in reduced accuracy of IC measurements,[3,18] patients with respiratory instability, those that needed frequent adjustment of mechanical ventilation parameters, and those that had surgical complications requiring timely treatment were excluded from this study. Prior to formal enlistment, the sample size was determined using an online sample size calculator (http://powerandsamplesize. com/), drawing from previously published literature and pilot study results.[19] Following this calculation, it was established that a minimum of 124 participants would be required. After appropriate expansion, we finally recruited 135 people.

Statement of ethics
This study was approved by the Ethics Committee of the Hospital with the approval number XHEC-C-2017-086 and with the participants' informed consent in compliance with the Helsinki Declaration. Written informed consents were obtained from the patients.

Indirect calorimetry (IC)
After the clinician confirmed that the patient's hemodynamics were stable following cardiac surgery, the REE was measured. Assessment of REE was then repeated every morning until the patient was off the mechanical ventilator. IC was conducted over a continuous 20-min session with a metabolic cart (GE Datex Ohmeda s / 5tm). It was imperative that all patients were fasted for at least 6 h prior to the IC procedure and the ambient temperature between 20-25 °C. During the measurements, patients were administered sedatives and analgesics via the intravenous route. They showed no sign of physical activity and did not receive any energy-containing liquid, such as injections of glucose or amino acid. Inspiratory and expiratory air samples were collected through the unique port of the endotracheal tube and measured by the machine analyzer, which was calibrated before each measurement in accordance with the manufacturer's instructions. The RQ data were presented in ratio form, while the REE data were presented as 24-h energy consumption (kcal/day).[3,18] The first measurement was conducted from 3:00 to 6:00 p.m. after entering the ICU, and the situation was initially stable. The second and third measurements were conducted from 9:00 a.m. to 11:00 a.m. All measurements were completed by two nutritionists.

Clinical data collection
The following clinical data were documented for each patient: personal information (including age, gender, body height and body weight), pre-operative characteristics (such as disease and diagnosis), post-operative characteristics (such as body temperature, heart rate, APACHE II score, duration of mechanical ventilation, LOS in ICU, and LOS in hospital) and details of surgical procedure (including operative duration, CPB duration, aortic cross-clamp time) based on the medical history. Weight and height measurements were taken by trained medical staff following standard procedures for anthropometric measurements using the same equipment when

the patients were admitted to the hospital. BMI was calculated as weight/height^2 (kg/m^2). Blood glucose and lactate levels were measured by nurses in the cardiothoracic surgery intensive care unit using a specialized blood gas analyzer (Radiometer ABL800 FLEX) following the manufacturer's instruction. The instrument has been confirmed to produce reliable results in previous studies.[20-22]

Calculation of parenteral and enteral energy intake

Post-operative liquid therapy for patients was performed by cardiothoracic surgeons. If the patient requires individualized parenteral nutrition treatment, a nutrition professional unrelated to this study will evaluate the patient's nutritional status, develop a nutritional plan, and implement parenteral nutrition. All patients were fasting on the first day after operation (no enteral nutrition intake) and were supplemented with energy-containing fluids (such as glucose or amino acid injection) through intravenous infusion. Cardiothoracic surgeons gradually provided enteral nutrition to patients based on their condition on the second day after surgery. Professionals qualified as nutritionists recorded the energy intake of patients through intravenous infusion within 24 h after admission to the ICU and during 24-48 h, as well as the energy intake through the gastrointestinal tract. The results were expressed in kcal/d. The researchers fully communicated with the patients and obtained written informed consent prior to the study. Further research findings pertaining in this study can be identified in previously published literature.[3,18]

Statistical analysis

Statistical analysis was performed using SPSS Statistics 25.0 statistical software (IBM Co., Armonk, NY, USA). Continuous variables were presented as mean ± SD. Repeated measured ANOVA (based on Generalized Linear Model) was used, and the mixed-effects model (uses the maximum likelihood method) was employed in case of missing values. Tukey's method was applied for post hoc comparisons. Pearson's correlation analysis was used to assess the correlation between RQ and other indicators, while partial correlation analysis was used after controlling variables. Multiple linear regression was used for further analysis of the relationship between RQ and other indicators. Collinearity diagnostics were carried out according to the variance inflation factor (VIF).[23] The prognosis-predictive performances of RQ and lactate levels were assessed using the area under the curve (AUC) measurements for receiver-operating characteristic (ROC) curves, and statistical significance was measured using p-values ($p<0.05$). The figures were generated using R-language and Prism 9.0.

RESULTS

Characteristics of the test participants

This study included 135 patients, of whom 57.04% were males, all of whom underwent IC measurement after cardiac surgery. On the first day of ICU admission, all 135 patients completed the measurement at an average measurement time of 1.74 ± 1.02 h post-operation. On the second day of ICU, 97 patients who were still undergoing mechanical ventilation completed the IC measurement,

with an average measurement time of 19.16 ± 0.89 h post-operation. On the third day of ICU, 15 patients who were still undergoing mechanical ventilation completed the measurement, with an average measurement time of 58.23 ± 0.41 h post-operation. Table 1 summarizes the demographic characteristics and related parameters of patients with various diseases.

RQ level of patients after operation

The RQ levels of patients on the first, second, and third days of admission to the ICU were 0.77±0.09 (n=135), 0.80±0.07 (n=97), and 0.78±0.05 (n=15), respectively. After cardiac surgery, the RQ levels for all 135 patients varied at different durations after surgery (F=3.889, p=0.0257). Compared to the day of admission to the ICU, the RQ of patients on the second day increased significantly. For patients with coronary arteries, the RQ on the first, second, and third days of admission to the ICU were 0.74±0.05 (n=55), 0.77±0.05 (n=39), and 0.77±0.03 (n=6), respectively. For those with valve surgery, the RQ was 0.80±0.08 (n=80) on the first day of admission to the ICU, 0.82±0.07 (n=58) on the second day, and 0.78±0.06 (n=9) on the third day. Among patients with coronary arteries, the RQ level on the second day in the ICU was significantly higher than on the first day; for those with valve surgery, no significant difference was found. The RQ levels and the change trends over time are presented in Figure 1.

To evaluate the RQ level of patients with different surgical treatments and their change after surgery, we first calculated the "duration after operation" in hours (h) based on the time point of measuring RQ after surgery for each patient and the patient's surgery time. We then generated scatter plots and performed linear regression analysis. As depicted in Figure 2, the RQ levels of coronary artery and valve patients at various time points after surgery are presented. Although the linear regression results were not statistically significant (all p>0.05), Figure 2 shows that the RQ levels of patients who underwent valve surgery were comparatively higher and remained at higher levels up to 21 h post-surgery. On the other hand, the RQ level of patients with coronary arteries gradually increased after surgery and then gradually decreased on the second day post-surgery.

Related influencing factors of RQ in patients after cardiac surgery

Subsequently, the factors that may influence RQ in patients after cardiac surgery were analyzed. The results of the Pearson correlation analysis indicate that the RQ level of the patients on the day of ICU admission was positively correlated with several postoperative indices: body temperature (r = 0.241, p = 0.005), heart rate (r = 0.301, p = 0.001), blood glucose (r = 0.333, p < 0.0001), and lactate level (r= 0.588, p < 0.0001). The RQ level was also positively correlated with the parenteral energy intake on the first day after the operation (r = 0.215, p = 0.012). The RQ level was also positively correlated with the mechanical ventilation duration (r = 0.192, p = 0.026), LOS in ICU (r = 0.240, p = 0.005), and LOS in hospital (r = 0.285, p = 0.001). After adjusting for patient's age, body height, and weight, the partial correlation analysis showed

Table 1. Demographic characteristics and related indicators

	Coronary artery (n=55)	Valve surgery (n=80[§])	Total (n=135)	p-value[¶]
Age (years)	64.2±9.74	56.0±11.1	59.3±11.3	<0.0001
Male, n (%)	43 (78.2)	34 (42.5)		-
Height (cm)	168±7.17	163±6.93	165±7.36	<0.0001
BW (kg)	67.7±9.84	62.6±11.5	64.7±11.1	0.009
BMI (kg/m^2)	24.0±2.61	23.4±3.23	23.6±2.99	0.282
Surgery duration (min)				
Operative duration	247±53.1	255±50.3	252±51.4	0.348
CPB duration	-	120±50.3	-	-
Aortic cross-clamp	-	70.9±27.9	-	-
Pre-op. characteristics				
LVEF (%)	57.1±11.5	61.7±8.23	59.8±9.90	0.008
Pre-op. diabetes (n)	9	4	13	-
Pre-op. hypertension (n)	21	18	39	-
Post-op. characteristics				
APACHE II[†]	7.87±2.40	6.90±2.39	7.30±2.43	0.022
Body temperature (℃)[†]	36.2±1.04	37.0±0.68	36.7±0.93	<0.0001
Heart rate (bpm)[†]	87.9±17.7	94.5±14.6	91.9±16.1	0.025
RQ[†]	0.74±0.05	0.80±0.08	0.77±0.09	<0.0001
RQ[‡]	0.77±0.05 (n=39)	0.82±0.07 (n=58)	0.80±0.07 (n=97)	0.0002
DMV (d)	2.65±6.66	2.13±3.45	2.34±4.99	0.556
LOS in ICU (d)	5.73±6.96	5.66±8.92	5.69±8.15	0.963
LOS in hospital (d)	21.6±11.3	25.3±16.7	23.8±14.8	0.156
Energy expenditure and intake[†]				
mREE (kcal/d)	1853±478	1956±446	1914±460	0.202
mREE/BW (kcal/d.kg)	27.2±5.68	31.5±4.84	29.8±5.59	<0.0001
EN (kcal/d)	0	0	0	-
PN (kcal/d)	538±198	594±180	571±189	0.089
EN+PN (kcal/d)	538±198	594±180	571±189	0.089
Biological characteristics				
Glucose (mmol/L)[†]	8.65±3.12	10.9±3.22	9.99±3.36	<0.0001
Lactate (mmol/L)[†]	2.21±1.23	5.27±3.41	4.02±3.12	<0.0001
Lactate (mmol/L)[‡]	2.37±1.18 (n=39)	5.22±2.99 (n=58)	4.08±2.90 (n=97)	<0.0001

CPB: cardiopulmonary bypass; BW: body weight; BMI: body mass index; LVEF (%): left ventricular ejection fraction; APACHE II: acute physiology and chronic health evaluation II; RQ: respiratory quotient; DMV: Duration of mechanical ventilation; LOS: length of stay; mREE: measured resting energy expenditure; EN: energy intake of enteral nutrition; PN: energy intake of intravenous infusion fluid on the first day after surgery
[†]Parameters on the 1st day of admission to the ICU.
[‡]Parameters on the 2nd day of admission to the ICU.
[§]Two of the 80 patients underwent both coronary artery bypass grafting and valve surgery.
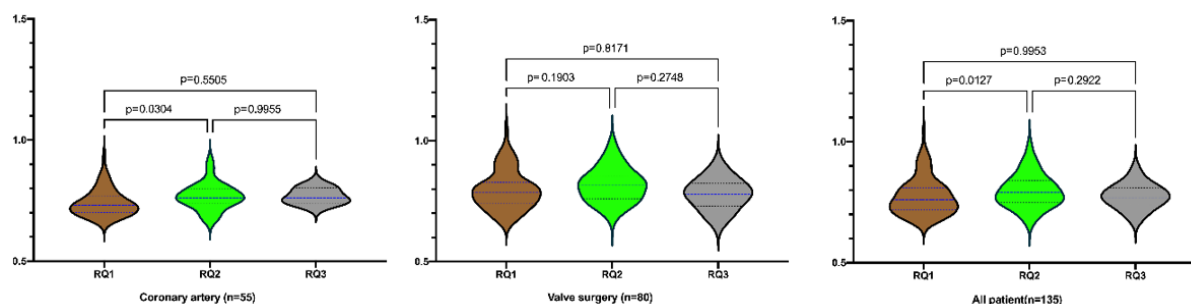[¶]Results of ANOVA analysis between two different disease groups.

Figure 1. RQ of cardiac patients after operation. RQ1: respiratory quotient on the 1st day of admission to ICU; RQ2: respiratory quotient on the 2nd day of admission to ICU; RQ3: respiratory quotient on the 3rd day of admission to ICU. Repeated measured ANOVA (based on Generalized Linear Model) was used, and the mixed-effects (maximum likelihood) model was used for missing values. Tukey's method was used for post hoc comparisons. The p-value refers to the result of post hoc comparisons using Tukey's method.

that the RQ level of patients on the day of admission to the ICU was still positively correlated with several factors: body temperature (r = 0.184, p = 0.047), heart rate (r = 0.250, p = 0.007), blood glucose (r = 0.322, p<0.0001), and lactate level (r = 0.564, p<0.0001). The RQ level was also positively correlated with parenteral energy intake (r = 0.251, p = 0.006), mechanical ventilation duration (r =

0.224, p = 0.015), LOS in ICU (r = 0.285, p = 0.002), and LOS in hospital (r = 0.328, p<0.0001). On the second day after admission to the ICU, Pearson correlation analysis showed that the patient's RQ was negatively correlated with BMI (r = -0.320, p = 0.001). It was also positively correlated with parenteral energy intake (r = 0.224, p = 0.028) and lactate levels on the second day of ICU

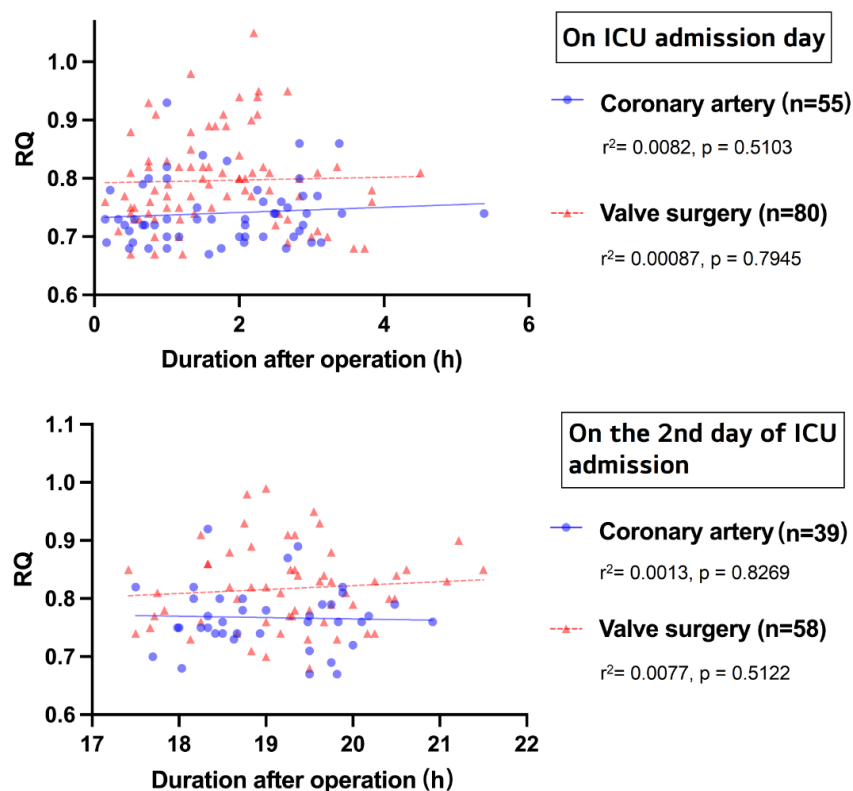**Figure 2.** Scatter plots of RQ. RQ: respiratory quotient; r^2 and *p*-value are statistical values of linear regression

admission (r = 0.339, *p* = 0.001). RQ also had a positive linear relationship with LOS in hospital (r = 0.210, *p* = 0.042). After adjusting for the patient's age, body height, and weight, the partial correlation analysis showed that RQ was positively correlated with several factors: APACHE II score (r = 0.280, *p* = 0.010), LOS in hospital(r = 0.234, *p* = 0.033), and parenteral energy intake (r = 0.266 , *p* = 0.015) and lactate levels on the second day after admission to ICU (r = 0.337, *p* = 0.002). As is shown in Figure 3, we presented the above relationship through a heat map, with the correlation coefficient being represented by the color intensity of each block.

After conducting the collinearity diagnosis, we incorporated the candidate indicators with significant correlations from the correlation analysis into the multiple linear regression model to assess the relationship between RQ and associated indicators. Employing the stepwise regression method, we introduced lactate, LOS in hospital, BMI, and PN into the model. At this time, two conditions were set: (1) the overall model was significant (*p* < 0.05), and (2) the independent variable coefficient was significant (*p* < 0.05). The specific statistics are smmarized in Table 2. On the day after operation, RQ displayed a positive correlation with LOS in hospital. Furthermore, RQ was positively correlated with lactate and PN on both the first and second days post-operation.

ROC curve for duration of mechanical ventilation, LOS in ICU, and LOS in hospital

Finally, we plotted the ROC curves for duration of mechanical ventilation, LOS in ICU, and LOS in hospital. The median values for DMV (0.98 days), LOS in ICU (3.78 days), and LOS in hospital (19.81 days) were set as cut-off points. Values above the median were considered

positive outcomes, refer to previous research.[24] Based on the ROC curve analysis, on the first day of ICU admission, RQ was a better predictor of longer durations of mechanical ventilation, LOS in ICU, and LOS in hospital than lactate levels. However, on the second day of ICU admission, neither RQ nor lactate levels could predict longer duration of mechanical ventilation, LOS in ICU, or LOS in hospital. The relevant results are presented in Figure 4 and Table 3.

DISCUSSION

We initially examined the RQ level and trend changes in patients after cardiac surgery. Our findings indicated that the overall RQ levels in patients who underwent valve surgery were higher than those in patients with coronary heart disease. Among patients with coronary artery disease, the RQ level tend to be higher on the second day of ICU admission compared to the first day. However, when compared to valve surgery patients, the difference was not significant. Prior studies have demonstrated that patients are in a heightened metabolic state following surgery. Even when adequate energy and nutrients are provided to match their increased metabolic rate, maintaining a catabolic state is very probable.[10,18] Caloric deprivation may cause a delay in wound healing, weakness in skeletal and respiratory muscles, and decreased resistance to infections.[9,25] In the present study, patients experienced insufficient energy intake in the early postoperative period (PN energy intake is significantly lower than REE). Although this is a short-term condition following surgery, variations in RQ performance and significant differences in REE/BW among patients were observed. The findings indicated substantial disparities in energy consumption and substrate metabolism between the two patient groups.
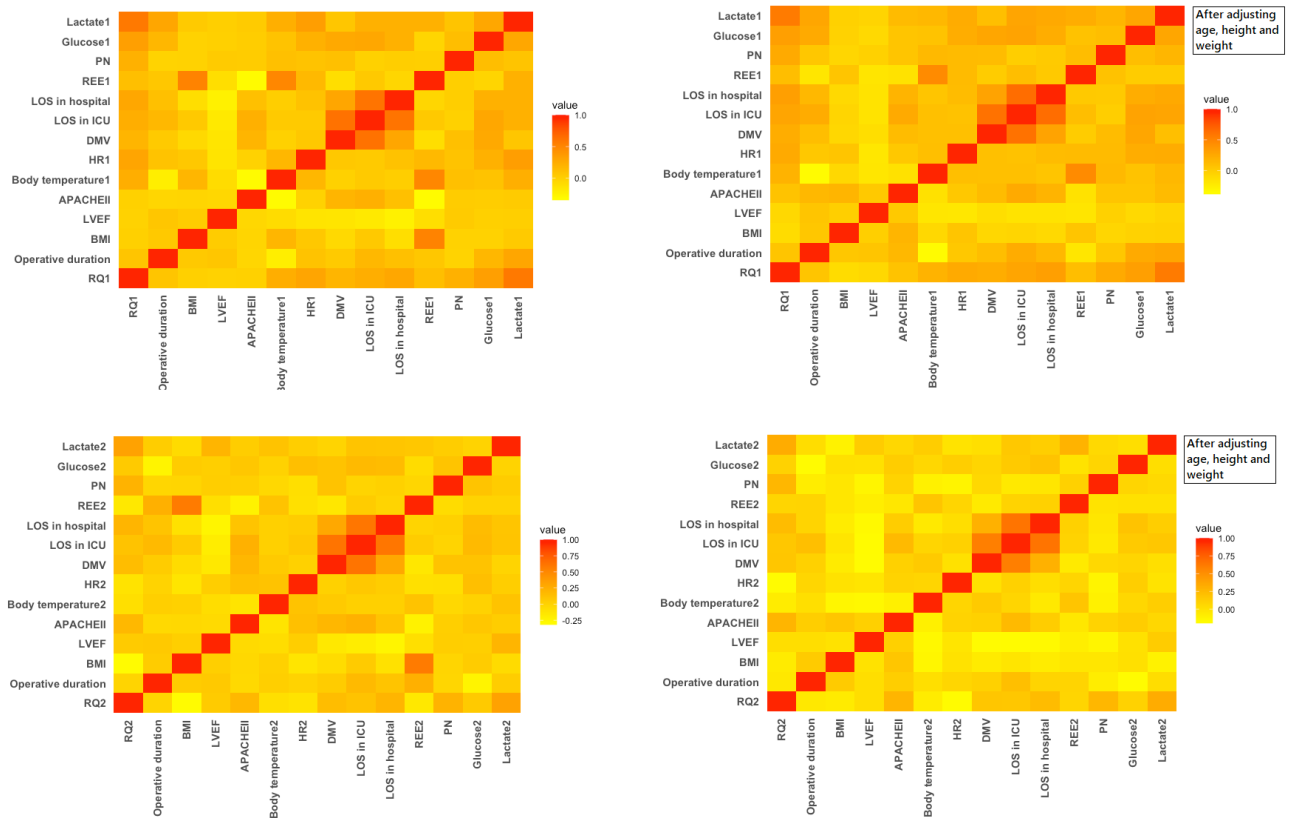
Figure 3. Heat Map of RQ. Each block signifies a pair of variables, and the color intensity within the block denotes the strength and direction of their relationship. A darker hue represents a stronger positive correlation, while a lighter shade suggests a weaker or no correlation. The correlation coefficient is expressed by the color depth of the block; Lactate 1, glucose 1, REE 1, HR1, Body temperature 1, RQ1 refer to the values of parameters on the day after operation; Lactate 2, glucose 2, REE 2, HR2, Body temperature 2, RQ2 refer to the values of parameters on the second day after operation; PN: energy intake of intravenous infusion fluid on the first day after surgery

Table 2. Statistics of multiple linear regression

Dependent variables and factors	Standardization coefficient β	p	R	R2	Adjusted R2
1st day					
RQ					
Lactate[†]	0.506	0.000	0.634	0.402	0.386
LOS in hospital	0.196	0.009			
PN[†]	0.166	0.024			
2nd day					
RQ					
Lactate[‡]	0.298	0.002	0.507	0.257	0.232
BMI	-0.310	0.001			
PN[†]	0.220	0.018			

RQ: respiratory quotient; PN: energy intake of intravenous infusion fluid; LOS: length of stay; BMI: body mass index
[†]Results on the day of admission to the ICU.
[‡]Results on the second day of admission to the ICU.

The reason for the metabolic differences among patients with different disease types may firstly stem from the differences in patient characteristics. In this study, patients with coronary heart disease had notably higher body weight than those with valvular disease, although BMI differences were insignificant. In the case of insufficient exogenous energy supply in the early post-operative period, patients with coronary heart disease may utilize more body fat reserves, which lead to lower RQ values. Several studies have indicated that overweight and obese people have low RQ values, suggesting that the lipid oxidation level of overweight women was significantly higher than that the normal weight group.[26] Furthermore, peri-operative hormonal stress responses and therapeutically administered catecholamines may contribute to the shift towards fat oxidation.[27]

Another possible reason for the post-operative metabolic differences among patients with different diseases may be due to variations in surgical procedures. In this study, higher blood glucose levels, blood lactate levels, and mREE per kg of body weight were observed among cardiac patients, indicating that valve surgery patients may exhibit greater energy consumption and substrate metabolism imbalance after surgery. Cardiopulmonary bypass (CPB) utilizes a pump-oxygenator device to partially or completely replace heart and lung functions for
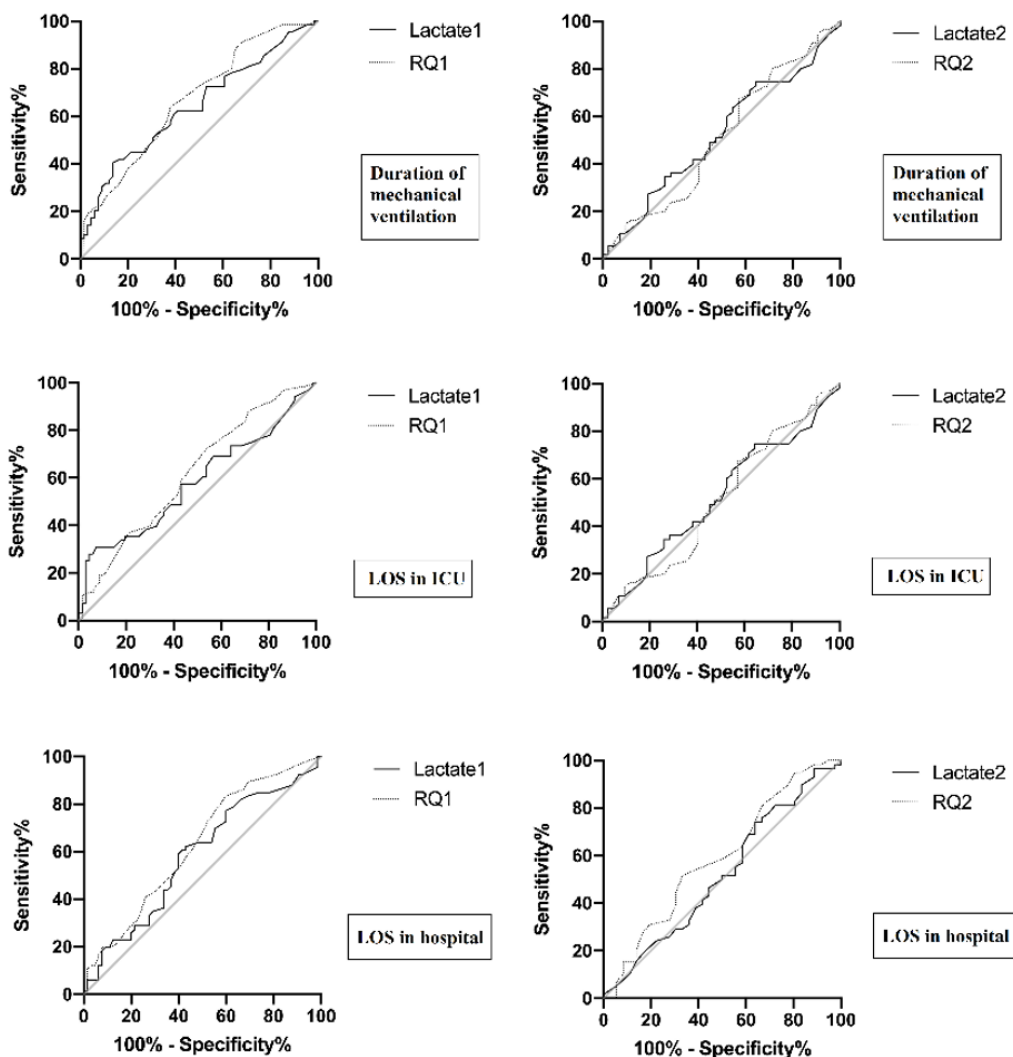
Figure 4. ROC curve for lactate and RQ. RQ1 refers to the respiratory quotient on the day of admission to the ICU; RQ2 refers to the respiratory quotient on the second day of admission to the ICU; Lactate1 refers to the lactic acid level on the day of admission to the ICU, and the interval between the determination time and RQ1 was less than 2 h; Lactate2 refers to the lactic acid level on the second day of admission to the ICU, and the interval between the determination time and RQ1 was less than 2 h. LOS: length of stay. The median values of DMV, LOS in ICU, and LOS in hospital were set as cut-off points, and those larger than the median were set as positive outcomes

Table 3. Statistical values for the ROC curves for duration of mechanical ventilation, LOS in ICU, and LOS in hospital[†]

Variable	DMV				LOS in ICU			
	AUC	Std. Error	95%CI	p-value	AUC	Std. Error	95%CI	p-value
RQ1[‡]	0.669	0.046	0.579-0.760	0.001	0.618	0.048	0.523-0.712	0.018
Lactate1[§]	0.641	0.047	0.548-0.734	0.005	0.581	0.049	0.484-0.678	0.104
RQ2[‡]	0.540	0.064	0.414-0.666	0.516	0.511	0.060	0.393-0.629	0.853
Lactate2[§]	0.562	0.061	0.443-0.682	0.306	0.522	0.059	0.406-0.638	0.710

Variable	LOS in hospital			
	AUC	Std. Error	95%CI	p-value
RQ1[‡]	0.626	0.049	0.531- 0.722	0.013
Lactate1[§]	0.581	0.050	0.483- 0.680	0.109
RQ2[‡]	0.590	0.062	0.469- 0.710	0.146
Lactate2[§]	0.519	0.063	0.396- 0.642	0.756

AUC: area under the curve; DMV: duration of mechanical ventilation; LOS: the length of stay
[†]The median values of DMV, LOS in ICU, and LOS in hospital were set as cut-off points, and those larger than the median were set as positive outcomes.
[‡]RQ1 refers to the respiratory quotient on the day of admission to ICU; RQ2 refers to the respiratory quotient on the second day of admission to ICU.
[§]Lactate1: refers to the lactic acid level on the day of admission to the ICU, and the interval between the determination time and RQ1 was less than 2 h; Lactate2 refers to the lactic acid level on the second day of admission to the ICU, and the interval between the determination time and RQ1 was less than 2 h.

safer cardiac operations.[28] Patients with valvular disease usually require CPB technology, while those with coronary heart disease usually do not, leading to metabolic differences (e.g., blood glucose and lactate levels). Besides eliciting systemic responses, CPB can disrupt the integrity of red blood cells, causing the release of hemoglobin from excessive foreign surface contact and mechanical stresses.[29] CPB can affect vital organs such as the brain, kidneys, and small intestines and may lead to adverse consequences.[29] Through the IC method, a precise means of assessing respiratory quotient, we can provide adequate nutritional support for these critically ill patients by modulating the formulation to reduce RQ and improve ventilation.[30]

To date, our understanding of the factors influencing RQ, particularly in critically ill patients, remains limited.[26] Therefore, we conducted further investigations into the factors affecting RQ in these patients.[31] In this study, we discovered a positive correlation between body temperature and RQ. Valvular patients had significantly higher post-operative body temperature and heart rate compared to those with coronary heart disease. One study found that changes in ambient temperature could lead to changes in the oxidation substrate of the body.[32] The disorder of myocardial energy metabolism may be one of the potential causes. During the first hours after a cardiac procedure, the myocardial uptake of substrates is markedly deranged, with no uptake of the normally dominant energy substrates. This suggests that endogenous substrates might constitute the majority of myocardial energy production in the heart.[33] In clinical practice, proper management of the patient's heart rate and temperature during the peri-operative period can minimize the stressful stimulus to catabolism, thereby slowing the wasting process to the point where much less nutrition is required to meet metabolic requirements.[34-36] However, the mechanism of the relationship between RQ and temperature/heartbeat needs further study. Glucose and lactate metabolism are linked by a number of intracellular metabolic pathways.[37] As glucose can be metabolized to lactate (also lactate to glucose), they are both nutrient metabolic substrates and can reflect the acute stress response of patients after cardiac surgery,[37] which may be related to global tissue hyperfunction.[38] In this study, RQ was found to be positively correlated with blood glucose and lactic acid. Similar to previous literature, the results of this study showed that RQ can reflect the acute stress level of patients.[39]

LOS in ICU and duration of mechanical utilization are indicators reflecting the clinical outcome of ICU patients,[40] while LOS in hospital is a widely used indicator to reflect the prognosis and health outcomes of patients with various diseases.[41-44] Using reasonable parameters to predict or estimate a patient's ICU LOS or hospital LOS may improve resource allocation and patient care.[45-46] One study found that RQ was associated with ICU mortality in post-cardiac arrest patients but not among those with neurological illnesses.[39] Another concluded that RQ could be used to predict 30-day mortality after cardiac surgery.[17] While numerous studies have explored the use of RQ in predicting mortality, none have explored its association with hospitalization time. In this study, it was found that RQ, like lactate, can be used as a potential indicator for

evaluating hospitalization outcomes. Furthermore, we also compared the ability of RQ and lactate to predict longer mechanical ventilation duration, LOS in the ICU, and LOS in the hospital on the first day and the second day after surgery, respectively. The results showed that on the first post-operative day, RQ demonstrated a slightly better predictive ability than lactate. Considering that RQ can be obtained through IC, which is non-invasive, its predictive use can improve clinical practice and aid in more reasonable clinical interventions. However, it is crucial to highlight that RQ measurement necessitates specialized equipment, is time-intensive, and comes with a higher expense compared to lactate testing. While lactate testing is an invasive procedure, it offers a quicker detection speed and a lower cost. Consequently, the decision between these two methods should be contingent on the specific circumstances and objectives, taking into account their respective pros and cons.

This study has several limitations that should be considered when interpreting the results. It is a single-center prospective research with a small sample size, involving only post-operative patients admitted to the ICU showing early post-operative RQ levels. The majority of patients were weaned from mechanical ventilation within three days after surgery. Due to the application scope of the metabolic cart used in this study, RQ levels of those weaned from mechanical ventilation were not measured, potentially limiting the generalizability of our findings. Patients with severe post-operative conditions were excluded from the study because they might require frequent ventilator adjustments or regular drug support and rescue. RQ measurement was not performed continuously (e.g., 24-h continuous measurement) due to patient treatment needs. Body composition analysis (e.g., bioelectrical impedance method, DXA method) and several influencing factors of RQ, such as race, heredity, and the use of sedatives, analgesics, and anesthetics, were not analyzed in this study, possibly leading to information bias.[32,47] Finally, although the energy intake on the first day after operation (parenteral energy intake) was discussed in this study, the relationship between the types of energy intake and RQ was not explored. Despite the limitations of this study, future research could explore how body composition and different types of energy intake affect RQ. Additionally, influencing factors such as race, heredity, and medication use should be considered to reduce information bias.

Research, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine (23XHCR17C).

REFERENCES

1. Barichella M, Cereda E, Faierman SA, Piuri G, Bolliri C, Ferri V. Resting energy expenditure in Parkinson's disease patients under dopaminergic treatment. Nutr Neurosci. 2022;25:246-55. doi: 10.1080/1028415X.2020.1745427.
2. Orozco-Ruiz X, Pichardo-Ontiveros E, Tovar AR, Torres N, Medina-Vera I, Prinelli F. Development and validation of new predictive equation for resting energy expenditure in adults with overweight and obesity. Clin Nutr. 2018;37:2198-205. doi: 10.1016/j.clnu.2017.10.022.
3. Ruan H, Tang Q, Yang Q, Hu F, Cai W. Resting Energy Expenditure Early after Cardiac Surgery and Validity of Predictive Equations: A Prospective Observational Study. Ann Nutr Metab. 2021:77:271-8. doi: 10.1159/000518676.
4. Wasserman K, Beaver WL, Whipp BJ. Gas exchange theory and the lactic acidosis (anaerobic) threshold. Circulation. 1990;81:14-30.
5. Patel H, Kerndt CC, Bhardwaj A. Physiology, Respiratory Quotient. Treasure Island (FL): StatPearls Publishing; 2023.
6. Price ER, Mager EM. Respiratory quotient: Effects of fatty acid composition. J Exp Zool A Ecol Integr Physiol. 2020;333:613-8. doi: 10.1002/jez.2422.
7. Belarmino G, Singer P, Gonzalez MC, Machado NM, Cardinelli CS, Barcelos S. Prognostic value of energy expenditure and respiratory quotient measuring in patients with liver cirrhosis. Clin Nutr. 2019;38:1899-904. doi: 10.1016/j.clnu.2018.07.001.
8. Sugihara K, Yamanaka-Okumura H, Teramoto A, Urano E, Katayama T, Mori H. Recovery pattern of non-protein respiratory quotient and non-esterified fatty acids after liver resection. Nutrition. 2014;30:443-8. doi: 10.1016/j.nut.2013.09.012.
9. Gebara BM, Gelmini M, Sarnaik A. Oxygen consumption, energy expenditure, and substrate utilization after cardiac surgery in children. Crit Care Med. 1992;20:1550-4. doi: 10.1097/00003246-199211000-00012.
10. Maxwell J, Gwardschaladse C, Lombardo G, Petrone P, Policastro A, Karev D. The impact of measurement of respiratory quotient by indirect calorimetry on the achievement of nitrogen balance in patients with severe traumatic brain injury. Eur J Trauma Emerg Surg. 2017;43:775-82. doi: 10.1007/s00068-016-0724-z.
11. Rosales A, Elli E, Lynch S, Ames G, Buchanan M, Bowers SP. Preoperative high respiratory quotient correlates with lower weight loss after bariatric surgery. Surg Endosc. 2020;34:3184-90. doi: 10.1007/s00464-019-07090-5.
12. Minton J, Sidebotham DA. Hyperlactatemia and Cardiac Surgery. J Extra Corpor Technol. 2017;49:7-15.
13. Pendino JC, Hess L, Beltrame S, Castillo GA, Trujillo J. Oxygen saturation and lactate concentration gradient from the right atrium to the pulmonary artery in the immediate postoperative following cardiac surgery with extracorporeal circulation. Rev Bras Ter Intensiva. 2017;29:287-92. doi: 10.5935/0103-507X.20170042.
14. Cheifetz IM, Kern FH, Schulman SR, Greeley WJ, Ungerleider RM, Meliones JN. Serum lactates correlate with mortality after operations for complex congenital heart disease. Ann Thorac Surg. 1997;64:735-8. doi: 10.1016/s0003-4975(97)00527-4.
15. Hayashi K, Matsui H. Case Report: Novel Monitoring for Anaerobic Conditions Detected by Respiratory Quotient in a Critically Ill Pediatric Patient. Front Pediatr. 2022;10:874969. doi: 10.3389/fped.2022.874969.
16. Renew JR, Barbara DW, Hyder JA, Dearani JA, Rivera M, Pulido JN. Frequency and outcomes of severe hyperlactatemia after elective cardiac surgery. J Thorac Cardiovasc Surg. 2016;151:825-30. doi: 10.1016/j.jtcvs.2015.10.063.
17. Piot J, Hébrard A, Durand M, Payen JF, Albaladejo P. An elevated respiratory quotient predicts complications after cardiac surgery under extracorporeal circulation: an observational pilot study. J Clin Monit Comput. 2019;33:145-53. doi: 10.1007/s10877-018-0137-0.
18. Ruan H, Zhao X, Yang Q, Feng Y, Zhang Y, Cai W. Relationship between energy intake, prognosis and related indicators in adults after cardiac, thoracic, and vascular surgery: A prospective observational study. Asia Pac J Clin Nutr. 2021;30:365-73. doi: 10.6133/apjcn.202109_30(3).0003.
19. Dell RB, Holleran S, Ramakrishnan R. Sample size determination. Ilar j. 2002;43:207-13. doi: 10.1093/ilar.43.4.207.
20. Yilmaz O, Karapinar T. Evaluation of the i-STAT analyzer for determination of ionized calcium concentrations in bovine blood. Vet Clin Pathol. 2019;48:31-5. doi: 10.1111/vcp.12705.
21. Vera MA, Sutphin A, Hansen L, El-Khoury JM. Resolving Pseudohyponatremia: Validation of Plasma Sodium on Radiometer ABL800 Blood Gas Analyzers for Immediate Reflex Testing. Lab Med. 2022;53:e105-e8. doi: 10.1093/labmed/lmab114.
22. Bargnoux AS, Beaufils O, Oguike M, Lopasso A, Dupuy AM, Sebbane M. Point-of-care creatinine testing in patients receiving contrast-enhanced computed tomography scan. Clin Chim Acta. 2018;478:111-3. doi: 10.1016/j.cca.2017.12.025.
23. Kim JH. Multicollinearity and misleading statistical results. Korean J Anesthesiol. 2019;72:558-69. doi: 10.4097/kja.19087.
24. Enriquez CAG, Diestro JDB, Omar AT, 2nd, Geocadin RG, Legaspi GD. Safety and Clinical Outcome of Good-Grade Aneurysmal Subarachnoid Hemorrhage in Non-Intensive Care Units. J Stroke Cerebrovasc Dis. 2020;29:105123. doi: 10.1016/j.jstrokecerebrovasdis.2020.105123.
25. Mehta NM, Bechard LJ, Dolan M, Ariagno K, Jiang H, Duggan C. Energy imbalance and the risk of overfeeding in critically ill children. Pediatr Crit Care Med. 2011;12:398-405. doi: 10.1097/PCC.0b013e3181fe279c.
26. Bugatto F, Quintero-Prado R, Vilar-Sánchez JM, Perdomo G, Torrejón R, Bartha JL. Prepregnancy body mass index influences lipid oxidation rate during pregnancy. Acta Obstet Gynecol Scand. 2017;96:207-15. doi: 10.1111/aogs.13058.
27. Sanchez JA, Sanchez LL, Dudrick SJ. Nutritional considerations in adult cardiothoracic surgical patients. Surg Clin North Am. 2011;91:857-75, ix. doi: 10.1016/j.suc.2011.06.001.
28. Holman WL, Timpa J, Kirklin JK. Origins and Evolution of Extracorporeal Circulation: JACC Historical Breakthroughs in Perspective. J Am Coll Cardiol. 2022;79:1606-22. doi: 10.1016/j.jacc.2022.02.027.
29. Govender K, Jani VP, Cabrales P. The Disconnect Between Extracorporeal Circulation and the Microcirculation: A Review. Asaio j. 2022;68:881-9. doi: 10.1097/MAT.0000000000001618.
30. Brandi LS, Grana M, Mazzanti T, Giunta F, Natali A, Ferrannini E. Energy expenditure and gas exchange measurements in postoperative patients: thermodilution versus indirect calorimetry. Crit Care Med. 1992;20:1273-83. doi: 10.1097/00003246-199209000-00014.
31. Marra M, Scalfi L, Contaldo F, Pasanisi F. Fasting respiratory quotient as a predictor of long-term weight changes in non-obese women. Ann Nutr Metab. 2004;48:189-92. doi: 10.1159/000079556.

32. De Nardi M, Bisio A, Della Guardia L, Facheris C, Faelli E, La Torre A. Partial-Body Cryostimulation Increases Resting Energy Expenditure in Lean and Obese Women. Int J Environ Res Public Health. 2021;18:4127. doi: 10.3390/ijerph18084127.

33. Håkanson E, Svedjeholm R, Vanhanen I. Physiologic aspects in postoperative cardiac patients. Ann Thorac Surg. 1995;59:S12-4. doi: 10.1016/0003-4975(94)00902-j.

34. Jakob SM, Stanga Z. Perioperative metabolic changes in patients undergoing cardiac surgery. Nutrition. 2010;26:349-53. doi: 10.1016/j.nut.2009.07.014.

35. Chiara O, Giomarelli PP, Biagioli B, Rosi R, Gattinoni L. Hypermetabolic response after hypothermic cardiopulmonary bypass. Crit Care Med. 1987;15:995-1000. doi: 10.1097/00003246-198711000-00001.

36. Jakob SM, Ensinger H, Takala J. Metabolic changes after cardiac surgery. Curr Opin Clin Nutr Metab Care. 2001;4:149-55. doi: 10.1097/00075197-200103000-00012.

37. Watha K, Davenport A, Tangvoraphonkchai K. Changes in blood glucose and lactate concentrations with hemodialysis. Artif Organs. 2022;46:138-45. doi: 10.1111/aor.14097.

38. Das S, Ghosh K, Hazra A, Sen C, Goswami A. Is elevated blood glucose a marker of occult tissue hypoperfusion in off-pump coronary artery bypass grafting? Ann Card Anaesth. 2018;21:393-401. doi: 10.4103/aca.ACA_202_17.

39. Lundin A, Dell'anna AM, Peluso L, Nobile L, Annoni F, Creteur J. Veno-arterial CO(2) difference and respiratory quotient after cardiac arrest: An observational cohort study. J Crit Care. 2021;62:131-7. doi: 10.1016/j.jcrc.2020.12.002.

40. Vahedian-Azimi A, Rahimibashar F, Ashtari S, Guest PC, Sahebkar A. Comparison of the clinical features in open and closed format intensive care units: A systematic review and meta-analysis. Anaesth Crit Care Pain Med. 2021;40:100950. doi: 10.1016/j.accpm.2021.100950.

41. Ashkenazi I, Gefen L, Hochman O, Tannous E. The 4-hour target in the emergency department, in-hospital mortality, and length of hospitalization: A single center-retrospective study. Am J Emerg Med. 2021;47:95-100. doi: 10.1016/j.ajem.2021.03.049.

42. Trotzky D, Tsur AM, Fordham DE, Halpern P, Ironi A, Ziv-Baran T. Medical expertise as a critical influencing factor on the length of stay in the ED: A retrospective cohort study. Medicine (Baltimore). 2021;100(19):e25911. doi: 10.1097/MD.0000000000025911.

43. Li P, Lu X, Teng C, Cai P, Kranis M, Dai Q. The Impact of COPD on in-Hospital Outcomes in Patients with Takotsubo Cardiomyopathy. Int J Chron Obstruct Pulmon Dis. 2020;15:2333-41. doi: 10.2147/COPD.S267289.

44. Wathne JS, Harthug S, Kleppe LKS, Blix HS, Nilsen RM, Charani E. The association between adherence to national antibiotic guidelines and mortality, readmission and length of stay in hospital inpatients: results from a Norwegian multicentre, observational cohort study. Antimicrob Resist Infect Control. 2019;8:63. doi: 10.1186/s13756-019-0515-5.

45. Henzi A, Kleger GR, Hilty MP, Wendel Garcia PD, Ziegel JF. Probabilistic analysis of COVID-19 patients' individual length of stay in Swiss intensive care units. PLoS One. 2021;16:e0247265. doi: 10.1371/journal.pone.0247265.

46. Higgins SD, Erdogan M, Coles SJ, Green RS. Early mobilization of trauma patients admitted to intensive care units: A systematic review and meta-analyses. Injury. 2019;50:1809-15. doi: 10.1016/j.injury.2019.09.007.

47. Gould LM, Cabre HE, Brewer GJ, Hirsch KR, Blue MNM, Smith-Ryan AE. Impact of Follicular Menstrual Phase on Body Composition Measures and Resting Metabolism. Med Sci Sports Exerc. 2021;53:2396-404. doi: 10.1249/MSS.0000000000002702.