A Systematic Review of Studies Examining Outcomes in Geriatric Surgical Oncology

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ABSTRACT:

Objective: To examine the predictive value of different components of a geriatric assessment in surgical oncology.

Method: We searched Medline, EMBASE, and the Cochrane Library to find prospective studies that examined geriatric patients undergoing elective surgery and used components of the Comprehensive Geriatric Assessment (CGA) as the primary variables in predicting surgical outcome. Outcome parameters were 30 day post-surgical mortality, complications within 30 days post-surgery, and discharge to a non-home care institution. For each outcome, we evaluated which CGA components had predictive value.

Results: The search identified 125 potentially relevant articles, and 10 articles base off of 7 studies were ultimately included. Despite differences in the surgical setting, poorer function as determined by components of CGA was consistently found to be associated with more adverse surgical outcomes.

Conclusion: This study supports that assessments of functional fitness by components of the CGA have predictive value for geriatric surgical patients. In addition, age was consistently not found to be an independent predictor of poor outcomes.

INTRODUCTION:

Geriatric patients present with a wide range of physiologic ages, and they also often have a greater number of geriatric syndromes and medical comorbidities. This challenge has a profound impact on treatment and care when working with geriatric patients in surgical oncology. Individual levels of functional fitness must be taken into account for determining the best approach to treatment in this patient population.

Cancer is a disease of aging, and there is a growing population of elderly patients. From 2004-2008, the median age at diagnosis for cancer of all sites was 66 years of age [1]. Studies by the American Cancer Society predict that by 2030, the population of people over 64 will increase to 20%, and that 70% of all cancers will be found in this patient group. There is a growing need for more information about how to treat elderly cancer patients. Despite the increasing need, there continues to be a lack of information in this field.

Conducting additional pre-surgical assessments of patient fitness would help stage their disease and direct their treatment. However, geriatric patients are often excluded from cancer clinical trials because it is difficult to isolate the different variables that may affect their health. In some cases, patients are denied standard surgical treatments that would be offered to younger patients because of fear of complications due to comorbidities, toxicity, and post-surgical
complications. There is a lack of data on these potentially curative treatments in geriatric patients because of the small number of clinical trials that enroll patients 65 and older. Age has been consistently found not to be an independent predictor of surgical outcome [2].

There is no standard definition for what qualifies as a geriatric patient, and this makes it difficult to direct treatment [5]. However, there are currently a number of different assessments that are used amongst geriatricians and primary care providers to measure a patient’s physiologic fitness. In geriatric clinics, a Comprehensive Geriatric Assessment (CGA) is often used to assess components of a patient’s physical, mental, and social wellbeing to give a whole picture of the patient’s physiological age and capabilities, regardless of their temporal age. A full CGA can take a few hours to complete, and it includes items such as Activities of Daily Living, Geriatric Depression Score, and Get-Up and Go assessments. However, in a setting of surgical oncology it is sometimes not clinically feasible to conduct and entire CGA for each patient because of the time constraints [2].

Several studies have looked at creating a shorter, more efficient geriatric assessment to stage cancer patients to see if they may be eligible for surgery. By analyzing different parts of the CGA, they have looked at ways to describe patients as being frail, moderately frail, and fit. Intuitively, patients who are staged as frail will trend towards having worse outcomes than those who are fit. However, for the moderately frail group, additional staging could be beneficial in the decision making process for what type of treatment to pursue. Studies looking at the predictive value of different screening tests have found relatively consistent benefits of using these assessments for surgical oncology across different types of cancer [1-7].

With this review, we synthesize the existing studies to determine whether frailty predicts surgical outcomes. The results will provide support and direction in developing new screening protocols and possibly identify what aspects of the CGA to target for pre-surgical interventions.

METHODS:

Eligibility Criteria:

Type of studies – All prospective studies in which patients were scheduled to undergo elective surgery for cancer treatment and used components of a CGA to predict surgical outcomes were eligible. Studies that looked at patients undergoing surgery in general were also included.

Types of participants – Geriatric patients undergoing elective surgery.

Types of observations – Any combination of components of the CGA including components of: fitness assessment, mental cognition, depression, nutrition, comorbidities, fatigue, and laboratory values.

Types of outcome measures
Primary outcomes – The main outcomes of interest were 30 day post-surgical mortality, complications within 30 days, and discharge to an institution.

Secondary outcomes – Midterm all-cause mortality, and long-term six month mortality

**Search Methods:**

**Electronic Searches**

For this review, we identified relevant studies by conducting searches of Medline via PubMed, EMBASE, and the Cochrane Library for articles published between 2000-2011. For Medline, the following search terms were used: Aged, Surgical Procedures, Operative, Neoplasms/Surgery, Neoplasm metastasis, geriatric assessment, prospective studies, prospective, prospectively, and logistic models. See Appendix 1 for the full search strategy. In EMBASE, the search terms used were 'cancer surgery'/exp or 'cancer surgery' or 'surgery' or 'surgery'/exp or surgery and ('geriatric assessment'/exp or 'geriatric assessment') and ('prediction' or 'prediction'/exp or prediction or 'prognosis' or 'prognosis'/exp or prognosis or 'treatment outcome'/exp or 'treatment outcome' or 'survival' or 'survival'/exp or survival or 'complication'/exp or 'complication') and ('prospective' or 'prospective study'/exp or 'prospective study' or 'prospectively'). The Cochrane Library was searched for ‘Neoplasms/Surgery[Mesh].’

**Searching Other Resources**

The reference lists of relevant articles were further searched for additional relevant studies.

**Selection of Studies**

The studies selected for inclusion in this review met the following criteria: prospective study design; a study population of geriatric patients who underwent elective surgical treatment; studies that used pre-surgical assessments containing components of the CGA as predictors of negative patient outcomes; measurements of at least one of the following outcomes: post-surgical complications, 30 day mortality, and discharge to an institution; published in English and a publication year between 2000 and 2011. Publications focusing on delirium as the primary post-surgical complication were excluded.

**Data Collection and Quality Assessment**

Data was independently extracted from the reports. The risk of bias in each study was assessed by six criteria. Each criterion was scored from 0-1, depending on if it was met or not met. The total quality score ranged from 0-6.
Data Items

Data was sought about which components of the geriatric assessment were used. The data was organized into separate categories including: fitness assessment, mental cognition, depression, nutrition, laboratory values, comorbidity, fatigue, and other. We assume that the odds ratio of the results from the different types of screening in each category were comparable between studies.

The three main outcomes of interest were post-surgical complications, 30 day mortality, and discharge to an institution. Some studies listed many complications that were specific to their surgery of interest, but for the purpose of this study they were all included as a post-surgical complication.

Risk of Bias in Individual Studies

Table 1. Study Quality

<table>
<thead>
<tr>
<th>Prospective study</th>
<th>Multiple institutions</th>
<th>Clearly defined inclusion/exclusion criteria</th>
<th>Validated questionnaire</th>
<th>Short term FU</th>
<th>Long term FU</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fukuse</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Kothari</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Kristjansson</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1**</td>
<td>6</td>
</tr>
<tr>
<td>Lee</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Makary</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>PACE, Audisio</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Robinson</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1***</td>
<td>5</td>
</tr>
</tbody>
</table>

* 90 day follow up
** 3 month follow up
*** 6 month mortality

RESULTS:

The studies for inclusion were selected by two authors. The keyword search yielded 125 results: 71 from Medline via Pubmed, 54 from EMBASE, and none from the Cochrane Library. By reading the abstracts, 27 potentially relevant articles were selected for further examination, not including nine duplicates which were removed. The remaining articles were further reviewed for inclusion criteria by reading the full text. Three articles were removed because they were published in non-English languages. Several articles were further excluded because they were not prospective studies, or they were review articles. Ultimately 10 articles were selected to be included in this study, and they were based on seven different prospective studies.

The studies and their characteristics are presented in Table 2.
Table 2. Study Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>PACE (Audisio)</th>
<th>Fukuse</th>
<th>Kothari</th>
<th>Kristjansson</th>
<th>Lee</th>
<th>Makary</th>
<th>Robinson</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td>UK (n=3), Italy (n=6), Belgium (n=1), The Netherlands (n=1), Japan (n=1) (07/03-12-05)</td>
<td>Otsu Red Cross Hospital. 08/00 – 05/03</td>
<td>Norwegian University Hospitals (n=3). 11/06-06/08</td>
<td>Norway, University Hospitals (n=3). 11/06-06/08</td>
<td>Nova Scotia, Johns Hopkins Hospital. 06/05-07/06</td>
<td>United States, Johns Hopkins Hospital. 06/05-07/06</td>
<td>Denver Veterans Affairs Medical Center 10/06-02/08</td>
</tr>
<tr>
<td>Types of surgical patients</td>
<td>Solid tumors. 47.2% breast. 31.3% GI. 15.4% GU. 6.1% other</td>
<td>Thoracic surgery. 60% lung. 52% lobectomy.</td>
<td>Thoracic oncology. 34 lung (5 met.), 18 esophageal, 1 tracheal, 2 (pleural or thymic)</td>
<td>Colorectal cancer</td>
<td>Cardiac</td>
<td>Patients at anesthesia preoperative evaluation center for elective surgery</td>
<td>Major operation req postop ICU admission. 47% General/ urology, 43% thoracic, 10% vascular</td>
</tr>
<tr>
<td>Sample size</td>
<td>460 (157M 303W) Age: ≥70 (avg. 76.9)</td>
<td>120 Age: ≥60y</td>
<td>60 (32M 28W) Age:≥70y (med 76)</td>
<td>185 Age:≥70y (avg. 79.6)</td>
<td>3826 (3669 non frail, 157 frail) Age:57-78 (med 71)</td>
<td>594 Age:≥65</td>
<td>110 (104M 6W) Age: ≥65 (avg. 74)</td>
</tr>
<tr>
<td>Exclusions</td>
<td>Emergency, MMSE ≤18. Unable to give written consent</td>
<td>Surgery must be acceptable by current practices. Unable to give written consent</td>
<td>Unable to give written consent</td>
<td>Parkinsons, stroke, MMSE&lt;18, carbi/levodopa, donepezil HCL, or antidepressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fitness assessment</td>
<td>Katz, Lawton Barthal</td>
<td>Katz, IADL*</td>
<td>Barthal, Lincoln</td>
<td>Katz, ambulation</td>
<td>Makary</td>
<td>Katz</td>
<td></td>
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<tr>
<td>Mental cognition</td>
<td>Folstein</td>
<td>Folstein</td>
<td>---</td>
<td>Folstein</td>
<td>Prev. Dx</td>
<td>---</td>
<td>Borson</td>
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<td>---</td>
<td>Brink</td>
<td>Brink</td>
<td>---</td>
<td>---</td>
<td>Prev. Dx</td>
</tr>
<tr>
<td>Nutrition</td>
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<td>deGroot</td>
<td>Guigoz</td>
<td>---</td>
<td>---</td>
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<tr>
<td>Comorbidity</td>
<td>SIC</td>
<td>Yes</td>
<td>---</td>
<td>CRS</td>
<td>Yes</td>
<td>Yes</td>
<td>Charlson Index</td>
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<tr>
<td>Fatigue</td>
<td>BFI</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>BFI</td>
<td>Makary</td>
<td>Falls</td>
</tr>
<tr>
<td>Laboratory values</td>
<td>---</td>
<td>Yes</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>Yes</td>
</tr>
<tr>
<td>Other</td>
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<td>---</td>
<td>Yes</td>
<td>---</td>
<td>Yes</td>
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<td>Yes</td>
</tr>
</tbody>
</table>
Methodological Quality

The studies were ranked on their quality based off several factors (Table 1). All of the studies were prospective studies with clearly defined inclusion and exclusion criteria. Most of them included validated questionnaires. All of the studies contained short term follow up including 30 day post operative complications and 30 day mortality. One study looked at 6m mortality as their primary adverse outcome [7]. Only a few of the studies were conducted at multiple institutions. Very few of the studies followed long term outcomes. Kristjansson looked at 3m follow up, and the study by Robinson looked at 6m mortality, but these were the longest follow up measures of the studies in this review [3, 7].

Complications

Complications were recorded as a dependent variable in all but one of the studies. In one study, complications were assessed by the patient’s physician and included a list of complications that were specific to the type of operations performed, including thoracic and cardiac operations [1, 4]. In some studies, post-operative complications were defined as a major complication or as any adverse events that occurred post-operatively within 30 days and required medical treatment that is not typical for the given operation [2, 3]. One used the American College of Surgical National Surgical Quality Improvement Program (NSQIP) definitions for complications within 30 days of surgery [5]. One divided complications into major and minor categories based off whether it was systemic or local [6].

One study found that patients with dependencies in ADLs and MMSE had a higher chance of post-operative complications. If surgical factors were added, operation time was found to be another major risk factor in complications. ADLs were also found to be more sensitive than PS [1]. However, another found that ADLS were not useful in predicting post-operative complications. This may have been due to the fact they had a small sample size for patients with deficiencies in ADLs [2]. Two studies found that dependence in IADLs were useful in predicting complications [6, 2]. Furthermore, Kotharti et al examined the predictive value of specific questions in IADLS and found that deficiencies in shopping alone were predictive of complications [2]. Moderate to severe BFI, abnormal PS, and ASA were also found to have significant correlations with post-operative complications [6]. Patients with dementia and deficiencies in single nutritional indexes had a higher risk as well [1]. Age alone was not found to be significantly correlated with complications [6, 4]. Age, ASA, tumor stage, and sex did not predict complications [3].

Post-Surgical Mortality

Frailty was found to be a predictor of mortality, and age was not [4]. In addition, one study found that there were six factors that had the highest predictive power of 6m mortality: cognitive dysfunction, lower albumin, having fallen in the past 6m, lower hematocrit, functional
dependence, and increased comorbidities. The presence of 4+ markers was related to 6m mortality with high sensitivity and specificity [7].

**Discharge to an Institution**

Deficiencies in IADL in shopping only were enough to be predictive of complications and discharge to a non-home institution. Geriatric depression screening was also helpful for both of these [2]. Frailty as a was associated with discharge to an institution as well [5], and age was not found to be an independent predictor [4].

**DISCUSSION:**

This review synthesizes the evidence that pre-surgical geriatric assessments have predictive value in regards to surgical outcomes, and they are a valuable tool for patients and their physicians. Despite differences in patient populations and surgical conditions, it has consistently been found that frailty is associated with adverse surgical outcomes. It is important for doctors to take into account the heterogeneity present in the elderly population in order to determine the best course of action for treatment.

Two of the studies looked at frailty as a whole, rather than as individual components-Kristjansson and Lee. In Lee, they found that mortality, discharge to an institution, post-operative complications and longer length of stay were all more prevalent in frail patient populations when compared to fit populations. Frailty was consistently found to be an independent risk factor for surgery. It was also found to be superior to age in predicting adverse surgical outcomes. Multiple studies found that age was not an independent predictor of complications.

One limitation present in some of the studies was that a small number of patients in some of the groups decreased the power of the study. Another factor that may have caused selection bias was that most of the studies were conducted at only one institution, and we may not be able to apply the results to the general geriatric population. Two studies, Audisio and Kristjansson were conducted at multiple institutions. Audisio is a global project with institutions in multiple countries, and the study by Kristjansson was conducted at multiple sites in Norway.

It is important to have a geriatric assessment that can efficiently and effectively stage patients into different groups based off function and comprehensive health. In each of the studies examined, the assessments took 10 to 80 minutes, with most being around 20 minutes. They show that this is a feasible amount of time to be spent with the patient what would make pre-surgical assessments more practical in the clinical setting. In addition, some of the components could also be filled out by the patient at home prior to their appointment.

The review supports that further research using prospective study designs are needed. This will help address the diversity of the population, and prevent both over and under treating patients. This could also help patients in with the decision making process for patients in
determining whether they are fit enough for surgery, or if they would benefit from less aggressive treatments. There have been several studies done in the geriatric population for patients undergoing chemotherapy or orthopedic surgery, but there are a limited number of studies that look at the outcomes of surgical oncology. Future studies could provide additional information to patients and physicians to help determine the best course of treatment for each individual.

References

1. Fukuse, T., Satoda, N., Hijiya, K. and Fujinaga, T. Importance of a comprehensive geriatric assessment in prediction of complications following thoracic surgery in elderly patients 2005