

Evaluation of the effect of ERAS to nutritional status of patients with elective craniotomy using bioelectrical impedance analysis: a prospective and randomized controlled trial

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Abstract

Background The aim of the present study was to test the body composition changes of patients undergoing elective craniotomy using bioelectrical impedance analysis, so as to evaluate the effect of enhanced recovery after surgery (ERAS) to nutritional status of patients. **Methods** 140 patients who needed elective craniotomy were randomly divided into two groups: observation group (ERAS group) and control group (traditional treatment group). The age was 45.6 ± 12.7 years old. Patients in ERAS group were treated with a set of enhanced recovery measures, while control group patients underwent conventional treatment. Bioelectrical impedance analysis was used to test body composition before and after the surgery. **Results** The body mass (BM), body mass index (BMI), fat mass (FM), muscle mass (MM), fat mass index (FMI), free-fat mass index (FFMI), body cell mass (BCM), body cell mass index (BCMI), in both groups were decreased after surgery. The decrease of FM and FMI in the control group was significantly different from that in the observation group ($p < 0.05$). However, the decrease of BM, BMI, MM, FFMI, BCM and BCMI in both groups were not statistically significant. **Conclusion** Patients undergoing elective craniotomy showed various degrees of nutritional injuries, and ERAS could alleviate nutritional injuries caused by operation. **Keywords** Enhanced Recovery after Surgery • Bioelectrical impedance analysis • Elective craniotomy Trail Registration Chinese Clinical Trial Registry, ChiCTR-INR-16009662. Registered on 27 October 2016. Trail Registration Chinese Clinical Trial Registry, ChiCTR-INR-16009662. Registered on 27 October 2016.

Background

Initiated by Professor Henrik Kehlet in 1997, Enhanced Recovery after Surgery (ERAS) programs attempt to attenuate the body's response to surgery, decrease postoperative complications, and shorten the length of hospital stay by optimizing a set of perioperative measures [1]. So far, ERAS has been studied in a variety of surgical specialties, including colorectal surgery [2], pancreaticoduodenectomy [3], gastrectomy [4], et al. Perioperative nutritional status is critical for the surgical patients, and the perioperative nutritional support has been introduced in many guidelines of ERAS [2-4]. Compared with patients undergoing other operations, patients for craniotomy had a low prevalence of malnutrition. Nevertheless, nausea, vomiting, dysphagia, headaches and other symptoms apparently affected normal diet, leading to weight loss or even malnutrition [5].

Changes of nutritional status results in cell membrane change and body fluid imbalance. Therefore, body composition analysis plays an important role in the assessment of nutritional status. Classic parameters includes anthropometric parameters and plasma proteins such as BM, BMI, skinfold thickness, albumin, prealbumin, etc. However, no marker is relatively sensitive or specific. Bioelectrical impedance analysis (BIA) is a quick, safe, inexpensive, noninvasive and especially accurate method to evaluate body composition changes. The principle of BIA involves passing a small multiple-frequency alternating current through the body and measuring the resulting resistance and reactance [6].

The aim of this study is to test the body composition changes of patients undergoing elective craniotomy before and after operation, and evaluate the effect of ERAS program to nutritional status of patients. To the best of our knowledge, no studies have investigated nutritional status using BIA within an ERAS program.

Methods

Patient recruitment

140 patients who were admitted for elective craniotomy in our hospital between October 2016 and May 2017 were enrolled. Participants were randomly divided into two groups by computerized random number generation: the observation group (ERAS group) (n=70) and the control group (traditional treatment group) (n=70). Inclusion criteria: All patients between 18 to 65 years of age (18 and 65 were included) without sex limitation, who had a single intracranial lesion, and were medically eligible for elective craniotomy were included. Exclusion criteria: Patients with intracranial trauma, pathology requiring emergent surgery, preoperative disturbance of consciousness, and presence of a confounding condition (e.g., pregnancy) or disease that could potentially impact postoperative recovery (e.g., paralysis, spinal deformity, autoimmune diseases, myocardial infarction, severe infection, liver and renal malfunction, or severe psychological or mental illness) were excluded from this study.

Perioperative measures

Our study was supported by local institutional ethical committee to develop a neurosurgical ERAS protocol through a quality patient care initiative. We set up a Neurosurgical ERAS Working Group in June 2016, including clinicians and ancillary staff from neurosurgery, anesthesiology, in-patient and operative nursing and clinical nutrition. This multidisciplinary working group developed and applied the neurosurgical ERAS protocol outlined in this study.

In ERAS group, patients underwent preoperative counseling, stopping smoking and alcohol consumption, nutritional risk screening and nutritional status assessment, nutritional therapy if necessary, anti-thrombotic prophylaxis, postoperative nausea and vomiting (PONV) management, glycerine enema induction if long history of constipation or ≥ 2 days without defecation, antimicrobial prophylaxis and skin preparation, shortening preoperative fasting and carbohydrate loading, preoperative respiratory protection, scalp blocks, minimally invasive craniotomies and endoscopic skull base approaches, non-opioid analgesia, avoiding hypothermia, early feeding after surgery, early removal of the urinary drainage within 6h, rapid de-escalation of fluids, early mobilization[7].

The perioperative care of patients in the conventional care (i.e. control) group was based on traditional neurosurgical protocols.

Nutritional risk screening (NRS-2002)

Nutritional status was assessed by NRS2002 [8]. It consists of a nutritional score, a severity of disease score and an age-adjustment for patients aged over 70 years. Nutritional score was calculated as the total score of the nutritional state, severity of disease and the age adjustment. Patients with NRS2002 score <3 were classified as having no nutritional risk, and NRS2002 score ≥ 3 were classified as existing nutritional risk.

Anthropometric measurement and bioelectrical impedance analysis before and after surgery

Height was measured with an accordant tool accurate to 0.1 centimeter. BIA measurement was taken using Healthy Keeper body composition analyzer (Korea). Patients were on an empty stomach, emptying urine and feces, calming down if exercising or sweating. Shoes, socks and metal accessories were removed. Pelmas attached to the two electrodes while thumb and forefinger squeezed the other two electrodes. Whole-body resistance and reactance between frequencies of 1 kHz and 1 MHz were measured. Body mass (BM), body mass index (BMI), fat mass (FM), free-fat mass (FFM), muscle mass (MM), body fat percentage (BFP), total body water (TBW), intracellular fluid (ICF) and extracellular fluid (ECF) values of patients were recorded. Body fat mass (BCM), fat mass index (FMI) and fat-free mass index (FFMI) were calculated by the following formulas: $FMI(kg/m^2) = FFM(kg)/height^2(m^2)$, $FFMI(kg/m^2) = (BM-FM)(kg)/height^2(m^2)$ [9], $BCM(kg) = ICF(kg)/0.7$, $BCMI(kg/m^2) = BCM(kg)/height^2(m^2)$ [10].

Perioperative nutritional support

In the ERAS group, patients were permitted solid food 6 hours before surgery and given 400 mL of 12.5% carbohydrate-rich beverage 2-3 hours before induction of anaesthesia to whom without suffering diabetes mellitus. The program of early feeding after surgery is as follows: feeding was started 4-6 hours after operation with water, when most of patients revived from anesthesia. During 6-24 hours after operation, patients could drink oral nutritional supplement (250 kcal/day) and other liquid diet. On POD 2, patients were suggested to drink oral nutritional supplement (500 kcal/day) and feed with some soft diet. From POD 3 until discharge, patients were allowed to eat regular diet, and ONS were given only if subjects were unable to eat 1000kcal/day from normal food. As ONS, we used homogenized diet (Leskon, Xi'an Li Bang clinical nutrition Co, LTD, China). The composition per 100 mL is: kcal, 104; carbohydrates, 14.6 g; proteins, 4.28 g; lipids, 2.82 g.

While, in control group, fasting is from midnight before surgery, no carbohydrate loading, no early feeding after surgery. Feeding was started 24h or more after surgery with the return of passing wind and faeces.

Discharge criteria

All the patients in ERAS and control group were discharged if they met our predefined discharge criteria: adequate pain management with oral analgesia, adequate intake of solid food, no need for intravenous fluids, no fever, independent mobility and a safe disposition at home. The decision of discharge was made by the consensus of two senior attending physicians in the department of Neurosurgery, who were instructed to follow the discharging criteria, and were independent of the researchers involved in this study.

Statistical analysis

All data were analyzed using the SPSS software (version 20.0). Data were shown as mean \pm standard deviation for normally distributed variables and as median for distributed continuous variables. Normally distributed continuous variables were analyzed using paired and un-paired *t-test* and ANOVA. Non-normally distributed variables were compared by Mann-Whitney U-test test. A two-sided level of $p < 0.05$ was considered as statistically significant.

Results

Clinical characteristics

A total of 197 patients were assessed for eligibility, prior to enrollment in this study. Fifty-seven patients were excluded for not meeting the inclusion criteria, refusal to participate, refusal to consent for surgery, special physique or refusal to measure after the operation. At last, a total of 140 patients (70 patients in the ERAS group and 70 patients in the control group) patients were enrolled in this study after exclusion, (Oct 2016 – May 2017), 48 patients were male, and 92 were female, with the age of 45.6 ± 12.7 years old. The height, BM and BMI were 1.62 ± 0.06 m, 62.0 ± 9.43 kg, 23.7 ± 3.25 kg/m², respectively (Table 1). The height, BM and BMI for ERAS group were 1.62 ± 0.07 m, 61.4 ± 9.75 kg and 23.5 ± 3.39 kg/m², while those for control group were 1.62 ± 0.06 m, 64.8 ± 7.48 kg and 24.7 ± 2.34 kg/m² (Table 2). There was no statistical difference among age, height, BM and BMI between two groups. All the patients did not have nutritional risk with NRS2002 score < 3 . They underwent craniotomy by the same experienced surgical team, and received allocated intervention. The median total hospital stay were 10 and 13 days respectively in ERAS and control group, and the median postoperative length of stay were 4 and 7 days respectively.

Changes of body composition

The levels of BM, BMI, FM, MM, BCM, FMI, FFMI and BCMI were reduced after surgery in both groups, which were reduced more in the control group (Table 3, Fig.1). The reduction of FM and FMI in ERAS and

control groups were statistically different ($p < 0.05$) (Fig.1). The reduction of FM and FMI were (0.16 ± 1.23) vs (0.99 ± 0.99) kg ($p = 0.017$, 95%CI: -1.50 to -0.15), (0.06 ± 0.47) vs (0.38 ± 0.38) kg/m² ($p = 0.016$, 95%CI: -0.57 to -0.06) respectively. The reduction of BM, BMI, MM, BCM, FFMI and BCMI in these two groups showed no statistical difference, and the Mean \pm SD were (1.17 ± 1.20) vs (2.45 ± 3.57) kg ($p = 0.189$, 95%CI: -3.27 to 0.71), (0.46 ± 0.47) vs (0.92 ± 1.32) kg/m² ($p = 0.203$, 95%CI: -1.20 to 0.28), (0.95 ± 1.37) vs (1.43 ± 2.91) kg ($p = 0.541$, 95%CI: -2.12 to 1.15), (0.64 ± 6.55) vs (0.94 ± 2.16) kg ($p = 0.860$, 95%CI: -3.72 to 3.12), (0.39 ± 0.57) vs (0.53 ± 1.18) kg/m² ($p = 0.485$, 95%CI: -0.55 to 0.26), (0.25 ± 0.39) vs (0.37 ± 0.83) kg/m² ($p = 0.414$, 95%CI: -0.41 to 0.17).

Discussion

In recent years, ERAS program has been widely used in many specialties and formed the expert consensus or guidelines. Nutritional measurement is an important intervention to rapid rehabilitation, including nutritional risk screening, preoperative nutritional support, the use of a carbohydrate-rich isotonic solution preoperatively, restarting early oral feeding within 24 hours postoperatively and postoperative immunonutrition [9][12][13]. Perioperative nutritional support reduces the catabolism, complication rates, and the occurrence of postoperative insulin resistance with a positive impact on perioperative glucose control, muscle preservation and intestinal mucosal function [9][12][13]. Our study, for the first time, tested the body composition changes of patients undergoing elective craniotomy before and after operation, and evaluated the validity of perioperative nutritional support in ERAS program. It also showed that BIA was effective for assessing the nutritional status of patients in ERAS program.

BM is the most direct, simple and widely used indicator of nutritional status. BMI is another index of nutritional status and a BMI less than 18.5 is considered as malnutrition [14]. Surgery induces "stress response" and activation of the immune-hypothalamic-pituitary-adrenal axis and sympathetic nervous systems, which lead to metabolic changes such as insulin resistance, protein catabolism, and lipid oxidation [15][16][17]. In our study, patients needed elective craniotomy showed a lower prevalence of malnutrition compared with patients undergoing other operations, the control group lost an average of 2.45 ± 3.57 kg during perioperative period, while in ERAS group, the weight loss was 1.17 ± 1.20 kg. In addition, our results indicated that the stress lead to enhanced catabolism. In spite of ERAS program, nutritional status was deteriorated during perioperation. Some studies demonstrated that inflammation caused by acute phase response may often promote a catabolic state, including increased protein decomposition and nitrogen loss, suppressed protein synthesis, and accelerated weight loss, a lower BMI even protein energy malnutrition [18][19][20][21]. Inflammation was also found to be involved in the development of insulin resistance[22]. Previous studies have identified that the preoperative fasting could aggravate the surgical stress response [15], exacerbate insulin resistance [23], and weaken gastrointestinal function [24], leading to aggravation of weight loss. In addition, patients undergoing preoperative overnight fasting were more inclined to be thirsty, hungry, and anxious [23]. Patients in ERAS group undergoing fasting solid food 6 hours before surgery and 12.5% carbohydrate drinks 2-3 hours

before induction of anaesthesia were considered to achieve maximal glycogen storage, alleviate insulin resistance, reduce postoperative protein and nitrogen loss, so as to maintain better lean body weight and muscle strength [25][26][27][28]. Furthermore, early feeding postoperatively and oral nutritional supplement are feasible. Previous studies showed that the early oral feeding was effective. Luca Gianotti et al [29] found that patients receiving early oral feeding postoperatively had a more efficient protein synthesis with a higher level of short half-life protein. Early feeding plays a more important role in nourish intestinal mucosa so as to avoid intestinal flora migration rather than providing nutrients for the body. In our study, we performed oral nutritional supplement in the first days after surgery, which possessed a more favorable ratio between volume taken and calorie/protein intake compared with ordinary food. Further more, minimally invasive craniotomies and endoscopic skull base approaches, avoiding hypothermia, early removal of the urinary drainage, early mobilization and other ERAS measures could also alleviate stress response. In our study, the reduction of BM and BMI in the control group was more than that in the ERAS group, suggesting that ERAS program alleviated body catabolism.

BMI alone cannot differentiate the respective contributions of FM and FFM to body weight, which are main components of body composition. And body weight and BMI are not adequate measurements to assess underlying changes in FM and FFM during illness [30]. Moreover, excess fat mass reduces the sensitivity of BMI to detect nutritional depletion [31]. Therefore, FM was tested. Because FM changes with height, weight, and age, we also calculated FMI, which was height-independent and could provide more meaningful information about nutritional status [8]. Insulin resistance usually means reduced glucose uptake and oxidation and glycogen synthesis [15]. In order to meet elevated energy demands, fat oxidation accelerates and becomes the principle source of fuel postoperatively. Furthermore, increased cortisol and epinephrine levels stimulate gluconeogenesis, with triglycerides being converted to glycerol and fatty acids [15]. Similar to previous reports [30], our results showed a reduced FM and FMI, indicating an increased body fat consumption when suffering stress response. And the reduction of FM and FMI was statistically different between the ERAS and control group, suggesting ERAS program and perioperative nutritional support alleviated stress response and fat catabolism.

Stress response caused by surgery is often accompanied with elevation of protein breakdown and increased nitrogen loss [15]. However, protein intake and synthesis are inadequate because of stress and fasting, which lead to a negative protein balance. Protein breakdown principally involves skeletal muscle protein loss [32]. FFM includes muscle and water, and BCM is the metabolically active component of FFM. Therefore, BCM and FFM are usually considered as better predictors of nutritional status [30][33]. Similar to BMI, FMI and FFMI, BCMI also eliminates the influence associated with height. It is more sensitive than BMI in monitoring changes in muscle mass and protein in illness-caused abnormality [34] [35]. In addition, it is a prognostic factor of the inflammation status and associated with skeletal muscle [35]. In our study, a decrease in MM, BCM, FFMI and BCMI was observed both in the ERAS and control group, demonstrating the protein breakdown and muscle loss during perioperative period. Compared with the control group, MM, BCM, FFMI and BCMI in ERAS group decreased much less. However, there was no statistically significant difference. We speculate that craniotomy has less influence on gastrointestinal function, compared with other surgeries especially gastrointestinal surgery. Most of the patients in both

groups could return to normal diet a few days after surgery. In addition, due to changes in intracranial pressure and the residual effects of narcotic drugs, some patients (including ERAS and control group) experienced postoperative nausea and vomiting, and carbohydrate enriched fluid treatment could not reduce postoperative discomfort [36], which affected the recovery of postoperative diet. Although less evidences support the postoperative nutritional support is typically needed for brain tumor patients, with the exception of patients who are in a prolonged comatose state [37], our data demonstrated the validity of ERAS program.

Conclusions

In summary, we firstly used the bioelectrical impedance method to analyze the changes of body composition in patients undergoing elective craniotomy before and after surgery. Our data showed that the changes of metabolic and nutritional status caused by surgery in ERAS group are less obvious to those in control group, demonstrating that the perioperative nutritional optimization is an essential part of ERAS program, and the application of ERAS in patients undergoing elective craniotomy is safe and effective. Considering the relatively small sample size, our findings warrant further studies on a larger scale.

Abbreviations

BM: body mass, BMI: body mass index., FM: fat mass, MM: muscle mass, BCM: body cell mass, FMI: fat mass index, FFMI: free-fat mass index, BCMI: body cell mass index.

Declarations

Acknowledgments

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Availability of data and materials

All data generated or analysed during this study are included in this published article.

Authors' contributions

LY and SMH were responsible for the conception and design of the study. JY performed the nutritional management in this study, analyzed and interpreted the patient data, and wrote the manuscript. SSW performed the nutritional management and analyzed the patient data. YW, TZZ and BFZ were major contributors in performing ERAS protocol. All authors approved the final version of the manuscript.

Ethics approval and consent to participate

The review and analysis of patient information for this study was approved by the Ethical Committee of Tangdu Hospital, and complied with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in this study.

Consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

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Tables

Table 1 Clinical characteristics of the study sample at admission*

	Overall (n=140)	Male (n=48)	Female (n=92)	P value
Age (years)	45.6±12.7	45.2±13.3	45.7±12.5	0.939
Height (m)	1.62±0.06	1.69±0.05	1.59±0.04	0.000
BM (kg)	62.0±9.43	68.1±9.50	59.7±8.36	0.000
BMI (kg/m ²)	23.7±3.25	23.9±3.26	23.7±3.27	0.274

*Values are mean ± standard deviation

Abbreviations: BM: body mass, BMI: body mass index.

Table 2 patient characteristics of the study sample at admission*

	Overall (n=140)	ERAS group (n=70)	Control group (n=70)	P value
Age (years)	45.6±12.7	45.4±12.0	46.1±11.9	0.864
Height (m)	1.62±0.06	1.62±0.07	1.62±0.06	0.834
BM (kg)	62.0±9.43	61.4±9.75	64.8±7.48	0.205
BMI (kg/m ²)	23.7±3.25	23.5±3.39	24.7±2.34	0.208

*Values are mean ± standard deviation

Abbreviations: BM: body mass, BMI: body mass index.

Table 3 Changes of body composition before and after surgery

Parameters	ERAS group (n=70)		Control group (n=70)		<i>P</i> value
	Admission	Discharge	Admission	Discharge	
					Changes of parameters during hospitalization
BM (kg)	61.4±9.74	60.2±9.56	64.8±7.48	62.4±6.2	0.189
BMI (kg/m ²)	23.5±3.39	23.1±3.28	24.7±2.34	23.8±1.99	0.203
FM (kg)	18.2±4.80	18.1±4.88	19.8±3.38	19.6±3.40	0.017
MM (kg)	40.1±7.25	39.2±7.04	42.1±6.48	40.7±5.10	0.541
BCM (kg)	30.6±5.22	29.9±5.03	31.8±4.34	30.9±3.39	0.860
FMI (kg/m ²)	7.1±2.06	7.0±2.10	7.5±1.58	7.2±1.50	0.016
FFMI (kg/m ²)	16.4±2.12	16.1±1.97	17.1±1.83	16.6±1.32	0.485
BCMI (kg/m ²)	11.7±1.43	11.4±1.36	12.1±1.12	11.7±0.81	0.414

*Values are mean ± standard deviation

Abbreviations: BM: body mass, BMI: body mass index., FM: fat mass, MM: muscle mass, BCM: body cell mass, FMI: fat mass index, FFMI: free-fat mass index, BCMI: body cell mass index

Figures

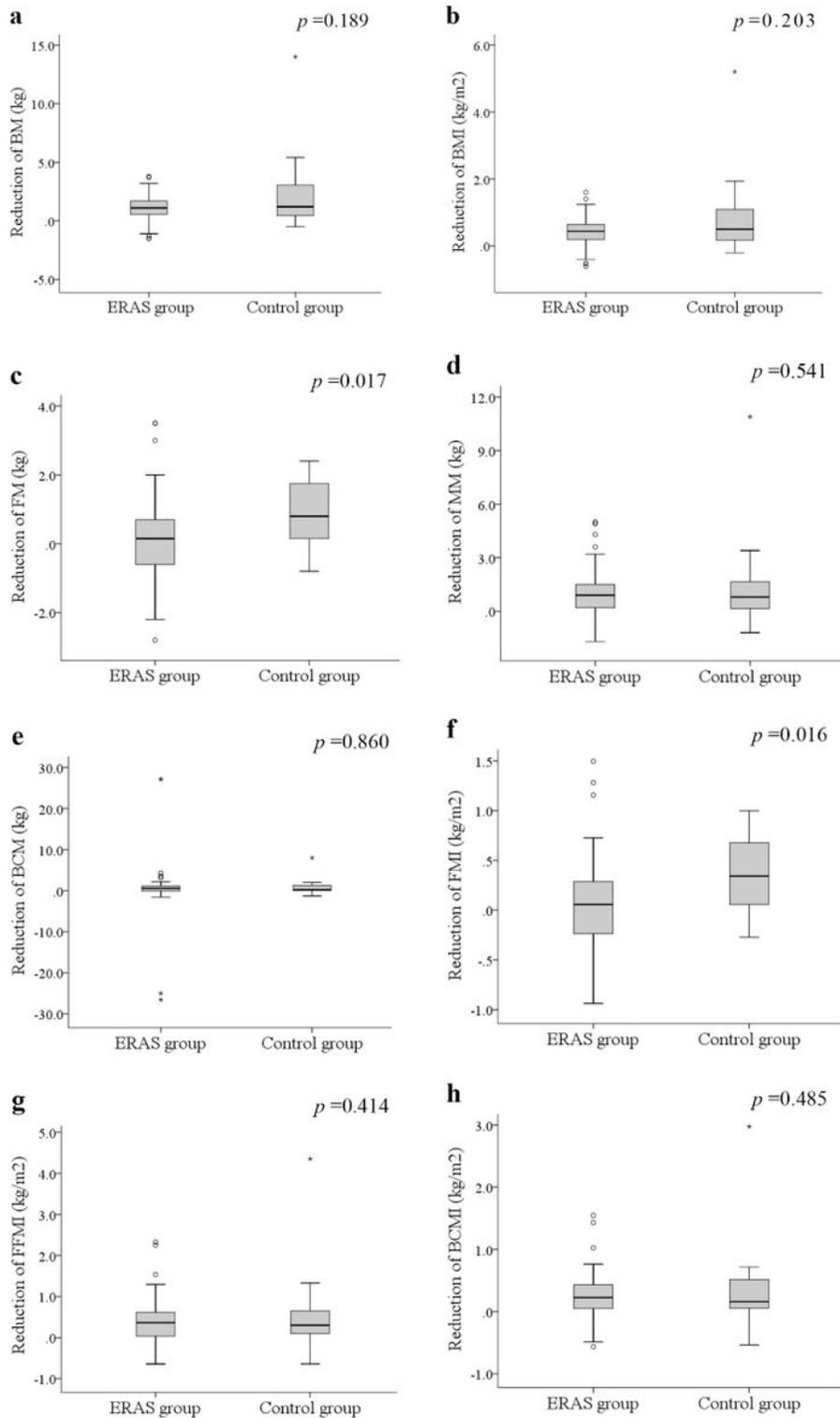


Figure 1

Changes of body composition for patients in control and ERAS group before and after surgery. (a-h) boxplots showing the parameters with statistical difference. (a). reduction of BM (kg). (b). reduction of BMI (kg/m²). (c). reduction of FM (kg). (d). reduction of MM (kg). (e). reduction of BCM (kg). (f). reduction of FMI (kg/m²). (g). reduction of FFMI (kg/m²). (h). reduction of BCMI (kg/m²).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [supplement1.docx](#)
- [supplement2.doc](#)