An update on a systematic review of the use of geriatric assessment for older adults in oncology

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Background: Our previous systematic review of geriatric assessment (GA) in oncology included a literature search up to November 2010. However, the quickly evolving field warranted an update. Aims of this review: (i) provide an overview of all GA instruments developed and/or in use in the oncology setting; (ii) evaluate effectiveness of GA in predicting/modifying outcomes (e.g., treatment decision impact, treatment toxicity, mortality, use of care).

Materials and methods: Systematic review of literature published between November 2010 and 10 August 2012. English, Dutch, French and German-language articles reporting cross-sectional or longitudinal, intervention or observational studies of GA instruments were included. Data sources: MEDLINE, EMBASE, PsycINFO, CINAHL and Cochrane Library. Two researchers independently reviewed abstracts, abstracted data and assessed the quality using standardized forms. A meta-analysis method of combining proportions was used for the outcome impact of GA on treatment modification with studies included in this update combined with those included in our previous systematic review on the use of GA.

Results: Thirty-five manuscripts reporting 34 studies were identified. Quality of most studies was moderate to good. Eighteen studies were prospective, 11 cross-sectional and 5 retrospective. Three studies examined treatment decision-making impact and found decisions changed for fewer than half of assessed patients (weighted percent modification is 23.2% with 95% confidence interval (20.3% to 26.1%). Seven studies reported conflicting findings regarding predictive ability of GA for treatment toxicity/complications. Eleven studies examined GA predictions of mortality, and reported that instrumental activities of daily living, poor performance status and more numerous GA deficits were associated with increased mortality risk. Other outcomes could not be meta-analyzed.

Conclusion: Consistent with our previous review, several domains of GA are associated with adverse outcomes. However, further research examining effectiveness of GA on treatment decisions and oncologic outcomes is needed.

Key words: systematic review, cancer treatment, comprehensive geriatric assessment, frail elderly, geriatric oncology, newly diagnosed cancer

Introduction

Cancer is a disease that predominantly affects older adults [1]. In addition to cancer, older adults often have other medical conditions. Cancer treatment decisions can be complicated by the presence of this multimorbidity, since it can complicate life expectancy estimation, affect treatment tolerability and modify treatment efficacy [2–4]. In order to help cancer specialists determine the best treatment of their older patients, the US National Comprehensive Cancer Network (NCCN), the International Society of Geriatric Oncology (SIOG), the European Society of Breast Cancer Specialists (EUSOMA) and the European Organisation for Research and Treatment of Cancer (EORTC) have recommended that some form of geriatric assessment (GA) should be conducted for all older patients for whom chemotherapy is considered [5–9]. Despite these recommendations, there is no solid evidence regarding either the best type of GA for use in the oncology setting or how outcomes are improved as a result of GA [10].

We previously published a systematic review on the use of GA in the oncology setting [10]. In that review, we reported that although there were many studies reporting on the use of GA and it was feasible to conduct in various settings, most studies only used a GA to describe their study population. Few studies examined the psychometric properties of GA tools, the impact on treatment decision-making or the predictive validity of GA for...
outcomes such as mortality, complications of treatment or use of care [10].

The field of geriatric oncology is evolving rapidly, so we have updated our systematic review to reflect the most recent available evidence for clinicians and other researchers interested in GA. We focused on two of the three previous reviews’ objectives: (i) to provide an overview of all GA instruments developed and/or in use in the oncology setting for older adults with cancer and (ii) systematically evaluate their impact on the treatment decision-making process and their effectiveness in predicting outcomes from cancer and its treatment. The objective describing the feasibility and psychometric properties of GA is not included as our previous review showed that GA is feasible and another recent review reported in detail on the psychometric properties of screening [11]. We also attempted to provide a quantitative estimate of the effects of GA on various outcomes as this has not been done previously.

carrier of the initial article selection (MP and BS). The abstracted information included study design, aim of study, location of study, sampling method, source of data, recruitment, characteristics of study participants, results of the study, outcomes of the assessment and details of statistical analysis. If any aspect of the study design and conduct was unclear, the authors of the study were contacted. We contacted authors of all studies except one for which no additional info was required [18]: all but six authors responded and provided additional details, which were included in our data abstraction.

quality assessment

The Reporting of Observational Studies in Epidemiology (STROBE) and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [19, 20] were used for assessing the quality of included studies. Quality assessment was carried out independently by two reviewers (MP and BS) and disagreements were resolved through consensus. To provide a comprehensive overview of all studies examining GA in the oncology setting for older adults with cancer, no study was excluded based on the quality assessment.

meta-analysis

We combined the studies included in this update with those included in our previous review [10] to examine if a meta-analysis examining the impact of GA on the number of cancer treatment modifications, treatment toxicity and overall survival. For

<table>
<thead>
<tr>
<th>Potentially relevant citations identified and screened for retrieval (n = 540): Bibliographic databases (n = 538) Suggested by research team (n = 2)</th>
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<tbody>
<tr>
<td>Citations excluded based on abstract and title review (n = 494). Reasons:</td>
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<tr>
<td>No geriatric assessment (n = 134)</td>
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<tr>
<td>Editorial/Review (n = 133)</td>
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<tr>
<td>No cancer (n = 12)</td>
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<tr>
<td>Study design only (n = 3)</td>
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<tr>
<td>Included in previous systematic review (n = 1)</td>
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<tr>
<td>Citations included based on abstract and title review (n = 46)</td>
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<td>Excluded abstract only (n = 1)</td>
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<tr>
<td>Studies excluded (n = 10). Reasons: Editorial/Review (n = 2) No geriatric assessment (n = 8)</td>
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<tr>
<td>Relevant citations for inclusion (n = 35, describing 34 studies)</td>
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</tbody>
</table>

Figure 1. Flow chart of study selection.
our outcome number of treatment modifications, as all studies published percentages/number of changes univariately, the weighted percentage of cancer treatment modifications and the 95% confidence interval (CI) was calculated using a binomial distribution (yes modification/no modification) and based on a method of combining proportions (using inverse of variance as weight) in a meta-analysis, by an experienced statistician (EA).

For our outcome treatment toxicity and overall survival, we examined if there were a minimum of three studies that had examined similar GA domains using the same tool or a different tool but similar domains that were dichotomously scored and could be compared across studies (e.g. yes/no depressed based on a score above an established cutoff point for the tool used). In addition, to be able to estimate an pooled risk estimate, the risk estimate from each of the individual studies had to come from a multivariable analysis adjusted for relevant confounders. Our research team considered relevant confounders to be age, cancer stage and performance status as the study samples varied in age range from 65 to 99 years and stage I to stage IV cancers. A meta-analysis was not possible for our outcomes treatment in age range from 65 to 99 years and stage I to stage IV cancers.

results

Thirty-five manuscripts reporting on 34 studies were included. Of the 34 manuscripts included, all except one were written in English (one was written in French [21]). The percentage refers to the proportion of the total of 34 studies in the sections below.

quality assessment

The quality of most studies was moderate to good (see supplementary Table S1, available at Annals of Oncology online). Most studies (n = 23, 68%) did not report response rates [12, 14–17, 22–36] or the reasons for refusal [12, 14–18, 21–29, 32, 34, 36–39], and therefore, the extent of selection bias could not be assessed. All studies except one (3%) [36] described the study design and all studies except three (9%) [21, 23, 36] reported the setting in which the study was conducted. Of the prospective studies (n = 14, 42%) [13, 14, 16, 17, 21–26, 33, 34, 37, 40–42], the follow-up methods were not described in four studies (12%) [13, 14, 17, 26]. In more than half of the studies (n = 19, 56%), the extent of missing data and/or how study authors dealt with missing data were not described [12, 14–16, 21, 22, 24, 26–30, 32, 33, 36, 39, 40, 42–45]. The statistical analyses were not well detailed in three studies (9%) [23, 46, 47].

characteristics of included studies

Characteristics of the selected studies are reported in supplementary Table S2, available at Annals of Oncology online. GA was examined in longitudinal observational studies (n = 14, 41%) [13, 14, 16, 17, 21, 22, 25, 26, 31, 33, 34, 37, 40, 42], cross-sectional observational studies (n = 7, 20%) [12, 15, 18, 29, 36, 39, 43, 48], retrospective studies (n = 5, 15%) [38, 44–47] and other study designs (n = 8, 23%) (all examining new therapeutic regimens) [23, 24, 27, 28, 30, 32, 35, 41]. No randomized, controlled trials (RCTs) were identified that examined the effectiveness of GA.

In 85% of studies (n = 29), participant assessments were conducted through primary data collection using interview or questionnaire with or without data abstraction from the patients’ medical charts [12–18, 21–43, 45, 48]. Almost all studies recruited participants through convenience (n = 12, 35%) [13, 16, 23, 24, 26–29, 32, 37, 41, 42] or consecutive (n = 13, 38%) [12, 14, 15, 18, 22, 25, 34–36, 38–40, 43, 48] sampling techniques, while 12% (n = 4) were chart reviews [33, 44–46], and 15% (n = 5) failed to specify the sampling methods [17, 21, 30, 31, 33]. Of the reviewed studies, 18% (n = 6) failed to report clear and explicit inclusion criteria [21, 23, 25, 36, 38, 40]. Sample sizes ranged from 31 [23] to 660 [37] participants and response rates ranged from 57.8% [37] to 99.5% [41].

objective 1: to provide an overview of all GA instruments developed and/or in use in the oncology setting for older adults with cancer

Where was GA assessment conducted and what was included in the GA?

All the assessments were completed in the hospital setting. Most studies (n = 22, 65%) did not specify the exact location where the assessments took place [12, 13, 16, 17, 21–24, 26–32, 34, 35, 37, 39, 41, 45–48]. Where reported, assessments took place in outpatient oncology (n = 2, 6%) [14, 15, 42], on inpatient wards (n = 3, 9%) [25, 36, 43] or in geriatric oncology clinics (n = 5, 15%) [18, 33, 38, 40, 44]. Most assessments took place before the start of cancer treatment (n = 21, 62%) [12–17, 21, 22, 26, 29–35, 39–42, 44, 45, 48], some were conducted during treatment (n = 3, 9%) [24, 30, 33] and some after (partial) treatment completion (n = 2, 6%) [30, 37]. In two studies (6%), the assessment took place before treatment of most patients although a proportion had already received treatment [18, 39]. In one study (3%), the GA took place at day 1 of cycle 1 of the chemotherapy [24]. For more description of the GAs conducted, please see the additional description in the supplementary File S5, available at Annals of Oncology online.

Supplementary Table S3, available at Annals of Oncology online, provides an overview of all the domains of the GA included in each study. The most commonly assessed domains included Basic Activities of Daily Living (ADL)(n = 30, 88%) [12, 14–18, 21–25, 27–36, 38–41, 43–47], Instrumental Activities of Daily Living (IADL) (n = 28, 82%) [12–18, 21–33, 35, 36, 38, 39, 41, 43, 44, 46–48], comorbidities (n = 34, 100%), depression/mood (n = 25, 74%) [13–18, 21, 24–27, 29–34, 36, 40, 41, 43, 44, 46, 48] and cognitive functioning (n = 26, 76%) [12–18, 21, 22, 24–27, 29–32, 36, 38–41, 43–48].

objective 2: to evaluate the effectiveness of the GAs in predicting outcomes from cancer and its treatment

One or more outcomes of interest were examined in 50% of studies (n = 17) [13, 14, 16–18, 21–23, 25, 26, 30, 32, 34, 37, 38, 40–42]. Two outcomes of interest, the use of GA (followed by interventions) to avoid complications of treatment and the impact of GA on Health and Functional status, were not evaluated in the included studies. The results for each outcome of interest are described below.
GA and treatment decision. Three studies (9%) examined the impact of GA on the cancer treatment decisions [18, 21, 40]. Horgan et al. [18] enrolled 30 patients with lung or gastrointestinal cancer. Most of these patients had locally advanced or metastatic disease and six patients had not yet received their oncological treatment plan. For five of those six patients (83%), the GA results informed final treatment decisions. For the 24 patients for whom the oncologic treatment decision was made at the time of referral, the GA affected only the treatment decision for 1 patient (4%).

Caillet et al. [40], in a prospective study of 375 patients with mixed cancer types and stages, reported that initial treatment plans developed by the oncologist changed for 78 patients (20%) as a result of the CGA conducted by a geriatrician; 8 participants received intensification of their proposed treatment, 63 received a reduction in treatment intensity and the start of treatment was delayed for 7 participants. The final treatment decision was made by the multidisciplinary oncology team.

Aliamus et al. [21] examined the relationship between multimodal GA and treatment decisions in 49 older adults with lung cancer (stage not reported). For 22 patients (45%), the initial decisions of the tumor board were changed based on the GA. Scores below 26 of 30 on the MMSE and IADL disability were associated with changes in treatment plans.

Meta-analysis results. The studies above were combined with three of the four studies included in our previous review [10, 49–51] (see supplementary Table S4, available at Annals of Oncology online). The study by Barthelemy et al. [52] was excluded from the meta-analysis as it was a retrospective chart review. The estimated weighted percent modification with GA across the six included studies was 23.2% (95% CI 20.3% to 26.1%).

GA and complications/toxicity of treatment. Seven studies (26%) examined the relationship between GA and complications/toxicity of treatment [13, 16, 26, 32, 34, 41, 42] (Table 1). With the exception of the studies by Kristjansson et al. [16] and Courtney-Brooks et al. [42] who examined postoperative surgical complications, all other studies focused on complications/toxicity related to chemotherapy.

Biesma et al. [41] reported that nonsmall-cell lung cancer patients with better functioning in terms of ADL, IADL or physical functioning were more likely to complete chemotherapy and those with higher depression scores or poor role or emotional functioning were more likely to experience grade 2 or higher psychiatric toxicity. In a group of participants with diffuse large B-cell lymphoma, no difference in grade 3 or higher toxicity was found between three groups (based on GA: fit, unfit and frail) [32]. Olivieri et al. [34], also separated participants with diffuse large B-cell lymphoma into three groups based on the GA (fit, with comorbidities and frail). They found that few patients developed grade 3 or higher toxicities across all groups. Courtney-Brooks et al. [42] separated the participants into three groups (nonfrail, intermediate frail and frail) and reported a similar frequency of postoperative complications in all groups.

Kristjansson et al. [16] compared frailty based on the GA and based on the definition by Fried et al. [53] in patients with colorectal cancer undergoing surgery. Frailty was observed in 43% and 13% of participants based on the CGA and Fried definitions, respectively. However, only the GA-frailty definition was associated with greater postoperative surgical complications.

Hurria et al. [26] and Extermann et al. [13] developed chemotherapy toxicity prediction scores in mixed cancer populations undergoing various chemotherapy regimens. In the study by Hurria et al., 53% of 500 patients experienced grade 3 or higher toxicity. Hurria’s final model included 11 variables: age 72 years and above, cancer type (gastrointestinal or genitourinary), standard dosing of chemo, polychemotherapy, low hemoglobin, creatinine clearance <34 ml/min, hearing impairment, one or more falls, limited in walking a block, need for assistance taking medications and decreased social activities due to physical or emotional health. The receiver-operating characteristic (ROC) curve of the model was 0.72. In the study by Extermann et al. [13], of 518 participants, 64% experienced severe toxicity, 32% had grade 4 hematologic toxicity and 56% had grade 3 or higher nonhematologic toxicity. Only hemoglobin and creatinine clearance were correlated with severe toxicity as individual variables. The best predictive model for hematological toxicity included the variables diastolic blood pressure, lactate dehydrogenase (LDH), IADL and a ‘chemotox’ score from a previously validated model [54, 55], with a C-statistic of 0.76. The best predictive model for nonhematological toxicity, yielding a C-statistic of 0.66, included the variables Eastern Collaborative Oncology Group Performance Status (ECOG-PS), Mini Mental Status Examination (MMSE), Mini Nutritional Assessment (MNA) and chemotox. The combination of both models yielded a C-statistic of 0.65.

GA and prediction of mortality. Eleven studies examined the ability of GA to predict mortality [14, 16, 17, 23, 25, 30, 32, 34, 37, 38, 41] with sample sizes ranging from 37 to 660 (Table 2). Of the studies that conducted multivariable analysis, Clough-Gorr et al. [37] reported that having three or more deficits on the GA predicted all-cause and breast cancer specific mortality at 5 and 10 years after the assessment. Kanesvaran et al. [38] reported that age, serum albumin, ECOG-PS, GDS and stage were associated with overall survival in a mixed cancer population. Winkelmann et al. [17] showed that IADL was associated with survival in patients with lymphoma. Spina et al. [32] showed that frail and unfrail persons had a higher risk of death compared with fit persons in patients with diffuse large B-cell lymphoma. Hamaker et al. [25] concluded that none of the GA variables in inpatients with cancer were associated with mortality. Kristjansson et al. [16] reported that frailty based on a GA as well as based on the Fried definition predicted overall survival in patients with early and advanced colorectal cancer.

GA and use of care and other outcomes studied. Robinson et al. [45] examined the cost of care up to 6 months for patients who had received colorectal surgery. Forty percent of patients were nonfrail, 22% prefrail and 38% frail. Preoperative comorbidities and intraoperative variables were the same across the different frailty groups. However, need for discharge to a care facility and 30-day readmission rates increased with increased frailty. Increasing frailty was also associated with higher surgical
<table>
<thead>
<tr>
<th>First author, year (reference)</th>
<th>Type of statistical analysis used</th>
<th>Was multivariable analysis conducted and were adjustments appropriate?</th>
<th>Sample size, number of events (treatment studied)</th>
<th>Complications of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biesma, 2011 [41] Logistic regression</td>
<td>Yes, adjusted for age, gender and extent of disease</td>
<td>181, unclear, (chemotherapy)</td>
<td>Patients with better ADL, IADL or physical functioning were more likely to finish all chemotherapy cycles. Patients with worse emotional functioning, role functioning or GDS scores were more likely to experience grade ≥2 psychiatric toxicity. However, none of the variables were associated with ≥3 toxicity and the occurrence of serious adverse events.</td>
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<tr>
<td>Courtney-Brooks, 2012 [42] Analysis of variance</td>
<td>No multivariable analysis was conducted</td>
<td>37, 10 (surgery for gynecologic cancer)</td>
<td>Of the nonfrail patients, 5 of 24 had 30-day postoperative complications, 1 of 10 of the intermediate and 4 of 6 frail patients (P = 0.04).</td>
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<td>Extermann, 2012 Logistic regression</td>
<td>Yes, variables were selected using a forward selection approach of predictors being selected when P &lt; 0.10</td>
<td>518, 320 (chemotherapy)</td>
<td>The best performing model for hematological toxicity included the variables chemotox, LDH, IADL and diastolic blood pressure. C-statistic 0.75. The best model for nonhematological toxicity included chemotox, MMSE, MNA and ECOG PS. The C-statistic was 0.64.</td>
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<tr>
<td>Hurria, 2011 [26] Logistic regression</td>
<td>Yes, variables that reached P &lt; 0.1 in univariate analyses, 500, 265 (chemotherapy) or that were deemed clinically relevant were included in a multivariable logistic model</td>
<td>The 11 variables that were retained in the predictive model included: age 72 and above, cancer type (GI and GU), standard dosing of chemo, polychemotherapy, hemoglobin, creatinine clearance &lt;34 ml/min, hearing impairment, one or more falls, limited in walking a block, need for assistance taking meds, decreased social activities due to physical or emotional health problems. The ROC was 0.72.</td>
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<tr>
<td>Kristjansson, 2012 Chi-square tests for trends</td>
<td>No multivariable analysis was conducted</td>
<td>176, 82 (colorectal cancer surgery)</td>
<td>CGA-based frailty predicted postoperative complications (P = 0.001).</td>
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<tr>
<td>Olivieri, 2012 Descriptive analysis</td>
<td>No multivariable analysis was conducted</td>
<td>91, unclear (chemotherapy)</td>
<td>In the fit group (n = 54), three patients experienced mucositis, four had infections and four hematological toxicities grade 3–4. In the group with comorbidities (n = 22), three had microsites, six had infections and three had Hand-Foot syndrome. In the frail group (n = 15), three had infections, one had cardiac, two neurologic and one liver and renal toxicity and one had hematological toxicity.</td>
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<tr>
<td>Spina, 2012 [32] Not described</td>
<td>Not described</td>
<td>81, 40 (chemotherapy)</td>
<td>Grade 4 toxicity was present in 31% of fit, 48% of unfit and 58% of frail patients (P = 0.11).</td>
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ADL, activities of daily living; CGA, Comprehensive Geriatric Assessment; ECOG PS, Eastern Collaborative Oncology Group Performance Status; GDS, geriatric depression scale; GI, gastrointestinal cancer; GU, genitourinary cancer; IADL, Instrumental Activities of Daily Living; HR, hazard ratio; KPS, Karnofsky Performance Status; LDL, lactate dehydrogenase; MNA, Mini Nutritional Assessment; MMSE, Mini Mental State Examination; ROC, receiver operating characteristic.
Table 2. Predictive validity of geriatric assessment for mortality

<table>
<thead>
<tr>
<th>First author, year (reference)</th>
<th>Type of statistical analysis used</th>
<th>Was multivariable analysis conducted and were adjustments appropriate?</th>
<th>Sample size, number of events (treatment studied)</th>
<th>Mortality</th>
</tr>
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<tbody>
<tr>
<td>Biesma, 2011 [41]</td>
<td>Survival analysis</td>
<td>Univariate analysis (Kaplan–Meier). No multivariable analysis was conducted examining the relationship between GA and mortality</td>
<td>181, 14 (chemotherapy)</td>
<td>Hazard ratios (HR) for overall survival and 95% CI: ADL HR 0.80 (0.70–0.91), IADL HR 0.82 (0.67–0.99), TUG HR 0.86 (0.78–0.94), GDS HR 0.66 (0.52–0.84), GFI HR 0.68 (0.56–0.84), physical functioning subscale EORTC QLQ C30 HR 0.62 (0.49–0.79), Role subscale HR 0.62 (0.46–0.84), emotional subscale HR 0.78 (0.62–0.98), Social subscale HR 0.78 (0.69–0.88), WHO PS 2 versus 0 HR 0.75 (0.65–0.86).</td>
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<tr>
<td>Clough-Gorr, 2012 [37]</td>
<td>Cox proportional hazards regression</td>
<td>Yes, the analysis was adjusted for age and stage (all were women)</td>
<td>660, 272 (breast cancer therapy)</td>
<td>Age, having three or more deficits, and advanced stage predicted all-cause mortality (5 and 10 years) as well as breast-cancer specific mortality (5 and 10-years). HR ≥3 deficits 5-year all-cause mortality 1.95 (1.42–2.67), HR 10-year all-cause mortality 1.76 (1.40–2.20), HR 5-year breast cancer-specific mortality 2.08 (1.27–3.39) HR 10-year breast cancer-specific mortality 2.13 (1.30–3.49)</td>
</tr>
<tr>
<td>Corsetti, 2011 [23]</td>
<td>Kaplan–Meier and Log-rank tests</td>
<td>No multivariable analysis was conducted</td>
<td>31, all patients were followed until death (chemotherapy)</td>
<td>There was no difference in survival time between frail and nonfrail patients (P = 0.52) or those who were IADL impaired versus not (P = 0.40).</td>
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<tr>
<td>Girone, 2012 [14]</td>
<td>Kaplan–Meier analysis</td>
<td>No multivariable analysis was conducted</td>
<td>83, unclear (treatment not reported)</td>
<td>ECOG PS status, IADL, dementia, depression, weight loss and albumin levels were significantly associated with survival (P &lt; 0.05). Age, comorbidity, social support and frailty were not significantly associated with survival.</td>
</tr>
<tr>
<td>Hamaker, 2012 [25]</td>
<td>Cox proportional hazards regression</td>
<td>Yes, variables that had a P-value of &lt;0.2 in univariate analysis and with &lt;20% missing data were included in the multivariable analysis. The factors age, sex and comorbidity were included in all models as potential confounders</td>
<td>292, 189 (150 patients received active cancer treatment and 137 received supportive care only, for the remaining 5 it could not be determined)</td>
<td>None of the GA variables were associated with mortality. Metastatic disease was associated with mortality HR 1.67 (1.23–2.29) and tumor-related admission HR 1.57 (1.12–2.21).</td>
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<tr>
<td>Kanesvaran, 2011 [38]</td>
<td>Cox proportional hazards regression</td>
<td>Yes, all variables were included in multivariable analysis and backward step-down approach was used to remove nonsignificant variables</td>
<td>249, 172, (treatment not reported)</td>
<td>The final model included age HR 1.04 (1.01–1.07), serum albumin normal = reference group, abnormal HR 1.97 (1.23–3.15), ECOG PS ≤ 1 = reference group, ECOG PS &gt; 1 HR 1.77 (1.15–2.72), GDS abnormal score versus normal HR 1.81 (1.29–2.56), Stage Late versus Early HR 1.71 (0.98–2.95), DETERMINE nutritional index Good = reference Group, moderate risk HR 1.23 (0.81–1.87), high-risk HR 1.84 (1.17–2.87).</td>
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<tr>
<td>Kristjansson, 2012 [16]</td>
<td>Cox proportional hazards regression</td>
<td>No, the analysis was adjusted for cancer stage and age but not gender</td>
<td>176, 46 (colorectal cancer surgery)</td>
<td>HR CGA classification frail compared with nonfrail 3.39 (1.82–6.29), HR Modified Fried Frailty Phenotype Robust = reference group, prefrail HR 2.33 (1.16–4.67), Frail HR 2.67 (1.11–6.83).</td>
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<tr>
<td>Olivieri, 2012 [34]</td>
<td>Cox proportional hazards regression</td>
<td>Variables were selected for the multivariable model if in univariate analysis, the P-value was &lt;0.1. However, in the final model, only the groups were maintained</td>
<td>98, 39 (chemotherapy)</td>
<td>The fit group is the reference group. HR Group with comorbidities 2.36 (1.20–4.64), frail group HR 2.89 (1.39–6.13).</td>
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Four deaths were unexplained by tumor progression, toxicity or comorbidity. Of those four, all had impaired ADL, all scored abnormal on the GDS, and two of four had low MMSE. FIT 5th (1.95; 1.15–3.66), HR IP 1 or 2 (1.04–3.36), HR IP 4 or 5 (1.03–15.64).

The final model included the variables age, treatment, ADL and IADL were not associated with mortality.

The GA variables ADL, IADL, performance status, depression and an increased number of deficits/frailty markers were associated with poor health outcomes such as toxicity of treatment and mortality, which is consistent with the findings of our previous review [10]. In our previous review, most studies reported that comorbidity was associated with adverse outcomes, whereas the studies in this review had mixed findings with regard to the impact of comorbidity.

New in this review are the inclusions of two large studies that examined new tools for prediction of chemotherapy toxicity that both featured large samples (≥500) and used an internal model validation approach, which no prior study had done. Hurria et al. [26] and Extermann et al. [13] included cancer characteristics, biological data and GA variables in their tools which predicted chemotherapy toxicity. The final model in the study by Hurria et al. [26] included having a hearing deficit, having one or more falls in the past 6 months as well as difficulty walking a block which were all assessed with simple 1-item questions and these variables were independently predictive of treatment toxicity while taking into account cancer treatment variables such as number of chemotherapy drugs, dosing, hemoglobin and creatinine clearance. The final model for nonhematological toxicity in the study by Extermann et al. [13] included cognition (using the MMSE) and nutrition (using the MNA) while adjusting for the toxicity of each individual regime. The final model for hematological toxicity did not include any of the GA domains. However, it is very promising that these tools showed the independent contributions of several GA domains. However, both tools require further validation in other populations.

Similar to our previous systematic review [10], there were conflicting findings with regard to the ability of GA to predict adverse outcomes. The GA variables ADL, IADL, performance status, depression and an increased number of deficits/frailty markers were associated with poor health outcomes such as toxicity of treatment and mortality, which is consistent with the findings of our previous review [10]. In our previous review, most studies reported that comorbidity was associated with adverse outcomes, whereas the studies in this review had mixed findings with regard to the impact of comorbidity.

hospital costs, increased costs after discharge and total costs up to 6 months [45].

discussion

In this update, we have summarized all published evidence available between 2010 and 2012 regarding the use and effectiveness of GA in the oncology setting. Encouragingly, the studies that have been published recently were generally of higher quality than those included in the first review [10]. However, no RCT examining the effectiveness of GA in altering the treatment plan or improving outcomes for older adults with cancer has yet been published.

Although evidence is sparse and of moderate strength, these studies suggest that GA may influence treatment decisions in up to 23% of older patients. However, to date, only seven studies have examined the impact of GA on the treatment decision, of which six took place in France and none were randomized studies. Additional studies from other countries are needed to better determine the usefulness of a GA for the treatment decision-making process.
An important aim of conducting a GA is to identify potential medical and functional status issues that were previously unidentified and that require intervention to promote and restore health and well-being [58]. However, as reported in our previous review [10], no study described the interventions (if any) that were carried out based on the results of the GA, nor how they impacted outcomes. As these assessments, particularly the comprehensive GAs, are time-consuming and thus resource-intensive, it is important that future studies demonstrate improved patient outcomes based on the GA in order to convince policymakers and other health care professionals of their benefit. A recent nonrandomized study by Kenis et al. [59], which was published after the completion of our literature search, reported that the GA identified previously unknown problems in 51% of patients, this resulted in a change in treatment decision for 25% of patients, and determined intervention plans for 25% of patients.

The four fundamental barriers to advancing the field of geriatric oncology defined in our previous review [10] are still relevant: (i) the lack of consensus on the gold standard of a GA; (ii) the lack of standardization in classifying patients in risk groups; (iii) the lack of information about psychometric properties of GA tools; and (iv) gaps in the quality of reporting. While the quality of reporting has increased since our previous review, we needed to contact all study authors except one to obtain details on the study design, response rates, details of assessment and follow-up. This information is critical for evaluating generalizability of the study findings, and therefore, it is important that study details are adequately reported in future studies.

Strengths of this review include the systematic methodology used to identify all relevant articles using two independent reviewers. We conducted a comprehensive search of articles published in four languages and no studies were excluded based on quality assessment criteria. This review also has several limitations. We were unable to conduct a meta-analysis for the outcomes of treatment toxicity and overall survival due to the heterogeneity of the studies included with regard to many different assessment methods used, different study populations included in studies and many studies have not used multivariable modeling adjusting for age and cancer stage, which is crucial to be able to calculate an pooled risk estimate taking into account the large heterogeneity in the ages and cancer stages of participants. To be able to conduct a meta-analysis of the effects of GA to improve cancer treatment outcomes it is crucial that, in future, researchers use validated tools that are commonly used and have well established cutoff points, and conduct statistical modeling with age and stage adjustment which will improve the generalizability of each individual study. Lastly, we have included studies with heterogeneous cancer populations, and thus we were not able to examine the usefulness of GA by cancer type or stage.

Although the top 10 priorities of SIOG include the development of multidisciplinary geriatric oncology clinics in comprehensive cancer centers and academic institutions, as well as the incorporation of GA in the oncology treatment-decision-making [60], convincing policymakers and other health professionals of their benefits will require further evidence of improved cancer treatment decision-making and/or outcomes for older adults with cancer.

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**disclosure**

The authors have declared no conflicts of interest.

**references**

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