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Impact of patients nutritional status on major surgery outcome

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Abstract. – OBJECTIVE: Surgery is a major stress factor that activates several inflammatory and catabolic pathways in man. An appropriate nutritional status allows the body to react properly to this stressor and recover in a faster and more efficient manner. On the other hand, malnutrition is related to a worse surgery outcome and to a higher prevalence of comorbidities and mortality.

The aims of this study were to evaluate the nutritional status of patients undergoing major surgery and investigate the potential correlation between malnutrition and surgical outcomes.

PATIENTS AND METHODS: Mini Nutritional Assessment (MNA) and global clinical examination (including biochemical parameters and comorbidities existence) were undertaken in 50 consecutive patients undergoing major surgery. Patients' clinical conditions were re-evaluated at 3 and 6 days after surgery, recording biochemical parameters and systemic and/or wound-related complications.

RESULTS: A compromised nutritional status was present in more than half (54%) of patients (malnutrition in 10% and risk of malnutrition in 44% of patients, respectively). Females were slightly more at risk of malnutrition (48% vs. 41%, *p*=NS, females *vs.* males) and clearly malnourished (14% *vs.* 7%, *p*<0.05, females *vs.* males). Age was an independent risk factor for malnutrition and within the elders' group (> 80 years old) 16.70% of patients was diagnosed with malnutrition and 58.3% was at risk of malnutrition. Systemic complications were registered in all patients both at 3 and 6 days after surgery. However, well-nourished and at-risk of malnutrition patients had earlier complications that only partially resolved within six days after the operation. Malnourished patients showed fewer complications at the 3rd post-surgery follow-up day but had a worse outcome six days after surgery.

CONCLUSIONS: Older age and but not female sex are independent risk factors for malnutrition development in patients undergoing major surgery. More interestingly, more than half of patients with an impaired nutritional status presented a less appropriated stress response to surgery. These data suggest that nutritional status assessment may be important to recognize patients at potential risk of surgical complications and that early nutritional interventions must be promptly arranged.

Key Words:
Surgery, Nutritional status, Malnutrition.

Introduction

Major and minor surgery may severely alter the physiology of our organism. In fact, surgery is followed by an inflammatory response and stimulates body catabolism also[1].

Initially, surgery determines catecholamines increase through activation of hypothalamus-hypophysis system with anti-diuretic hormone (ADH), growth hormone (GH) and adrenocorticotropic hormone (ACTH) secretion[2]. These immune-endocrine storm determines the aforementioned catabolism: increase of glucagon and corticosteroids secretion, activation of hepatic glycogenolysis and, on the other hand, gluconeogenesis, insulin-resistance occurrence together with muscle proteolysis[1].

Thus, surgery is strongly associated with malnourishment and may be linked to a negative post-operative outcome. In an eight-week observational study on 460 patients 52% of them having emergency surgery and 38% being a candidate to elective surgery, respectively, were at risk of malnutrition[3]. These data were significantly associated with a negative post-surgery outcome.

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Indeed, malnourishment alters both immune response and tissues repairing in surgical patients[4].

Among the described increased postoperative complications we recognize[5]: systemic infections, delayed surgical wounds healing, pressure lesions, respiratory failure, hospitalization duration increase and relative healthcare costs rise, higher mortality rate.

Another factor potentially affecting postoperative malnourishment is represented by patients' preoperative clinical conditions. Cancer patients[6] (especially those with gastrointestinal, brain and neck localizations[7]) have the highest prevalence of postoperative malnourishment development. Esophageal cancer patients, for example, show the highest malnourishment prevalence (about 79%) in the frame of oncologic patients[8]. This is due to the admittance nutritional conditions, comorbidities, elderly, malabsorption and gastrointestinal obstruction/gastric stasis occurrence, dysphagia[9].

We aimed to prospectively assess the nutritional status of patients undergoing elective surgery; we aimed also to evaluate the eventual correlation of malnutrition presence with post-operative complications occurrence and severity.

Patients and Methods

Study Population

We consecutively enrolled patients undergoing elective major surgery at the Surgery Unit of "Madonna del Soccorso" General Hospital of San Benedetto del Tronto, Area Vasta 5 ASUR Marche, Italy, between April and October 2015. The study was approved by the regional ASUR Marche Ethical Committee

Study Design

The day before, and three and six days after surgery, respectively, all anthropometrics and clinical parameters of patients were collected. Consensually patients were asked to fill in the Mini Nutritional Assessment (MNA) test[10]. Postsurgical outcome and surgical complications were registered at three and six days after the operation.

The assessment scheme adopted is shown in Figure 1.

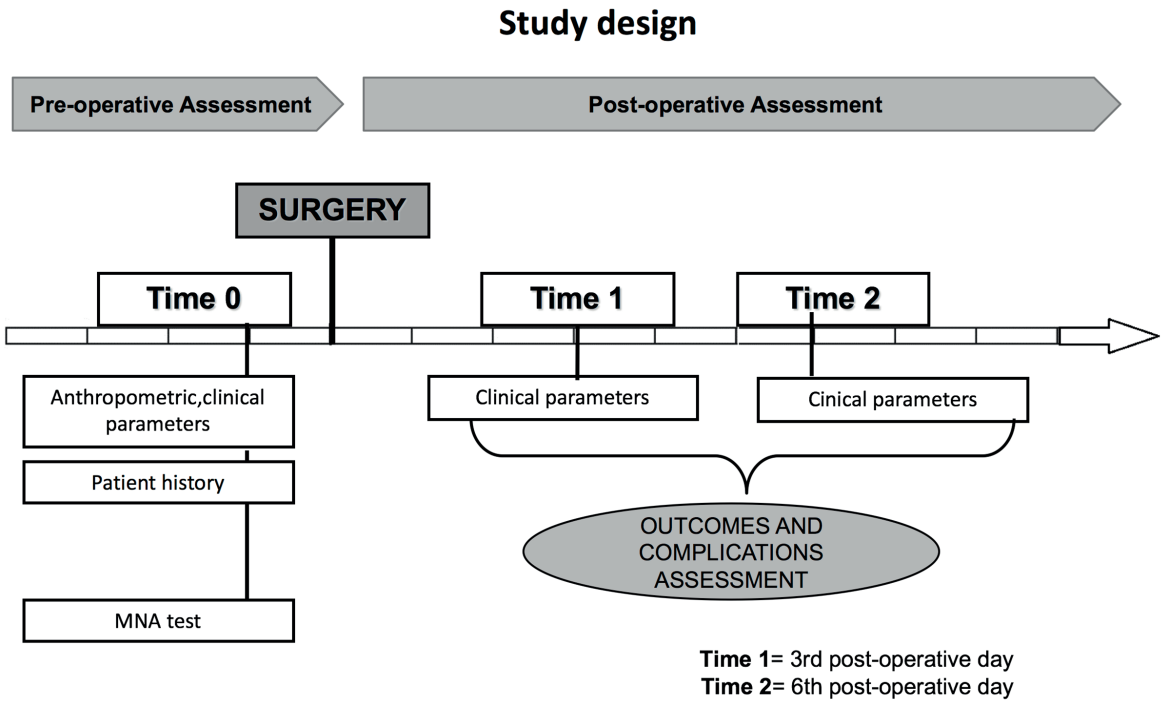

Figure 1. Overview of the study design. Before surgery (T0) MNA was performed in order to identify patients at risk of malnutrition and those frankly malnourished. In the pre-operative assessment, also medical history, anthropometric parameters and clinical and laboratory data were included. Post-operative assessment consisted of recording patients' data three (T1) and six days after surgery (T2). During both follow-up points, systemic and operative-related complications were collected. MNA: Mini Nutritional Assessment.

MNA Test

The Mini Nutritional Assessment is a multidimensional screening tool, validated in many clinical settings. More specifically, it is an integrated nutrition index that evaluates different nutritional parameters in order " to obtain a synthetic information and a more accurate nutritional diagnosis"[11]. According to meta-analysis, MNA has 96% sensitivity, 98% specificity, and 97% predictive value to describe nutritional status of patients[12]. Moreover, MNA is easily repeatable even by non-trained nutrition professionals[11].

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends its use both as a first level screening and for successive follow-ups among the elderly[13].

Among hospitalized elderly patients, MNA scores are inversely correlated with healthcare costs, length of stay, short-term and long-term mortality[14,15].

Several studies have validated it as a reliable index of muscle disability and motility as well as a complementary tool for nutritional status assessment in patients[16].

MNA test consists of 18 items divided into three sections: one about anthropometry and weight changes; one that considers quality and quantity of food intake; one about disabilities and cognitive status[17].

MNA consists of two steps:

– **Screening** (with a maximum score of 14 over six variables): story of weight loss in the previous three months, food intake, motility, acute stress, cognitive status, Body Mass Index (BMI) assessment. A score of 0-7 is predictive of malnutrition, a score of 8-11 suggests that patients are at risk of malnutrition, a score of 12-14 indicates that the person is well nourished and needs no further investigation. If the score is less than 11 it is strongly recommended to continue with the remaining questions; this is necessary to obtain additional information on factors that may impact nutritional status.

  A MNA score higher than 24 indicates that the patient is well-nourished, a score between 17-23.5 suggests a risk of malnutrition and scores lower than 17 clearly pinpoints malnutrition.

– **Self Global assessment** (drugs assumption, food habits, fluid intake, residence place, patient's considerations on personal health status and on nutritional status).

Other Anthropometric Parameters For Nutritional Status Assessment

Other anthropometric values were recorded: middle-arm circumference and calf circumference.

Middle-arm circumference (mean values: 34.1 cm for males and 31.9 cm for females, respectively)[18] is measured at the mid-point between the acromial surface of the scapula and the olecranon process of the elbow. It is nowadays used as validated index predictive of malnutrition both in child and in adult patients[19]. In the latter, middle-arm circumference reflects weight variations, changes in muscular mass and subcutaneous fat deposition (both of them are important predictive factors for survival of patients)[20].

Calf circumference (maximal values of 33 and 34 cm form males and female, respectively)[18] is an anthropometric measure taken around the widest part of the calf, with the patient sitting with the left leg hanging or standing with their weight distributed on both feet[21,22].

Statistical Analysis

All data are presented as mean ± standard deviation (SD). Paired Student's *t*-test, chi-square, ANOVA and Fisher's exact tests were used to compare values of variables between groups. Bonferroni test was used for correction of multiple testing errors of results from ANOVA. Pearson regression test was used to evaluate the correlation between nutritional status and age, mental status impairment, type of systemic postoperative complication; between age and hospitalization stay. Differences were considered to be significant at the 5% level.

Results

Fifty Caucasian patients undergoing major surgery were enrolled (21 females, mean age 73.5±7.76 years, BMI 26.32 ± 4.47 kg/m^2) (Table Ia,b). The highest percentage of patients underwent the operation for cancer treatment. Fifty percent of patients underwent abdominal surgery (Table Ia,b).

According to MNA evaluation, 10% of patients were malnourished, 44% at risk of malnourishment and 46% had a normal nutritional status (Figure 2).

Malnutrition diagnosis was found in 14% of female patients and in 7% of males only (*p=NS, chi-square*, females *vs.* males, respectively). Mal-

Table Ia. Patients classification by site and type of surgical intervention.

Surgical site of intervention	Number of patients	Percentages	Reason for intervention	Type of intervention
Bowel	25	50%	Oncology (n=18), intestinal occlusion (n=5), acute appendicitis (n=2) Appendicectomy (n=2)	Emicolectomy (n=18), colostomy (n=5), Appendicectomy (n=2)
Stomach	12	24%	Oncology	Partial gastrectomy (n=8), gastro-jejunal anastomosis (n=4)
Breast	3	6%	Oncology	Mastectomy (n=3)
Liver	4	8%	Oncology	Partial hepatectomy (n=4)
Kidney	1	2%	Oncology	Radical nephrectomy (n=1)
Ovaries	1	2%	Oncology	Ovariectomy (n=1)
Others	4	8%	Acute abdomen	Exploratory laparectomy (n=4)

nutrition risk was 48% and 41%, respectively, for female and male patients (*p=NS, x^2*, females *vs.* males, respectively). Adequate nutritional status was found in 48% and 52% of females and males, respectively (*p=NS, x^2*, females *vs.* males, respectively) (Figure 3a,b).

Malnutrition but not risk of malnutrition diagnosis significantly correlated with elder age (*r=0.034*) (Figure 4).

Impaired mental status was found in 33% of patients undergoing surgery (11% with Alzheimer type dementia, 12% with non-Alzheimer type dementia and 10% with chronic vascular encephalopathy diagnosis). An impaired mental status did not significantly correlate with malnutrition diagnosis (*r=NS*).

Systemic and local complications were registered separately. Local complications (namely hematoma and surgical wound infection) were registered in 5 patients (10%) and three of them lasted from the third to the sixth postoperative day. All the patients with local complications presented also systemic complications.

Table Ib. Patients' characteristics at baseline.

Patients included	50 (n)
Gender (M/F)	29/21 (n)
(M/F)%	58/42 (%)
Mean age (years)	73.5 ± 7.76
Mean height (cm)	164.24 ± 9.56
Mean weight (kg)	71.16 ± 14.61
Body Mass Index (kg/m^2)	26.32 ± 4.47
Albumin (g/dl)	12.12 ± 2.02
Creatinine (mg/dl)	0.97 ± 0.47
White blood cells (n x 10^9/L)	7.50 ± 3.11
Number of absent teeth	8.5 ± 5.03

Systemic complications were represented by: sepsis (n=14), acute haemorrhage (6), heart failure (n=5), renal insufficiency (n=2), pneumonitis (n=7), urinary tract infection (n=5).

Grade of systemic complications was: Grade I (n=16), grade II (n=12), grade IIIa (n=6), grade IIIb (n=3), grade IVa (n=1), V (n=1)[23].

Ten patients (20%) had systemic complications on the third postoperative day with resolution within the sixth day; seven patients (14%) had postoperative complications on the sixth day only. Eleven patients (22%) developed complications long-lasting from the third until the sixth postoperative day.

Comparing complications with nutritional status we observed that 31% of systemic complications on the third postoperative day were registered in well-nourished patients while 65.5% in those at risk of malnutrition and 3,5% in malnourished patients (ANOVA, *p<0.05*, patients at risk of malnutrition *vs.* well-nourished and malnourished).

On the sixth postoperative day, systemic complications were registered in 26,7% of well-nourished patients, in 50% of those at risk of malnutrition and in 23.3% of malnourished patients (ANOVA, *p=NS,* patients at risk of malnutrition *vs.* well-nou-

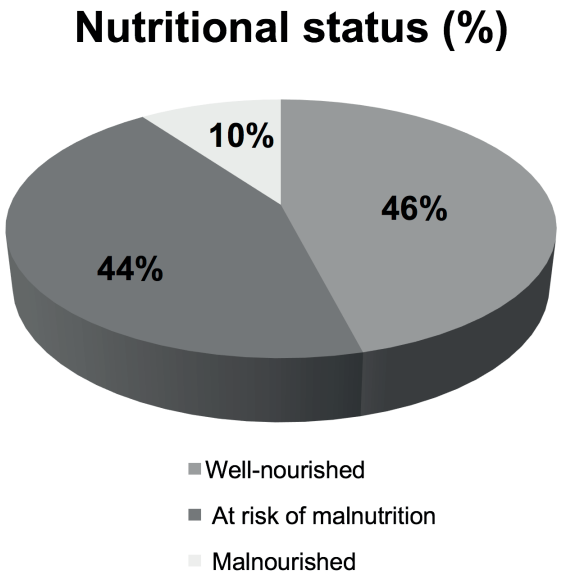

Figure 2. Distribution of sample by nutritional status. Patients distribution by nutritional status. Results were obtained from Mini Nutritional Assessment. The respondents whose score was ≥ 24 accounted for 46% of the total, those with scores between 17 and 23.5 were 44%, those whose score was ≤ 17 were 10% of the total. The scores were suggestive of good nutritional status, at risk of malnutrition and malnutrition of patients, respectively.

rished and malnourished) (Figure 5a,b).

More in particular, systemic complications appeared in 17.4% of well-nourished subjects within the third postoperative day; in 13% of these subjects on the sixth postoperative day.

In the group of patients at risk of malnutrition, 27.3% showed systemic complications on third postoperative day while 13.6% showed these complications on the sixth day.

Finally, 20% of malnourished patients presented systemic complications on the third postoperative day while 40% of these subjects on the sixth postoperative day. This group only recorded one death due to cardiovascular complications (namely heart failure due to systemic sepsis).

Interestingly, we did not find a significant correlation between nutritional status and type of systemic complication.

Surgical wounds healing were successful in the majority of patients. However, 5 of them had a late healing. In particular, one was well nourished, three at risk of malnutrition and one frankly malnourished (Figure 5). The well-nourished patient had delayed wound healing on the third postoperative day until resolution on the sixth day. On the other hand, subjects at risk of malnutrition presented surgical wound delayed healing that maintai-

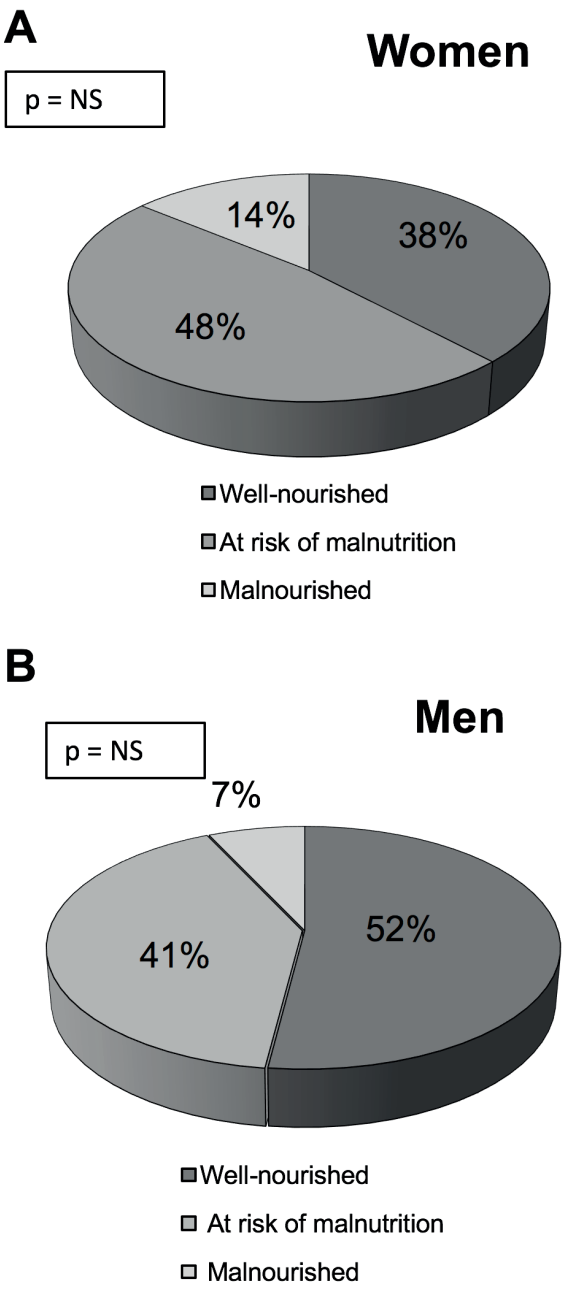

Figure 3. Nutritional status distribution. **(A)** Distribution of nutritional status in female subgroup. MNA shows that well-nourished female are 38% of the total, those with a nutritional risk are 48%, those malnourished are 14% of the total. Results were obtained from Mini Nutritional Assessment. The well-nourished respondents are 52% of the total, those with a nutritional risk are 41%, those who result malnourished are 7% of the total. **(B)** Distribution of nutritional status in male subgroup. The well-nourished respondents are 52% of the total, those with a nutritional risk are 41%, those who results malnourished are 7% of the total. Although malnourished women were more represented than malnourished men, the association between nutritional status and sex did not reach statistical significance ($p = NS$).

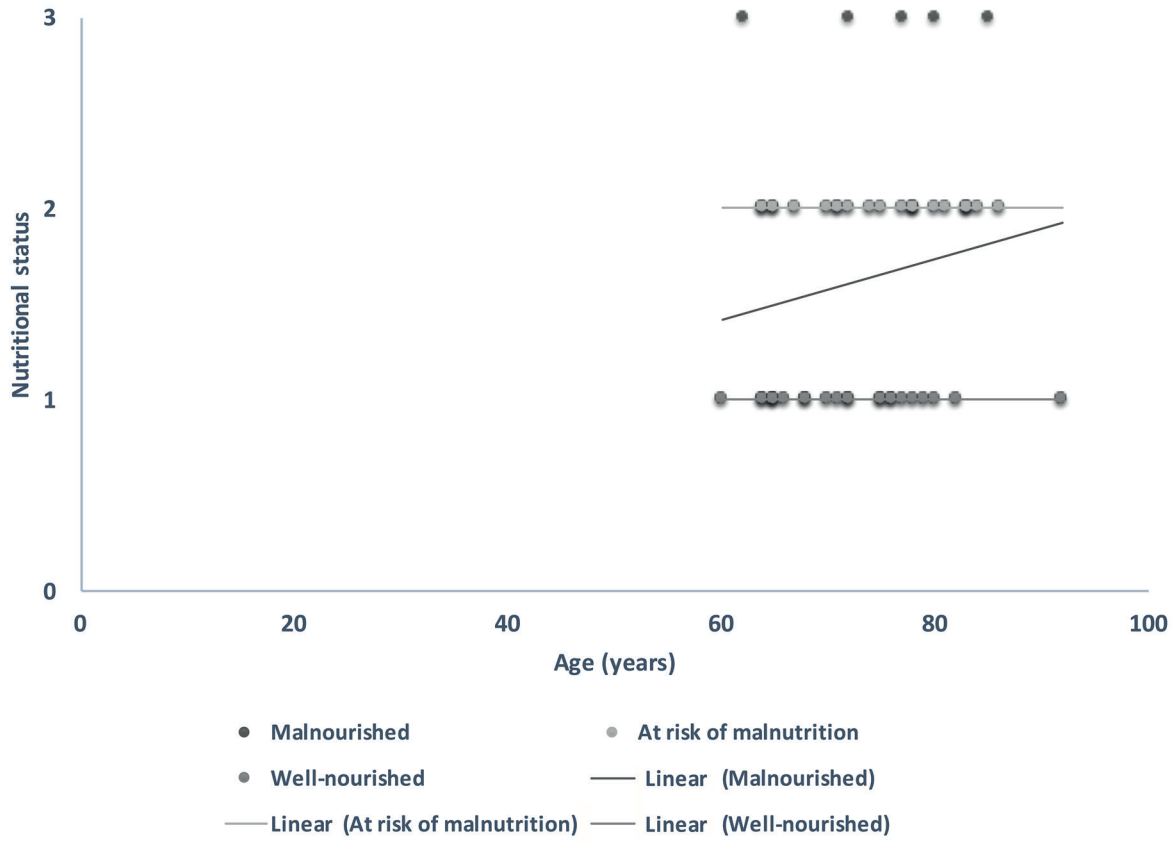

Figure 4. Correlation between age and malnutrition prevalence. There was a significant correlation between older age and growing prevalence of frank malnutrition (*r=0.034*). MNA categories: 1 indicates the score for well-nourished; 2 that for at risk of malnutrition; 3 that for malnourished patients.

ned until and over the sixth postoperative day.

Older age correlated with hospitalization stay without reaching statistical significance (*r=NS*).

Patients at risk of malnutrition and frankly malnourished had a longer hospital stay than well nourished but this difference did not reach a statistical significance (8.6±1.0 and 9.1±0.8 *vs.* 7.2±0.9 days, for patients at risk of malnutrition, malnourished and well nourished, both *p=NS*).

Discussion

Malnutrition is a staple problem in hospital settings. The imbalance between energy and nutrients needs and real dietary intake may compromise the body reaction to environmental stresses, including surgery[24].

Several studies[25-27] revealed the correlation of an impaired nutritional status and worse perioperative outcomes due to an overtriggered inflammatory response in the frame of lack of proteins and energy sources for the injured body. Furthermore, the surgery itself may have a negative impact on nutritional status especially in geriatric patients[28,29].

The aim of the present study was to evaluate the possible association between nutrition and postoperative complications, both local (namely surgical wound healing) and systemic, in patients undergoing elective surgery at the Surgery Unit of "Madonna del Soccorso" General hospital of San Benedetto del Tronto, Area Vasta 5 ASUR Marche.

During the enrollment period, the Mini Nutritional Assessment (MNA) was filled in for every patient. The MNA is a well-known nutritional screening tool, approved for its reliability, sensibility, and convenience[17]. The analysis of the MNA results showed that, even before surgery, 44% of the patients were at risk of malnutrition and 10% were pointedly malnourished. These results can be explained by both the older age and comorbidities of patients studied. In fact, both older age and lung, heart and metabolic diseases could have im-

paired nutritional status and physical autonomy responsible for malnutrition risk or status in our population[30,31].

Irrespective of literature findings women had higher malnutrition rate than man, 14% and 7% respectively[32]. However, this difference did not reach statistical significance due to the small sample size.

The risk of malnutrition showed similar results among males and females. This finding is in agreement with literature that doesn't recognize a specific impact of sex on malnutrition prevalence in the elderly or surgical patients except for the major prevalence of osteoporosis in females orthopedic patients[32,33].

Age was a critical risk factor for malnutrition because of its physiological effects on body composition and function (34). Indeed, 66.7% of patients older than 80 years had an impaired nutritional status; this rate was significantly higher than that shown in the younger group (47%) ($p<0.05$), perhaps in line with previous reports from literature.

Moreover, malnutrition presence was significantly correlated with older age within our sample in the study ($r=0.034$). The lack of significant correlation between risk of malnutrition and older age can be explained by the small sample

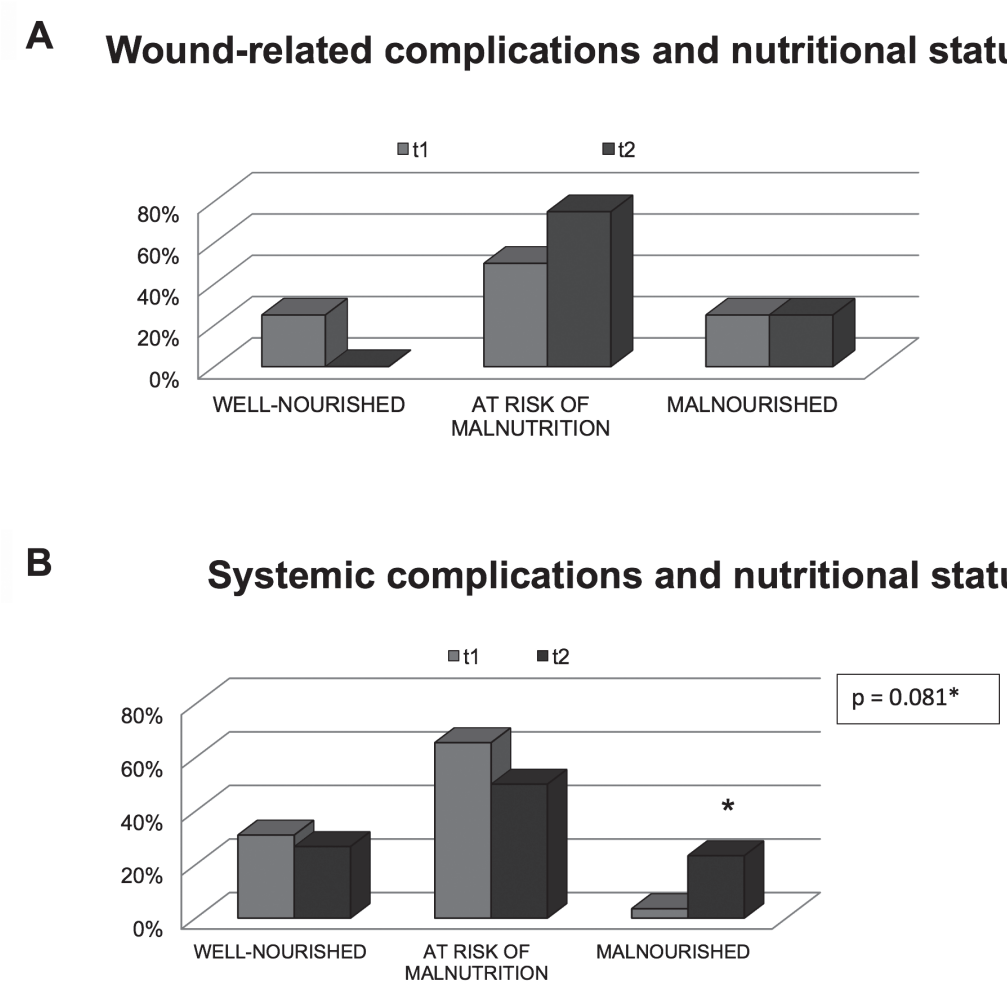

Figure 5. Local ***(A)*** and systemic ***(B)*** complications at time 1 and 2. ***(A)*** Wound-related complications distribution (shown as percentage) and nutritional status. Complications observed at T1 and those observed at T2 are represented separately. Wound-related complications include hematoma, infection, cutaneous dehiscence, evisceration. Due to small sample size and to small number of wound-related complications, no statistical differences was found ($p=NS$). ***(B)*** Percentages of systemic complications and nutritional status. Complications observed at T1 and those observed at T2 are represented separately. There is a trend toward significance ($p=0.08$) in the relationship between nutritional status and systemic complications.

size in this study. On the other hand, this finding describes the real tendency of less old people to have a frank state of malnutrition but a subclinical tendency towards it that is one of the main target of preventive medicine in this field[30].

Indeed, elderly is associated with a lower food intake and macro- and micronutrients malabsorption. Moreover, limited physical activity reduces body metabolism leading to protein loss, calcium deposits depletion, insulin resistance that contributes to perpetuate the impaired nutritional status[30,31].

One of the factors responsible for malnutrition development such as mental status impairment and its relative altered eating disturbances (e.g., dysphagia, hyperphagia, anorexia, etc.) did not significantly correlate with malnutrition or risk of malnutrition diagnosis. This result can be explained by the paucity of our sample, irrespective of other studies in the literature that have shown a clear association between eating pattern and cognitive function derangement in elderly Polish patients at risk of metabolic syndrome development[35].

Of note, the overall rate of postoperative complications, in well-nourished patients, at risk of malnutrition and malnourished patients showed a distribution conditioned by malnutrition. In fact, well-nourished subjects had complications mostly in the early follow-up (three days after surgery) but they recovered either partially either completely within six days after surgery. On the other hand, patients with an impaired nutritional status developed both systemic and wound-related complications not only at T1 but also at T2.

According to the post-operative assessment scheme, wound-related complications tended not only to appear early, but also to not heal within six days after surgery both in patients at risk of malnutrition and in those who were clearly malnourished *vs.* well-nourished ones ($p<0.05$).

Notably, systemic complications had been a few and mostly not life-threatening (e.g., fever, nausea, and vomiting). However, there was a recognizable timing of complications appearance according to the nutritional status: patients at risk of malnutrition had complications mostly at T1 (65.5%) and showed better outcomes six days after surgery (50%) *vs.* malnourished patients that had less systemic complications at T1 but showed worse outcome at T2. These findings are in line with literature and can be explained by the lower energetic reserve of the malnutrition state that affects the suboptimal recovery from post-operative complications in several kinds of surgical patients (e.g., gastrointestinal, urologic, bone, and neck surgery)[36].

Statistical analysis on the correlation between age and complications showed that 47% of patients in the younger group did not have postoperative complications. In particular, 20% of younger patients had complications that solved within three days after surgery. In the group aged 70-79 years old, complications were recorded in the 65% of patients (older *vs.* younger patients, $p<0.05$). This rate is comprehensive of patients who had complications both at T1 and T2 (47%).

In the elderly group (age > 80 years) 50% of patients had complications. It's interesting to note that in this group the majority of wound-related complications was recorded. This finding is in agreement with the suggestion that advanced age limits the efficacy of tissue regeneration after insults starting from a condition of sarcopenia linked to nutrients malabsorption and subclinical hyponutrition, irrespective of malnutrition diagnosis[37,38].

Older age tended to be correlated with a longer hospitalization stay without reaching statistical significance. This finding is apparently in disagreement with literature[36,39,40]. However, it can be explained by the small sample size that shows a tendency without reaching statistical significance. We can find an explanation for the lack of significance of the correlation between hospitalization stay and nutritional status within the same issue. In this case, also we can recognize a tendency towards difference in the hospitalization time according to the nutritional status, perhaps in agreement with the literature[36,39,40].

The first part of results (namely those on the prevalence of malnutrition in patients undergoing major surgery) clearly underlines the importance of an early diagnosis of the risk of malnutrition and malnutrition itself: focusing on an impaired nutritional status paves the road to a faster and more efficient approach to this issue. Thus, perioperative nutritional support can be important in order to solve one of the major factor affecting the outcome both of surgery and of patient's quality of life[36,39].

The second part of the results (namely those on the correlation of complications with both malnutrition and older age) brings the attention to the importance of knowing the "nutritional frailty", a peculiar subclinical entity indicative of sarcopenia of the elderly with an apparently good nutritional status[40]. This condition can affect how patients react to stressful events such as surgery[41,42]. Thus, the significant prevalence of local and sys-

temic complications *vs.* adult populations can be explained by ageing and malnutrition, two independent but physiopatologically linked factors affecting surgery outcome.

Limitations of our study are mainly the small numerosity of sample, the heterogeneity of surgical interventions, and the short-term of follow-up.

The former two have mainly conditioned the non-statistical significance of certain results such as the prevalence of early and late systemic complications in malnourished patients *vs.* well-nourished and at risk of malnutrition.

About the latter, three and six days after surgery can be argued to be both a short-term follow up as many of the post-operative complications can appear later. Thus, additional surveys are required in order to evaluate the development of complications even after weeks or months from the operation.

Conclusions

This observational prospective single-center study showed the significant association between nutritional status and early and late surgical complications onset. Moreover, in this research, we have showed how advanced age is an independent risk factor for a higher number and more severe surgical complications, both local and systemic.

Further randomized prospective larger studies are needed to confirm these observations perhaps extending the follow-up of the studied patients.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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