Optimal management of elderly cancer patients: usefulness of the Comprehensive Geriatric Assessment

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Background: Cancer is common in older patients, who raise specific treatment challenges due to aging-related, organ-specific physiologic changes and the presence in most cases of comorbidities capable of affecting treatment tolerance and outcomes. Identifying comorbid conditions and physiologic changes due to aging allows oncologists to better assess the risk/benefit ratio and to adjust the treatment accordingly. Conducting a Comprehensive Geriatric Assessment (CGA) is one approach developed for this purpose. We reviewed the evidence on the usefulness of CGA for assessing health problems and predicting cancer treatment outcomes, functional decline, morbidity, and mortality in older patients with solid malignancies.

Methods: We searched Medline for articles published in English between January 1, 2000 and April 14, 2014, and reporting prospective observational or interventional studies of CGA feasibility or effectiveness in patients aged ≥65 years with solid malignancies. We identified studies with at least 100 patients, a multivariate analysis, and assessments of at least five of the following CGA domains: nutrition, cognition, mood, functional status, mobility and falls, polypharmacy, comorbidities, and social environment.

Results: All types of CGA identified a large number of unrecognized health problems capable of interfering with cancer treatment. CGA results influenced 21%–49% of treatment decisions. All CGA domains were associated with chemotoxicity or survival in at least one study. The abnormalities that most often predicted mortality and chemotoxicity were functional impairment, malnutrition, and comorbidities.

Conclusion: The CGA uncovers numerous health problems in elderly patients with cancer and can affect treatment decisions. Functional impairment, malnutrition, and comorbidities are independently associated with chemotoxicity and/or survival. Only three randomized published studies evaluated the effectiveness of CGA-linked interventions. Further research into the effectiveness of the CGA in improving patient outcomes is needed.

Keywords: cancer, geriatric assessment, elderly, mortality, chemotoxicity, outcomes

Introduction

The management of older cancer patients has become a major public health concern in Western countries because of the aging of the population and the steady increase in cancer incidence with advancing age. Today, over 60% of all cancers are diagnosed in patients older than 65 years in Europe and the USA. This percentage is expected to rise to 70% within the next 30 years. The care of older patients thus constitutes an important part of everyday oncology practice. However, despite the rapid growth of the geriatric oncology population in the real-life setting, older patients are underrepresented in the clinical trials that set the standards of care in oncology. As a result, there is a lack of evidence on the risk/benefit ratio of cancer treatments in older patients. Comorbidities...
and disabilities become increasingly prevalent with advancing age and are associated with treatment-related side effects and poorer outcomes. Thus, a major issue for oncologists treating older cancer patients is determination of the intensity of cancer treatment best suited to each patient. There is considerable heterogeneity among patients of the same age, so that chronologic age alone provides little information regarding an individual’s tolerance to cancer treatments.

Identifying comorbid conditions and aging-related, organ-specific physiologic changes that increase the risk of toxicities may allow oncologists to better assess the risk/benefit ratio in individual patients, to develop customized treatment adjustments, and to implement interventions designed to decrease the risk of toxicity. The Comprehensive Geriatric Assessment (CGA) is one approach developed for this purpose. The CGA was designed by geriatricians as a multidimensional assessment of general health status based on validated geriatric scales and tests that produce an inventory of health problems, allowing the development of an individualized geriatric intervention program. Since the mid-1990s, oncologists and geriatricians have worked to integrate CGA approaches into oncologic practice. The International Society of Geriatric Oncology created a task force to determine the best CGA format for use in oncology. Independent of these recommendations, the feasibility and effectiveness of the CGA in managing older cancer patients and the evidence of its usefulness in everyday oncology practice deserve consideration. Only two systemic reviews have focused on the CGA in older cancer patients.

The objectives of this review were to depict CGA components in everyday oncology practice and to assess the usefulness of the CGA in assessing health problems, guiding decisions about cancer treatments, predicting outcomes, and developing a coordinated program of tailored geriatric interventions. We also reviewed the available data on the benefits of specific CGA-based interventions.

Materials and methods

Data sources

We conducted a systematic comprehensive search of Medline (PubMed) for articles published in English between January 1, 2000, and April 14, 2014.

Study eligibility criteria

We used four eligibility criteria to select studies for our review: a focus on older patients (65 years or older) with solid cancer (excluding hematologic malignancies) who were seen in oncology or surgery or geriatric-oncology clinics (as outpatients or inpatients); prospective data collection and observational or interventional design; a sample size of at least 100 patients; and assessment of at least five CGA domains (from nutrition, cognition, mood, functional status, mobility and falls, polypharmacy, comorbidities, and social environment). We excluded editorials, case studies, studies published as abstracts, and review articles other than the two most recent systematic reviews of the CGA in geriatric oncology.

For assessment of the ability of the CGA to detect previously unrecognized health problems, the studies had to contain information on the frequencies of CGA domain alterations or on the data needed to compute these frequencies. We therefore excluded articles that did not report the frequencies of CGA domain alterations. To assess the usefulness of the CGA in predicting outcomes such as postoperative complications, feasibility of chemotherapy, chemotoxicity, functional decline/disability, and mortality, we included only studies involving a multivariate analysis. To enable an evaluation of the impact of CGA-based geriatric interventions, a randomized design was required.

We designed a specific algorithm for each objective:

1) Algorithm 1 to assess the usefulness of the CGA in assessing health problems (Figure 1): (“Neoplasms” [Mesh] OR “cancer” [Text Word]) AND (“Geriatric Assessment” [Mesh] OR “Comprehensive Geriatric Assessment” [Text Word]);


For the three algorithms, we used the following limits: Article Types, Clinical Trial OR Observational Study; Publication Dates from January 1, 2000 to April 14, 2014; Species, Humans; Language, English; Subjects, Cancer; and Ages, 65+ years.

Limits: Article types: Clinical trial OR observational study; Publication dates: from 01/01/2000 to 14/04/2014;
Species: Humans; Languages: English; Subjects: Cancer; Ages: 65+ years.
Source: Medline (PubMed).

n=67 records identified

Excluded (n=30) due to:
- No cancer population: n=8
- Hematological malignancies: n=6
- No CGA or GA: n=16

n=37 abstracts screened

Excluded (n=22) due to:
- No cancer population: n=1
- Retrospective design: n=1
- N<100: n=16
- < four domains explored in the GA: n=4

n=15 full-length articles assessed for eligibility

n=19 full-length articles from references, related contents of included publications, and two previous systematic reviews regarding CGA*

Excluded (n=5) due to:
- No information on frequencies of CGA domains: n=2
- < four domains explored in the GA: n=2
- Duplicate study: n=1

n=29 articles included

Figure 1 Search results and study selection for ability of the CGA to detect health problems in elderly patients with solid malignancies.

Notes: N, number of patients; n, number of articles. *Data from Hamaker et al9 and Puts et al10,11

Abbreviations: CGA, Comprehensive Geriatric Assessment; GA, Geriatric Assessment.


Limits: Article types: Clinical trial OR observational study; Publication dates: from 01/01/2000 to 14/04/2014;
Species: Humans; Languages: English; Subjects: Cancer; Ages: 65+ years.
Source: Medline (PubMed).

n=59 records identified

Excluded (n=15) due to:
- No cancer population: n=9
- Hematological malignancies: n=6

n=44 abstracts screened

Excluded (n=28) due to:
- Retrospective design: n=1
- N<100: n=13
- No CGA or GA: n=14

n=15 full-length articles assessed for eligibility

n=11 full-length articles from references, related contents of included publications, and two previous systematic reviews regarding CGA*

Excluded (n=9) due to:
- No matching outcomes: n=6
- Duplicate study: n=1
- No CGA or GA: n=2

n=17 articles included

Figure 2 Search results and study selection for usefulness of the CGA in predicting outcomes in elderly patients with solid malignancies.

Notes: N, number of patients; n, number of articles. *Data from Hamaker et al9 and Puts et al10,11

Abbreviations: CGA, Comprehensive Geriatric Assessment; GA, Geriatric Assessment.
Study selection

Articles were selected initially by three senior medical doctors specialized in geriatric oncology (PC, FCP, and EP), based on the titles and abstracts and on the eligibility criteria described above. When one or more of these three investigators were uncertain about whether the article fulfilled the eligibility criteria, the abstract was included and the full-length article was analyzed by the same three investigators. Disagreements were resolved by consensus. We also reviewed the reference lists of all selected articles, related contents of the Medline search, and reference lists of the three above-mentioned reviews to look for relevant articles.

The three investigators used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines (http://www.prisma-statement.org/statement.htm) to assess the quality of included studies. Disagreements were resolved by consensus.

What is the CGA?

Definition

The CGA was defined in 1988 as

[...] a multidisciplinary evaluation in which the multiple problems of older persons are uncovered, described, and explained, if possible, and in which the resources and strengths of the person are catalogued, need for services assessed, and a coordinated care plan developed [...].

CGA components and assessment tools

The core components of the CGA are functional status, cognition, mood and emotional status, social support, financial concerns, nutritional status, comorbidities and polypharmacy, geriatric syndromes (fall risk, confusion, urinary incontinence, visual or hearing impairments), goals of care, and advance care planning. The CGA uses validated geriatric scales and tests to produce an inventory of health problems, which can then serve to develop an individualized geriatric intervention plan. The content of the assessment varies with the care setting (eg, home, clinic, hospital, or nursing home). In many settings, the CGA process relies on a core team consisting of a physician, a nurse, and a social worker, who obtain assistance as needed from other health care professionals (eg, nutritionist, physical therapist, and/or psychologist).

The effects of implementing a CGA-based approach have been evaluated in a number of controlled studies conducted in inpatients and community-dwelling...
outpatients. A meta-analysis of 28 controlled trials comprising 4,959 patients who underwent one of five CGA types and 4,912 controls showed that the CGA, when used to guide management decisions and combined with long-term follow-up, detected a greater number of health problems and improved survival, functional status, and unplanned admissions in older patients with nonmalignant diseases, compared with usual care. However, the effect size was greater for inpatients than for community-dwelling patients. A meta-analysis of 21 trials with 10,315 patients indicated that the CGA increased the likelihood of patients being alive and in their own homes 6 months after an emergency admission.14

**Conducting the CGA in oncology**

To help oncologists select the best treatment for older patients, the US National Comprehensive Cancer Network, International Society of Geriatric Oncology, and European Organisation for Research and Treatment of Cancer recommend a CGA-based approach for elderly cancer patients. However, the best CGA type and implementation method for cancer patients in everyday practice remain to be defined. Limitations to the widespread use of the CGA in everyday practice are the considerable time and human resources needed to conduct the assessment and the failure of some health insurance systems to reimburse it. The abundance of studies investigating the effectiveness of the CGA or using CGA components supports the feasibility of this assessment in geriatric oncology. Only one large prospective multicenter study carried out in ten hospitals in Belgium, including 1,967 older cancer patients, has specifically addressed the feasibility of the CGA. In this study, the high inclusion rate involving 71% of patients indicated that the implementation of a geriatric assessment was very feasible. Nevertheless, this study showed that the information revealed by the CGA did not always reach treating physicians and efforts were needed to improve the interaction between the oncologist, geriatrician, and trained health care worker.

**Ability to detect previously unrecognized health problems in the elderly with solid malignancies**

Table 1 recapitulates the results of 29 studies describing CGA findings in elderly patients with solid malignancies.5,7,16–42 Functional status was consistently assessed using the Eastern Cooperative Oncology Group-Performance Status (ECOG-PS), Activities of Daily Living (ADL) index, and/or instrumental ADL index. Functional impairment defined as an ECOG-PS grade ≥2 was noted in 2%–50% of patients. Deficiency in at least one ADL or instrumental ADL item was found in 10%–61% and 25%–73% of patients, respectively. Mobility or fall risk was assessed in 22/29 (75.9%) studies. The Timed Get-Up-and-Go test of gait and balance indicated a risk of falls in 14%–55% of patients. Of the 29 studies selected for this review, 13 (44.8%) used the Mini-Nutritional Assessment to evaluate nutritional status. Malnutrition or a high risk for malnutrition was found in 27%–83% of patients. The Mini-Mental State Examination was performed to evaluate cognition in 20/29 (69%) studies and showed cognitive dysfunction in 6%–42% of patients. The Geriatric Depression Scale (in its variants with 2, 4, 15, or 30 items) was the most widely used tool to assess depressive symptoms (19/29 studies, 65.5%) and showed depression in 10%–65% of patients. All 29 studies evaluated comorbidities, generally using the Cumulative Illness Rating Scale for Geriatrics (12/29 studies, 41%) or the Charlson Comorbidity Index (10/29 studies, 34.5%). Using these tools, at least one comorbidity was found in 23%–70% of patients, at least two comorbidities in 16%–59%, and at least three comorbidities in 50%–81%.

Thus, all CGA types identified large numbers of geriatric problems and multiple comorbidities likely to interfere with cancer treatment and to compete with cancer as a cause of death. Identifying these problems is therefore a crucial initial step when implementing comprehensive care for older patients with cancer.

**Influence of CGA on treatment decisions**

The CGA is recommended in older cancer patients to help physicians determine whether the best option is standard anticancer treatment, anticancer treatment adjusted according to existing health problems other than cancer, or supportive care only. Nevertheless, the relationship between CGA findings and the treatment decision-making process remains unclear. To date, few studies have addressed the influence of CGA on decision-making.

A prospective study of 1,967 older cancer patients (87.2% with solid malignancies and 12.8% with hematologic malignancies) evaluated the prevalence of changes in treatment decisions based on CGA findings. The oncologists were aware of the CGA results at the time of treatment decision-making for only 61.3% of patients and, among these, 25.3% had changes in the final treatment decision in response to the CGA results. This study did not assess relationships between individual CGA parameters and cancer treatment decisions.
### Table 1: Studies of health problem identification using Comprehensive Geriatric Assessment

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Sample size</th>
<th>Cancer type and metastatic status</th>
<th>Age, mean ± SD or median (range)</th>
<th>Dependency</th>
<th>Mobility impairment – fall risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laurent et al</td>
<td>P</td>
<td>385</td>
<td>NHL 31.8%, breast 23.1%, GI non-CRC 19.2%, urinary tract 13.2%, prostate 10.9%, other 4.9% M+ 47.0%</td>
<td>78.9±5.4</td>
<td>21% ADL 40.2% PS ≥2</td>
<td>34.5% walking problems 47.2% fall risk</td>
</tr>
<tr>
<td>Pottel et al</td>
<td>P</td>
<td>100</td>
<td>HNC 100% 69% stages III–IVb</td>
<td>72 (65–86)</td>
<td>10.2% ADL 59.2% IADL</td>
<td>26.5% (Tinetti)</td>
</tr>
<tr>
<td>Kanesvaran et al</td>
<td>P</td>
<td>803</td>
<td>Lung 32.1%, CRC 21.0%, breast 7.2%, prostate 2.1%, other 37.5% M+ 56.3%</td>
<td>72 (65–94)</td>
<td>29.4% ADL 63.7% IADL</td>
<td>NR</td>
</tr>
<tr>
<td>Kenis et al</td>
<td>P</td>
<td>937</td>
<td>Breast 40.4%, CRC 20.6%, lung 7.8%, ovarian 6.3%, prostate 9%, hematologic malignancies 15.9% M+ 51.8%</td>
<td>76 (70–95)</td>
<td>51.4% ADL 57.4% IADL</td>
<td>3.7% ≥2 falls without injury 11.2% ≥2 falls with injury</td>
</tr>
<tr>
<td>Decoster et al</td>
<td>P</td>
<td>937</td>
<td>Breast 40.4%, CRC 20.6%, lung 7.8%, ovarian 6.3%, prostate 9%, hematologic malignancies 15.9%</td>
<td>76 (70–95)</td>
<td>51.4% ADL 57.4% IADL</td>
<td>3.7% ≥2 falls without injury 11.2% ≥2 falls with injury</td>
</tr>
<tr>
<td>Aaldriks et al</td>
<td>P</td>
<td>143</td>
<td>CRC (colon 83%, rectum 17%)</td>
<td>75 (70–92)</td>
<td>2% PS ≥2</td>
<td>NR</td>
</tr>
<tr>
<td>Hoppe et al</td>
<td>P</td>
<td>299</td>
<td>NHL 31.8%, colon 25.8%, stomach 11.4%, lung 10.0%, pancreas 5.7%, prostate 5.4%, bladder 4.7%, ovary 4.0%, primary unknown 1.3% M+ 37.5%</td>
<td>77.35 (70–93)</td>
<td>31.8% ADL 72.9% IADL</td>
<td>22.4% TGUG</td>
</tr>
<tr>
<td>Bouzereau et al</td>
<td>P</td>
<td>111</td>
<td>Lung 26.1%, GI 18%, HNC 12.6%, genitourinary tract 6.3%, breast 9.9%, gynecologic 5.4%, prostate 4.5%, hematologic malignancies 10.8%, skin 4.5%, other 1.9%</td>
<td>80.6 (65–96)</td>
<td>33.3% ADL 58.6% IADL</td>
<td>NR</td>
</tr>
<tr>
<td>Falandry et al</td>
<td>P</td>
<td>111</td>
<td>Ovarian cancer 100% M+ 35%</td>
<td>79 (71–93)</td>
<td>55% ADL 69% IADL</td>
<td>NR</td>
</tr>
<tr>
<td>Kenis et al</td>
<td>P</td>
<td>1,967</td>
<td>Breast 40.5%, CRC 21.5%, lung 12.0%, ovary 5%, prostate 8.2%, hematologic malignancies 12.8% M+ 44.9%</td>
<td>76 (70–96)</td>
<td>56.5% ADL 64.5% IADL</td>
<td>4.4% ≥2 falls without injury 13.7% ≥2 falls with injury</td>
</tr>
<tr>
<td>Beitar A et al</td>
<td>P</td>
<td>170</td>
<td>Urinary tract 29%, digestive tract 19%, HNC 16%, breast 15%, lung 11%, others 11% M+ 57%</td>
<td>77 (66–97)</td>
<td>33% ADL 52% IADL</td>
<td>35% TGUG</td>
</tr>
<tr>
<td>Soubeyran et al</td>
<td>P</td>
<td>348</td>
<td>Colon/stomach 37.1%, NHL 30.7%, other 32.2% M+ 81.3%</td>
<td>77.45 (70–99)</td>
<td>18.1% ADL 73.0% IADL</td>
<td>24.1% TGUG</td>
</tr>
<tr>
<td>Bellara et al</td>
<td>CS</td>
<td>364</td>
<td>NHL 30%, colon 28%, stomach 10%, lung 10%, pancreas 6%, prostate 6%, bladder 5%, ovary 4%, unknown primary 1% M+ 53%</td>
<td>77 (70–99)</td>
<td>17% ADL 72% IADL</td>
<td>23% TGUG</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Cognitive impairment</td>
<td>Depression</td>
<td>Comorbidities</td>
<td>Polypharmacy</td>
<td>Social difficulties</td>
<td>Frailty</td>
</tr>
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</tr>
<tr>
<td>41.8% MNA</td>
<td>12.3% MMSE</td>
<td>27.9% GDS-4</td>
<td>% NR (CIRS-G)</td>
<td>% NR (number of drugs/day)</td>
<td>36.1% living alone</td>
<td>NR</td>
</tr>
<tr>
<td>46.9% risk of MNA</td>
<td>22.4% MMSE</td>
<td>20.4% GDS</td>
<td>69.4% ≥ 1 comorbid condition (CIRS-G)</td>
<td>NR</td>
<td>NR</td>
<td>75% vulnerable</td>
</tr>
<tr>
<td>25.4% with 25% food intake reduction in last week</td>
<td>% NR (QLQC30)</td>
<td>% NR (QLQC30)</td>
<td>55.4% ≥ 3 comorbidities</td>
<td>28.4% ≥ 3 drugs/day</td>
<td>8.7% living alone</td>
<td>NR</td>
</tr>
<tr>
<td>63.7% MNA-SF</td>
<td>10.6% MMSE</td>
<td>20.6% GDS-15</td>
<td>29.1% CCI ≥ 2</td>
<td>% NR</td>
<td>30.2% living alone</td>
<td>NR</td>
</tr>
<tr>
<td>63.7% MNA-SF</td>
<td>10.6% MMSE</td>
<td>20.6% GDS-15</td>
<td>29.1% CCI ≥ 2</td>
<td>53.1% ≥ 5 drugs/day</td>
<td>30.2% living alone</td>
<td>73.5% geriatric risk</td>
</tr>
<tr>
<td>27.3% MNA</td>
<td>13.3% IQCODE 7.7% MMSE</td>
<td>NR</td>
<td>49% ≥ 2 comorbid organ systems CCI</td>
<td>50% ≥ 4 drugs/day</td>
<td>NR</td>
<td>24% GFI</td>
</tr>
<tr>
<td>10.7% BMI &lt;19 kg/m²</td>
<td>17.1% MMSE</td>
<td>44.5% GDS-15</td>
<td>39.1% grade 3 or 4 comorbidities by CIRS-G</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>70% weight loss</td>
<td>42.2% MMSE</td>
<td>46.7% GDS-4</td>
<td>58.6% ≥ 2 comorbidities CCI</td>
<td>NR</td>
<td>24.3% social worker</td>
<td>37% fit</td>
</tr>
<tr>
<td>21% BMI &lt;21 kg/m²</td>
<td>29% MMSE</td>
<td>36% GDS-15</td>
<td>24% ≥ 3 comorbidities</td>
<td>68% ≥ 4 drugs/day</td>
<td>17% home care</td>
<td>NR</td>
</tr>
<tr>
<td>61% albumin &lt;35 g/L</td>
<td>13.2% MMSE</td>
<td>37% HADS</td>
<td>33.8% ≥ 2 comorbidities CCI</td>
<td>% NR (number of drugs/day)</td>
<td>35.2% living alone</td>
<td>70.7% geriatric profile by G8</td>
</tr>
<tr>
<td>53% MNA</td>
<td>9% MMSE</td>
<td>24% GDS-30</td>
<td>35% ≥ 1 grade 3 or 4 comorbidities by CIRS-G</td>
<td>NR</td>
<td>20% MOS-SSS</td>
<td>47% vulnerable</td>
</tr>
<tr>
<td>34.9% MNA</td>
<td>19.0% MMSE</td>
<td>44.0% GDS-15</td>
<td>38.2% ≥ 1 grade 3 or 4 comorbidities by CIRS-G</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>64% MNA</td>
<td>17% MMSE</td>
<td>45% GDS-15</td>
<td>39% ≥ 1 grade 3 or 4 comorbidity by CIRS-G</td>
<td>NR</td>
<td>NR</td>
<td>82% impaired G8 score</td>
</tr>
</tbody>
</table>

(continued)
### Table 1 (Continued)

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Sample size</th>
<th>Cancer type and metastatic status</th>
<th>Age, mean ± SD or median (range)</th>
<th>Dependency</th>
<th>Mobility impairment – fall risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biesma et al28</td>
<td>P</td>
<td>181</td>
<td>Lung 100%, Stages III–IV, M+ 68% GI 58.7%, including 58.6% CRC, breast 16.3%, prostate and urinary tract 18.4%, lung 1.6%, others 5.1%, M+ 54.6%</td>
<td>74 (70–81)</td>
<td>23.0% ADL</td>
<td>14% TGUG</td>
</tr>
<tr>
<td>Caillet et al29</td>
<td>P</td>
<td>375</td>
<td>CRC 33%, GI non-CRC 17%, breast 19%, lung 9%, gynecologic 7%, other 15% Advanced or M+ 53%</td>
<td>82.4 (73–97)</td>
<td>32% ADL</td>
<td>20% TGUG</td>
</tr>
<tr>
<td>Chaïbi et al30</td>
<td>P</td>
<td>161</td>
<td>Breast 11%, lung 29%, prostate, GI 27%, gynecologic 17%, urinary tract 10%, others 6%, M+ 61%</td>
<td>73±6.2 (65–91)</td>
<td>21% KPS 60%</td>
<td>80% 1 fall in last 6 months</td>
</tr>
<tr>
<td>Hurria et al3</td>
<td>P</td>
<td>500</td>
<td>Lung 100%, NHL 9%, breast 41%, NHL 9%, gynecologic or genitourinary tract 17%, GI 19%, other 14%, M+ 36%</td>
<td>74.9 (65–96)</td>
<td>38.1% ADL</td>
<td>47.9% mobility limitation</td>
</tr>
<tr>
<td>Hamaker et al31</td>
<td>P</td>
<td>292</td>
<td>CRC 14%, GI non-CRC 34.2%, hematologic malignancies 17.8%, breast 6.2%, lung 6.2%, prostate 5.5%, bladder 4.8%, other 11.3%, M+ 43.2%</td>
<td>76.7±4.9 (70–92)</td>
<td>45% ADL</td>
<td>22% ≥1 falls in past 6 months</td>
</tr>
<tr>
<td>Owusu et al32</td>
<td>CS</td>
<td>117</td>
<td>Breast 59%, other 41%, 41% stages II–IV</td>
<td>73 (69–80)</td>
<td>19% ADL</td>
<td>23% fall risk (≥2 falls in past 6 months, TGUG)</td>
</tr>
<tr>
<td>To et al33</td>
<td>CS</td>
<td>200</td>
<td>GI 32%, lung 24%, genitourinary 13%, breast 13%, other 18%, M+ 63%</td>
<td>76.7±4.9 (70–92)</td>
<td>45% ADL</td>
<td>22% ≥1 falls in past 6 months</td>
</tr>
<tr>
<td>Luciani et al34</td>
<td>CS</td>
<td>419</td>
<td>Lung 32%, CRC 29%, breast 8.4%, HNC 2.7%</td>
<td>76±5 (70–97)</td>
<td>30% ADL</td>
<td>36% mobility problems by VES-13</td>
</tr>
<tr>
<td>Kristjansson et al35</td>
<td>P</td>
<td>178</td>
<td>CRC (colon 71%, rectum 29%) M+ 12%</td>
<td>76±5.7 (70–94)</td>
<td>15.7% Barthel Index</td>
<td>NR</td>
</tr>
<tr>
<td>Kellen et al36</td>
<td>CS</td>
<td>113</td>
<td>Prostate 32%, lung 11%, breast 15%, colon 15%, other 27%</td>
<td>77±4</td>
<td>61% ADL</td>
<td>NR</td>
</tr>
<tr>
<td>Hurria et al37</td>
<td>CS</td>
<td>245</td>
<td>Breast 41%, NHL 9%, gynecologic or genitourinary tract 17%, GI 19%, other 14%, M+ 36%</td>
<td>76±7 (65–95)</td>
<td>45.8% IADL</td>
<td>20.1% ≥1 fall in past 6 months</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Cognitive impairment</td>
<td>Depression</td>
<td>Comorbidities</td>
<td>Polypharmacy</td>
<td>Social difficulties</td>
<td>Frailty</td>
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<tr>
<td>NR</td>
<td>7.5% MMSE</td>
<td>27.5% GDS</td>
<td>% NR (CIRS-G, CCI)</td>
<td>NR</td>
<td>% NR (GFI)</td>
<td>% NR (number of altered CGA parameters)</td>
</tr>
<tr>
<td>57.5%</td>
<td>27.1% MMSE</td>
<td>28.3% GDS-4</td>
<td>% NR (CIRS-G)</td>
<td>66.9% ≥5 drugs/day</td>
<td>17.6% inappropriate social environment</td>
<td>40.1% living alone</td>
</tr>
<tr>
<td>65% MNA</td>
<td>26% MMSE</td>
<td>34% GDS-15</td>
<td>46.5% ≥1 grade 3 or 4 comorbidity by CIRS-G</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>12% BMI</td>
<td>Blessed Orientation Memory Concentration test</td>
<td>% NR (HADS)</td>
<td>90% ≥1 comorbid condition</td>
<td>NR</td>
<td>21% living alone</td>
<td>NR</td>
</tr>
<tr>
<td>38% unintentional weight loss &gt;5% in last 6 months</td>
<td>% NR (albumin)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46.0% SNAQ and/or BMI</td>
<td>15.1% IQCODE-SF 65.3% GDS-2</td>
<td>21.5% CAM</td>
<td>% NR (CCI)</td>
<td>48.0% ≥5 drugs/day</td>
<td>5.0% not living independently</td>
<td>91.1% ≥1 geriatric condition</td>
</tr>
<tr>
<td>NR</td>
<td>6% MMSE</td>
<td>12% GDS-15</td>
<td>36% CCI ≥2</td>
<td>9% ≥10 drugs/day</td>
<td>42% living alone</td>
<td>43% ≥2 geriatric abnormalities</td>
</tr>
<tr>
<td>34% &gt;5% weight loss</td>
<td>22% self-reported memory problems</td>
<td>17.5% psychologic distress</td>
<td>19% ≥4 comorbidities</td>
<td>38% &gt;5 drugs/day</td>
<td>30% living alone</td>
<td>28% fit</td>
</tr>
<tr>
<td>% NR (MNA-SF)</td>
<td>% NR (MMSE)</td>
<td>NR</td>
<td>81% ≥3 comorbidity condition (CIRS-G)</td>
<td>57% ≥3 drugs/day</td>
<td>39% support service</td>
<td>60% vulnerable</td>
</tr>
<tr>
<td>9.0% MNA</td>
<td>6.7% MMSE</td>
<td>10.1% GDS-30</td>
<td>23.0% severe comorbidities by CIRS-G</td>
<td>6.2% ≥8 drugs/day</td>
<td>26% help from relatives or friends</td>
<td>42.7% frail</td>
</tr>
<tr>
<td>NR</td>
<td>14% MMSE</td>
<td>30% GDS</td>
<td>76% ≥1 comorbidity</td>
<td>NR</td>
<td>34% living alone</td>
<td>28% CGA impairment</td>
</tr>
<tr>
<td>32.2% weight loss in past 6 months % NS (BMI)</td>
<td>NR</td>
<td>% NR (MOS emotional)</td>
<td>50.0% ≥3 comorbidities</td>
<td>% NR (number of drugs/day)</td>
<td>32.7% living alone</td>
<td>68% ≥5 altered CGA domains</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td>15.0% support service</td>
<td>31% vulnerable by GFI</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>49% vulnerable by YES-13</td>
</tr>
<tr>
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<td>NR</td>
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</tbody>
</table>

(continued)
Table 1 (Continued)

<table>
<thead>
<tr>
<th>References</th>
<th>Study design</th>
<th>Sample size</th>
<th>Cancer type and metastatic status</th>
<th>Age, mean ± SD or median (range)</th>
<th>Dependency</th>
<th>Mobility impairment – fall risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mohile et al&lt;sup&gt;38&lt;/sup&gt;</td>
<td>CS</td>
<td>2,349</td>
<td>Lung 5.1%, colon 14.0%, breast 25.6%, uterus 11.6%, prostate 22.3%, bladder 5.2%, ovarian 3.6%, other 25.7% (some patients with more than one cancer)</td>
<td>76.2</td>
<td>Self-reported</td>
<td>25.9% with self-reported falls</td>
</tr>
<tr>
<td>Girre et al&lt;sup&gt;39&lt;/sup&gt;</td>
<td>CS</td>
<td>105</td>
<td>Breast 60.9%; lung 5.7%; CRC 6.7%; gynecologic 7.5%, prostate 1.9%, hematologic malignancies 1.9%, others 15.1%</td>
<td>79 (70–97)</td>
<td>42% ADL</td>
<td>19.8% ≥2 falls in past year</td>
</tr>
<tr>
<td>Marenco et al&lt;sup&gt;40&lt;/sup&gt;</td>
<td>P</td>
<td>571</td>
<td>CRC 29.9%, GI non-CCR 16.3%, kidney and bladder 14.2%, lung 10%, breast 6%, prostate 10%, others 13.6%</td>
<td>78.0±4.8</td>
<td>28.2% ADL</td>
<td>% NS (IADL, KPS)</td>
</tr>
<tr>
<td>Wedding et al&lt;sup&gt;41&lt;/sup&gt;</td>
<td>CS</td>
<td>200</td>
<td>% NR (hematologic malignancies, GI, lung, breast, ovary, prostate, bladder, pancreas, liver, skin, larynx)</td>
<td>75.9 (70–94)</td>
<td>50% ADL</td>
<td>23% fall risk (Tinetti)</td>
</tr>
<tr>
<td>Hurria et al&lt;sup&gt;42&lt;/sup&gt;</td>
<td>CS</td>
<td>250</td>
<td>Breast 41%, NHL 9%, gynecologic or genitourinary 17%, GI 19%, others 15%</td>
<td>76±7 (65–95)</td>
<td>49% IADL</td>
<td>21% with history of falls</td>
</tr>
</tbody>
</table>

Note: This table lists only prospective studies with 100 or more patients and assessment of at least four CGA domains. The CGA was performed within 30 days of diagnosis or initiation of treatment in 91% of cases. The treatment plan was modified after CGA in 38.7% of cases. By univariate analysis, body mass index ≤23 and absence of depression were associated with treatment changes. In another prospective study of 161 patients with solid malignancies, the CGA influenced cancer treatment decisions in 49% of cases. Chemotherapy intensity was diminished in 21% of patients (by using less intensive regimens in 18% and by delaying treatment initiation in 3%) and augmented in 28% of patients.

Only two prospective studies involved multivariate analyses to identify CGA parameters associated with treatment decisions. In 571 older patients with solid malignancies, factors independently associated with receiving supportive care only were older age, living alone, ADL impairment, and low body mass index, whereas a higher instrumental ADL score was associated with receiving active cancer treatment. The other study<sup>29</sup> included 375 older patients with solid malignancies, of whom 20.8% had CGA-based changes in their treatment plan, which consisted of decreased treatment intensity in 81% of cases. By multivariate analysis, factors independently associated with treatment changes were a lower ADL score and malnutrition.

**References**: This table lists only prospective studies with 100 or more patients and assessment of at least four CGA domains. The CGA was performed within 30 days of diagnosis or initiation of treatment in 91% of cases. The treatment plan was modified after CGA in 38.7% of cases. By univariate analysis, body mass index ≤23 and absence of depression were associated with treatment changes. In another prospective study of 161 patients with solid malignancies, the CGA influenced cancer treatment decisions in 49% of cases. Chemotherapy intensity was diminished in 21% of patients (by using less intensive regimens in 18% and by delaying treatment initiation in 3%) and augmented in 28% of patients.

Two studies used univariate analyses to investigate associations between CGA parameters and treatment decisions. In a prospective study of 105 older cancer patients (98.1% with solid malignancies), the treatment plan was modified after CGA in 38.7% of cases. By univariate analysis, body mass index ≤23 and absence of depression were associated with treatment changes. In another prospective study of 161 patients with solid malignancies, the CGA influenced cancer treatment decisions in 49% of cases. Chemotherapy intensity was diminished in 21% of patients (by using less intensive regimens in 18% and by delaying treatment initiation in 3%) and augmented in 28% of patients.
These five studies suggest that some CGA parameters may influence treatment decisions. Function and nutritional status may have the strongest effect.

CGA components predicting cancer-treatment outcomes, functional decline, morbidity, and mortality in older patients with solid malignancies

Determining the optimal therapeutic strategy is a major challenge in older cancer patients. An important goal of the CGA is prediction of mortality and cancer treatment toxicities. Table 2 shows the findings from 17 studies reporting associations that link CGA components to cancer treatment outcomes, functional decline, and mortality in elderly patients with solid malignancies. Four studies investigated relationships between CGA components and chemotoxicity. Dependency as indicated by impaired instrumental ADL or ECOG-PS values, mobility impairment, cognitive dysfunction, malnutrition, social difficulties, and polypharmacy were significantly associated with chemotoxicity. Nine studies assessed the ability of CGA components to predict mortality. Dependency assessed by instrumental ADL and/or ECOG-PS, mobility impairment, cognitive dysfunction, depressive mood, malnutrition, and
Table 2 | Effectiveness of CGA components in predicting cancer treatment outcomes, functional decline, morbidity, and mortality in older patients with solid malignancies

<table>
<thead>
<tr>
<th>CGA components</th>
<th>Treatment outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Postoperative complications</td>
</tr>
<tr>
<td>Dependency</td>
<td>Audisio et al(^\text{13}): (460 patients, mixed tumor sites), IADL and ECOG-PS were associated with 1-month postsurgical complications</td>
</tr>
<tr>
<td></td>
<td>Laurent et al(^\text{1d}): (385 patients, mixed solid malignancies), better ADL (or ECOG-PS) associated with greater likelihood of chemotherapy completion</td>
</tr>
<tr>
<td></td>
<td>Makary et al(^\text{e}): (594 patients, 60% operated for solid tumor), frailty assessed by Fried criteria-associated postoperative complications</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Extermann et al(^\text{a}): altered MNA score associated with nonhematologic toxicity Falandry et al(^\text{1d}): (111 patients, ovarian cancer), geriatric vulnerability score (GVS) including albuminemia associated with severe chemotoxicity</td>
</tr>
<tr>
<td>Depression</td>
<td>Kanesvaran et al(^\text{1f}): (249 patients, mixed cancer sites), GDS associated with overall survival Giantin et al(^\text{g}): (160 patients, mixed cancer sites), GDS associated with 6-month and 12-month survival</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>Extermann et al: decreased MMSE score associated with nonhematologic toxicity</td>
</tr>
<tr>
<td>---------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Comorbidities/ polypharmacy/ number of CGA components</td>
<td>Giantin et al**: (160 patients, mixed cancer sites), MMSE associated with 6-month and 12-month survival</td>
</tr>
</tbody>
</table>

Social difficulties | Huria et al**: decreased social activities associated with chemotoxicity |

Note: This table lists only prospective studies with 100 or more patients and a multivariate analysis.

**Abbreviations:** CGA, Comprehensive Geriatric Assessment; GVS, geriatric vulnerability score; NSCLC, non-small cell lung carcinoma; ADL, activities of daily living; IADL, instrumental activities of daily living; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; MMSE, Mini-Mental State Examination; QLQC30, Quality of Life Questionnaire; TGUG, Timed Get-Up-and-Go test; BMI, body mass index; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics.
comorbidities was associated with mortality independently from cancer parameters. Finally, each CGA domain was associated with chemotoxicity and survival in at least one study. The domains most often reported as predicting mortality and chemotoxicity were functional impairment, malnutrition, and comorbidities.

**CGA-based individually tailored coordinated care plans**

An important aim in conducting a CGA is to develop and implement individually tailored geriatric interventions. Few studies have described the interventions carried out based on CGA results in older patients with cancer. In one study, a geriatrician performed a CGA, then suggested multidisciplinary interventions based on the results in 375 patients, the results of CGA of 1,967 patients, the results of CGA led to intervention plans targeting all CGA domains in 25% of patients.

Very few randomized trials have assessed the potential effect on patient outcomes of CGA-based management and follow-up of health problems in older cancer patients (Figure 3). Two randomized trials in older post-surgical cancer patients showed significant survival gains with home care by advanced practice nurses or improved appropriateness of treatment strategies with nurse case management. A secondary subset analysis of data from a randomized 2×2 factorial trial comparing care in a geriatric inpatient unit, geriatric outpatient clinic, both, and neither in frail older cancer inpatients showed that inpatient geriatric assessment and management significantly improved quality of life but not 1-year survival. In a recent randomized trial in older patients undergoing elective surgery for solid cancer, an individualized geriatric intervention plan based on patient-related risk factors for delirium failed to decrease the occurrence of postoperative delirium, other complications, or death. We urgently need randomized controlled trials of patient outcomes after CGA-based geriatric interventions. The available data suggest that these trials will demonstrate significant improvements, thus helping to convince health authorities that geriatric oncology teams must receive strong support. Seven such trials are ongoing and are registered on clinicaltrials.gov (Table 3).

**Conclusion**

All CGA types detect numerous unrecognized health problems that may interfere with cancer treatment and/or compete with cancer as a cause of death. CGA results affected...
treatment decisions in 21%–49% of patients in available studies. The results of 17 studies with large sample sizes and multivariate analyses indicate independent associations linking functional impairment, malnutrition, depressive symptoms, and comorbidities to chemotherapy toxicity and/or overall survival. Only three randomized trials of the effectiveness of CGA-based interventions have been published. Further research to produce high-level evidence about the effects of CGA on patient outcomes are needed.

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Disclosure
The authors report no conflicts of interest in this work.

References


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