Surgery in the Aged Population

Surgical Oncology

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It is estimated that health care expenditures will triple in the next 70 years, with Medicare expenses alone accounting for 8% of the gross domestic product. While part of this will be due to increasing expenditures per person, the most significant cause will be the expanding elderly population. Cancer occurs predominantly in elderly people, and the growing size of this age group in the United States will certainly increase the prevalence of this health problem. While the definition of “elderly” is an area of controversy, the increased life expectancy of a person born this year is anticipated to lead to a dramatic increase in the number of people who will require care for cancer during their lifetimes. Assuming that the recent trends in the incidence of disease and life expectancy continue, it is estimated that cancer will bypass cardiac disease and become the leading cause of death in the United States by the year 2010. Couple this with the increase in the absolute number of elderly people requiring medical care, and it seems reasonable to envision the emergence of geriatric oncology!

CHANGES IN CANCER INCIDENCE AND PREVALENCE

The annual age-adjusted cancer incidence has slowly increased during the last 30 years, by approximately 15%, to nearly 450 cases per 100,000 people. The associated age-adjusted cancer mortality rate is slightly less than 200 cases per 100,000 people. For reference, the rate of death from cardiac diseases is just greater than 250 cases per 100,000, a decline of almost 60% in the last 50 years. Heart disease was responsible for almost 40% of all deaths in the United States in 1973, while cancer accounted for just 17.7%; in 1999, heart disease was responsible for 30% of deaths, while cancer was the cause in 23%. This represents a 30% relative increase in cancer-related mortality, with a concomitant 25% relative decrease in cardiac-related mortality. It is easily understandable why cancer will become the leading cause of death given the significant decline in mortality from cardiac diseases.

The increase in life expectancy coupled with the increased incidence of cancer has had a profound effect on the prevalence of cancer. It is estimated that there are more than 1.3 million Americans who are currently living with cancer. The lifetime probability of developing an invasive cancer is almost 45% in men (nearly 1 in 2) and 38% in women (greater than 1 in 3). The growth of the aged population of the United States is clearly responsible for this increase in lifetime risk—most of the risk occurs after the age of 60 years. Cancer development is uncommon in people younger than 40 years (1 in 72 for men and 1 in 51 for women). This dramatically increases so that the risk of a man developing cancer during the 20 years between ages 60 and 70 years is 32%, which represents most of his lifetime risk. Therefore, as the population lives longer, it is subjected to an increasing risk of cancer development.

These effects are clearly seen when the age-adjusted incidence of breast can-
cancer is examined in conjunction with the review of the size of each age group at risk. Breast cancer is extremely uncommon in young women, with an annual incidence of fewer than 20 cases per 100,000 women aged 20 to 39 years. This rate dramatically increases during each subsequent decade to reach a peak of 380 per 100,000 people for the 70- to 79-year age group, nearly 40 times the risk for the younger population. Both the incidence and population at risk drop off after this decade, but it remains a significant health problem for the nonagenarian. While the fraction of the population of these older age groups is currently small (only 3.4% of the population, or an estimated 9.2 million people older than 80 years in the year 2000), it is anticipated that these numbers will explode in the coming years (by 2025, this group will increase to 14.9 million, or nearly 5% of the population).11

THE IMPACT OF AGING ON CANCER TREATMENT

The decision to treat cancer in elderly patients often includes evaluation of 2 additional factors: (1) Is survival limited by the cancer or age-related illnesses? and (2) To what degree do age-related illnesses interact with the delivery of optimal cancer treatment? The first question is not necessarily related to elderly patients, as every surgeon has seen the “high-mileage” 50-year-old man who would be anticipated to die of medical diseases much earlier than the “low-mileage” 75-year-old woman. Therefore, it seems as though there are no hard and fast guidelines that can be applied to patients in various age groups, but treatment strategies must be individualized. However, neglecting to provide adequate cancer treatment to elderly patients is not appropriate, as there are data to suggest that elderly patients can be anticipated to live an additional period of years. It is estimated that the mean life expectancy of a 65-year-old person is an additional 17 years (women have an expected 19 more years while men have an expected 16 more years). Even an 85-year-old person can be expected to live an average of 6 additional years.12

A variety of chronic medical conditions are associated with age such that it is uncommon for a 65-year-old to be healthy without any comorbidities. The most common diseases seen in cancer patients include hypertension, diabetes, atherosclerotic disease, chronic respiratory diseases, and arthritis.13,14 The incidence of these in elderly cancer patients was reviewed by Ogle et al15 in a population-based analysis of 15,626 people using the Surveillance, Epidemiology, and End Results data. Across all age groups studied, less than 30% of patients were without a chronic preexisting comorbidity at the time of cancer diagnosis. More than one third of patients had at least 1 disease, one quarter had 2 diseases, and the remaining had at least 3 medical diseases. The most common medical condition was hypertension, occurring in nearly half of patients aged 70 years and older, although more than one third had atherosclerotic disease, and one quarter had chronic pulmonary disease.

Any of these medical conditions may limit a patient’s life expectancy depending on the severity; it is beyond the scope of this review to summarize the significance of these diseases in anticipated survival. However, a variety of scoring systems have been developed that can be used to quantify overall medical health. In elderly cancer patients, the 2 best validated scales are the Charlson comorbidity index16 and the Cumulative Illness Rating Scale–Geriatric.17 These 2 scales represent distinct approaches to the assessment of the medical health of the elderly patient; the Charlson comorbidity index was developed for its simplicity, focusing on a short list of selected diseases, while the Cumulative Illness Rating Scale–Geriatric is comprehensive, including analysis of 14 organ systems. Both of these scales have been shown to identify those cancer patients who will die of their comorbid illnesses.18-20 The predictive ability of these scales is independent of the type of cancer, the stage at initial examination, and the aggressiveness of therapy administered. Another method of evaluating the medical health of cancer patients is based on scoring systems of functional performance. The 2 most commonly used methods are the Eastern Cooperative Oncology Group or World Health Organization performance status21 and the Karnofsky score.22 Neither of these specifically scores comorbidities but instead they both assess a patient’s overall level of functional performance. Both of these systems were developed by oncologists to evaluate whether a patient would likely tolerate the administration of systemic chemotherapy. These performance-assessment models have been repeatedly validated to predict survival independent of therapy in a variety of cancers, including non–small cell lung cancer and ovarian cancer.23-26 Owing to the significant impact that medical comorbidities have on survival, current cancer trials are stratified based on performance score, especially in elderly patients.27 This seems logical but does not offer much guidance for the evaluation of individual patients with few and/or mild comorbid medical illnesses.

ARE ELDERLY CANCER PATIENTS UNDERTREATED?

A detailed discussion as to whether elderly patients with various types of cancer are undertreated is beyond the scope of this article. Therefore, a focused discussion of breast cancer will cover aspects of the interaction of patient age and cancer treatment: (1) the effect of patient age on treatment recommendations, (2) the magnitude of undertreatment that currently exists, (3) the effect of undertreatment of cancer patients, and (4) reasons that have been proposed to explain the undertreatment.

It is well established that survival following breast-conserving therapy (BCT) (segmental mastectomy with breast irradiation) is equivalent to that following mastectomy.28 However, BCT continues to be underutilized in patients who are considered to be appropriate candidates.29 The reasons that women continue to undergo mastectomy when BCT is a reasonable alternative are multifactorial, including patient wishes and physician bias. While it has been hard to sort out these 2 reasons, Liang et al30 demonstrated that when the surgeon engaged in an interactive discussion of surgical options, patients were much more likely to receive BCT. Withholding the option of BCT for elderly women, therefore, represents an unreasonable physician bias based solely on age; elderly...
women treated with BCT have equivalent outcomes to younger women. Finally, the medical health of elderly women cannot explain the persistent high rate of mastectomy, as comorbid conditions are uncommon contraindications to BCT.

The discussion of BCT vs mastectomy relates to the provision of equivalent treatments of breast cancer in the elderly woman. Unfortunately, it is clear that appropriate treatment is being withheld and that this may have a significant effect on cancer-free survival. The clearest example of this is the performance of axillary lymph node dissection (ALND) for early-stage invasive breast cancer. Two reports that examined large databases (Breast Cancer Outcomes Unit Database [N=8038] and National Cancer Data Base [N=47944]) noted that the omission of ALND is related to age and increases dramatically in patients older than 65 years. The incidence of omission of ALND reached greater than 60% in women older than 80 years. The reasons for this are unclear, although several have been postulated. There is some belief that breast cancer in elderly patients may be less aggressive, and the risk of nodal disease is lower in the elderly patient and therefore, the yield of ALND is lower than that in younger women. Others believe that the clinical consequences of ALND (especially lymphedema) are greater in elderly women, and as with the yield (both histopathologically and in terms of utility in treatment planning), the risks outweigh the benefits, and ALND can be omitted.

The impact of omission of appropriate therapy for these elderly breast cancer patients can be significant. An analysis of the National Cancer Data Base identified 84877 women treated for stage I breast cancer with a variety of treatment regimens; in every scenario of BCT in which ALND was omitted, women sustained a significantly lower rate of survival. The 10-year survival rate was 85% for lumpectomy with ALND and 66% for lumpectomy without ALND; the addition of systemic therapy could not overcome the adverse effect of omission of ALND. This adverse effect has been reported in other studies, but there are also reports that elderly women who receive appropriate radiation therapy and systemic therapy can have ALND omitted from their treatment strategy. Given the potential adverse outcome associated with omitting ALND in elderly women with early-stage invasive breast cancer, the need for careful discussion of risks and benefits on an individual basis is clear.

The omission of appropriate therapy is not just limited to surgery; elderly breast cancer patients are just as likely to have systemic therapy withheld. This applies to both hormone therapy and systemic chemotherapy. This may be due to the concern among oncologists that elderly patients are unlikely to tolerate systemic chemotherapy, which has a higher incidence of significant adverse effects. While elderly patients may have medical conditions that interact with the administration of chemotherapy, it does not appear that the risk of adverse events is any different when chemotherapy is properly administered. Du et al identified 35060 women in the Surveillance, Epidemiology, and End Results database who received systemic chemotherapy for breast cancer. In this analysis, the risk of hospitalization for chemotherapy-related events was equivalent among all age groups, including persons older than 80 years. However, elderly persons were at higher risk for the development of dehydration, anemia, and neutropenia, although these chemotherapy-related adverse effects were mild and easily managed without sequelae. Although the potential benefit of systemic therapy on the survival of elderly cancer patients has not been fully defined due to intentional exclusion of these patients from clinical trials of chemotherapy, it would seem reasonable to include this as part of the potential treatment plan. This discussion has been limited to breast cancer, but the same conclusions are true for most other malignancies. Cancer therapy for elderly patients is being modified simply on the basis of age.

WHAT ARE THE BENEFITS OF TREATMENT IN ELDERLY PATIENTS?

The potential benefit of chemotherapy or radiation in elderly cancer patients appears to be no different than in younger patients. Studies suggest that older patients sustain a similar benefit when these modalities are included in their care. In the elderly patient with colon cancer, adjuvant chemotherapy with fluorouracil and either leucovorin or levamisole is associated with improved survival rates. Elderly patients with stage II and III colon cancer who received standard chemotherapy regimens had 5-year survival rates of 67% compared with 62% with surgery alone.44 Chemotherapy was also associated with better disease-free survival (69% vs 57% at 5 years).45 The use of adjuvant chemotherapy and radiation in elderly patients with stage III rectal cancer is also associated with a 29% decrease in the risk of death compared with surgery alone. Unfortunately, the large randomized breast cancer trials have not specifically addressed the treatment of patients older than 70 years. However, a meta-analysis of a number of these studies has shown that the use of tamoxifen is associated with improved overall survival (annual odds of death decreased by 21%) for postmenopausal women, including those older than 70 years, with early-stage disease. Additionally, the study by Extermann et al estimates the absolute reduction in mortality from systemic polychemotherapy for older breast cancer patients at 1% to 3%, similar to the 2.3% absolute benefit expected for young patients.

Substantial data suggest that elderly patients enjoy increased survival following curative oncologic surgery. Elderly patients undergoing potentially curative colorectal cancer surgery experience overall and disease-free 5-year survival rates comparable with those of their younger counterparts (55%-75%). For patients undergoing curative resection of esophageal cancers, median survival was 32 months for patients older than 70 years, and 33 months for patients younger than 70 years. Similarly, the 5-year survival rate for older patients undergoing gastrectomy is 26%, which is comparable with that for younger patients. Curative pancreatic resections are associated with a 5-year survival rate of 17% to 21% in elderly patients and 19% to 29% in younger patients. Liver resection for hepatocellular carcinoma or colorectal cancer is associated with a median survival of 22.9 vs 33.5 months, and a 5-year survival rate of 42% vs 40% in older patients vs younger patients, respectively.
These data suggest that in appropriately selected elderly patients, similar oncologic benefits from multimodality therapy can be achieved compared with those achieved in younger patients. Furthermore, the survival benefit of appropriate treatment for cancer in elderly patients is similar to that in younger patients, suggesting that malignancy in elderly patients is not any less or more aggressive than in younger patients.

**WHAT ARE THE REAL RISKS OF TREATMENT TO ELDERLY PATIENTS?**

Contrary to commonly held beliefs, there is a substantial amount of evidence indicating that major surgical procedures can be performed safely in elderly patients. The morbidity and mortality for major surgical procedures for cancer (eg, esophagectomy, gastrectomy, colectomy, hepatectomy, and pancreactectomy) are presented in the Table and demonstrate acceptable rates of complications in elderly patients. When a higher incidence of complications is noted for these procedures, the conclusion that elderly patients are at higher risk is somewhat misleading because these studies have not adequately addressed the influence of preexisting medical conditions. Because elderly patients may have a higher incidence of age-related cardiopulmonary dysfunction, the incidence of cardiopulmonary complications may be slightly higher, as noted for colectomy. In certain instances, the surgical procedure may need to be tailored to the elderly patient to account for preexisting disease. Recent studies investigating the role of laparoscopic colectomy for colon cancer in elderly patients have shown lower rates of cardiopulmonary-related (7.7% vs 22.4%) and overall (20% vs 54%) morbidity compared with open colectomy. Collectively, these studies suggest that major oncologic procedures may be undertaken in older patients in whom operative risk is good, with acceptable rates of complications; the presence of advanced age alone is not a contraindication to appropriate surgical intervention for cancer.

Most malignancies are treated with a combination of therapeutic modalities. Recent studies suggest that age by itself is not a risk factor for increased rates of complications from chemotherapy or radiation. The physiologic changes associated with aging (eg, decreased glomerular filtration rate) that affect the pharmacokinetics and toxicities of chemotherapeutic agents can be compensated without forgoing efficacy. The use of reduced doses or less toxic regimens, and hematopoietic growth factors (eg, granulocyte colony stimulating factor), have been effective. Studies have shown that treatment of elderly colorectal cancer patients with fluorouracil and levamisole (or levamisole) is well tolerated. With the exception of leukopenia, toxicity in elderly patients appears to be the same as in younger patients (31% vs 17%, respectively). The rate of hospitalization for complications due to this type of treatment is 8% to 13% for patients aged 70 to 89 years and ~7% for younger patients. Studies have shown that radiotherapy also is well tolerated by fit older patients. Although acute toxicity of radiotherapy may be more severe for elderly patients, late toxicities and severe complications are similar to those in younger patients.

**THERAPY DIRECTED AT QUALITY OF LIFE**

The elderly cancer patient frequently has advanced disease on initial examination. For a multitude of reasons, supportive care alone has often been offered to these patients. However, recent studies suggest a benefit of palliative surgery to the older cancer patient with advanced disease. In addition, non-treatment is associated with its own set of complications, such as bleeding, perforation, and obstruction. Mortality rates for incurable colorectal cancer are significantly higher for diversion or fulguration (~17%) vs resection (5%) and are associated with median survival rates of 7 months and 15 months, respectively. The median relief of preoperative cancer symptoms was only 1 month for nonresected patients and 4 months for resected patients. Moreover, operative morbidity and mortality rates significantly increase with emergent surgery to the order of 20% to 30%, compared with less than 10% for elective procedures. Patients with gastric cancer who underwent emergent surgery for perforation or bleeding had...
perioperative mortality rates of 12.5% and 30.7%, respectively.\textsuperscript{77} Mortality rates from colorectal cancer surgery in patients older than 70 years rose from 7.5% in an elective setting to 23.3% when emergent operation was required.\textsuperscript{80} The extensive review by Yancik et al\textsuperscript{81} suggests that undertreating older breast cancer patients leads to premature death. In this study, the most aged (\textgeq 85 years) also were most likely to be understaged and undertreated; 68% of these patients died within a 30-month follow-up. The data indicate that elderly patients live longer and may enjoy better quality of life if surgery or dose-adjusted chemotherapy is instituted, rather than supportive care alone, for patients who are not candidates for curative therapy.\textsuperscript{27,82-84}

While generally unnecessary in the treatment of most young patients, the assessment of existing support systems is paramount to the management of older patients. The loss of spouses and family as patients age is inevitable and may be detrimental to their outcome. In addition, care of elderly persons, in many circumstances, may best be aimed at improving quality of life, rather than survival; this raises the issue of palliative procedures again. Unfortunately, quality of life is difficult to assess and traditionally has not been an evaluable end point of most studies. More difficult than assessing quality of life is assessing the risks and benefits of intervention for elderly patients with decreased cognitive ability or dementia. Should the presence of dementia alter medical and surgical decision-making? There is limited evidence that impaired cognition may contribute to a worse outcome.\textsuperscript{85}

The elderly population is growing, and the number of elderly patients with both malignancies and comorbid medical conditions has significantly increased. A dilemma regarding the treatment of these patients now exists and is not easily resolved. The medical community has not agreed on the significance of age in treatment decision-making for patients with cancer. Analyses of current medical practices in the United States for elderly patients suggest that many cancer patients are denied treatment based solely on age.\textsuperscript{25,38,82,83} These practices are likely due to multiple preconceptions: (1) the elderly cancer patient does not tolerate procedures, chemotherapy, or radiation as well as the young patient; (2) overall medical health will determine survival and not the malignancy; and (3) older cancer patients have less aggressive tumors.\textsuperscript{86} Most of the medical literature, on the other hand, supports the idea that age, independent of coexisting medical conditions, is not a significant risk factor in outcome from oncologic procedures or in survival.

Studies stratifying outcome by medical condition, tumor stage, and type of treatment suggest that disease-free and actuarial survival are the same for young and elderly patients.\textsuperscript{31,82,86,89,97,98} Furthermore, studies also indicate that the clinical behavior of malignancies (such as breast cancer) in elderly persons are not indolent, and that systemic or even radiation therapy (as opposed to hormone-based treatment alone) may prolong survival in older breast cancer patients.\textsuperscript{39,99-102} Unfortunately, most of these data come from studies that are small, retrospective, biased as to the selection of patients (ie, at the discretion of the operating surgeon), and report a significant number of deaths from other causes. Although it is difficult to draw firm conclusions from these somewhat limited studies, there is very little evidence in the literature to suggest that cancer in elderly patients is more favorable or that therapy should be any less aggressive in aged vs young patients.

The physician must assess risks to the elderly patient of the malignancy, the proposed procedure, and preexisting comorbidities. These risks frequently are difficult to estimate in older patients and historically have been based on the inaccurate perceptions of normal physiologic processes in elderly patients.\textsuperscript{103} Studies have shown that “fit” older patients experience the same benefits and toxicities of chemotherapy as do younger patients.\textsuperscript{77,82,83} When normalized for preexisting medical conditions, older patients also tolerate major surgical procedures as well as younger patients.\textsuperscript{52,60,84,87,88}

In conclusion, the lack of evidence-based medicine for elderly persons has impaired the definition of disease-based strategies for these patients. Historically, the treatment of older patients with cancer was based largely on anecdotal evidence and unduly excluded a number of these patients from appropriate care. More recently, a number of studies suggest that “fit” older patients with cancer do as well with various forms of treatment as do their younger counterparts. The evidence available indicates that patients should not be denied treatment based solely on age. Instead, treatment for elderly cancer patients needs to be tailored more specifically not only to obvious medical limitations, but also to subtle decreases in organ functioning, social circumstances, and quality of life.

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