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ORIGINAL ARTICLE

Acute Postoperative Changes in Body Composition and Muscle Function Among Patients with Pancreatic Cancer Undergoing Pancreaticoduodenectomy

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ABSTRACT

AIM: To observe changes in the nutritional status of patients during the acute postoperative days following pancreaticoduodenectomy and to evaluate their influence on postoperative complications.

METHODS: Nutritional status was assessed in 72 patients on the preoperative day before surgery and postoperative days (PD) 3 and 8, included measurements of body composition by bioimpedance impedance analysis, biochemical values and muscle function by maximum handgrip strength (HGS). The presence of postoperative complications was collected over 30 post operative days. Changes at PD were calculated for all variables. Non-parametric statistics were used and results are given as median (25^{th}–75^{th} quartiles).

RESULTS: Significant changes occurred on PD 3 in body weight +2.3 (0.8–3.6) kg, total body water +2.8 (1.1–5.9) l, extracellular water +2.5 (1.2–3.7) l, intracellular water +1.1 (-0.4–1.9) l, phase angle -1.0 (-1.2 to -0.7)°, C-reactive protein +58.0 (36.0–100.8) mg/l, serum albumin -12 (-16.5 to -10.0) g/l, and HGS -4.8 (-7.3 to -3.0) kg. Higher but no significant changes were observed at PD 3 in patients with postoperative complications (n=28) compared to those without (n=44). The hospital stay was longer in patients with complications (12.5 days, p=0.005).

CONCLUSION: Changes in body composition, biochemical values and muscle function were observed during the first 8 PDs. Changes at PD 3 did not influence significantly the outcomes, but trends in body fluids and phase angle were found among patients with postoperative complications.

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States and Europe[1] and the 5-year survival rate after diagnosis is from 8.5 to 55%, depending on the tumour stage and type[2]. Pancreatic surgery is performed to

Conflict of Interest: none declared

treat patients suffering from various benign and malignant diseases such as pancreatic cancer, pancreatic cystic lesions and chronic pancreatitis and it differs according to the location of the lesion[3]. The Whipple procedure (WP), also known as pancreaticoduodenectomy (PD), is the standard operative technique performed for diseases involving the head of the pancreas or adjacent regions. Pancreatic cancer patients undergoing surgery have a median survival of 27 months, and a 3-year survival of 37%[4,5]. Patients with neoplastic or inflammatory disease of the pancreas have difficulties to digest all the nutrients in the food, and consequently, are more likely to be nutritionally depleted and to have lost weight when undergoing surgery[6]. The prevalence of malnutrition among patients submitted to surgery is high, ranging from 35 to 60% according to the criteria used, and it is associated with poor clinical outcomes[7]. Malnutrition affects body composition, skeletal muscle metabolism and alters skeletal and respiratory muscle functions. However, it is known that major surgical procedures have an additional negative impact on nutritional status[8]. Patients after pancreatic resections are at risk to develop long-term nutrition-related side effects, including alterations of gastrointestinal and hepatic function, glucose control, lack of pancreatic enzymes and malnutrition risk[2,9]. In addition, the complex nature of pancreatic operation makes it a high-risk and technically demanding major abdominal procedure, thus resulting in early pathophysiological alterations[10]. Early changes of body composition and function may be of big clinical significance and may provide a more direct measurement of surgical effects. Nevertheless, little work is available on the early nutritional status following pancreatic resections. Few authors reported small changes in body composition such as body weight increase, fluid accumulation and fat reduction, alteration in biochemical values as well as impaired function of respiratory and skeletal muscles in the short time after pancreatic surgery[11,12].

The assessment of the nutritional status should be included routinely in perioperative care of patients undergoing pancreatic surgery and several methods have been proposed. Beside the common body weight change and biochemical markers, recent works have suggested the usefulness of body composition measurements in the evaluation of nutritional status among surgical patients and in the prediction of outcomes[13]. Bioimpedance technique has been appreciated as a bedside approach, easy to use in hospital environments[14] and is based on the physical property of the body to conduct electrical current[12]. In particular, bioimpedence analysis (BIA) has a better ability to measure volume variations over a short period of time in case of fluid imbalance[14], which is common among severely ill and surgical patients[15]. The phase angle (PA) is an important clinical parameter measured by BIA that expresses cellular health status, including membrane capacitance, integrity, function, body cell mass, permeability and hydration[16]. This value has been recently considered as an important indicator for nutritional status as well as prognostic factor in several clinical situations[17] and normal values were defined as ≥5° for men and ≥4.6° for women[18]. Furthermore, other studies have shown that measurements of involuntary muscle function by maximum handgrip strength (HGS) were valuable indicators of nutritional status as well as predictors of operative outcomes[6]. The inclusion of this information as part of the nutritional assessment has also been suggested by ESPEN[19]. Therefore, in the current study measurements of body composition, biochemical values and muscle function were used to assess the pre and postoperative nutritional status of patients.

Nowadays, improvements in surgical techniques and perioperative management of patients undergoing pancreatic resections has reduced the postoperative death rate to less than 5%[13]. However, morbidity remains high with about 45-50% of patients developing complications after PD[11]. The most common complications following pancreatic surgery are delayed gastric emptying with a prevalence of 20-50% and pancreatic fistula occurring in 10-30% of cases. Bleeding is another quite common complication in 2-16% of cases, while abscess and pancreatitis have an incidence of 6 and 2-3% respectively (2). The occurrence of those complications has a big impact on the recovery, length of hospital stay (LOS) and survival[20]. Some authors emphasized the importance of identifying factors that could influence the risk of complications and mortality. In particular, limited surgical experience, greater age, extended resection and soft pancreatic texture are some of the identified independent risk factors for morbidity and mortality following PD. In addition, it has been reported that alterations in body composition following surgery had increased this risk[10]. Malnutrition, perioperative hypoalbuminemia, preoperative weight loss, high or low body mass index (BMI), high FM and especially high volume of visceral fat, low FFM and low PA have been recognized as potential risk factors[17,21,22]. Body fluid excess can also predispose the patients to tissue oedema and anastomotic leakage, thus increasing the risk for postoperative complications and longer LOS[23]. However, the role of nutritional status in the development of postoperative complications remains unclear and controversial[24].

Provision of more knowledge to the current literature on perioperative nutritional status of pancreatic surgical patients is of clinical importance to create and/or improve specific perioperative care and management as well as multimodality treatment plan and, consequently, to improve patients quality of life[25]. Therefore, the aim of the present study was to observe and quantify the changes of nutritional status, including body composition, biochemical values and muscle function in the early postoperative days (PDs) 3 and 8 in patients following pancreaticodudonectomy, and to evaluate their influence, if any, on the development of early postoperative complications.

MATERIALS AND METHODS

SUBJECTS

A prospective observational cohort study was carried out with patients candidates for Whipple procedure (WP) from September 2017 to January 2020 at Evaggelismos General Hospital (Athens, Greece). Initially, a total number of 87 patients were met and after the first interview, 15 patients were excluded because they did not give their written informed consent, underwent to a different operative procedure, were "open-close" cases or because they refused to continue the participation in the study. Therefore, a final number of 72 patients was measured the day before surgery (day -1) and followed at PDs 3 and 8 Data were collected and analysed by a trained dietitian.

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

All patients who consented to participate in the study were interviewed at the hospital admission. General information as gender, age, height, surgery type and diagnosed pathology were collected before the meeting from medical records. Weight was measured using a stand-up scale and BMI was consequently calculated according to the formula weight (kg)/height (m^2). The weight during the prior 6 months was asked to the patients and the weight loss % was then calculated. Information on preoperative malnutrition was gathered. Patients were defined to be at risk for malnutrition if they had involuntary weight lost (regardless time and extent) or eating disorders (loss of appetite, swallowing or chewing problem, powerlessness and motor disorder) or BMI <20 and 22 kg/m^2 respectively for patients younger and older than 70 years old (28). While the diagnosis of malnutrition was assessed considering a BMI <18.5 kg/m^2 or the following 3 criteria: unintentional weight loss $>10\%$ over an indefinite time with either BMI <20 (<70 years old) or <22 kg/m^2 (≥ 70 years old) and/or fat free mass index (FFM/height) <15 in women and <17 kg/m^2 in men[19]. Moreover, preoperative medical conditions were assessed using the American Society of Anaesthesiologists (ASA) class, where class 1 indicates a normal healthy patient, 2 a patient with mild systemic disease, 3 a patient with severe systemic disease, 4 a patient with life-threatening complication and 5 a moribund patient (29). Also, preoperative comorbidities were defined by Charlson Comorbidity Index (CCI), with severe comorbidities identified by CCI ≥ 6 (30).

The presence of complications developed during the first 30 post operative days was defined according to internationally accepted guidelines[26,27]. Postoperative complications were graded according to the Clavien-Dindo classification (CDC), which has been validated for pancreatic surgery. This classification is based on outcome management, with grade >3 indicating major and severe postoperative complications[2]. Furthermore, LOS was calculated for each patient.

BODY COMPOSITION MEASUREMENTS

BIA was performed using the In Body S10 (Japan) the day before surgery (day -1) and in the early morning (7.30-9.00 a.m.) at PDs 3 and 8. Patients removed all metal objects and other items that might interfere with the scan and were lying supine on a bed for at least 5 minutes with their legs separated and arms abducted from the body. This method requires only the placement of two single use electrodes on the dorsal surface of the right hand/wrist and other two on the right foot/ankle attaching leads according to the manufacturer's instructions. Specific data of sex, age, height and current weight were added to the machine before starting the impedance. BIA provides measurements of extracellular water (ECW) and intracellular water (ICW), and subsequent total body water (TBW) given by their sum[28]. FFM is predicted from ECW and ICW distribution and FM is calculated as the difference between body weight and FFM[29]. The PA measured at 50 kHz is determined by resistance of body fluid and reactance of cell membranes using the following formula: PA = arc-tangent (reactance/resistance) X180°/π and is expressed in degrees (36). Moreover, changes in all variables at PD 3 were calculated as "measurements at PD 3 – measurement at day -1" in order to study their influence on outcomes.

BIOCHEMICAL VALUES

Biochemical values including serum levels of C-reactive protein (CRP), haemoglobin (Hb) and albumin (Alb) were collected from medical laboratory records at preoperative day -1 and then at PDs 3 and 8. Changes at PD 3 were calculated.

MUSCLE FUNCTION MEASUREMENTS

Skeletal muscle function was assessed by measurements of HGS (kg), using a hand dynamometer (Jamar). The patients in a sitting position with shoulders adducted and the elbow of the dominant hand flexed at 90°, were asked to press the device with maximal strength for three times. The mean of those measurements was recorded. Both tests were performed at day -1 and then at PDs 3 and 8. Changes at PD 3 were calculated.

STATISTICAL ANALYSIS

The Kolmogorov-Smirnov test was applied and a non-normally distribution was found in most variables, so non-parametric statistics were used. All data are expressed as median (25^{th}–75^{th} quartiles) and categorical variables as number (%). Differences between groups were evaluated using Mann-Whitney U test. Comparison of perioperative changes was achieved by Freidman's test and, when it was statistically significant, a post hoc Wilcoxon signed-rank test was performed to detect postoperative differences compared to the preoperative values. These comparisons only test for differences in the setting of complete data, which were not available for all patients on PD 6 and 8. Spearman correlations tested the relationship between changes in variables at PD 3. Statistical significance was set at two-tailed p-value <0.05. All analyses were performed using the statistical software IBM SPSS (Statistical Package for Social Science, version 21).

ETHICAL APPROVAL

All patients received oral and written information about the project, before asking for their written informed consent. This study did not interfere with the current clinical practice in the hospital and it was approved by the Evangelismos Ethics Committee.

RESULTS

The study group of 72 patients included 38 females and 34 males with a median age of 70 years old. The patients had a median BMI of 24.4 and 36 patients had lost weight in the prior 6 months. From a preoperative assessment, 46 patients were at risk for malnutrition while no one underwent surgery had a malnutrition diagnosis. Moreover, with regard to the preoperative medical conditions and comorbidities, 42 patients had an ASA class III-IV and 18 patients a CCI ≥6. Postoperative complications were developed by 30 patients (16 women and 14 men) of which 12 having minor complications (CDC=2) and only 3 having major complications (CDC=3b). The median LOS was 10 days (Table 1).

The preoperative nutritional status stratified by gender is described in Table 2. The median age of females was 69.5 (63.5-72.3) and of males 73 (61.0-77.8), and the median BMI was 24.6 (21.2-27.8) and 24.3 (22.9-26.7) for females and males respectively. Significant differences were observed in body composition, with women having lower weight, TBW, ECW, ICW and FFM than men. No differences in the biochemical profile were detected, but the muscle function was significantly different with lower values of PEFR and HGS in women compared to men.

The absolute values for body composition, biochemical profile and muscle function as indicators of nutritional status during the perioperative period are shown in Table 3. Overall, significant perioperative changes were found. The body weight and TBW rose significantly on PD 3 (body weight +2.3 (0.8-3.6) kg; TBW +2.8 (1.1-5.9) l) and recovered by PD 8. Changes in body water compartments were observed. In particular, ECW increased significantly on PD 3 (+2.5 (1.2-3.7) l) and, despite a small reduction, remained higher than the preoperative value on PD 8. Whereas ICW increased slightly on PD 3 (+1.1 (-0.4-1.9) l) but fell significantly on PD 8. FFM rose and FM declined significantly on PD 3 (FFM +3.8 (1.6-8.0) kg; FM -1.8 (-4.6 to -1.3) kg) and then both recovered by the rest of the PDs. Moreover, PA reduced significantly on PD 3 (-1.0 (-1.2 to -0.7)°) and remained low on PD 8. With regard to the biochemical values, CRP level rose significantly on PD 3 (+78.0 (41.0-102.8) mg/l) and, despite a slow decrease on PD 8, it was significantly higher than the preoperative value. In contrast, Hb and Alb values fell sharply on PD 3 (Hb -34.5

TABLE 1. Demographic and clinical characteristics of 72 patients undergoing pancreatic surgery

	N (%)	Median (25^{th}-75^{th} quartiles)
Patients	72 (100)	
Gender		
Female	39 (54.1)	
Male	33 (45.9)	
Age (years)		67.0 (61.0-73.3)
BMI (kg/m^2)[a]		24.4 (22.5-27.1)
Normal weight	40 (54.5)	
Overweight	24 (33.4)	
Obesity	8 (11.1)	
Weight loss 6 months prior (%)	36 (55.9)	5.4 (1.9-7.2)
Risk for malnutrition (yes)[a]	46 (63.8)	
ASA Class[a]		
I-II	30 (41.8)	
III-IV	42 (58.2)	
CCI age adjusted[a]		
<6	54 (75.1)	
≥6	18 (24.9)	
Complications (yes)[b]	30 (41.2)	
CDC[b]		
1	26 (58.8)	
2	12 (35.3)	
3b	2 (5.9)	
Length of hospital stay (days)[b]		10.0 (8.0-13.3)

BMI: body mass index; IPMN: intraductal papillary mucinous neoplasms; ASA: American Society of Anesthesiologists class; CCI: Charlson Comorbidity Index; CDC: Clavien-Dindo Classification.
[a]preoperative; [b]postoperative.

TABLE 2. Gender differences of the preoperative body composition, biochemical values and muscle function

	Day -1		
	F =39	**M =35**	**P-value**
Body composition			
Body weight (kg)	68.2 (57.0-76.0)	78.5 (67.9-91.3)	0.022
TBW (l)	32.9 (29.1-35.3)	42.2 (38.0-48.3)	0.000
ECW (l)	14.4 (13.0-15.7)	20.4 (17.3-21.8)	0.000
ICW (l)	18.4 (15.3-20.5)	22.5 (19.3-25.1)	0.001
FFM (kg)	44.9 (39.7-48.2)	57.6 (51.9-66.0)	0.000
FM (kg)	21.2 (17-30.1)	21.2 (14.5-25.3)	NS
PA (°)	4.4 (3.7-5.4)	4.7 (4.1-5.3)	NS
Biochemical values			
CRP (mg/l)	3.5 (1.8-6.0)	2.5 (1.0-7.3)	NS
Hb (g/l)	127.0 (120.3-139.0)	134.0 (126.3-142.0)	NS
Alb (g/l)	36.0 (32.5-37.5)	35.0 (32.0-40.0)	NS
Muscle function			
HGS (kg)	21.8 (17.6-23.2)	40.0 (33.1-44.2)	0.000

Values expressed as median (25^{th}-75^{th} quartiles). F, females; M, males. TBW, total body water; ECW, extracellular water; ICW, intracellular water; FFM, fat free mass; FM, fat mass; PA, phase angle; CRP, C- reactive protein; HB, haemoglobin; Alb, albumin; HGS, maximum handgrip strength. Mann-Whitney U test; NS, non-significant.

(-45.8 to -26.0) g/l; Alb -12.0 (-16.5 to -10.0) g/l) and, although small increases on PD 8, remained lower than the preoperative values. In addition, the muscle function significantly changed over the study period. Both PEFR and HGS values fell dramatically on PD 3 (PEFR -250.0 (-407.5 to -125.0) l/m; HGS -5.4 (-7.3 to -3.0) kg) and remained significantly lower than the preoperative values by PD 8.

The relationship between changes in body composition, biochemical values and muscle function was investigated at PD 3, when the alterations were most pronounced (Table 4). There was a significant negative correlation between the change in PA and the change in ECW, a slight negative but non- significant correlation between changes in CRP and Alb, and a significant positive correlation was found between the changes in PEFR and HGS.

In order to investigate the influence on outcomes, a comparison of the changes in body composition, biochemical values and muscle function at PD 3 was made between patients that developed complications (n=30) within 30 days after surgery and those who did not (n=42). There were no significant differences between the two groups. However, we observed that changes were bigger in patients with postoperative complications. In particular, we found that body fluids volume changed more among patients with complications than those without (TBW= +3.4 (0.8-6.0) vs +2.5 (1.1-6.1); ECW= +2.6 (1.5-4.0) vs +2.3 (1.1-3.7); ICW= +1.3 (-0.6-1.8) vs +0.7 (-0.5-2.4). A similar but negative trend was shown in PA change (PA= -1.2 (-1.2 to -0.9) vs -0.9 (-1.4 to -0.6)) (Figure 1). Moreover, a significant difference in LOS was found between the two groups, with a median of 12.5 (10.8-16.0) days for patients with postoperative complications compared to 9.0 (8.0-10.8) days for those without (p=0.005).

DISCUSSION

This study investigated how the nutritional status, including measurements of body composition, biochemical values and muscle function, changed during the early postoperative period in 72 patients following WP surgery. Significant changes were observed during the perioperative period. The body weight increased 3 days after surgery as reflecting fluid reten-

TABLE 3. Body composition, biochemical values and muscle function of patients before (day -1) and after (PDs 3 and 8) pancreatic surgery

	Days			
	-1 (n = 72)	**+3 (n=72)**	**+8 (n=66)**	**P-value[1]**
Body composition				
Body weight (kg)	73.0 (62.4-81.3)	75.3*** (65.5-84.8)	72.6 (62.4-79.3)	***
TBW (l)	35.7 (32.1-42.8)	40.2*** (34.6-45.5)	34.7 (32.6-41.8)	***
ECW (l)	16.4 (14.4-20.4)	18.9 *** (16.3-23.1)	17.8 (15.6-19.8)	***
ICW (l)	20.2 (16.2-23.3)	20.4* (17.6-23.2)	18.1** (16.7-21.1)	**
FFM (kg)	48.8 (43.9-58.4)	54.9*** (47.3-62.2)	47.5 (44.6-57.2)	***
FM (kg)	21.2 (16.3-28.8)	18.4* (15.4-25.6)	20.9 (15.6-30.5)	*
PA (°)	4.5 (4.1-5.3)	3.7*** (3.1-4.3)	3.9*** (3.2-4.6)	***
Biochemical values				
CRP (mg/l)	3.0 (1.0-6.0)	85.0*** (52.3-113.3)	29.0** (12.0-71.5)	***
Hb (g/l)	130.5 (121.0-141.0)	92.0*** (83.5-102.0)	98.5*** (94.0-115.0)	***
Alb (g/l)	36.0 (32.0-38.5)	22.0*** (20.0-25.0)	22.5** (19.3-26.3)	*
Muscle function				
HGS (kg)	27.5 (20.3-37.7)	22.1*** (16.1-35.2)	25.2*** (15.0-34.3)	***

[1] P-value *<0.05, ***<0.01

TABLE 4. Correlations between changes in body composition, biochemical values and muscle function at PD 3

Spearman Correlation		**P-value**
Changes in PA and ECW	-0.452	0.021
Changes in CRP and Alb	-0.321	0.075
Changes in PEFR and HGS	0.402	0.022

Changes at PD 3 are calculated as "measurement at PD 3 – measurement at day -1"

tion. Patients undergoing abdominal surgery often receive excessive perioperative intravenous fluids, which hide fluid losses and result in weight gain of 3-6 kg[30]. The magnitude of fluid retention was lower in the present study, with a median weight increase of 2.3 kg at PD 3. Small increases in weight were also found in other studies over a period of 7 days[6,31]. In contrast, body weight reductions were observed after a median of 12 days following PD[11] and a loss of 1.3 kg was found 2 weeks after pancreatic surgery[32]. Previous works focusing on long-term changes, reported a significant reduction in BMI 3 months after PD and a recovery to the preoperative weight after 6-12 months[11].

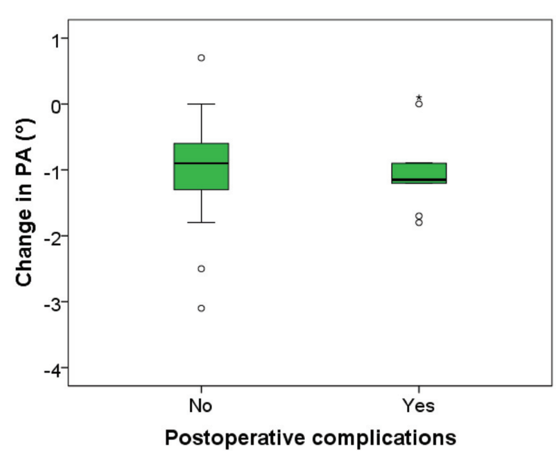

FIGURE 1. Change in phase angle (PA) at PD 3 between patients with and without postoperative complications.

The patients had a significant expansion of TBW on PD 3 suggesting the presence of oedema, which recovered on PD 9. Although this recovery, there was a shift in the distribution of body fluid compartments that persisted over the entire postoperative period. ECW rose significantly after the operation and remained higher than the preoperative volume suggesting a sequestration in the so- called "third space", a non-functional compartment normally having little or no fluid. Whereas ICW increased slightly on PD 3 followed by a significant decrease suggesting a loss of body cell mass, which is frequent in clinical populations[28]. Similarly, in a study of 71 patients followed before and immediately after general anaesthesia and surgery, the increase in TBW was paralleled by a rise in ECW, whereas the ICW increased but slowly without reaching statistical significance (40). What happens from a physiological point of view is that the inflammatory process, as a response to the surgical shock or trauma, increases the capillary permeability and causes a fluid shift of water, salt and small proteins, from the intravascular to the interstitial or other non-functional spaces. This results in localised oedema, which reaches a peak by 5-6 hours after operation and may persist for 72 hours depending on the extent of injury. A consequence of this fluid shift is the hypovolemia that clinically is treated with perioperative administration of intravenous fluid therapy[33]. Our patients had a median fluid accumulation of 2.8 l on PD 3 compared to an average of 4.1 l measured by segmental BIA in 8 patients during the first 2 hours after abdominal surgery[12]. Furthermore, our patients were given perioperative infusion of crystalloids that have been demonstrated to leave the intravascular space and cause interstitial oedema as compared to colloids (42). Another factor influencing the fluid overload is the epidural analgesia that leads to vasodilation and intravascular hypovolemia, which is interpreted as fluid depletion and treated by infusing more fluids[30]. The epidural analgesia was given to our patients until PD 5 and this may explain the recovery of TBW found on PD 6.

In the present study, an increase of FFM was observed on PD 3 and this can be explained by the rise in TBW. Since FFM includes skeletal and non-skeletal muscle, organs, bone and body fluids, it is difficult to identify lean tissue change because the postoperative excess of body water and especially of ECW may have masked its loss[34]. The lean body mass was measured in 27 pancreatic cancer patients after WP and the preoperative value of 44.9 kg was maintained for 2 weeks but fell to 42 kg after 5 weeks[32]. Our measurements also showed a significant reduction in FM on PD 3. Other studies reported a postoperative FM loss resulting from the hypermetabolic state following surgery. Moreover, most of the fat loss is said to occur in the first PDs when the energy intake is really in deficit[6]. However, in our study the nutritional intake was not included. A possible explanation is that this result was affected by the impedance measurement, since FM derives from the difference of body weight and FFM and, therefore, FM loss most likely results from the water retention[32].

Moreover, a very unstable situation characterized the postoperative period of our patients, as shown by the low PA compared to the normal values (PA $\geq 5^\circ$ for men and $\geq 4.6^\circ$ for women)[18]. The significant reduction in PA observed after surgery may suggest a cell loss and reduced cell integrity (36). In addition, the change in PA was negatively associated to the change in ECW on PD 3 indicating that a reduction in body cell mass is compensated by an increase in extracellular volume. PA may be considered as an indicator for nutritional status since it has been demonstrated that its reduction was parallel to a decline in nutritional status[17]. But its biological meaning has to be better understood[16].

With regard to the biochemical values, our results showed that CRP level significantly increased on PD 3 and remained high until PD 8, indicating the metabolic stress of the operative procedure[6]. Furthermore, there was a significant decrease in Hb and Alb on PD 3 that persisted for the entire postoperative period. The Hb level fell as a consequence of bleeding and hemodilution while the reduction in Alb was due to the increased permeability of capillary membrane with associated leakage to the interstitial room (39). These alterations are mostly caused by the systemic inflammatory response to surgery and are consistent with other works[11,35]. In fact, a negative but non- significant correlation was found between the changes in CRP and Alb occurred on PD 3, indicating that the increase in inflammation lowers albumin level.

The results of this study showed that the HGS value of our patients declined on PD 3 and remained low by the end of the study period. This finding is consistent with one work that found a reduction in handgrip on PD 3 and 7 among 12 patients after WP[36]. Also, the HGS values of 36 patients fell 3 days after an operation for pancreatic or hepatic disease and remained low by a week. In another study of 40 patients undergoing major abdominal surgery, a diminished handgrip was shown on PD 2[37]. Moreover, both measurements were found to be positively correlated between each other, indicating that the reduction in PEFR was associated to that of HGS. A common explanation to the observed decrease in HGS values is that anaesthesia, surgical trauma, bed rest, protein depletion, fatigue and pain affect muscle function after surgical procedure[38]. The simple changing from supine to a seated position in order to perform the tests was really challenging after surgery for the majority of our patients and their abdominal tension prevented them from hard blowing and pressuring.

The present study demonstrated that the nutritional status of patients changed after pancreatic resection and that the alterations were more pronounced on PD 3. Therefore, we investigated whether those earliest changes could play a role in the development of postoperative complications. It is important to highlight that changes in our measurements on PD 3 must be interpreted with caution since those are not representative of the nutritional status itself, but are confounded by the postoperative response to the surgical trauma in terms of fluid retention.

Few authors have reported potential risk factors for early complications after pancreatic surgery such as malnutrition, preoperative hypoalbuminemia, preoperative weight loss, high or low BMI, high FM and especially high volume of visceral fat, low FFM, low PA and high body fluids[7,17,24]. In the current study, no significant differences in changes of body composition, biochemical values and muscle function on PD 3 could be identified between patients with and without postoperative complications indicating that those alterations did not influence the outcomes. However, we observed some trends. In particular, higher volumes of TBW, ECW and ICW were found in patients with complications suggesting that an immediate postoperative rise in body fluids might represent a risk factor for developing early complications. An excessive fluid overload in the perioperative period has been shown to have a negative impact on the integrity of anastomosis and consequently to increase postoperative complications and prolong hospital stay[23]. Also, the fluid overload causes a local inflammation, alters the collagen regeneration and increases the risk for postoperative wound infection and rupture[39]. Our results, even if not significant, may suggest the importance to maintain the patient in a normovolaemic status, by preserving a normal intravascular volume and avoiding weight gains due to excessive fluid administration[23]. The Enhanced Recovery After Surgery (ERAS) concept strongly recommends to achieve a perioperative near-zero fluid balance because patients in fluid balance have been associated with reduced postoperative complications and LOS rather than those in fluid imbalance[30]. In addition, the reduction in the PA value was bigger in patients with complications than the others, but this difference was not significant. It has been previously demonstrated that low PA values were significantly associated with postoperative complications[17]. In fact, this parameter has been used as a prognostic marker in several clinical situations where smaller PA values were associated with poor prognosis and short survival[16]. Moreover, the occurrence of postoperative complications has a big impact on the LOS[20], as it was shown in the present study where patients developing early postoperative complications had longer hospitalization (12.5 days).

Strengths of the study include the prospective design, the randomized nature of the study group and the precise accuracy in performing the measurements without interfere with the current clinical practice. To our knowledge, this was the first study to measure body composition by BIA in the early postoperative period among pancreatic surgical patients and the additional evaluation of biochemical profile and muscle function to assess the nutritional status represents a further strength. Our results provide a valuable insight on how WP and TP influence the nutritional status in the immediate postoperative period. Weaknesses include the small sample size that limited the power of the study as well as the few severe postoperative complications. A further criticism is that not all patients had complete measurements in the postoperative period (PD 8=66) due to different LOS. Although statistical analysis considers missing values, the data must be interpreted with caution, especially with regard to comparisons on PD 9. Body composition measurements were not measured by independent methods like dilution or Dual-energy X-ray absorptiometry (DXA), thus introducing uncertainty on the interpretation of the results. However, it has been reported a similar magnitude of errors between bioimpedance and reference techniques as dilution[34] and it has been validated against DXA in the estimation of FFM and FM among healthy elderly Swedes[29]. BIA is a very sensitive method since several factors can influence its precision and accuracy, including skin temperature, degree of adiposity, proximity to metal or electronic devices, body position and electrodes placements. Although those limitations, BIA remains one of the few best options for clinicians[34,40].

Besides the common body weight change and biochemical markers, measurements of body composition and muscle function were also included in the present study to assess the nutritional status of the patients. In particular, body composition measurement was found to be useful in the evaluation of nutritional status among surgical patients and in the prediction of outcomes[13]. It can be measured by several methods such as tracer dilution or DXA. However, bioimpedance methods are bedside approaches, non-invasive, non-expensive, simple and easily available in the clinical setting, and allow assessing body composition repeatedly over a short period of time. In particular, BIA, which was the only tool available for the current project, has the advantage to separate TBW in ECW and ICW which ratio varies with age and illness[12]. Furthermore, many studies have shown that measurements of involuntary muscle function by HGS were valuable indicators of nutritional status as well as predictor of operative outcomes[6,41]. Also, the use of a peak flow meter and handgrip dynamometer represent a simple, portable and reliable way to easily assess physiological function among patients[6,38].

The present study has a big clinical significance as it adds knowledge to the current scarce literature on what changes occur in the body composition, biochemical profile and muscle function in patients during the early postoperative period following WP and TP. The nutritional status assessment must be encouraged as a fundamental clinical practice to develop and improve perioperative care and management and, consequently, improve outcomes.

To conclude, we observed significant changes in the early postoperative nutritional status of patients after pancreatic surgery. The main changes in body composition occurred on PD 3 with a partial recovery by PD 8, except for ICW and PA. The biochemical values had the greatest change on PD 3 and remained altered for the rest of the postoperative period. Similarly, the impairment in muscle function occurred after surgery and persisted for 9 days. No significant influences of the early changes in body composition, biochemical values and muscle function on outcomes were found. However, trends in TBW, ECW, ICW and PA were observed in patients with postoperative complications

CONCLUSION

The perioperative evaluation of body composition, biochemical values and muscle function may be useful for the nutritional and clinical assessment of surgical patients in order to improve the perioperative care and management and, consequently, provide a better quality of life for patients. Future research are necessary to show the accuracy of the use of BIA in patients undergoing pancreatic surgery and to confirm our findings. The inclusion of larger and more homogeneous groups of patients is needed. The evaluation of food intake could be considered for a better and complete assessment of nutritional status. Moreover, the observation of earlier changes, as on PD 1, is needed to clearly describe whether shifts in body composition are a prerequisite for the development of postoperative complications.

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