The Response to TPN

A Form of Nutritional Assessment

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Malnutrition in surgical patients is associated with an increased incidence of postoperative mortality and morbidity. Preoperative nutritional support has been shown to be efficacious in reducing the incidence of these complications, although the postoperative complication rate in these patients continues to be greater than in their wellnourished counterparts. This study attempts to determine whether the postoperative course can be either influenced by or predicted from the preoperative response to nutritional support. Thirty-two patients with nutritional depletion who received an average of 1 week of total parenteral nutrition prior to a major abdominal operation were studied. These patients were followed for postoperative complications. Of the 16 patients who exhibited the characteristic response to early nutritional support, diuresis of the expanded extracellular fluid compartment with a resultant loss of weight (127.9 ± 5.7 to 124.6 ± 5.8 (SEM) lbs, $p < .001$) and rise in serum albumin (3.21 ± 0.14 to 3.46 ± 0.15 gms%, $p < 0.001$), only one developed a complication in the postoperative period. The other 16 patients did not exhibit this response. They retained additional fluid, gained weight (119.3 ± 8.1 to 121.3 ± 8.2 lbs, $p < .025$), and showed a decrease in serum albumin levels (3.14 ± 0.14 to 3.00 ± 0.14%), $p < 0.01$). Eight of these patients developed a total of 15 postoperative complications ($p < 0.01$). This study demonstrates that the response to preoperative TPN is an important factor in assessing operative risk and morbidity. The need to individualize preoperative nutritional support and the timing of surgical intervention is clearly demonstrated.

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THE RELATIONSHIP BETWEEN the nutritional status of surgical patients and postoperative morbidity and mortality is well recognized. In 1936, Studley[1] noted that patients undergoing ulcer surgery who had lost greater than 20% of their normal body weight had an increase in postoperative complications, particularly wound disruption and pneumonia. In 1944, Cannon et al.[2] reported an association between protein deficiency and the frequency and severity of postoperative infections. In 1955, Rhoads and Alexander[3] found that postoperative complications, such as urinary tract infection, wound infection, and respiratory tract infection, were greater in patients who were hypoproteinemic prior to surgery. These investigators stressed the importance of restoring nutritional deficits before subjecting patients to elective operation. Despite a long history suggesting an association between malnutrition and surgical complications, the selection of patients for preoperative nutritional support continues to be a troublesome clinical problem.

The objective measurements of preoperative nutritional status commonly used as predictors of postoperative morbidity and mortality include serum levels of albumin and transferrin, cutaneous delayed hypersensitivity, and weight loss.[4-8] However, these parameters do not effectively predict which patients are at an increased operative risk due to malnutrition. There is a related problem: that of determining an adequate time period for the administration of nutritional support to those patients selected to receive it prior to operation. Initial trials which examined the efficacy of postoperative total parenteral nutrition (TPN)[9] and short courses (48–72 hours) of preoperative in conjunction with postoperative TPN[9,10] did not demonstrate any clear benefits. When preoperative nutritional support was applied for periods of 1 week or more, postoperative morbidity declined significantly.[11] This reduction in the total number of complications was mainly due to improved wound healing,[12,13] a decreased incidence of wound infection,[14] respiratory failure,[11] and generalized sepsis.[11,15,16] Thus, a few days of preoperative nutritional support appears to be inadequate, while a week is considered to be beneficial in reducing postoperative morbidity.

However, despite the reduction in morbidity and mortality which may result from preoperative TPN, a sig-

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nificant number of these patients continue to develop serious complications after operation. The present study was undertaken in an effort to better define the role of preoperative nutritional support in surgical patients. The timing of operation in relation to the response to nutritional support is examined.

Methods

Thirty-two patients were admitted into the study. All had been referred by primary physicians for preoperative nutritional support and all met three major criteria. The criteria for inclusion were: (1) the presence of malnutrition as defined below, (2) a preoperative nutritional support period of between 5 and 14 days, and (3) a major abdominal operation.

Malnutrition was considered to be present when there had been a recent weight loss of greater than 10% of normal body weight and the serum albumin level was less than 3.5%. The period of preoperative nutritional support was limited to between 5 and 14 days in order to assure that all patients were receiving at least the minimum amount of nutritional support, which has been shown to be efficacious. Finally, all patients in the study underwent a major abdominal operation.

Total parenteral nutrition (TPN) was instituted using a Broviac catheter placed *via* a cutdown in the cephalic or basilic vein. Patients received a caloric intake approximately 1.5 times their estimated resting energy expenditure.[17] Protein intake varied between 1.5 and 2.0 grams/kg and nonprotein calories were evenly divided between fat and glucose. All patients were continued on TPN in the postoperative period until such time as either oral intake was adequate as confirmed by calorie count or intravenous feeding was replaced by enteral nutritional support.

Venous blood was sampled three times per week and analyzed for serum albumin (Technicon®, Simultaneous Multiple Analyzer Computerized). Daily weights were obtained. These two parameters were used to assess the response to nutritional support. Based on response patterns, the patients were divided into two groups. Group 1, comprised of 16 patients, demonstrated a loss in weight and rise in serum albumin following the institution of TPN. This was due to a diuresis of the previously expanded extracellular space. Group 2, the remaining 16 patients, gained rather than lost weight and had no change or a decrease in serum albumin. This is consistent with fluid retention and an expansion of the ECF.[18]

The postoperative course of each patient was followed with respect to specific complications. The complications were subdivided under infectious and mechanical. Infectious complications included: (1) generalized infection, as defined by a temperature greater than 101 F, leukocytosis, and a positive blood culture, (2) abscess formation with a positive culture requiring drainage, (3) pneumonia, as diagnosed by chest roentgenogram and sputum culture, and (4) wound infection, defined as purulent drainage with a positive culture requiring opening of the operative incision. Mechanical complications were those related to an expanded extracellular fluid space and its influence on respiratory function, wound healing, and return of bowel function. They included: (1) prolonged postoperative mechanical ventilation (greater than 24 hours), (2) wound dehiscence (requiring operative closure), and (3) anastamotic leak and/or fistula formation with documentation by contrast studies.

TABLE 1. *Patient Diagnoses by Group*

Diagnosis	Group 1	Group 2
Gastric cancer	5	4
Pancreatic cancer	1	1
Bladder cancer	2	2
Colon cancer	1	0
Diverticular disease	0	2
Small bowel obstruction	2	2
Gastric outlet obstruction	2	1
Inflammatory bowel disease	2	3
Chronic pancreatitis	1	0
Hiatal hernia	0	1
Total	16	16

Results

The actual patients diagnoses in the two groups are listed in Table 1. Of the 16 patients in Group 1, 12 were men and four were women. The mean age was 57.0 ± 4.7 years (Mean ± SEM). Group 2 was comprised of 10 men and six women with a mean age of 62.1 ± 4.4 years.

All patients were extremely malnourished at the time of their referral (Table 2). Recent weight loss averaged 24% and there were no differences between groups. This degree of nutritional depletion is characteristically associated with an expansion of the extracellular fluid space and a decrease in serum albumin. This is consistent with the findings in both groups, which exhibited low serum albumin levels (Table 2).

During the administration of TPN, some patients demonstrated an improvement in body composition, characterized by a diuresis, reduction in body weight, and

TABLE 2. *Nutritional Parameters; (Mean ± SEM)*

Parameter	Group 1	Group 2
Weight loss (lbs)	24.0 ± 4.6	24.5 ± 4.1
% normal weight	83.8 ± 2.7	83.4 ± 2.4
Albumin gms %	3.21 ± 0.14	3.14 ± 0.14

TABLE 3. *Changes in Body Weight and Serum Albumin During TPN (Mean ± SEM)*

	Pre-TPN	Immediately Preoperative	
	Wt (lbs)		p<
Group 1	127.9 ± 5.7	124.6 ± 5.8	***
Group 2	119.3 ± 8.1	121.3 ± 8.2	**
	Albumin (%)		
Group 1	3.28 ± 0.14	3.46 ± 0.15	***
Group 2	3.14 ± 0.14	3.00 ± 0.14	*

Comparison of Pre-TPN to immediately preoperative, paired t-test.
* $p < .01$
** $p < .025$.
*** $p < .001$.

rise in serum albumin; they were placed in Group 1 (Table 3). The changes began to develop early in the course of nutritional repletion and reached a maximum by the sixth day of therapy (4.9 ± 0.2 days) in all patients. The diuresis of the expanded ECF was evidenced by a loss of weight (127.9 ± 5.7 to 124.6 ± 5.8 lbs, $p < .001$) and an increase in serum albumin (3.21 ± 0.14 to 3.46 ± 0.15 gms %, $p < .001$). This diuresis did not take place in the patients in Group 2. Rather, there appeared to be an expansion of ECF, where weight gains were associated with a progressive reduction in serum albumin levels (Table 3).

At the time of operation, the patients in Groups 1 had received 7.4 ± 1.0 days of preoperative TPN, while the patients in Group 2 had received 6.8 ± 1.0 days (NS). All patients underwent major intra-abdominal procedures (Table 4) with similar mean operative times (Group 1—3.6 ± 0.6 hrs, Group 2—4.4 ± 0.9 hrs).

The postoperative course of the patients in the two groups were remarkably different. Only one patient in Group 1 experienced a complication during the postoperative convalescent period. This patient developed pneumonia which resolved, but he eventually succumbed to a cerebral vascular accident. In Group 2, eight of the sixteen patients developed 15 postoperative complications

TABLE 4. *Operations by Group*

Operation	Group 1	Group 2
Exploratory laparotomy	2	1
Gastric/small bowel resection	4	4
Bypass	3	5
Colon resection with anastomosis	3	2
End colostomy	1	1
Cystectomy	2	2
Distal pancreatectomy	1	0
Hiatal hernia repair	0	1
Total	16	16

($p < .05$) (Table 5). Of particular note is the fact that four of these patients required mechanical ventilation for over 24 hours, while six developed a total of eight infectious complications (Table 5). Two of the patients in this group who developed pneumonia had required prolonged postoperative ventilation, and one patient eventually died from respiratory failure. Of the other two deaths in this group, one was a patient who developed postoperative sepsis and the other was apparently unrelated to the nutritional state.

Discussion

The changes in body composition that occur during nutritional depletion characteristically include an expansion of the extracellular fluid compartment. This expanded extracellular fluid compartment results in edema, which may delay normal wound healing and has been shown to be associated with an increased incidence of wound dehiscence, anastomatic breakdown, and wound infection.[19-22] Excess fluid may also be present as interstitial pulmonary edema and lead to respiratory failure in the postoperative period.[15] Malnutrition has also been associated with decreased immunocompetence and anergy. In this compromised immune state, surgical patients may also be subject to an increased number of septic complications.[23,24]

The unfavorable clinical setting may be reversed prior to operation by the institution of a nutritional support regimen. Following a 2–3 week course of nutritional support, there is a marked improvement in the levels of IgG,

TABLE 5. *Postoperative Complications*

Complications	Group 1	Group 2
Mechanical		
Prolonged mechanical ventilation	0	4
Fistula	0	0
Wound dehiscence	0	1
Anastamotic leak	0	0
Total	0	5*
Infectious		
Sepsis	0	2
Pneumonia	1	3
Wound infection	0	3
Abscess	0	0
Total	1	8*
Death	1	2
Total complications	1	15**
Total number of patients developing complications	1	8**

Comparison of Group 1 to Group 2 (chi-squared, with continuity correction).
* $p < .05$.
** $p < .01$.

IgM, and complement factor C_3[25,26] as well as an increase in the total lymphocyte count and the lymphocyte response to a challenge with phytohemaglutinin. However, reversal of anergy usually occurs only after longer periods of nutritional support.[26,27]

The relationship between improvement in the immune status and the characteristic changes in body composition (diuresis of the ECF) in response to nutritional support has been demonstrated by Forse et al.[28] Using the Na_e/K_e ratio as an indicator of body composition, they showed that this ratio was increased (with an expansion of the ECF) to levels considered to represent severe malnutrition in the majority of anergic patients. After receiving TPN, the patients who reversed their anergy also showed a significant decrease in their Na_e/K_e ratio with a decrease in the ECF. The patients who remained anergic showed no change in body composition and an increase in complications.

The different patterns of response seen during nutritional support appear to be related to the incidence of postoperative complications for the two groups of patients in this study. Patients in Group 1 exhibited the expected response of a malnourished patient following institution of nutritional support. The expanded ECF contracted as the patients diuresed, resulting in an increase in the serum albumin level. This immune state also presumably began to improve and thus the patients were at less risk for infectious complications. The patients in Group 2 did not respond in this fashion. Diuresis of the ECF did not occur. In fact, retention of fluid resulted in an expansion of the ECF as evidenced by weight gain and a decrease in the serum albumin level. The immune state of these patients presumably did not improve prior to undergoing operation. A significantly greater number of mechanical and infectious complications occurred in these patients as compared to those in Group 1.

While it might be possible to predict an altered response to nutritional support, in some instances, on the basis of admission diagnosis, state of malnutrition, or clinical assessment, it would not be accurate for most patients being considered for preoperative TPN. The response to nutritional repletion exhibited by the patients in Group 2 has previously been described as occurring in patients with ongoing stress.[18] The possibility that these patients were, as a group, more seriously ill than the patients in Group 1 cannot be overlooked. Certainly these patients did not appear to receive the same benefits of a 1-week course of pre-operative nutritional support as did those in Group 1. Longer courses of preoperative TPN might in fact have been beneficial to these patients. In a separate analysis of eight patients that did not diurese after 1 week of TPN but then went on to receive between 3–4 weeks of nutritional support before operation, there was only one postoperative complication, a wound infection (unpublished results).

The role of preoperative nutritional support appears to be multifaceted. The risks of a postoperative complication decrease in patients who receive TPN for 1 week and exhibit an early diuresis in response to repletion. For those patients that do not diurese, the question arises as to whether a prolonged course of preoperative nutritional support should be undertaken. Initial results suggest that this would be beneficial; however, each patient must be assessed individually to determine if the problem is more than one of poor nutritional response.

Body weight and albumin levels during preoperative nutritional support provide an important determinant of the risk of postoperative complications after 1 week of TPN. Patients who lose weight and show a rise in their serum albumin levels after 1 week of preoperative TPN have been shown to have a reduced risk of postoperative complications. Patients who do not diurese, but rather gain weight with a reduction in serum albumin levels remain at an increased risk for a postoperative complication. These patients should undergo further evaluation to investigate the reason for this response and may well be candidates for a prolonged course of TPN.

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