Clinical Significance of Preoperative Nutritional Status in 215 Noncancer Patients

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Preoperative nutritional status was assessed by: the percentage weight loss (% WL), body weight in relation to reference weight (WI), arm muscle circumference (AMC), and S-albumin (S-Alb) in a prospective study of 215 noncancer patients classified into three groups according to type of surgery: major vascular, minor vascular, and abdominal. The clinical significance of the nutritional markers was assessed by correlations to postoperative outcome and the time spent in the hospital after surgery. The influence of age on nutritional markers and clinical variables was evident but was ruled out in all correlations. If malnutrition was classified as two or more abnormal values in the nutritional markers (% WL, WI, AMC, S-Alb), the overall frequency was 12%, highest in the major vascular surgery group (18%) and lowest in the minor vascular group (4%). Patients with low nutritional status stayed an average of 29 days in the hospital compared to 14 days if the nutritional status was normal ($p < 0.01$). The overall complication frequency was higher in patients with low nutritional status compared to normal status (48% and 23%, respectively, $p < 0.01$). The frequency of serious complications was 31% in undernourished and 9% in well-nourished patients ($p < 0.05$). Various nonnutritional variables such as age, diagnosis, and duration of surgery were shown to increase the predictive ability of nutritional status. The results of this study confirm that nutritional state *per se* is predictive for postoperative outcome even when variables were stabilized for different backgrounds with covariation to nutritional status.

HOSPITALIZED PATIENTS often have an inappropriate food intake[1-3] and are frequently in negative energy balance.[4-5] According to the degree and the duration of negative balance, symptoms of malnutrition may appear and can be detected by measuring the energy and nutrient reserves and circulating proteins. In surgical patients several such nutritional markers have a proven correlation to complication frequency.[6-8] In certain combinations they have been shown to be of predictive value for surgical outcome.[9-12] In addition, even routine clinical judgments have been reported to be of predictive value.[13] However, since many of the nutritional markers are interrelated, regression analysis using such markers could lead to misinterpretations. Associated factors of nonnutritional origin, such as disease and age, may falsely influence the predictive ability of a prognostic nutritional index. This influence of nonnutritional variables may also vary among different groups of patients. Previous studies reporting predictive ability of nutritional state in surgical patients have not emphasized the importance of associated nonnutritional variables for the prognostic strength of nutritional state *per se* for the clinical outcome.

Therefore, the objectives of the present study were: 1) to find the least number of nutritional markers of clinical significance, *i.e.*, correlating to complication frequency and duration of hospital stay; 2) to test such a set of variables in a prospective study in relation to postoperative outcome; and 3) to evaluate the influence of nonnutritional variables in the prediction of complication frequency and duration of hospital stay in noncancer patients.

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Materials

Initially, the study comprised all patients admitted to one surgical ward at Sahlgrenska Hospital, Gothenburg, during a period of 6 months. Patients admitted for emergency surgery and those not subjected to surgery were then excluded. Cancer patients were also excluded. In the remaining patients (n = 215) the preoperative nutritional status was assessed within 1 day of admittance and the postoperative course was monitored until death or discharge from hospital. According to the type of surgery, the material was divided into four groups (see Table 1).

Methods

In addition to general clinical examinations, the following nutritional variables were examined.

TABLE 1. *Diagnosis of Patients Grouped According to Type of Surgery*

	Diagnosis	Number
Major vascular surgery	Aortic aneurysm	7
	Stenosis of major arteries	26
	Intermittent claudication	16
	Serious ischemia	29
Mean age 61.6 years	Subtotal	78
Minor vascular surgery	Stenosis of the carotid artery	16
	Varicose veins	40
Mean age 55.3 years	Subtotal	56
Abdominal surgery	Gallbladder disease	35
	Peptic ulcer	6
	Renal calculus	2
	Hernia and appendicitis	26
	Diagnostic laparotomy	3
	Coeliac plexus compression	1
Mean age 55.7 years	Subtotal	73
Other	Prostatic operation	4
	Papilloma of urinary bladder	1
	Raynaud's disease	1
	Hydrocele	1
	Keloid repair	1
Mean age 65.1 years	Subtotal	8
	Total number	215

Weight Loss

Weight loss, if present, was calculated from preillness weight, estimated by the patient. A weight loss of more than 5% was considered abnormal.

Anthropometry

Weight index was calculated as the actual weight divided by the reference weight for height. This reference weight (RW) was taken from a randomized population of middle-aged and elderly men and women in Gothenburg and calculated according to the equations: RW (women) = 0.65 × height − 40.4 and RW (men) = 0.80 × height − 62.0.[14] Normal weight index was 0.80 or greater. This comparatively wide range was deliberately chosen in order to minimize the risk for a false-positive indication of malnutrition in healthy, tall, and slim individuals. The arm circumference and the triceps skinfold were measured at the midpoint of the left arm and the arm muscle circumference was calculated.[15] The Swedish reference values for arm anthropometric measures used[16] were age-dependent. Values greater than the fifth percentile were classified as normal. Low values for arm muscle circumference in different age ranges are: 20 to 39 years: women ≤ 18 cm, men ≤ 22 cm; 40 to 49 years: women ≤ 19 cm, men ≤ 23 cm; 50 to 69 years: women ≤ 19 cm, men ≤ 22 cm; 70 to 79 years: women ≤ 18 cm, men ≤ 21 cm; and ≥ 80 years: women ≤ 17 cm, men ≤ 20 cm. All anthropometric measurements were performed by the same investigator (IW).

Serum Proteins

Blood samples were taken for analysis of S-albumin, S-transferrin, S-prealbumin, and S-retinol binding protein (S-RBP) using immunodiffusion technique. Reference values were collected from our own analysis of serum from 100 healthy persons (50 men and 50 women), mainly hospital staff. The age range in this reference population was 19 to 61 years. Low values were: S-albumin: women ≤ 33.0 g/l, men ≤ 38.3 g/l; S-transferrin: women and men ≤ 2.1 g/l; S-prealbumin: women ≤ 0.213 g/l, men ≤ 0.235 g/l; S-RBP: women and men ≤ 0.035 g/l.

Cell-mediated Immunity

A subgroup of 46 patients divided evenly between the four surgery groups were subjected to skin tests for delayed hypersensitivity to Candida, purified protein derivative (PPD), and phythemagglutinin (PHA). The induration was read after 48 hours and the reaction was classified

TABLE 2. *Means and Standard*

Type of Surgery	Sex	n	WI	n	TSF (mm)	n	AMC (cm)	n	S-Alb (g/l)	n	S-Prealb (mg/l)
Major vascular surgery	F	25	0.96 (±0.03)	26	18.1 (±1.5)	26	21.9 (±0.4)	26	37.9 (±0.9)	26	245 (±13)
	M	52	0.95 (±0.02)	52	11.2 (±0.9)	52	25.3 (±0.3)	51	40.3 (±0.7)	51	280 (±10)
Minor vascular surgery	F	24	1.11 (±0.06)	24	22.7 (±1.6)	24	23.3 (±0.6)	24	41.7 (±0.6)	24	285 (±12)
	M	32	0.94 (±0.02)	32	10.6 (±0.6)	32	25.7 (±0.4)	32	42.6 (±0.7)	32	284 (±8)
Abdominal surgery	F	32	0.99 (±0.04)	32	19.5 (±1.2)	32	22.4 (±0.4)	32	40.3 (±0.7)	32	266 (±15)
	M	40	0.95 (±0.02)	40	9.7 (±0.5)	40	25.9 (±0.4)	38	41.1 (±0.6)	38	291 (±13)
Other	F	3	1.03 (±0.04)	3	18.9 (±3.6)	3	22.2 (±0.8)	3	41.0 (±1.5)	3	266 (±17)
	M	5	0.90 (±0.05)	5	9.1 (±1.3)	5	23.8 (±1.0)	5	41.3 (±1.6)	5	297 (±22)

as normal if the sum of right angle diameters was greater than 10 mm.[17] If two skin tests were abnormal the patient was defined as relatively anergic. If all three skin tests were abnormal the patient was defined as anergic.

Clinical Data Registered During Surgery

The surgeon (senior or junior), the type of surgery, the duration of surgery, the estimated blood loss, and the amount of blood and plasma infused during the operation were recorded. The amount of replaced blood loss was used in our correlation computations.

Postoperative Outcome

Disturbances such as short-time fever and nausea and vomiting after surgery were registered. Complications were classified according to severity as minor (infections, mainly wound infections and trombophlebites) or major or serious (trombosis, myocardial infarction, pulmonary embolism wound rupture, and death). The complications were scored according to an arbitrarily chosen ranking scale. The scores were: no complication–0, fever less than 2 days–1, fever more than 2 days–2, infection–3, major trombophlebites–4, thrombosis–5, and myocardial infarction, wound rupture demanding reoperation, and death–6. Antibiotic medication and the number of days on parenteral infusion and liquid diet were also registered as well as the length of the total and postoperative stay. The length of preoperative hospital stay depended on medical, organizational, and social factors. All clinical data were continuously registered by the same nurse and physician (KL). Simms' modified prognostic index (PI) was used to predict complications and duration of hospital stay.[12]

Pilot Study

Prior to the main study, a pilot study was conducted in the same ward on 44 patients to find out which set of nutritional variables were of clinical significance if measured preoperatively, *i.e.*, were correlated to the duration of hospital stay and/or to complication frequency. The variables tested were the same as mentioned above with the exception of the skin tests. In addition to this the total body potassium[18] and lymphocyte count were measured. The patients of the pilot study were not included in the main study.

Statistical Calculations

The nonparametric Pitman's and Fisher's permutation tests were used with or without background variables.[19] Only the 5% ($p < 0.05$) and the 1% ($p < 0.01$) levels of significance were tested.

Results

Pilot Study

The pilot study indicated that weight index, arm muscle circumference, S-albumin, and weight loss correlated significantly to the postoperative outcome. [Weight index was chosen as an indicator of malnutrition among the variables reflecting fat mass of the body (body weight, triceps skinfold, and weight index).] The remaining markers from this group did not increase the predictive ability of weight index. The total body potassium was of similar significance as the arm muscle circumference, but in clinical routine the latter is to be preferred due to availability of the method. From the four serum proteins (albumin, transferrin, prealbumin, and retinol binding protein) albumin had the greatest predictive ability and the remaining proteins did not increase the prediction further. Weight loss in itself correlated closely to all clinical markers.

Main Study

The mean values and standard errors of all data recorded in the main study are given in Table 2. The frequency of abnormal values for the variables used (as selected from the pilot study) are given in Table 3. Individuals having abnormal values in at least two of the four

Errors of Registered Data

n	S-Transferrin (g/l)	n	S-RBP (mg/l)	n	% Weight Loss	n	Duration of Surgery (h)	n	Replaced Blood Loss (ml)	Hospital Stay Total (days)	Stay Postop (days)
76	2.8 (±0.1)	77	77 (±3)	78	2.9 (±0.5)	77	3.5 (±0.2)	77	629 (±84)	28.5 (±3.3)	20.7 (±3.1)
54	3.1 (±0.1)	56	67 (±2)	56	1.1 (±0.4)	56	1.6 (±0.1)	56	125 (±19)	6.6 (±0.7)	3.6 (±0.6)
69	3.0 (±0.1)	70	68 (±3)	72	2.2 (±0.6)	72	1.8 (±0.1)	72	231 (±43)	10.4 (±0.6)	6.4 (±0.4)
8	2.9 (±0.1)	8	67 (±7)	8	0.9 (±0.6)	8	1.2 (±0.3)	8	306 (±194)	8.4 (±1.8)	4.3 (±1.0)

TABLE 3. *Frequency of Abnormal Values in Weight Index (WI), Arm Muscle Circumference (AMC) S-Albumin, and Weight Loss and Frequency of Malnutrition According to Diagnosis*

Type of Surgery	WI (%)	AMC (%)	S-Albumin (%)	Weight Loss (%)	Malnutrition (%)*
Major vascular surgery	14	5	25	23	18
Minor vascular surgery	9	4	9	9	4
Abdominal surgery	17	7	13	15	13
Other	11	11	11	0	11
All patients	14	6	16	16	12

* If two or more values of WI, AMC, S-Albumin below reference value or per cent weight loss ≥ 5%.

variables (weight index, arm muscle circumference, S-albumin, and weight loss) are considered to be in a state of malnutrition. This definition of malnutrition is justified by the fact that this distinction was of clinical significance according to both complication frequency and duration of hospital stay.

Nutritional Variables

Low S-albumin levels were found in 16% of all patients. Weight loss correlated closely to S-albumin ($p < 0.01$) and was seen in 16% of these patients. Weight index was low in 14% of all patients. Arm muscle circumference was the least sensitive marker, abnormal in only 6% of all patients (significantly lower frequency compared to weight index, albumin, and weight loss, $p < 0.01$). For low values in the different surgery groups see Table 3. Malnutrition was most frequent in the major vascular surgery group (18%) and most infrequent in the minor vascular surgery group (4%, $p < 0.05$). In the abdominal surgery group 13% of the patients could be classified as malnourished.

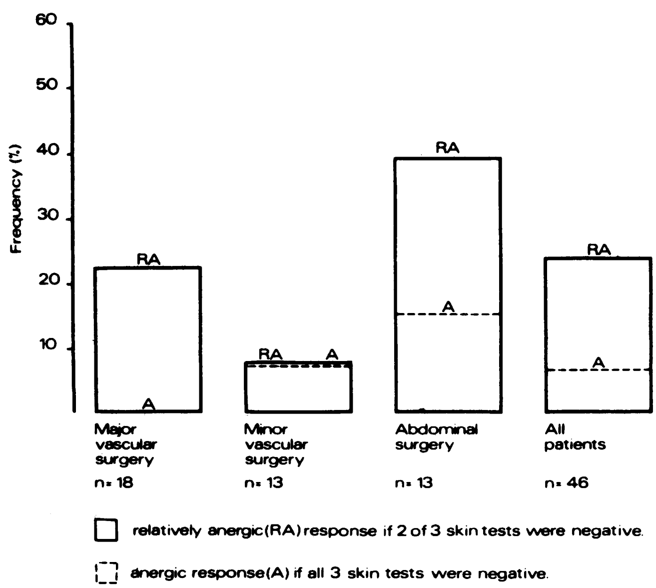

FIG. 1. Frequency of relatively anergic (RA) and anergic (A) response to skin tests with Candida, purified protein derivative, and phythemagglutinin.

Skin Tests

The results from the skin tests are given in Figure 1. Twenty-four per cent of all patients were classified as relatively anergic and only 7% as anergic. The highest frequency of poor responders was found in the abdominal surgery group (38% relative anergy and 15% anergy). None of the three skin tests nor the combined reactions correlated to any of the clinical variables or to the nutritional variables used. The number of skin-tested patients was too few to allow any use of the Mullen's prognostic nutritional index (PNI).[9] Simms' modified prognostic index[12] correlated closely to age ($p < 0.01$) and to complications ($p < 0.05$) and duration of hospital stay ($p < 0.05$) without influence of age.

Correlations

The age of the patients correlated significantly to S-albumin ($p < 0.01$), S-transferrin ($p < 0.01$), S-prealbumin ($p < 0.05$), per cent weight loss ($p < 0.05$), complications ($p < 0.01$), and duration of total as well as postoperative hospital stay ($p < 0.01$). To find the "true" correlation (age independent) between the preoperative nutritional status and postoperative complications and durations of hospital stay, age was selected as the background variable in the statistical analysis. The clinical experience of surgical risks in relation to age caused a division of the material into three age classes, which is accounted for in the statistical evaluations: patients below 60 years of age (low risk), between 60 and 70 years (intermediate risk), and above 70 years (increased risk). The significant correlations between the nutritional and the clinical variables are shown in Table 4. Taking all patients into one group, albumin correlated to the clinical variables (complication frequency, $p < 0.01$ and hospital stay, $p < 0.01$) and weight loss only to complication frequency ($p < 0.01$). In the major surgery group albumin only correlated to hospital stay ($p < 0.05$). In the minor surgery group per cent weight loss correlated to the clinical variables ($p < 0.05$ for complication frequency and $p < 0.01$ for duration of hospital stay). In the abdominal surgery group, the weight index correlated to the total ($p < 0.05$) and the postoperative hospital stay ($p < 0.01$). Within the abdominal surgery group the serum proteins with a short half-life correlated to complications ($p < 0.05$ for prealbumin and $p < 0.01$ for RBP). No significant correlations

TABLE 4. *Statistically Significant Correlations Between the Nutritional Variables and the Clinical Variables (Pitman's Permutation Test with Age as Background Variable)*

	Weight Index	Arm Muscle Circumference	Albumin	Transferrin	Prealbumin	Retinol Binding Protein	Per cent Weight Loss
Complications			All patients*		Abdominal surgery†	Abdominal surgery†	All patients* Minor surgery†
Total hospital stay	Abdominal surgery†		All patients* Major surgery†				Minor surgery*
Postoperative hospital stay	Abdominal surgery*		All patients*				Minor surgery*

* $p < 0.01$. † $p < 0.05$.

were found between arm muscle circumference or S-transferrin and any of the clinical variables.

The overall complication frequency was 48% in patients with abnormal nutritional status and 23% in patients with a normal nutritional state ($p < 0.01$; Table 5). The frequency of major complications was 31% in patients with abnormal nutritional status and 9% in patients with normal status ($p < 0.05$). Furthermore, four of five deaths were found in the malnourished group. Malnourished patients spent totally 29 ± 5 days (mean ± SEM) and wellnourished patients 14 ± 1 days in the hospital ($p < 0.01$), while the postoperative hospital stay was 20 ± 4 in malnourished patients compared to 10 ± 1 days in wellnourished patients ($p < 0.05$). These differences were also significantly different when the influence of age was stabilized for in the statistical computations.

Correlations were found between the experience of the surgeon and the outcome of the operation. The more experienced the surgeon was, the higher was the complication frequency ($p < 0.01$) and the longer was the hospital stay ($p < 0.01$). The patients operated on by the most experienced surgeons were more frequently in the need of postoperative nutritional support compared with other patients ($p < 0.01$). Significant relationships were also found between the duration of surgery and the recorded postoperative variables. The longer the operation time, the higher the complication frequency and the longer the hospital stay in all patients irrespective of their nutritional state ($p < 0.01$). This was true for the minor vascular surgery group and in the abdominal surgery group ($p < 0.01$), but not in the major vascular surgery group. Surgery of long duration *per se* caused the supply of higher amounts of blood and plasma during surgery ($p < 0.01$) and was followed by more days on parenteral support ($p < 0.01$).

Discussion

The clinical significance of preoperative nutritional status assessment has been documented in a variety of surgical patients.[9,11,13] The present study confirms that malnourished patients presented 48% overall complications compared to 23% in wellnourished patients. More important is that serious complications were present in 31% of the malnourished patients and in only 9% of the wellnourished patients (Table 5). Furthermore, four of five deaths occurred in malnourished patients. In the earliest studies of this kind, no attempt was made to combine nutritional markers. Each marker was separately analyzed and gave rise to its own frequency of malnutrition.[20-22] To be of value in the clinical routine, an assessment of individual risk is required. To achieve this, combinations of nutritional markers into prognostic indices have been created.[9-12,23] Unfortunately, many of the markers are both interrelated and may also correlate to important factors of nonnutritional origin. Regression analysis using such markers might therefore falsely influence on the predictive ability of the index.[13]

This study reports that the overall frequency of malnutrition was 12%, which is much lower than reported in previous studies by others. This wide difference in the frequency of malnutrition is probably due to the different combinations of nutritional markers, ununiformed definition of malnutrition among different studies, the quality of the reference values, and the type of patients and dis-

TABLE 5. *Overall Frequency of Malnutrition and Its Relationship to the Duration of Hospital Stay and PostOperative Complications in All Patients*

Nutritional Status	Frequency (%)	Hospital Stay (days) Total	Hospital Stay (days) Postoperative	Overall Complication Frequency (%)	Serious Complications (%)
Malnutrition	12	29*	20†	48*	31†
Normal nutritional status	88	14*	10†	23*	9†
Significant differences		$p < 0.01$	$p < 0.05$	$p < 0.01$	$p < 0.05$

eases examined. For obvious reasons, nutritional markers have wide normal ranges. This is especially true of the anthropometric measurements. The cutoff point between normal and abnormal values has previously been arbitrarily chosen and also influenced by the often asymmetric distribution of the values in a healthy population. As cutoff points for the anthropometric measures the principle of percentiles is to be preferred to standard deviations or per cent deviation from normal values. The fifth percentile was chosen as limits in the present study, but the results were similar even when using the 2.5 percentile. Unfortunately, in the body weight reference used[14] only per cent deviations were available. The plasma proteins of our reference population presented normal distributions, which allowed us to use −2 standard deviations as limit for low values. Correlations to age have previously been reported,[24] but significant changes occurred only over 80 years of age and were not included in the present study. Moreover, reference values must be collected from the same population as the patients. All reference values in the present study were controlled for such possible errors.

The nutritional prognostic indices have often been claimed to be universal for surgical patients.[9,11,12] However, the results of the present study indicate important variations in the prognostic ability of different nutritional markers in different subgroups of patients. S-albumin was found to have greatest prognostic value in the present study irrespective of diagnosis and has also been included in most indices.[9-12] Several sets of nutritional prognostic markers make use of transferrin,[7,9,12] but transferrin had no predictive value whatsoever in our patients. Theoretically, serum proteins with short half-lives would be of great value in rapidly changing conditions. However, in our study this relationship was only observed for S-prealbumin and S-RBP in the abdominal surgery group. In the present study the lack of any correlation between triceps skinfold and the clinical variables was evident. Very few patients actually showed abnormally low triceps skinfold. Arm muscle circumference is often measured as reflecting the nutritional status[10,20-22] but it failed to be significant in this study. Skin testing was of no value to predict complications among the few patients being anergic (n = 3). This was in conflict with results from larger series of patients.[25] So far, the preoperative weight loss or the weight index has not been included in reported prognostic indices. In the present study weight loss had predictive value in the minor vascular surgery group and weight index in the abdominal surgery group. It deserves to be emphasized that a history of even a small amount of weight loss in patients (approximately 2%) may objectively signal altered homeostasis, even if one would suspect that such small changes should be unpredictive.

Conflicting results among different studies might be explained by the fact that various studies have been performed in different patient populations with their specific risks to develop postoperative complications. Thus, the diagnosis must be taken into account when judging the predictive ability of any nutritional index. For example, in major surgery a low S-albumin level alone seems to be sufficient to detect a prolonged hospital stay, while in minor surgery several nutritional markers must be low before complications and prolonged hospital stay may be predicted. Recently, an attempt has been made to distinguish between different diagnosis (cancer versus noncancer) when discussing the significance of prognostic indices.[11] This distinction was reported to increase the predictive ability of the nutritional index. In addition, the present study confirms that patients above 70 years of age have more postoperative complications and prolonged hospital stay than younger patients irrespective of nutritional state. Therefore, nutritional prognostic indices should benefit by taking age into account. The possibility of analyzing relationships where the influence of age is to be ruled out depends either upon the size of the patient group or on the combinations of trends within each age group.[19]

In general, the duration of surgery is a powerful predictive factor for postoperative outcome reflecting the complexity of the procedure. In the present study, this factor was of importance for the postoperative outcome except within the major surgery group, since a major surgical procedure in itself represents an increased clinical risk for complications. The fact that when the most experienced surgeon performed the surgery, the highest complication frequency was obtained probably indicates that the more experienced surgeons did the most difficult operations. This further illustrates interrelated factors of different nature.

In conclusion, this study confirmed that it is possible to predict the postoperative outcome and duration of hospital stay by means of preoperative nutritional assessment. However, factors of nonnutritional origin such as diagnosis, age, and duration of surgery should also be taken into account as they might otherwise falsely influence the predictive ability of the nutritional state itself.

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