
Risk Factors for Postoperative Pneumonia

The Importance of Protein Depletion

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Pulmonary complications remain the most important cause of postoperative morbidity and mortality. The many advances of modern surgical care over the last 30 years have not appreciably altered the incidence of these complications. Many risk factors have been shown to contribute to this problem, but no studies have examined the impact of preoperative protein depletion on respiratory function and related this to the development of postoperative pulmonary complications. 80 patients (42 men, 38 women, median age of 64 years, with a range of 15–91 years) awaiting major elective gastrointestinal (G.I.) surgery were divided into two categories on the basis of a direct measurement of protein depletion: nonprotein-depleted patients ($n = 41$, mean protein loss, $2\% \pm 1.7$ SEM) and protein-depleted patients ($n = 39$, mean protein loss, $36\% \pm 3.5$ SEM). There was no significant difference between these two categories in regard to age, height, sex, surgical diagnosis, the presence of chronic lung disease, smoking, proportion of upper abdominal incisions, degree of obesity, the duration of anesthesia, and the use of prophylactic antibiotics and physiotherapy. There was a significant difference between these two categories of patients in regard to respiratory muscle strength ($p < .025$), vital capacity ($p < .05$), and peak expiratory flow rate ($p < .005$). Pneumonia developed in a significantly higher proportion of protein-depleted patients with atelectasis ($p < .05$), and their stay in the hospital after surgery was longer ($p < .05$). These data show that protein depletion is associated with an impairment of respiratory function, and is in itself a significant risk factor in the development of postoperative pneumonia.

DESPITE THE MANY ADVANCES in anesthetic and surgical techniques, the incidence of postoperative pneumonia has not changed appreciably over the past 30 years¹; it remains the most important cause of morbidity and mortality after major abdominal surgery.^{2,3} Although many risk factors for postoperative pulmonary complications have been identified,^{1,4–6} preoperative protein depletion has not

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been seriously examined.⁷ Protein depletion is common in general surgical patients,⁸ is associated with impairment of a wide range of physiologic functions (including respiratory function),^{9–13} and results in a higher incidence of postoperative complications and a longer hospital stay.^{14–16} In a prospective series of patients, we have examined the effect of preoperative protein depletion on respiratory function and its role as a risk factor of postoperative pulmonary complications.

Methods

Over a 15-month period, all adult patients presenting to the Department of Surgery at Auckland Hospital for elective surgical procedures in which a major resection of some part of the gastrointestinal (G.I.) tract was planned and who were not septic or immunocompromised and for whom preoperative intravenous (I.V.) nutrition was not considered essential were asked if they would be willing to take part in this study. On the day before surgery, 80 patients (42 men, 38 women, median age of 64 years, with a range of 15–91 years) were clinically assessed to identify risk factors for postoperative pulmonary complications, measurements of body composition, and respiratory function. Their clinical course was carefully monitored until discharge. This study was carried out with the consent of the Auckland Hospital Human Ethical Committee.

Body Composition Analysis

Prompt *in vivo* neutron activation analysis (IVNAA) and the tritiated water dilution technique were used to measure total body protein (TBP) and total body fat (TBF).¹⁷ The protein index,¹⁸ a measure of protein de-

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TABLE 1. *The Logistic Regression Analysis of Risk Factors for Postoperative Pneumonia Listed in Order of Relative Importance*

Risk Factor	Partial Regression Coefficient	Standard Error	Chi-Square	p
Incision site	2.27	0.94	5.84	0.015
Protein depletion	5.63	3.89	2.09	0.148
Age	0.03	0.03	0.90	0.343
Operation duration	0.29	0.36	0.66	0.417
Obesity	1.01	1.65	0.37	0.543
Smoking	0.39	0.85	0.21	0.645
(Intercept)	1.78	5.28)		

pletion, is the measured TBP divided by a predicted TBP. The predicted TBP was derived from regression equations, using the age, height, and sex of a local normal population that had had direct measurements of TBP. In the same way, a fat index was calculated from the measured and predicted TBP of each patient, and is used to measure the extent of body fat depletion. The patients were ranked on the basis of the protein index (PI) and divided into two categories: nonprotein-depleted patients and protein-depleted patients. Forty-one nonprotein depleted patients had a PI > 0.77, and 39 protein-depleted patients had a PI ≤ 0.77. This cutoff value represents 2 standard deviations from the mean of a study of normal volunteers using the same neutron activation facility.¹⁸

Respiratory Function Analysis

Respiratory muscle strength was assessed by measuring mouth pressure with a Validyne bidifferential pressure transducer (Model MP 45) (Validyne Engineering Corp., Northridge, CA) during maximal static inspiration (MIP) at functional residual lung capacity and during maximal static expiration (MEP) at total lung capacity.^{12,19} A respiratory muscle strength index was derived as the average of the per cent predicted MIP and MEP. These were derived from regression equations based on the patient's age, height, and sex.^{20,21} Forced expiratory volume in 1 second (FEV₁), vital capacity (VC),²² and peak expiratory flow rate (PEFR)^{23,24} were also measured and expressed as the percentage of a predicted value that were separately derived from regression equations for FEV₁,²⁵ VC,²⁶⁻²⁸ and PEFR.^{29,30} These gave similar results to equations derived from a study of 59 local normal volunteers (unpublished).

The Assessment of Risk Factors for Postoperative Pulmonary Complications

The important risk factors were identified and recorded in the following manner. The incision site^{1,30-33} was recorded as either upper or lower abdominal. Any

incision with a portion above the umbilicus was considered upper abdominal. The presence of pre-existent acute or chronic respiratory disease^{1,4} was identified by history and confirmed by both examination and measurement of respiratory function. Patients were classified through the measurements of FEV₁/VC and per cent predicted VC³⁴ as having obstructive, restrictive, and combined respiratory disease. Before surgery, patients independently assessed by the clinical team as having significant respiratory disease were seen by a physiotherapist, and received postoperative physiotherapy accordingly.³⁵ Patients receiving medication for asthma received nebulized bronchodilator both before and after surgery. Smokers^{1,33,36} were classified into three groups. Heavy smokers were those who had consumed at least 20 cigarettes per day for 20 years, while moderate smokers consumed less than 20 per day for less than 20 years. Those patients who had not smoked for 10 years, or who only smoked cigars and/or pipe were grouped with the nonsmokers. The body mass index (weight/height²) was used as an index of obesity.^{1,37,38} All patients received general anesthesia with an endotracheal tube. The duration of anesthetic^{6,39,40} was recorded. No patient required postoperative mechanical ventilation. A prophylactic antibiotic (second or third generation cephalosporin) was used with each patient. All patients had postoperative narcotic analgesia on an "as required" basis.⁴¹

Postoperative Course

Pulmonary complications were classified as either pneumonia (diagnosed if the patient had a fever higher than 38.5 C, purulent sputum, positive blood and/or sputum culture, as well as clinical and/or radiologic evidence of consolidation that was not present before surgery,^{42,5} or *atelectasis* (diagnosed if the patient had evidence of a fever and clinical and radiologic evidence of collapse).⁵ The number of days in hospital and from the time of the operation to that of discharge was recorded, as were all deaths that occurred within 14 days of the operation.

Statistical Analysis

To determine the significant difference between the means of the different measurements, the Student's *t* test was used according to variance equivalence. Categorical data in the two patient categories were evaluated using the chi-square test with Yates' correction, unless expected values were less than 5, in which case a two-tailed modification of the Fisher's exact test was used.⁴³ The risk factors for postoperative pneumonia were analyzed by multiple logistic regression analysis (Table 1).⁴³

Results

Table 2 shows the demographic data, details of the recognized risk factors for postoperative pulmonary complications, and the surgical diagnoses for the nonprotein-depleted and protein-depleted patient categories. There is no significant difference between them in regard to age, height, sex, or the ratio of benign to malignant disease. Malignant (G.I.) disease occurred in 66% of nonprotein-depleted patients and in 59% of depleted patients. There were no significant differences between the two patient categories for the recognized risk factors, except that, overall, the nonprotein-depleted patients were more obese (body mass index, $p < .0005$) and received anesthesia for a longer period ($p < .025$).

Table 3 shows that the two patient categories were significantly different in regard to the measurements of both body protein and fat depletion. The patients in the

TABLE 2. *The Demographic Data, Known Risk Factors for Postoperative Complications, and Surgical Diagnoses for Protein-depleted and Nonprotein-depleted Patients*

	Nonprotein Depleted Patients (n = 41)	Protein Depleted Patients (n = 39)	p
Age (years)	58.8 ± 2.3*	63.7 ± 2.5	NS
(range)	15-78	17-91	
Height (cm)	164.9 ± 1.5	164.3 ± 1.3	NS
Sex (M:F)	22:19	20:19	NS
Incision site			
Upper abdominal	12	16	NS
Lower abdominal	29	23	
Respiratory disease (No. of patients)			
None	34	33	NS
Obstructive			
Moderate	5	4	
Severe	0	0	
Restrictive			
Moderate	0	0	
Severe	0	1	
Combined			
Moderate	2	0	
Severe	0	1	
FEV ₁ /VC	75.4 ± 1.9	72.8 ± 1.8	NS
Smokers (No. of patients)			
Light or nonsmokers	25	22	NS
Moderate	12	15	
Heavy	4	2	
Obesity (body mass index)	2.56 ± 0.8	2.05 ± .04	<.0005
Duration of anesthesia (hours)	3.3 ± 0.2	2.6 ± 0.2	<.025
Upper G.I.			
Benign	6	8	NS
Malignant	7	8	NS
Lower G.I.			
Benign	5	4	NS
Malignant	20	15	NS
Inflammatory bowel disease	3	4	NS

* Mean ± SEM.
NS = not significant.

TABLE 3. *The Body Composition and Respiratory Function Data for Protein-depleted and Nonprotein-depleted Patients*

	Nonprotein Depleted Patients (n = 41)	Protein Depleted Patients (n = 39)	p
Body composition data			
Measured TBP (kg)	9.67 ± .49*	6.28 ± .31	<.0005
Predicted TBP (kg)	9.82 ± .37	9.73 ± .33	NS
Protein index	0.98 ± 0.03	0.64 ± 0.02	<.0005
Measured TBF (kg)	17.1 ± 1.5	13.4 ± 1.2	<.05
Predicted TBF (kg)	15.1 ± .61	16.2 ± .67	NS
Fat Index	1.17 ± 0.11	0.88 ± 0.13	<.05
Respiratory function data			
Resp. Muscle Strength Index (% predicted)	95.3 ± 6.9	78.9 ± 6.7	<.025
FEV ₁ (% predicted)	98.5 ± 3.8	89.2 ± 4.8	NS
VC (% predicted)	91.2 ± 2.5	83.8 ± 3.5	<.05
PEFR (% predicted)	89.3 ± 2.7	77.2 ± 3.6	<.005

* Mean ± SEM.
NS = not significant.

protein-depleted category had lost a mean of 36% of body protein, compared with 2% for the nonprotein-depleted patients ($p < .0005$). Also shown are the measurements of respiratory function in the two patient categories. It can be seen that the protein-depleted patient category underwent a significant reduction in respiratory muscle strength ($p < .025$), vital capacity ($p < .05$), and peak expiratory flow rate ($p < .005$), although no impairment was found for the measurement of forced expiratory volume.

There was no significant difference in the incidence of atelectasis between the two patient categories. It can be seen in Table 4 that postoperative atelectasis developed in 20 patients in the nonprotein-depleted group; pneumonia developed in three—significantly less (Fisher's exact test: $p = 0.048$) than in the protein-depleted patients; in whom pneumonia developed in eight of 16 patients. Three deaths occurred in this series, and all three were those of protein-depleted patients. Two of these deaths were due to pneumonia; the other was caused by massive pulmonary embolization. Although there was no significant difference in regard to overall hospital stay, the protein-depleted patients also had a longer stay in hospital after surgery ($p < .05$).

Table 1 shows the results of the logistic regression analysis of the risk factors of postoperative pneumonia. It can be seen that, as a risk factor for postoperative pneumonia protein depletion is relatively more important than any of the other risk factor except for incision site.

Discussion

These data show that surgical patients with preoperative protein depletion have a significant impairment of

TABLE 4. *The Details of Postoperative Course for Protein-depleted and Nonprotein-depleted Patients*

	Nonprotein Depleted Patients (n = 41)	Protein Depleted Patients (n = 39)	p
Pneumonia/Atelectasis	3/20	8/16	<.05
Death	0	3	NS
Postoperative stay (days)	13.3 ± 1.1*	17.3 ± 2.1	<.05
Overall hospital stay (days)	18.8 ± 1.3	22.9 ± 2.0	NS

* Mean ± SEM.

NS = not significant.

respiratory function and are at increased risk of developing pneumonia (but not atelectasis) after abdominal surgery.

The incidence of postoperative pneumonia has not changed significantly over the last three decades.¹ This suggests that the main determinants of postoperative pneumonia have been largely unaffected by changes in medical and surgical practice. The problem of postoperative pneumonia remains substantial: depending on the rigor of the diagnostic criteria and whether clinical and/or radiologic factors are considered, the incidence of pulmonary infections after upper abdominal surgery ranges from 5%⁴⁴ (if the criterion is a retrospective analysis of the hospital course done by the surgeon) to 70%⁴⁵ (if radiologic criteria alone are used). Most modern surveys agree on an incidence of postoperative pneumonia close to 20%.^{1,46-48} The overall incidence of pneumonia in this study was 13.7%.

Risk Factors for Postoperative Pulmonary Complications

A review of the literature indicates that the most important risk factor of postoperative pulmonary complications is the site of incision; the incidence of pneumonia after operations outside the chest or upper abdomen in fit patients is negligible.¹ Also, of importance is chronic respiratory disease.^{33,49-51} Obesity (greater than 120 kg),^{1,37} old age (more than 70 years), a history of smoking,¹ an anesthetic lasting longer than 2 hours, and a longer preoperative hospital stay¹ are also associated with a greater probability of postoperative pneumonia. Men have an incidence two to three times that of women,³³ although in one study, no difference was found when correction was made for operative site.¹ All of these recognized risk factors were analyzed in this study. Importantly, only two of the risk factors (duration of anesthesia and obesity) were significantly different between the two patient categories, and in both cases, the effect of this difference was to increase the risk of the nonprotein-depleted patients' sustaining pulmonary complications.

It has been known for more than 50 years that malnutrition is a risk factor of postoperative pneumonia.⁵² Although attempting to reduce the incidence of postoperative pulmonary complications, researchers nevertheless have not addressed the problem of malnutrition.¹

Protein Depletion and Respiratory Function

It has been suggested that protein-depleted patients are more susceptible to pulmonary complications because of an ineffective cough secondary to expiratory muscle weakness.¹² It is known that malnutrition has profound effects on skeletal muscle function,^{26,53,54} and it is therefore not surprising to find that protein depletion is associated with an impairment of respiratory muscle function. In particular, malnutrition is associated with a reduction in diaphragmatic muscular mass,⁵⁵ respiratory muscle strength in the remaining muscle fibers,^{11,12} and maximum voluntary ventilation.¹² The degree of reduction of VC appears to exceed what would be expected on the basis of the degree of muscle weakness alone. It has recently been suggested that the measurement of VC is the most useful way to monitor the evolution of a neuromuscular disease process or the response to treatment, because it reflects both the direct (loss of distending pressure) and secondary effects (alterations in the elastic properties of the lungs and chest wall) of respiratory muscle weakness on lung function.⁵⁶

There are also well-documented changes in respiratory function after surgery and anesthesia⁴ involving changes in lung volume,⁵⁷⁻⁶⁰ mechanics,²² gas exchange, and patterns of ventilation.³ These changes usually remain subclinical, but in protein-depleted patients, they are more likely to be significant and promote the progression from atelectasis to pneumonia.

Prevention of Postoperative Pulmonary Complications

The desire of the surgeon and anesthetist to prevent this progression from atelectasis to pneumonia has led to three main approaches to reduce the incidence of postoperative pulmonary complications. (1) Preoperative and postoperative management of chronic respiratory disease has included breathing exercises, postural drainage,⁶¹ physiotherapy with or without intermittent positive-pressure breathing,³⁵ and incentive spirometry.⁶² (2) Prophylactic antibiotics have not proved helpful when given to all patients undergoing abdominal surgery. They are considered to benefit primarily the high risk patient.¹ (3) Improving the relief of postoperative pain by a wide range of techniques has not been shown to reduce the incidence of pulmonary complications following abdominal surgery.⁷

Given that protein depletion is a significant risk factor of postoperative pulmonary complications, it has been largely overlooked, and because it is associated with an impairment of respiratory function, it is reasonable to suggest that nutritional intervention might be an effective means of reducing the incidence of pneumonia in some at-risk patients. A recent study has shown, by a multiple isotope dilution technique, that TPN is able to increase both body cell mass and inspiratory muscle strength.⁶³

The present study supports the move towards tests of function (dynamic testing) in the assessment of nutritional status.⁶⁴ This represents a departure from the more traditional, indirect measurements (static testing) of nutritional status (such as skinfold thickness, arm circumference, plasma proteins, and nutritional indices) for the identification of high-risk patients who stand to benefit from a course of TPN. Respiratory function testing has been used with mixed success in identifying patients at increased risk of postoperative pulmonary complications.^{4,30,36,48,65,66} In addition, the testing of respiratory function may provide a practical means of monitoring response to nutritional therapy as well.

In summary, the advances of modern surgical and anesthetic care have not had a significant impact on the incidence of postoperative pneumonia over the last 30 years, which remains the most important cause of morbidity and mortality after abdominal surgery. For more than 50 years, we have known that malnutrition is associated with an increased incidence of postoperative pneumonia. However, current recommended approaches to prophylaxis for postoperative pulmonary complications after surgery do not address the problem of protein depletion.^{4,7} If we are to see a further reduction in the incidence of postoperative pneumonia, the importance of protein depletion as a risk factor will need to be more widely recognized. The respiratory muscles are the only skeletal muscles vital to life, and the measurement of the impact of protein depletion on respiratory muscle function is a physiologic approach to measuring the problem. I.V. nutrition might be viewed as a practical means of reducing the incidence of postoperative pneumonia in patients with detectable impairment of respiratory function. It remains to be seen whether this impairment can be practically identified in the ward setting and whether preoperative nutritional replenishment can be shown to be cost-effective in reducing the incidence of postoperative pulmonary complications.

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