Original Article

Relative validity of an indirect calorimetry device for measuring resting energy expenditure and respiratory quotient

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Background and Objectives: Resting energy expenditure (REE) and respiratory quotient (RQ) are important for optimal nutritional care. The purpose of this study was to assess the accuracy and repeatability of an indirect calorimetry device (IIM-IC-100) in the measurement of REE and RQ in healthy Chinese adults. **Methods and Study Design:** A total of 38 healthy adults (19 male and 19 female) aged 18-52 years (25±6 years) were enrolled in this study. REE and RQ were measured by IIM-IC-100 and by VO2000, alternately and in duplicate. **Results:** There was a highly significant correlation between IIM-IC-100 REE and VO2000 REE (r=0.906, $p<0.001$), with mean IIM-IC-100 REE significantly higher than that of VO2000 (1475±269 vs 1394±313 kcal/d, $p=0.002$). Bland-Altman analysis revealed that the mean difference between IIM-IC-100 REE and VO2000 REE was 81.3 kcal/d, with limits of agreement of -185 to +347 kcal/d. There was no significant difference in RQ between the two devices. No significant differences were observed between the repeated measurements for both devices. Intra-subject coefficients of variation (CVs) of REE were smaller for IIM-IC-100 (5.8%) than for VO2000 (10.5%), while CVs of RQ were similar for IIM-IC-100 (7.2%) and VO2000 (6.9%). **Conclusions:** These preliminary data indicated that the IIM-IC-100 showed promise as an accurate and precise tool in the assessment of REE and RQ in healthy Chinese adults.

Key Words: indirect calorimetry, resting energy expenditure, respiratory quotient, oxygen consumption, validation

INTRODUCTION

The prevalence of obesity is increasing rapidly in China according to the data of the China Health and Nutrition Survey (CHNS),[1] and obesity, which is mainly caused by a positive energy balance, is considered as a risk factor for metabolic diseases such as type 2 diabetes, hypertension and hyperlipidemia.[2-5] Resting energy expenditure (REE), or resting metabolic rate (RMR), represents 60% to 70% of the total caloric expenditure in humans, with a higher proportion for sedentary individuals. Respiratory quotient (RQ) has been shown to have the potential to identify the metabolic consequences of over or underfeeding and serve as a predictor of weight changes.[6-10] Accurate determination of the REE and RQ are key for optimal nutritional care for weight management.

Predictive formulas have played a critical role in the assessment of the people's real caloric needs. These include the Harris-Benedict (H-B), World Health Organization (WHO), Owen, and Mifflin and Liu's equations. However, a number of studies have shown these widely used equations to significantly overestimate REE among Chinese individuals.[11-13] In this way, usage of these equations may place Chinese individuals at greater risk of becoming overweight or obese. Traditional indirect calorimetry may optimize nutrition care in that it allows the most precise determination of energy needs and substrate utilization.[14,15] Unfortunately, indirect calorimetry has not become widespread in China, especially not in small-scale hospitals and public health systems, because of its expense and the need for professional operators.

An indirect calorimetry device (IIM-IC-100, Institute of Intelligent of Machines, Hefei, China) that is cost-effective and has low operator dependency has been developed to measure gas exchange variables. The purpose of this work was to examine the accuracy and repeatability of the IIM-IC-100 against the MedGraphics (Medical Graphics Corp, St Paul, MN) VO2000 metabolic system (VO2000) for measuring REE and RQ in healthy Chinese adults.

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MATERIALS AND METHODS

Subjects

Healthy subjects were recruited among the staff of the Hefei Institutes of Physical Science of the Chinese Academy of Sciences through notice board postings. Inclusion criteria were as follows: being a non-smoker and having an age of more than 18 years old. Exclusion criteria were the presence of cardio-respiratory diseases, thyroid diseases, diabetes, claustrophobia sufficient to prohibit lying comfortably under a ventilated hood, or consumption of any medication likely to influence metabolic rate. A total of 38 eligible participants agreed to take part and underwent measurements. Height and weight were recorded with each participant wearing light clothing and no footwear, using a stadiometer to the nearest 0.1 kg and an electronic scale to the nearest 0.1 cm. They were measured by a trained physician's assistant. This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the ethics committee of Hefei Institutes of Physical Science (approval number 2015YX008). Written informed consent was obtained from all subjects.

MedGraphics VO2000

The VO2000 portable metabolic system employs a patented flow meter, which uses a proportional sampling valve and a 3-breath average for the measurement of oxygen uptake (VO2), carbon dioxide output (VCO2), and minute ventilation (VE). The flow pneumotach of the VO2000 is a bi-directional differential pressure preVent™ pneumotach. The low flow pneumotach (range 2-30 L/min), with an accuracy of ±3% of the absolute volume, should be selected when measuring resting energy expenditure. A galvanic fuel cell for the oxygen analyzer (range 0–96%) and a non-dispersive infrared carbon dioxide analyzer (range 0–10%) are used for gas concentration analysis. A mask that covered the participant's mouth and nose was used for gas collection. The system was calibrated according to the manufacturer's instructions prior to each test. It was an auto-calibration procedure involving a proprietary room air calibration of the oxygen and carbon dioxide analyzers, and auto-calibration procedure for the pneumotach.

IIM-IC-100

The IIM-IC-100 metabolic cart is an open circuit device that uses a gas dilution technique to measure gas exchange variables. The exhaust flow is measured using a bi-direction differential pressure preVent™ pneumotach which is the same as the VO2000. The oxygen content of the inspired and expired gas was measured using a zirconia sensor (range 0–100%), and carbon dioxide was measured using a non-dispersive infrared carbon dioxide analyzer (range 0–10%), with quite fast response times (<110 and 100 ms, respectively). VO2 and VCO2 can be measured and displayed for every breath. REE is calculated using a modified Weir equation[16] and RQ is calculated by VCO2/VO2.

Specifically, mixtures of gas exhaled from subjects and the atmosphere were pumped into the metabolic unit, followed by sampling, drying, and concentration analysis. The pumping rate could be automatically changed based on the weight of the subject in order to prevent the concentration of the CO2 from becoming too high, or the range of the mixed gas concentration too narrow. The degree of stability, which is defined as 100% minus maximum coefficient variation (CV) of VO2, VCO2 during last 5 consecutive 1-min intervals, is shown to operators on the interface. The measurement process could be stopped manually or automatically with a settable shortest test time and minimum degree of stability achieved. Results were derived from the average of the final five continuous minutes. The calorimeter was calibrated prior to each test. This consisted of a flow calibration by a 3-L syringe and a 2-point gas calibration, which could be executed automatically in sequences by the press of a button. Room temperature, humidity, and barometric pressure were measured during the calibration procedure.

Experimental design

Subjects were instructed to fast for at least four hours and to abstain from ingestion of alcohol for twenty-four hours and also from heavy physical activity for twelve hours before the tests. The IIM-IC-100 and VO2000 metabolic systems were used in a random and counterbalanced order to avoid confounding due to order effects (schedule shown in Figure 1). Thus, half of the subjects were randomly selected for measurement in the same manner as subject 1, and the other half were selected in the same manner as subject 2. Subjects were instructed to lie down for at least 20 minutes to achieve a complete resting state. After calibration during this period, metabolic measurement was initiated with one of the subjects equipped with a mask for the VO2000 device and another equipped with a canopy for the IIM-IC-100 system. Subjects were asked to maintain a supine position throughout the measurement period. The temperature of the testing room was kept within 20 to 25°C.

Gas exchange was collected continuously for 15 minutes. Data from the first five minutes were discarded to allow for subjects' familiarization with the mask or canopy hood. In the remaining 10 minutes, only the data from the 5-minute steady state were averaged to determine results. The 5-minute steady state condition, which was defined as 10% CV in 5 consecutive 1-minute meas-

Subject1	Resting and Calibrating	IIM-IC-100	Calibrating	VO2000	Calibrating	IIM-IC-100	Calibrating	VO2000
Subject2	Resting and Calibrating	VO2000	Calibrating	IIM-IC-100	Calibrating	VO2000	Calibrating	IIM-IC-100

Time (min) 0 20 35 40 55 60 75 80 95

Figure 1. Time schedule of each measurement session; two subjects were simultaneous measured; after resting for 20min and calibrating, measurements started by alternating used of the IIM-IC-100 and VO2000; the first 5min data was discarded and the remaining 10min was used for data analysis.

urements, was necessary to obtain accurate and reliable results.[17-20] If the steady state was not observed, the data were excluded from the analysis. For the IIM-IC-100, it was not necessary to hand out the first several minutes manually as with the VO2000, because the system was able to identify the last five useful minutes to identify parameters automatically. All procedures were performed by a trained physician's assistant.

Statistical analyses

All values are given as mean ± standard deviation (SD). Pearson's correlation coefficients (r) were used to compare the values obtained for VO2, VCO2, and REE by the two devices. Differences between IIM-IC-100 and VO2000 were examined using paired t-tests. Bland-Altman analysis[21] was also used to assess mean differences and the degree of general agreements between devices as expressed by the limits of agreement (LoA). The LoA was defined as the mean ± 2SD. Pearson's correlation coefficients were also calculated to analyze relationships between repeated measurements of each device. Analysis of intra-measurement variability, which was assessed by the CV calculated by dividing the SD of the differences by their mean, expressed as a percentage, was used to determine whether a time effect was present and to assess repeatability. $p<0.05$ was considered significant for all analyses.

RESULTS

Subject characteristics

Six subjects were excluded from the analysis because they could not reach the steady state protocol. Thus, 32 subjects (17 male and 15 female) were used for analysis. Table 1 shows the characteristics of the 32 subjects. The mean age was 25.3 years and the mean BMI was 21.5 kg/m^2. According to the criteria of the Working Group on Obesity in China,[22] three participants were overweight and the others were within the normal weight range.

Table 1. Characteristics of the study populations (n=32)

Variables	Mean±SD	Range
Male/Female	17/15	
Age (years)	25.3±5.9	18-52
Height (cm)	166±7.6	156-180
Weight (kg)	59.8±9.4	46.0-77.0
BMI	21.5±2.3	17.4-26.0

Values are numbers or Mean±SD

Repeatability of the IIM-IC-100

There were high and significant correlations between repeated measurements for both the IIM-IC-100 (VO2: r=0.95, VCO2: r=0.91, REE: r=0.95; p<0.001) and VO2000 (VO2: r=0.90, VCO2: r=0.85, REE: r=0.90; p<0.001). No significant difference was observed between the repeated measurements of VO2, VCO2, RQ and REE measured by IIM-IC-100 and VO2000. The mean differences of repeated measurements for both the IIM-IC-100 and VO2000 were small (4.0 mL/min and 2.8 mL/min for VO2; 1.6 mL/min and 5.5 mL/min for VCO2; -0.006 and 0.014 for RQ; 25.1 kcal/d and 24.8 kcal/d for REE), as shown in Table 2 and Table 3. The CVs were 5.9% and 10.3% for VO2, 8.3% and 13.0% for VCO2, 7.2% and 6.9% for RQ, and 5.8% and 10.5% for REE (Table 3). The mean values of repeated measurements were used for assessing accuracy.

Accuracy of the IIM-IC-100

VO2 (r=0.91, p<0.001), VCO2 (r=0.89, p<0.001) and REE (r=0.91, p<0.001) measured by the IIM-IC-100 were highly and significantly correlated with the same parameters measured by the VO2000. Paired t-tests showed significant differences for the mean of VO2, VCO2, and REE. However, there was no significant difference in RQ. Bland-Altman plots further revealed a small mean difference of 11.7 mL/min (5.88%), 9.2 mL/min (5.54%),

Table 2. Parameters measured by IIM-IC-100 and VO2000

Parameters	IIM-IC-100 (n=32)			VO2000 (n=32)		
	Test1	Test2	Mean	Test1	Test2	Mean
VO2(mL/min)	213±38.9	209±39.0	211±38.4*	201±47.9	198±44.5	199±45.1
VCO2(mL/min)	176±32.6	174±34.7	175±32.9*	168±40.6	163±35.0	166±36.4
RQ	0.83±0.05	0.83±0.05	0.83±0.04	0.84±0.06	0.83±0.05	0.83±0.05
REE(kcal/d)	1488±270	1463±275	1475±269*	1406±335	1381±307	1394±313

VO2: oxygen uptake; VCO2: carbon dioxide output; RQ: respiratory quotient; REE: resting energy expenditure.
All data were showed as mean±SD.
Test1: the first measurement of IIM-IC-100 or VO2000; Test2: the second measurement of IIM-IC-100 or VO2000.
*Significant different from the mean of VO2000 (p<0.05).

Table 3. Mean difference and coefficients of variation of the repeated measurements

Parameters	IIM-IC-100 (n=32)			VO2000 (n=32)		
	MD	CV (%)	*p*	MD	CV (%)	*p*
VO2 (mL/min)	4.0	5.9	0.083	2.8	10.3	0.444
VCO2 (mL/min)	1.6	8.3	0.537	5.5	13.0	0.154
RQ	-0.006	7.2	0.553	0.014	6.9	0.184
REE (kcal/d)	25.1	5.8	0.109	24.8	10.5	0.348

VO2: oxygen uptake; VCO2: carbon dioxide output; RQ: respiratory quotient; REE: resting energy expenditure.
MD: Mean difference of the first measurement of one device and the second measurement of the device.

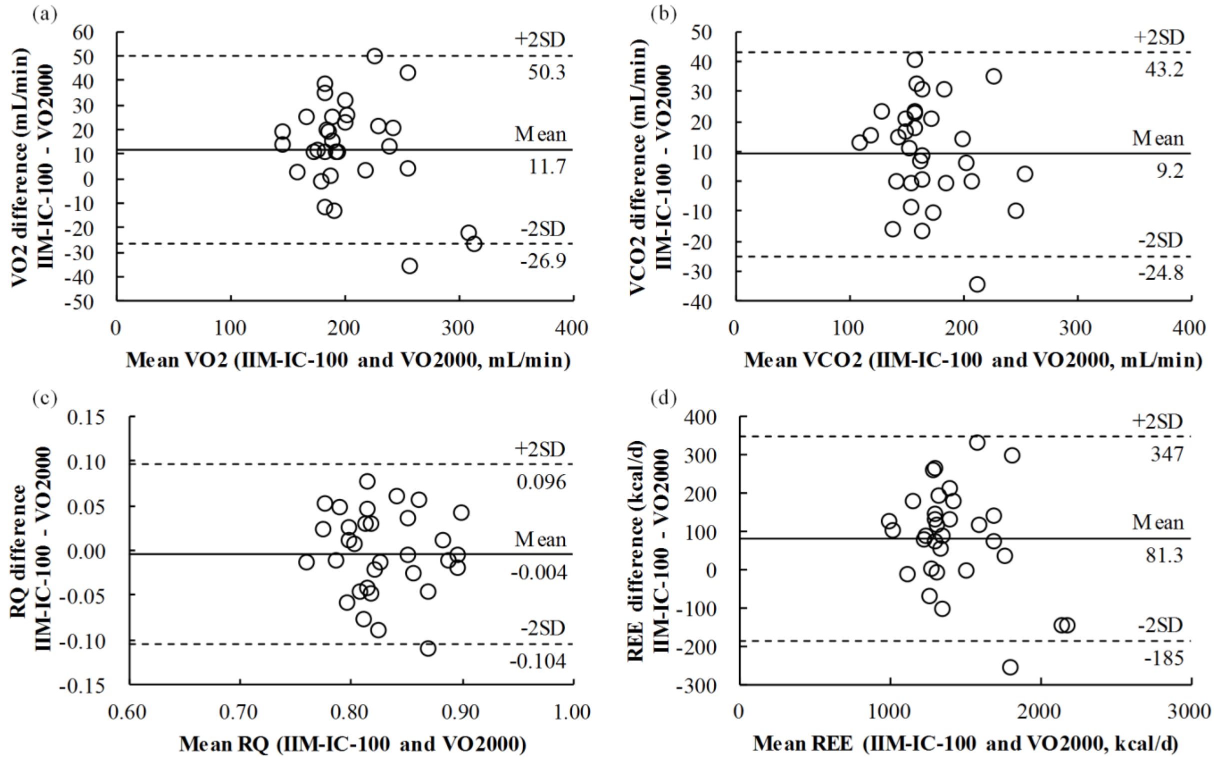

Figure 2. Bland-Altman plots show mean differences and limits of agreement of parameters measured by IIM-IC-100 and VO2000: (a) oxygen uptake (VO2), (b) carbon dioxide output (VCO2), (c) respiratory quotient (RQ) and (d) resting energy expenditure (REE).

-0.004 (0.5%) and 81.3 kcal/d (5.83%) with LoA of -26.9 to 50.3 mL/min (-13.1% to 24.5%), -24.8 to 43.2 mL/min (-14.5% to 25.4%), -0.10 to 0.10 (-12.0% to 12.0%) and -185 to +347 kcal/d (-12.8% to 24.1%) for VO2, VCO2, RQ and REE, respectively (Figure 2). Among these, positive values indicated over-estimation and negative values were under-estimation.

DISCUSSION

This is the first study to validate the IIM-IC-100 for measurement of REE and RQ. We investigated the validity of the IIM-IC-100 using the VO2000 as a reference device. The principal finding of the current study is that the IIM-IC-100 showed good accuracy and repeatability for measuring gas exchange variables.

There were no significant differences between the repeated measurements for the two devices, indicating good repeatability at the group level. Intra-subject CVs further demonstrated a good performance for IIM-IC-100 at the individual level, but moderate for the VO2000. Cooper et al tested the internal test-retest reliability of six metabolic monitors in different sites.[23] Results showed that, among these devices, only Deltatrac and TrueOne had smaller CVs than IIM-IC-100 in terms of REE. It was reasonable that the VO2000 used in the present study would have similar intra-subject CVs to the Ultima because they used the technology of the same company. Alam et al[24] found the CVs of Deltatrac to be similar to that reported by Cooper et al and the CVs of MedGem REE in their study were higher than IIM-IC-100 REE in the present study.

There are several possible explanations for the high intra-subject CVs of the VO2000. Gas leaks may be a contributing factor. The VO2000 metabolic system measured gas exchange parameters using a facemask covering the participants' face. Although the facemasks came in different sizes, it did not match all participants' faces well. Researchers could not make sure that there would be no gas leakage during the test, although much care was taken before starting a measurement. Discomfort may be another reason. All but one participant reported that the facemask of the VO2000 was less comfortable than the canopy hood of IIM-IC-100. The range of the differences can be expected to be higher since some subjects may have been more familiar with the uncomfortable facemask during the second measurement, or may have been impatient with the discomfort at any time.

Results showed that REE as measured by the IIM-IC-100 was significantly higher than that as measured by the VO2000. Gas collection methods of the two devices were different in this study (IIM-IC-100: canopy hood, VO2000: facemask), which may have contributed to the difference. This was consistent with a recent study that showed that the CCMexpress (CCM) facemask produced lower EE measurements than the CCM canopy.[25] However, in the work reported by Isbell et al[17] and McAnena et al,[26] there was no significant difference between collection methods observed. In contrast, Forse found VO2 and VCO2 to be 7.1% and 4.1% higher for the facemask than for canopy measurements.[27] Explanations for these different results are unclear but may be related to air leaks inherent to the facemask. An acceptable degree of error for comparisons of the reference instruments in clinical settings was ±10%.[15] Therefore, the mean difference in REE between IIM-IC-100 and V2000 was relatively small and lacked clinical significance, although it was statistically significant.

Wahrlich et al validated the VO2000 calorimeter for measuring RMR and reported that the VO2000 RMR was significantly lower than the Deltatrac RMR, by 34.6 kcal/d or corresponding to 2.76%.[28] This may suggest a closer reading of REE between IIM-IC-100 and Deltatrac. However, a dedicated study is needed to test this assumption. In addition, it should be aware that inherent error in the IIM-IC-100 (25.1 kcal/d) and VO2000 (24.8 kcal/d) may cause some uncertainty in the results. The true difference of the two devices may be smaller. Analogously, Fields et al. also pointed out a commonly held fallacy that any variation between an established technique and a new technique was always attributable to the new technique.[29]

Bland and Altman analysis showed the LoA for REE and RQ between the two devices to be somewhat wide, suggesting the accuracy at the individual level was moderate. This was somewhat in line with (or better than) the results reported by Fields et al.[29] The non-simultaneous measurements between the IIM-IC-100 and the reference device may act as a reason. The physical state may have varied subtly during the measurement session. Counterbalanced order may help eliminate the order effects (mean difference of the result of the two devices) to some extent. However, it may have no effect on the range of the LoA.

All except one participant reported that the facemask of the VO2000 was less comfortable than the canopy hood of IIM-IC-100. This indicated that people may become more relaxed under the canopy hood than under the facemask. The mixing chamber used by the VO2000 was actually a low-pass filter. It could underestimate the CVs of VO2, VCO2 and REE and then overestimate the degree of stability. Therefore, when performing a gas exchange measurement, canopy hood systems should be the first choice and much attention should be paid to whether the subject is really in a resting state.

Possible limitations of the methodology of this study should be emphasized. First, the non-simultaneous measurements may contribute to some of the differences between the two devices. However, to our knowledge, there has been no previous study comparing these two gas sample methods simultaneously. Second, the VO2000 was not the gold standard indirect calorimetry device. Deltatrac has been found to be a valid metabolic monitor and it was considered the gold standard for gas exchange measurement.[30-32] However, it is no longer in production and was not available for this study. Medgraphics is prominent in the field of gas exchange measurement. Its products, such as the VO2000 and CCM, have been confirmed to be valid tools.[28,33] They have been used in some clinical nutrition and research studies.[34,35] In addition, Schrack et al have assessed the accuracy of the CosmedK4b(2) portable metabolic analyzer, by using the Medgraphics D-Series as a reference method.[36] Therefore, using the VO2000 as the reference method was reasonable and acceptable.

In conclusion, these preliminary data indicated that the IIM-IC-100 showed promise as an accurate and precise tool in the assessment of REE and RQ in healthy Chinese adults. It may be a suitable alternative to the VO2000 and may promote the use of indirect calorimetry in the field of public health in China because it is cost-effective and easy to use. Further research is needed to assess the accuracy of IIM-IC-100 by comparing it to the Douglas bag method or Deltatrac.

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