Preoperative Assessment of Surgical Risk in Oncogeriatric Patients

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ABSTRACT
Cancer is a prevalent disease in our aging population; however, few oncologists are familiar with caring for oncogeriatric patients. Surgery is presently the treatment of choice for most solid tumors, but it is frequently delivered in a suboptimal way in this patient subsetting. Undertreatment is often justified with the concern of an unsustainable toxicity, while overtreatment can be related to the lack of knowledge in optimizing preoperative risk assessment. To draw new light on this issue, several surgeons presented their series, providing hard evidence that surgical options can be offered to the elderly with cancer, with only a limited postoperative mortality and morbidity. As it is likely that much of these data suffer from selection bias, we concentrated on Comprehensive Geriatric Assessment (CGA), which can add substantial information on the functional assessment of elderly cancer patients. A validated instrument such as the CGA allows a comparison of series, predicting short-term surgical outcomes more precisely, and offers appropriate information when consenting elderly patients. Preoperative Assessment of Cancer in the Elderly is a prospective international study conceived and launched to outline the fitness of elderly surgical patients with malignant tumors. This paper reports on preliminary results and analysis from the ongoing study. The Oncologist 2005;10:262–268

INTRODUCTION
Two-thirds of all solid tumors occur in patients aged 65 years or older, and most cancer-related deaths occur within this age group [1-3]. There is considerable evidence that this steadily expanding population receives substandard treatment when compared with younger age groups [4]. Possible explanations that have been suggested for this inequity in treatment include A) the perceived limitations to conventional treatments in the elderly [5, 6]; B) concerns about attendant serious associated medical conditions [7, 8], and C) a reluctance by clinicians to incorporate older patients either into clinical trials of novel agents or into existing screening programs [9-12]. Such a suboptimal approach to the management of oncogeriatric patients has prompted several surgical oncologists to review their series. This resulted in two positive outcomes. First, after a review of performance, including an audit of outcomes, and a comparison of results, evidence of superimposable long-term cancer-related outcomes was established, irrespective of patient’s age [13, 14]. Second, it was noted that, after accurate selection and expert management, short-term complications and mortality rates did not significantly differ. From this initial consultation it was clear that further collaboration was warranted and, to this end, dedicated teams are being established, educational programs are being developed,
and associated research is being promoted through meetings, conferences, and curricula.

**SURGICAL RISK IN THE ELDERLY: TO OPERATE OR NOT**

**Comprehensive Geriatric Assessment**

Operating on the elderly for cardiac, orthopedic, or vascular diseases is becoming increasingly accepted. However, there is a continued reluctance to recommend aggressive intervention for malignant conditions [1] even though surgical resection has so far been accepted as the only curative therapy for solid tumors [2]. Elderly subjects may be denied surgery because of the presumed higher risk of mortality and morbidity, a belief held since the beginning of the last century [3]. Reluctance to advise or accept an operation is often unrelated to the presence of coexisting debilitating conditions or impaired functional status [4].

In the first half of the last century, operative mortality under elective conditions was high for patients aged 70 years or greater (19% compared with 5% in modern series). The increasing elderly population and the frequency of surgical problems among the elderly were clearly described by Brooks in 1937 [3].

In 1948 Welch reported a large series of abdominal operations in patients over 70 years of age with a perioperative mortality of 20.7% [5]; he concluded that the surgery itself was safe but that aged subjects required greater attention in perioperative management, thus drawing a basis for invasive monitoring.

In 1975 a report by Greenfield showed how over a 40-year period, operative mortality was halved in patients over 70 years of age [6]. This was the consequence of improvements in anesthetic and surgical technique, availability of new drugs, and optimized postoperative care. Given these advancements it is surprising that it is still common clinical practice to exclude the elderly from optimal surgical treatment [7].

It was only in the 1980s and 1990s that the prognostic importance of comorbidities was realized, with several surgeons reporting on the presence of risk factors as powerful prognostic indicators. Weight loss and obstructive conditions were perceived to negatively impact short-term outcomes, as well as a number of medical conditions such as cardiovascular, pulmonary, renal, hepatic, and metabolic conditions [8–11].

The hypothesis that comorbidities can have a direct impact on cancer management is supported by recent research. A significant step forward was made when a predictive value in toxicity and outcome of treatment was noticed among elderly cancer patients mainly receiving nonsurgical treatment [12–17]. Some studies indicate that the inclusion of a vast list of comorbidities in patient pre-treatment assessment increases prognostic value [18, 19].

It was also suggested that a simple list of associated medical conditions is not sufficient to impact prognosis, but what is required is assessment of the complexity of comorbidity information that can be gathered through a Comprehensive Geriatric Assessment (CGA) tool. CGA has proven useful in predicting mortality and disability in several clinical settings, including hospital geriatric evaluation, inpatient geriatric consultation, home assessment service, hospital home assessment service, and outpatient assessment service, for a number of chronic diseases [20–24].

In a previous investigation of nonsurgical elderly cancer patients [25], it was demonstrated that the CGA can add substantial information to the functional assessment of elderly cancer patients through the performance status (PS) index. Among elderly cancer patients, the role of PS as a unique indicator of functional status resulted insufficient.

**Frailty**

The term “frail” is a quarter of a century old, but its medical meaning is still undefined. It has been described as representing the dependency of someone with poor physiological reserve who has a high occurrence of repeated chronic illness and hospital admissions and where there may be complex medical and psychosocial problems in addition to a limited social support structure. This is coupled with an increase in the age-related prevalence of significant cardiac and respiratory comorbidities together with major functional impairment that, in the elderly subsetting, increases the risk of treatment-related complications and mortality [26–34]. The lack of sound, evidence-based information concerning the treatment of elderly patients with cancer can mean that such treatment in clinical practice is often ill informed [35, 36], resulting in an exclusion of a significant number of geriatric cancer patients from surgery, radiotherapy, and chemotherapy [37, 38].

**Surgical Risk**

The choice whether to operate on a patient is one of the most important decisions a surgeon is asked to make. This choice is considerably more difficult when working with a patient who is a poor surgical candidate.

The elderly population is a large and heterogeneous group, ranging from competent, active, and well individuals to those who are frail and cognitively impaired. A number of demands (i.e., greater need for information, more effective use of available resources, advances in perioperative management, and surgical techniques) requires an improved and individualized risk definition to be shared between the surgeon and the patient. Although this can be a difficult task in an emergency setting, risk prediction should be appreciated and disclosed to the patient when asking them for their consent.
As in the case of medical oncology, abnormal laboratory tests are not capable of predicting post-treatment-operative adverse outcomes. Consequently, a number of risk classifications aimed at predicting outcomes for specific conditions have been developed and tested. Unfortunately, results have been disappointing. To date no scoring method relating to candidacy for surgery has ever been attempted specifically on the oncogeriatric population.

Currently available assessment tools include the widely known American Society of Anesthesiologists (ASA) physical status system [39]. ASA is not aimed at measuring operative risk, but rather assessing the degree of sickness or physical state prior to anesthesia and surgery. The ASA does not specifically relate to the assessment of elderly individuals. Unfortunately, ASA is not sufficiently sensitive in differentiating between the largest proportion of patients falling in the ASA II and III categories [40]. Recently, a nationwide investigation led by Tekkis on behalf of the Association of Coloproctology in Great Britain and Ireland suggests that ASA may predict operative mortality among colorectal cancer patients, including the elderly. Noticeably, ASA I and II had to be cumulated to achieve statistical significance, so again it could be argued that the ASA might not be sufficiently sensitive.

The assessment of cardiac risk has been addressed by the Goldman Cardiac Risk Index (CRI) [41]. This instrument is designed to assess cardiac risk in noncardiac surgery but is rarely used by surgeons [42]. The modified CRI and the algorithm for cardiac risk assessment laid down by the American College of Physicians have been applied by anesthesiologists as determinants of outcome [43, 44].

Respiratory complications have been analyzed by Kroenke [45] who described the following as associated with respiratory complications following thoracic and major abdominal surgery: A) age over 70 years; B) perioperative bronchodilator use; C) abnormal chest x-ray, and D) high ASA grade. Lawrence et al. [46] identified four preoperative variables that were associated with postoperative respiratory complications, including abnormal respiratory examination, abnormal chest x-ray, Goldman CRI, and the Charlson comorbidity index [47]. These variables have not been formalized as a score or validated.

Undernourishment is highly prevalent among the healthy geriatric population; it can affect up to 12% of males and 8% of females. Moreover, nutritional deficiencies occur in 60% of hospitalized elderly subjects in Europe [38]. These figures have an impact on postsurgical outcomes, with a six-fold increase in surgical complications observed in patients who are malnourished preoperatively [48].

Acute Physiological and Chronic Health Evaluation (APACHE) is probably the best known of the physiological scoring systems [49]. It is based on 34 physiological variables, taking the worst values in the first 24 hours after the patient’s admission to an intensive care unit. Various modifications of this APACHE system are now available: APACHE II [50] uses 12 physiological variables. It is currently being used in general and surgical intensive care patients. Its application in the intensive care unit seems very appropriate but its development to general surgical patients who may not require respiratory support in intensive care is limited.

Another physiological scoring system developed in the UK is the Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity (POSSUM) [51, 52]. Portsmouth (P) POSSUM, a modification of the POSSUM [53], has been developed in an attempt to counter the over-prediction of mortality that was observed when POSSUM had been used previously. P POSSUM is used to produce a different formula for the calculation of risk value.

Both of these scoring systems comprise two parts: a physiological score and an operative score. The second part is highly relevant to the final result. Unfortunately, the necessity to record postoperative variables compromises its usefulness as a preoperative assessment tool.

The Broad Picture
Given the lack of reliable instruments capable of predicting risk and allowing a comparison between series, it was felt appropriate to audit and present personal and institutional results. Series of Ivor-Lewis transthoracic-abdominal resections for esophageal cancer, abdominal procedures for large bowel malignancies or liver primary tumors and metastatic conditions, pancreatic resections, and others were audited and published [54–79]. Some reviews were also performed [80] as well as multi-institutional data collections [81]. Two major themes were identified: A) that long-term outcomes (i.e., cancer-related survival rates) are age independent. Whenever a surgical option is feasible, it should be considered and offered no matter what the patient’s anagraphic age, and B) that even aggressive procedures may be undertaken on subjects beyond 70 years of age. The results and recommendations were presented at international meetings with the aim of sending the message that major surgery in the elderly should no longer be an issue. Clearly, selection bias was associated with the collection of these data and thus the presentation of results and thus major conclusions are limited. The findings are only representative of the restricted number of very fit elderly cancer patients who managed to reach the operative room. However, it is still an important observation that elderly patients, although exposed to a higher operative risk, may still undergo major surgery. Second, it was important to demonstrate that short-term outcomes in the elderly are not significantly different from individuals of a younger
Preoperative Assessment of Cancer in the Elderly

In order to address the limitations above in terms of recruiting and presenting surgical data on elderly cancer patients, the international Preoperative Assessment of Cancer in the Elderly (PACE) project has been launched with the aim of defining the general health condition of oncogeriatric surgical candidates. PACE is a new instrument generated from previous experience [23], this time focusing on the surgical candidate. In addition to CGA, PACE incorporates a number of validated tools currently used for surgical risk assessment. Specifically, PACE encompasses Mini Mental State (MMS) [82]; Satariano’s modified index of comorbidities [25]; Activities of Daily Living (ADL) [46]; Instrumental Activities of Daily Living (IADL) [47]; Geriatric Depression Scale (GDS) [48]; Brief Fatigue Inventory (BFI) [49]; Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) [50]; ASA physical status system [51]; POSSUM [52, 53]; and P POSSUM [54].

PACE is administered to elderly cancer patients by a trained health carrier prior to surgery. Thirty-day surgical mortality and morbidity are assessed and recorded by a physician, taking into consideration local and systemic complications. The total number of days spent in hospital after the day of surgery is also recorded.

Preliminary data have been collected and analyzed. The series was dichotomized based on whether the patient experienced 30-day morbidity. No mortality was recorded in these patients. Scores from each component of PACE were compared between the two groups, and the observed differences were assessed for statistical significance with the use of SPSS software. Face validity was measured by discussing PACE with the patients after completion. The practical utility of PACE as a presurgical assessment tool was assessed first by the duration of time taken to complete the interview, and second by establishing possible associations between components of the PACE and postoperative morbidity.

A pilot study was completed on a sample of 73 patients and found PACE to be comprehensible (good face validity), inexpensive, and feasible in terms of time taken to administer (approximately 20 minutes on average) [83]. Participation rate was 97%, with patient age ranging from 70–92 years (median age, 77 years). Patients with breast, colorectal, and upper gastrointestinal malignancies formed the study sample.

The number of comorbidities did not differ between the two groups, but there was evidence of an association between scores on MMS, BFI, GDS, and ASA, as well as whether patients had experienced a postoperative complication. However, none achieved statistical significance.

Conversely, two components of PACE were associated with 30-day morbidity: PS was found to be significantly lower in patients who developed 30-day morbidity, and a lower ADL score was associated with postoperative complications (p < .001).

Results from an interim analysis of the PACE database are shown in Table 1. This analysis has recently been conducted on a sample of 215 patients who were considered for a surgical procedure. The largest proportion of these patients received surgery for breast cancer (142 patients), with an additional 27 patients receiving surgery for urogenital cancer, 27 for colorectal cancer, nine for gastroesophageal cancer, nine for head and neck cancer, and one for gynecological cancer. To date, the refusal rate is 0.9% (two patients) and the median age is 76 years (range, 70–100 years).

Table 1. Results from interim analysis of components of PACE with 30-day morbidity

<table>
<thead>
<tr>
<th>Pace component</th>
<th>Complications (n = 64)</th>
<th>No complications (n = 149)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>IQR</td>
<td>Median</td>
</tr>
<tr>
<td>n of comorbidities</td>
<td>2</td>
<td>0-3</td>
<td>1</td>
</tr>
<tr>
<td>MMS</td>
<td>28</td>
<td>27-30</td>
<td>28</td>
</tr>
<tr>
<td>GDS</td>
<td>3</td>
<td>1-6</td>
<td>2</td>
</tr>
<tr>
<td>BFI</td>
<td>2.2</td>
<td>0.2-4.4</td>
<td>1.2</td>
</tr>
<tr>
<td>PS = 0</td>
<td>30</td>
<td>46.9</td>
<td>122</td>
</tr>
<tr>
<td>ADL = Dependent</td>
<td>38</td>
<td>59.4</td>
<td>55</td>
</tr>
<tr>
<td>IADL = Independent</td>
<td>38</td>
<td>59.4</td>
<td>114</td>
</tr>
<tr>
<td>ASA = 1, 2</td>
<td>29</td>
<td>45.1</td>
<td>72</td>
</tr>
</tbody>
</table>

Abbreviations: ADL = activities daily living; ASA = American Society of Anesthesiologists; BFI = Brief Fatigue Inventory; GDS = Geriatric Depression Scale; IADL = Instrumental Activities Daily Living; IQR = interquartile range; MMS = Mini Mental State; PACE = Preoperative Assessment of Cancer in the Elderly; PS = performance status
The median number of comorbidities was one for the 149 patients who did not report a postsurgical complication, and two for the 64 patients who did report a complication ($p = .024$; Table 1). MMS, GDS, and BFI were not found to be related to 30-day morbidity. Of the patients who experienced complications, 30 (46.9%) had a PS = 0, compared with 122 (81.9%) of patients who did not develop postoperative complications ($p < 0.0001$). Similarly, a significant difference was identified in ADL score among the 38 patients (59.4%) with postoperative complications. However, aspects relating to physical frailty and morbidity (i.e., PS, ADL, and IADL) seem to be significantly associated with 30-day morbidity.

These preliminary results should be interpreted with caution, and a larger sample is required to produce a more definitive analysis. This cooperative project is ongoing at present under the auspices of the International Society of Geriatric Oncology [84], and further expressions of interest in actively participating in this investigation are welcome.

**DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST**

The authors indicated no potential conflicts of interest.

**REFERENCES**


84 International Society of Geriatric Oncology. Available at: http://www.cancerworld.com/siog/default.asp