Nutritional factors predicting postoperative infectious complications in the Mekong Delta, Vietnam

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**Nutritional factors predicting
postoperative infectious complications
in the Mekong Delta, Vietnam**

Nutritional factors predicting postoperative infectious complications in the Mekong Delta, Vietnam

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit van Maastricht,
op gezag van de Rector Magnificus, Prof. mr. G.P.M.F. Mols
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
op woensdag 27 mei 2009 om 16.00 uur

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Nutritional factors predicting postoperative infectious complications in the Mekong Delta, Vietnam

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To my parents, my wife Thao, my children Ngoc and Khanh,
and my sisters and brother.

CHAPTER 1

Introduction and Outline of the Thesis

Introduction and Outline of the Thesis

Methods to assess nutritional status

In developed countries and several developing countries, clinicians have become increasingly aware of the prevalence of malnutrition among hospitalized patients (1-11). These surveys have shown that 20-50% of hospital admissions suffer from nutritional depletion. Clinicians have also learnt that malnourished patients are at a higher risk of developing complications while undergoing treatment (12). These complications include increased mortality, sepsis, abscess formation, other infections such as pneumonia, postoperative wound healing difficulties and organ failure (respiratory, renal, hepatic, immune function etc). Some authors have used the term “nutrition-associated complications” to highlight the relationship between malnutrition and these adverse events (13-16).

There is a lot of methods of assessing the nutritional status of hospitalized patients. The four widely applied traditional methods (body weight loss as a marker of nutritional status, anthropometry, plasma proteins as markers of protein-energy malnutrition and as part of prognostic nutritional indexes) rely heavily on objective anthropometric measurements and laboratory test results. Nutritional assessment can also be based on the findings of routine history taking and physical examination, the so-called subjective global assessment (SGA) of nutritional status. SGA was originally used to predict outcome in surgical patients; however, its use has been applied for other purposes and in other populations. Validation of SGA as a screening tool for surgical patients was done by Detsky et al in 1984 (17). Since that time, SGA has been modified by different researchers and clinicians to make the method applicable to other patient groups (18-20). Validation of these modified SGA applications has not been thoroughly done. Further work in establishing validity and reliability of each version of SGA in different patient populations should be done to enable clinicians and researchers to properly use this nutritional assessment tool. At present many methods are propagated that bear resemblance to the SGA method (MUST, PNI, NRF), and that all suffer from the same problems: they do measure nutritional status only to a limited degree and instead assess factors that increase the risk of developing malnutrition. The specificity, sensitivity and predictive value of these methods is therefore limited.

In terms of objective methods of assessing nutritional status, several methods are available to measure body composition and function. A very important component of the body is muscle mass which is the major part of body cell mass. Body cell mass is the active living part of the organism and its size may be considered to reflect health or depletion. Malnutrition has been defined as lack of intake or uptake of food, leading to diminished function. Depletion of cell mass would due to its size specifically regard muscle mass. A very important aspect of diminished function would therefore be diminished muscle strength. There are several ways to determine muscle strength, the most often used

Introduction and Outline of the Thesis

method being hand dynamometry. Hand grip strength has been used successfully to predict postoperative complications and mortality and has been directly related to nutritional status (16, 21-26). This measurement has been shown to be reproducible when care is taken to execute the measurement carefully. Muscle strength is not only related to the absolute muscle mass but also to muscle metabolism. In inflammatory states, muscle force is compromised (27-30). Insight in these complex relationships may be obtained by relating muscle strength to levels of serum albumin, which is known to be especially decreased during inflammation, and much less by starvation without inflammation (28, 31).

Bioelectrical impedance spectroscopy (BIS) is another technique to assess nutritional status. This technique allows measurement of body extracellular water (ECW), intracellular water (ICW) and total body water (TBW). BIS is based on differences in conducting properties of different tissues and measures resistance of a current when it passes through the body. During the measurement an alternating current of different frequencies is sent through the body, via electrodes placed on hands and feet. At low frequencies the current is unable to penetrate the cell membrane which acts as a capacitor. The measured resistance is the result of conductance through the extracellular fluid. At higher frequencies the current is able to pass through the cell membrane and the measured resistance is a reflection of both ECW and ICW. From all measured resistance values the resistance of ECW and ICW can be extrapolated. These values are used in equations from mixture sciences to calculate ECW and ICW. TBW is calculated as the sum of ECW and ICW. BIS has the potential benefits of being non-invasive, portable and able to provide instant results. However, prediction equations for body composition have the tendency to be population-specific (32). Many factors can be responsible for this "population specificity". Factors known to have an impact on the prediction of total body water from bioelectrical impedance are gender, age, and body water distribution (32). Body impedance is also affected by body built. It has been shown in various studies that the contribution of the limbs to total body impedance is disproportional to the amount of body water in these body segments (33),(34). Ethnic groups can differ in body built. Therefore, theoretically, the relationship between total body impedance and total body water may differ among different ethnic groups (35-37). At present, almost all BIS studies to measure body composition have been carried out in Europe and North America, thus most assumptions are based on data obtained from Caucasians (35, 38).

The dilution of compartment specific indicators or tracers is often used as the gold standard for the measurement of the volume of different body compartment. Deuterium dilution is used as reference method for TBW (39) and Bromide dilution for ECW (40). At present, these dilution methods are the best methods available yielding acceptable accuracy in clinical studies (41). Both the dilution methods and BIS primarily measure the volume of fluid compartments.

BIS has been criticized regarding two assumptions underlying the measurement and calculations.

The first assumption is that specific resistivity of fluid compartments is constant, while in fact resistivity may change during disease (42). The common denominator underlying a

multitude of disease processes consists of inflammatory activity. One of the underlying assumptions of the BIS method is that total cell size and volume determine its capacitance. This is unlikely however because the integrity of the membrane and consequently its membrane potential (its porosity) is an additional factor determining its capacity to store an electrical charge. In this respect capacitance and muscle strength may be influenced by similar factors: size and inflammatory activity (43). Of the BIA/BIS measure specifically Phase angle (PA) and membrane capacitance (Cm) are of interest because they are determined by cell volume and integrity of the cell membrane. This may explain why strong correlations have been found between basal metabolic rate and Cm in healthy persons (44). The Phase angle (PA) can be calculated from R and Xc at any frequency, but usually 50 kHz is used. Several studies on the PA in relation to malnutrition and severity of illness have been published (45, 46). PA decreases with age (47) and with nutritional depletion (48),(49) and has prognostic value in different disease states like HIV (50), colon cancer (51), and lung disease (52). PA has also been found to correlate well with basal metabolic rate (53). On the basis of these considerations these measures may be hypothesized to be valuable for assessment of overall health status and to have predictive power for outcome.

The second assumption is that the human body behaves as a cylinder that homogeneously conducts the electrical current while in fact the geometry of the human body is much more complex (see previous page).

Vietnam is located in South East Asia. Its population amounts to approximately 85 million on an area of 330,363 square kilometers. There are two deltas in Vietnam. These are the Mekong River Delta in the South and the Red River Delta in the North. To the best of our knowledge, only two of the studies directly or indirectly dealing with nutrition in Vietnam (54-63), dealt with investigations of anthropometric measures of nutritional state of the adult and labouring population of Vietnam in the recent decade (54, 63). The nutritional screening of patients at risk of depletion is not routine in most hospitals of Vietnam in general and of the Mekong Delta region in particular. As a consequence, many malnourished surgical patients continue to be ignored and untreated. Therefore, malnutrition associated morbidity and mortality are still occurring frequently.

BIA/BIS mediated assessment of body composition has, till now, not been reported in a Vietnam population. To assess the value of these techniques to measure body composition it is necessary to validate BIS with a gold standard in a Vietnamese population. Ideally a solid measure for body cell mass should be employed, based on tracer dilution methods. Although we tried to use deuterated water to measure fat free mass and Bromide to measure extracellular volume, the results suggested that we had dealt with technical difficulties. This did not allow us to attach much significance to the data obtained. Anthropometry yields reliable data at the group level, but is less reproducible at the individual level. We nevertheless attached much importance to the measures obtained by this technique, due to little variance if applied by well trained investigators.

Aims of the thesis

- 1- To investigate the prevalence of malnutrition in elective abdominal surgical patients.
- 2- To determine the relationship between preoperative nutritional status and the outcome of major abdominal surgery.

Outline of the thesis

In chapter 2, SGA of nutritional status will be applied in patients who are scheduled to undergo abdominal surgery. Also, the incidence of malnutrition in patients undergoing minor and major abdominal operations is investigated. We will try also to establish, whether SGA class is indicative of infectious complications after major surgery Can Tho university hospital in the Mekong River Delta, Vietnam.

In chapter 3 we will determine in a prospective study which variable or which group of variables predicts the development of postoperative complications. Anthropometric measurements, laboratory tests, BIA and postoperative complications will be investigated in patients undergoing abdominal surgery.

In chapter 4 SGA of nutritional status in surgical patients is compared with objective anthropometric and functional measurements. We will try to confirm that there is a strong association between handgrip strength and MAMC and will test the hypothesis that there is also an association between handgrip strength and inflammation.

In chapter 5 we will apply indicator dilution methods in healthy volunteers to validate BIA/BID techniques in assessing body composition. Both the use of mixture equations and the use of single frequency BIS with application of a proposed equation specific for three Singapore ethnic groups will be evaluated.

In chapter 6 the relationship between different BIS variables (FFM, FM, fluid volumes, PA, Cm) on the one hand and anthropometric, biochemical and functional variables on the other hand in preoperative patients will be studied.

In chapter 7 the results will be comprehensively discussed.

In chapter 8 a short summary of the study will be presented in English and Vietnamese.

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Introduction and Outline of the Thesis

CHAPTER 2

Application of subjective global assessment as a screening tool for malnutrition in surgical patients in Vietnam

Subjective Global Assessment as Screening Tool for Malnutrition

**Application of subjective global assessment as a
screening tool for malnutrition in surgical patients in
Vietnam**

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Abstract

Background & aims: In most hospitals in Vietnam, clinical assessment of nutritional status has yet to become part of the routine clinical history taking and physical examination. It is the aim of this study to apply subjective global assessment (SGA) of nutritional status in the Mekong Delta, Vietnam, to determine the incidence of malnutrition according to SGA and to know whether there was an association between SGA class and infectious complications.

Methods: A prospective, cross-sectional study design was used. SGA of nutritional status was applied. Patients were rated as well-nourished (A), moderately-malnourished (B), or severely-malnourished (C). Infectious complications (wound infection, intra-abdominal abscesses, anastomotic leakage) were recorded.

Results: Of the 438 patients assessed, 194 (44.3%) were classified as A, 126 patients (28.8%) were classified as B and 118 patients (26.9%) were classified as C. Of the 274 patients who underwent major abdominal surgery assessed, 61 patients (22.3%) were classified as A, 97 patients (35.4%) were classified as B and 116 patients (42.3%) were classified as C. Weight loss and percent weight loss, muscle wasting, loss of subcutaneous fat, functional capacity and significant gastrointestinal symptoms correlate significantly with the severity of SGA class ($p < 0.001$). The rate of postoperative infectious complications was higher in patients classified as SGA class C (33.6%) than as class A (6%) and B (11%).

Conclusions: A high rate of malnutrition was found, applying SGA of nutritional state in surgical patients in Vietnam. Malnutrition was associated with an increase in infectious complications. Special attention should be paid to weight loss, muscle wasting, loss of subcutaneous fat, functional capacity, and gastrointestinal symptoms.

Keywords: Subjective Global Assessment, malnutrition, surgical patients, Mekong Delta, Vietnam

Introduction

Malnutrition occurs among patients either because of their primary disease (e.g. malignancy, tuberculosis), because the procedures they undergo in order to treat the primary disease prevent them from receiving adequate nutritional intake for prolonged periods of time (e.g. surgery) or because they do not eat enough or do not have enough food to eat.

During the past four decades clinicians have become increasingly aware of the prevalence of malnutrition among hospitalised patients.¹⁻¹¹ These surveys have shown that 20-50% of the patients admitted to the hospital suffer from nutritional depletion. Clinicians have also recognized that malnourished patients are at a higher risk of developing complications while undergoing treatment.¹² These complications include death, sepsis, abscess formation, other infections such as pneumonia, postoperative wound healing difficulties and respiratory failure. Some authors have used the term “nutrition-associated complications” to highlight the relationship between malnutrition and these adverse events.¹³⁻¹⁶

The nutritional status of hospitalised patients can be assessed by a variety of methods. The four widely applied traditional methods (the use of body weight loss as a marker of nutritional status, anthropometric methods of nutritional assessment, the use of plasma proteins as markers of protein-energy malnutrition and the prognostic nutritional indexes) rely heavily on objective anthropometric measurements and laboratory test results. Nutritional assessment can also be based on the findings of routine history taking and physical examination, the so-called subjective global assessment (SGA) of nutritional status. SGA was originally used to predict outcome in surgical patients; however, its use has been applied for other purposes and in other populations. Validation of SGA as a screening tool for surgical patients was performed by Detsky et al.¹⁷ in 1984. Since that time, SGA has been altered by different researchers and clinicians to make the method applicable to other patient groups.¹⁸⁻²⁰ Validation of the altered SGA formats has not been thoroughly done. Further work in establishing validity and reliability of each version of SGA in different patient populations should be done to enable clinicians and researchers to properly use this nutritional assessment tool.

In Vietnam, till now, a limited number of surveys have been reported in this area. They regard nutritional factors, dietary intake, food consumption pattern, macronutrient intake, child malnutrition, micronutrient status of primary school girls, nutritional status of middle-aged Vietnamese in Ho Chi Minh City and use of body mass index in the assessment of adult nutritional status in Vietnam.²¹⁻²⁹ Only one report has been published regarding malnutrition in the clinical setting. This study was performed in the provincial hospital of Quang Ngai in the period from 1965 to 1971.³⁰ We have not found publications regarding SGA or malnutrition in hospitalized patients. In Can Tho General Hospital, nutritional assessment was not a routine part of the work-up of patients that

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were scheduled for surgery. Some surgeons and physicians considered the presence of low albumin and the presence of ankle edema to reflect a compromised nutritional state. The first aim of this study was therefore to apply SGA of nutritional status in patients who were about to undergo abdominal operation. The second aim of the study was to determine the incidence of malnutrition in patients who underwent minor and major abdominal operations and to know whether SGA class was indicative of infectious complications after operation in the Mekong River Delta, Vietnam.

Subjects and methods

Study population

The study group consisted of patients who were scheduled to undergo elective abdominal surgery. These were consecutive patients who were admitted to Can Tho General Hospital with 580 beds in a city with 1,300,000 inhabitants and a total of 2,000 beds. The hospital attracts referrals from a region with 2,700,000 inhabitants. A major abdominal operation was defined as an operation in which the length of the laparotomy wound was more than 5 cm. All patients who underwent laparotomy with the length of incision less than 5 cm and who underwent laparoscopic surgery, such as laparoscopic cholecystectomy, choledocholithotomy, deroofting of liver cyst were categorized as minor abdominal surgery. Patients with dementia, status after cerebrovascular accident were excluded. Other exclusion criteria were the necessity to undergo emergency operations, such as for peritonitis and acute intestinal obstruction. From 14 November 2002 to 6 May 2004, 438 patients were included in the study.

Study methods

The study was a prospective, cross-sectional study. SGA of nutritional status of each patients was performed by one member of a group of three surgeons. Each was taught to perform SGA in a similar fashion. SGA is based on patient's history i.e. degree and pattern of weight loss, change of oral intake, presence of gastrointestinal symptoms (nausea, vomiting, diarrhea and anorexia), functional level and physical examination (loss of subcutaneous tissue, muscle wasting, presence of edema or ascites). Three of these features of physical examination are recorded as normal (0), mild (1+), moderate (2+), or severe (3+). After all of the features have been assessed, patients are rated as well nourished (A), mildly malnourished (B), or severely malnourished (C).

After operation all patients are monitored on a daily basis for the occurrence of complications. All complications either documented on the chart or observed by study group are recorded. Daily monitoring continues from the beginning day until the day of death, discharge, or postoperative day (POD) # 30, whichever comes first. Patients

discharged before POD # 30 were monitored for complications that had occurred between discharge and POD # 30 by personal letter or telephone interview. Some complications are progressive. On a given day, a patient can have more than one complication, but only one complication in a given class is recorded – the one that is most severe in that class. Definition and classification of postoperative complications is described in the study protocol.³¹ Infectious complications (wound or intra-abdominal infection) were recorded.

Statistical methods

Statistical techniques

SGA class is a categorical variable. Some variables such as gastrointestinal symptoms, change in dietary intake, functional capacity, loss of subcutaneous fat, muscle wastage, edema and ascites are also categorical. On the contrary, weight loss and percentage of weight loss are continuous variables. However, in order to compare our results with other authors, a continuous variable can be transformed into a categorical one, e.g. percentage of weight loss, when we use it as continuous variable to calculate mean values of continuous variables and their correlation with SGA class. On the other hand, when we recode the percentage of weight loss to three levels for instance, < 5%, between 6% and 10% and >10%, to calculate the proportion of subjects in these three categories and their correlation with SGA class, it is transformed into a categorical variable. To describe means and proportions across the three SGA classes, χ^2 and one-way analysis of variance were used. In addition, rank correlation coefficients (Kendall's tau_b) were calculated and tested for statistical significance using SPSS 11.5 software for windows.

Results

Gender

Of the 438 patients assessed, 218 (49.8%) were men and 220 (50.2 %) were women. In the major surgical group, 151 (55.5%) were men and 123 (44.9%) were women.

Classification of diseases

Two hundred and seventy-four patients (62.6%) underwent major abdominal operations and 164 patients (37.4%) underwent minor abdominal operations.

Groups of diseases are shown in table 1.

All patients with cancer underwent major surgery (142 patients) and 132 patients with benign GI disease, common bile duct stones, other bilio-pancreatic benign diseases were investigated in major surgery group.

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Table 1 Classification of diseases

Diagnosis	Frequency	Percentage
Gastrointestinal cancer	113	25.8
Esophagus	2	
Stomach	50	
Duodenum	3	
Colorectum	58	
Bilio-pancreatic cancer	29	6.6
Gastrointestinal benign diseases	42	9.6
Cholecystolithiasis	134	30.6
Choledocholithiasis	70	16.0
Other bilio-pancreatic benign diseases	11	2.5
Liver cyst	3	0.7
Abdominal hernias	36	8.2
Total	438	100.0

SGA for total population

Of the 438 patients assessed, 194 (44.3%) were classified as A, 126 patients (28.8%) were classified as B and 118 patients (26.9%) were classified as C (Table 2).

Table 2 Classification of Subjective Global Assessment

	SGA class*			Total
	A	B	C	
<i>Total patient group</i>				
Male	79	60	79	218
Female	115	65	40	220
Total	194	126	118	438
<i>Major surgery</i>				
Male	22	51	78	151
Female	39	46	38	123
Total	61	97	116	274

* A = well nourished, B = moderately malnourished, C = severely malnourished

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Of the 274 patients who underwent major abdominal surgery, 61 patients (22.3%) were classified as A, 97 patients (35.4%) were classified as B and 116 patients (42.3%) were classified as C (Table 2).

In the major surgical group, four SGA-A patients (6%) developed complications, whereas the number of patients in SGA-B and SGA-C that developed complications amounted to 9 (11%) and 39 (33.6%), respectively. The incidence of complications developing in patients with SGA-C class was significantly higher than in patients with SGA-A and SGA-B.

Regarding the clinical features, weight loss and percent weight loss increased consistently across the SGA classes, with the highest values of each occurring in class C. Each variable was significantly correlated with SGA class, as shown by the values of Kendall's tau τ_b ($p < 0.001$).

In table 3, the association between clinical features of SGA of nutritional status presented as categorical or ordinal variables and the SGA class is shown. For each clinical characteristic, a large proportion of the patients with "normal" levels are classified as A, fewer are classified as B and fewer again are classified as C. On the contrary, the most "severe" levels of these characteristics are seen in class C, fewer in class B and much fewer in class A. Table 3 also shows that the degree of abnormality of each variable is clearly correlated with the SGA class. Muscle wastage, loss of subcutaneous fat, categorical weight loss, functional capacity and significant gastrointestinal symptoms have the highest correlation coefficients.

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Table 3 Proportion of subjects in categorical variable levels and their correlation with SGA class

Characteristic	Level	SGA class*			Correlation Coefficient (Kendall's tau b) [†]
		A	B	C	
Weight loss category	< 5%	0.86	0.50	0.08	0.65
	6 – 10%	0.13	0.36	0.17	
	> 10%	0.01	0.14	0.75	
Change in dietary intake	Normal	0.56	0.25	0.01	0.50
	Suboptimal solid	0.43	0.72	0.81	
	Suboptimal liquid	0.00	0.02	0.13	
	Hypocaloric liquids	0.00	0.01	0.05	
	Starvation	0.01	0.00	0.00	
Significant GI [‡] symptoms	Absent	0.76	0.25	0.03	0.60
	Present	0.24	0.75	0.97	
	Normal	0.64	0.31	0.00	
Functional capacity	Suboptimal	0.35	0.59	0.42	0.61
	Bed rest	0.01	0.10	0.58	
	None	0.95	0.16	0.01	
Loss of subcutaneous fat	Mild	0.04	0.56	0.08	0.84
	Moderate	0.01	0.26	0.37	
	Severe	0.00	0.02	0.54	
	None	0.98	0.11	0.02	
Muscle wastage	Mild	0.01	0.75	0.08	0.88
	Moderate	0.01	0.14	0.57	
	Severe	0.00	0.00	0.33	
	None	1.00	0.95	0.72	
Edema	Mild	0.00	0.03	0.20	0.34
	Moderate	0.00	0.01	0.06	
	Severe	0.00	0.01	0.02	
	None	1.00	1.00	0.85	
Ascites	Mild	0.00	0.00	0.11	0.26
	Moderate	0.00	0.00	0.03	
	Severe	0.00	0.00	0.01	

* A, well nourished; B, moderately malnourished; C, severely malnourished.

[†] p < 0.001.

[‡] GI is abbreviated for gastrointestinal.

Discussion

In principle, employing meticulous history taking of the patient and careful physical examination, SGA is not a difficult method to assess nutritional status.^{8, 32, 33} When we assessed 438 patients, the results give similar conclusions as published by other authors.^{8, 34} Weight loss is one of the most important features of the history. Weight loss and percent weight loss correlate significantly with the severity of SGA class. At the time of writing the proposal to apply SGA of nutritional status to patients in our department, we were concerned regarding the reliability of weight reports of the patients, who came to a large extent from rural regions. If they would not know their usual weights, it would be impossible to use SGA to assess their nutritional status. Fortunately, only very few patients did not weigh themselves. Consequently, only few of these patients together with patients suffering from memory loss needed to be excluded from the study. Detsky recommended that in addition to considering the degree of weight loss, it is important to know the pattern of the weight loss. Patients who lost weight in the period of 6 months before operation but had regained some weight prior to admission (although their current weights are still less than their usual weights) are considered to have a better nutritional state than patients with continuous weight loss. In our study, the pattern of weight loss was assessed in a small number of patients, precluding analysis. Besides weight loss, muscle wasting, loss of subcutaneous fat, functional capacity and significant gastrointestinal symptoms are crucial physical findings when SGA is performed. Changes in dietary intake, edema (ankle and sacral) and ascites are important features, but they are less important than those mentioned above.

Different methods of assessing nutritional status in surgical patients have been used, and different prevalences of malnutrition have been reported. In this chapter, we report the prevalence of malnutrition in surgical patients as assessed by SGA. Detsky et al.⁸ studied 202 patients who underwent major gastrointestinal surgery in Toronto, Canada. He found that SGA class B and C comprised 31% of the total population studied. Ten out of a total of 202 patients developed major complications during their hospitalization. These 202 patients had all undergone GI major surgery. In another study of Gupta et al.³⁵ in advanced colorectal cancer, a prevalence of malnutrition of 52% was reported. This prevalence was especially high because of the advanced stage of colorectal cancer. In the study of Rojratsirikul et al.³⁶ in Songkla, Thailand, the prevalence of malnutrition was also high. However, these data were obtained in a pediatric patient population about to undergo surgery. In the study of Bauer and Capra³³ in Brisbane, Australia, the prevalence of malnutrition was very high because of cancer in patients aged 56 ± 15 years. Although we had anticipated that the prevalence of malnutrition in hospitalized patients in Vietnam would be high, the incidence that we found (55.7%) was higher than we expected. Awareness that this is the case should be increased among surgeons, who plan surgery for

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this patient population, because undernutrition may lead to an increase in postoperative infectious complications. Better insight in the risks involved while performing operations in malnourished patients may change our surgical approach, diminishing the incidence of complications. The high incidence of postoperative infectious complications in SGA class C patients indicates that preoperative nutritional repletion should be applied and assessed in these patients.

Conclusion

Application of SGA of nutritional state in surgical patients is feasible in Vietnam. Special attention should be paid to weight loss, muscle wasting, loss of subcutaneous fat, functional capacity, and significant gastrointestinal symptoms.

The incidence of malnutrition determined by SGA was very high in patients that were about to undergo abdominal surgery in the Mekong River Delta, Vietnam. Patients considered to be severely malnourished (SGA class C) had a higher rate of infectious complications than patients in classes A and B.

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CHAPTER 3

Nutritional risk factors for postoperative infectious morbidity in patients undergoing abdominal surgery in the Mekong River Delta, Vietnam.

Nutritional Risk Factors in Patients in the Mekong River Delta

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Nutritional risk factors for postoperative infectious morbidity in patients undergoing abdominal surgery in the Mekong River Delta, Vietnam.

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Abstract

Background: Malnutrition compromises postoperative recovery of patients. The aim of the present study was to identify nutrition related factors that predict the development of postoperative complications in patients undergoing elective surgery.

Methods: Nutritional assessment was performed in 262 patients before major elective abdominal operations. Postoperative infectious complications were recorded until postoperative day # 30, discharge or death. The independent samples Student t-test, log likelihood chi-squares, odds ratio and multiple logistic regression analysis were used to analyze the data.

Results: Seventeen patients (6.6%) developed minor and 46 patients (17.6%) major infectious complications. Age and percentage of weight loss were significantly higher, and mid arm muscle circumference/m², handgrip strength/m², BIA phase angle, membrane capacitance/m² and fat free mass index significantly lower in the complicated group. In a multivariate analysis only handgrip strength/m² (OR=0.699, 0.602-0.812) and percentage weight loss (OR=1.056, 1.009-1.105) remained significant risk factors. Men had a higher risk to develop infectious complications than women. *Conclusion:* Simple bedside tests like handgrip strength corrected for length and a history of weight loss identify patients with a high risk to develop postoperative infectious complications. Men have a higher risk than women.

Keywords:

Percentage weight loss (%WL), bioelectrical impedance analysis (BIA), handgrip strength, midarm muscle circumference (MAMC), fat free mass index (FFMI), phase angle (PA), membrane capacitance (Cm), infectious complications, abdominal surgery, gender

Introduction

In surgical practice, many factors play a role in the development of postoperative infectious complications. Important variables are the overall physical health of the patient, including nutritional status¹, the magnitude of the planned operative procedure, organ dysfunction of the patient, the experience of the surgeon, the pathology encountered and the quality of the anesthetic and postoperative care. In recent decades, involuntary weight loss, various anthropometric indices, muscle function (handgrip strength), plasma albumin, plasma transferrin, plasma protein and combinations of these variables have been used as potential risk indicators for postoperative complications²⁻⁷.

More recently, bioelectrical impedance analysis (BIA) has been used and improved and is potentially applicable for monitoring nutritional status of hospitalized patients. BIA is an easy, non-invasive, portable bedside technique allowing measurement of fat free mass and fat mass and changes therein during treatment. Some studies have revealed that lean body mass depletion at hospital admission is associated with an increased length of hospital stay^{8, 9} and with postoperative infectious complications¹⁰. The data obtained by bioelectrical impedance analysis and specifically phase angle (PA) have been found to be a prognostic marker in several clinical conditions, such as HIV infection, liver cirrhosis, chronic obstructive pulmonary disease, hemodialysis, sepsis, lung cancer, advanced colorectal cancer and advanced pancreatic cancer¹¹⁻¹⁸. PA is determined by both resistance and reactance values and therefore reflects a composite of cellular mass and function^{11, 15}, which may therefore theoretically and hypothetically be a good parameter for the general condition of the patient and therefore the risk of a poor outcome.

In order to determine which variable or which group of variables can be used to obtain a more precise prediction of the development of postoperative complications, we studied prospectively a consecutive group of patients scheduled for elective abdominal surgery. Anthropometric, laboratory and BIA measures were obtained. Another objective was to assess whether simple bedside methods like anthropometric measures and values for muscle strength had similar discriminative capacity as modern sophisticated techniques. This is relevant because simple measures enhance applicability in less wealthy or less well equipped intra- and extramural health care facilities around the world.

Patients and methods

Study population

The study was performed in a prospective fashion in Can Tho General Hospital - the affiliated hospital of Can Tho University School of Medicine, Mekong River Delta, Vietnam. From 14 November 2002 to 6 May 2004 all patients who were consecutively admitted to Can Tho General Hospital for elective major abdominal surgery were included in the study. A major abdominal operation was considered to be performed if the length

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of the laparotomy wound amounted to more than 5 cm. All patients who underwent laparotomy with the length of incision less than 5 cm and who underwent laparoscopic surgery, such as laparoscopic cholecystectomy, removal of common bile duct stones, deroofting of liver cysts were excluded. Patients suffering from dementia, or having a history of cerebrovascular accidents were also excluded. Other exclusion criteria were the necessity to undergo emergency operations, such as for peritonitis or acute intestinal obstruction.

Study methods

On the day prior to the elective operation, nutritional assessment was performed in all patients. Subjective global assessment of nutritional status of each patient was performed by one member of a group of three surgeons. To obtain percentage of weight loss during the past six months (%WL), current weight was measured and usual weight, defined as the body weight of 6 months previously, was recorded. Percentage of weight loss (%WL) was subsequently calculated as:

$$\% \text{ WL} = \frac{\text{usual weight} - \text{current weight}}{\text{usual weight}} \times 100.$$

Anthropometric measurements consisting of height, triceps skinfold thickness and mid-arm circumference of the dominant arm were performed. Based on current weight and height, the body mass index was calculated ($\text{BMI} = \text{weight} / \text{height}^2 = \text{kg/m}^2$). For measurement of triceps skinfold thickness (TSF), a Holtain skinfold caliper was used. The TSF of the dominant arm was measured with the arm extended, half-way between the tip of the acromion and the olecranon process. This procedure was carried out on three occasions, and the mean value was calculated. Midarm circumference (MAC) was measured with a tape at the same site and in the extended position. Subsequently midarm muscle circumference (MAMC) was calculated ($\text{MAMC} = \text{MAC} - \pi \text{ TSF}$). MAMC was corrected for height by calculating MAMC divided by height squared and expressed as MAMC/m^2 .

Handgrip strength of the dominant hand was measured with a mechanical JAMAR handgrip dynamometer. This dynamometer can be adjusted for hand size by changing the concave unit to fit the size of the hand. Patients were required to sit with the arm flexed in the elbow in a 90° angle. The dominant arm was measured in triplicate. This allowed familiarization with the technique and provided the opportunity to improve performance. After an instruction, the patient squeezed the handle as forcefully as possible for a few seconds and then released their grip. Patients were encouraged verbally and the highest score was used in the analysis. Handgrip strength was also corrected for height by calculating handgrip strength divided by height squared (kg/m^2).

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A fasting blood sample was obtained to measure albumin, total serum protein, C-reactive protein (CRP), hemoglobin and lymphocytes. These laboratory tests were validated by the Laboratory of Clinical Chemistry, Maastricht University Hospital, The Netherlands. Bioelectrical impedance measurements were performed with a Hydra ECF/ICF (Model 4200) bio-impedance spectrum analyzer (Xitron Technologies, Inc. San Diego, California, USA) using 50 programmed frequencies ranging from 5KHz to 1MHz. Patients were lying supine on a bed with legs separated and arms abducted from the body. A tetrapolar electrode arrangement as described by Lukaski et al. was used¹⁹. Phase angle (PA) at 50 kHz frequency is composed of the mean of the right and the left PA ($PA = (Reactance * 180) / (Resistance * \pi)$). From all impedance measurements at the 50 frequencies Xitron software calculated the membrane capacitance and the resistance of intracellular (Ricw) and extracellular fluid (Recw) by fitting the data to a Cole-Cole plot²⁰. Recw and Ricw were used to calculate fat free mass (FFM) by use of Hanai mixture equations provided by the manufacturer. Membrane capacitance (Cm) is a measure of the ability of the membrane to store electrical charge. Cm of the whole body is determined by total cell surface area and membrane thickness and porosity. Cm is affected by the aspect ratio (length to cross-sectional area) of the body's conductor. Therefore, values were corrected for height² (Cm/m²). In addition to these BIA variables also body composition (FFM and FM) was calculated based on resistance measurements. These were based on prediction equations provided by the manufacturer. FFM index (FFMI) was calculated by dividing FFM values by height squared (m²).

After operation all patients were monitored on a daily basis for the occurrence of complications. All complications either documented in the patient files or observed by the project group were recorded. Daily monitoring continued from the first preoperative day until the day of death, discharge, or postoperative day (POD) # 30. Patients discharged before POD# 30 were monitored for post discharge complications by personal, letter or telephone interview until POD # 30. When patients had more than one complication, only the severest complication in a given class was recorded. Definitions and classifications of postoperative complications were determined by the study protocol²¹ and as indicated in the guidelines for prevention of surgical site infection²². In order to analyze data, all minor complications i.e. urinary infection due to catheterization before operation, grade I and grade II wound infection and respiratory tract infection not requiring mechanical ventilation were excluded from further analysis. The rationale for this is that these infections are difficult to diagnose correctly and are generally self limiting.

Statistical methods

Continuous variables were expressed as means and standard deviations (sd). The Kolmogorov-Smirnov test was used to test the normality of distribution of variables. To compare the means of continuous variables for both uncomplicated and complicated patients the independent samples Student t-test was used. If variables were not normally distributed, the Mann-Whitney test was applied. Categorical variables were expressed as frequencies and percentages. To analyze the association between cancer and non-cancer patient groups on the one hand and complicated and non-complicated groups on the other

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a cross tabulation with the chi-square test was used. For the univariate relationship between risk (or protective) variables (or factors) the log likelihood chi-squares (and its p-value) and the odds ratio with its 95% confidence interval (CI) were used. The multiple logistic regression analysis was firstly used to search for the best-fitting model. For this purpose all relevant risk or protective variables were entered into the regression model and by backward elimination each non- significant effect was removed from the model. Subsequently, the resulting model containing only significant effects (the 'direct effects' model) was enlarged by the forward testing of each first-order interaction effect between all pairs of its risk or protective variables. The finally resulting model is presented as a table with net odd ratios with 95% Confidence Intervals (CI) for each variable. A p-value of less than 0.05 was considered to be statistically significant. All data analyses were performed by SPSS-pc version 12.

Results

During the 18 months study period, 262 patients were admitted for major abdominal procedures. Gastrointestinal cancer and hepato-bilio-pancreatic cancer accounted for 51.5 percent of the indications for operation (Table 1). The second most common disease was tropical common bile duct stones, resulting from infestation with *Ascaris lumbricoides*.

Table 1: Type of disease diagnosis for major surgery

DIAGNOSIS	FREQUENCY	PERCENTAGE
Gastrointestinal cancer	108	41.2
Esophagus	2	
Stomach	49	
Duodenum	2	
Colorectum	55	
Gastrointestinal benign diseases	39	14.9
Hepatobilio-pancreatic cancer	27	10.3
Common bile duct stones	67	25.6
Other bilio-pancreatic benign diseases	21	8.0
Total	262	100.0

An uncomplicated postoperative course was observed in 195 (75.6%) patients. Seventeen patients (6.6%) developed minor infectious complications and forty six patients (17.6%) developed major infectious complications (table 2). Nine patients died (3.4%) within the postoperative period. The diagnoses of these nine patients were gastrointestinal cancer (7/9), cancer of the pancreatic head (1/9) and tropical common bile duct stones (1/9). Of

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the 135 cancer patients, 34 (25.2%) developed complications. Postoperative mortality and morbidity was higher in cancer patients than in non-cancer patients ($p < 0.05$).

Table 2: Severity and type of postoperative complications

Complications	Number
None	195 (75.6%)
Minor	17 (6.6%)
Major	46 (17.8%)
Wound infection	32
Anastomotic leakage	9*
Septic shock	4
Upper GI hemorrhage	1

* included 5 deaths due to anastomotic leakage.

GI : gastrointestinal

Age and percentage of weight loss were significantly higher in the group with complications (table 3). MAMC/m², handgrip strength/m², PA, Cm/m² and FFMI were significantly lower in the group with complications compared with the group without complications. The values of serum albumin, protein and hemoglobin were not significantly different between both groups.

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Table 3: Characteristics of nutritional parameters in groups with or without complications in men and women. (n=262)

Parameters	Outcome		P value
	Complication	No complications	
Men			
n	31	111	
Age	59.7 ± 15.8	51.3 ± 16.1	0.01
% weight loss	12.7 ± 10.4	8.7 ± 7.0	< 0.05
MAMC/m ²	7.3 ± 0.7	8.0 ± 0.9	0.001
Handgrip strength/m ²	7.5 ± 2.9	10.4 ± 3.0	< 0.001
Albumin	35.8 ± 5.2	37.3 ± 5.5	0.193
Protein	70.5 ± 8.1	69.9 ± 8.5	0.748
Hemoglobin	10.7 ± 2.6	11.5 ± 2.2	0.098
PA	5.3 ± 0.9	5.7 ± 0.9	< 0.05
Cm/m ²	0.37 ± 0.13	0.45 ± 0.15	0.009
FFM index	12.7 ± 1.7	14.3 ± 2.1	< 0.001
Women			
n	15	105	
Age	64.1 ± 18.8	49.3 ± 16.2	0.001
% weight loss	13.5 ± 10.2	6.0 ± 6.5	< 0.001
MAMC/ m ²	7.8 ± 0.9	8.5 ± 1.1	< 0.05
Handgrip strength/ m ²	5.4 ± 1.6	8.1 ± 2.5	< 0.001
Albumin	36.7 ± 6.3	37.5 ± 5.1	0.604
Protein	68.0 ± 9.6	71.2 ± 8.2	0.162
Hemoglobin	10.5 ± 1.8	11.2 ± 2.0	0.222
PA	4.7 ± 0.9	5.4 ± 0.8	0.001
Cm/m ²	0.29 ± 0.13	0.40± 0.13	0.002
FFM index	11.8 ± 2.0	12.9 ± 1.9	< 0.05

MAMC: midarm muscle circumference, PA: phase angle, Cm: membrane capacitance, FFM: fat free mass

After removal of the 9 deceased patients from follow-up, the morbidity rate amounted to 16.2 % in 253 patients. The most important risk or protective factors proved to be handgrip strength/m², MAMC/m², percentage weight loss, SGA, age, Cm/m², FFMI , PA and gender. Handgrip/m², MAMC/m², Cm/m², FFMI and PA are protective: when values are higher, there is less post-operative morbidity (table 4).

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Table 4: Univariate relationships between postoperative morbidity and eleven relevant variables (n=253)

Predictors	OR	95% CI		Log likelihood Chi-square	p value
		Lower	Upper		
Age	1.04	1.02	1.06	13.47	0.001
Gender	0.44	0.21	0.90	5.34	0.021
SGA	0.35	0.18	0.70	4.57	0.022
%Weight loss	1.09	1.05	1.14	16.88	0.001
MAMC/ m ²	0.41	0.27	0.62	21.59	0.001
Handgrip/ m ²	0.73	0.64	0.84	25.28	0.001
Albumin	0.96	0.90	1.02	1.53	0.22
Protein	0.98	0.94	1.02	0.86	0.35
Hemoglobin	0.90	0.78	1.05	1.80	0.18
FFM index	0.75	0.63	0.90	10.86	0.001
PA	0.58	0.40	0.85	8.28	0.004
Cm/m ²	0.013	0.001	0.19	11.41	0.001

MAMC: midarm muscle circumference, PA: phase angle, Cm: membrane capacitance, FFMI: fat free mass index, OR: odds ratio, CI: confidence interval, SGA: subjective global assessment (malnourished and well nourished)

Risk factors appear to be percentage of weight loss and age. Female patients had a significantly lower post-operative morbidity than male patients (10% versus 20 %). Serum albumin, protein and hemoglobin in this study were not significantly associated with post-operative morbidity. Multiple logistic regression analysis was performed with these eleven variables and gender as a twelfth factor. The 'direct effects' model found, contained eventually only the statistically significant effects of handgrip strength/m², percentage weight loss and gender (table 5). The sensitivity of the model amounted to 73.4% and the specificity to 74.5% (Area under the curve parameter: 0.816 (0.754-0.878); standard error: 0.032). To correct these effects for age, this variable was deliberately added to the 'direct effects' model, regardless whether it had statistically significant effects or not. The six pair-wise first-order interactions between the four remaining variables were not statistically significant.

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Table 5: Logistic regression results for postoperative morbidity (n=253, 0=no morbidity, 1=morbidity)

Predictors	OR	95% CI		Log likelihood Chi-square	p value
		Lower	Upper		
Gender	0.239	0.101	0.564	10.74	0.001
Handgrip strength / m ²	0.699	0.602	0.812	17.93	0.001
% weight loss	1.056	1.009	1.105	5.62	0.018

OR: odds ratio, CI: confidence interval

Discussion

Major surgery is still fraught with complications. Complication rates vary in many studies between 10 –40% ^{2, 7}. In a large study of Khuri et al it was documented that at least one complication occurred in 17% of general surgical patients ²³. Our study showed that minor and major complications amounted to 6.6% and 17.8%, respectively. In surgery for cancer postoperative morbidity is usually higher. In a study in patients with head and neck cancer, minor and major complication rates were 25% and 31% ³. Because of the increased risk of morbidity and mortality in malnourished surgical patients ^{24, 25}, much research has been done to define clinical and laboratory parameters to assess nutritional status. No agreement exists as to how patients at risk should be identified. Many indices and scoring systems have been developed, but no single scoring system is used as a standard. In this study we wanted to explore whether relatively simple bedside or laboratory measures were specific enough to identify patients truly at risk to develop postoperative infectious complications.

In 1936, Studley documented that in patients operated for chronic peptic ulcer disease, complication rate, including mortality, was 33,5% in patients with weight loss > 20% and 3,5 % in patients who had lost less weight. Patients undergoing head and neck surgery for squamous cell carcinoma, that had lost more than 10% of their body weight during the six months before surgery had also a high risk for the occurrence of major postoperative complications³. In Windsor's study of patients undergoing elective surgery involving the upper GI tract, weight loss was a basic indicator of surgical risk, providing it is associated with clinically obvious impairment of organ function ²⁶. In Sungurtekin's study, weight loss alone was not a good predictor of complications, but when used in the scoring system (SGA and NRI), the scoring systems were predictive for postoperative complications ⁴. In our study, percentage weight loss was significantly higher in the group

with complications than in the group without complications and was one of the most potent predictors of postoperative infectious complications. SGA however, was different between the two groups but lost its predictive value in the multiple logistic regression analysis.

Handgrip strength is the most commonly used method to measure upper extremity muscle strength. It is a simple bedside test, which can be easily performed. It has been used successfully to predict postoperative complications and mortality²⁷⁻³⁰. Moreover, Mahalakshmi found in 2004 that handgrip strength was a better predictor of postoperative complications than serum albumin³¹.

Handgrip strength values in developing country populations are published only sparsely. Examples are values of Rwandan refugees³² and people from rural Malawi, Thailand and Urban India³³. Normal handgrip strength values of Vietnamese population are not available. In our study, logistic regression analysis identified handgrip strength to be the most prominent predictive parameter for the occurrence of major postoperative infectious complications. A grip strength of 85% of the standard for age and sex was found to be the most decisive cut-off value for the prediction of postoperative complications in terms of sensitivity and specificity, predicting 74% of the complications ($p < 0.05$)³⁴. Following statistical rules we did not include the deceased patients into the analysis, although they died as a result of postoperative infection. When these would have been included the effects would have been similar but stronger.

In one study on preoperative nutritional parameters and postoperative complications in 440 patients with gastric cancer, PA was one of the three indices predicting postoperative complications³⁵. Bioelectrical impedance phase angle (PA) has been found to be a prognostic marker in several clinical conditions¹¹⁻¹⁸. Our present study showed that phase angle, membrane capacitance/m² and FFMI were significantly lower in the complicated group than in the uncomplicated one. However, in the final model, the effects of these predictors were not statistically significant any more. In the present patient population we found that SGA identifies a higher number of malnourished patients compared with data derived from anthropometry (MAMC) and function (handgrip strength)³⁶. Depletion of body cell mass (muscle mass) and plasma albumin concentrations as an indicator of inflammatory activity have been found to be separate risk factors for the development of postoperative infectious complications. In the present study these factors scored less well than handgrip strength. In the study mentioned above we found that handgrip strength was not only associated with MAMC but also with plasma albumin level. This last association persisted also when handgrip strength was controlled for MAMC, suggesting that low albumin levels, reflecting inflammatory activity, have an independent effect on handgrip strength. This may explain why handgrip strength as a composite measure of muscle mass and inflammatory activity is a more important risk factor than MAMC and albumin concentrations individually. PA has also been suggested to be an independent risk factor for the development of postoperative infectious complications. Cm has been less well studied in this respect. In principle they

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are influenced by the same factors as handgrip strength, namely total body cell mass (largely muscle mass) and inflammation. This might explain why they are not statistically significant predictors to the model once handgrip strength has been incorporated. However, if handgrip strength is deleted from the model, the final model includes the protective effect of MAMC next to the risk of percentage weight loss, while the gender effect is replaced by the risk factor of age.

Consequently we did not confirm the value of PA and Cm as prognostic indicators of morbidity and mortality. The advantage of these tools would have been that they do not rely on a sometimes unreliable history of weight loss or on laborious (anthropometry) or expensive (laboratory values) measurements or on the ability of the patient to actively cooperate to optimally measure handgrip strength. The usage of Cm as a risk factor only requires correction for height or height squared. The disadvantage of these tools is that somewhat sophisticated equipment is required (BIA/BIS), which not every hospital administrator is willing to purchase, and that special care should be taken to acquire reproducible results.

In conclusion we have found that handgrip strength/ m^2 and percentage weight loss are the most important nutritional risk factors for the development of postoperative infectious complications. Although Cm/ m^2 and PA are significantly different between the patients that develop infectious complications and those that do not, they do not add to the model once handgrip strength has been incorporated. These findings are fortunate because percentage weight loss and handgrip strength can be easily obtained without great financial investment all around the world. However, when undergoing elective major abdominal surgery one might prefer to be a woman.

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SGA and Measures for Muscle Mass and Strength

CHAPTER 4

SGA and measures for muscle mass and strength in surgical Vietnamese patients

SGA and Measures for Muscle Mass and Strength

SGA and measures for muscle mass and strength in surgical Vietnamese patients

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Abstract

Objective:

This study compared the outcome of the Subjective Global Assessment (SGA) in preoperative surgical patients with objective measurements of muscle mass and strength and with biochemical data. A secondary aim was to test the influence of inflammatory activity on muscle strength.

Methods:

Two hundred seventy-four consecutive patients who were admitted for elective major abdominal surgery were assessed using the SGA, anthropometry, muscle strength, and laboratory measurements (hemoglobin, protein, albumin, C-reactive protein, and lymphocytes). Normal values for midarm muscle circumference (MAMC) and handgrip strength were obtained in a healthy control group. For all other variables, normal values available for the Vietnamese population were used.

Results:

Of 274 patients (151 men, 123 women) assessed, 61 (22.3%) were classified as SGA class A (well nourished), 97 patients (35.4%) as class B (moderately malnourished), and 116 patients (42.3%) as class C (severely malnourished). There were significant differences in age, body weight, percentage of weight loss, triceps skinfold thickness, MAMC, and serum albumin across the three SGA classes. Almost all patients rated class A had normal MAMC and handgrip strength. However, a large proportion of patients rated as B or C also had normal MAMC and handgrip strength (38% of men, 50% of women). Handgrip strength per square meter correlated with serum albumin ($r = 0.278$, $P < 0.001$) and this correlation persisted when handgrip strength was controlled for MAMC ($r = 0.296$, $P < 0.001$ in men; $r = 0.237$, $P < 0.01$ in women).

Conclusion:

The SGA correctly identifies patients with normal muscle mass and strength but a substantial number of patients rated SGA B or C have normal muscle mass and strength. Muscle strength is not only positively associated with muscle mass but also negatively with inflammatory activity.

Keywords:

Subjective Global Assessment; Body mass index; Midarm muscle circumference; Handgrip strength; Malnutrition; Albumin; Inflammatory activity; Surgical patients

Introduction

Nutritional assessment is subject to much confusion. This is the result of the lack of consensus regarding the definition of malnutrition. Several ways to assess malnutrition have been proposed, which use dietary and medical histories, weight loss, anthropometry, and biochemical variables in varying degrees. The Subjective Global Assessment (SGA) is an example of this approach, employing history, weight loss, and physical examination to arrive at a score without actually measuring body composition precisely. If we define malnutrition as a state in which body cell mass is diminished, leading to diminished function, nutritional assessment should actually include measurement of cell mass and function. In practice in the third world and in our hospitals, body cell mass is diminished not only by deficient uptake or intake of food (components) but also by disease and more specifically an inflammatory state. By now it has become clear that disease decreases body cell mass by its catabolic effect, but also that inflammatory activity independently diminishes the ability of the organism to respond adequately to an exterior challenge (trauma, infection) even when body cell mass is still relatively well preserved. More precise measurement of nutritional state and the function of the organism should therefore include not only measurement of cell mass but also assess inflammatory state. Ideally one should arrive at measurements that are a composite of these two aspects.

Several investigators have shown that 20–50% of patients admitted to the hospital have nutritional depletion, which is indicated by several factors including weight loss [1–4]. A loss greater than 10% within 6 mo may decrease the ability to heal wounds or to generate an adequate immune response to trauma and infection [1,5]. Operative mortality has been shown to increase in patients with a weight loss greater than 15–25% [6]. The SGA evaluates nutritional status (and severity of illness) by encompassing the patient's history and physical parameters [1,7]. This method has been shown to be reproducible. We found in a recent study that patients classified as severely malnourished with SGA (class C) have significantly higher rates of infectious complications than do patients rated class A (well nourished) and class B (moderately malnourished) [8]. Nevertheless, many patients rated class C have favorable outcomes, and the question arises as to whether the SGA adequately identifies patients at risk for a poor postoperative outcome.

In the patient cohort under study we have identified in a multivariate analysis the most significant risk factors for postoperative infectious complications, i.e., preoperative weight loss, handgrip strength, and gender (unpublished observations). In a univariate analysis the SGA showed a significant relation with postoperative complications but in the multivariate analysis the SGA lost its predictive value. Handgrip strength has been used successfully by other investigators to predict postoperative complications and death and has been directly related to nutritional status [9–15]. In the present study we assessed whether those patients in the Mekong delta of Vietnam rated moderately or severely malnourished by the SGA were truly malnourished, when we define malnutrition

as a state of decreased body cell mass and diminished function. The same patients were studied and anthropometry was employed as a measurement of body cell mass and hand dynamometry as a measurement of function. Muscle strength is related not only to absolute muscle mass but also to muscle metabolism. In inflammatory states, muscle force is compromised [16–19]. Insight into these complex relations may be obtained by relating muscle strength to levels of serum albumin, which is known to be especially decreased during inflammation and much less by starvation without inflammation.

We and other investigators have found the SGA to have predictive value with regard to postoperative outcome. The main aim of this study was to compare the SGA of nutritional status with objective anthropometric and functional measurements that equally have been found to predict poor outcome. A secondary aim was to confirm that there is a strong association between handgrip strength and midarm muscle circumference (MAMC) and to explore the hypothesis that there is also an association between handgrip strength and inflammation.

Materials and methods

Study population

The study was performed prospectively in Can Tho General Hospital, the affiliated hospital of Can Tho University of Medicine and Pharmacy, Mekong River Delta in Vietnam. The study was approved by the medical ethical committee of this hospital. All consecutive patients who were admitted to Can Tho General Hospital for elective major abdominal surgery were included in the study. A major abdominal operation was considered to be performed when the laparotomy wound was longer than 5 cm. All patients who underwent laparotomy with an incision shorter than 5 cm and who underwent laparoscopic surgery, such as laparoscopic cholecystectomy, common bile duct exploration, and deroofting of liver cysts, were excluded. Patients who had a history of dementia or cerebrovascular accidents were also excluded. Other exclusion criteria were the necessity to undergo emergency operations, such as for peritonitis and acute intestinal obstruction. From November 14, 2002 to May 6, 2004, 274 patients were included in the study.

Study methods

On admission, all patients underwent nutritional assessment. A medical history was obtained and a physical examination performed. The SGA of nutritional status was executed using the protocol developed by Detsky et al. [1]. Patients were classified as class A (well nourished), B (moderately malnourished), or C (severely malnourished) [1].

Anthropometric assessment of weight, height, triceps skinfold (TSF), and midarm circumference (MAC) of the dominant arm was performed. Based on current weight and height, body mass index (BMI; weight in kilograms divided by height squared in meters)

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was calculated. For measurement of TSF thickness, a Holtain skin fold caliper was used. The TSF of the dominant arm was measured with the arm extended, half-way between the tip of the acromion and the olecranon process. This procedure was carried out on three occasions, and the mean value was calculated. MAC was measured at the same site and in the extended position.

Table 1
Types of diseases for major surgery

DIAGNOSIS	FREQUENCY	%
Gastrointestinal cancer	113	41.2
Esophagus	2	
Stomach	50	
Duodenum	3	
Colorectum	58	
Gastrointestinal benign diseases	41	15.0
Bilio-pancreatic cancer	29	10.6
Common bile duct stones	70	25.5
Bilio-pancreatic benign diseases	21	7.7
Total	274	100.0

Subsequently MAMC was calculated ($MAMC = MAC - \pi \text{ TSF}$). MAMC was corrected for height by dividing the measured value by height (meters) squared.

Handgrip strength of the dominant hand was measured with a dynamometer. A mechanical JAMAR handgrip dynamometer (Sammons Preston, Bolingbrook, IL, USA) was used. This dynamometer can be adjusted for hand size by adapting the concave unit to the size of the hand under study. Patients were required to sit with the arm flexed at the elbow in a 90° angle. The dominant arm was measured in triplicate. This allowed familiarization with the technique and provided the opportunity to improve performance. After explaining the procedure to the patients, they squeezed the handle as forcefully as possible for a few seconds and then released their grip. Patients were encouraged verbally and the best score was used in the analysis. Handgrip strength was also corrected for height by dividing the measured value by height (meters) squared.

A fasting blood sample was obtained to measure albumin, total protein, C-reactive protein, hemoglobin, and lymphocytes. These laboratory tests were validated by the laboratory of Clinical Chemistry, Maastricht University Hospital, Maastricht, The Netherlands.

To compare the values obtained in patients for BMI, serum albumin, serum total protein, serum C-reactive protein, hemoglobin, and lymphocytes with normal values, we employed normal values used in Vietnam [20–22]. Because no good references were available for handgrip strength and MAMC, we measured values in 40 healthy adults including 20 men and 20 women (men: age range 24–77 y, mean age 42.3 ± 17.1 y; women: age range 23–84

y, mean age 47.4 ± 16.5 y) from the Mekong River Delta. These individuals were randomly selected and used as controls when the SGA according to Detsky et al. [1] had rated them in class A (well nourished) [1]. In a previous study we found that class A individuals have normal MAMC and handgrip strength [8]. Mean values and standard deviations were calculated. Cutoff points were set at mean of -2 SD. Subsequently MAMC and handgrip strength were corrected for height by dividing the measured value by height (meters) squared. Cutoff values for all other variables were set at values that were below the normality range given for the Vietnamese population [20].

Statistical methods

The data were analyzed with SPSS 11.5 for Windows (SPSS, Inc., Chicago, IL, USA). Differences between continuous variables (e.g., results of anthropometry, functional capacity, and laboratory tests) of different groups that were classified according to the SGA were assessed with one-way analysis of variance. Spearman's rank correlation coefficients were calculated for association between scores and variables. Data are presented as mean $\pm$ SD. Differences were considered to be statistically significant at $P < 0.05$. Agreement between the two levels of subnormal limits and normal limits of each objective measurement and each pair of three classes of SGA was analyzed by the κ statistic. The value of κ varies from 0 to 1; a value ≤ 0.4 indicates that chance alone can account for the observed agreement and a value of 1 indicates perfect concordance.

Results

During the 18-mo study period, 274 patients (151 men, 123 women) were admitted for major abdominal procedures. The diagnoses of these patients are presented in Table 1.

Of the 274 patients who were assessed, 61 (22.3%) were classified as SGA class A, 97 (35.4%) were classified as class B, and 116 (42.3%) were classified as class C (Table 2). Men were considered to be at risk for severe malnutrition (51.6%) more often than women (30.9%). There were differences in age, body weight, percentage of weight loss, TSF, MAMC, and serum albumin across the three SGA classes. There were only significant differences in handgrip strength and serum total protein between SGA-A and SGA-C and between SGA-B and SGA-C, but not between SGA-A and SGA-B. Differences in hemoglobin levels existed across SGA groups. It is striking that even in class A almost 50% of patients had hemoglobin levels below the reference values for the Vietnamese population (reference for men 14.6 ± 0.6 , for women 13.2 ± 0.5). One of the main causes of low hemoglobin in well-nourished patients as determined by the SGA was cancer (Table 3). Hemoglobin in cancer patients was lower than that in non-cancer patients in men and women. No significant differences in C-reactive protein and lymphocyte count were found across the three SGA classes (Table 4).

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Table 2
Classification of SGA in patients undergoing major surgery.

Sex	SGA class (%)			Total
	A	B	C	
Male	22(8.0)	51(18.6)	78(28.4)	151(55)
Female	39(14.3)	46(16.8)	38(13.9)	123(45)
Total	61(22.3)	97(35.4)	116(42.3)	274(100)

A = well nourished, B = moderately malnourished, C = severely malnourished; SGA, Subjective Global Assessment

Table 3
*Hemoglobin concentration (g/dL) **

	Cancer patients		Non-cancer patients		<i>P</i>
Male	90	11.1 ± 2.5	61	11.9 ± 2.2	< 0.05
Female	52	10.4 ± 2.2	71	11.6 ± 1.6	0.001

** Data are presented as numbers of patients and mean ± SD*

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Table 4
*Patient characteristics, anthropometric and laboratory data**

	Total population	Class A	Class B	Class C
Age (y) [†]	52.5 ± 16.8	44.6 ± 15.2	51.2 ± 15.5 [§]	57.8 ± 16.9 ^{§††}
Weight (kg) [†]	46.7 ± 7.1	52.2 ± 7.0	46.9 ± 5.5 [§]	43.3 ± 6.6 ^{§††}
Percent WL (%) [†]	8.4 ± 7.8	1.6 ± 3.6	5.5 ± 5.5 [§]	14.2 ± 6.8 ^{§††}
BMI (kg/m ²) [†]	18.5 ± 2.8	21.3 ± 2.7	18.8 ± 2.0 [§]	16.9 ± 2.1 ^{§††}
Skin fold (mm) [†]	9.0 ± 5.2	13.6 ± 6.4	8.9 ± 4.5 [§]	6.6 ± 3.2 ^{§††}
MAMC (cm) [†]	20.3 ± 2.3	21.5 ± 2.6	20.6 ± 1.9 [§]	19.3 ± 1.9 ^{§††}
Handgrip (kg) [†]	22.3 ± 8.8	24.8 ± 8.9	23.7 ± 8.3	19.6 ± 8.6 ^{§††}
Albumin (g/L) [†]	37.1 ± 5.3	40.0 ± 4.5	37.4 ± 5.1 [§]	35.3 ± 5.2 ^{§††}
Protein (g/L) [†]	70.3 ± 8.3	73.6 ± 6.6	71.2 ± 8.3	67.8 ± 8.5 ^{§††}
Hemoglobin (g/dL) [†]	11.3 ± 2.2	12.4 ± 1.3	11.5 ± 2.0 [§]	10.5 ± 2.5 ^{§††}
CRP (mg/dL) [†]	9.5 ± 5.9	10.3 ± 6.6	9.4 ± 6.5	9.3 ± 5.0
Lymphocyte/nL [†]	2.073 ± 848	2.132 ± 936	2.118 ± 967	2.005 ± 660

A, well nourished; B, moderately malnourished; C, severely malnourished; BMI, body mass index; MAMC, mid-arm muscle circumference; CRP, C reactive protein; SGA, Subjective Global Assessment; WL, weight loss.

** Data are presented as mean ± SD*

† Correlated significantly with SGA (p < 0.05 – 0.001).

‡ Did not correlate significantly with SGA.

§ significantly different with class A (p < 0.05 – 0.001).

†† significantly different with class B (p < 0.05 – 0.001).

Figure 1 shows that almost all SGA-A male patients and all SGA-A female patients had normal MAMC and handgrip strength but that a substantial number (for men: 37 of 51 patients in class B [73%], 20 of 78 patients in class C [26%]; for women: 41 of 46 patients in class B [89%], 20 of 38 patients in class C [55%]) had normal values. Some SGA-C patients had good handgrip strength but low MAMC. Figure 1 also shows a good correlation between MAMC and handgrip strength in men but a poor correlation in women. At the group level MAMC did not differ substantially between men and women, whereas handgrip strength was greater in men than in women, which implies that at a given MAMC men have greater handgrip strength than do women.

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Fig.1. The relation between handgrip strength and midarm muscle circumference per square meter (dashed lines represent cutoff values) and according to the SGA for male and female patients. SGA, Subjective Global Assessment.

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A relatively high level of agreement was found between low BMI in severely malnourished patients and a normal BMI in the well-nourished ones ($\kappa = 0.670$, $P < 0.001$). Nevertheless, of 116 considered to have a high risk for malnutrition, 22 patients had a normal BMI (Fig. 2). In addition, most patients in the SGA-A group had normal BMI and MAMC per meter squared and a substantial proportion of SGA-B and SGA-C patients had a low BMI but a normal MAMC/m². Especially in SGA-B patients low BMI did not correlate well with handgrip strength per square meter (Fig. 3).

A fair correlation was observed between handgrip strength per square meter and serum albumin ($r = 0.278$, $P < 0.001$). When handgrip strength was controlled for MAMC this correlation persisted ($r = 0.296$, $P < 0.001$ in men; $r = 0.237$, $P < 0.01$ in women).

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Fig.2. The relation between body mass index (vertical dashed lines represent cutoff values) and midarm muscle circumference per square meter (horizontal dashed lines represent cutoff values) specified for SGA scores for male and female patients. SGA, Subjective Global Assessment.

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Fig.3. The relation between body mass index (vertical dashed lines represent cutoff values) and handgrip strength per square meter (horizontal dashed lines represent cutoff values) according to SGA score for male and female patients. SGA, Subjective Global Assessment.

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Fig.4. *Body mass index and serum albumin according to SGA (dashed lines represent cutoff values for body mass index and serum albumin). SGA, Subjective Global Assessment.*

No good correlation was observed between BMI and serum albumin. Almost all patients considered to belong to SGA-A had normal BMI and normal serum albumin (Fig. 4). Figure 4 shows that many lean patients with a low BMI had normal serum albumin.

Discussion

Malnutrition in patients is caused by a combination of a decreased uptake of food and inflammatory activity. Although different definitions are used for malnutrition, agreement exists that the malnourished state is characterized by loss of body cell mass, in turn leading to compromised body functions. The lack of an accepted valid reference method complicates the discussion about the best method to assess nutritional status. Several recent and older reports indicated that weight loss and handgrip strength were the most important risk factors for the development of postoperative infectious complications. In a recent study we found that gender also is a major risk factor for the development of infectious complications (unpublished observations). In the present study we compared the results of the SGA with objective measurements for muscle mass and muscle strength and with biochemical data, indicative of inflammatory activity. The different measurements often used to assess nutritional status focus on different

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aspects of disease-related malnutrition and can not be used interchangeably. Used in combination, however, they can broaden our insight.

We found in this study that according to the SGA 42.3% of patients were considered to be at risk for severe malnutrition (class C) and 35.4% for moderate malnutrition (class B), and 77.7% for malnutrition when combining classes B and C. Men were considered to be at risk for moderate (33.8%) and severe (51.6%) malnutrition more often than women (37.4% and 30.9%, respectively). These figures are approximately similar as the highest incidences of malnutrition in surgical patients reported in the literature (Table 5).

Table 5
Incidence of malnutrition in surgical patients

Study	Country	No. of patients	Malnutrition determined by SGA
Detsky et al. [1]	Canada	202	31.0 %
Gupta et al. [29]	USA	217	52.0 %
Rojratsirikul et al.[30]	Thailand	78	35.9 %
Bauer and Capra [31]	Australia	65	75.0 %
Sungurtekin et al. [32]	Turkey	100	44.0 %
Present study	Vietnam	274	77.7 %

SGA, Subjective Global Assessment

The lowest incidences are reported by groups from Thailand and Canada (31% and 36%, respectively). The SGA-B and SGA-C scores found in our study may be explained by the large proportion of cancer patients with advanced cancer stages, but most likely also by the fact that there still is endemic malnutrition in the Mekong delta [20]. We found low hemoglobin levels in our control group, which supports this possibility. We could not compare MAMC and handgrip strength measurements in the control group with those in other studies in Vietnam because, to the best of our knowledge, such studies do not exist.

In our study, BMI was the only measurement of anthropometry in which there was substantial concordance with the SGA in classifying well-nourished and severely malnourished patients. This is probably because the first clinical impression of the patient is very much determined by the presence of body fat and therefore has a major influence on the final attribution to an SGA class. However, we found in this study that BMI did not prove to be a good objective parameter because many patients with a low BMI had normal MAMC, normal handgrip strength, normal serum albumin, and normal hemoglobin. This means that BMI provides only a very general impression of the relation between the weight and height of a patient. It does not furnish reliable information regarding body composition and muscle function and is therefore not a very good indicator of nutritional status of surgical patients.

The definition of malnutrition that we used includes normal body cell mass (predominantly muscle) and function. We assessed body cell mass and function by

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measuring MAMC and handgrip strength. Our data indicate that almost all patients considered not at risk for malnutrition by the SGA (class A) had normal MAMC and handgrip strength. However, in the SGA-B and SGA-C groups a substantial number of patients had normal muscle mass and strength. Especially in men the percentage of patients considered to be malnourished by the SGA had normal MAMC and hand-grip strength. The reason may be that men are leaner than women, leading to low BMI values, which may have a major effect on the final attribution to SGA classes. It follows that especially low BMI should have less effect in assessment methods than is presently the case. The data obtained do not allow us to explain the modest correlation between MAMC and handgrip strength in women. It is also striking that MAMC in women was similar to that in men, whereas strength was weaker. We have the impression that women tried as hard as men to achieve optimal force. Potential influences may be exerted by gender or level of physical labor.

Measurement of muscle strength is subject to inter- and intraobserver variabilities when not executed properly and is influenced not only by muscle mass but also by disease - related factors. However, this also applies to some degree to more sophisticated measurements such as the bioimpedance measurement. The advantage is that it is a rapid and cheap method that can be applied and executed in any hospital setting. Further, the present patients under study were about to undergo elective surgery and were not acutely ill or in pain. In such patients these measurements have been shown to be reproducible when care is taken to execute the measurements carefully.

Hemoglobin, total protein, and specifically albumin are often called nutritional parameters. In this population, hemoglobin proved to be low in patients in all SGA classes and in patients with normal MAMC and handgrip strength. This may be due to endemic anemia in the Mekong delta. Albumin levels were normal in SGA-A but varied from normal to low in SGA-B and SGA-C. There was a modest correlation between albumin and handgrip strength per square meter. This may be explained by the fact that longstanding inflammatory activity as evidenced by low albumin may lead to low MAMC or by the fact that muscle cannot contract adequately in the presence of inflammation. The finding of a persistent correlation when controlled for MAMC suggests that inflammation independently diminishes muscle strength. This is a real possibility because evidence has been presented in the literature that inflammatory activity negatively influences muscle strength [16–19].

In the literature the prevalence of patients estimated to be malnourished as determined by the SGA differs widely from 31% to 52% because of different study populations [1,23,24].

In our study, as in those by Hirsch et al. [25] and Sungurtekin et al. [26], body weight, serum albumin, serum total protein, hemoglobin, and anthropometric data were significantly lower in the malnourished group, and age and percentage of weight loss correlated significantly with malnutrition scores.

In one study of 100 surgical patients, Mourao et al. [27] also recognized the importance of weight loss in nutritional assessment. They found that weight loss > 10% was the only measurement that agreed with Kondrup's Nutritional Risk Assessment,

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British Association for Parenteral and Enteral Nutrition (BAPEN) Malnutrition Screening Tool, Nutrition Screening Initiative, Admission Nutritional Screening Tool, and the SGA ($\kappa = 0.86 - 0.94$, $P \leq 0.05$). The SGA was highly sensitive (100%) and specific (69%) and was the only method with a significant Youden value (0.7).

In Spain, Planas et al. [28] assessed the nutritional status of patients by using anthropometric measurements (BMI, TSF thickness, and upper-arm muscle circumference) and the SGA technique [28]. They found that anthropometric data and the SGA technique were not concordant, reflecting the limitations of markers of nutritional status.

In conclusion, the SGA classes correlate significantly with age and percentage of weight loss. Body weight, BMI, MAMC, handgrip strength, serum albumin and total protein, and hemoglobin differed significantly across SGA classes. BMI was the only measurement of anthropometry that was relatively well concordant with the SGA in classifying patients as class A or C. The concordance in the attribution of patients to class B was low. A substantial portion of these patients had normal MAMC and handgrip strength and normal biochemical variables. We must therefore conclude that the SGA qualifies a larger proportion of patients as malnourished when compared with the aforementioned measurements. It is likely that very low BMI values correctly indicate malnutrition but that BMI values below the cutoff point, but not extremely low, are not good indicators of malnutrition in this Vietnamese population. Similarly high BMI values are not good indicators of adequate muscle mass and function.

As expected, there was a close correlation between MAMC and handgrip strength in men, but the correlation in women did not reach significance. However, there also was an independent effect of albumin levels on handgrip strength. We propose that these findings imply that muscle strength is positively associated with muscle mass but negatively with inflammatory activity.

Based on our results we recommend using the SGA in combination with simple objective measurements such as MAMC and handgrip strength to assess nutritional status in surgical patients.

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CHAPTER 5

Validation of bioelectrical impedance spectroscopy in healthy Vietnamese adults

Validation of bioelectrical impedance spectroscopy

**Validation of bioelectrical impedance
spectroscopy in healthy Vietnamese adults**

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Abstract

Background

Bioelectrical impedance spectroscopy (BIS) is an attractive, noninvasive method for measuring body composition. However, prediction equations for body composition are generally population-specific. Results of body composition research using BIA or BIS in a Vietnamese population have not been reported. The aim of this study was therefore to apply BIS in healthy volunteers to validate this technique in assessing body composition.

Methods

Thirty healthy volunteers (13 males and 17 females) were included in the study. Impedance measurements were performed at the same time with a gold standard method in which Deuterium dilution is used as reference method for total body water (TBW) and Bromide dilution for extracellular water (ECW). Both the use of mixture equations and the use of single frequency BIA with application of a proposed equation, specific for three Singapore ethnic groups were evaluated.

Results

A good correlation between TBW measured by Deuterium dilution technique and by BIS was obtained ($r = 0.892$, $p < 0.001$). However, BIS underestimated TBW (4 litres) compared with the dilution method. The correlation between ECW determined by the dilution method and BIS was 0,769. ECW determined by BIS was 2,1 L overestimated compared with the Br-dilution method. Furthermore, a negative correlation between the error and the size of ECW was found. The correlation between TBW predicted by the equation of Deurenberg and TBWdil was 0,850, comparable with the correlation between TBWbis and TBWdil. TBWdeurenberg also underestimated TBW by almost 4 L. In contrast, comparison of TBWbis with TBWdeurenberg showed a higher correlation coefficient (0,949, $P < 0,001$) and a mean difference between the methods of only 0,7 L. The fact that the bias for ECW is negative indicates that not incomplete ingestion is the potential error source but probably evaporation of indicator mixture. This leads to a decrease of the Deuterium intake but not of the Bromide intake. In this case the assumed Deuterium intake was higher than the actual intake leading to a higher dilution.

Conclusion

The dilution method may not have been performed accurately. The error source may reside in evaporation of the deuterium oxide from the indicator mixture. More comparative studies in healthy people but also in diseased subjects should be conducted in Vietnam.

Introduction

Multiple studies have demonstrated that malnutrition is one of the major causes of increased morbidity and mortality among hospitalized patients. The nutritional status of hospitalized patients can be assessed by a variety of methods in which measurement of body composition is becoming a standard assessment in many clinical and nutrition-related studies ¹. There is great need for a simple valid method to measure body composition in a clinical setting. Laboratory methods such as indicator dilution techniques, computerized tomography, whole-body counting of ⁴⁰K and neutron activation analysis for total body nitrogen are very accurate but also expensive, cumbersome, and require sophisticated instrumentation and highly trained technicians ². Densitometry, underwater weighing, is less expensive but not suited for patients. Techniques based on anthropometric measurement are not reliable enough for use in the individual patient. Furthermore, many indirect methods that rely on assumptions are not valid during disease states. Changes in fluid balance leading to over- or underhydration will alter the density of the fat free mass. In these situations hydrodensitometry and skinfold measurement are not applicable.

Bioelectrical impedance spectroscopy (BIS) is a technique to measure body extracellular water (ECW), intracellular water (ICW) and total body water (TBW). BIS is based on differences in conducting properties of different tissues. BIS measures resistance of a current when it passes through the body. During the measurement an alternating current of different frequencies is sent through the body, via electrodes placed on hands and feet. At low frequencies the current is unable to penetrate the cell membrane which acts as a capacitor. The measured resistance is the result of conductance through the extracellular fluid. At higher frequencies the current is able to pass through the cell membrane and the measured resistance is a reflection of both ECW and ICW. From all measured resistance values, the resistance of ECW and ICW can be extrapolated. These values are used in equations from mixture sciences to calculate ECW and ICW. TBW is calculated as the sum of ECW and ICW.

BIS has the potential benefits of being non-invasive, portable and able to provide instant results. However, prediction equations for body composition have the tendency to be population-specific ³. Many factors can be responsible for this “population specificity”. Factors known to have an impact on the prediction of total body water from bioelectrical impedance are gender, age, and body water distribution ³. Body impedance is also affected by body build. It has been shown in various studies that the contribution of the limbs to total body impedance is disproportional to the amount of body water in these body segments ^{4,5}. Ethnic groups can differ in body build. Therefore, theoretically, the relationship between total body impedance and total body water may differ among different ethnic groups. At present, almost all BIS studies to measure body composition have been carried out in Europe and North America, thus most assumptions are based on data obtained from Caucasians.

Validation of bioelectrical impedance spectroscopy

In Vietnam, till now, no body composition research using BIA or BIS has been reported. In order to apply BIS to Vietnamese patients, it is necessary to validate BIS with a gold standard. The dilution of compartment specific indicators or tracers is often used as the gold standard for the measurement of the volume of different body compartment. Deuterium dilution is used as reference method for TBW⁶ and Bromide dilution for ECW⁷. At present, these dilution methods are the best methods available yielding acceptable accuracy in clinical studies^{8,9,10}. Both the dilution methods and BIS primarily measure the volume of fluid compartments.

The aim of this study was therefore to apply BIS in healthy volunteers to validate this technique in assessing body composition. Both the use of mixture equations and the use of single frequency BIS with application of a proposed-equation specific for three Singapore ethnic groups¹ will be evaluated.

Subjects and methods

Study population

Thirty healthy volunteers (13 males and 17 females) were included in the study. Written informed consent was obtained from all participants. The study was approved by Scientific and Ethic Committee of Can Tho General Hospital which is affiliated with Can Tho University of Medicine and Pharmacy, Vietnam.

Study methods

Anthropometric measurements

Before anthropometry was measured, by taking the history and doing physical examination, all volunteers had been confirmed to have good health. Weight was measured to the nearest 0.1kg and height to the nearest 0.1cm after subjects had voided. From weight and height, body mass index (BMI) (kg/m²) was calculated.

Bioelectrical impedance measurement

Impedance measurements were performed just before the subjects drank the indicator mixture and after the subjects had been in a supine position for 10 minutes. Subjects were lying supine on a bed with legs separated and arms abducted from the body. A tetrapolar electrode arrangement as described by Lukaski et al. was used¹¹. Impedance was measured with a Hydra ECF/ICF (Model 4200) bio-impedance spectrum analyzer (Xitron Technologies, Inc. San Diego, California, USA) using 50 programmed frequencies ranging from 5 kHz to 1 MHz. The extrapolated resistance of ECW and ICW were used in mixture equations provided by manufacturer to calculate body composition. Because the relationship between total body impedance and total body water can differ among different ethnic groups, we also use Deurenberg's prediction equation to estimate total body water¹ using the impedance index at 100 kHz frequency:

for females: $TBW = 0.545 \cdot H^2 / Z_{100} + 4.3$

for males: $TBW = 0.549 \cdot H^2 / Z_{100} + 4.5$

Subsequently these TBW values were compared with results from mixture equations and with deuterium TBW.

Body fluid compartments

Total body water (TBW) and extracellular water (ECW) were measured by Deuterium oxide (D_2O) dilution and Sodium Bromide (NaBr) dilution respectively. The bottles containing the indicator dilution mixture were prepared in Maastricht, The Netherlands and subsequently shipped to Vietnam. They were kept at room temperature (about 26 °C) during one month. Approximately three weeks before the experiment the indicator dilution mixture was distributed into 50 small bottles of 50ml by the pharmacist. These bottles were sealed by rubber caps and then covered by plastic paper and kept at room temperature, before they were ingested by the volunteers during two weekends.

In the morning, overnight fasted volunteers emptied their bladder. Blood samples were collected followed by ingestion of 50 ml of a mixture which contained 20 ml D_2O (D_2O : 99.84 atom percentage excess) and 30 ml 150 mM NaBr. After 4 hour interval, the second blood samples were also obtained for Deuterium and Bromide analysis respectively. During the 4 hour interval, volunteers stayed in the hospital. They were allowed to move freely and to drink 500 ml water during the first three hours after ingestion of the mixture. Eating was not allowed. Blood samples coagulated for 1 hour and then, coagulated blood samples were centrifuged for 10 minutes. All serum samples were stored at – 20 °C and were sent to University Hospital Maastricht to be analyzed. Deuterium was analyzed by a mass spectrometric method described by van Kreelr⁶. Bromide was analyzed by ion chromatography¹².

TBWdil was calculated by correcting the Deu-dilution space with 4% for exchange of labile hydrogen¹³. ECWdil was calculated by correcting the Br-dilution space with 0.9 for non-extracellular distribution of Br and with 0.95 for the Donnan equilibrium¹⁴. The Br-dilution method for ECW is estimated to have an accuracy of 5%^{7,8}. The accuracy of TBW measurements by Deu-dilution has been reported to be 1.5%^{8,9}.

Statistical methods

All data were analyzed by using SPSS 11.5 for Windows (SPSS Inc. Chicago, IL, USA). Results are expressed as an mean (SD). Absolute values of variables were compared between methods by paired-samples T tests. Results of TBW and ECW which were measured by BIS were compared with those measured by the dilution method by Bland and Altman analysis¹⁵. *P*-values of less than 0.05 were considered significant.

Results

Thirty-three healthy volunteers were included in the study. Data of three persons were excluded because results of dilution methods were irrational with a Deuterium TBW/body weight ratio higher than 73 percent. Subsequently data of thirty healthy volunteers (13 male and 17 female) with a mean age of 48.2 (16.8) years and a mean BMI of 22.4 (2.6) kg/m² were analyzed. The characteristics of population are shown in table 1.

Validation of bioelectrical impedance spectroscopy

Table 1: Population characteristics

Parameters	Mean $\pm$ sd
Age (y)	48.2 $\pm$ 16.8
Height (cm)	158.6 $\pm$ 7.0
Weight (kg)	56.5 $\pm$ 8.8
Body mass index (kg/m ²)	22.4 $\pm$ 2.6
Total body water (dilution) (L)	35.7 $\pm$ 6.4
Extracellular water (dilution)(L)	11.7 $\pm$ 1.7
Total body water (BIS) (L)	31.3 $\pm$ 7.3
Extracellular water (BIS) (L)	13.7 $\pm$ 2.4

A good correlation between TBW measured by Deuterium dilution technique and by BIS was obtained ($r = 0.892$, $p < 0.001$) (as shown in figure 1A). However, the mean difference between the methods (bias) was more than 4 litres (table 2). This means that BIS underestimated TBW compared with the dilution method. The standard deviation of the difference was also large (table 2). This results in wide limits of agreement (figure 1B). There was no significant correlation between the difference of the 2 methods and the volume of TBW.

Figure 1. Comparison of total body water (TBW) measured with deuterium dilution (Deu) and bioelectrical impedance spectroscopy (BIS). A: The correlation between the two methods. B: Difference between the two methods against their mean value. The horizontal line indicates the mean difference (bias) and the dotted lines indicate the 95% limits of agreement.

For ECW the dilution method and BIS showed a correlation of 0,769. ECW was 2,1 L overestimated (table 2) compared with the Br-dilution method. Furthermore, a negative correlation between the error and the size of ECW (see figure 2B) was found.

Validation of bioelectrical impedance spectroscopy

Figure 2. Comparison of extracellular water (ECW) measured with Bromide dilution (Br) and bioelectrical impedance spectroscopy (BIS). A: The correlation between the two methods. B: Difference between the two methods against their mean value. The horizontal line indicates the mean difference (bias) and the dotted lines indicate the 95% limits of agreement.

The correlation between TBW predicted by the equation of Deurenberg and TBWdil was 0,850, comparable with the correlation between TBWbis and TBWdil. TBWdeurenberg also underestimated TBW by almost 4 L (fig. 3, table 2). In contrast, comparison of TBWbis with TBWdeurenberg showed a higher correlation coefficient (0,949, $P < 0,001$) and a mean difference between the methods of only 0,7 L (fig 3).

Validation of bioelectrical impedance spectroscopy

Figure 3. Comparison of total body water (TBW) measured with bioelectrical impedance spectroscopy (BIS) and Deurenberg's equation (using the impedance index at 100 KHz frequency). A: The correlation between the two methods. B: Difference between the two methods against their mean value. The horizontal line indicates the mean difference (bias) and the dotted lines indicate the 95% limits of agreement.

Table 2 : Comparison of body fluid compartments measured with dilution techniques and bioimpedance spectroscopy (BIS)¹

	Volume (L) (SD)	Difference between methods	Correlation coefficient with dilution
TBW			
dilution	35.7 (6.4)		
BIS mixture	31.3 (7.3)*	4.4 (3.3)	0.892
BIA Deurenberg's	32.0 (6.3)*	3.7 (3.5)	0.850
ECW			
Dilution	11.7 (1.7)		
BIS	13.7 (2.4)*	-2.1 (1.5)	0.784

¹ Mean values, SD in parentheses.

* Significant different from dilution value, paired T-test ($P<0.001$).

Discussion

The majority of body composition studies, reported in the literature is performed in Caucasians and much of the information on validity methods and assumptions are available only for this ethnic group¹⁶. It is assumed that these assumptions are also valid for other ethnic groups. However, this is not the case. Prediction equations for body composition have the tendency to be population specific³. As far as we know, no studies regarding bioelectrical impedance spectroscopy in Vietnam have been published. It is therefore necessary to validate BIS with a gold standard in healthy people before BIS is clinically applied. Unfortunately, this study demonstrates that the results of BIS and dilution techniques are different. In the current study BIS underestimated TBW by 4.4 L and overestimated ECW by 2.1 L. This is not acceptable because this study was performed in healthy individuals with a normal hydration state. In the study of van Marken Lichtenbelt¹⁷ on 29 healthy adults better correlations were achieved, $r = 0.990$ for TBWBIS and TBWdeuterium and $r = 0.970$ for ECWBIS and ECWbromide dilution. In another study of Simpson¹⁸ in healthy volunteers, there was a good correlation ($r = 0.870$) between estimates of ECW using dual frequency BIA and NaBr dilution, with the former overestimating ECW by approximately 1 L. Although TBW measurements obtained by single and dual frequency BIA correlated well with estimates using tritium dilution ($r = 0.980$ and 0.970 respectively), single frequency BIA underestimated TBW by approximately 1 L and dual frequency BIA by approximately 5 L compared to tritium dilution. In the study of Cox-Reijven²³, the authors validated the spectrum approach and compared different methods for screening nutritional depletion in patients with gastrointestinal disease. They found that BIS underestimated TBW by 3 L and overestimated ECW by 0.64 L.

Because the correlation coefficient between Deurenberg TBW and TBWdil was comparable with the correlation between TBWbis and TBWdil and lower than values reported in the literature, our data appear to indicate that the dilution method may not have been performed accurately. The high correlation between Deurenberg TBW and TBWbis can be explained by the fact that resistance values used in the equation correlate with each other. In Deurenberg's study, the impedance index at 100 KHz frequency was used to construct a regression equation based on TBW measured by deuterium dilution. Our results show that the mean difference between TBWbis and TBWdilution is comparable with the difference between TBWdeurenberg and TBWdilution. In both cases the bias is positive and large (about 4 L underestimation by BIA and BIS). This finding also points in the direction of limitation of the dilution method. The fact that the bias for ECW is negative indicates that not incomplete ingestion is the potential error source but probably evaporation of indicator mixture. This leads to a decrease of the Deuterium intake but not of the Bromide intake. In this case the assumed Deuterium intake was higher than the actual intake leading to a higher dilution. Calculation of TBW then would result in falsely high values.

Validation of bioelectrical impedance spectroscopy

The finding that TBW_{BIS} was consistent with results obtained by Deurenbergs' equations for TBW justifies the use of BIS, but proper validation studies should be repeated in the future.

At present, many studies addressing BIS validity with dilution methods as gold standard in hospitalized patients have been published such as in hemodialysis patients (19, 20), in obese patients (21), in patients with severe weight loss (22), with gastrointestinal disease (23) and in elderly patients (24). Such validation studies have not been carried out in Vietnam in healthy, nor in diseased populations. In order to apply BIS in Vietnamese populations the technique should be validated not only in healthy people but also in diseased subjects.

Conclusion

BIS estimates of TBW and ECW did not correlate well with dilution methods and showed for a large bias for TBW. Evaporation of the deuterium oxide from the indicator mixture may explain the discrepant results. BIS results computed with mixture equations yields results for TBW that are comparable with results obtained employing specific equations published by Deurenberg for populations in Singapore. More studies not only in healthy people but also in diseased subjects should be conducted in Vietnam

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CHAPTER 6

The value of bioelectrical impedance spectroscopy in assessing nutritional status of surgical patients in Vietnam

Bioelectrical Impedance Spectroscopy in Assessing Nutritional Status

**The value of bioelectrical impedance spectroscopy in
assessing nutritional status of surgical patients in
Vietnam**

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Abstract

Background and aims

Bioelectrical impedance spectroscopy (BIS) is attractive for nutritional assessment because it is a bedside method, easy to perform and non-invasive. The aim of the study was to evaluate the relationship between different BIS variables (fat free mass (FFM), fat mass (FM), fluid volumes, phase angle (PA), membrane capacitance (Cm)) on the one hand and anthropometric, biochemical and functional variables on the other hand in patients before surgery.

Methods:

262 consecutive patients who were admitted for elective major abdominal surgery were included in the study. On the day prior to the elective operation, nutritional assessment consisting of percentage of weight loss, anthropometry, handgrip strength, biochemical tests and BIA were performed in all patients. Phase angle was calculated directly from body resistance and reactance. All the values of different BIS variables (FFM, FM, fluid volumes, PA, Cm) were compared with other objective measures indicative of nutritional and functional disturbances.

Results:

The best correlation was found between Cm and Handgrip strength ($r = 0.652$, $p < 0.001$) and between PA and handgrip measures and MAMC were good but lower than with handgrip strength. FFM index also significantly correlated with MAMC and handgrip strength but correlations were less significant than with Cm and PA. Values of Cm and PA exhibit fairly good correlations with albumin and handgrip strength when controlling for muscle mass (MAMC or FFM) for both sexes. The sensitivity and specificity of Cm/m² (73.6% and 72.3%, respectively) and PA in classifying malnourished and well nourished patients (75.5% and 71.8%, respectively) when used with handgrip strength/m² as reference method were higher than with MAMC/m² as a reference. (For Cm/m²: 70.0% and 72.1%, respectively; for PA: 58.3% and 68.8%, respectively).

Conclusions:

Simple, quick objective measurements like BIS, handgrip strength, midarm muscle circumference can furnish a good indication of nutritional status. The advantage of these measures is that no complicated equations to calculate fat free mass and fat mass at the whole body level are required.

Keywords:

Bioelectrical impedance spectroscopy (BIS), handgrip strength, midarm muscle circumference, fat free mass (FFM), fat mass (FM), phase angle (PA), membrane capacitance (Cm),

Introduction

Undernutrition has been documented to occur frequently in surgical patients (1-3), and has been associated with a higher incidence of morbidity and mortality (4-8). Undernutrition is characterized by loss of body cell mass by functional disturbances in muscle force, immune function and cognition. Body compartments are changed in undernutrition (9). Therefore, measurement of body composition is an important component of overall nutritional evaluation in hospitalized patients (10-12).

Bioimpedance analysis (BIA) was the first technique making use of measuring the resistance against an alternating electrical current of 50 Hz to assess body compartments. Bioelectrical impedance spectroscopy (BIS) theoretically is a technique to measure total body water (TBW), extracellular water (ECW) and intracellular water (ICW). BIS is based on differences in conducting properties of different fluid compartments. BIS, like BIA, measures resistance to a current when it passes through the body. During the measurement, unlike BIA, an alternating current of different frequencies is sent through the body, making use of electrodes placed on hands and feet. At low frequencies the current is unable to penetrate the cell membrane which acts as a capacitor. The measured resistance is the result of conductance through the extracellular fluid and therefore is a measure of extracellular water (ECW). At higher frequencies the current is able to pass through the cell membrane. With the use of the Cole-Cole model the resistance of the ECW and ICW can be extrapolated. These resistance values can be used in Hanai mixture equations to calculate ECW, ICW and TBW (13). Based on these fluid volumes fat free mass and fat mass can be calculated. BIS has been validated in different types of hospitalized patients (14),(15). BIS has the benefit of being non-invasive, makes use of portable equipment and is able to provide instant, relatively accurate results. However, BIS also has been criticized regarding two assumptions underlying the measurement and calculations. The first is that specific resistivity of fluid compartments is constant, while in fact resistivity may change during disease (16). The second assumption is that the human body behaves as a cylinder that homogeneously conducts the electrical current while in fact the geometry of the human body is much more complex. Recently, it has been proposed that phase angle (PA) in case of single frequency (BIA) and membrane capacitance (Cm) in case of multiple frequencies can be used to classify nutritional status of patients. Cm theoretically measures the capacitance of all membranes in the body to store electricity and is therefore dependent on body cell mass, which predominantly consists of muscle mass. Consequently on theoretical grounds Cm should correlate well with muscle mass. An additional factor that may influence Cm however is the integrity of the cell membrane which may be compromised in patients that are undernourished or subject to inflammatory activity (13). In the literature strong correlations have been found between basal metabolic rate and Cm in healthy persons (17).

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The Phase angle (PA) can be calculated from R and Xc at any frequency, but usually 50 kHz is used. Several studies on the PA in relation to malnutrition and severity of illness have been published (18,19). PA decreases with age (20) and with nutritional depletion (21),(22) and has prognostic value in different disease states like HIV (23), colon cancer (24) , and lung disease (25) . PA has also been found to correlate well with basal metabolic rate (26) .

The exact biological meaning of Cm and PA is not completely understood. Because they not only reflect BCM, but also appear to be indicators of cell membrane function, these measures might be valuable for assessment of overall health status and may have predictive power for outcome.

In an earlier study we found that handgrip strength is positively influenced by muscle mass and negatively by inflammatory activity as indicated by albumin levels. We therefore undertook a study to analyse the value of different BIS variables by comparing them with other objective measures indicative of nutritional and functional disturbances. We hypothesized that correlations should exist between Cm or PA and albumin levels, mid arm muscle circumference and handgrip strength. The strongest correlation should exist between Cm and handgrip strength because both have been found to correlate with muscle mass and inflammatory activity. To the best of our knowledge such studies have not been performed previously in Vietnam.

It was the aim of the present research to study the relationship between different BIS variables (FFM, FM, fluid volumes, PA, Cm) on the one hand and anthropometric, biochemical and functional variables on the other hand in patients before surgery.

Subjects and methods

Study population

This prospective study was performed in Can Tho General Hospital - the affiliated hospital of Can Tho University School of Medicine, Mekong River Delta, Vietnam.

All consecutive patients who were admitted to Can Tho General hospital for elective major abdominal surgery were included in the study. A major abdominal operation was considered to be performed when the length of laparotomy amounted to more than 5 cm. All patients who underwent laparotomy with the length of incision less than 5 cm and who underwent laparoscopic surgery, such as laparoscopic cholecystectomy, choledocholithotomy, deroofing of liver cysts were excluded. Patients with dementia or a history of a cerebrovascular accident were also excluded. Other exclusion criteria were the necessity to undergo emergency operations, such as for peritonitis and acute intestinal obstruction. From 14 November 2002 to 6 May 2004, two hundred sixty two patients were included in the study.

Study methods

During the first 72 hours after admission, a medical history of the patient was obtained and a physical examination performed. Height and weight were measured. A fasting blood sample was obtained to measure albumin, total serum protein, C-reactive protein (CRP),

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hemoglobin and lymphocytes. These laboratory tests were validated by the Laboratory of Clinical Chemistry, Maastricht University Hospital, The Netherlands.

In addition all patients underwent the following tests of nutritional assessment:

- Anthropometric assessment of triceps skinfold and mid-arm circumference of the dominant arm. For measurement of triceps skinfold (TSF) thickness, a Holtain skin fold caliper was used. The TSF of dominant arm was measured with the arm extended, half-way between the tip of the acromion and the olecranon process. This procedure was carried out three times, and the mean value was calculated. For measurement of midarm circumference (MAC) the MAC was measured at the same site and in the extended position. Midarm muscle circumference (MAMC) was calculated using the formula:

$$\text{MAMC} = \text{MAC} - \pi \text{ TSF}$$

MAMC was corrected by height squared (MAMC / m^2) in order to allow comparison with values of a reference population.

- Handgrip strength of the dominant hand was measured with a mechanical JAMAR handgrip dynamometer. This dynamometer can be adjusted for hand size by changing the concave unit which is set together with the handle. Patients were required to sit with the arm flexed in the elbow in a 90° angle. The dominant arm was measured in triplicate. This allowed familiarization with the technique and provided the opportunity to improve performance. After an explanation the patient squeezed the handle as forcefully as possible for a few seconds and released. Patients were encouraged verbally and the best score was used in the analysis. Handgrip strength was also corrected by height squared (m^2).

- Bioelectrical impedance measurements were performed with a Hydra ECF/ICF (Model 4200) bio-impedance spectrum analyzer (Xitron Technologies, Inc. San Diego, California, USA) using 50 programmed frequencies ranging from 5 kHz to 1 MHz. Patients were lying supine on a bed with legs separated and arms abducted from the body. A tetrapolar electrode arrangement as described by Lukaski et al. was used (27). PA at 50 KHz frequency is the mean of the right and the left PA. PA can be calculated with the following equation:

$$\text{PA} = (\text{Capacitance} * 180) / (\text{Resistance} * \pi).$$

Membrane capacitance (C_m) is a measure of the ability of membrane to store electrical charge. C_m of the whole body is determined by total cell surface area and membrane thickness and porosity. C_m is affected by the aspect ratio (height to cross-sectional area) of the body's conductor. PA and C_m with other BIA data i.e. fat free mass (FFM), fat mass (FM), TBW, ECW and ICW were collected. FFM index, FM index (FMI), TBW index and ICW index are calculated by dividing absolute values by height squared (m^2).

To obtain normal values for hemoglobin, MAMC and handgrip strength, we undertook a study in 40 healthy adults (20 men and 20 women) from urban and suburban areas of Can Tho city. These individuals were randomly selected and used as controls when subjective global assessment (SGA) according to Detsky (28) had rated them in class A (well nourished). In an earlier study we found that class A individuals have normal MAMC and handgrip strength (29). Mean and standard deviations were calculated for the absolute

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values as well as for the values corrected for height squared. Cut-off points were set at mean minus 2 standard deviations (sd). Characteristics of the control group are shown in table 1.

Table 1: Demography of control group

Parameters	Unit	Male (20)		Female(20)	
		Mean $\pm$ sd	Range	Mean $\pm$ sd	Range
Age	year	42.1 $\pm$ 16.8		47.5 $\pm$ 15.8	
Weight	kg	59.9 $\pm$ 8.1	43.7-76.1	52.9 $\pm$ 7.7	37.5-68.3
Height	cm	163.4 $\pm$ 5.4	152.6-174.2	154.4 $\pm$ 5.4	143.2-165.2
MAMC	cm	23.9 $\pm$ 1.9	20.1-27.7	19.5 $\pm$ 1.6	16.3-22.7
MAMC/ height ²	cm/m ²	8.9 $\pm$ 0.7	7.6-10.2	8.3 $\pm$ 0.8	6.7-9.7
Handgrip	kg	40.3 $\pm$ 10.5	19.3-61.3	22.5 $\pm$ 4.2	14.1-30.9
Handgrip/height ²	kg/m ²	15.0 $\pm$ 3.5	8.0-22.0	9.1 $\pm$ 2.0	5.1-13.1
Hemoglobin	g/dL	13.9 $\pm$ 1.4	11.2-16.6	12.4 $\pm$ 1.4	9.7-15.1

MAMC: midarm muscle circumference

In order to calculate the sensitivity and specificity of FFM index, Cm/m² and PA for classifying patients as malnourished or well nourished, we used the cut-off values of MAMC/m² and handgrip strength/m² of the male and female control groups.

Statistical methods

All data were analysed by using SPSS 11.5 for Windows (SPSS Inc. Chicago, IL, USA). Differences of continuous variables between male and female were assessed with independent samples T test. Data are presented as mean $\pm$ standard deviation. Pearson product-moment correlations coefficient analysis was performed to test the linear relationship between continuous variables. Partial correlation was performed to test whether the third factor can have influence to the relationship between the first two factors. To compare the ability of FFM index, Cm/m² and phase angle to identify patients with nutritional depletion, the sensitivity (percentage of depleted patients classified as depleted) and specificity (percentage of not depleted patients classified as not depleted) were calculated with normal values for MAMC/m² and handgrip strength/m² as reference methods. For all tests *P*-values of less than 0.05 were considered significant.

Results

During the 18 months study period, 262 patients were admitted for major abdominal procedures. Gastrointestinal cancer and hepato-bilio-pancreatic cancer accounted for 51.5 percent of the patients (table 2). The second commonest disease was tropical common bile duct stones on the basis of infestation with *Ascaris lumbricoides*.

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Table 2: Types of diseases for major surgery

DIAGNOSIS	FREQUENCY	PERCENTAGE
Gastrointestinal cancer	108	41.2
- Esophagus	2	
- Stomach	49	
- Duodenum	2	
- Colorectum	55	
Gastrointestinal benign diseases	39	14.9
Hepatobilio-pancreatic cancer	27	10.3
Choledocholithiasis	67	25.6
Benign bilio-pancreatic diseases	21	8.0
Total	262	100.0

Height, MAMC/m², handgrip strength, handgrip strength/m², FFM index, TBW index, FM index, ICW index Cm, Cm/m² and PA, were significantly different between male and female patients, (table 3).

Table 3: Characteristics of the study population

Parameters	All patients Mean $\pm$ sd	Males(142) Mean $\pm$ sd	Females(120) Mean $\pm$ sd
Age (year)	52.2 $\pm$ 16.7	53.1 $\pm$ 16.3	51.1 $\pm$ 17.1
Weight (kg)	46.6 $\pm$ 7.3	47.4 $\pm$ 6.8	45.6 $\pm$ 7.7*
Height (m)	1.59 $\pm$ 0.07	1.63 $\pm$ 0.06	1.53 $\pm$ 0.05**
MAMC (cm)	20.3 $\pm$ 2.3	20.7 $\pm$ 2.1	19.8 $\pm$ 2.4*
MAMC/ m ² (cm/ m ²)	8.1 $\pm$ 1.1	7.8 $\pm$ 0.9	8.4 $\pm$ 1.1**
Handgrip strength (kg)	22.5 $\pm$ 8.7	26.0 $\pm$ 8.8	18.3 $\pm$ 6.4**
Handgrip /m ² (kg/m ²)	8.8 $\pm$ 3.1	9.7 $\pm$ 3.2	7.8 $\pm$ 2.7**
FFM index (kg/ m ²)	13.4 $\pm$ 2.1	14.0 $\pm$ 2.1	12.8 $\pm$ 2.0**
TBW index (L/m ²)	10.1 $\pm$ 1.6	10.5 $\pm$ 1.5	9.6 $\pm$ 1.4**
FM index (kg/m ²)	5.1 $\pm$ 2.3	3.8 $\pm$ 1.5	6.6 $\pm$ 2.2**
ICW index (L/m ²)	5.4 $\pm$ 1.1	5.6 $\pm$ 1.1	5.1 $\pm$ 1.0**
ECW/ICW	0.90 $\pm$ 0.15	0.89 $\pm$ 0.15	0.92 $\pm$ 0.15
PA	5.5 $\pm$ 0.9	5.6 $\pm$ 0.9	5.3 $\pm$ 0.8*
Cm (n.Farad)	1.05 $\pm$ 0.38	1.2 $\pm$ 0.4	0.9 $\pm$ 0.3**
Cm /m ² (n.Farad/m ²)	0.41 $\pm$ 0.14	0.43 $\pm$ 0.15	0.39 $\pm$ 0.13*

MAMC: midarm muscle circumference; FFM: fat free mass; TBW: total body water; TBW: total body water; FM: fat mass; ICW: intracellular water; ECW: extracellular water; PA: phase angle, Cm: membrane capacitance, m²: height squared
Significant differences between males and females: * $P < 0.05$ ** $P < 0.001$

We compared Cm, PA and FFM index on the one hand with MAMC and Handgrip strength on the other hand. The best correlation was found between Cm and Handgrip strength ($r = 0.652$, $p < 0.001$) and between PA and handgrip measures and MAMC were good but lower than with handgrip strength (table 4). FFM index also significantly correlated with MAMC and handgrip strength but correlations were less significant than with Cm and PA (table 4).

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Table 4: Correlation coefficients (r) between anthropometric, laboratory data and BIA phase angle, membrane capacitance and FFM index

Parameters	Phase angle	Membrane capacitance	Fat free mass index
	r	r	r
Age	- 0.487**	- 0.316**	- 0.200*
% weight loss	- 0.235**	- 0.275**	- 0.310**
BMI	0.335**	0.422**	0.601**
MAMC	0.407**	0.522**	0.661**
Handgrip	0.607**	0.652**	0.509**
Albumin	0.359**	0.307**	0.146*
Protein	0.417**	0.362**	0.217**
Hemoglobin	0.397**	0.389**	0.323**
CRP	- 0.007	0.023	0.053
Lymphocyte	0.139*	0.126*	0.062

* $P < 0.05$; ** $P < 0.001$

BMI: body mass index

MAMC: midarm muscle circumference

CRP: C reactive protein

FFM : fat free mass

Impedance values PA, Cm, FFM index and ICW index, obtained in men correlated better with handgrip strength than values obtained in women (table 5). Similar differences between correlations in men and women were obtained for impedance values and MAMC (table 5). Serum albumin, protein and hemoglobin correlated with PA, Cm, FFM index and ICW index as shown in table 5. However, CRP and lymphocytes did not correlate with any of the BIS variables.

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Table 5: Correlation between anthropometric, laboratory data and BIA phase angle, membrane capacitance and FFM index in men and women

MALE				
PARAMETERS	Phase angle	Cm	FFM index	ICW index
	r	r	r	r
Age	-0.506**	-0.408**	-0.362**	-0.421**
% weight loss	-0.238 *	-0.323**	-0.396**	-0.368**
BMI	0.412**	0.567**	0.757**	0.692**
MAMC	0.526**	0.674**	0.660**	0.644**
MAMC/m ²	0.458**	0.515**	0.634**	0.601**
Handgrip	0.597**	0.640**	0.482**	0.558**
Handgrip/m ²	0.616**	0.631**	0.518**	0.591**
Albumin	0.412**	0.420**	0.243 *	0.316**
Protein	0.431**	0.373**	0.249 *	0.322**
Hemoglobin	0.428**	0.410**	0.326**	0.373**
CRP	-0.009	-0.004	-0.084	-0.017
Lymphocyte	0.132	0.123	0.068	0.108
FEMALE				
PARAMETERS	Phase angle	Cm	FFM index	ICW index
Age	-0.506**	-0.283 *	-0.067	-0.156
% weight loss	-0.317**	-0.397**	-0.355**	-0.280 *
BMI	0.415**	0.595**	0.752**	0.682**
MAMC	0.327**	0.546**	0.628**	0.558**
MAMC/m ²	0.295 **	0.466**	0.617**	0.550**
Handgrip	0.572**	0.542**	0.394**	0.430**
Handgrip/m ²	0.599**	0.548**	0.424**	0.460**
Albumin	0.316**	0.212**	0.060	0.104
Protein	0.434**	0.439**	0.229 *	0.252 *
Hemoglobin	0.339**	0.355**	0.309 **	0.314**
CRP	0.028	0.137	0.036	0.034
Lymphocyte	0.124	0.084	0.008	0.042

* $p < 0.05$

** $p = 0.001$

BMI: body mass index, MAMC: midarm muscle circumference, CRP: C reactive protein, Cm: membrane capacitance, FFM : fat free mass, ICW: intracellular water.

Values of Cm and PA exhibit fairly good correlations with albumin and handgrip strength when controlling for muscle mass (MAMC or FFM) for both sexes (table 6), but the correlation is better with absolute handgrip strength. This partial correlation between handgrip strength and Cm or PA controlled for MAMC was significantly stronger in females compared with males. The correlation between albumin and BIS variables also decreased by controlling for MAMC or FFM but to a lesser extent.

Table 6: Correlation matrix for albumin, handgrip strength, Cm and PA with and without correction for MAMC or FFM by partial correlation.

		Albumin		Handgrip strength	
	Control variables	Male	Female	Male	Female
Cm	No Control	0.42**	0.21*	0.64**	0.54**
	MAMC	0.34**	0.19*	0.43**	0.50**
	FFM	0.35**	0.19*	0.41**	0.50**
PA	No Control	0.41**	0.32**	0.60**	0.57**
	MAMC	0.33**	0.30**	0.43**	0.53**
	FFM	0.33**	0.28**	0.39**	0.42**

Cm: membrane capacitance, PA: phase angle, MAMC: midarm muscle circumference, FFM: fat free mass. (* $p < 0.05$ and ** $p < 0.005$).

In the patients in which MAMC and handgrip strength were below the cut-off values determined in the control group mean FFMI, Cm/m² and PA were lower than in patients with normal values both in males and females (table 7).

Table 7: Mean values of FFM index, Cm/m² and PA in patients with MAMC/m² and handgrip/m² below or above the lower cut-off values found in the control group. A: for men and B: for women.

A				
Men	FFM index	Cm/m ²	PA	
MAMC/m ²				
< limit	12.6 ± 1.6**	0.34 ± 0.11**	5.2 ± 0.8**	
≥ limit	14.9 ± 1.9	0.49 ± 0.14	5.9 ± 0.9	
Handgrip/m ²				
< limit	12.6 ± 1.7**	0.32 ± 0.10**	4.9 ± 0.8**	
≥ limit	14.4 ± 2.1	0.47 ± 0.15	5.8 ± 0.9	
B				
Women	FFM index	Cm/m ²	PA	
MAMC/m ²				
< limit	10.4 ± 1.2**	0.21 ± 0.09**	4.7 ± 0.8*	
≥ limit	12.9 ± 1.9	0.40 ± 0.13	5.3 ± 0.8	
Handgrip/m ²				
< limit	11.4 ± 2.0**	0.28 ± 0.14**	4.4 ± 0.8**	
≥ limit	13.0 ± 1.9	0.41 ± 0.13	5.5 ± 0.7	

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Significant difference between groups (* $p < 0.05$, ** $p < 0.005$). MAMC: midarm muscle circumference, FFM: fat free mass, Cm: membrane capacitance. PA: phase angle. The lower limits for MAMC/ m^2 and handgrip/ m^2 calculated from control group and used for men and women to classify them as well or malnourished.

Table 8 shows the sensitivity and specificity of FFM index, Cm/ m^2 and PA in classifying malnourished and well nourished patients with MAMC or handgrip strength as reference method. The sensitivity and specificity of Cm/ m^2 (73.6% and 72.3%, respectively) and PA (75.5% and 71.8%, respectively) when used with handgrip strength/ m^2 as reference method were higher than with MAMC/ m^2 as a reference. (For Cm/ m^2 : 70.0% and 72.1%, respectively; for PA: 58.3% and 68.8%, respectively).

Table 8: Sensitivity and specificity of FFM index, Cm/ m^2 and PA in classifying malnourished and well nourished patients based on MAMC/ m^2 and handgrip strength/ m^2 references.

	Sensitivity(%)	Specificity(%)
FFM index		
MAMC/ m^2 (reference)	72.1	70.7
Handgrip strength/ m^2 (ref.)	70.7	68.9
Cm/m^2		
MAMC/ m^2 (reference)	70.0	72.1
Handgrip strength/ m^2 (ref.)	73.6	72.3
PA		
MAMC/ m^2 (reference)	58.3	68.8
Handgrip strength/ m^2 (ref.)	75.5	71.8

MAMC: midarm muscle circumference, FFM: fat free mass, Cm: membrane capacitance. PA: phase angle.

Discussion

In this study we confirmed that BIS derived estimates of FFM correlate well with MAMC and BMI. More importantly, it was found in this study that Cm and PA correlated with MAMC and Alb, but most strongly with handgrip strength. With this finding we provided supportive evidence for the hypothesis that Cm and handgrip strength are not only influenced by body cell (muscle) mass but also by muscle function. In the literature very few data exist regarding Cm. Phase angle, however, has been demonstrated to be influenced by the relative contributions of fluid (resistance) and cellular membranes (capacitance) of the human body (30), (31). By definition, phase angle is positively associated with capacitance and negatively associated with resistance (30).

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Lower phase angles suggest cell death or decreased cell integrity, whereas higher phase angles suggest large quantities of intact cell membranes (31). In earlier studies we have shown that handgrip strength is not only influenced by muscle size but also by inflammation, because inflammatory activity decreases the ability to contract (29),(32),(33). In other areas of medicine this also has been demonstrated (34), (35). In view of the fact that muscle size and disease influence both handgrip strength and Cm in similar ways we investigated relationships between BIS derived variables and handgrip strength. The present study shows that there were good correlations between handgrip strength, and PA or Cm. In addition, MAMC was also positively associated with PA and Cm but the correlation coefficient was lower than for handgrip strength. Miki Nagano et al also reported a correlation between PA and MAMC in pediatric patients (36).

In the present study correlations between handgrip strength, and PA and Cm in men were significantly better than in women. When corrected for MAMC this correlation was still higher for men. This implies that other factors than muscle mass must influence muscle strength. Potential influences may be the fact that men perform more manual labour, and possibly are more inclined to do their best to perform well in a physical test than women. Finally hormonal differences may also influence muscle strength.

Among BIA parameters, we focused on PA because it can be obtained directly from resistance and reactance. Also, PA values can be obtained in patients whose weight and height cannot be measured. Moreover, it does not depend on regression equations, thereby eliminating a large source of random error.

Whether PA can be used as a nutritional assessment tool in hospitalized patients depends on its sensitivity and specificity. In an earlier study we found that SGA correctly identifies well nourished patient but overestimates the number of malnourished patients. Our data suggest that in fact PA and Cm perform just as well or even better than SGA. Some previous studies have tried to address this question. For example, Selberg et al showed that PA was higher in control subjects than in hospitalized patients. Schwenk et al (23) hypothesized that PA could be interpreted as a global marker of malnutrition in HIV-infected patients. In patients with liver cirrhosis, PA was speculated to be a marker of clinically relevant malnutrition characterized by both increased extracellular volume and decreased body cell mass (31). In the study of Ploumis Passadakis et al.(37) , it was found that there was a proportional decrease in PA with the severity of malnutrition determined by SGA. Similarly, Miki Nagano et al. (36) in one study of pediatric patients also found that malnourished patients showed lower PA than well nourished children. In another study in Brasil, Barbosa-Silva et al.(9) also showed that PA decreased significantly with worsening nutritional status according to SGA, which implies that BIA-PA is to some degree allows detection of changes in nutritional status. In patients with advanced colorectal cancer and with advanced pancreatic cancer, it was found that patients with higher PA had longer median survival time (24),(38). Our study showed that if we considered cut-off values of MAMC/m² and handgrip strength/m² of control group as references, not only PA, but also Cm and FFM index were significantly lower in the malnourished than in the well nourished group. PA is derived from single frequency BIA whereas membrane capacitance (Cm) is derived from multiple frequency BIS. Our

study showed that there was good correlation between PA and Cm. Unfortunately few data exist regarding Cm and the assessment of nutritional status. Theoretically Cm furnishes a better measure of the ability of the body to store an electric current, and should therefore be a better measure of the complex of total body cell membranes and their integrity. Indeed we found that Cm correlated as well or better than PA with MAMC and especially handgrip strength. The role of PA and Cm in assessing a composite of body cell mass and its integrity depends on their value to identify patients that are malnourished (low body cell mass: low MAMC) and have limited functional capacity (handgrip strength). Despite the fact that at the group level there is a highly significant correlation between these parameters, specificity and sensitivity were not high enough to detect an individual as being malnourished with high reliability. However, in comparison with the results obtained from validation of SGA with simple techniques to estimate muscle mass and function Cm (in BIS) or PA (in BIA) were as reliable or better than SGA. This conclusion only applies to the population of preoperative patients that we studied.

The value of PA at the group level is supported by the study of Maggiore Q (16) in renal failure patients, who also showed that post-hemodialysis PA appeared to be the best index of nutritional status, being significantly correlated with serum albumin and MAMC. In the study of Fein (39) it was also concluded that PA was correlated with all of the biochemical markers of nutrition, such as albumin and total protein. The value of FFM index in nutritional assessment has been confirmed by Pichard (40). He concluded that FFM index was significantly lower in patients than in control subjects. In our present study, FFM index was also significantly lower in the malnourished than in the well nourished group.

In the available literature no data exist regarding body composition analysis performed with BIS in Vietnam. The data obtained in the present study demonstrate that the value of BIA or BIS is as high or higher than SGA when used as a screening tool. To increase its performance more insight is necessary in the pathogenesis of malnutrition and the effects that pathophysiology has on electrophysiologic events occurring in health and disease.

Conclusion

Simple, quick objective measurements like BIS, handgrip strength, midarm muscle circumference can furnish a good indication of nutritional status. The advantage of these measures is that no complicated equations to calculate fat free mass and fat mass at the whole body level are required. Their value is strengthened by the possibility that they do not only furnish information regarding body composition but that they also may be risk factors for the development of infectious complications. These factors should therefore be taken into account when surgery is considered and should guide the surgeon in considering extensive aggressive or limited defensive surgery to diminish the occurrence of life threatening postoperative complications.

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General Discussion

CHAPTER 7

General discussion

General Discussion

Assessment of nutritional status

Assessment of nutritional state includes both subjective and objective measurements. However, no agreement exists with regard to the definition of malnutrition. Generally, malnutrition is defined as a state resulting from lack of uptake or intake of nutrition leading to diminished body weight and diminished function. Over the years, general agreement has developed that of the components of body weight especially Fat Free Mass (FFM) and more specifically cellular mass are the crucial determinants of nutritional state. Cells constitute the living active part of the organism and their size and integrity determine the health and ability of the organism to function properly. In health this means that the body feels well, is able to perform manual labour, can concentrate and perform intellectual labour. In acute disease, it implies that the body can generate an adequate healing response to the acute trauma or the acute illness.

The confusing issue in the definition is that it focuses on nutrition whereas shrinkage of cellular mass may also be caused by inflammatory activity. Almost without exception, malnutrition is the result of the combined action of overnutrition/undernutrition and inflammatory/infectious activity. Most children suffering from endemic malnutrition are infected with parasites or other microorganisms in the non-oedematous but especially in the oedematous malnourished groups. Malnutrition in these children very likely results from a vicious circle, including insufficient food intake, parasitic infection, inflammatory activity in the intestine, leading to diarrhoea and insufficient intake. In later stages inflammatory activity may continue without demonstrable parasitic infection.¹ Along the same lines chronic inflammatory diseases like rheumatoid arthritis, psoriasis, Crohn's disease, COPD, end stage renal failure also induce shrinkage of cellular mass, which cannot be completely countered by nutritional measures, but which contributes to the malnourished state.

The importance of inflammatory activity is supported by the fact that in many "nutritional risk indexes" both anthropometric data and inflammatory parameters are included, because they have been shown to be significantly correlated with the occurrence of complications, bad quality of life etc. The risk indexes that include inflammatory parameters have higher predictive power than when anthropometric data are taken alone²⁻⁸. The screening methods also include crude anthropometric measures as well as severity of disease, but the only true measurement consists of weighing (body weight; BW) and measuring height (meter) to calculate body mass index (BMI) expressed as kg/m². These screening methods include the assessment of the risk of insufficient food uptake and the degree of inflammation/ size of the operative trauma/ severity of disease. The view that diminution of the body cell mass (BCM) may result from combinations of insufficient nutrition and inflammatory activity has led to endeavours to include metabolism in the definition. It has also led to the practice to call patients depleted rather than undernourished. Depletion as a term to indicate loss of BCM has met some political resistance however because the term may obscure the notion that lack of sufficient

nutrition is a major factor, contributing to the depleted/ undernourished state, necessitating implementation of worldwide programs to supply sufficient food to the many populations at risk. Taking this into account, it may be preferable to maintain the term "Malnutrition". Another problem with "depletion" as definition is that overnutrition (more calories taken up than expended) is not included in the definition whereas "Malnutrition" includes both over- and undernutrition (fewer calories taken up than expended). In view of these considerations, malnutrition should be viewed as a situation in which body composition is abnormal and simultaneously in which there is diminished function.

Undernutrition (negative nutrient balance) leads to loss of adipose tissue but importantly also to loss of body cell mass. The amount of adipose tissue present is a major factor determining the duration of successful starvation during which body cell mass and protein can be spared, and consequently determining the duration of survival. When more adipose tissue is available, more fat will be lost and less body cell mass.⁹ Loss of body cell mass diminishes the ability to respond adequately to trauma or disease. It is difficult to acquire a reliable measure of body cell mass in practice, especially because in starvation, severe obesity and even more so in disease the ratio BCM/FFM and also the ratio tissue solids/tissue water (normally 27/73%) substantially decrease.¹⁰⁻¹⁴ Consequently many data on FFM, relying on the assumptions that these ratios are stable in starvation/obesity/disease overestimate BCM and tissue solids, which represent the active metabolizing part of the body. In spite of the fact that FFM may overestimate the amount of tissue solids, low FFM/Height² remains a significant predictor of mortality in logistic regression analyses in many populations.¹⁵⁻¹⁷

The above mentioned description of malnutrition emphasizes that function should be diminished. The changes in body composition should have interfered with normal function (muscle, cognitive, immune function). When weight loss is modest or if there are only slight losses of body fat mass, this may not be the case and the weight loss and the changes in body composition are irrelevant. Function may also be compromised by inflammatory activity, already present before the new trauma or disease. Inflammatory activity of longer duration leads also to shrinkage of body cell mass, specifically muscle mass. However, the presence of inflammatory activity also interferes independently with the ability to recover successfully from trauma or disease.¹⁸⁻²² Inflammatory activity also diminishes quality of life, longevity, physical mobility²²⁻³⁵, as well as the ability to cope successfully with exogenous noxious influences (acute disease, trauma).^{5, 36-38}

Patients lose BCM and are in a negative protein balance after (surgical) trauma. When they do not recover well for instance due to infection, they continue to lose BCM and become malnourished. In this situation the inflammatory state persists and the body will not respond well to a renewed or ongoing challenge (second hit).³⁹⁻⁴³

If patients recover well from the inflammatory response they develop polyuria and a negative fluid balance (decreasing body weight as a sign of shrinking extracellular water), their plasma albumin increases, edema is lost, they improve clinically, and plasma Na, Hb, Alb increase. If recovery of surgical trauma is successful, these clinical signs start occurring approximately 3 days after operation. After prolonged periods of sepsis the

turning point is only reached when sepsis is adequately cleared, but the recovery process develops much slower and may require months to a year.

The fact that inflammatory markers in most nutritional risk indexes ^{2-7, 44} improve the sensitivity/specificity of indexes predicting the risk of malfunction (e.g. infectious complications) has led to the practice of naming them nutritional markers, which they are not since they do not adequately reflect body composition. However, when there is chronic inflammatory activity the body becomes catabolic and body cell mass (especially muscle mass) decreases, which explains why there is generally a crude correlation between inflammatory parameters and parameters for body composition. ¹⁰ After acute trauma or disease, inflammatory parameters may be elevated but cell mass may still be relatively normal. On the other hand, due to insufficient uptake or intake of food, but only modest inflammatory activity, substantial amounts of body cell mass may have been lost while inflammatory parameters are only mildly elevated.

The strong negative predictive value of these inflammatory parameters with regard to an adequate immune/host response results from the fact that the body responds less well in the presence of inflammatory activity, still present after an earlier stressful event (“second hit” phenomenon; see above), even when body cell mass is still well preserved. In clinical practice, this may explain why patients that are re-operated within 24–48 hours after the first operation tolerate this second surgical trauma relatively well, whereas after longer intervals between the first operation and the re-operation, patients are more prone to heal badly and to develop infectious complications. Similarly, an infection occurring in the post-traumatized state may have much more deleterious consequences (multiple organ failure) than when the infection occurs (as a first hit) in a metabolically stable situation. ^{39-43, 45}

Regardless of how malnutrition is described, adequacy of function should be considered as the most important factor, determining the quality of defence mechanisms of the organism and quality of life. In conclusion, it should be born in mind that several different factors may influence body composition and function. ^{39-43, 45}

How to separate the influence of changes in body composition from the effect of inflammatory activity?

In this thesis we tried to separate the influence of changes in body composition from the influence of inflammatory activity on clinical outcome. We found that, as usual, measures of body composition were significantly different between patients developing infectious complications and those that did not. Especially the difference in loss of body weight (BW), midarm muscle circumference (MAMC), and handgrip strength were highly significant just as values of BIA/BIS (FFM index, ICW index, phase angle, membrane capacitance). In the multivariate analysis loss of BW and handgrip strength remained significant. In this model PA and Cm did not add to the model once handgrip strength was incorporated.

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Interestingly in this patient group albumin did only show a trend as a predictor whereas in many studies it had a significant predictive effect with regard to infectious outcome.⁴⁶⁻⁴⁸ This may be explained by the fact that the range of albumin levels was rather small. Handgrip strength scored better than MAMC but correlated well with albumin levels especially when handgrip strength was expressed per unit of muscle mass, namely MAMC. It follows that in the presence of low Albumin levels, muscle is less strong than in its absence. This is confirmed in studies in neurobiology^{26,49}.

On the basis of these findings we propose that the high predictive value of handgrip strength results from the fact that this measure is determined by at least two factors: muscle size and inflammatory activity. This explains its high predictive value with regard to the development of infectious complications. Many studies also showed that handgrip strength has been used successfully to predict postoperative complications and mortality.⁵⁰⁻⁵⁵

Interestingly in our patient cohort, women were less strong than men when strength was controlled for size. Apart from a true gender difference, this may also be explained by other factors like for instance men performing more manual labour. Also the correlations between handgrip strength and MAMC were much less strong in women than in men. Comparable findings have been found in patients with renal disease.⁵⁶ Muscle force was much less influenced by inflammatory activity in women than in men.

It is possible that phase angle (PA) and membrane capacitance (Cm) would score as well or better than handgrip strength as predictors of infection. This requires somewhat more sophisticated equipment, which not every hospital would want to purchase. Importantly PA does not require any body measure and Cm only body length. A practical advantage of handgrip strength is that the equipment to measure it, is cheap and easy to purchase. In addition, little training is required to achieve good reproducibility.

Our study showed that not only PA, but also Cm was significantly lower in the malnourished than in the well nourished group. Theoretically, Cm furnishes a better measure of the ability of the body to store an electric current, and should therefore be a better measure of the complex of total body cell membranes and their integrity.

The fact that PA and Cm are significantly different between groups with and without complications agrees with the high predictive value of handgrip strength because these BIA/BIS parameters are also very much dependent on cell mass and inflammatory activity. PA has indeed been found by other authors to be a risk factor for the development of postoperative complications.⁵⁷⁻⁵⁹ Few data exist regarding Cm and the assessment of nutritional status. When using BIS, further studies addressing the potential value of Cm as a risk factor are needed.

Malnutrition in Vietnamese hospitalized surgical patients

In Vietnam, a very limited number of surveys has been reported regarding the assessment of nutritional status. In the adult population, nutritional factors have been published, including dietary intake, food consumption pattern, and macronutrient intake. Nutritional status of middle-aged Vietnamese in Ho Chi Minh City has been assessed and body mass index has been used in the assessment of adults in Vietnam.⁶⁰⁻⁶⁴ In the paediatric population, surveys have been produced addressing rates of malnutrition and micronutrient status of primary school girls.⁶⁵⁻⁶⁷ No reports are available regarding malnutrition in hospitalized patients. In all hospitals of this country, nutritional assessment was not a routine part of the work-up of patients, scheduled for surgery. We therefore conducted these studies. The present study is the first to perform SGA, to evaluate the role of anthropometry and handgrip strength, and to use BIS in the assessment of nutritional state in hospitalized patients.

Although we had anticipated that the prevalence of malnutrition in hospitalized patients in Vietnam would be high, the incidence found (55.7%) was higher than we expected. Awareness should be increased among surgeons, who plan surgery for this patient population, because undernutrition may lead to an increase in postoperative infectious complications. Better insight in the risks involved while performing operations in malnourished patients may change the surgical approach, diminishing the incidence of complications. Application of SGA, handgrip strength, and bioelectrical impedance spectroscopy in surgical patients is feasible in Vietnam.

Screening methods are increasingly applied in developed countries.^{68,69} True assessment of nutritional state can be performed by assessing muscle force, inflammatory activity (albumin levels), and body composition (anthropometry). A crucial question to ask is whether the patient has lost weight in view of the fact that we found that this is a strong predictor of the development of complications. It is necessary to be aware of these risk factors, and to perform a good clinical examination for loose skin, oedema etc and then relate the values obtained to control values. In this study, we have focused on muscle function. There is no consensus how to measure muscle force, and it is important to achieve consensus how to acquire reliable measures for muscle force but also for immune function and cognitive function. These last two functions were not addressed in this thesis.

Recommendations for the future

Because of very high prevalence of malnutrition in hospitalized surgical patients and the high incidence of postoperative infectious complications in severely malnourished patients, application of methods for nutritional screening and risk assessment for not only

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inpatients but also outpatients should preferably be done routinely in all hospitals in Vietnam. Subsequently, preoperative nutritional intervention should be considered for malnourished patients that are about to undergo abdominal surgery. In addition, surgeons should adapt their surgical strategy in patients that are malnourished, including limiting the risk and the size of the operative trauma.

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SUMMARY

The prevalence of malnutrition of hospitalized patients is still very high in every country in the world and especially in developing countries. A compromised nutritional state has adverse effects on recovery and increases postoperative morbidity and mortality. Therefore, early diagnosis and treatment of the malnourished state can improve the quality of treatment.

There are several methods of assessing nutritional status of hospitalized patients. However, each method has its advantages and limitations. No method has been proved to be superior and to be applicable in all clinical settings. The question is raised which method or which combination of methods identifies patients at risk to develop postoperative complications best. At present, no studies regarding subjective global assessment (SGA), handgrip strength and bioelectrical impedance spectroscopy (BIS) in Vietnamese patients have been published.

The aims of the studies presented in this thesis were to investigate the prevalence of malnutrition in elective abdominal surgical patients in Vietnam, to determine the relationship between preoperative nutritional status and postoperative infectious complications of major abdominal surgery, and to compare SGA with anthropometry, handgrip strength, laboratory measures and BIS.

Prevalence of malnutrition in Vietnamese surgical patients

In a population of 438 patients who underwent abdominal operations (chapter 2) the prevalence of malnutrition was 55,7% rated by SGA. If only patients who underwent major abdominal operations were taken into account (274 patients), the prevalence of malnutrition was 77.7%. It is concluded that SGA yields a high rate of malnutrition in surgical patients in Vietnam.

Malnutrition and infectious complications

In the patients undergoing major abdominal surgery (chapter 2) the rate of postoperative infectious complications was higher in patients classified as SGA class C (33.6%) than patients classified as class A (6%) and B (11%). We concluded that malnutrition was associated with an increase in infectious complications.

Risk factors of infectious complications

Handgrip strength m^2 and percentage weight loss were found to be the most important nutritional risk factors for the development of postoperative infectious complications in abdominal surgical patients (chapter 3). Although C/m^2 and PA are significantly different between the patients that develop infectious complications and those that do not, they do not add to the model once handgrip strength has been incorporated. These findings are fortunate because percentage weight loss and handgrip strength can be easily obtained without high costs all around the world.

SGA and measures for muscle mass and strength

In chapter 4 we compared SGA of nutritional status with objective anthropometric and functional measurements that were found to be the best predictors of poor outcome (chapter 3). We found that the SGA correctly identifies patients with normal muscle mass and strength. However a substantial number of patients rated SGA B or C have normal muscle mass and strength. An additional finding was that muscle strength is not only positively associated with muscle mass but also negatively with inflammatory activity.

The value of bioelectrical impedance spectroscopy in assessing nutritional status of Vietnamese surgical patients

In chapter 5 we aimed to validate BIS in healthy volunteers with indicator dilution methods (deuterated water and bromide). Good correlations were found between BIS and TBWdil ($r = 0.892$, $p < 0.001$) and BIS and ECWdil ($r = 0.769$, $p < 0.001$). Similar correlations were found ($r = 0.850$, $p < 0.001$) when equations of Deurenberg derived from a Singapore Asian population were applied to the outcome of our BIS measures. However, BIS underestimated TBW (4 L) and overestimated ECW (2.1 L) compared with the dilution methods. On the basis of these discrepant results and values for TBWdil as percentage of BW higher than 73% in three patients we conclude that evaporation of the water in the indicator mixture may have occurred in some indicator mixtures.

Relationship between BIS variables and conventional measures of nutritional state

In chapter 6, the relationship between different BIS variables (fat free mass (FFM), fat mass (FM), fluid volumes, phase angle (PA), membrane capacitance (Cm) on the one hand and anthropometric, biochemical and functional variables on the other hand was evaluated patients before surgery. In view of the fact that handgrip strength was found to be the best predictor of postoperative infectious morbidity we used handgrip strength as the predominant reference value. We found that the best correlation was found between Cm and handgrip strength ($r = 0.652$, $p < 0.001$) and between PA and handgrip strength ($r = 0.607$, $p < 0.001$).

Conclusion

We conclude that several simple, quick objective measurements like BIS and handgrip strength furnish a good indication of nutritional status. The advantage of these measures is that no complicated equations are required to calculate fat free mass and fat mass at the whole body level. Handgrip strength and preoperative weight loss as the best predictors of postoperative infectious complications, furnish easily accessible tools to estimate risks in surgery.

Samenvatting

Ondervoeding komt overal ter wereld veel voor en zeker in ontwikkelingslanden. Het woord ondervoeding is een minder goede term dan het Engelse “malnutrition” om twee redenen. In de eerste plaats houdt het Engelse woord zowel overvoeding als ondervoeding in. In de tweede plaats suggereert het Nederlandse woord “ondervoeding” dat er louter sprake is van een negatieve nutriënt balans. In werkelijkheid is “ondervoeding” praktisch altijd het gevolg van een negatieve nutriëntbalans en van ontstekingsactiviteit als gevolg van ziekte, trauma, stress etc. Daar in het Nederlandse spraakgebruik “malnutritie” een ongewone term is, wordt “ondervoeding” als benaming van “malnutritie” gebruikt.

Ondervoeding heeft negatieve effecten op het resultaat van behandeling, leidt tot een verminderde kwaliteit van leven, en tot verhoogde morbiditeit en mortaliteit. Het is daarom van belang ondervoeding snel op te sporen en zo mogelijk te behandelen.

Er zijn verschillende manieren om de voedingstoestand van patiënten vast te stellen. Al deze methoden hebben echter hun voor- en nadelen. Geen enkele methode heeft echter bewezen superieur te zijn en toepasbaar in alle mogelijke situaties. Het is de vraag welke methode zich het beste leent om bij patiënten die operaties moeten ondergaan het voedinggerelateerde risico vast te stellen om postoperatieve complicaties te krijgen.

Subjective Global Assessment (SGA), spierkrachtmetingen (handknijpkracht) en Bioimpedantie metingen zijn nooit eerder in Vietnam bij klinische patiënten verricht.

Het doel van de studies, beschreven in dit proefschrift, was om de prevalentie van ondervoeding vast te stellen bij Vietnamese patiënten die electieve buikoperaties moesten ondergaan. Tevens was het de bedoeling de gevolgen vast te stellen van de preoperatieve voedingstoestand voor postoperatieve infecties, en om vast te stellen in hoeverre SGA als screeningsmethode de voedingstoestand juist inschat, vergeleken met anthropometrie, handknijpkracht, laboratoriumgegevens en biopedantiemeting.

Prevalentie van ondervoeding in Vietnamese chirurgische patiënten

De prevalentie van ondervoeding bij 438 patiënten die buikoperaties ondergingen (hoofdstuk 2) bedroeg 55.7%, gemeten met SGA. Bij de patiënten die alleen grote buikoperaties ondergingen (274 patiënten), werden 77.7% geclassificeerd als ondervoed. Deze prevalentie is hoger dan in het algemeen gepubliceerd is. Het is mogelijk dat dit het gevolg is van het feit dat in dit deel van Vietnam ondervoeding endemisch is.

SGA en postoperatieve infecties

Het percentage postoperatieve infecties was hoger bij de patiënten die geclassificeerd werden in SGA klasse C (33.6%) dan bij patiënten in SGA klasse A (6%) en B (11%). Met name in patiënten in SGA klasse C is de kans op postoperatieve infecties sterk verhoogd. Er zijn geen belangrijke verschillen tussen patiënten in klasse SGA A en B.

Voedingsgerelateerde risicofactoren en postoperatieve infecties

Handknijpkracht/m² en percentage gewichtsverlies zijn de belangrijkste metabole risicofactoren voor het ontstaan van postoperatieve infecties (hoofdstuk 3). Hoewel Cm/m² en PA verschillen tussen patiënten die complicaties ontwikkelen en patiënten die een ongecompliceerd postoperatief beloop hebben, voegen zij niet toe aan het model, als handknijpkracht in het model is opgenomen. Dit is een gelukkige bevinding omdat percentage gewichtsverlies en handknijpkracht gemakkelijk vastgesteld kunnen worden zonder grote financiële kosten. Zij kunnen daarom wereldwijd worden toegepast.

SGA, spiermassa en spierkracht

In hoofdstuk 4 is SGA van de voedingstoestand vergeleken met anthropometrie en metingen van functie, die de belangrijkste risicofactoren bleken te zijn in het onderzoek beschreven in hoofdstuk 3. Het bleek dat SGA patiënten correct identificeert met normale spiermassa en spierkracht. Echter, een belangrijk deel van de patiënten, geklassificeerd in SGA klasse B en C, bleken een normale spiermassa en spierkracht te hebben. Spierkracht bleek niet alleen positief geassocieerd te zijn met spiermassa maar ook met het plasma-albumine als maat voor inflammatoire activiteit.

De waarde van BIS voor het bepalen van de voedingstoestand van Vietnamese chirurgische patiënten

In hoofdstuk 5 zijn de resultaten beschreven van validering van BIS met indicator-verdunningsmethoden in gezonde vrijwilligers (gedeuteerd water en bromide). Goede correlaties werden gevonden tussen BIS en TBWdil ($r = 0.892$, $p < 0.001$) en BIS en ECWdil ($r = 0.769$, $p < 0.001$). Vergelijkbare correlaties werden gevonden ($r = 0.850$, $p < 0.001$) als de formules van Deurenberg werden toegepast op de uitkomst van de BIS metingen. BIS onderschatte totaal lichaamswater (TBW) echter (4 liter) en overschatte extracellulair water (ECW) (2.1 liter) vergeleken met de verdunningsmethoden. Op basis

van waarden voor TBW die hoger zijn 73% van het actuele lichaamsgewicht in drie patiënten concluderen we dat verdamping van water uit het indicatormengsel plaats moet hebben gevonden.

Relatie tussen BIS variabelen en conventionele metingen van de voedingstoestand

In hoofdstuk 6 werd de relatie onderzocht tussen verschillende BIS variabelen vetvrije massa (FFM), vetmassa (FM), vloeistof volumina, fasehoek (PA), membraan capacitantie (Cm) enerzijds en anthropometrische, biochemische en functionele variabelen anderzijds. Patienten werden geëvalueerd voor operatie. Daar handknijpkracht de beste voorspeller van postoperatieve infecties bleek te zijn, gebruikten we handknijpkracht als de belangrijkste referentiewaarde. De beste correlatie werd gevonden tussen Cm en handknijpkracht ($r = 0.652$, $p < 0.001$) en tussen PA en handknijpkracht ($r = 0.607$, $p < 0.001$).

Concluderend geven BIS uitkomsten zoals PA en Cm, en handknijpkracht een goede indruk van de functionele status van de patiënt. Afhankelijk van de definitie voor ondervoeding kunnen BIS en handknijpkracht ook beschouwd worden als maat voor de voedingstatus. Het voordeel van deze metingen is dat geen ingewikkelde berekeningen hoeven te worden uitgevoerd om vetvrije massa en vetmassa te berekenen. Handknijpkracht en preoperatief gewichtsverlies zijn de beste voorspellers van postoperatieve infectieuze complicaties en zijn overal ter wereld eenvoudig te bepalen.

TÓM TẮT

Tỷ lệ mắc bệnh suy dinh dưỡng trong số bệnh nhân nhập viện điều trị nội trú vẫn còn rất cao ở mọi nước trên thế giới, đặc biệt ở các nước đang phát triển. Suy dinh dưỡng làm chậm quá trình hồi phục và làm gia tăng tỷ lệ biến chứng cũng như tỷ lệ tử vong sau mổ. Vì vậy, chẩn đoán và điều trị sớm tình trạng suy dinh dưỡng có thể cải thiện được chất lượng điều trị.

Có một số phương pháp đánh giá tình trạng dinh dưỡng của bệnh nhân. Tuy nhiên, mỗi phương pháp đều có ưu điểm và giới hạn của nó. Chưa có phương pháp nào chứng tỏ được tính ưu việt vượt trội và có thể áp dụng cho mọi tình huống lâm sàng. Vấn đề đặt ra là phương pháp nào hoặc sự kết hợp của những phương pháp nào có thể nhận biết được một cách chính xác nhất những bệnh nhân có nguy cơ bị biến chứng sau mổ. Hiện nay, chưa có công trình nghiên cứu nào được công bố về phương pháp đánh giá lâm sàng toàn diện (SGA, subjective global assessment), phương pháp đo lực cơ cơ bàn tay (handgrip strength) và đo phổ trở kháng sinh điện học trên bệnh nhân Việt Nam.

Mục tiêu của những nghiên cứu trình bày trong luận án này là khảo sát tỷ lệ mắc bệnh suy dinh dưỡng trên bệnh nhân Việt Nam được mổ chương trình về bụng, xác định mối tương quan giữa tình trạng dinh dưỡng trước mổ và xuất độ biến chứng nhiễm trùng sau phẫu thuật lớn về bụng, và so sánh phương pháp đánh giá lâm sàng toàn diện với phương pháp nhân trắc học, phương pháp đo lực cơ cơ bàn tay, các phương pháp xét nghiệm và phương pháp đo phổ trở kháng sinh điện học (BIS).

Tỷ lệ mắc bệnh suy dinh dưỡng của bệnh nhân ngoại khoa Việt Nam

Trong tổng số 438 bệnh nhân được phẫu thuật bụng (chương 2) tỷ lệ suy dinh dưỡng theo phương pháp đánh giá lâm sàng toàn diện là 55,7%. Nếu chỉ tính số bệnh nhân mổ đại phần (274 bệnh nhân), tỷ lệ suy dinh dưỡng là 77,7%. Có thể kết luận rằng phương pháp đánh giá lâm sàng toàn diện đã phát hiện tỷ lệ mắc bệnh suy dinh dưỡng của bệnh nhân ngoại khoa Việt Nam là rất cao.

Suy dinh dưỡng và biến chứng nhiễm trùng

Trong số bệnh nhân được mổ đại phần (chương 2) xuất độ biến chứng nhiễm trùng sau mổ cao hơn hẳn trong suy dinh dưỡng mức độ C (33,6%) so với mức độ A (6%) và mức độ B (11%). Chúng tôi kết luận rằng suy dinh dưỡng sẽ đi kèm với nguy cơ gia tăng về biến chứng nhiễm trùng sau mổ.

Các yếu tố nguy cơ của biến chứng nhiễm trùng

Lực cơ cơ bàn tay/ m^2 và tỷ lệ % sụt cân là những yếu tố nguy cơ dinh dưỡng quan trọng nhất dự đoán khả năng xảy ra biến chứng nhiễm trùng sau phẫu thuật bụng (chương 3). Mặc dù Cm/m^2 và góc phase (PA) có sự khác biệt có ý nghĩa giữa bệnh nhân bị biến chứng nhiễm trùng so với bệnh nhân không bị biến chứng nhiễm trùng, nhưng hai yếu tố này bị loại ra khỏi biểu mẫu thống kê khi đưa lực cơ cơ bàn tay vào biểu mẫu thống kê. Những kết quả này là điều may mắn vì tỷ lệ % sụt cân và lực cơ cơ có thể dễ dàng thu thập được ở mọi nơi trên thế giới mà không phải tốn kém nhiều.

Phương pháp đánh giá lâm sàng toàn diện và các phương pháp đo khối cơ và lực cơ

Trong chương 4 chúng tôi so sánh SGA với các phương pháp đo nhân trắc và đo chức năng - phương pháp đã được chứng minh là yếu tố tiên đoán tốt nhất về kết quả sau mổ (chương 3). Chúng tôi phát hiện ra rằng SGA có thể nhận biết chính xác tình trạng dinh dưỡng của những bệnh nhân có khối cơ và lực cơ cơ bình thường. Tuy nhiên, vẫn có một số bệnh nhân được phân loại có mức độ B và C vẫn có khối cơ và lực cơ cơ bình thường. Lực cơ cơ không chỉ tỷ lệ thuận với khối cơ mà còn tỷ lệ nghịch với hoạt tính viêm.

Giá trị của phương pháp đo phổ trở kháng sinh điện học trong việc đánh giá tình trạng dinh dưỡng của bệnh nhân ngoại khoa Việt Nam

Trong chương 5, chúng tôi nghiên cứu BIS trên người tình nguyện Việt Nam khỏe mạnh với tiền chuẩn vàng là phương pháp pha loãng chất chỉ thị nước trung tính và bromide). Chúng tôi ghi nhận có mối tương quan tốt giữa thể tích nước toàn phần và thể tích nước ngoại bào của phương pháp BIS và phương pháp pha loãng ($r = 0.892$, $p < 0.001$) và ($r = 0.769$, $p < 0.001$). Tương tự, mối tương quan tốt cũng đã được tìm thấy khi áp dụng các phương trình của Deurenberg nghiên cứu từ người Singapore gốc Á với phương pháp BIS của chúng tôi ($r = 0.850$, $p < 0.001$). Tuy nhiên, khi so sánh với các phương pháp pha loãng, BIS đã tính hụt thể tích nước toàn phần (dưới 1 lit) và tính thừa thể tích nước ngoại bào (quá 2.1 lit). Với những kết quả hơi trái ngược này và kết quả thể tích nước toàn phần của phương pháp pha loãng lại cao hơn cân nặng thực tế trên một số người tình nguyện, chúng tôi kết luận rằng sự bốc hơi nước từ hỗn hợp chất chỉ thị rất có thể đã xảy ra.

Trong chương 6, trước phẫu thuật chúng tôi đánh giá mối liên hệ giữa các thông số khác nhau của phương pháp BIS: khối cơ (FFM), khối mỡ (FM), thể tích dịch, góc pha (PA), capacitance màng tế bào (Cm) với các thông số của phương pháp đo nhân trắc, sinh hóa và chức năng. Với kết quả nghiên cứu trước đó ghi nhận lực cơ cơ bàn tay là yếu tố tiên đoán tốt nhất khả năng xảy ra biến chứng nhiễm trùng, chúng tôi lấy sức cơ cơ bàn tay làm giá trị đối chiếu chính. Chúng tôi phát hiện ra rằng mối tương quan tốt nhất xảy ra giữa Cm và sức cơ cơ bàn tay ($r = 0.652$, $p < 0.001$) và giữa góc pha và sức cơ cơ bàn tay ($r = 0.607$, $p < 0.001$).

Chúng tôi kết luận các phương pháp đo khách quan, nhanh chóng, đơn giản như BIS và sức cơ cơ bàn tay đánh giá được tình trạng dinh dưỡng. Tính tiện lợi của các phương pháp này là không phải cần đến những phương trình phức tạp để tính khối mỡ không mỡ, khối mỡ của cơ thể. Sức cơ cơ bàn tay và tỷ lệ phần trăm sụt cân trước mổ - những yếu tố tiên đoán tốt nhất biến chứng nhiễm trùng có thể dễ dàng thực hiện được để tiên đoán các nguy cơ trong phẫu thuật tiền thể giới.

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Pham Van Nang was born on December 18, 1962 in Thai Binh, Vietnam. In 1980 he graduated from high school at Nguyen Trung Truc High School, Kien Giang. He began studying medicine at Can Tho University School of Medicine from 1981 and graduated in 1987 with distinction and received a MBBS (Bachelor of Medicine and Bachelor of Surgery). From October 1987 to July 1991 he started his internship training at the Surgical Department of Ho Chi Minh City University of Medicine and Pharmacy (Head and Vice Head: Prof. Dr. Truong Cong Trung , Prof. Dr. Nguyen Dinh Hoi). From September 1991 to January 1996 he worked as both a lecturer at Can Tho University School of Medicine and an abdominal surgeon in Can Tho General Hospital, Can Tho City, Vietnam. From February 1996 to February 1997 he worked as clinical and research fellow at Flinders Medical Centre, Adelaide, Australia (Head: Prof. Dr. James Tooli). Since March 1997 to now he is both a lecturer of Department of Surgery at Can Tho University of Medicine and Pharmacy and an abdominal surgeon in Can Tho General Hospital, Can Tho City, Vietnam. Since 2002 he conducted a study in a “sandwich program” on nutrition in Vietnamese surgical patients with supervision of Prof. Dr. Peter B. Soeters and Prof. Dr. Jan Willem Greve from Maastricht University, The Netherlands.