Effects of Age and Nutritional Status on Surgical Outcomes in Head and Neck Cancer

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Older and younger malnourished and well-nourished head and neck cancer patients scheduled for surgery were studied. More of the young (75%) compared with the old (58%) underwent curative surgery, and only the old with lower clinical stages of cancer were selected. When data on those undergoing surgery were analyzed in regard to older and younger malnourished and well-nourished men, the malnourished old had the poorest surgical outcomes of any group, with significantly more complications and morbidity rates. The well-nourished old had outcomes that did not differ from younger patients. On further examination, 60% of the young malnourished and only 20% of the old malnourished received preoperative enteral or parenteral nutritional support. Findings suggest that more attention to the needs of the older malnourished patients could improve surgical outcomes.

FIFTY YEARS AGO, most surgeons were cautious about operating on elderly patients in the belief that older age was a surgical risk. There is little doubt that age is still a factor in decisions about surgery and that evaluating operative risk is complex. Although morbidity and mortality rates are often similar in old and young after elective surgery, the risk in emergency surgery is much greater in the elderly than in younger patients.[1,2] Furthermore, coexisting morbidity increases with age. Thus, increased surgical risk with age can be attributed in part to multiple pathology, more advanced disease, and more frequent emergency surgery. At the same time, biologic variability increases with age. Although some elderly are frail, most are not. A positive factor for surgery in older patients is often their age, in that they are survivors who have outlived many of their birth cohorts. Numerous studies have shown that good results can be obtained in operating on the elderly when they are properly managed.

Nutritional and immune status are two interrelated factors known to influence surgical outcomes[3,4]; both of these are related to aging. The elderly are more susceptible than younger individuals to nutritional deficiencies because of age-related physiologic changes as well as psychosocial factors.[5] Furthermore, immune function is thought to decline with age.[6] There is increased frequency of cancer with aging, and nutrition and immunocompetence are also associated with cancer.[7]

Malnutrition is known to be high in head and neck cancer. The present study was undertaken to determine whether surgical outcomes differed by older and younger malnourished and well-nourished patients with head and neck cancer.

Methods

Data are taken from a larger 4-year ongoing study of the relationship of nutritional status to surgical outcomes in head and neck cancer patients. The study was initiated in 1984 in Miami at the VA Medical Center. Men admitted for treatment for squamous cell head and neck cancer to surgical wards were selected for study. A total of 120 men (94%) agreed to participate in the study by signing informed consent.

A research nurse collected information describing age, ethnicity, social class, education, marital status, pack/yr of cigarette smoking, diagnosis of alcoholism in the medical record, symptoms, months since onset of symptoms, type and stage of cancer, prior treatments for cancer, and number of days from admission to surgery. In addition, number of current diagnoses and a measure

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of severity of illness were obtained using the Cumulative Illness Rating Scale.[8]

Nutritional status was measured 2 days before surgery with a 23-item Protein Energy Malnutrition Scale (PEMS).[9] The scale provides four subscores as well as an overall score for degree of malnutrition. The research nurse obtained anthropometric data and provided ratings for the history and physical subscores on the PEMS. The anthropometric score is derived from per cent ideal body weight, per cent weight loss, triceps skinfold measurement, and midarm muscle circumference. The clinical history score is based on four-point ratings for degree of adequate nutritional intake, excessive nutrient losses, increased metabolic needs, and catabolic medications. The physical examination score is based on four-point ratings for degree of cachexia, hepatomegaly/ascites, muscle atrophy, edema, change in hair/nails, and changes in condition of the skin. A 24-hour dietary intake was recorded for calculation of caloric intake, and a 24-hour urine sample, covering the same time, was ordered for analysis so that creatinine height index and nitrogen balance could be computed. The Multitest CMI (Merieux Institute), consisting of seven delayed hypersensitivity skin tests, was given and read 48 hours later. Blood samples were drawn for laboratory tests. The laboratory score on the PEMS is derived from values for serum albumin, hemoglobin, lymphocyte counts, transferrin, retinol-binding proteins, creatinine height index, nitrogen balance, and skin tests. Higher scores indicate more malnutrition.

The day before surgery, between 8:00 and 10:00 A.M. blood samples were drawn in a heparinized syringe from the patients and their matched controls. The immune tests were done by laboratory personnel blind to patient or control status and to rating time. Blood samples were drawn again 3 and 30 days after surgery and the same immune tests repeated. Lymphocyte response in culture to phytohemagglutinin (PHA), concanavalin A (con A), and pokeweed mitogen (PWM) were studied using a fixed number of purified lymphocytes as previously described.[10] All cultures were done in triplicate, with the means calculated and responses expressed as counts per minute (cpm) in the stimulated minus unstimulated cultures, with log transformation of the cpm for statistical analyses. Neutrophil chemotaxis was used to assess migration of PMN cell according to methods described by Maderazo,[11] using a Boyden chamber and filters 13 mm in diameter with 5-μm pores with and without zymosan-activated guinea pig serum. Means of triplicate counts of stimulated minus unstimulated cultures were used as the neutrophil response to chemotaxis.

Data were also collected describing the operative procedure and outcome of surgery. Operative data included type of operation, times for anesthesia and surgery, blood loss, whether surgery was performed by ENT or general services, level of operating surgeon, and type of anesthesia.

After surgery, patients were monitored daily for 30 days or until discharge or death to determine signs of complications. Severity of each complication was rated by a surgeon who reviewed the daily records of the research nurse at the end of 30 days. A list of possible complications was scored for degree of severity on a 0 (none) to 4 (extremely severe) scale. Other outcome data included number of days from surgery to discharge, whether the patients were readmitted within 90 days after surgery, and number of days from discharge to readmission for those readmitted.

Data were analyzed in a 2 × 2 factorial design for ANOVA, in which one factor was age (older × younger) and the other factor was nutritional status (well-nourished × malnourished). Age was stratified by 60 or over (older) and under 60 (younger). The PEMS score was used to define nutritional status with a score of 8 and over meaning malnourished and a score under 8 meaning well-nourished.

Results

Of the 120 men admitted to be evaluated for possible surgery, 65 were in the older age group (mean age: 64; SD, 5) and 55 were in the younger age group (mean age: 44; SD, 6). Only 72 actually underwent curative surgery with more of the younger (75%) than the older (58%) men being operated upon.

Operated Versus Nonoperated

A higher average clinical stage of cancer (3.3) was associated with operating upon the young and with not operating upon the old (interaction effect of age with surgery was $F = 6.8$, $p < 0.01$). Thus, older patients with a higher clinical stage of cancer were not selected for surgery even though their average stage was identical to that of the younger patients undergoing surgery. The exclusion of higher stage cancers in older patients accounts for the fact that clinical stage differed significantly by age ($F = 5.4$, $p < 0.01$), with the old being 2.7 and the young 3.3. Although the older group had a greater number of diagnoses than the younger group (4.9 *vs.* 2.6; $F = 7.8$, $p < 0.01$), number of diagnoses did not discriminate significantly between those who were and were not operated upon (3.3 *vs.* 4.2, with those having surgery having more diagnoses). Severity of illness scores did not differ either by age or having surgery. Degree of malnutrition did not differ by age groups; however, there was a trend toward those who were less well-nourished being excluded from surgery, particularly in the older group, but this was not statistically significant. Prior treatment with radiation did not differ

TABLE 1. *Background Characteristics of Old and Young Malnourished and Well-nourished Patients Undergoing Surgery*

	Groups				*F* Ratios		
	Old		Young				
Variables	Malnourished (N = 22)	Well-nourished (N = 16)	Malnourished (N = 23)	Well-nourished (N = 18)	Old *vs.* Young	Malnourished *vs.* Well-nourished	Age × Nutrition
Black (%)	22	7	43	25	3.7	2.0	0.1
Education (yr)	11	11	11	10	0.3	0.4	0.5
Social class*	3.7	3.9	4.3	4.1	3.4	0.1	0.2
Married (%)	77	47	31	58	1.2	0.1	4.3§
ETOH diagnosis (%)	78	73	81	50	0.3	2.2	1.1
Alcohol use past†	3.4	3.4	3.9	3.3	1.2	2.6	2.4
Alcohol use present†	1.9	2.2	2.7	2.3	1.6	0.1	1.2
No. of medications	1.9	1.3	1.0	1.3	0.8	0.0	1.0
Pack/yr smoking habit	55	77	52	74	0.7	6.1‡	0.1

* Social class was rated 1–5, with higher numbers referring to lower class.
† Alcohol use was rated by patient as 1–4, with 4 being extreme.
‡ $p < 0.01$.
§ $p < 0.05$.

significantly, with about one fourth of all groups operated or not having received radiation. However, none of the older, as compared with 17% of the younger patients, had received prior chemotherapy ($F = 7.2$, $p < 0.01$). Records of each of the patients excluded from surgery were reviewed. In the groups, 22% of the old and 33% of the young were not operated upon because their biopsies indicated unresectable tumors. Also, one patient in each group expired before surgery. The remaining patients were referred for either radiation or chemotherapy as the treatment of choice, except for one patient in each group who selected one of these treatments rather than undergoing extensive surgery. In summary, there were no clear indications as to why fewer of the old than the young were selected for surgery. The remaining results focus upon those patients who had surgery.

Background Characteristics

Table 1 shows characteristics of the sample by age and nutritional status. It can be seen that none of the variables differed significantly at a statistical level by older and younger age of the patients. Pack/years of smoking was significantly higher among the well-nourished compared with the malnourished patients ($p < 0.01$). In addition, less of the malnourished young but more of the malnourished old were currently married ($p < 0.05$).

Symptoms and Types of Cancer

Table 2 shows months from onset of symptoms to diagnosis of cancer, types of symptoms, and types of cancer for the four groups. Older men came in sooner than younger men after onset of symptoms, with an average of about 2.9 months in the old as compared with about 5 months in the young ($p < 0.05$). This, however, may also reflect the lower clinical stage of cancer in the old than in the young who received surgery. More of the young than old had symptoms of trouble swallowing ($p < 0.05$) and weight loss ($p < 0.001$). A number of symptoms differed in malnourished *versus* well-nourished groups: nausea ($p < 0.05$), hoarseness ($p < 0.01$), trouble swallowing ($p < 0.01$), and weight loss ($p < 0.001$). There were no statistically significant interaction effects of age with malnutrition, indicating that older and younger malnourished differed from well-nourished in a similar manner.

In regard to types of head and neck cancer, some of the younger but none of the older patients had tonsillar carcinoma ($p < 0.05$). Likewise, there were more cancers of the hypopharynx in malnourished than well-nourished patients ($p < 0.05$). Again, no interaction effects of age and nutritional status were found.

Nutritional Status

Table 3 shows the total PEMS scores for old and young malnourished and well-nourished patients. Although the proportion of patients who were malnourished did not differ by age (58% of old and 55% of young were malnourished), there was a significant interaction effect of age with nutritional status, in that the malnourished old had higher scores than any other group ($p < 0.05$). It can be seen that the old malnourished became more malnourished (about the same degree more as well-nourished patients) after surgery; however, the malnourished younger patients remained essentially at the same level of malnutrition.

Immune Status

Table 4 shows that lymphocyte responses to con A were lower in the old malnourished patients than in any other group after surgery. As expected, malnourished

TABLE 2. *Symptoms and Type of Cancer of Old and Young Malnourished and Well-nourished Patients*

	Groups				F Ratios		
	Old		Young				
Variables	Malnourished (N = 22)	Well-nourished (N = 16)	Malnourished (N = 23)	Well-nourished (N = 18)	Old *vs.* Young	Malnourished *vs.* Well-nourished	Age × Nutrition
Symptoms (%)							
Months since onset	2.8	3.0	5.7	4.5	5.4*	0.3	0.4
Pain	62	23	57	60	1.9	1.2	1.9
Trouble chewing	23	7	29	40	2.1	0.0	1.1
Nausea	13	0	21	0	0.8	4.1*	0.3
Hoarseness	50	15	71	30	3.4	7.5‡	0.6
Ulcer in mouth	38	15	35	40	0.9	0.3	0.8
Trouble swallowing	63	23	85	40	4.5*	9.7‡	0.2
Vomiting	0	0	14	0	1.8	1.5	1.3
Weight loss	62	0	86	50	16.6†	16.8†	1.3
Type of cancer (%)							
Tongue	10	22	12	23	0.1	1.3	0.0
Floor mouth	10	22	6	23	0.2	2.3	0.6
Palate	20	5	0	8	1.2	0.1	2.6
Tonsil	0	0	18	15	5.3*	0	0.1
Larynx	30	39	47	31	0.1	0.1	0.9
Hypopharynx	30	6	12	0	0.9	4.8*	0.6
Neck only	0	6	6	0	0.9	0.9	0.3

* $p < 0.05$.
† $p < 0.001$.
‡ $p < 0.01$.

and well-nourished patients differed significantly, with malnourished having lower immune function as reflected by lymphocyte responses to con A and by anergy. Doses yielding maximal responses were selected for analysis of lymphocyte function. Although response to delayed hypersensitivity skin testing was considered part of nutritional status measurement, it is shown here since it demonstrated the same *in vivo* cellular immune function pattern as that found for the *in vitro* lymphocyte response, with 60% of the old malnourished and 20% of the young malnourished being anergic (no response to all seven antigens).

Surgical Outcomes

Table 5 shows how the groups compared in regard to surgical outcomes. Days after surgery in the hospital were significantly more for malnourished than well-nourished patients ($p < 0.05$). Furthermore, more malnourished than well-nourished had greater degrees of postoperative complications ($p < 0.05$). However, significantly more of the old malnourished had more complications and significantly more of the old malnourished died within 1 year after surgery than any other group (both significant at the 0.05 levels). The relationship between nutritional status before surgery and surgical outcomes were examined. Greater degree of malnutrition, as reflected by the PEMS score, was correlated significantly with postoperative complications ($r = .42$, $p < 0.01$) and death within the year ($r = .59$, $p < 0.01$).

Preoperative Nutritional Support

In trying to account for the fact that the old malnourished became more malnourished after surgery while the younger malnourished did not, as well as for why the old

TABLE 3. *Nutritional Status before and after Surgery in Old and Young Malnourished and Well-nourished Patients*

	Groups				F Ratios		
	Old		Young				
Variables	Malnourished (N = 22)	Well-nourished (N = 16)	Malnourished (N = 23)	Well-nourished (N = 18)	Old *vs.* Young	Malnourished *vs.* Well-nourished	Age × Nutrition
Before surgery total PEMS	11.9	5.1	10.3	5.9	2.6	89.2*	3.8†
After surgery total PEMS	14.9	7.1	10.9	7.8	0.7	25.3*	5.9†

Note: Higher PEMS scores indicate more malnutrition.
* $p < 0.001$.
† $p < 0.05$.

TABLE 4. *Immune Function before and after Surgery in Old and Young Malnourished and Well-nourished Patients*

	Groups				*F* Ratios		
	Old		Young				
Variables	Malnourished (N = 22)	Well-nourished (N = 16)	Malnourished (N = 23)	Well-nourished (N = 18)	Old *vs.* Young	Malnourished *vs.* Well-nourished	Age × Nutrition
Before surgery							
Lymphocyte response							
to PHA	4.7	4.8	4.8	5.0	1.5	2.9	3.6
to con A	4.3	4.7	4.4	4.7	2.0	4.1*	1.2
Anergic (%)	60	0	20	0	5.1*	7.2†	4.8*
After surgery							
Lymphocyte response							
to PHA	4.5	4.7	4.7	5.0	3.3	2.4	1.0
to con A	4.1	4.6	4.3	4.6	2.6	4.4*	3.9*
Anergic (%)	60	0	20	10	4.6*	5.0*	4.3*

Note: Lymphocyte responses are given as counts per minute (cpm) in the stimulated minus control cultures with $\log_{10}$ transformation.

* $p < 0.05$.
† $p < 0.01$.

malnourished had the poorest outcomes of any group, the question of nutritional intervention before surgery was examined. None of the well-nourished in either age group received any type of nutritional support. Sixty per cent of the younger malnourished patients received either enteral or parenteral nutritional support before surgery. On the other hand, only 20% of the older malnourished patients received nutritional intervention before surgery.

Discussion

The major finding was that malnourished older patients had poorer surgical outcomes than any other group. The well-nourished elderly were similar in postoperative morbidity rates to younger patients. Since preoperative level of malnutrition was associated significantly with postoperative complications and death within 1 year, it seems likely that improving nutritional status before surgery, particularly in the elderly, might lead to decreased postoperative morbidity rates. This presents a dilemma for two reasons. One is that there is some suggestion here that the attitudes of staff about operating on the elderly and offering nutritional intervention may have played a role in their poorer surgical outcomes. If only older patients with lower clinical stages of cancer were selected for surgery then there is some systematic age bias in selection of patients. Further, if almost none of the malnourished old, but a sizeable proportion of the malnourished young, received nutritional intervention, and taking into account that the malnourished old were more malnourished than the malnourished young, then again there appears to be some age bias in the selection, unfortunately (in this case) for a clinical problem (malnutrition) that is remediable. What this suggests is that attitudes of the staff about treating the elderly may need to be explored further.

If chronologic age, rather than physiologic age, is the determinant of medical care, then the elderly may be given care that can result in premature morbidity and mortality rates.[12] There are additional suggestions of this

TABLE 5. *Surgical Outcomes in Old and Young Malnourished and Well-nourished Patients*

	Groups				*F* Ratios		
	Old		Young				
Variables	Malnourished (N = 22)	Well-nourished (N = 16)	Malnourished (N = 23)	Well-nourished (N = 18)	Old *vs.* Young	Malnourished *vs.* Well-nourished	Age × Nutrition
Days after surgery	40	18	39	13	0.4	4.2*	0.3
Complication score	7.6	4.0	4.4	2.5	3.7	5.4*	4.5*
Death (% 1 yr)	50	11	17	15	0.7	3.1	3.9*

Note: Complication score range is 0–12, with higher score being more severe.

* $p < 0.05$.

from other studies. One study[13] found that elderly patients with cancer received less curative treatments than younger patients with cancer even after taking stage of the disease into account. Likewise, a study[14] of 1680 women with breast cancer treated in 17 hospitals showed a linear trend for older patients to receive fewer services such as biopsies, number of lymph nodes examined, chemotherapy, and radiation therapy, even though stage of cancer and estrogen receptor status were not associated with age. Another recent study[15] controlled for comorbidity, functional status, and tumor stage, as well as for type and size of seven hospitals from which 374 cancer patients were selected. They found that even after controlling for all of these factors, age itself affected medical care in that physicians provided less than optimal care for older patients even with mild or no comorbid disease. Wetle[16] concluded that lack of data about treatment effectiveness and side effects for older patients made clinicians reluctant to use new treatments with the elderly or overly cautious by using less than optimal dosages. In turn, this leads to a self-fulfilling prophecy in which older patients treated for cancer *do not do well* because appropriate treatment was not provided. We have recently reported[17] that medical student attitudes about surgery in the elderly could be changed positively by a better understanding of the normal aging process and the need to evaluate each older person individually in regard to surgical risk based on his or her biologic and not chronologic age. Whether some emphasis in continuing medical education for staff or in the quality assurance review and feedback to staff would change attitudes about treating the elderly could be tested.

There is, however, another complicating factor that needs to be considered. Even if attitudes about operating on the elderly were improved and staff were motivated to offer nutritional intervention, the latter may be difficult to accomplish. Cost containment goals and diagnostic related groups (DRGs) have led to patients coming in only a day or two before elective surgery. We have found[18] that head and neck cancer patients admitted since institution of DRGs had significantly more malnutrition at the time of surgery and more postoperative complications than patients admitted before institution of DRGs. There is currently no system for reimbursement under DRGs for treating malnutrition. Thus, if preoperative nutritional support is needed, it may have to be offered in the home before hospital admission. The lack of time for intervention in the hospital applies equally to the young and old. However, there have been questions raised[19] about operations for the elderly and their necessity, with suggestions made that a third of the procedures may be unnecessary and that second opinions should be required for operations in the elderly. If such attitudes center only around the old, this can lead in a dangerous direction as a means of cost containment, because death, of course, can become the ultimate economy. The longer the elderly survive, the more costly their care.

At the same time that one might argue for equal treatment for all regardless of age, there are questions about the value of nutritional intervention in cancer. The role of cancer cachexia is not fully understood, particularly in how metabolism and immune function may be related. Malnutrition is known to suppress immune function. There is agreement that both malnutrition and immune function before surgery are associated with postoperative complications. However, studies have not clearly demonstrated that nutritional intervention in cancer patients can improve survival. There are questions as to whether total parenteral nutrition or overnutrition may in fact promote tumor growth.[20] The lack of effect of aggressive nutritional therapy on survival, however, should not be used to deny any cancer patient nutritional support during the course of illness. A better understanding, however, is needed about the effects of nutritional intervention, and most would agree that it should be used only for malnourished patients and perhaps then only in amounts adequate to supply needs and not tumor growth.

The comparison of old and young head and neck cancer patients showed several differences that require further study. Older patients seem to seek medical care earlier for symptoms than younger ones. The older patients also had fewer tonsillar cancers, which raises a question of whether this might be associated with the common practice of removing tonsils when the older men were children. Older patients never received preoperative chemotherapy, which also raises the question of possible age bias in clinical management. Why more pack/years of smoking was associated with being well-nourished, instead of being malnourished, cannot be answered, but the magnitude of the difference was 20 pack/years and occurred in both old and young groups between malnourished and well-nourished groups. Overall, there were perhaps more similarities than differences between old and young head and neck cancer patients. Mortality rates were very high in the malnourished old (50%) but lowest of any group in the well-nourished old (11%). In general, the findings suggest that more attention to the needs of the elderly in areas that could improve surgical outcome such as nutritional repletion might prove beneficial.

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