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Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Short title: The accuracy of bioelectrical impedance analysis in estimating visceral fat area

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Key words: gastric cancer, visceral fat area, visceral obesity, computed tomography, bioelectrical impedance analysis
Abstract

Objectives: As the gold standard method for measuring body composition, computer tomography (CT) still has several shortcomings which limit its wide application. Bioelectrical impedance analysis (BIA) is a simple and inexpensive method for body composition estimation. However, the accuracy of BIA was unknown. Visceral obesity was associated with adverse prognosis in gastric cancer. Therefore, we aimed to assess the accuracy of BIA in estimating visceral fat in gastric cancer. Methods: From 1st January 2017 to 1st December 2018, patients diagnosed of gastric cancer were enrolled. VFA (visceral fat area) was measured both by CT and BIA. VFA by CT \( \geq 100\text{cm}^2 \) was considered as visceral obesity. The reliability between two methods were assessed by intraclass correlation coefficient (ICC) and Bland-Altman method (95% limits of agreement). Area under receiver operating characteristic curve (AUROC) was used to assess the performance of diagnosing visceral obesity by BIA. Results: A total of 157 patients diagnosed of gastric cancer were enrolled. The VFA by CT and BIA in the overall patients were 84.39\( \pm \)46.43 cm\(^2\) and 71.94\( \pm \)22.44 cm\(^2\), respectively. VFA estimated by BIA was positively correlated with VFA measured by CT (r=0.650, p<0.001). ICC for two methods in overall patients was 0.675. The mean bias between two measurements was 12.45\( \pm \)36.13cm\(^2\). The 95% limits of agreement ranges from -58.36 to 83.26 cm\(^2\) and the bias of 96% patients were within the 95%LOA range. The cut-off value for diagnosing visceral obesity by BIA was 81cm\(^2\) (AUROC: 0.822, p<0.001, 95%CI: 0.758-0.887). Conclusions: VFA measured by BIA showed satisfactory reliability with that measured by CT. Though consistent in statistical level,
the bias between two methods was not clinically acceptable. The cut-off value of VFA by BIA for diagnosing visceral obesity was 81 cm$^2$ for gastric cancer patients in Chinese population.

Key words: visceral fat area, gastric cancer, bioelectronic impedance analysis, computed tomography

Strengths and limitations of this study

To our knowledge, this is the first study to assess the accuracy of visceral fat area estimated by BIA in gastric cancer patients.

We compared visceral fat area estimated by BIA with that measured by CT scan as the ‘gold standard’.

The sample size of the study was small. However, considering the prospective recruitment of patients, the access of data for analyzing was strict which could compensate for the bias in some extent.
Introduction

Gastric cancer is a common malignancy type worldwide with a high mortality rate [1]. The prevalence of gastric cancer is comparatively higher in the Asian countries than that in the westerns [2]. Previous studies suggested that the alteration of body composition could affect the outcomes of multiple malignancies [3-6]. The negative effect of sarcopenia on the prognosis of cancer was reached in consensus [4-6]. In addition, the present of visceral obesity could bring difficulty in surgery operation, increase the post-operation infection rate and reduce the overall survival rate in gastric cancer [3,7]. Go et al demonstrated that the present of visceral obesity of gastric cancer subjects undergone laparoscopy-assisted distal gastrectomy significantly affected the number of retrieved lymph node [7]. In addition, visceral fat tissues contain more large adipocytes and androgen receptors than subcutaneous fat tissues and could result in insulin resistance, which was a negative hallmark for tumor progression [8]. Visceral obesity plays an essential role in the adverse prognostic factors of gastric cancer patients. Therefore, it was necessary to screen out visceral obesity in such population.

Several medical imaging methods were used for analyzing body composition, including computed tomography (CT), dual-energy X-ray absorptiometry (DXA), magnetic resonance imaging (MRI) [9]. Among them, CT as a routine imaging examination prior to cancer diagnosis and therapy was accurate and considered the gold standard method for evaluating body composition [9, 10]. The area of skeletal muscle and visceral fat tissue at L3 vertebra level by CT highly correlated with total body skeletal muscle mass and visceral fat mass [9-11]. According to previous researches,
111 100cm$^2$ as the threshold of visceral fat area for discriminating visceral obesity was accepted in clinic [7,8]. However, the use of CT in evaluating body composition has many drawbacks, such as radiation exposure, high expenses and the need of specialist in medical imaging. Bioelectrical impedance analysis (BIA) method was a non-invasive alternate for body composition evaluation and was widely used in clinic [12]. The advantages of BIA lie in the low cost and none radiation to subjects, which is suitable for repeated monitoring for nutrition status. The accuracy of visceral fat area (VFA) was investigated in a Korean cohort in healthy subjects, revealing that VFA estimated by BIA correlated well with that measured by CT method, but an accurate equation was needed to match that measured by CT [12]. However, the accuracy of BIA was highly dependent on ethnicity and hydration status [13]. Patients with malignancies may have alteration in body composition and hydration status, which affect the performance of BIA in estimating VFA. Moreover, researches on validation of its accuracy was limited in Chinese patients. The aim of the present study was to investigate the accuracy of BIA in estimating VFA in gastric cancer subjects in Chinese population, as well as to identify the threshold for diagnosing visceral obesity by BIA.

128 **Materials and Methods**

129 **Patients**

130 From 1st January 2017 to 1st December 2018, patients with a clear diagnosis of gastric cancer either by pathology or radiology admitted to Gastroenterology or General Surgery department of Drum Tower Hospital affiliated to Nanjing University Medical
School were prospectively enrolled. Exclusion criteria were patients with age younger than 18 or older than 80 years old, primary tumor originated from other organs, heart failure, kidney failure, cirrhosis, unmeasurable CT visceral fat area, application of diuretics or lipid regulation medications, unable to stand still or patients who refused to undergo CT and BIA. The observational study was in accordance with the principles of Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the medical center. Written consent was obtained from all participants.

Clinical information collection

The clinical information of all the patients were recorded. Baseline clinical characteristics, including age, gender, body weight, body height, body mass index (BMI, defined as body weight in kilogram (kg)/ [body height in meters]²), tumor stage, tumor tissue type, and comorbidities were recorded. Body weight was measured with patient wearing thin clothes and to the nearest 0.1kg. Body height was measured with patient bare feet and to the nearest 0.1kg. Tumor stage classification was based on the criteria established by the American Joint Committee on Cancer (AJCC) [14, 15]. Neoadjuvant therapy before the study was recorded. Laboratory tests were performed with fasting blood samples when admitted to hospital. Laboratory parameters included white blood cell count (WBC), hemoglobin level, albumin level, triglyceride level, cholesterol level, C-reactive protein level. Tumor markers were also performed once admitted and parameters included, carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199), carbohydrate antigen 724 (CA724),
carbohydrate antigen 242 (CA242).

**Body composition assessment by CT**

CT scans were performed before treatment. According to previously published method [10, 16], a single slice at the third lumbar vertebra (L3) level was selected and the area of different body compositions were analyzed by Matlab software (MathWorks, Massachusetts State, USA). Different body composition tissue compartments were manually outlined and segmented with different Hounsfield unit (HU) threshold ranges. Tissues with Hounsfield unit ranges from -29 to 150 were considered as skeletal muscle and the total skeletal muscle area (SMA) was calculated. Areas with HU ranges from -150 to -50 were considered as visceral fat and the total visceral fat area (VFA) was calculated. Areas with HU ranges from -190 to -30 were considered as subcutaneous fat and the total subcutaneous fat area (SFA) was calculated.

**Body composition assessment by BIA**

BIA assessment was performed the same day with CT scan. An Inbody 720 multifrequency BIA Inbody720 machine (Inbody corporation, Seoul, Korea) was adopted to measure body composition. The method was in accordance with previously described protocol [10]. To be brief, patients with fasting condition and empty bladder stand with both arms 45 angles apart from the body trunk and with both feet bared on the spots of the platform. Total body water, visceral fat area in cm$^2$, total fat mass, body fat percentages, lean body mass, skeletal body mass, fat free mass were estimated and
the values were output.

Definition of visceral obesity

Based on the Japan Society for the Study of Obesity and widely accepted criteria in clinic [7,17], the threshold for visceral obesity was 100cm² measured by CT images. Visceral obesity was defined as patients with visceral fat area ≥100cm².

Statistical analysis

Data analysis was performed by SPSS for windows version 20.0 (IBM, New York State, USA) and MedCalc for windows version 15.2.2 (MedCalc Software corporation, Ostend, Belgium). Continuous variables were expressed as mean± standard deviation (SD) if data were normally distributed and were compared by paired t-test. Skewed distributed data were expressed as median (25th percentile, 75th percentile) and were compared by Mann-Whitney U-test. Categorical variables were expressed by number and percentages and were compared by Chi-square (χ²-test) test or Fisher’s exact test when appropriate. The correlation between parameters were assessed by Pearson’s correlation test. The reliability and consistency between two measurements were assessed by intraclass correlation coefficient (ICC) and Bland-Altman statistical method [18] with 95% limits of agreements (95% LOA) calculated. Patients with VFA ≥100cm² measured by CT were classified as visceral obesity. The performance of VFA estimated by BIA in diagnosing visceral obesity was assessed by area under the receiver characteristic curve (AUROC). The cut-off value of VFA estimated by BIA in
stratifying visceral obesity was obtained with the maximum Youden index (sensitivity + specificity -1). A two-tailed p-value <0.05 was considered statistically significant. Shrout et al proposed that ICC value ranges from 0.00 to 0.49 was interpreted as poor reliability, ranges from 0.50 to 0.74 was interpreted as satisfactory and ranges from 0.75 to 1.00 was interpreted as excellent reliability [19].

Results

Baseline characteristics of the study population

A total of 35 patients were excludes from the research, finally 157 patients with gastric cancer were enrolled, included 48 females and 109 males (Supplementary figure 1). The mean age of the overall patients was 60.61±11.95 years old. The mean body weight and body height of the overall patients were 61.27±9.14kg and 162.10±7.07cm, respectively. The BMI of the overall group was 23.28±2.93kg/m$^2$. According to classification standard of China [20], 5 patients were underweight (3.2%), 85 patients were within normal range of BMI (54.1%), 61 patients were overweight (38.9%) and 6 patients were obesity (3.8%). Number of patients with gastric cancer tumor stage I, II, III, IV were 48 (30.6%), 31 (19.7%), 49 (31.2%) and 29 (18.5%), respectively. The majority of patients were diagnosed with adenocarcinoma tissue type. Laboratory indicators and demographic characteristics were summarized in Table 1.

The VFA measured by CT in overall patients was 84.39±46.43cm$^2$. There was 65 (41.4%) patients were diagnosed with visceral obesity. The VFA estimated by BIA in overall patients was 71.94±22.44cm$^2$. (Table 2)
Comparison of VFA measured by CT (VFA-CT) and estimated by BIA (VFA-BIA) in overall patients

In the overall patients, VFA measured by CT was positively correlated with that estimated by BIA (r=0.650, p<0.001) (Table 3, Figure 1 A). ICC value between VFA-CT and VFA-BIA was 0.675, indicating satisfactory reliability. With Bland-Altman analysis, the mean bias between two measurements was 12.45±36.13 cm$^2$, indicating that BIA underestimated VFA by 12.45±36.13 cm$^2$ in overall patients (Table 4). The 95% limits of agreement ranged from -58.36 to 83.26 cm$^2$. The bias of 96% of patients (151 patients) were within the 95% LOA range, indicating overall satisfactory consistency in statistical level (Figure 1 B). However, the bias was too large and was considered not clinically acceptable. In addition, the Bland-Altman plot showed that VFA was overestimated in patients with smaller VFA and underestimated in patients with larger VFA (Figure 1 B).

Subgroup analysis

VFA measured by CT was significantly correlated with that estimated by BIA in both female (r=0.559, p<0.001) and male (r=0.714, p<0.001) groups. The mean bias of two methods between genders was not significantly different (5.04±31.57 cm$^2$, 15.71±37.64 cm$^2$, respectively, p=0.088). In both gender groups, the two methods showed satisfactory reliability (ICC=0.659, 0.683, respectively). Patients were divided into groups according to median BMI. In both BMI groups, VFA-CT and VFA-BIA
were significantly correlated \( (r=0.315, \ p=0.010 \) in BMI\( >24 \) kg/m\(^2\) group; \( r=0.551, \ p<0.001 \) in BMI\( \leq24 \) kg/m\(^2\) group). The mean bias of VFA between two BMI categories was significantly different \( (25.50\pm31.00 \) cm\(^2\), \( 2.99\pm36.78 \) cm\(^2\); \( p<0.001 \)), indicating that BIA largely underestimated VFA in overweight or obesity subjects. ICC value in BMI\( >24 \) kg/m\(^2\) group indicated poor reliability in this subcategory. In both older (>60 years old) and younger (\( \leq60 \) years old) groups, two methods showed significant correlation \( (r=0.640, \ p<0.001; \ r=0.656, \ p<0.001, \) respectively) and satisfactory reliability \( (ICC=0.668, 0.678, \) respectively). The bias between patients with different age groups was not statistically significant \( (p=0.855) \). The bias between different tumor stages was not significantly different \( (p=0.424) \). In all subgroups, Bland-Altman analysis showed consistency in statistical level, however, the biases were not clinically acceptable.

### VFA-BIA in diagnosing visceral obesity

The criteria of VFA\( \geq100\)cm\(^2\) [7,17] measured by CT at L3 level was adopted as threshold in diagnosing visceral obesity. The VFA estimated by BIA showed an good to excellent performance in diagnosing visceral obesity in overall patients in the present study \( (AUROC=0.822, \ p<0.001, 95\%CI \ 0.758-0.887) \), with a sensitivity of 65.6%, and specificity of 88.2%. (Figure 2). The best cut-off value of VFA-BIA was 81cm\(^2\), indicating that gastric cancer patients with VFA larger than 81 cm\(^2\) estimated by BIA should be highly suspected of visceral obesity.
Discussions

The present study revealed that VFA estimated by BIA significantly correlated with that measured by CT at L3 level in gastric cancer patients in Chinese population.

This was in accordance with a previous Korean study [12]. Lee et al compared VFA-CT with VFA-BIA in healthy subjects with wide ranges of age and BMI. The mean bias of VFA between two methods was 21.4±45.6cm$^2$, and tend to increase with BMI [12]. Our study also demonstrated the positive correlation of bias with BMI, indicating the drawback of BIA in analyzing body composition in overweight or obesity subjects.

This limitation of BIA for obesity was proposed by several studies [21-24]. Bosaeus et al discovered that BIA underestimated total fat mass in overweight and obese women compared with MRI measurement [21]. Neovius et al discovered that compared with DXA, the bias of fat mass was increased with degree of adiposity [25]. The equations of body composition estimation by BIA was based on fixed hydration status, age, normal weight condition and certain ethnicity [26]. Adiposity was suggested to have effect on body trunk resistance [27], leading to alteration of body composition estimation by BIA.

CT slice at L3 level serves as the gold standard for body composition assessment. VFA larger than 100cm$^2$ [7,17] was widely accepted for diagnosing visceral obesity. However, the exposure to radiation and high cost restricted the use of CT as nutritional assessment in clinic. Moreover, the need for expertise in medical imaging also restricted its application. The BIA method compensated for these shortcomings and was suitable for extensive nutritional screening and monitoring [11]. Though with satisfactory
reliability, considering the wide range of 95%LOA by Bland-Altman analysis in our research, the bias of VFA by two methods was not clinically acceptable. This indicated that VFA measurement by BIA and CT were interchangeable in statistics level, but not interchangeable in the clinic. Lee at al [12] postulated a formula to predict actual VFA with BIA variables. However, this formula was too complicated in calculation and difficult to implement routinely. In addition, previous formulas were based on healthy subjects with different ethnicities, which were not applicable for Chinese patients with gastric cancer. To our knowledge, this was the first research investigating accuracy of BIA in estimating VFA in gastric cancer patients in Chinese ethnicity. In our study, we identified 81cm$^2$ as the cut-off value of VFA-BIA in gastric cancer patients in Chinese population. BIA could serve as an alternate for CT in estimating VFA and patients with VFA estimated by BIA larger than 81cm$^2$ should both be highly suspected for visceral obesity.

The body composition substantially altered in patients with tumor bearing state [3-6, 28] and during anti-tumor therapies [29]. Previous researches mainly focused on sarcopenia as the negative prognostic factor in multiple malignancies [3-6]. The importance of screening and monitoring sarcopenia or cachexia was reached in consensus. Methods for measuring skeletal muscle mass has been comprehensively studied. A study by Lee et al [30] suggested that BIA overestimated whole body muscle mass and appendicular skeletal muscle mass by 1.97kg to 2.28kg in comparison with DXA. In contrast, researches on accuracy of BIA in estimating VFA were relatively limited. The adverse effects of visceral fat tissues on insulin resistance and coronary
risk were well established [31]. Choe et al found that lung function improves with reduced visceral fat mass [32]. Recent years, the roles of visceral obesity on the progression of cancer and cancer-related comorbidities were investigated in several studies [33,34]. Ozoya et al retrospectively analyzed 110 patients with colon cancer and concluded that visceral obesity was associated with metabolic comorbidities and post-operative morbidities [33]. Go et al indicated that the present of visceral obesity could bring technical difficulties in operation, and could significantly reduce the number of retrieved lymph nodes and overall survival in gastric cancer patients undergone laparoscopy-assisted distal gastrectomy [7]. Masashi et al retrospectively studied 75 patients underwent gastrectomy for gastric cancer, and concluded that VFA was a risk factor for postoperative complications via multivariate regression analysis. Visceral obesity was more useful than BMI in predicting anastomotic leakage rate and surgical site infection rate [35]. A Japan research by Tanaka et al identified VFA as an indicator for pancreatic fistula in postoperative complications after total gastrectomy [36]. Therefore, visceral obesity should be discriminated prior to surgery, and operations should be conducted by more experienced surgeons [7].

Visceral obesity serves as an adverse hallmark for outcome of patients with malignancies. Excessive visceral fat tissues predisposed to insulin resistance and dysfunction of inflammatory response via hepatic PPARα and PPARγ expression [33,37]. The low-grade chronic inflammation produced by excessive visceral fat tissues was considered suitable microenvironment for tumor growth [33]. In addition, growth factors released by visceral fat tissues also mediated in cancer progression [33].
animal experiment, visceral fat tissues transplanted from growth hormone receptor
knockout mice into normal mice could improve insulin sensitivity and tumor progression [38]. Furthermore, visceral obesity attributed to technical difficulties in tumor resection surgeries, especially in laparoscopic approach [7,39]. Moreover, for gastrectomy operations, comorbidity of visceral obesity predisposed to post-surgery infection and delayed wound healing [40]. Therefore, the present of visceral obesity was essential in tumor progression and poor outcome of cancer patients. Gastric cancer was one of the most common malignancies worldwide and was lethal with high mortality rate [41]. To identify patients with visceral obesity prior to operation could help surgeons optimize the selection of patients suitable for laparoscopic approach and take interventions for prophylaxis of surgical incision infection. Dietary intervention for reducing visceral fat mass in these subjects was warranted to apply for inhibiting progression of malignancies.

There were several limitations in the present research. First, the study was conducted in a single center and only included patients of Southeast China. The conclusions might not be generalized to patients from other parts of China. Multicenter design study was warranted to apply to validate our conclusions. Second, the sample size of the study was small, which may lead to certain bias. However, considering the prospective recruitment of patients, the access of data for analyzing was strict which could compensate for the bias in some extent. Third, only few patients were extreme obese in the present study, the accuracy of BIA for estimating VFA in extreme obese patients remained unclear.
In conclusion, it was necessary to identify visceral obesity in gastric cancer patients via body composition analysis. The present study revealed that VFA measured by CT and BIA showed significant correlation and satisfactory reliability in overall gastric cancer patients. Though consistent in statistical level, the bias between two methods was not clinically acceptable. BIA overestimated VFA in patients with smaller VFA and underestimated VFA in patients with larger VFA. The cut-off value of VFA-BIA for diagnosing visceral obesity in the present study was 81 cm$^2$, indicating Chinese gastric cancer patients with VFA estimated by BIA larger than the threshold should be highly suspected for visceral obesity.

**Contributors**

BG was responsible for methodology, data curation, project administration, and writing; YL was responsible for methodology, statistical analysis, data analyzing and writing; CD was responsible for data collection; SLL was responsible for data curation, project administration, Software management; XJB was responsible for BIA management and data collection; XTC was responsible for study design and manuscript supervision. All authors gave their final approval of the final version of the manuscript.

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work as co-corresponding authors.

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Competing interests

No declared.

Patient consent

Obtained.

Ethics approval

The study was in accordance with the principles of Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the Nanjing Drum Tower Hospital.

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Not commissioned; externally peer reviewed.

Data sharing statement

The data was available at the corresponding authors with reasonable request.
Patient and Public Involvement Statement

They were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

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Figure Legends

Figure 1 Correlation between VFA measured by CT and BIA (A) and Bland-Altman plot for comparing the two methods (B).

(A) The Pearson’s correlation coefficient between the two methods was 0.065, with p<0.001. (B) The mean bias between two measurements was 12.45±36.13 cm², 95% limits of agreements range from -58.36 cm² to 83.26 cm². The bias of 96% patients (151 patients) were within the 95%LOA range, indicating that the bias was acceptable in statistical level.
Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients

The AUROC=0.822, p<0.001, 95%CI: 0.758-0.887, the best cut-off value for diagnosing visceral obesity by VFA-BIA was 81cm², with a sensitivity of 65.6% and specificity of 88.2%.

Supplementary Figure 1 The flow diagram of the research.

Tables

Table 1 Baseline characteristics

| Age (year) | Overall | 60.61±11.95 |
| <60 y (%) | 66 (42.0) |
| ≥60 y (%) | 91 (58.0) |
| Gender (Male, %) | 109 (69.4) |
| Body weight (kg) | 61.27±9.14 |
| Body height (cm) | 162.10±7.07 |
| BMI (kg/m²) | 23.28±2.93 |
| <18.5 | 5 (3.2) |
| 18.50-23.99 | 85 (54.1) |
| 24-27.99 | 61 (38.9) |
| ≥28 | 6 (3.8) |
| Tumor stage (AJCC) | 1 48 (30.6) |
| II | 31 (19.7) |
| III | 49 (31.2) |
| Tissue type                        | Count (Percent) |
|-----------------------------------|-----------------|
| Adenocarcinoma                    | 124 (79.0)      |
| Signet ring cell carcinoma        | 7 (4.5)         |
| Others                            | 11 (7.0)        |
| Unknown                           | 15 (9.5)        |

| Neoadjuvant (yes, %)              | 2 (1.3)         |
| Diabetes (yes, %)                 | 8 (5.1)         |

### Laboratory

| Blood parameter                          | Value            |
|------------------------------------------|------------------|
| WBC (<10^9/L)                            | 5.3 (4.5, 6.25)  |
| Hemoglobin (g/L)                         | 126 (109.5, 139.5) |
| Albumin (g/L)                            | 38.30±4.18       |
| Triglyceride (mmol/L)                    | 1.18±0.70        |
| Cholesterol (mmol/L)                     | 3.75±0.86        |
| C-reactive protein (mg/L)                | 3.2 (2.5, 4.45)  |
| CEA (ng/ml)                              | 1.12 (0.52, 2.22) |
| CA125 (ng/ml)                            | 7.2 (4.9, 13.55) |
| CA199 (ng/ml)                            | 10.43 (6.08, 18.96) |
| CA724 (ng/ml)                            | 1.84 (1.01, 4.15) |
| CA242 (ng/ml)                            | 9.97±17.86       |

**BMI: body mass index; WBC: white blood cell; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125; CA 199: carbohydrate antigen 199; CA724: carbohydrate antigen 724; CA242: carbohydrate antigen 242. Normally distributed variables were expressed as mean± standard deviation, skewed variables were expressed as median (25th percentile, 75th percentile).**

### Table 2 Body composition assessment by CT and BIA in overall patients

| Body composition assessment | Overall N=157 |
|-----------------------------|---------------|
| **Body composition by CT**  |               |
| Skeletal muscle mass area (cm²) | 117.32±24.97  |
| Subcutaneous fat mass area (cm²) | 103.56±50.01  |
| Visceral fat area (cm²) | 84.39±46.43   |
| SMI (cm²/m²)                | 44.44±8.13    |
| Sarcopenia (n, %)           | 65 (41.4)     |
| Visceral obesity (n, %)     | 65 (41.4)     |
| **Body composition by BIA** |               |
| Total body water (L)        | 33.43±5.23    |
| Visceral fat area (cm²)     | 71.94±22.44   |
| Total fat mass (kg)         | 16.03±5.12    |
| Body fat percentage %       | 25.83±6.84    |
| Lean body mass (kg)         | 42.88±6.73    |
| Skeletal muscle mass (kg)   | 24.86±4.29    |
| Fat free mass (kg)          | 45.42±7.08    |
SMI: skeletal muscle mass index.

| Table 3 Pearson’s correlation of VFA measured by CT and BIA |
|---------------------------------|-----------------|-----------------|-----|-----|
|                                | n               | VFA by CT (cm²)  | VFA by BIA (cm²) | r   | p    |
| Overall                        | 157             | 84.39±46.43      | 71.94±22.44      | 0.650 | <0.001 |
| Female                         | 48              | 85.10±38.04      | 80.06±22.67      | 0.559 | <0.001 |
| Male                           | 109             | 84.08±49.84      | 68.37±21.48      | 0.714 | <0.001 |
| BMI>24 kg/m²                   | 66              | 113.57±32.22     | 88.07±15.24      | 0.315 | 0.010  |
| BMI≤24 kg/m²                   | 91              | 63.23±43.70      | 60.24±19.39      | 0.551 | <0.001 |
| Age≤60 year                    | 66              | 84.94±42.66      | 73.11±20.67      | 0.640 | <0.001 |
| Age>60 year                    | 91              | 83.99±49.21      | 71.09±23.71      | 0.656 | <0.001 |
| Stage I                        | 48              | 86.78±47.18      | 72.49±21.87      | 0.671 | <0.001 |
| Stage II                       | 31              | 84.26±36.56      | 74.53±18.90      | 0.564 | <0.001 |
| Stage III                      | 49              | 88.15±47.00      | 70.63±21.15      | 0.726 | <0.001 |
| Stage IV                       | 29              | 74.22±53.99      | 70.46±28.97      | 0.605 | 0.001  |

BMI: body mass index; VFA: visceral fat area. r for Pearson’s correlation coefficient.

| Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA |
|---------------------------------|-----------------|-----------------|-----|-----|-----|-----|
|                                | n               | CT-BIA VFA (cm²) | p   | ICC | 95%LOA |
| Overall                        | 157             | 12.45±36.13      | ——— | 0.675 | -58.36, 83.26 |
| Female                         | 48              | 5.04±31.57       | 0.088 | 0.659 | -56.84, 66.92 |
| Male                           | 109             | 15.71±37.64      | 0.683 | -58.06, 89.48 |
| BMI>24 kg/m²                   | 66              | 25.50±31.00      | 0.000* | 0.392 | -35.26, 86.26 |
| BMI≤24 kg/m²                   | 91              | 2.99±36.78       | 0.580 | -69.10, 75.08 |
| Age≤60 year                    | 66              | 11.83±33.45      | 0.855 | 0.668 | -53.73, 77.39 |
| Age>60 year                    | 91              | 12.90±38.13      | 0.678 | -61.83, 87.63 |
| Stage I                        | 48              | 14.28±36.32      | 0.424 | 0.677 | -56.91, 85.47 |
| Stage II                       | 31              | 9.73±30.23       | 0.631 | -49.25, 68.98 |
| Stage III                      | 49              | 17.51±34.83      | 0.704 | -50.76, 85.78 |
| Stage IV                       | 29              | 3.77±43.15       | 0.670 | -80.80, 88.34 |

BMI: body mass index; VFA: visceral fat area; ICC: intraclass correlation coefficient; 95%LOA: 95% limits of agreement. p for comparison of CT-BIA VFA between subgroups by independent t-test.
Figure 1 Correlation between VFA measured by CT and BIA (A) and Bland-Altman plot for comparing the two methods (B).

227x113mm (150 x 150 DPI)
Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients.

AUROC = 0.822, p<0.001
95%CI: 0.758-0.887
192 patients with gastric cancer

35 patients were excluded
- Tumor originated from other organ (n=19)
- Heart failure (n=1)
- Kidney failure (n=5)
- Cirrhosis (n=1)
- Unmeasurable CT VFA (n=5)
- Unable to standstill (n=2)
- Refused to participate (n=2)

157 primary gastric cancer patients

VFA measured by CT (n=157)

VFA estimated by BIA (n=157)

171 x 119 mm (150 x 150 DPI)
1STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

| Section/Topic       | Item # | Recommendation                                                                 | Reported on page # |
|---------------------|--------|--------------------------------------------------------------------------------|--------------------|
| Title and abstract  | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1                  |
|                     |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 3-4                |
| Introduction        | 2      | Explain the scientific background and rationale for the investigation being reported | 5                  |
| Objectives          | 3      | State specific objectives, including any prespecified hypotheses                  | 6                  |
| Methods             | 4      | Present key elements of study design early in the paper                            | 6                  |
| Study design        | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7                |
| Setting             | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants | 7                  |
| Participants        | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-9                |
| Variables           | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-9                |
| Data sources/       |        | measurement                                                                      |                    |
| Bias                | 9      | Describe any efforts to address potential sources of bias                          | 9-10               |
| Study size          | 10     | Explain how the study size was arrived at                                          | 6                  |
| Quantitative variables | 11  | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 10                 |
| Statistical methods | 12     | (a) Describe all statistical methods, including those used to control for confounding | 9-10               |
|                     |        | (b) Describe any methods used to examine subgroups and interactions                | 9-10               |
|                     |        | (c) Explain how missing data were addressed                                       | No missing data    |
|                     |        | (d) If applicable, describe analytical methods taking account of sampling strategy | 9-10               |
|                     |        | (e) Describe any sensitivity analyses                                              | 9-10               |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 10 |
| Participants | 13* | (b) Give reasons for non-participation at each stage | 10 |
| Participants | 13* | (c) Consider use of a flow diagram | 10 |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 10 |
| Descriptive data | 14* | (b) Indicate number of participants with missing data for each variable of interest | No missing data |
| Outcome data | 15* | Report numbers of outcome events or summary measures | 11-12 |
| Main results | 16 | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11-12 |
| Main results | 16 | (b) Report category boundaries when continuous variables were categorized | 10 |
| Main results | 16 | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 11 |
| Discussion | 18 | Summarise key results with reference to study objectives | 13 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 16 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-16 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 13-16 |
| Other information | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 18 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Short title: The accuracy of bioelectrical impedance analysis in estimating visceral fat area

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Key words: gastric cancer, visceral fat area, visceral obesity, computed tomography, bioelectrical impedance analysis
Abstract

Objectives: As the gold standard method for measuring body composition, computer tomography (CT) still has several shortcomings which limit its wide application. Bioelectrical impedance analysis (BIA) is a simple and inexpensive method for body composition estimation. However, the accuracy of BIA is unknown. Visceral obesity is associated with adverse prognosis in gastric cancer. Therefore, we aimed to assess the accuracy of BIA in estimating visceral fat area (VFA) in gastric cancer. Methods: From 1st January 2017 to 1st December 2018, patients diagnosed of gastric cancer were enrolled. VFA was measured both by CT and BIA. VFA by CT at umbilical level ≥100 cm$^2$ was considered as visceral obesity. The reliability between two methods was assessed by intraclass correlation coefficient (ICC) and the consistency was assessed by Bland-Altman method (95% limits of agreement). Area under receiver operating characteristic curve (AUROC) was used to assess the performance of diagnosing visceral obesity by BIA. Results: A total of 157 patients diagnosed of gastric cancer were enrolled. The VFA by CT and BIA in the overall patients were 84.39±46.43 cm$^2$ and 71.94±22.44 cm$^2$, respectively. VFA estimated by BIA was positively correlated with VFA measured by CT by Pearson’s test ($r=0.650, p<0.001$). ICC for two methods in overall patients was 0.675. The mean bias between two measurements was 12.45±36.13 cm$^2$. The 95% limits of agreement ranged from -58.36 to 83.26 cm$^2$. The cut-off value for diagnosing visceral obesity by BIA was 81 cm$^2$ (AUROC: 0.822, $p<0.001$, 95%CI: 0.758-0.887). Conclusions: The VFA measured by BIA showed satisfactory reliability with that measured by CT. However, the absolute values of the
two methods were not interchangeable. The cut-off value of the VFA by BIA for diagnosing visceral obesity was 81 cm$^2$ for gastric cancer patients in the Chinese population.

**Key words:** visceral fat area, gastric cancer, bioelectronic impedance analysis, computed tomography

**Strengths and limitations of this study**

To our knowledge, this is the first study to assess the accuracy of visceral fat area estimated by BIA in gastric cancer patients. We compared visceral fat area estimated by BIA with that measured by CT scan as the ‘gold standard’.

The sample size of the study was small. However, the access of data for analyzing was strict which could compensate for the bias in some extent.
Introduction

Gastric cancer is a common malignancy type worldwide with a high mortality rate [1]. The prevalence of gastric cancer is comparatively higher in the Asian countries than that in the westerns [2]. Previous studies suggested that the alteration of body composition could affect the outcomes of multiple malignancies [3-6]. The negative effect of sarcopenia on the prognosis of cancer has reached in consensus [4-6]. In addition, the presence of visceral obesity could bring difficulty in surgery operation, increase the post-operation infection rate and reduce the overall survival rate in gastric cancer [3,7]. Go et al demonstrated that the presence of visceral obesity in gastric cancer subjects undergone laparoscopy-assisted distal gastrectomy significantly affected the number of retrieved lymph node [7]. In addition, visceral fat tissues contain more large adipocytes and androgen receptors than subcutaneous fat tissues and could result in insulin resistance, which is a negative hallmark for tumor progression [8]. Patients with gastric cancer need post-operative aftercare and individualized nutritional intervention. The measurement of VFA and muscle mass plays a role in the formulation of total energy and carbohydrate proportion in dietary instructions. Therefore, it is necessary to measure VFA and screen out visceral obesity in such population.

Several medical imaging methods has been used for analyzing body composition [9]. Among them, CT as a routine imaging examination prior to cancer diagnosis and therapy is accurate and considered the gold standard method for evaluating body composition [9, 10]. The area of skeletal muscle and visceral fat tissue by CT highly correlate with total body skeletal muscle mass and visceral fat mass [9-11]. However,
the use of CT in evaluating body composition has many drawbacks, such as radiation exposure, high expense and the need of specialists in medical imaging, which is not suitable for periodical measurements aftercare. In addition, only a few radiologists in central cities in China master the method of body composition by CT. Bioelectrical impedance analysis (BIA) method is a non-invasive alternate method for body composition evaluation and is widely used in a clinic setting [12]. The advantages of BIA lie in the low cost and none radiation to subjects, which is suitable for repeated monitoring for nutrition status. The accuracy of visceral fat area (VFA) was investigated in a Korean cohort in healthy subjects, revealing that VFA estimated by BIA correlated well with that measured by CT method, but an accurate equation was needed to match that measured by CT [12]. However, the accuracy of BIA is highly dependent on ethnicity and hydration status [13]. Patients with malignancies may have alteration of body composition and hydration status, which affects the performance of BIA in estimating VFA. Moreover, researches on validation of its accuracy is limited in the Chinese patients. The aim of the present study was to investigate the accuracy of BIA in estimating VFA in gastric cancer subjects in the Chinese population, as well as to identify the threshold for diagnosing visceral obesity by BIA.

Materials and Methods

Patients

From 1st January 2017 to 1st December 2018, patients with a clear diagnosis of gastric cancer either by pathology or radiology admitted to Gastroenterology or General
Surgery department of Drum Tower Hospital affiliated to Nanjing University Medical School were prospectively enrolled. Exclusion criteria were patients with age younger than 18 or older than 80 years old; primary tumor originated from other organs; heart failure; kidney failure; cirrhosis; unmeasurable CT visceral fat area; use of diuretics or lipid regulation medications; unable to stand still or patients who refused to undergo CT and BIA. The observational study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Nanjing Drum Tower Hospital (209-173-01). Written consent was obtained from all participants.

Clinical information collection

The clinical information of all the patients were recorded. Baseline clinical characteristics included age, gender, body weight, body height, body mass index (BMI, defined as body weight in kilogram (kg)/[body height in meters]^2), tumor stage, tumor tissue type, and comorbidities. Body weight was measured with patient wearing thin clothes and to the nearest 0.1 kg. Body height was measured with patient bare feet and to the nearest 0.1 cm. Body weight and body height were measured directly via the Inbody 720 instrument at the time of BIA testing. For most patients, body weight and height were measured only once, or was measured in replicate if the trained researcher found the patient was not stand still or stand straight. Tumor stage classification was based on the criteria established by the American Joint Committee on Cancer (AJCC) [14, 15]. Neoadjuvant therapy before the study was recorded. Laboratory tests were
performed with fasting blood samples when admitted to hospital. Laboratory
parameters included white blood cell count (WBC), hemoglobin level, albumin level,
triglyceride level, cholesterol level, C-reactive protein level. Tumor markers were also
performed once admitted and parameters included, carcinoembryonic antigen (CEA),
carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199), carbohydrate
antigen 724 (CA724), carbohydrate antigen 242 (CA242).

**Body composition assessment by CT**

CT scans were performed before treatment. According to previously published
method [10, 16], a single slice at the umbilical level was selected and the area of
different body compositions were analyzed by Matlab software (MathWorks, Massachusetts State, USA). Different body composition tissue compartments were
manually outlined and segmented with different Hounsfield unit (HU) threshold ranges.
Tissues with Hounsfield unit ranges from -29 to 150 were considered as skeletal muscle
and the total skeletal muscle area (SMA) was calculated. Areas with HU ranges from -150 to -50 were considered as visceral fat and the total visceral fat area (VFA) was
calculated. Areas with HU ranges from -190 to -30 were considered as subcutaneous
fat and the total subcutaneous fat area (SFA) was calculated [17,18]. CT assessment
was performed by two radiologists independently. They were blinded to each other in
CT measurement. They were both blinded to patients’ personal information and BIA
values. Mean values by two radiologists were used in the study.
Body composition assessment by BIA

BIA assessment was performed the same day with CT scan. An Inbody 720 multifrequency BIA Inbody720 instrument (Inbody corporation, Seoul, Korea) was adopted to measure body composition. The method was in accordance with previously described protocol [10]. To be brief, patients with fasting condition and empty bladder stand with both arms 45 angles apart from the body trunk and with both feet bared on the spots of the platform. Total body water, visceral fat area in cm$^2$ at the umbilical level, total fat mass, body fat percentages, lean body mass, skeletal body mass, fat free mass were estimated and the values were output. The measurement process was standard and was strictly supervised by an experienced researcher. If the BIA measurement process was not standard or the researcher consider potential mistakes, another measurement by BIA was performed to replace the former result.

Definition of visceral obesity

Based on the Japan Society for the Study of Obesity and widely accepted criteria in clinic [7,19], the threshold for visceral obesity was 100 cm$^2$ at umbilical level measured by CT images. Visceral obesity was defined as patients with visceral fat area at umbilical level $\geq$100 cm$^2$.

Statistical analysis

Data analysis was performed by SPSS for windows version 20.0 (IBM, New York State, USA) and MedCalc for windows version 15.2.2 (MedCalc Software corporation,
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199 Ostend, Belgium). Continuous variables were expressed as the means± standard
deviation (SD) if data were normally distributed and were compared by independent or
paired t-test when appropriate. Skewed distributed data were expressed as the medians
(25th percentile, 75th percentile) and were compared by Mann-Whitney U-test.

202 Categorical variables were expressed by number and percentages and were compared
by Chi-square (χ²-test) test or Fisher’s exact test when appropriate. Paired-t test and
intra-class correlation coefficient (ICC) for reliability and agreement were applied to
compare the difference of VFA between CT and BIA. Pearson’s correlation coefficient
was used to investigate any correlations between these two methods of measurement.

210 The consistency between two measurements was assessed by Bland-Altman statistical
method [20] with 95% limits of agreements (95% LOA) calculated. Patients with VFA
≥100 cm² measured by CT were classified as visceral obesity. The performance of VFA
estimated by BIA in diagnosing visceral obesity was assessed by the area under the
receiver characteristic curve (AUROC). The cut-off value of the VFA estimated by BIA
in stratifying visceral obesity was obtained with the maximum Youden index
(sensitivity + specificity -1). A two-tailed p-value <0.05 was considered statistically
significant. Shrout et al proposed that ICC value ranges from 0.00 to 0.49 was
interpreted as poor reliability, ranges from 0.50 to 0.74 was interpreted as satisfactory
and ranges from 0.75 to 1.00 was interpreted as excellent reliability [21].

219 Results

220 Baseline characteristics of the study population
A total of 35 patients were excluded from the research, finally 157 patients with
gastric cancer were enrolled, included 48 females and 109 males (Supplementary figure
1). The mean age of the overall patients was 60.61±11.95 years old. The mean body
weight and body height of the overall patients were 61.27±9.14 kg and 162.10±7.07
cm, respectively. The mean BMI of the overall group was 23.28±2.93 kg/m². According
to classification standard of China [22], 5 patients were underweight (3.2%), 85 patients
were within normal range of BMI (54.1%), 61 patients were overweight (38.9%) and 6
patients were obesity (3.8%). The number of patients with gastric cancer tumor stage I,
II, III, IV were 48 (30.6%), 31 (19.7%), 49 (31.2%) and 29 (18.5%), respectively. The
majority of patients were diagnosed with adenocarcinoma tissue type. Laboratory
indicators and demographic characteristics are summarized in Table 1.

The ICC between the two radiologists was 0.999. The mean value of VFA
measured by CT in overall patients was 84.39±46.43 cm². There were 65 (41.4%)
patients diagnosed with visceral obesity. The VFA estimated by BIA in overall patients
was 71.94±22.44 cm². (Table 2)

Comparison of VFA measured by CT (VFA-CT) and estimated by BIA (VFA-BIA)
in overall patients

The difference of the VFA between CT and BIA was statistically significant via
paired-t test (p<0.001). There was a mean 14.75% difference (based on CT) between
the values of the two methods in the overall patients (Table 2). The VFA measured by
CT was positively correlated with that estimated by BIA in overall patients by Pearson’s
correlation test \( r=0.650, p<0.001 \) (Table 3). ICC value between the VFA-CT and the VFA-BIA was 0.675, indicating satisfactory reliability and agreement. With Bland-Altman analysis, the mean bias between the two measurements was 12.45±36.13 cm², indicating that BIA underestimated VFA by 12.45±36.13 cm² in overall patients (Table 4, Figure 1). In addition, the Bland-Altman plot also showed that the VFA was overestimated in patients with smaller VFA and underestimated in patients with larger VFA (Figure 1). The 95%LOA of the bias ranged from -58.36 cm² to 83.26 cm², indicating that the absolute values of the two measurements were not interchangeable directly and the bias was not clinically acceptable.

**Subgroup analysis**

The VFA measured by CT was significantly correlated with that estimated by BIA in both the female \( r=0.559, p<0.001 \) and the male \( r=0.714, p<0.001 \) groups by Pearson’s correlation test. The mean difference of the two methods between genders was not significantly different \( 5.04±31.57 \) cm², 15.71±37.64 cm², respectively, \( p=0.088 \). In both gender groups, the two methods showed satisfactory reliability (ICC=0.659, 0.683, respectively). Patients were divided into groups according to the median of BMI. In both BMI groups, the VFA-CT and the VFA-BIA were significantly correlated by Pearson’s correlation test \( r=0.315, p=0.010 \) in BMI>24 kg/m² group; \( r=0.551, p<0.001 \) in BMI≤24 kg/m² group). The mean bias of VFA between the two BMI categories was significantly different \( 25.50±31.00 \) cm², 2.99±36.78 cm²; \( p<0.001 \), indicating that BIA largely underestimated VFA in overweight or obesity
subjects. ICC value in BMI>24 kg/m² group interpreted as poor reliability in this subcategory. In both older (>60 years old) and younger (≤60 years old) groups, the two methods showed significant correlation by Pearson’s correlation test (r=0.640, p<0.001; r=0.656, p<0.001, respectively) and satisfactory reliability (ICC=0.668, 0.678, respectively). The bias between patients with different age groups was not statistically significant (p=0.855). The bias between different tumor stages was not significantly different (p=0.424).

VFA-BIA in diagnosing visceral obesity

The criteria of VFA≥100 cm² [7,19] measured by CT at umbilical level was adopted as threshold in diagnosing visceral obesity. The VFA estimated by BIA showed a good to excellent performance in diagnosing visceral obesity in overall patients in the present study (AUROC=0.822, p<0.001, 95%CI: 0.758-0.887), with a sensitivity of 65.6%, and specificity of 88.2%. (Figure 2). The best cut-off value of the VFA-BIA was 81 cm², indicating that the gastric cancer patients with VFA larger than 81 cm² estimated by BIA should be highly suspected of visceral obesity.

Discussions

The present study revealed that the VFA estimated by BIA significantly correlated with that measured by CT at umbilical level in gastric cancer patients in the Chinese population with satisfactory reliability (ICC=0.675). This was in accordance with a previous Korean study [12]. Lee et al compared VFA-CT with VFA-BIA in healthy subjects with wide ranges of age and BMI. The mean bias of VFA between two methods
was 21.4±45.6 cm², and tended to increase with BMI [12]. Our study also demonstrated
the positive correlation of bias with BMI, indicating the drawback of BIA in analyzing
body composition in overweight or obese subjects. This limitation of BIA for obesity
was proposed by several studies [23-27]. Bosaeus et al discovered that BIA
underestimated total fat mass in overweight and obese women compared with MRI
measurement [23]. Neovius et al discovered that compared with DXA, the bias of fat
mass was increased with degree of adiposity [27].

CT slice at umbilical level serves as the gold standard for VFA assessment [7,19].
However, the exposure to radiation and the high cost restrict its use as periodical
nutritional assessment in clinic settings. Moreover, the need for expertise in medical
imaging also restricts its application. In China, the reality is that only a few doctors
working in regional central hospitals master the body composition quantification
technique by CT. Body composition assessment is important for these gastric cancer
patients in post-operative aftercare and individualized nutritional intervention. Patients
with distinct VFA status requires different formulation of energy and proportion of
macro nutrients [28]. Periodical measurement of VFA could provide clues for
nutritionists with individualized dietary instructions. Unfortunately, CT for body
composition assessment is not applicable to non-central city hospitals in China and is
also not suitable for periodical nutritional assessment in follow up. It has clinical value
to evaluate the accuracy of BIA in estimating VFA in gastric cancer patients since the
BIA method compensate for the shortcomings of CT and is suitable for extensive
nutritional screening and monitoring [11]. But what need to be clarified is that the
principle of BIA instruments is based on the electrical property, impedance of the
tissues in the conductive path between the sense electrodes [9]. The quantifications of
adipose tissue by BIA are only estimations rather than direct measurements [9].
Therefore, we still recommend CT as a priority when there are enough professionals
and economic conditions for routine VFA assessment by CT. Otherwise, BIA could be
an alternate. To supplement, the present study only enrolled patients could stand still
and undertake BIA measurement by the Inbody 720. However, there are many cancer
patients who are too weak to stand, the Inbody S10 for supine subjects to measure VFA is a choice [29]. The accuracy of VFA estimation by the Inbody S10 warrants further investigation.

Recent years, the roles of visceral obesity on the progression of cancer and cancer-related comorbidities has been investigated in several studies [30,31]. Ozoya et al retrospectively analyzed 110 patients with colon cancer and concluded that visceral obesity was associated with metabolic comorbidities and post-operative morbidities [30]. Go et al indicated that the presence of visceral obesity could bring technical difficulties in operation, and could significantly reduce the number of retrieved lymph nodes, as well as the overall survival in gastric cancer patients undergone laparoscopy-assisted distal gastrectomy [7]. Therefore, visceral obesity should be discriminated prior to surgery, and operations should be conducted by more experienced surgeons [7].

Pre-operative quantification of VFA could help surgeons optimize the selection of patients suitable for laparoscopic approach and take interventions for prophylaxis of surgical incision infection. In addition, the low-grade chronic inflammation produced by excessive visceral fat tissues is considered suitable microenvironment for tumor growth [30]. Growth factors released by visceral fat tissues also mediate in cancer progression [30-32]. Therefore, to reverse visceral obesity state is essential in gastric cancer subjects. Tumor of gastrointestinal origin apparently affects the digestion and absorption of nutrients. Many patients suffer from weight loss, sarcopenia or even cachexia after gastrectomy or under tumor bearing state [33]. The metabolic characteristics and nutritional management are different between patients with distinct body composition [34]. How to provide scientific, accurate and reasonable individualized nutritional support for these patients is a major challenge and difficulty.

Some cancer patients, especially those in the earlier stage, prone to excessive daily energy intake and restricted daily physical activity, may consequently develop sarcopenia obesity. For patients with similar skeletal muscle mass but different VFA status, the total energy and micronutrient proportions required daily will be distinctive [28], as well as the physical exercise regimen [35]. Therefore, it is essential to distinct
visceral obesity both prior to surgery and in aftercare period.

In the present study, the values of the two methods were significantly different by paired-t test (p<0.001), and the mean bias of the two methods was 12.45±36.13 cm$^2$, with a wide range of 95%LOA, indicating that the absolute values of the two methods were not interchangeable directly. This was in accordance with Lee’s research [12]. Lee et al [12] postulated a formula to predict actual VFA with BIA variables. However, this formula was too complicated in calculation and difficult to implement routinely. In addition, previous formulas were based on healthy subjects with different ethnicities, which were not applicable for the Chinese patients with gastric cancer. Therefore, the present study identified a cut-off value of VFA by BIA in diagnosing visceral obesity. The Chinese patients with gastric cancer with VFA exceeding 81 cm$^2$ by BIA should be highly suspected of visceral obesity. What we need to clarify here is that, BIA data is based on certain in-built equations suitable for different ethnicities [36,37]. The equations will be modified when the instruments installed in different regions worldwide. Therefore, our conclusions were only applicable to the Asian population, especially to the Chinese population, when they take BIA by instruments installed in China.

There were several limitations in the present research. First, the study was conducted in a single center with a relatively small sample size, and only included patients from China. The conclusions might not be generalized to patients from other regions. A multicenter design study with a larger sample size was warranted to validate our conclusions. Second, the ROC result in the present study could distinct visceral obesity by BIA, but could not directly convert the VFA-BIA absolute value into the VFA-CT absolute value. It was unable to obtain the exact and accurate values of VFA via BIA. Third, the study design applied the Inbody 720 as BIA instrument, which is a relatively older product. Further studies to validate the conclusions with the promotion product Inbody 770 should be performed [38].

In conclusion, it is necessary to identify visceral obesity in gastric cancer patients both prior to surgery and in aftercare period via body composition analysis. The present
study revealed that the VFA measured by CT and BIA showed significant correlation and satisfactory reliability. However, the bias between the two methods was within a wide range, indicating that the absolute values of the two methods were not interchangeable directly. The cut-off value of the VFA-BIA for identifying visceral obesity in the present study was $81 \text{ cm}^2$, indicating the Chinese gastric cancer patients with VFA estimated by BIA larger than the threshold should be highly suspected for visceral obesity.

**Contributors**

BG was responsible for methodology, data curation, project administration, and writing; YL was responsible for methodology, statistical analysis, data analyzing and writing; CD was responsible for data collection; SLL was responsible for data curation, project administration, Software management; XJB was responsible for BIA management and data collection; XTC was responsible for study design and manuscript supervision. All authors gave their final approval of the final version of the manuscript.

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Competing interests

No declared.

Patient consent

Obtained.

Ethics approval

The study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the Nanjing Drum Tower Hospital.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

The data was available at the corresponding authors with reasonable request.

Patient and Public Involvement Statement
They were not involved in the design, or conduct, or reporting, or dissemination
plans of our research.

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**Figure Legends**

**Figure 1** Bland-Altman plot for comparing the two methods

The mean bias between the two measurements was 12.45±36.13 cm² (Line of the Mean and its 95%CI were shown), 95% limits of agreements ranged from -58.36 cm² to 83.26 cm² (Lines of the Mean±1.96SD and their 95%CI were shown).

**Figure 2** ROC of VFA by BIA for diagnosing visceral obesity in overall patients
The AUROC=0.822, p<0.001, 95%CI: 0.758-0.887, the best cut-off value for diagnosing visceral obesity by VFA-BIA was 81 cm², with a sensitivity of 65.6% and specificity of 88.2%.

Supplementary Figure 1 The flow diagram of the research.

Tables

Table 1 Baseline characteristics

Table 2 Body composition assessment by CT and BIA in overall patients

Table 3 Pearson’s correlation of VFA measured by CT and BIA

Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

Table 1 Baseline characteristics

|                      | Overall | N=157 |
|----------------------|---------|-------|
| Age (year)           | 60.61±11.95 |
| <60y (%)             | 66 (42.0) |
| ≥60y (%)             | 91 (58.0) |
| Gender (Male, %)     | 109 (69.4) |
| Body weight (kg)     | 61.27±9.14 |
| Body height (cm)     | 162.10±7.07 |
| BMI (kg/m²)          | 23.28±2.93 |
| <18.5                | 5 (3.2) |
| 18.50-23.99          | 85 (54.1) |
| 24-27.99             | 61 (38.9) |
| ≥28                  | 6 (3.8) |
| Tumor stage (AJCC)   |         |
| I                    | 48 (30.6) |
| II                   | 31 (19.7) |
| III                  | 49 (31.2) |
| IV                   | 29 (18.5) |
| Tissue Type            | Count (Percentage) |
|------------------------|--------------------|
| Adenocarcinoma         | 124 (79.0)         |
| Signet ring cell carcinoma | 7 (4.5)      |
| Others                 | 11 (7.0)           |
| Unknown                | 15 (9.5)           |

| Laboratory Test        | Result             |
|------------------------|--------------------|
| WBC (×10^9/L)          | 5.3 (4.5, 6.25)    |
| Hemoglobin (g/L)       | 126 (109.5, 139.5) |
| Albumin (g/L)          | 38.30±4.18         |
| Triglyceride (mmol/L)  | 1.18±0.70          |
| Cholesterol (mmol/L)   | 3.75±0.86          |
| C-reactive protein (mg/L) | 3.2 (2.5, 4.45) |
| CEA (ng/ml)            | 1.12 (0.52, 2.22)  |
| CA125 (ng/ml)          | 7.2 (4.9, 13.55)   |
| CA199 (ng/ml)          | 10.43 (6.08, 18.96)|
| CA724 (ng/ml)          | 1.84 (1.01, 4.15)  |
| CA242 (ng/ml)          | 9.97±17.86         |

BMI: body mass index; WBC: white blood cell; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125; CA 199: carbohydrate antigen 199; CA724: carbohydrate antigen 724; CA242: carbohydrate antigen 242. Normally distributed variables were expressed as mean± standard deviation, skewed variables were expressed as median (25th percentile, 75th percentile).

Table 2 Body composition assessment by CT and BIA in overall patients

| Body Composition Assessment | Overall N=157 |
|-----------------------------|---------------|
| Body composition by CT      |               |
| Skeletal muscle mass area (cm²) | 117.32±24.97 |
| Subcutaneous fat mass area (cm²) | 103.56±50.01 |
| Visceral fat area (cm²)     | 84.39±46.43   |
| Visceral obesity (n, %)     | 65 (41.4)     |
| Body composition by BIA     |               |
| Total body water (L)        | 33.43±5.23    |
| Visceral fat area (cm²)     | 71.94±22.44   |
| Total fat mass (kg)         | 16.03±5.12    |
| Body fat percentage %       | 25.83±6.84    |
| Lean body mass (kg)         | 42.88±6.73    |
| Skeletal muscle mass (kg)   | 24.86±4.29    |
| Fat free mass (kg)          | 45.42±7.08    |

SMI: skeletal muscle mass index. The difference of VFA between CT and BIA was statistically significant (p<0.001) via paired-t test. There was a mean 14.75% difference (based on CT) between the
Table 3 Pearson’s correlation of VFA measured by CT and BIA

|               | n  | VFA by CT (cm²) | VFA by BIA (cm²) | r   | p      |
|---------------|----|----------------|------------------|-----|--------|
| Overall       | 157| 84.39±46.43    | 71.94±22.44      | 0.650 | <0.001 |
| Female        | 48 | 85.10±38.04    | 80.06±22.67      | 0.559 | <0.001 |
| Male          | 109| 84.08±49.84    | 68.37±21.48      | 0.714 | <0.001 |
| BMI>24 kg/m² | 66 | 113.57±32.22   | 88.07±15.24      | 0.315 | 0.010  |
| BMI≤24 kg/m² | 91 | 63.23±43.70    | 60.24±19.39      | 0.551 | <0.001 |
| Age≤60 year   | 66 | 84.94±42.66    | 73.11±20.67      | 0.640 | <0.001 |
| Age>60 year   | 91 | 83.99±49.21    | 71.09±23.71      | 0.656 | <0.001 |
| Stage I       | 48 | 86.78±47.18    | 72.49±21.87      | 0.671 | <0.001 |
| Stage II      | 31 | 84.26±36.56    | 74.53±18.90      | 0.564 | <0.001 |
| Stage III     | 49 | 88.15±47.00    | 70.63±21.15      | 0.726 | <0.001 |
| Stage IV      | 29 | 74.22±53.99    | 70.46±28.97      | 0.605 | 0.001  |

BMI: body mass index; VFA: visceral fat area. r for Pearson’s correlation coefficient. p for statistical significance of Pearson’s correlation test.

Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

|               | n  | CT-BIA VFA (cm²) | p          | ICC | 95%LOA          |
|---------------|----|-----------------|------------|-----|-----------------|
| Overall       | 157| 12.45±36.13     | 0.675      | -58.36, 83.26 |
| Female        | 48 | 5.04±31.57      | 0.088      | 0.659 | -56.84, 66.92  |
| Male          | 109| 15.71±37.64     | 0.683      | -58.06, 89.48 |
| BMI>24 kg/m² | 66 | 25.50±31.00     | 0.000*     | 0.392 | -35.26, 86.26  |
| BMI≤24 kg/m² | 91 | 2.99±36.78      | 0.580      | -69.10, 75.08 |
| Age≤60 year   | 66 | 11.83±33.45     | 0.855      | 0.668 | -53.73, 77.39  |
| Age>60 year   | 91 | 12.90±38.13     | 0.678      | -61.83, 87.63 |
| Stage I       | 48 | 14.28±36.32     | 0.424      | 0.677 | -56.91, 85.47  |
| Stage II      | 31 | 9.73±30.23      | 0.631      | -49.25, 68.98 |
| Stage III     | 49 | 17.51±34.83     | 0.704      | -50.76, 85.78 |
| Stage IV      | 29 | 3.77±43.15      | 0.670      | -80.80, 88.34 |

BMI: body mass index; VFA: visceral fat area; ICC: intraclass correlation coefficient; 95%LOA: 95% limits of agreement. p for comparison of CT-BIA VFA between subgroups by independent t-test.
Figure 1 Bland-Altman plot for comparing the two methods

209x135mm (300 x 300 DPI)
Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients

AUROC = 0.822, p < 0.001
95% CI: 0.758 - 0.887

209x189mm (300 x 300 DPI)
192 patients with gastric cancer

35 patients were excluded
- Tumor originated from other organ (n=19)
- Heart failure (n=1)
- Kidney failure (n=5)
- Cirrhosis (n=1)
- Unmeasurable CT VFA (n=5)
- Unable to standstill (n=2)
- Refused to participate(n=2)

157 primary gastric cancer patients

VFA measured by CT (n=157)

VFA estimated by BIA (n=157)
# 1STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

| Section/Topic | Item # | Recommendation | Reported on page # |
|---------------|--------|----------------|-------------------|
| **Title and abstract** | 1 | (a) Indicate the study’s design with a commonly used term in the title or the abstract | 1 |
| | | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | 3-4 |
| **Introduction** | 2 | Explain the scientific background and rationale for the investigation being reported | 5 |
| **Objectives** | 3 | State specific objectives, including any prespecified hypotheses | 6 |
| **Methods** | 4 | Present key elements of study design early in the paper | 6 |
| Study design | | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7 |
| Participants | 6 | (a) Give the eligibility criteria, and the sources and methods of selection of participants | 7 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-10 |
| Data sources/measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-10 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9-10 |
| Study size | 10 | Explain how the study size was arrived at | 6 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 10 |
| Statistical methods | 12 | (a) Describe all statistical methods, including those used to control for confounding | 9-10 |
| | | (b) Describe any methods used to examine subgroups and interactions | 9-10 |
| | | (c) Explain how missing data were addressed | No missing data |
| | | (d) If applicable, describe analytical methods taking account of sampling strategy | 9-10 |
| | | (e) Describe any sensitivity analyses | 9-10 |
| **Results** | | | |

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
Participants

13* (a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed 10-11
(b) Give reasons for non-participation at each stage 10-11
(c) Consider use of a flow diagram 10-11

Descriptive data 14*

(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders 10-11
(b) Indicate number of participants with missing data for each variable of interest No missing data

Outcome data 15*

Report numbers of outcome events or summary measures 11-13

Main results 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included 11-13
(b) Report category boundaries when continuous variables were categorized 10-11
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period _

Other analyses 17

Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses 11

Discussion

Key results 18
Summarise key results with reference to study objectives 13-14

Limitations 19
Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias 16

Interpretation 20
Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence 13-16

Generalisability 21
Discuss the generalisability (external validity) of the study results 13-16

Other information

Funding 22
Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based 18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Comparison of visceral fat area measured by Computed Tomography and 
Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-
sectional study

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Short title: The accuracy of bioelectrical impedance analysis in estimating visceral 
fat area

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29 **Key words:** gastric cancer, visceral fat area, visceral obesity, computed tomography, bioelectrical impedance analysis
Abstract

Objectives: Bioelectrical impedance analysis (BIA) is a simple and inexpensive method for body composition estimation. However, the accuracy of BIA is unknown. We aimed to assess the accuracy of BIA in estimating visceral fat area (VFA) in gastric cancer patients.

Study design: This study was a cross-sectional study comparing accuracy of BIA in estimating VFA with the gold standard method measured by computer tomography (CT). The VFA was measured both by CT and BIA for the enrolled patients. VFA by CT at umbilical level ≥100 cm² was considered as visceral obesity. The reliability between two methods was assessed by intraclass correlation coefficient (ICC) and the consistency was assessed by Bland-Altman method (95% limits of agreement). Area under the receiver operating characteristic curve (AUROC) was used to assess the performance of diagnosing visceral obesity by BIA.

Setting: The study was conducted in China.

Participants: From 1st January 2017 to 1st December 2018, a total of 157 patients diagnosed of gastric cancer were enrolled.

Results: The VFA by CT and BIA in the overall patients were 84.39±46.43 cm² and 71.94±22.44 cm², respectively. VFA estimated by BIA was positively correlated with VFA measured by CT by Pearson’s test (r=0.650, p<0.001). ICC for the two methods in overall patients was 0.675. The mean bias between the two measurements was 12.45±36.13 cm². The 95% limits of agreement ranged from -58.36 to 83.26 cm². The cut-off value for diagnosing visceral obesity by BIA was 81 cm² (AUROC: 0.822,
Conclusions: The VFA measured by BIA showed satisfactory reliability with that measured by CT. However, the absolute values of the two methods were not interchangeable. The cut-off value of the VFA by BIA for diagnosing visceral obesity was 81 cm$^2$ for gastric cancer patients in the Chinese population.

Key words: visceral fat area, gastric cancer, bioelectronic impedance analysis, computed tomography

Strengths and limitations of this study

To our knowledge, this is the first study to assess the accuracy of visceral fat area estimated by BIA in gastric cancer patients in China. We compared visceral fat area estimated by BIA with that measured by CT scan as the ‘gold standard’.

We assessed the reliability and consistency of BIA in estimating visceral fat area with that measured by CT.

We identified the cut-off value of visceral fat area estimated by BIA to diagnose visceral obesity.

Though the sample size of the study was small, the access of data for analyzing was strict which could compensate for the bias in some extent.
Introduction

Gastric cancer is a common malignancy type worldwide with a high mortality rate [1]. The prevalence of gastric cancer is comparatively higher in the Asian countries than that in the westerns [2]. Previous studies suggested that the alteration of body composition could affect the outcomes of multiple malignancies [3-6]. The negative effect of sarcopenia on the prognosis of cancer has reached in consensus [4-6]. In addition, the presence of visceral obesity could bring difficulty in surgery operation, increase the post-operation infection rate and reduce the overall survival rate in gastric cancer [3,7]. Go et al demonstrated that the presence of visceral obesity in gastric cancer subjects undergone laparoscopy-assisted distal gastrectomy significantly affected the number of retrieved lymph node [7]. In addition, visceral fat tissues contain more large adipocytes and androgen receptors than subcutaneous fat tissues and could result in insulin resistance, which is a negative hallmark for tumor progression [8]. Patients with gastric cancer need post-operative aftercare and individualized nutritional intervention. The measurement of VFA and muscle mass plays a role in the formulation of total energy and carbohydrate proportion in dietary instructions. Therefore, it is necessary to measure VFA and screen out visceral obesity in such population.

Several medical imaging methods has been used for analyzing body composition [9]. Among them, CT as a routine imaging examination prior to cancer diagnosis and therapy is accurate and considered the gold standard method for evaluating body composition [9, 10]. The area of skeletal muscle and visceral fat tissue by CT highly correlate with total body skeletal muscle mass and visceral fat mass [9-11]. However,
the use of CT in evaluating body composition has many drawbacks, such as radiation exposure, high expense and the need of specialists in medical imaging, which is not suitable for periodical measurements aftercare. In addition, only a few radiologists in central cities in China master the method of body composition by CT. Bioelectrical impedance analysis (BIA) method is a non-invasive alternate method for body composition evaluation and is widely used in a clinic setting [12]. The advantages of BIA lie in the low cost and none radiation to subjects, which is suitable for repeated monitoring for nutrition status. The accuracy of visceral fat area (VFA) was investigated in a Korean cohort in healthy subjects, revealing that VFA estimated by BIA correlated well with that measured by CT method, but an accurate equation was needed to match that measured by CT [12]. However, the accuracy of BIA is highly dependent on ethnicity and hydration status [13]. Patients with malignancies may have alteration of body composition and hydration status, which affects the performance of BIA in estimating VFA. Moreover, researches on validation of its accuracy is limited in the Chinese patients. The aim of the present study was to investigate the accuracy of BIA in estimating VFA in gastric cancer subjects in the Chinese population, as well as to identify the threshold for diagnosing visceral obesity by BIA.

Materials and Methods

Patients

From 1st January 2017 to 1st December 2018, patients with a clear diagnosis of gastric cancer either by pathology or radiology admitted to Gastroenterology or General
Surgery department of Drum Tower Hospital affiliated to Nanjing University Medical School were prospectively enrolled. Exclusion criteria were patients with age younger than 18 or older than 80 years old; primary tumor originated from other organs; heart failure; kidney failure; cirrhosis; unmeasurable CT visceral fat area; use of diuretics or lipid regulation medications; unable to stand still or patients who refused to undergo CT and BIA. The observational study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Nanjing Drum Tower Hospital (209-173-01). Written consent was obtained from all participants.

**Clinical information collection**

The clinical information of all the patients were recorded. Baseline clinical characteristics included age, gender, body weight, body height, body mass index (BMI, defined as body weight in kilogram (kg)/[body height in meters]^2), tumor stage, tumor tissue type, and comorbidities. Body weight was measured with patient wearing thin clothes and to the nearest 0.1 kg. Body height was measured with patient bare feet and to the nearest 0.1 cm. Body weight and body height were measured directly via the Inbody 720 instrument at the time of BIA testing. For most patients, body weight and height were measured only once, or was measured in replicate if the trained researcher found the patient was not stand still or stand straight. Tumor stage classification was based on the criteria established by the American Joint Committee on Cancer (AJCC) [14, 15]. Neoadjuvant therapy before the study was recorded. Laboratory tests were
performed with fasting blood samples when admitted to hospital. Laboratory
parameters included white blood cell count (WBC), hemoglobin level, albumin level,
triglyceride level, cholesterol level, C-reactive protein level. Tumor markers were also
performed once admitted and parameters included, carcinoembryonic antigen (CEA),
carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199), carbohydrate
antigen 724 (CA724), carbohydrate antigen 242 (CA242).

**Body composition assessment by CT**

CT scans were performed before treatment. According to previously published
method [10, 16], a single slice at the umbilical level was selected and the area of
different body compositions were analyzed by Matlab software (MathWorks,
Massachusetts State, USA). Different body composition tissue compartments were
manually outlined and segmented with different Hounsfield unit (HU) threshold ranges.
Tissues with Hounsfield unit ranges from -29 to 150 were considered as skeletal muscle
and the total skeletal muscle area (SMA) was calculated. Areas with HU ranges from -
150 to -50 were considered as visceral fat and the total visceral fat area (VFA) was
calculated. Areas with HU ranges from -190 to -30 were considered as subcutaneous
fat and the total subcutaneous fat area (SFA) was calculated [17,18]. CT assessment
was performed by two radiologists independently. They were blinded to each other in
CT measurement. They were both blinded to patients’ personal information and BIA
values. Mean values by two radiologists were used in the study.
Body composition assessment by BIA

BIA assessment was performed the same day with CT scan. An Inbody 720 multifrequency BIA Inbody720 instrument (Inbody corporation, Seoul, Korea) was adopted to measure body composition. The method was in accordance with previously described protocol [10]. To be brief, patients with fasting condition and empty bladder stand with both arms 45 angles apart from the body trunk and with both feet bared on the spots of the platform. Total body water, visceral fat area in cm$^2$ at the umbilical level, total fat mass, body fat percentages, lean body mass, skeletal body mass, fat free mass were estimated and the values were output. The measurement process was standard and was strictly supervised by an experienced researcher. If the BIA measurement process was not standard or the researcher consider potential mistakes, another measurement by BIA was performed to replace the former result.

Definition of visceral obesity

Based on the Japan Society for the Study of Obesity and widely accepted criteria in clinic [7,19], the threshold for visceral obesity was 100 cm$^2$ at umbilical level measured by CT images. Visceral obesity was defined as patients with visceral fat area at umbilical level $\geq$100 cm$^2$.

Statistical analysis

Data analysis was performed by SPSS for windows version 20.0 (IBM, New York State, USA) and MedCalc for windows version 15.2.2 (MedCalc Software corporation,
Ostend, Belgium). Continuous variables were expressed as the means± standard deviation (SD) if data were normally distributed and were compared by independent or paired t-test when appropriate. Skewed distributed data were expressed as the medians (25th percentile, 75th percentile) and were compared by Mann-Whitney U-test. Categorical variables were expressed by number and percentages and were compared by Chi-square (χ²-test) test or Fisher’s exact test when appropriate. Paired-t test and intraclass correlation coefficient (ICC) for reliability and agreement were applied to compare the difference of VFA between CT and BIA. Pearson’s correlation coefficient was used to investigate any correlations between these two methods of measurement. The consistency between two measurements was assessed by Bland-Altman statistical method [20] with 95% limits of agreements (95% LOA) calculated. Patients with VFA ≥100 cm² measured by CT were classified as visceral obesity. The performance of VFA estimated by BIA in diagnosing visceral obesity was assessed by the area under the receiver characteristic curve (AUROC). The cut-off value of the VFA estimated by BIA in stratifying visceral obesity was obtained with the maximum Youden index (sensitivity + specificity -1). A two-tailed p-value <0.05 was considered statistically significant. Shrout et al proposed that ICC value ranges from 0.00 to 0.49 was interpreted as poor reliability, ranges from 0.50 to 0.74 was interpreted as satisfactory and ranges from 0.75 to 1.00 was interpreted as excellent reliability [21].

Results

Baseline characteristics of the study population
A total of 35 patients were excluded from the research, finally 157 patients with gastric cancer were enrolled, included 48 females and 109 males (Supplementary figure 1). The mean age of the overall patients was 60.61±11.95 years old. The mean body weight and body height of the overall patients were 61.27±9.14 kg and 162.10±7.07 cm, respectively. The mean BMI of the overall group was 23.28±2.93 kg/m². According to classification standard of China [22], 5 patients were underweight (3.2%), 85 patients were within normal range of BMI (54.1%), 61 patients were overweight (38.9%) and 6 patients were obesity (3.8%). The number of patients with gastric cancer tumor stage I, II, III, IV were 48 (30.6%), 31 (19.7%), 49 (31.2%) and 29 (18.5%), respectively. The majority of patients were diagnosed with adenocarcinoma tissue type. Laboratory indicators and demographic characteristics are summarized in Table 1.

The ICC between the two radiologists was 0.999. The mean value of VFA measured by CT in overall patients was 84.39±46.43 cm². There were 65 (41.4%) patients diagnosed with visceral obesity. The VFA estimated by BIA in overall patients was 71.94±22.44 cm². (Table 2)

### Comparison of VFA measured by CT (VFA-CT) and estimated by BIA (VFA-BIA) in overall patients

The difference of the VFA between CT and BIA was statistically significant via paired-t test (p<0.001). There was a mean 14.75% difference (based on CT) between the values of the two methods in the overall patients (Table 2). The VFA measured by CT was positively correlated with that estimated by BIA in overall patients by Pearson’s
correlation test ($r=0.650$, $p<0.001$) (Table 3). ICC value between the VFA-CT and the VFA-BIA was 0.675, indicating satisfactory reliability and agreement. With Bland-Altman analysis, the mean bias between the two measurements was $12.45\pm36.13 \text{ cm}^2$, indicating that BIA underestimated VFA by $12.45\pm36.13 \text{ cm}^2$ in overall patients (Table 4, Figure 1). In addition, the Bland-Altman plot also showed that the VFA was overestimated in patients with smaller VFA and underestimated in patients with larger VFA (Figure 1). The 95%LOA of the bias ranged from $-58.36 \text{ cm}^2$ to $83.26 \text{ cm}^2$, indicating that the absolute values of the two measurements were not interchangeable directly and the bias was not clinically acceptable.

Subgroup analysis

The VFA measured by CT was significantly correlated with that estimated by BIA in both the female ($r=0.559$, $p<0.001$) and the male ($r=0.714$, $p<0.001$) groups by Pearson’s correlation test. The mean difference of the two methods between genders was not significantly different ($5.04\pm31.57 \text{ cm}^2$, $15.71\pm37.64 \text{ cm}^2$, respectively, $p=0.088$). In both gender groups, the two methods showed satisfactory reliability (ICC=0.659, 0.683, respectively). Patients were divided into groups according to the median of BMI. In both BMI groups, the VFA-CT and the VFA-BIA were significantly correlated by Pearson’s correlation test ($r=0.315$, $p=0.010$ in BMI$>24 \text{ kg/m}^2$ group; $r=0.551$, $p<0.001$ in BMI$\leq24 \text{ kg/m}^2$ group). The mean bias of VFA between the two BMI categories was significantly different ($25.50\pm31.00 \text{ cm}^2$, $2.99\pm36.78 \text{ cm}^2$; $p<0.001$), indicating that BIA largely underestimated VFA in overweight or obesity.
subjects. ICC value in BMI>24 kg/m² group interpreted as poor reliability in this subcategory. In both older (>60 years old) and younger (≤60 years old) groups, the two methods showed significant correlation by Pearson’s correlation test (r=0.640, p<0.001; r=0.656, p<0.001, respectively) and satisfactory reliability (ICC=0.668, 0.678, respectively). The bias between patients with different age groups was not statistically significant (p=0.855). The bias between different tumor stages was not significantly different (p=0.424).

VFA-BIA in diagnosing visceral obesity

The criteria of VFA≥100 cm² [7,19] measured by CT at umbilical level was adopted as threshold in diagnosing visceral obesity. The VFA estimated by BIA showed a good to excellent performance in diagnosing visceral obesity in overall patients in the present study (AUROC=0.822, p<0.001, 95%CI: 0.758-0.887), with a sensitivity of 65.6%, and specificity of 88.2%. (Figure 2). The best cut-off value of the VFA-BIA was 81 cm², indicating that the gastric cancer patients with VFA larger than 81 cm² estimated by BIA should be highly suspected of visceral obesity.

Discussions

The present study revealed that the VFA estimated by BIA significantly correlated with that measured by CT at umbilical level in gastric cancer patients in the Chinese population with satisfactory reliability (ICC=0.675). This was in accordance with a previous Korean study [12]. Lee et al compared VFA-CT with VFA-BIA in healthy
subjects with wide ranges of age and BMI. The mean bias of VFA between two methods was 21.4±45.6 cm$^2$, and tended to increase with BMI [12]. Our study also demonstrated the positive correlation of bias with BMI, indicating the drawback of BIA in analyzing body composition in overweight or obese subjects. This limitation of BIA for obesity was proposed by several studies [23-27]. Bosaeus et al discovered that BIA underestimated total fat mass in overweight and obese women compared with MRI measurement [23]. Neovius et al discovered that compared with DXA, the bias of fat mass was increased with degree of adiposity [27].

CT slice at umbilical level serves as the gold standard for VFA assessment [7,19]. However, the exposure to radiation and the high cost restrict its use as periodical nutritional assessment in clinic settings. Moreover, the need for expertise in medical imaging also restricts its application. In China, the reality is that only a few doctors working in regional central hospitals master the body composition quantification technique by CT. Body composition assessment is important for these gastric cancer patients in post-operative aftercare and individualized nutritional intervention. Patients with distinct VFA status requires different formulation of energy and proportion of macro nutrients [28]. Periodical measurement of VFA could provide clues for nutritionists with individualized dietary instructions. Unfortunately, CT for body composition assessment is not applicable to non-central city hospitals in China and is also not suitable for periodical nutritional assessment in follow up. It has clinical value to evaluate the accuracy of BIA in estimating VFA in gastric cancer patients since the BIA method compensate for the shortcomings of CT and is suitable for extensive
nutritional screening and monitoring [11]. But what need to be clarified is that the
principle of BIA instruments is based on the electrical property, impedance of the
tissues in the conductive path between the sense electrodes [9]. The quantifications of
adipose tissue by BIA are only estimations rather than direct measurements [9].
Therefore, we still recommend CT as a priority when there are enough professionals
and economic conditions for routine VFA assessment by CT. Otherwise, BIA could be
an alternate. To supplement, the present study only enrolled patients could stand still
and undertake BIA measurement by the Inbody 720. However, there are many cancer
patients who are too weak to stand, the Inbody S10 for supine subjects to measure VFA
is a choice [29]. The accuracy of VFA estimation by the Inbody S10 warrants further
investigation.

Recent years, the roles of visceral obesity on the progression of cancer and cancer-
related comorbidities has been investigated in several studies [30,31]. Ozoya et al
retrospectively analyzed 110 patients with colon cancer and concluded that visceral
obesity was associated with metabolic comorbidities and post-operative morbidities
[30]. Go et al indicated that the presence of visceral obesity could bring technical
difficulties in operation, and could significantly reduce the number of retrieved lymph
nodes, as well as the overall survival in gastric cancer patients undergone laparoscopy-
assisted distal gastrectomy [7]. Therefore, visceral obesity should be discriminated
prior to surgery, and operations should be conducted by more experienced surgeons [7].
Pre-operative quantification of VFA could help surgeons optimize the selection of
patients suitable for laparoscopic approach and take interventions for prophylaxis of
surgical incision infection. In addition, the low-grade chronic inflammation produced by excessive visceral fat tissues is considered suitable microenvironment for tumor growth [30]. Growth factors released by visceral fat tissues also mediate in cancer progression [30-32]. Therefore, to reverse visceral obesity state is essential in gastric cancer subjects. Tumor of gastrointestinal origin apparently affects the digestion and absorption of nutrients. Many patients suffer from weight loss, sarcopenia or even cachexia after gastrectomy or under tumor bearing state [33]. The metabolic characteristics and nutritional management are different between patients with distinct body composition [34]. How to provide scientific, accurate and reasonable individualized nutritional support for these patients is a major challenge and difficulty. Some cancer patients, especially those in the earlier stage, prone to excessive daily energy intake and restricted daily physical activity, may consequently develop sarcopenia obesity. For patients with similar skeletal muscle mass but different VFA status, the total energy and micronutrient proportions required daily will be distinctive [28], as well as the physical exercise regimen [35]. Therefore, it is essential to distinct visceral obesity both prior to surgery and in aftercare period.

In the present study, the values of the two methods were significantly different by paired-t test (p<0.001), and the mean bias of the two methods was 12.45±36.13 cm², with a wide range of 95%LOA, indicating that the absolute values of the two methods were not interchangeable directly. This was in accordance with Lee’s research [12]. Lee at al [12] postulated a formula to predict actual VFA with BIA variables. However, this formula was too complicated in calculation and difficult to implement routinely. In
addition, previous formulas were based on healthy subjects with different ethnicities, which were not applicable for the Chinese patients with gastric cancer. Therefore, the present study identified a cut-off value of VFA by BIA in diagnosing visceral obesity. The Chinese patients with gastric cancer with VFA exceeding 81 cm² by BIA should be highly suspected of visceral obesity. What we need to clarify here is that, BIA data is based on certain in-built equations suitable for different ethnicities [36,37]. The equations will be modified when the instruments installed in different regions worldwide. Therefore, our conclusions were only applicable to the Asian population, especially to the Chinese population, when they take BIA by instruments installed in China.

There were several limitations in the present research. First, the study was conducted in a single center with a relatively small sample size, and only included patients from China. The conclusions might not be generalized to patients from other regions. A multicenter design study with a larger sample size was warranted to validate our conclusions. Second, the ROC result in the present study could distinct visceral obesity by BIA, but could not directly convert the VFA-BIA absolute value into the VFA-CT absolute value. It was unable to obtain the exact and accurate values of VFA via BIA. Third, the study design applied the Inbody 720 as BIA instrument, which is a relatively older product. Further studies to validate the conclusions with the promotion product Inbody 770 should be performed [38].

In conclusion, it is necessary to identify visceral obesity in gastric cancer patients both prior to surgery and in aftercare period via body composition analysis. The present
study revealed that the VFA measured by CT and BIA showed significant correlation and satisfactory reliability. However, the bias between the two methods was within a wide range, indicating that the absolute values of the two methods were not interchangeable directly. The cut-off value of the VFA-BIA for identifying visceral obesity in the present study was 81 cm², indicating the Chinese gastric cancer patients with VFA estimated by BIA larger than the threshold should be highly suspected for visceral obesity.

Contributors

BG was responsible for methodology, data curation, project administration, and writing; YL was responsible for methodology, statistical analysis, data analyzing and writing; CD was responsible for data collection; SLL was responsible for data curation, project administration, Software management; XJB was responsible for BIA management and data collection; XTC was responsible for study design and manuscript supervision. All authors gave their final approval of the final version of the manuscript.

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Competing interests

No declared.

Patient consent

Obtained.

Ethics approval

The study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the Nanjing Drum Tower Hospital.

Provenance and peer review

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Data sharing statement

The data was available at the corresponding authors with reasonable request.

Patient and Public Involvement Statement
They were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Reference

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Figure Legends

Figure 1 Bland-Altman plot for comparing the two methods
The mean bias between the two measurements was 12.45±36.13 cm³ (Line of the Mean and its 95%CI were shown), 95% limits of agreements ranged from -58.36 cm³ to 83.26 cm³ (Lines of the Mean±1.96SD and their 95%CI were shown).

Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients
The AUROC=0.822, p<0.001, 95%CI: 0.758-0.887, the best cut-off value for diagnosing visceral obesity by VFA-BIA was 81 cm², with a sensitivity of 65.6% and specificity of 88.2%.

**Supplementary Figure 1** The flow diagram of the research.

**Tables**

**Table 1** Baseline characteristics

**Table 2** Body composition assessment by CT and BIA in overall patients

**Table 3** Pearson’s correlation of VFA measured by CT and BIA

**Table 4** Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

| Table 1 Baseline characteristics | Overall N=157 |
|----------------------------------|--------------|
| Age (year)                       | 60.61±11.95  |
| <60y (%)                         | 66 (42.0)    |
| ≥60y (%)                         | 91 (58.0)    |
| Gender (Male, %)                 | 109 (69.4)   |
| Body weight (kg)                 | 61.27±9.14   |
| Body height (cm)                 | 162.10±7.07  |
| BMI (kg/m²)                      | 23.28±2.93   |
| <18.5                            | 5 (3.2)      |
| 18.50-23.99                      | 85 (54.1)    |
| 24-27.99                         | 61 (38.9)    |
| ≥28                              | 6 (3.8)      |
| Tumor stage (AJCC)               |              |
| I                                | 48 (30.6)    |
| II                               | 31 (19.7)    |
| III                              | 49 (31.2)    |
| IV                               | 29 (18.5)    |
| Tissue type                      |              |
Adenocarcinoma 124 (79.0)
Signet ring cell carcinoma 7 (4.5)
Others 11 (7.0)
Unknown 15 (9.5)
Neoadjuvant (yes, %) 2 (1.3)
Diabetes (yes, %) 8 (5.1)

Laboratory
- WBC (×10^9/L) 5.3 (4.5, 6.25)
- Hemoglobin (g/L) 126 (109.5, 139.5)
- Albumin (g/L) 38.30±4.18
- Triglyceride (mmol/L) 1.18±0.70
- Cholesterol (mmol/L) 3.75±0.86
- C-reactive protein (mg/L) 3.2 (2.5, 4.45)
- CEA (ng/ml) 1.12 (0.52, 2.22)
- CA125 (ng/ml) 7.2 (4.9, 13.55)
- CA199 (ng/ml) 10.43 (6.08, 18.96)
- CA724 (ng/ml) 1.84 (1.01, 4.15)
- CA242 (ng/ml) 9.97±17.86

BMI: body mass index; WBC: white blood cell; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125; CA 199: carbohydrate antigen 199; CA724: carbohydrate antigen 724; CA242: carbohydrate antigen 242. Normally distributed variables were expressed as mean± standard deviation, skewed variables were expressed as median (25th percentile, 75th percentile).

Table 2 Body composition assessment by CT and BIA in overall patients

| Body composition assessment | Overall N=157 |
|----------------------------|--------------|
| **Body composition by CT**  |              |
| Skeletal muscle mass area (cm²) | 117.32±24.97 |
| Subcutaneous fat mass area (cm²) | 103.56±50.01 |
| Visceral fat area (cm²)  | 84.39±46.43  |
| Visceral obesity (n, %)  | 65 (41.4)    |
| **Body composition by BIA** |              |
| Total body water (L)        | 33.43±5.23   |
| Visceral fat area (cm²)     | 71.94±22.44  |
| Total fat mass (kg)         | 16.03±5.12   |
| Body fat percentage %       | 25.83±6.84   |
| Lean body mass (kg)         | 42.88±6.73   |
| Skeletal muscle mass (kg)   | 24.86±4.29   |
| Fat free mass (kg)          | 45.42±7.08   |

SMI: skeletal muscle mass index. The difference of VFA between CT and BIA was statistically significant (p<0.001) via paired-t test. There was a mean 14.75% difference (based on CT) between the
values of two methods.

### Table 3 Pearson’s correlation of VFA measured by CT and BIA

|       | n   | VFA by CT (cm²) | VFA by BIA (cm²) | r   | p       |
|-------|-----|-----------------|------------------|-----|---------|
| Overall| 157 | 84.39±46.43     | 71.94±22.44      | 0.650 | <0.001  |
| Female | 48  | 85.10±38.04     | 80.06±22.67      | 0.559 | <0.001  |
| Male   | 109 | 84.08±49.84     | 68.37±21.48      | 0.714 | <0.001  |
| BMI>24 kg/m² | 66  | 113.57±32.22    | 88.07±15.24      | 0.315 | 0.010   |
| BMI≤24 kg/m² | 91  | 63.23±43.70     | 60.24±19.39      | 0.551 | <0.001  |
| Age≤60 year | 66  | 84.94±42.66     | 73.11±20.67      | 0.640 | <0.001  |
| Age>60 year | 91  | 83.99±49.21     | 71.09±23.71      | 0.656 | <0.001  |
| Stage I | 48  | 86.78±47.18     | 72.49±21.87      | 0.671 | <0.001  |
| Stage II| 31  | 84.26±36.56     | 74.53±18.90      | 0.564 | <0.001  |
| Stage III| 49  | 88.15±47.00     | 70.63±21.15      | 0.726 | <0.001  |
| Stage IV| 29  | 74.22±53.99     | 70.46±28.97      | 0.605 | 0.001   |

BMI: body mass index; VFA: visceral fat area. r for Pearson’s correlation coefficient. p for statistical significance of Pearson’s correlation test.

### Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

|       | n   | CT-BIA VFA (cm²) | p      | ICC  | 95%LOA   |
|-------|-----|-----------------|--------|------|----------|
| Overall| 157 | 12.45±36.13     | 0.675  | -58.36, 83.26 |
| Female | 48  | 5.04±31.57      | 0.088  | 0.659 | -56.84, 66.92 |
| Male   | 109 | 15.71±37.64     | 0.088  | 0.659 | -56.84, 66.92 |
| BMI>24 kg/m² | 66  | 25.50±31.00     | 0.000*| 0.392 | -35.26, 86.26 |
| BMI≤24 kg/m² | 91  | 2.99±36.78      | 0.000*| 0.392 | -35.26, 86.26 |
| Age≤60 year | 66  | 11.83±33.45     | 0.855  | 0.668 | -53.73, 77.39 |
| Age>60 year | 91  | 12.90±38.13     | 0.855  | 0.668 | -53.73, 77.39 |
| Stage I | 48  | 14.28±36.32     | 0.424  | 0.677 | -56.91, 85.47 |
| Stage II| 31  | 9.73±30.23      | 0.631  | 0.677 | -56.91, 85.47 |
| Stage III| 49  | 17.51±34.83     | 0.704  | 0.677 | -56.91, 85.47 |
| Stage IV| 29  | 3.77±43.15      | 0.670  | 0.677 | -56.91, 85.47 |

BMI: body mass index; VFA: visceral fat area; ICC: intraclass correlation coefficient; 95%LOA: 95% limits of agreement. p for comparison of CT-BIA VFA between subgroups by independent t-test.
Figure 1 Bland-Altman plot for comparing the two methods

209x135mm (300 x 300 DPI)
Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients

209x189mm (300 x 300 DPI)
192 patients with gastric cancer

35 patients were excluded:
- Tumor originated from other organ (n=19)
- Heart failure (n=1)
- Kidney failure (n=5)
- Cirrhosis (n=1)
- Unmeasurable CT VFA (n=5)
- Unable to standstill (n=2)
- Refused to participate (n=2)

157 primary gastric cancer patients

VFA measured by CT (n=157)

VFA estimated by BIA (n=157)
| Section/Topic                | Item # | Recommendation                                                                                                                                                                                                 | Reported on page # |
|-----------------------------|--------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Title and abstract          | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract                                                                                                                         | 1                 |
|                             |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found                                                                                                          | 3-4               |
| Introduction                | 2      | Explain the scientific background and rationale for the investigation being reported                                                                                                                        | 5                 |
| Objectives                  | 3      | State specific objectives, including any prespecified hypotheses                                                                                                                                           | 6                 |
| Methods                     | 4      | Present key elements of study design early in the paper                                                                                                                                                    | 6                 |
| Study design                | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection                                                                                 | 6-7               |
| Setting                     | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants                                                                                                               | 7                 |
| Participants                | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable                                                                         | 7-10              |
| Variables                   | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-10              |
| Data sources/measurement    | 9      | Describe any efforts to address potential sources of bias                                                                                                                                                    | 9-10              |
| Bias                        | 10     | Explain how the study size was arrived at                                                                                                                                                                     | 6                 |
| Study size                  | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why                                                                                   | 10                |
| Statistical methods         | 12     | (a) Describe all statistical methods, including those used to control for confounding                                                                                                                        | 9-10              |
|                             |        | (b) Describe any methods used to examine subgroups and interactions                                                                                                                                         | 9-10              |
|                             |        | (c) Explain how missing data were addressed                                                                                                                                                                   | No missing data   |
|                             |        | (d) If applicable, describe analytical methods taking account of sampling strategy                                                                                                                           | 9-10              |
|                             |        | (e) Describe any sensitivity analyses                                                                                                                                                                         | 9-10              |

**1STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies**
| Section            | Check | Details                                                                                                                                                                                                 | Page(s) |
|--------------------|-------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Participants       | 13*   | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed                                    | 10-11   |
|                    |       | (b) Give reasons for non-participation at each stage                                                                                                                                                     |         |
|                    |       | (c) Consider use of a flow diagram                                                                                                                                                                | 10-11   |
| Descriptive data   | 14*   | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders                                                                | 10-11   |
|                    |       | (b) Indicate number of participants with missing data for each variable of interest                                                                                                                     | No missing data |
| Outcome data       | 15*   | Report numbers of outcome events or summary measures                                                                                                                                                | 11-13   |
| Main results       | 16    | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 11-13   |
|                    |       | (b) Report category boundaries when continuous variables were categorized                                                                                                                              | 10-11   |
|                    |       | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period                                                                                       |         |
| Other analyses     | 17    | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses                                                                                                         | 11      |
| Discussion         |       |                                                                                               |         |
| Key results        | 18    | Summarise key results with reference to study objectives                                                                                                                                             | 13-14   |
| Limitations        | 19    | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                      | 16      |
| Interpretation     | 20    | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                  | 13-16   |
| Generalisability   | 21    | Discuss the generalisability (external validity) of the study results                                                                             | 13-16   |
| Other information  |       |                                                                                               |         |
| Funding            | 22    | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based                                                  | 18      |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.
Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Comparison of visceral fat area measured by Computed Tomography and Bioelectrical impedance analysis in Chinese gastric cancer patients: A cross-sectional study

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Short title: The accuracy of bioelectrical impedance analysis in estimating visceral fat area

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Key words: gastric cancer, visceral fat area, visceral obesity, computed tomography, bioelectrical impedance analysis
Abstract

**Objectives:** Bioelectrical impedance analysis (BIA) is a simple and inexpensive method for body composition estimation. However, the accuracy of BIA is unknown. We aimed to assess the accuracy of BIA in estimating visceral fat area (VFA) in gastric cancer patients.

**Study design:** This study was a cross-sectional study comparing accuracy of BIA in estimating VFA with the gold standard method measured by computer tomography (CT). The VFA was measured both by CT and BIA for the enrolled patients. VFA by CT at umbilical level ≥100 cm² was considered as visceral obesity. The reliability between two methods was assessed by intraclass correlation coefficient (ICC) and the consistency was assessed by Bland-Altman method (95% limits of agreement). Area under the receiver operating characteristic curve (AUROC) was used to assess the performance of diagnosing visceral obesity by BIA.

**Setting:** The study was conducted in China.

**Participants:** From 1st January 2017 to 1st December 2018, a total of 157 patients diagnosed of gastric cancer were enrolled.

**Results:** The VFA by CT and BIA in the overall patients were 84.39±46.43 cm² and 71.94±22.44 cm², respectively. VFA estimated by BIA was positively correlated with VFA measured by CT by Pearson’s test (r=0.650, p<0.001). ICC for the two methods in overall patients was 0.675. The mean bias between the two measurements was 12.45±36.13 cm². The 95% limits of agreement ranged from -58.36 to 83.26 cm². The cut-off value for diagnosing visceral obesity by BIA was 81 cm² (AUROC: 0.822,
Conclusions: The VFA measured by BIA showed satisfactory reliability with that measured by CT. However, the absolute values of the two methods were not interchangeable. The cut-off value of the VFA by BIA for diagnosing visceral obesity was 81 cm$^2$ for gastric cancer patients in the Chinese population.

Key words: visceral fat area, gastric cancer, bioelectronic impedance analysis, computed tomography

Strengths and limitations of this study

To our knowledge, this is the first study to assess the accuracy of visceral fat area estimated by BIA in gastric cancer patients in China. The in-built equations of the BIA instrument will be modified when installed in different regions worldwide, so the single center nature of the study consisting only of Chinese population made the generalization of the study limit to Asian population. The study design applied the Inbody 720 as BIA instrument, which is a relatively older product than the Inbody 770. The estimation of visceral fat area by BIA was compared with the measurement by the gold standard method of CT scan, which improved the reliability of the results. Though the sample size of the study was small, the access of data for analyzing was strict which could compensate for the bias in some extent.
Introduction

Gastric cancer is a common malignancy type worldwide with a high mortality rate [1]. The prevalence of gastric cancer is comparatively higher in the Asian countries than that in the westerns [2]. Previous studies suggested that the alteration of body composition could affect the outcomes of multiple malignancies [3-6]. The negative effect of sarcopenia on the prognosis of cancer has reached in consensus [4-6]. In addition, the presence of visceral obesity could bring difficulty in surgery operation, increase the post-operation infection rate and reduce the overall survival rate in gastric cancer [3,7]. Go et al demonstrated that the presence of visceral obesity in gastric cancer subjects undergone laparoscopy-assisted distal gastrectomy significantly affected the number of retrieved lymph node [7]. In addition, visceral fat tissues contain more large adipocytes and androgen receptors than subcutaneous fat tissues and could result in insulin resistance, which is a negative hallmark for tumor progression [8]. Patients with gastric cancer need post-operative aftercare and individualized nutritional intervention. The measurement of VFA and muscle mass plays a role in the formulation of total energy and carbohydrate proportion in dietary instructions. Therefore, it is necessary to measure VFA and screen out visceral obesity in such population.

Several medical imaging methods has been used for analyzing body composition [9]. Among them, CT as a routine imaging examination prior to cancer diagnosis and therapy is accurate and considered the gold standard method for evaluating body composition [9, 10]. The area of skeletal muscle and visceral fat tissue by CT highly correlate with total body skeletal muscle mass and visceral fat mass [9-11]. However,
the use of CT in evaluating body composition has many drawbacks, such as radiation
exposure, high expense and the need of specialists in medical imaging, which is not
suitable for periodical measurements aftercare. In addition, only a few radiologists in
central cities in China master the method of body composition by CT. Bioelectrical
impedance analysis (BIA) method is a non-invasive alternate method for body
composition evaluation and is widely used in a clinic setting [12]. The advantages of
BIA lie in the low cost and none radiation to subjects, which is suitable for repeated
monitoring for nutrition status. The accuracy of visceral fat area (VFA) was
investigated in a Korean cohort in healthy subjects, revealing that VFA estimated by
BIA correlated well with that measured by CT method, but an accurate equation was
needed to match that measured by CT [12]. However, the accuracy of BIA is highly
dependent on ethnicity and hydration status [13]. Patients with malignancies may have
alteration of body composition and hydration status, which affects the performance of
BIA in estimating VFA. Moreover, researches on validation of its accuracy is limited
in the Chinese patients. The aim of the present study was to investigate the accuracy of
BIA in estimating VFA in gastric cancer subjects in the Chinese population, as well as
to identify the threshold for diagnosing visceral obesity by BIA.

Materials and Methods

Patients

From 1st January 2017 to 1st December 2018, patients with a clear diagnosis of
gastric cancer either by pathology or radiology admitted to Gastroenterology or General
Surgery department of Drum Tower Hospital affiliated to Nanjing University Medical School were prospectively enrolled. Exclusion criteria were patients with age younger than 18 or older than 80 years old; primary tumor originated from other organs; heart failure; kidney failure; cirrhosis; unmeasurable CT visceral fat area; use of diuretics or lipid regulation medications; unable to stand still or patients who refused to undergo CT and BIA. The observational study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of Nanjing Drum Tower Hospital (209-173-01). Written consent was obtained from all participants.

Clinical information collection

The clinical information of all the patients were recorded. Baseline clinical characteristics included age, gender, body weight, body height, body mass index (BMI, defined as body weight in kilogram (kg)/ [body height in meters]²), tumor stage, tumor tissue type, and comorbidities. Body weight was measured with patient wearing thin clothes and to the nearest 0.1 kg. Body height was measured with patient bare feet and to the nearest 0.1 cm. Body weight and body height were measured directly via the Inbody 720 instrument at the time of BIA testing. For most patients, body weight and height were measured only once, or was measured in replicate if the trained researcher found the patient was not stand still or stand straight. Tumor stage classification was based on the criteria established by the American Joint Committee on Cancer (AJCC) [14, 15]. Neoadjuvant therapy before the study was recorded. Laboratory tests were
performed with fasting blood samples when admitted to hospital. Laboratory parameters included white blood cell count (WBC), hemoglobin level, albumin level, triglyceride level, cholesterol level, C-reactive protein level. Tumor markers were also performed once admitted and parameters included, carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199), carbohydrate antigen 724 (CA724), carbohydrate antigen 242 (CA242).

**Body composition assessment by CT**

CT scans were performed before treatment. According to previously published method [10, 16], a single slice at the umbilical level was selected and the area of different body compositions were analyzed by Matlab software (MathWorks, Massachusetts State, USA). Different body composition tissue compartments were manually outlined and segmented with different Hounsfield unit (HU) threshold ranges. Tissues with Hounsfield unit ranges from -29 to 150 were considered as skeletal muscle and the total skeletal muscle area (SMA) was calculated. Areas with HU ranges from -150 to -50 were considered as visceral fat and the total visceral fat area (VFA) was calculated. Areas with HU ranges from -190 to -30 were considered as subcutaneous fat and the total subcutaneous fat area (SFA) was calculated [17,18]. CT assessment was performed by two radiologists independently. They were blinded to each other in CT measurement. They were both blinded to patients’ personal information and BIA values. Mean values by two radiologists were used in the study.
Body composition assessment by BIA

BIA assessment was performed the same day with CT scan. An Inbody 720 multifrequency BIA Inbody720 instrument (Inbody corporation, Seoul, Korea) was adopted to measure body composition. The method was in accordance with previously described protocol [10]. To be brief, patients with fasting condition and empty bladder stand with both arms 45 angles apart from the body trunk and with both feet bared on the spots of the platform. Total body water, visceral fat area in cm$^2$ at the umbilical level, total fat mass, body fat percentages, lean body mass, skeletal body mass, fat free mass were estimated and the values were output. The measurement process was standard and was strictly supervised by an experienced researcher. If the BIA measurement process was not standard or the researcher consider potential mistakes, another measurement by BIA was performed to replace the former result.

Definition of visceral obesity

Based on the Japan Society for the Study of Obesity and widely accepted criteria in clinic [7,19], the threshold for visceral obesity was 100 cm$^2$ at umbilical level measured by CT images. Visceral obesity was defined as patients with visceral fat area at umbilical level $\geq$100 cm$^2$.

Statistical analysis

Data analysis was performed by SPSS for windows version 20.0 (IBM, New York State, USA) and MedCalc for windows version 15.2.2 (MedCalc Software corporation,
Ostend, Belgium). Continuous variables were expressed as the means± standard deviation (SD) if data were normally distributed and were compared by independent or paired t-test when appropriate. Skewed distributed data were expressed as the medians (25th percentile, 75th percentile) and were compared by Mann-Whitney U-test. Categorical variables were expressed by number and percentages and were compared by Chi-square ($\chi^2$-test) test or Fisher’s exact test when appropriate. Paired-t test and intraclass correlation coefficient (ICC) for reliability and agreement were applied to compare the difference of VFA between CT and BIA. Pearson’s correlation coefficient was used to investigate any correlations between these two methods of measurement. The consistency between two measurements was assessed by Bland-Altman statistical method [20] with 95% limits of agreements (95% LOA) calculated. Patients with VFA $\geq$100 cm$^2$ measured by CT were classified as visceral obesity. The performance of VFA estimated by BIA in diagnosing visceral obesity was assessed by the area under the receiver characteristic curve (AUROC). The cut-off value of the VFA estimated by BIA in stratifying visceral obesity was obtained with the maximum Youden index (sensitivity + specificity -1). A two-tailed p-value <0.05 was considered statistically significant. Shrout et al proposed that ICC value ranges from 0.00 to 0.49 was interpreted as poor reliability, ranges from 0.50 to 0.74 was interpreted as satisfactory and ranges from 0.75 to 1.00 was interpreted as excellent reliability [21].

Results

Baseline characteristics of the study population
A total of 35 patients were excluded from the research, finally 157 patients with gastric cancer were enrolled, included 48 females and 109 males (Supplementary figure 1). The mean age of the overall patients was 60.61±11.95 years old. The mean body weight and body height of the overall patients were 61.27±9.14 kg and 162.10±7.07 cm, respectively. The mean BMI of the overall group was 23.28±2.93 kg/m². According to classification standard of China [22], 5 patients were underweight (3.2%), 85 patients were within normal range of BMI (54.1%), 61 patients were overweight (38.9%) and 6 patients were obesity (3.8%). The number of patients with gastric cancer tumor stage I, II, III, IV were 48 (30.6%), 31 (19.7%), 49 (31.2%) and 29 (18.5%), respectively. The majority of patients were diagnosed with adenocarcinoma tissue type. Laboratory indicators and demographic characteristics are summarized in Table 1.

The ICC between the two radiologists was 0.999. The mean value of VFA measured by CT in overall patients was 84.39±46.43 cm². There were 65 (41.4%) patients diagnosed with visceral obesity. The VFA estimated by BIA in overall patients was 71.94±22.44 cm². (Table 2)

Comparison of VFA measured by CT (VFA-CT) and estimated by BIA (VFA-BIA) in overall patients

The difference of the VFA between CT and BIA was statistically significant via paired-t test (p<0.001). There was a mean 14.75% difference (based on CT) between the values of the two methods in the overall patients (Table 2). The VFA measured by CT was positively correlated with that estimated by BIA in overall patients by Pearson’s
correlation test ($r=0.650$, $p<0.001$) (Table 3). ICC value between the VFA-CT and the VFA-BIA was 0.675, indicating satisfactory reliability and agreement. With Bland-Altman analysis, the mean bias between the two measurements was $12.45\pm36.13$ cm$^2$, indicating that BIA underestimated VFA by $12.45\pm36.13$ cm$^2$ in overall patients (Table 4, Figure 1). In addition, the Bland-Altman plot also showed that the VFA was overestimated in patients with smaller VFA and underestimated in patients with larger VFA (Figure 1). The 95%LOA of the bias ranged from $-58.36$ cm$^2$ to $83.26$ cm$^2$, indicating that the absolute values of the two measurements were not interchangeable directly and the bias was not clinically acceptable.

Subgroup analysis

The VFA measured by CT was significantly correlated with that estimated by BIA in both the female ($r=0.559$, $p<0.001$) and the male ($r=0.714$, $p<0.001$) groups by Pearson’s correlation test. The mean difference of the two methods between genders was not significantly different ($5.04\pm31.57$ cm$^2$, $15.71\pm37.64$ cm$^2$, respectively, $p=0.088$). In both gender groups, the two methods showed satisfactory reliability (ICC=0.659, 0.683, respectively). Patients were divided into groups according to the median of BMI. In both BMI groups, the VFA-CT and the VFA-BIA were significantly correlated by Pearson’s correlation test ($r=0.315$, $p=0.010$ in BMI>24 kg/m$^2$ group; $r=0.551$, $p<0.001$ in BMI≤24 kg/m$^2$ group). The mean bias of VFA between the two BMI categories was significantly different ($25.50\pm31.00$ cm$^2$, $2.99\pm36.78$ cm$^2$; $p<0.001$), indicating that BIA largely underestimated VFA in overweight or obesity.
subjects. ICC value in BMI>24 kg/m\(^2\) group interpreted as poor reliability in this subcategory. In both older (>60 years old) and younger (≤60 years old) groups, the two methods showed significant correlation by Pearson’s correlation test (r=0.640, p<0.001; r=0.656, p<0.001, respectively) and satisfactory reliability (ICC=0.668, 0.678, respectively). The bias between patients with different age groups was not statistically significant (p=0.855). The bias between different tumor stages was not significantly different (p=0.424).

VFA-BIA in diagnosing visceral obesity

The criteria of VFA≥100 cm\(^2\) [7,19] measured by CT at umbilical level was adopted as threshold in diagnosing visceral obesity. The VFA estimated by BIA showed a good to excellent performance in diagnosing visceral obesity in overall patients in the present study (AUROC=0.822, p<0.001, 95%CI: 0.758-0.887), with a sensitivity of 65.6%, and specificity of 88.2%. (Figure 2). The best cut-off value of the VFA-BIA was 81 cm\(^2\), indicating that the gastric cancer patients with VFA larger than 81 cm\(^2\) estimated by BIA should be highly suspected of visceral obesity.

Discussions

The present study revealed that the VFA estimated by BIA significantly correlated with that measured by CT at umbilical level in gastric cancer patients in the Chinese population with satisfactory reliability (ICC=0.675). This was in accordance with a previous Korean study [12]. Lee et al compared VFA-CT with VFA-BIA in healthy...
subjects with wide ranges of age and BMI. The mean bias of VFA between two methods
was 21.4±45.6 cm$^2$, and tended to increase with BMI [12]. Our study also demonstrated
the positive correlation of bias with BMI, indicating the drawback of BIA in analyzing
body composition in overweight or obese subjects. This limitation of BIA for obesity
was proposed by several studies [23-27]. Bosaeus et al discovered that BIA
underestimated total fat mass in overweight and obese women compared with MRI
measurement [23]. Neovius et al discovered that compared with DXA, the bias of fat
mass was increased with degree of adiposity [27].

CT slice at umbilical level serves as the gold standard for VFA assessment [7,19].
However, the exposure to radiation and the high cost restrict its use as periodical
nutritional assessment in clinic settings. Moreover, the need for expertise in medical
imaging also restricts its application. In China, the reality is that only a few doctors
working in regional central hospitals master the body composition quantification
technique by CT. Body composition assessment is important for these gastric cancer
patients in post-operative aftercare and individualized nutritional intervention. Patients
with distinct VFA status requires different formulation of energy and proportion of
macro nutrients [28]. Periodical measurement of VFA could provide clues for
nutritionists with individualized dietary instructions. Unfortunately, CT for body
composition assessment is not applicable to non-central city hospitals in China and is
also not suitable for periodical nutritional assessment in follow up. It has clinical value
to evaluate the accuracy of BIA in estimating VFA in gastric cancer patients since the
BIA method compensate for the shortcomings of CT and is suitable for extensive
nutritional screening and monitoring [11]. But what need to be clarified is that the principle of BIA instruments is based on the electrical property, impedance of the tissues in the conductive path between the sense electrodes [9]. The quantifications of adipose tissue by BIA are only estimations rather than direct measurements [9]. Therefore, we still recommend CT as a priority when there are enough professionals and economic conditions for routine VFA assessment by CT. Otherwise, BIA could be an alternate. To supplement, the present study only enrolled patients could stand still and undertake BIA measurement by the Inbody 720. However, there are many cancer patients who are too weak to stand, the Inbody S10 for supine subjects to measure VFA is a choice [29]. The accuracy of VFA estimation by the Inbody S10 warrants further investigation.

Recent years, the roles of visceral obesity on the progression of cancer and cancer-related comorbidities has been investigated in several studies [30,31]. Ozoya et al retrospectively analyzed 110 patients with colon cancer and concluded that visceral obesity was associated with metabolic comorbidities and post-operative morbidities [30]. Go et al indicated that the presence of visceral obesity could bring technical difficulties in operation, and could significantly reduce the number of retrieved lymph nodes, as well as the overall survival in gastric cancer patients undergone laparoscopy-assisted distal gastrectomy [7]. Therefore, visceral obesity should be discriminated prior to surgery, and operations should be conducted by more experienced surgeons [7]. Pre-operative quantification of VFA could help surgeons optimize the selection of patients suitable for laparoscopic approach and take interventions for prophylaxis of
surgical incision infection. In addition, the low-grade chronic inflammation produced by excessive visceral fat tissues is considered suitable microenvironment for tumor growth [30]. Growth factors released by visceral fat tissues also mediate in cancer progression [30-32]. Therefore, to reverse visceral obesity state is essential in gastric cancer subjects. Tumor of gastrointestinal origin apparently affects the digestion and absorption of nutrients. Many patients suffer from weight loss, sarcopenia or even cachexia after gastrectomy or under tumor bearing state [33]. The metabolic characteristics and nutritional management are different between patients with distinct body composition [34]. How to provide scientific, accurate and reasonable individualized nutritional support for these patients is a major challenge and difficulty. Some cancer patients, especially those in the earlier stage, prone to excessive daily energy intake and restricted daily physical activity, may consequently develop sarcopenia obesity. For patients with similar skeletal muscle mass but different VFA status, the total energy and micronutrient proportions required daily will be distinctive [28], as well as the physical exercise regimen [35]. Therefore, it is essential to distinct visceral obesity both prior to surgery and in aftercare period.

In the present study, the values of the two methods were significantly different by paired-t test (p<0.001), and the mean bias of the two methods was 12.45±36.13 cm², with a wide range of 95%LOA, indicating that the absolute values of the two methods were not interchangeable directly. This was in accordance with Lee’s research [12]. Lee at al [12] postulated a formula to predict actual VFA with BIA variables. However, this formula was too complicated in calculation and difficult to implement routinely. In
addition, previous formulas were based on healthy subjects with different ethnicities, which were not applicable for the Chinese patients with gastric cancer. Therefore, the present study identified a cut-off value of VFA by BIA in diagnosing visceral obesity. The Chinese patients with gastric cancer with VFA exceeding 81 cm² by BIA should be highly suspected of visceral obesity. What we need to clarify here is that, BIA data is based on certain in-built equations suitable for different ethnicities [36,37]. The equations will be modified when the instruments installed in different regions worldwide. Therefore, our conclusions were only applicable to the Asian population, especially to the Chinese population, when they take BIA by instruments installed in China.

There were several limitations in the present research. First, the study was conducted in a single center with a relatively small sample size, and only included patients from China. The conclusions might not be generalized to patients from other regions. A multicenter design study with a larger sample size was warranted to validate our conclusions. Second, the ROC result in the present study could distinct visceral obesity by BIA, but could not directly convert the VFA-BIA absolute value into the VFA-CT absolute value. It was unable to obtain the exact and accurate values of VFA via BIA. Third, the study design applied the Inbody 720 as BIA instrument, which is a relatively older product. Further studies to validate the conclusions with the promotion product Inbody 770 should be performed [38].

In conclusion, it is necessary to identify visceral obesity in gastric cancer patients both prior to surgery and in aftercare period via body composition analysis. The present
study revealed that the VFA measured by CT and BIA showed significant correlation and satisfactory reliability. However, the bias between the two methods was within a wide range, indicating that the absolute values of the two methods were not interchangeable directly. The cut-off value of the VFA-BIA for identifying visceral obesity in the present study was 81 cm², indicating the Chinese gastric cancer patients with VFA estimated by BIA larger than the threshold should be highly suspected for visceral obesity.

Contributors

BG was responsible for methodology, data curation, project administration, and writing; YL was responsible for methodology, statistical analysis, data analyzing and writing; CD was responsible for data collection; SLL was responsible for data curation, project administration, Software management; XJB was responsible for BIA management and data collection; XTC was responsible for study design and manuscript supervision. All authors gave their final approval of the final version of the manuscript.

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Competing interests

No declared.

Patient consent

Obtained.

Ethics approval

The study was in accordance with the principles of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the Nanjing Drum Tower Hospital.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

The data was available at the corresponding authors with reasonable request.

Patient and Public Involvement Statement
They were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

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Figure Legends

Figure 1 Bland-Altman plot for comparing the two methods

The mean bias between the two measurements was 12.45±36.13 cm² (Line of the Mean and its 95%CI were shown), 95% limits of agreements ranged from -58.36 cm² to 83.26 cm² (Lines of the Mean±1.96SD and their 95%CI were shown).

Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients
The AUROC=0.822, p<0.001, 95%CI: 0.758-0.887, the best cut-off value for diagnosing visceral obesity by VFA-BIA was 81 cm², with a sensitivity of 65.6% and specificity of 88.2%.

Supplementary Figure 1 The flow diagram of the research.

Tables

Table 1 Baseline characteristics

Table 2 Body composition assessment by CT and BIA in overall patients

Table 3 Pearson’s correlation of VFA measured by CT and BIA

Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

Table 1 Baseline characteristics

| Overall | N=157 |
|---------|-------|
| Age (year) | 60.61±11.95 |
| <60y (%) | 66 (42.0) |
| ≥60y (%) | 91 (58.0) |
| Gender (Male, %) | 109 (69.4) |
| Body weight (kg) | 61.27±9.14 |
| Body height (cm) | 162.10±7.07 |
| BMI (kg/m²) | 23.28±2.93 |
| <18.5 | 5 (3.2) |
| 18.50-23.99 | 85 (54.1) |
| 24-27.99 | 61 (38.9) |
| ≥28 | 6 (3.8) |
| Tumor stage (AJCC) | |
| I | 48 (30.6) |
| II | 31 (19.7) |
| III | 49 (31.2) |
| IV | 29 (18.5) |

Tissue type
Adenocarcinoma 124 (79.0)
Signet ring cell carcinoma 7 (4.5)
Others 11 (7.0)
Unknown 15 (9.5)
Neoadjuvant (yes, %) 2 (1.3)
Diabetes (yes, %) 8 (5.1)

Laboratory
- WBC (>10⁹/L) 5.3 (4.5, 6.25)
- Hemoglobin (g/L) 126 (109.5, 139.5)
- Albumin (g/L) 38.30±4.18
- Triglyceride (mmol/L) 1.18±0.70
- Cholesterol (mmol/L) 3.75±0.86
- C-reactive protein (mg/L) 3.2 (2.5, 4.45)
- CEA (ng/ml) 1.12 (0.52, 2.22)
- CA125 (ng/ml) 7.2 (4.9, 13.55)
- CA199 (ng/ml) 10.43 (6.08, 18.96)
- CA724 (ng/ml) 1.84 (1.01, 4.15)
- CA242 (ng/ml) 9.97±17.86

BMI: body mass index; WBC: white blood cell; CEA: carcinoembryonic antigen; CA125: carbohydrate antigen 125; CA 199: carbohydrate antigen 199; CA724: carbohydrate antigen 724; CA242: carbohydrate antigen 242. Normally distributed variables were expressed as mean± standard deviation, skewed variables were expressed as median (25th percentile, 75th percentile).

Table 2 Body composition assessment by CT and BIA in overall patients

| Body composition assessment | Overall |
|-----------------------------|---------|
| N=157                        |         |
| Body composition by CT       |         |
| Skeletal muscle mass area (cm²) | 117.32±24.97 |
| Subcutaneous fat mass area (cm²) | 103.56±50.01 |
| Visceral fat area (cm²)      | 84.39±46.43 |
| Visceral obesity (n, %)      | 65 (41.4) |
| Body composition by BIA      |         |
| Total body water (L)         | 33.43±5.23 |
| Visceral fat area (cm²)      | 71.94±22.44 |
| Total fat mass (kg)          | 16.03±5.12 |
| Body fat percentage %        | 25.83±6.84 |
| Lean body mass (kg)          | 42.88±6.73 |
| Skeletal muscle mass (kg)    | 24.86±4.29 |
| Fat free mass (kg)           | 45.42±7.08 |

SMI: skeletal muscle mass index. The difference of VFA between CT and BIA was statistically significant (p<0.001) via paired-t test. There was a mean 14.75% difference (based on CT) between the
values of two methods.

Table 3 Pearson’s correlation of VFA measured by CT and BIA

|                | n   | VFA by CT (cm²) | VFA by BIA (cm²) | r   | p       |
|----------------|-----|-----------------|------------------|-----|---------|
| Overall        | 157 | 84.39±46.43     | 71.94±22.44      | 0.650 | <0.001  |
| Female         | 48  | 85.10±38.04     | 80.06±22.67      | 0.559 | <0.001  |
| Male           | 109 | 84.08±49.84     | 68.37±21.48      | 0.714 | <0.001  |
| BMI>24 kg/m²   | 66  | 113.57±32.22    | 88.07±15.24      | 0.315 | 0.010   |
| BMI≤24 kg/m²   | 91  | 63.23±43.70     | 60.24±19.39      | 0.551 | <0.001  |
| Age≤60 year    | 66  | 84.94±42.66     | 73.11±20.67      | 0.640 | <0.001  |
| Age>60 year    | 91  | 83.99±49.21     | 71.09±23.71      | 0.656 | <0.001  |
| Stage I        | 48  | 86.78±47.18     | 72.49±21.87      | 0.671 | <0.001  |
| Stage II       | 31  | 84.26±36.56     | 74.53±18.90      | 0.564 | <0.001  |
| Stage III      | 49  | 88.15±47.00     | 70.63±21.15      | 0.726 | <0.001  |
| Stage IV       | 29  | 74.22±53.99     | 70.46±28.97      | 0.605 | 0.001   |

BMI: body mass index; VFA: visceral fat area. r for Pearson’s correlation coefficient. p for statistical significance of Pearson’s correlation test.

Table 4 Intraclass correlation coefficient and Bland-Altman analysis of VFA measured by CT and BIA

|                | n   | CT-BIA VFA (cm²) | p   | ICC | 95%LOA            |
|----------------|-----|------------------|-----|-----|-------------------|
| Overall        | 157 | 12.45±36.13      | 0.675 | -58.36, 83.26 |
| Female         | 48  | 5.04±0.04        | 0.088 | 0.659 | -56.84, 66.92   |
| Male           | 109 | 15.71±37.64      | 0.683 | -58.06, 89.48 |
| BMI>24 kg/m²   | 66  | 25.50±31.00      | 0.000* | 0.392 | -35.26, 86.26  |
| BMI≤24 kg/m²   | 91  | 2.99±36.78       | 0.580 | -69.10, 75.08 |
| Age≤60 year    | 66  | 11.83±33.45      | 0.855 | 0.668 | -53.73, 77.39  |
| Age>60 year    | 91  | 12.90±38.13      | 0.678 | -61.83, 87.63 |
| Stage I        | 48  | 14.28±36.32      | 0.424 | 0.677 | -56.91, 85.47  |
| Stage II       | 31  | 9.73±0.23        | 0.631 | -49.25, 68.98 |
| Stage III      | 49  | 17.51±34.83      | 0.704 | -50.76, 85.78 |
| Stage IV       | 29  | 3.77±43.15       | 0.670 | -80.80, 88.34 |

BMI: body mass index; VFA: visceral fat area; ICC: intraclass correlation coefficient; 95%LOA: 95% limits of agreement. p for comparison of CT-BIA VFA between subgroups by independent t-test.
Figure 1 Bland-Altman plot for comparing the two methods.
Figure 2 ROC of VFA by BIA for diagnosing visceral obesity in overall patients

209x189mm (300 x 300 DPI)
192 patients with gastric cancer

35 patients were excluded
- Tumor originated from other organ (n=19)
- Heart failure (n=1)
- Kidney failure (n=5)
- Cirrhosis (n=1)
- Unmeasurable CT VFA (n=5)
- Unable to standstill (n=2)
- Refused to participate (n=2)

157 primary gastric cancer patients

VFA measured by CT (n=157)
VFA estimated by BIA (n=157)
### 1STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

| Section/Topic          | Item # | Recommendation                                                                                      | Reported on page # |
|------------------------|--------|-----------------------------------------------------------------------------------------------------|--------------------|
| **Title and abstract** | 1      | *(a)* Indicate the study's design with a commonly used term in the title or the abstract            | 1                  |
|                        |        | *(b)* Provide in the abstract an informative and balanced summary of what was done and what was found | 3-4                |
| **Introduction**       | 2      | Explain the scientific background and rationale for the investigation being reported                | 5                  |
| **Objectives**         | 3      | State specific objectives, including any prespecified hypotheses                                    | 6                  |
| **Methods**            | 4      | Present key elements of study design early in the paper                                             | 6                  |
|                        | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 6-7                |
|                        | 6      | *(a)* Give the eligibility criteria, and the sources and methods of selection of participants       | 7                  |
| **Participants**       | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-10               |
|                        | 8*     | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-10               |
| **Variables**          | 9      | Describe any efforts to address potential sources of bias                                           | 9-10               |
| **Bias**               | 10     | Explain how the study size was arrived at                                                           | 6                  |
| **Study size**         | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 10                 |
| **Statistical methods**| 12     | *(a)* Describe all statistical methods, including those used to control for confounding             | 9-10               |
|                        |        | *(b)* Describe any methods used to examine subgroups and interactions                               | 9-10               |
|                        |        | *(c)* Explain how missing data were addressed                                                      | No missing data    |
|                        |        | *(d)* If applicable, describe analytical methods taking account of sampling strategy               | 9-10               |
|                        |        | *(e)* Describe any sensitivity analyses                                                              | 9-10               |

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| Section                  | Items | Description                                                                                                                                                                                                 | Page(s) |
|--------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Participants             | 13*   | (a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed                                      | 10-11   |
|                          |       | (b) Give reasons for non-participation at each stage                                                                                                                                                        |         |
|                          |       | (c) Consider use of a flow diagram                                                                                                                                                                          | 10-11   |
| Descriptive data         | 14*   | (a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders                                                                 | 10-11   |
|                          |       | (b) Indicate number of participants with missing data for each variable of interest                                                                                                                                               | No missing data |
| Outcome data             | 15*   | Report numbers of outcome events or summary measures                                                                                                                                                              | 11-13   |
| Main results             | 16    | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included                        | 11-13   |
|                          |       | (b) Report category boundaries when continuous variables were categorized                                                                                                                                       | 10-11   |
|                          |       | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period                                                                                                   |         |
| Other analyses           | 17    | Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses                                                                                                                  | 11      |
| Discussion               |       |                                                                                                                                                                                                            |         |
| Key results              | 18    | Summarise key results with reference to study objectives                                                                                                                                                        | 13-14   |
| Limitations              | 19    | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                                                              | 16      |
| Interpretation           | 20    | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence                                                   | 13-16   |
| Generalisability         | 21    | Discuss the generalisability (external validity) of the study results                                                                                                                                         | 13-16   |
| Other information        |       |                                                                                                                                                                                                            |         |
| Funding                  | 22    | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based                                                             | 18      |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.