P.O.Box 2345, Beijing 100023,China
Fax: +86-10-85381893
E-mail: wcjd@public.bta.net.cn www.wjgnet.com

World J Gastroenterol 2002;8(6):1149-1152
World Journal of Gastroenterology
 ISSN 1007-9327

• CLINICAL RESEARCH •

Sequential changes of body composition in patients with enterocutaneous fistula during the 10 days after admission

Xin-Bo Wang, Jian-An Ren, Jie-Shou Li

Xin-Bo Wang, Jian-An Ren, Jie-Shou Li, Clinical School of Medical College, Nanjing University, Research Institute of General Surgery, Nanjing General Hospital, People' s Liberation Army, Nanjing 210002, Jiangsu Province, China
Correspondence to: Dr. Xin-Bo Wang, Research Institute of General Surgery, Nanjing General Hospital, People' s Liberation Army, 305 East Zhongshan Road, Nanjing 210002, Jiangsu Province, China. wang_xb@sohu.com
Fax: +86-25-4803956
Received 2002-06-01 **Accepted** 2002-07-22

Abstract

AIM: To investigate the sequential changes of body composition in the metabolic response that occurred in a group of patients with enterocutaneous fistula after admission to the hospital.

METHODS: Sixty-one patients with enterocutaneous fistula admitted to our hospital had measurements of body composition by multiple-frequency bioelectrical impedance analysis after admission and 5, 10 days later. Sequential measurements of plasma constitutive proteins were also made.

RESULTS: The body weight, fat-free mass, body mass index, and body cell mass were initially well below the normal range, especially the body mass index and body cell mass. And all the data gradually moved up over the 10-day study period, only a highly significant difference was found in body cell mass. Once the patients received nutrition supplement, ECW began to return to normal range slowly as well as ICW and TBW began to rise up, and ECW/TBW significantly declined to near normal level by day 10 in either male or female patients. There was a reprioritization of plasma constitutive protein synthesis that was obligatory and independent of changes in FFM.

CONCLUSION: Serial measurements can quantify the disturbance of body composition in enterocutaneous fistula patients. The early nutritional intervention rapidly ameliorates the abnormal distribution of body water while the state-of-the-art surgical management prevents the further deterioration in cellular composition.

Wang XB, Ren JA, Li JS. Sequential changes of body composition in patients with enterocutaneous fistula during the 10 days after admission. *World J Gastroenterol* 2002; 8(6):1149-1152

INTRODUCTION

Malnutrition is common in patients with enterocutaneous fistula, over a period of time, giving rise to alterations in body composition, as well as systemic and multiorgan manifestations. Malnutrition is also associated with adverse outcomes, whereas clinical stability is associated with nutritional stability[1]. Unfortunately, accurate nutritional assessment is difficult in patients with enterocutaneous fistula because standard laboratory methods are inaccurate and the techniques used to precisely assess metabolic compartments are complex, expensive, and of limited availability, especially in China. Assessment of body composition may provide important information about the nutritional status[2] .The applicability of one safe and convenient methods for body composition analysis, multiple-frequency bioelectrical impedance analysis (MFBIA) in malnourished patients with enterocutaneous fistula has been sparsely elucidated[3] .

Thus, the aim of the present study is to investigate the sequential changes of body composition in the metabolic response that occurred in a group of patients with enterocutaneous fistula after admission to the hospital.

MATERIALS AND METHODS

Patients

Between December 1, 2000, and November 30, 2001, 86 patients suffering from enterocutaneous fistula (EF) were admitted to the EF Treatment Group of Institute of General Surgery at Jinling Hospital, Nanjing, China. All of these patients wholly recruited from other inpatient clinic were included in the study. EF care at our hospital took place more than thirty years ago in a well coordinated system of pre-hospital and in-hospital care that includes good co-operation with other hospitals, radio-telephone communication, and a high-level, in-hospital EF team response and experience, which includes rapid assessment, resuscitation, stabilization, and sequential therapeusis according to well-established principles[4].

At the time of admission, all patients studied were able to accomplish the analysis of body composition in standing position for 3 minutes. None of the patients were treated with diuretics and prednisolone and they had exclusion of any metabolic disease. For each patient, diagnosis was made on clinical presentation: definite history of operation, temperature spikes, elevated white cell counts, increasing abdominal tenderness, wound infection, and drainage of succus entericus from intraperitonal drains. Initial management of the patients invariably involved fluid resuscitation, repletion of depleted electrolytes, maintenance of systemic and multi-organic function, active suction drainage of succus entericus, appropriate broad-spectrum antibiotic therapy to control sepsis, pharmacological approaches including H_2 antagonists, somatostatin and growth hormone if needed[5] ,and nutritional supplementation. Some patients who needed prompt exploration of the abdominal cavity to control generalized peritonitis or definitive pus were excluded from the study.

Nutrition was given enterally (Peptide, Nutricia, Dutch) when possible[4]. The caloric distribution of the formula was 16.5 % protein, 22.7 % fat, and 60.8 % carbohydrate administered by the nasogastric, nasojejunal, gastrostomic, jejunostomic, or any available intestinal route[4, 6] . Nutritional intake was increased up to 2000Kcal/d according a standard protocol. Patients with contraindications to enteral feeding were given parenteral nutrition by dedicated single-lumen central venous catheters. The initial daily prescription of 17 g nitrogen, 1000Kcal from glucose, and 500Kcal from fat was modified on the basis of size, renal function, and indirect calorimetry.

Study protocol

Patients underwent serial measurements of plasma protein concentrations and body composition during a period of 10 days. The first studies were performed as soon as hemodynamic stability was achieved without either colloid infusion or increasing inotropic support (day 0). The body composition measurements were repeated 5, 10 after admission in the Department of General Surgery by one medician. Measurements of the plasma protein were also made 10 days later.

Techniques of body composition analysis

Body composition measurements were made in all subjects using an multiple-frequency bioelectrical impedance (MFBIA) model InBody 3.0 (Biospace, Seoul, Korea). As one of the latest impedance analyzers, InBody 3.0 uses state-of-the-art technology, an 8-point tactile electrode system that measures the total and segmental impedance and phase angle of alternating electric current at four different frequencies (5 kHz, 50 kHz, 250 kHz, and 500 kHz).

Impedance measurements were made with the subject standing in an upright position, on foot electrodes in the platform of the instrument, with the legs not touching the thighs and the arms not touching the torso. The subject stood on the four foot electrodes: two oval shape electrodes and two heel shape electrodes, and gripped the two Palm-and-Thumb electrodes in order to yield two thumb electrodes and two palm electrodes, without shoes or excess clothing (coats, sweaters, vests). The skin and the electrodes were precleaned using the specific electrolyte tissue according to the manufacturer’ s instructions. Prior to this, height (stadiometry) was recorded to the nearest 0.1 cm. All the subjects were instructed to fast and to avoid exercise 8 h before measurement and had been resting for at least 30 min before measurement.

All the body composition data were performed in the instrument by inner software and typed in the result sheet immediately after measuring. The software performs provides a plot of reactive and resistive components of the measured impedance at each frequency, as well as body weight, fat-free mass (FFM), total body water (TBW), intra-/extra-cellular water (ICW/ECW), segmental fluid distribution, fat mass (FM), body cell mass (BCM) and body mass index (BMI).

Plasma proteins

Fibronectin, transferrin, and prealbumin were measured as markers of the constitutive plasma proteins. These were determined by ELISA assay using kits of Pointe, UK.

Statistical methods

Analyses were performed using SPSS10.0. Paired student’ s *t* test was used to detect significant changes over time. Values are expressed as means ±SD. *P* values less than 0.05 were considered significant.

RESULTS

Patients

Sixty-one of the 86 patients who were recruited into the study completed the protocol, and their clinical diagnostic details are listed in Table 1. During the 10 days after admission, Of the 25 patients who did not complete the protocol, 11 underwent prompt laparotomy exploration to control sepsis, the remaining 14 were too weakness to stand up to complete the body composition measurement. The 61 enterocutaneous fistula patients were all secondary to alimentary tract operation, 18 secondary to cancer, 10 secondary to inflammatory bowel diseases, 2 secondary to pancreatitis, 5 secondary to digestive ulcer, 26 secondary to trauma, intestinal obstruction, and cholelithiasis.

Of the 51 male patients, 24 received total parenteral nutrition, the remaining 27 received enteral nutrition with or without parenteral feeding. Of the 10 female patients, 3 received TPN, and the remaining 7 received total or partial enteral feeding. Nutrition was administered continuously. There was no apparent clinical manifestation of peripheral extremity edema, ascites, or other intra-abdominal fluid collections just before body composition measurement. The median time from admission to receiving the nutritional support was 2 days (range 1 to 3 days).

Table 1 Clinical data of patients recruited for the study

	Male	Female
Esophageal and gastric fistula	4	0
Duodenal fistula	11	3
High-output intestinal fistula	9	2
Low-output intestinal fistula	18	4
Colonic fistula	10	2
Pancreatic and biliaric fistula	5	0
Total	51[a]	10[a]

[a]Some patients had multiple-origin enterocutaneous fistulas.

Body composition measurements

The body weight, BMI, FFM, and BCM in the male patients were initially well below the normal range (in our own data), especially BMI and BCM, which can be accounted for the severely malnutritional state of these enterocutaneous fistula patients. All the data gradually moved up over the 10-day study period (in Table 2), only a highly significant difference was found in BCM. As is also shown in Table 3, except for the female patients received a significant increase in FFM as well as in BCM. As to the differences of FFM in gender-specific, the causes may be attributed to the small case number, the gentle state of illness, and the high proportion of enteral feeding of the female patients. The latter intensifies the benefits of enteral nutrition in the treatment of enterocutaneous fistula in early course and needs further refinement in future research.

Once the patients received nutrition supplement, ECW began to return to normal slowly as well as ICW and TBW began to raise to normal, and ECW/TBW (which should be the index of edema) significantly declined to near normal by day 10 in either male or female patients. Finally, TW and TW/TBW in male patients significantly increased on Day 5 and then slowly decreased on Day 10, which may be attributable to excess fluid locating in the trunk for abdominal infection or intolerance to early enteral feeding.

Plasma proteins

Twenty of 61 patients at random underwent serial measurement of plasma protein concentration (Shown in Table 4). We found that fibronectin, transferrin, and prealbumin concentrations, which were initially well below the normal range increasingly raised up without significance by Day 10 (P>0.05).

Table 2 Demographic and body composition data for male (*n*=51)

Age (years)	41.9±13.5			
Height (cm)	170.2±8.5			

	Day0	Day5	Day10	*P*
Weight (kg)	51.19±11.00	51.09±10.88	51.39±10.89	0.58
BMI (kg/m²)	17.62±3.08	17.56±3.06	17.71±3.00	0.44
TBW (kg)	29.41±5.09	29.61±5.03	29.61±5.07	0.18
ECW (kg)	10.51±1.97	10.43±1.91	10.35±1.87	0.12
ICW (kg)	18.89±3.26	19.16±3.23[b]	19.24±3.31[b]	0.005
ECW/TBW	0.357±0.0171	0.351±0.0194[b]	0.350±0.0161[b]	<0.0001
FFM (kg)	42.55±7.27	42.84±7.16	42.80±7.25	0.21
FM (kg)	8.64±5.00	8.27±4.67[b]	8.59±4.68	0.009
% FM (wt/wt)	15.97±6.47	15.26±6.15[b]	15.82±5.97	0.006
BCM (kg)	29.61±5.10	29.98±5.04[b]	30.02±5.14[a]	0.010
TW (kg)	13.71±2.41	13.92±2.34[b]	13.84±2.42	0.007
TW/TBW (%)	46.58±2.25	47.00±1.76[a]	46.69±1.90	0.015

BMI=body mass index, TBW=total body water, ECW=extracellular water, ICW=intracellular water, FM=fat mass, FFM=fat-free mass, BCM=body cell mass, TW=trunk water [a]*P*<0.05, [b]*P*<0.01 *vs* Day0.

Table 3 Demographic and body composition data for female (*n*=10)

Age (years)	50.1±11.4			
Height (cm)	157.9±5.4			

	Day0	Day5	Day10	*P*
Weight cm)	46.78±8.52	46.92±8.83	47.63±8.57[a]	0.04
BMI (kg)	18.81±3.74	19.11±3.60	19.18±3.69[a]	0.04
TBW (kg)	23.44±4.38	24.29±3.54	24.86±3.29	0.057
ECW (kg)	8.59±1.09	8.53±1.25	8.56±1.20	0.38
ICW (kg)	15.54±2.18	15.75±2.32	16.19±2.12[b]	0.001
ECW/TBW	0.358±0.0157	0.351±0.015[a]	0.348±0.0127[a]	0.017
FFM (kg)	35.11±4.49	35.26±5.04	36.09±4.68[b]	0.005
FM (kg)	10.59±7.11	11.64±6.02	11.56±4.68	0.31
% FM (wt/wt)	23/.26±9.89	23.90±8.82	23.24±8.83	0.49
BCM (kg)	24.48±3.21	24.71±3.52	25.36±3.22[b]	0.004
TW (kg)	11.26±1.46	11.48±1.81	11.21±1.56	0.07
TW/TBW (%)	48.98±7.80	46.06±1.21	46.18±1.24	0.30

BMI=body mass index, TBW=total body water, ECW=extracellular water, ICW=intracellular water, FM=fat mass, FFM=fat-free mass, BCM=body cell mass, TW=trunk water, [a]*P*<0.05, [b]*P*<0.01 *vs* Day0.

Table 4 Results of plasma proteins over 10 days

	Day0	Day5	Day10	[a]*P*
FN (mg/L)	109.4±36.4	117.9±37.4	128.6±46.6	0.06
TF (mg/dl)	232.2±40.7	230.4±48.0	243.4±44.2	0.07
PA (mg/dl)	17.4±7.5	19.4±7.1	21.0±6.9	0.054

FN=fibronectin, TF=transferrin, PA=prealbumin [a]*P* *vs* Day0.

DISCUSSION

Estimation of body composition is important in the assessment and monitoring of enterocutaneous fistula patients. Enterocutaneous fistula is a condition in which overnutrition, edema, and undernutrition can coexist simultaneously, or successively, over a period of time, giving rise to alterations in body composition, as well as systemic and multiple-organic manifestations. The development of a noninvasive, inexpensive, and accurate technique to assess body water and nutritional compartment would be of great clinical value to identify those patients with impaired morbidity and mortality in enterocutaneous fistula, and enhanced nutritional support is indicated in those patients with persisting nutritional deficits[4, 7].

Bioelectrical impedance analysis is a technique of assessing body composition such as total body water and thus fat-free mass in the healthy population[8]. And in a number of conditions such as hemodialysis[9], pregnancy[10], hepatic cirrhosis[11], after surgery[12], and in critical illness[13], changes in TBW have been shown to be accompanied by changes in impedance. However, in situations where there are clinically important changes in intraceullar and extracellular water distribution, such as ascites[11] and critical illness[14], the value of single-frequency BIA is limited. It is proposed that multiple-frequency BIA (MFBIA) may be of particular use in patients with altered distribution of body water[2]. At low frequency, the current passes through the extracellular fluids because of the capacitance effect of cell membranes and tissue interfaces, whereas at high frequencies, the current is conduced through both intra-and extracellular fluids. The Biospace InBody 3.0 body-composition analyzer is a novel device to estimate body water compartments and body fat. It differs from other impedance systems, which uses an 8-point tactile electrode system that measures the total and segmental impedance and phase angle of alternating electric current at four different frequencies between 5 and 500 kHz.

BMI was found to be an important predictor of mortality in clinic study, with the association between body mass index and mortality suggesting the U-shaped relation corroborated by many studies[15]. Although BMI in our study was initially well below the normal range, there were no significant differences in BMI over the study period for male and female patients as well as in body weight and FFM. However, there were highly significant differences in BCM changes over the study period (Table 2 and Table 3). Weight and BMI do not definitely evaluate changes in body compartments and therefore do not reveal if loss of FFM or gain in FM occurs[16]. The keenness and speediness in the response of BCM to medical intervention made a strong impression on us. BCM provides an ideal reference for metabolic studies in enterocutaneous fistula, while less specific parameters such as body weight, BMI or FFM (which include non-metabolic compartments such as ECW) should be interpreted with caution[17]. Therefore, we emphasize the importance of measurement of the growth of the metabolically active body compartment, the BCM, in accurately assessing nutritional status in enterocutaneous fistula. And it would be useful in future research to investigate whether the relation between BCM and mortality is also U-shaped in critical illness especially in enterocutaneous fistula. This question may be more amenable to investigate in relatively small, short studies, provided that an appropriate tool for assessment of body composition in enterocutaneous fistula patients is used.

Our results show once again that there is a reprioritization of hepatic protein synthesis in enterocutaneous fistula[18] that is obligatory and independent of changes in FFM. Concentrations of the constitutive plasma proteins fallen initially raised up over the study period without significance (*P*>0.05) because of their well known turnover rates. There were no significant correlations between the changes of FFM and those of the constitutive plasma proteins. These obligatory changes may occur in face of continuing proteolysis and high energy expenditure in critical illness. And our results confirm that the measurements of the constitutive plasma proteins have no significant values in demonstrating changes in cellular composition early in the course of enterocutaneous fistula.

Once the patients received nutrition supplement, ECW began to return to normal slowly as well as ICW and TBW began to rise to normal, while ECW/TBW (which should be the index of edema) significantly declined to near normal range by day 10 in either male or female patients (P<0.0001 in male, and P=0.017 in female). These results are partially similar to those obtained in the critical illness study[19,20]. In our experience, these findings may be relevant to the clinical manifestations of enterocutaneous fistula patients, especially when persistent severe malnutrition was detected. There may be a reduction in ICW by a compensation for increased ECW in the patients especially those received inappropriate nutritional supplement. And in the early course of nutritional intervention, the rapid amelioration was found not in body protein but in body water compartments. These findings in our study have two implications. First, the present understanding of the degree of abnormal body water distribution that occurs in such patients is largely correct. In the second, it is clear from this study that most effects of the early administered nutritional intervention lie in the rapid improvement of body water distribution. It seems unlikely that much more can be done to preserve cellular composition in early stage of treatment, but state-of-the-art surgical management appears to have prevent further deterioration.

Finally, BIA is a technique that can be readily applied in clinical situations, easy, portable, noninvasive, and inexpensive. Because of these advantages, it can be repeated frequently as necessary and therefore gives a picture of the patient' s body composition status and responses to therapy. However, there are still many debates on the validity of MFBIA in clinical assessment of nutritional status especially body water compartment[21, 22]. MFBIA may not accurately predict water compartments in critically illness especially in those with greatly altered distribution of water, which may alter the capacitant effect of all membranes on conductance through the fluid compartment, although this is highly speculative. It is also recognized that the whole-body BIA is insensitive to fluid changes in the trunk. In our data, we found that the BCM correlated with resting energy expenditure (r^2=0.61, P<0.001 on Day0, and r^2=0.59, P<0.001 on Day10) in 12 enterocutaneous fistula patients who were admitted to our hospital consecutively. The slope of the line relating BCM to REE was the same on Day0 and on Day10 (P=0.34) in these 12 patients. These findings encouraged us to elucidate the applicability of MFBIA in the enterocutaneous fistula patients. We also suggest that patients with enterocutaneous fistula during treatment phases be followed periodically with BIA measurements. Longitudinal follow-up would permit evaluation of treatment side effects (eg, overfeeding, undernutrition) or sepsis, which are known to have catabolic effects on FFM and FM. And in the future, we will introduce more sophisticated and more invasive techniques such as dual-energy x-ray absorptiometry (DXA).

In conclusion, we have for the first time quantified the changes of body composition during 10 days after admission in enterocutaneous fistula patients by use of MFBIA and have shown that the early nutritional intervention rapidly ameliorates the disturbance of body water while the state-of-the-art surgical management prevents the further deterioration in cellular composition.

REFERENCES

1 **Huang YC**. Malnutrition in the critically ill. *Nutrition* 2001; **17**: 263-264

2 **Ellis K**. Human body composition: In vivo methods. *Physiol Rev* 2000; **80**: 649-680

3 **Gross E**, Holbrook IB, Thornton M. Assessment of the nutritional state of patients with an intestinal fistula. *Br J Surg* 1978;**65**:740-743

4 **Li JS**, Ren JA, Yin L, Han JM. Management of enteric fistula-Thirty year's experience. *Zhonghua Waike Zazhi* 2002; **40**: 100-103

5 **Li JS**, Ren JA, Wang XB, Gu J, Jiang J. Somatostatin and growth hormone promote spontaneous closure of enterocutaneous fistula. *Zhonghua Waike Zazhi* 2000; **38**: 447-449

6 **Levy E**, Frileux P, Cugnenc PH, Honigor J, Olivier JM, Parc R. High-output external fistulae of the small bowel: Management with continuous enteral nutrition. *Br J Surg* 1989; **76**: 676-679

7 **Dudrick SJ**, Maharaj AR, McKelvey AA. Artificial nutritional support in patients with gastrointestinal fistulas. *World J Surg* 1999; **23**: 570-576

8 **Kyle UG**, Genton L, Karsegard L, Slosman DO, Pichard C. Single prediction equation for bioelectrical impedance analysis in adults aged 20-94 years. *Nutrition* 2001; **17**: 248-253

9 **Cooper BA**, Aslani A, Ryan M, Zhu FYP, Ibels LS, Allen BJ, Pollock AP. Comparing different methods of assessing body composition in end-stage renal failure. *Kidney Int* 2000; **58**: 408-414

10 **Lukaski HC**, Siders WA, Nielsen EJ, Hall CB. Total body water in pregnancy: Assessment by using bioelectrical impedance. *Am J Clin Nutr* 1994; **59**: 578-585

11 **Lehnert ME**, Clarke DD, Gibbons JG, Ward LC, Golding SM, Shepherd RW, Cornish BH, Crawford DHG. Estimation of body water compartments in cirrhosis by multiple-freqyency bioelectrical impedance analysis. *Nutrition* 2001; **17**: 31-34

12 **Meguid MM**, Lukaski HC, Tripp MD, Rosenburg JM, Parker FB. Rapid bedside method to assess changes in postoperative fluid status with bioelectrical impedance analysis. *Surgery* 1992; **112**:502-508

13 **Sluys TEMS**, Ende MEVD, Swart GR, van den Berg JWO, Wilson JHP. Body composition in patients with acquired immunodeficiency syndrome: A validation study of bioelectrical impedance analysis. *JPEN* 1993; **17**: 404-408

14 **Foley K**, Keegan M, Campbell I, Murby B, Hancox D, Bpharm BP. Use of single-frequency bioimpedance at 50 kHz to estimate total body water in patients with multiple organ failure and fluid overload. *Crit Care Med* 1999; **27**: 1472-1477

15 **Apovian CM**. Nutritional assessment in the elderly: Facing up to the challenges of developing new tools for clinical assessment. *Nutrition* 2001; **17**: 62-63

16 **Frankenfield D**, Rowe WA, Cooney RN, Smith JS, Becker D. Limits of body mass index to detect obesity and predict body composition. *Nutrition* 2001; **17**: 26-30

17 **Shepherd RW**, Greer RM, McNaughton SA, Wotten M, Cleghorn GJ. Energy Expenditure and the Body Cell Mass in Cystic Fibrosis. *Nutrition* 2001; **17**: 22-25

18 **Kuvshinoff BW**, Brodish RJ, McFadden DW, Fischer JE. Serum transferring as a prognostic indicatorof spontaneous closure and mortality in gastrointestinal cutaneous fistulas. *Ann Surg* 1993; **217**: 615-623

19 **Plank LD**, Hill GL. Sequential metabolic changes following induction of systemic inflammatory response in patients with severe sepsis or major blunt trauma. *World J Surg* 2000; **24**: 630-638

20 **Cheng ATH**, Plank LD, Hill GL. Prolonged overexpansion of extracellular water in elderly patients with sepsis. *Arch Surg* 1998; **133**: 745-751

21 **Haderslev KV**, Staun M. Comparison of dual-energy X-ray absorptiometry to four other methods to determine body composition in underweight patients with chronic gastrointestinal disease. *Metabolism* 2000; **49**: 360-366

22 **Ellis KJ**, Shypailo RJ, Wong WW. Measurement of body water by multifrequency bioelectrical impedance spectroscopy in a multiethnic pediatric population. *Am J Clin Nutr* 1999;**70**:847-853

Edited by Ren SY