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# Predictive value of each geriatric assessment domain for older patients with cancer: A systematic review

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ABSTRACT

*Background:* A geriatric assessment (GA) is increasingly used to help guide treatment decisions in older patients with cancer. However, there is no consensus regarding which domains should be included in the GA. In addition, the field of geriatric oncology moves very fast and as a result many new studies have been published since the last review in 2015. Therefore, the objective of this systematic review is to evaluate which domains of the GA could predict patient-related treatment outcomes of older patients with cancer and thereby should be included in a GA.

*Methods:* A systematic literature search was performed for publications in English or Dutch between September 2006 and July 2017 addressing the association between individual domains of the GA and mortality, postoperative complications, or systemic treatment-related outcomes in older patients with cancer.

*Results:* Eight different domains were evaluated in 46 publications, namely functional status, nutritional status, cognition, mood, physical function, fatigue, social support, and falls. All eight domains were predictive for at least one of the investigated outcomes but the results were quite variable across studies. Physical function and nutritional status were the domains most often associated with mortality and systemic treatment-related outcomes, and the domain physical function was most often associated with postoperative complications.

*Conclusion:* Overall, this review demonstrates that the GA should minimally consist of physical function and nutritional status, when the aim is to predict patients-related outcomes of older patients with cancer, although the results are quite heterogeneous. For the other domains, the findings are too inconsistent to draw conclusions about their overall predictive ability.



**Contents**



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## 1. Introduction

More than half of patients newly diagnosed with cancer today are 65 years of age or older [1]. The number of older patients with cancer substantially increases as a result of increasing life expectancy, population aging, and steady increase of cancer incidence with advancing age. Unfortunately, because this group is underrepresented in clinical trials, there are less results on which to base treatment decisions [2]. This means that older patients with cancer are more likely to be treated according to recommended treatment guidelines for younger patients, resulting in over-treatment. On the other hand, some older patients are incorrectly denied treatment according to recommended guidelines for fear of higher complications and toxicity rates resulting in under-treatment. Both over-treatment and under-treatment have a strong negative impact on survival. Moreover, older patients often have other chronic health conditions in addition to cancer, which can further complicate life expectancy estimation, affect treatment tolerability, and modify treatment efficacy [3].

Furthermore, treatment decisions are complicated by the heterogeneity of the older population with regard to co-morbidity, physiological reserves, functional status, social network, and geriatric conditions, making treatment decisions complex. As a result, the biological or functional age can differ significantly from chronological age [4]. Because chronological age alone is a poor descriptor of the highly individualized process of aging, a systematic way of describing the heterogeneity is needed to help guide oncology treatment decisions. A geriatric assessment (GA) can fill this knowledge gap [5].

A GA is a multidisciplinary, multidimensional, and systematic assessment, and consists of validated scales to identify impairments in geriatric domains [6]. A GA-guided treatment improves survival, quality of life, functional status, and decreases the risk of hospitalization and nursing home placement in non-oncological patients [6]. Over the past decade, the GA has been suggested as a useful geriatric oncology tool for identifying any underlying undetected medical, functional, and psychosocial impairment that may complicate treatment, thereby helping to select the most appropriate treatment [7–9]. Also, several studies have shown associations between items of the GA and the risk of toxicity, morbidity, and mortality during cancer treatment in older patients [10].

The International Society of Geriatric Oncology (SIOG) has therefore recommended conducting some form of geriatric assessment in the older patient with cancer [4,11,12]. Despite their recommendation, there is no consensus regarding which domains should be included in the GA for patients with cancer. The SIOG suggests exploring several domains (functional status, fatigue, cognition, mental health status, social support, nutrition, and geriatric syndromes), but provides no clear recommendation [5]. In addition, several different measurement tools are available for investigating these domains, but no one tool has been proven superior to the others. There is also a variation in the cutoff scores for impairment of the tools, resulting in various compositions of the GA, making inter-study comparison difficult. For that reason, there is a need for uniformity in the GA.

To help decide which domains should be included in the GA, the predictive value of each individual domain should be known. To our knowledge, the most recently published overviews of the predictive abilities of individual domains of the GA were published in 2015, reporting literature searches performed in 2013 [13,14]. We have therefore concluded that a new systematic review is needed in order to arrive at an overview of the most recent evidence. The aim of this systematic review is to systematically evaluate which domains of the GA could predict patient-related treatment outcomes defined as mortality, postoperative complications of elective surgery for solid tumors, systemic treatment-related outcomes as toxicity, completion of planned treatment, and dose modifications, and should be included in a GA for older patients with cancer.

## 2. Methods

### 2.1. Data Sources

In July 2017, a systematic search was conducted in four databases: MEDLINE, EMBASE, Cochrane, and Cinahl. The search strategy combined synonyms for 'older patients', 'cancer', 'geriatric assessment', 'mortality', 'treatment outcomes', and 'postoperative complications'. The search was executed in 'title and/or abstract', and was restricted to articles in English or Dutch with a publication date between September 2006 and July 2017 (to avoid outdated evidence). An experienced university librarian assisted in the literature search. The full search syntax is presented in Supplementary 1. The PRISMA statement was used for reporting this systematic review [15].

### 2.2. Study Selection

After duplicates were deleted, the studies were selected in two steps. In the first step, the results were screened based on potentially relevant title and abstract using predefined criteria. A study was eligible for inclusion if all of the following criteria were fulfilled: (1) the study reported on patients 65 years or older diagnosed with cancer (any type of solid tumors or hematological malignancies, except skin cancer), and (2) the study reported on longitudinal, observational, interventional, or retrospective studies that addressed the association between baseline geriatric assessment and the following patient-related outcomes: mortality, postoperative complications of elective surgery for solid tumors, and systemic treatment-related outcomes defined as toxicity of systemic treatment, completion of planned treatment, and dose modifications. Editorials, case studies, reviews, expert opinion papers, and studies that were published as abstracts only were excluded. Because comorbidity is a routine part of the oncological work-up and therefore not considered part of the geriatric assessment, studies assessing the association between comorbidity and patient-related outcomes were excluded. Furthermore, frailty was not considered as an individual domain of the GA since frailty has frequently been defined as the presence of one or more impairments in geriatric domains, e.g. weight loss, fatigue, or low physical activity.

The selection was performed independently by two authors (CB and DH). When one author was uncertain about whether the study met the inclusion criteria or the abstract was unavailable, the study was selected for full text screening. In the second step, the full text was independently reviewed by these authors using the same inclusion and exclusion criteria. Disagreements between authors were resolved by consensus. To obtain the one unavailable full text article, we contacted the authors by email. Finally, the reference list of each selected study was reviewed to identify any additional relevant article.

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### 2.3. Quality Assessment

The two authors appraised the methodological quality of each of the selected studies independently. The Quality In Prognosis Studies (QUIPS) tool was used to assess the risk of bias for the following five domains (1) the study participation, (2) the study attrition, (3) the assessment of the domains of the GA, (4) the measurement of the outcomes, and (5) statistical analysis and reporting (Supplementary 2) [16,17]. These potential bias domains were rated as having high (0 points), moderate (0.5 points), or low risk of bias (1 point), based on the QUIPS study of Hayden et al. [17]. Next, we rated the study design. A prospective study was ranked as a low risk of bias (1 point) because the inclusion criteria, the prognostic factors, and outcomes are defined in advance, and the baseline and follow-up data are more often complete, which reduces the risk for data dragging [18]. As a result, a retrospective study was ranked as a high risk of bias (0 points).

Subsequently, the scores of the six items were added. The total score reflected the overall risk of bias of the study: the maximum total score of 6 was regarded as the study with the lowest risk of bias. All discrepancies were resolved by consensus. No study was excluded based on the quality assessment since our aim was to provide a comprehensive overview of all studies assessing the predictive ability of individual domains of the GA for older adults with cancer.

### 2.4. Data Abstraction, Synthesis and Analysis

The two authors extracted the data of each study included independently. A formal meta-analysis was not possible due to the heterogeneity in study designs, diversity in study populations, the use of different geriatric assessment tools with different cutoff points, and the diversity in outcomes. Therefore, we summarized the results of the predictive ability of individual geriatric domains per outcome measure.

## 3. Results

The literature search in four databases yielded 881 citations. After removing duplications (n = 50) and screening on titles and abstracts, 122 full texts were reviewed. The full text of one citation remained unavailable, despite contacting the authors [19]. After this review, 46 publications remained eligible for inclusion (Fig. 1). Next, one publication was excluded because this publication reported the exact same cohort, data, and results as another publication included [20,21]. Reference checking yielded one additional relevant publication. In the end, 46 eligible publications remained for quality assessment and data analysis.

Overall, scores of the quality assessments ranged from 2.0 to 6.0, with a median value of 4.5 (Supplementary 3). Five publications had the lowest risk of bias with a maximum score of 6 [21–25].

## 4. Study Characteristics

An overview of the characteristics of the 46 eligible publications is shown in Table 1. More than half of the studies were published in 2014 or later (24 out of 46 studies, 52%). Of the 46 publications, 38 were prospective studies, six were retrospective studies, and two had an unclear study design. None of the publications reviewed reported a randomized controlled trial specifically designed to examine the effectiveness of geriatric assessment.

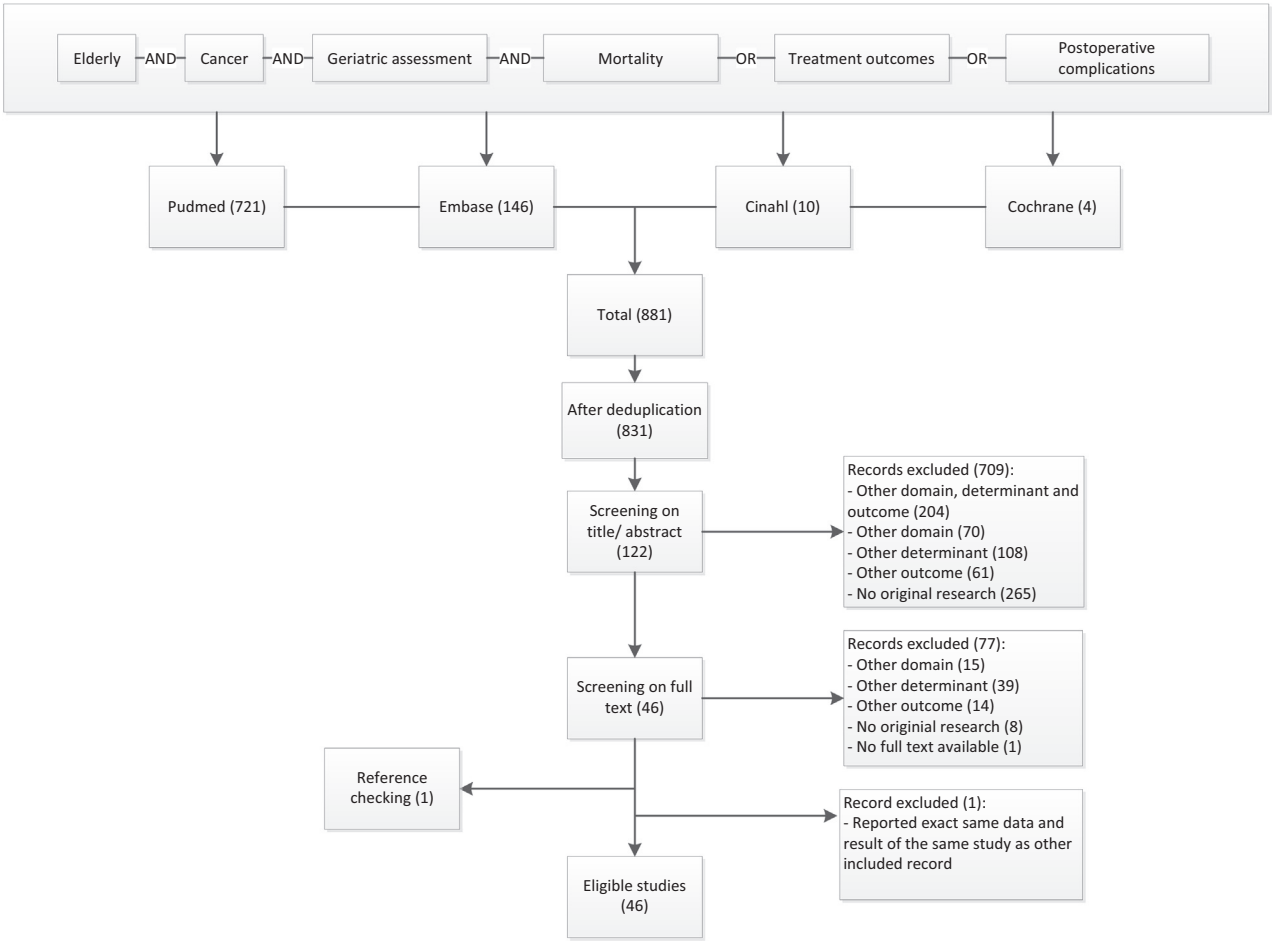


**Fig. 1.** Flowchart of study selection.

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**Table 1**
Study characteristics.

| Author (year) | Design | Aim of study | Sample size (% males)/country | Min. age | Age, median years (range) | Tumor type | Follow-up | Inclusion criteria | Geriatric domains of GA | Measurement tool of geriatric domain | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Aaldriks [31] | Pros | To study the prognostic value of GA | 55* (4) Netherlands | ≥70 yr | 76[a] (70–88) | Breast cancer | 0–57 months | Advanced cancer for whom chemotherapy was prescribed | Nutrition<br>Cognition | MNA<br>MMSE/IQCODE-N | Early withdrawal chemotherapy<br>Mortality |
| Aaldriks [51] | Pros | To investigate the prognostic value of GA | 44 (43) Netherlands | ≥70 yr | 78[a] (70–86) | Non-Hodgkin Lymphoma | 0–101 months | Fit for chemotherapy | Nutrition<br>Cognition | MNA<br>MMSE/IQCODE-N | Early withdrawal chemotherapy<br>Mortality |
| Aaldriks [8] | Pros | To assess the prognostic value of GA for treatment with chemotherapy | 202* (45) Netherlands | ≥70 yr | 77[a] (71–92) | All cancer types | 1–33 months | Chemotherapy was prescribed | Nutrition<br>Cognition | MNA<br>MMSE/IQCODE-N | < 4 cycles chemotherapy vs ≥4 cycles |
| Aaldriks [32] | Pros | To analyze which elements of geriatric screening program were predictive for chemotherapy and mortality | 494 (49.9)* Netherlands | ≥70 yr | 75 (70–92) | All cancer types | 1–101 months | Considered fit enough for chemotherapy | Nutrition<br>Cognition | MNA<br>MMSE/IQCODE-N | Mortality<br>< 4 cycles chemotherapy vs ≥4 cycles |
| Aaldriks [33] | Pros | To assess the predictive value for tolerance of treatment | 143 (59)* Netherlands | ≥70 yr | 75[a] (70–92) | Colorectal | 0.5–62 months | Eligible for chemotherapy treatment | Nutrition<br>Cognition | MNA<br>MMSE/IQCODE-N | Mortality<br>< 4 cycles chemotherapy vs ≥4 cycles |
| Aparicio [66] | Pros | To identify predictive factors of treatment feasibility and toxicity | 123 (54) France | ≥75 yr | 80.4[a] (NR) | Colorectal | 4 months | Fit for chemotherapy | Functional status:<br>IADL<br>Cognition<br>Mood | Lawton-scale<br>MMSE<br>GDS | Mortality<br>Grade 3 to 4 toxicity<br>Dose reduction >33%<br>Hospitalization |
| Audisio [43] | Pros | To investigate the value of a GA in assessing the suitability for surgical intervention | 460 (34) Europe and Japan | ≥70 yr | 76.9[a] (70–95) | Solid tumors | 1 months | Elective cancer surgery<br>No emergency surgical management | Functional status:<br>ADL<br>IADL<br>Cognition<br>Mood<br>Fatigue | Katz-scale<br>Lawton-scale<br>MMSE<br>GDS<br>BFI | Morbidity<br>Post-operative hospital stay |
| Badgwell [44] | Pros | To identify factors which may be associated with increased risk in older patients undergoing abdominal surgery | 111 (55) United States of America | ≥65 yr | 72 (62–89) | Abdominal cancer | 3 months | Abdominal cancer surgery | Functional status:<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Fatigue<br>Falls | Lawton-scale<br>Amount of weight/6 months<br>Mini-Cog Test<br>GDS<br>BFI<br>Number of falls/6 months | Post-operative complications according to Clavien-Dindo scale<br>Discharge to nursing facility<br>Hospital readmission |
| Baier [47] | Pros | Use of GA to predict risks and benefits of interventions | 200 (69) Germany | ≥70 yr | 75 (70–88) | Abdominal cancer | 6 months | Planned for elective surgery in curative intention, expected survival >6 months | Functional status:<br>IADL<br>Nutrition<br>Cognition<br>Physical function | Lawton-scale<br>MNA<br>MMSE<br>GUG | Dependence: ADL < 95 |

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| Baitar [67] | Pros | To evaluate the association between the Geriatric 8 and Groninger Frailty Index and severe treatment toxicity | 85 (48) Belgium | ≥65 yr | 66 (66–88) | All cancer types | 1 months | (Radio)chemotherapy <3 weeks after screening | Functional status[b]: ADL IADL Nutrition[b] Cognition Mood[b] Social support[b] | Katz-scale Lawton-scale MNA MMSE GDS MOS-SSS | SAE after first cycle of (radio) chemotherapy |
| Biesma [68] | Pros | To evaluate whether a GA can be used as a tool to predict which patients benefit from chemotherapy | 181 (77) Netherlands | ≥70 yr | 74 (70–87) | Non-Small Cell Lung Carcincoma | NR | Inoperable, WHO-performance score ≤ 2 | Functional status: ADL IADL Cognition Mood Physical function | Katz-scale Lawton-scale MMSE GDS TUG | Survival |
| Bila [69] | NR | To analyze the prognostic and treatment effect of IADL on the outcome of older patients | 110 (50) Serbia | ≥65 yr | NR | Multiple myeloma | NR | Treatment with chemotherapy | Functional status: IADL | Lawton-scale | AE Overall survival |
| Brunello [42] | Retro | To develop a cancer-specific multidimensional Prognostic Index for mortality prediction | 658 (34) Italy | ≥70 yr | 77.16[a] (70–96) | All cancer types | 0–8. years | NR | Functional status: ADL IADL Cognition Mood Social support | Katz-scale Lawton-scale MMSE GDS Presence of caregiver | One-year mortality |
| Choi [45] | Retro | To evaluate the role of a scoring model in predicting adverse surgical outcomes | 281 (0) Korea | ≥65 yr | 76.3[a] (NR) | All cancer types | 100 days | Low ASA risk, female, Korean patients undergoing curative cancer surgery | Functional status: ADL IADL Nutrition Cognition Mood | Barthel-index Lawton-scale MNA MMSE GDS | Post-operative complication Length of hospital stay |
| Clough-Gorr [41] | NR | To evaluate GA domains in relation to important outcomes | 660 (0) United States of America | ≥65 yr | NR | Breast cancer | 7 years | Stage I, II or IIIA | Mood Social support | MHI5 MOS-SSS | Poor treatment tolerance according to opinion patient Mortality |
| Denewet [70] | Pros | To assess to which extent GA could be seen as determinant of survival | 205 (53) Belgium | ≥70 yr | 79 (70–93) | All cancer types | 12 months | New diagnosis or disease progression | Functional status: ADL IADL Nutrition[b] Cognition[b] Mood[b] | Katz-scale Lawton-scale MNA-SF MMSE GDS | Survival |
| Dubruille [71] | Pros | To investigate the predictive value of the different GA items | 90 (51) Belgium | ≥65 yr | 74 (65–89) | Hematological cancer | 1 year | Hospitalized for chemotherapy | Functional status: ADL IADL Nutrtion Cognition Mood Fatigue Falls | Katz-scale Lawton-scale MNA MMSE GDS Mob-t Number of falls/last year | 1-year overall survival |
| Extermann [49] | Pros | To create and validate in independent patients a predictive score with potential for clinical application | 518(49.8) United States of America | ≥70 yr | 75.5 (70–92) | All cancer types | 6 months | Histologically proven cancer and were initiating a new first line to fourth line | Functional status: IADL Nutrition | Lawton-scale MNA MMSE GDS | Grade 4 hematologic toxicity and/or grade 3–4 |

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**Table 1** (*continued*)

| Author (year) | Design | Aim of study | Sample size (% males)/country | Min. age | Age, median years (range) | Tumor type | Follow-up | Inclusion criteria | Geriatric domains of GA | Measurement tool of geriatric domain | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | source of chemotherapy | Cognition<br>Mood | | non-hematologic toxicity |
| Ferrat [26] | Pros | To identify GA findings associated with mortality | 993 (51)<br>France | ≥70 yr | 80.2[a]<br>(NR) | All cancer types | 1 year | NR | Functional status:<br>ADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function | Katz-scale<br>MNA<br>MMSE<br>GDS<br>GUG | Overall 1-year mortality |
| Ghosn [72] | Pros | To evaluate the predictive value of and abridged GA for mortality in older patients with cancer | 100 (53)<br>Lebanon | ≥70 yr | 76 | All cancer types | Median 1418 days | A performance score ≥ 60 and a MMSE ≥23 | Functional status<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function | Katz-scale<br>Lawton-scale<br>MNA<br>MMSE<br>GDS<br>TUG | Overall surivival |
| Giantin [22] | Pros | To test the Multidimensional Prognostic Index | 160 (45)<br>Italy | ≥70 yr | 79.4[a]<br>(69–93) | Solid tumors | 12 months | Inoperable or metastatic solid cancer | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | Katz-scale<br>Lawton-scale<br>MNA<br>SPMSQ/MMSE<br>GDS | Mortality |
| Gírones [34] | Pros | To investigate the association of GA variables with function and survival | 83 (97.6)<br>Spain | ≥70 yr | 77[a]<br>(NR) | Lung cancer | 2 years | Lung cancer at any stage | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | Katz-scale<br>?<br>Amount of weight loss/3 months<br>MMSE<br>GDS | Mortality |
| Goede [30] | Pros | To investigate the association between GA and treatment outcome | 75 (61)<br>Germany | No cutoff point: 8% below 65 years | 75<br>(48–87) | Chronic Lymphocytic Leukemia | 5 years | Treatment with chemotherapy in the Chronic Lymphocytic Leukemia-9 trial | Functional status:<br>IADL<br>Cognition<br>Physical function | Lawton-scale<br>DEMTECT<br>TUG | Dose reduction<br>Treatment delay<br>Treatment discontinuation<br>Overall survival |
| Hamaker [73] | Pros | To evaluate the association between baseline GA and toxicity | 78 (0)<br>Netherlands | ≥65 yr | 75.9<br>(65.8–86.8) | Breast cancer | Median 32 months | Metastatic breast cancer patients treated with first line chemotherapy | Functional status:<br>IADL<br>Nutrition<br>Cognition<br>Mood | Lawton-scale<br>BMI<br>MMSE<br>GDS | Grade 3–4 toxicity<br>Mortality |
| Hamaker [28] | Pros | To assess the value of Geriatric 8 in predicting 1-year mortality | 108 (53)<br>Austria | ≥67 yr | 78.2<br>(67.1–98.9) | Hematological malignancy | 12 months | Newly diagnosed with a hematological malignancy | Functional status:<br>ADL<br>IADL<br>Nutrition | Barthel-index<br>Lawton-scale<br>BMI<br>MMSE<br>GDS | 1-year mortality |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Cognition<br>Mood<br>Physical function | TUG | |
| Hamaker [39] | Pros | To assess which geriatric conditions are associated with mortality | 292 (51.2)<br>Netherlands | ≥65 yr | 74.9<br>(65–96.2) | All cancer types | 12 months | Patients admitted to general medicine or oncology | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Social support | Katz-scale<br>Modified Katz-scale<br>SNAQ<br>IQ-CODE-SF<br>GDS<br>EDIZ | 12-month mortality |
| Hoppe [48] | Pros | To determine factors associated with functional early functional decline during first-line chemotherapy in older patients | 364 (59.2)<br>France | ≥70 yr | 77.35<br>(70–93) | Colon, pancreatic, stomach, ovarian, bladder, prostate, lung, non-Hodgkin lymphoma, or cancer of unknown primary origin | 4 weeks | Patients scheduled to receive first-line chemotherapy | Functional status<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function | Katz-scale<br>Lawton-scale<br>MNA<br>MMSE<br>GDS<br>TUG | Functional decline after first cycle of chemotherapy: any decrease in ADL score |
| Huisman [21] | Pros | To investigate the predictive ability of screening tools | 328 (38.1)**<br>Europe | ≥70 yr | 76<br>(70–96) | Solid tumors | 1 month | Elective surgery for a solid tumor under general anesthesia | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function<br>Fatigue | Katz-scale<br>Lawton-scale<br>NRS<br>MMSE<br>GDS<br>TUG<br>BFI | Major complication <30 days according to Clavien-Dindo scale |
| Huisman [23] | Pros | To determine the predictive value of the TUG | 263(33.5)<br>Europe | ≥70 yr | 76<br>(70–96) | Solid tumors | 1 month | Elective surgery for a solid tumor | Physical function | TUG | Major complication (gr 3–5) < 30 days according to Clavien-Dindo scale |
| Hurria [7] | Pros | To develop a predictive model for grade 3 to 5 toxicity | 500(44)<br>United States of America | ≥65 yr | 73[a]<br>(65–91) | Solid tumors | Until the end of chemotherapy | Diagnosis of cancer Stage I-IV and scheduled to receive a new chemotherapy | Functional status[b]:<br>ADL<br>IADL<br>Nutrition[b]<br>Cognition[b]<br>Mood[b]<br>Physical function<br>Falls<br>Social support[b] | Subscale of MOS Physical Health<br>Subscale of OARS<br>BMI<br>BOMC<br>HADS<br>TUG<br>Number of falls/6 months<br>MOS-SSS | Grade 3 to 5 toxicity of chemotherapy |
| Jonna [74] | Retro | To identify factors associated with shorter survival after following hospitalization | 803(51.8)<br>United Stated of America | ≥65 yr | 72.5<br>(?) | All cancer types | 6 years | All patients admitted to the oncology acute care for elders unit who underwent GA | Functional status:<br>ADL<br>IADL<br>Cognition | Katz-scale<br>Lawton-scale<br>Clock | Overall survival |

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**Table 1** (*continued*)

| Author (year) | Design | Aim of study | Sample size (% males)/country | Min. age | Age, median years (range) | Tumor type | Follow-up | Inclusion criteria | Geriatric domains of GA | Measurement tool of geriatric domain | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Kanesvaran [35] | Retro | To determine the impact of each GA domain on overall surivial | 249(61.4) Singapore | ≥70 yr | 77 (70–94) | All cancer types | 3 years | Diagnosis at any stage | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | Katz-scale<br>Lawton-scale<br>DETERMINE-NI<br>Clock/MMSE<br>GDS | Overall survival |
| Kenig [24] | Pros | To compare prevalence of frailty depending on the number of incorporated domains of GA and to evaluate its accuracy in predicting postoperative outcomes | 75(56) Poland | ≥65 yr | 73 (65–93) | Solid abdominal tumors | 1 month | In need of elective surgery under general anesthesia | Functional status:<br>ADL[b]<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function<br>Fatigue<br>Social support | Katz-scale<br>Lawton-scale<br>MNA<br>BOMC/Clock/MMSE<br>GDS<br>TUG<br>BFI<br>MOS-SSS | Any event within 30 days of surgery that required treatment<br>Major complication |
| Kristjansson [36] | Retro | To identify independent predictors of post-operative complications and early mortality from a GA | 182(43) Norway | ≥70 yr | 80 | Colorectal cancer | 14–34 months | Planned for surgery of a confirmed or suspected colorectal cancer | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | Barthel-index<br>NEADL<br>MNA<br>MMSE<br>GDS | Any and severe complications <30 days of surgery<br>Mortality |
| Marinello [75] | Pros | To analyze the role of several factors, including GA, in predicting the occurrence of adverse events during chemotherapy | 110(64) Italy | ≥70 yr | 75.1 (70–87) | Any stage of breast, lung and colorectal cancer | The whole treatment period (about 6 months) | Considered sufficiently fit to tolerate chemotherapy | Functional status:<br>ADL<br>IADL<br>Cognition | Katz-scale<br>Lawton-scale<br>SPMSQ | Death<br>Toxicity<br>Treatment interruption |
| Merli [76] | Pros | To evaluate which among the GA components could help better identify patients | 94(34) Italy | ≥65 yr | 78 (65–93) | Diffuse large B-cell lymphoma (DLBCL) | Median 36 months | DLBCL and ECOG 0–3<br>This study describes the results of the frail patients according to GA | Functional status:<br>ADL | NR | Overall survival |
| Mokutani [46] | Pros | To determine whether GA could predict complications of colorectal cancer surgery | 156(57) Japan | ≥75 yr | 80.2[a] (75–94) | Colorectal cancer | Complications retrospectively analyzed | With planned radical surgery of confirmed or suspected colorectal cancer | Functional status:<br>ADL<br>Cognition<br>Mood | Barthel-index<br>MMSE<br>GDS | Postoperative complications <30 days of surgery |
| Naito [50] | Retro | To examine whether items in the GA were associated with survival time | 93(46) Japan | ≥65 yr | 77 (NR) | Non-Hodgkin Lymphoma | 5 years | Who were admitted for the first time for the treatment of Non-Hodgkin Lymphoma | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | Barthel-index<br>Lawton-scale<br>BMI<br>Hasegawa's scale<br>GDS | Adverse events<br>Overall survival |
| Ommundsen | Pros | To explore whether GA also predict | 178(43) | ≥70 yr | 80 | Colorectal cancer | 5 years | Scheduled for elective | Functional | Barthel-index | 1-year survival |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| [37] | | 1-year and 5-year survival | Norway | | (70–94) | | | surgery for confirmed or suspected colorectal cancer | status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood | NEADL<br>MNA<br>MMSE<br>GDS | 5-year survival |
| Park [38] | Pros | To evaluate the relation of the GA to tolerability and survival of chemotherapy | 70(54.3)<br>Korea | ≥65 yr | 73.5<br>(65–92) | Aggressive Non-Hodgkin Lymphoma (NHL) | 11.8–31.3 months | NHL and treated with chemotherapy for curative intent | Nutrition<br>Cognition<br>Mood | MNA-SF<br>MMSE<br>GDS | Maintenance the planned therapy for 12 weeks or more |
| Puts [40] | Pros | To explore the association between frailty and treatment toxicity | 112(30.4)<br>Canada | ≥65 yr | 74.1<br>(65–92) | All cancer types | 6 months | New diagnosis of solid tumor with or without metastasis, or hematological malignancy | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function<br>Fatigue | Katz-scale<br>OARS<br>Weight loss<br>MMSE<br>HADS<br>Self-report questions, 4 m gait speeds, hand grip strength with dynamometer<br>EORTC QOL C30 | Overall survival<br>Severe toxicity grade 3–5 at 3 and 6 months<br>Death at 6 months |
| Spina [77] | Pros | To evaluate the feasibility and efficacy of chemotherapy modulated according to a modified GA | 100(41)<br>Italy | ≥70 yr | 75<br>(70–89) | Diffuse large B-cell lymphoma | Minimal 5 years | No previous chemotherapy | Functional status:<br>ADL<br>IADL | Katz-scale<br>Lawton-scale | Overall survival |
| Soubeyran [29] | Pros | To use GA to search for factors associated with higher risk of early death | 364(59.5)<br>France | ≥70 yr | 77.45<br>(70–99.4) | All cancer types (breast excluding) | 6 months | Scheduled to receive first-line chemotherapy | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function | Katz-scale<br>Lawton-scale<br>MNA<br>MMSE<br>GDS<br>TUG | Death <6 months of chemotherapy |
| Suh [25] | Pros | To evaluate the associations of GA with surgical complications | 60(0)<br>Korea | ≥70 yr | 73<br>(70–85) | Gynaecologic cancer | 30 days | Who were scheduled to undergo selective surgery | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Fatigue | Barthel-index<br>Lawton-scale<br>MNA<br>MMSE<br>GDS<br>BFI | Postoperative complications <30 days |
| Ugolini [27] | Pros | To investigate the variables capable of predicting the long-term risk of mortality | 46(52)<br>Italy | ≥70 yr | 80.5 | Colorectal cancer | Median follow-up 4.6 years (range 2.9–5.7) | Undergoing elective surgery for colorectal cancer | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Physical function<br>Fatigue | Katz-scale<br>Lawton-scale<br>MNA<br>MMSE<br>GDS<br>TUG<br>BFI | Long-term mortality<br>Living situation: but number of surviving patients were to small |

(continued on next page)

**Table 1** (*continued*)

| Author (year) | Design | Aim of study | Sample size (% males)/country | Min. age | Age, median years (range) | Tumor type | Follow-up | Inclusion criteria | Geriatric domains of GA | Measurement tool of geriatric domain | Outcomes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Wildes [78] | Pros | To determine whether geriatric assessments are associated with completion of a chemotherapy course | 65(41.5) United States of America | ≥65 yr | 73 (65–89) | Colorectal, lung or breast cancer or lymphoma | 0.01–47 months | Who were likely to begin a course of chemotherapy | Functional status:<br>ADL<br>IADL<br>Nutrition<br>Cognition<br>Mood<br>Falls | Katz-scale<br>Lawton-scale<br>BMI<br>Unknown<br>Unknown<br>Number of falls/past month | Completion of chemotherapy<br>Grade III/IV toxicity of chemotherapy<br>Survival |

**Abbreviations:** ADL, Activities of Daily Living; AE, Adverse Event; ASA, American Society of Anesthesiologists; BFI, Brief Fatigue Inventory; BMI, Body Mass Index; BOMC, Blessed Orientation-Memory-Concentration Test; GA, Comprehensive Geriatric Assessment; DEMTECT, Dementia Detection Test; DETERMINE-NI, DETERMINE nutritional index; ECOG, Eastern Cooperative Oncology Group; EDIZ, Experienced Burden of Informal Care; EORTC QOL C30, Organization for Research and Treatment of Cancer Quality of life questionnaire fatigue subscale; GDS, Geriatric Depression Scale; GUG, Get-up and Go test; HADS, Hospital Anxiety and Depression Scale; IADL, Instrumental Activities of Daily Living; IQCODE-N, Informant Questionnaire on Cognitive Decline in the Older patients the short Dutch translation; MIH5, Five-item Mental Health Index; Mini-Cog, Mini Cognition Test; MMSE, Mini Mental State Examination; MNA, Mini-Nutritional Assessment; MNA-SF, Mini-Nutritional Assessment Short-Form (MNA-SF); Mob-t, Mobility-tiredness scale; MOS, Medical Outcomes Study; MOS-SSS, Medical Outcomes Study Social Support Scale; NEADL, Nottingham Extended Activities of Daily Living Scale; NR, not reported; NRS, Nutritional Risk Screening; OARS, Older Americans Resources and Services European; Pros, Prospective; Retro, Retrospective; SAE, Severe Adverse Event; SNAQ, Short Nutritional Assessment Questionnaire; SPMSQ, Short Mental Status Questionnaire; TUG, Time Up and Go test; WHO, World Health Organization.

* Same cohort

** Same cohort

[a] Mean age instead of median age

[b] Results of this domains not described

welve studies focused on patients with one specific solid tumor type, nine studies included patients with a hematological malignancy, and 25 studies focused on patients with various types of cancer. In total, the 46 publications comprised data of 9985 unique patients of 44 different cohorts. An average of 49% of the patients were males. The median number of patients enrolled was 150 (range 44–993). The age of the patients ranged from 65 to 99 years. The following geriatric domains were assessed as being part of a GA: functional status, nutritional status, cognition, mood, physical function, fatigue, social support, and falls. The median number of geriatric domains of the GA reported by study was four (range one-seven).

## 5. Mortality

Thirty-two studies analyzed which domains of the geriatric assessment were predictive for mortality (Table 2). Physical function, assessed with the Time-up and Go-test (TUG), Get-up and Go test (GUG), four-meter gait speed, or hand grip strength, was found to be the domain most often associated with mortality in five out of eight studies (63%) [26–30].

Nutritional status was associated with mortality in thirteen out of 23 studies (57%) [8,26,29,31–40]. For Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), cognition, mood, fatigue, and falls, <50% of the studies found an association with mortality. In the three studies that assessed the association between social support, no association was found [39,41,42].

## 6. Postoperative Complications

As shown in Table 3, nine studies addressed the association between individual geriatric domains and postoperative complications within 30 days [21,23–25,36,43–46], while one study assessed the association with postoperative dependency [47].

Physical function was also the most associated geriatric domain for postoperative complications in three out of four studies (75%) [21,23,24]. In the only study that assessed this domain, social support was a statistically significant predictive factor for postoperative complications [24].

For ADL, IADL, nutrition, cognition, mood, fatigue, and falls, <50% of the studies found an association.

## 7. Systemic Treatment-Related Outcomes

Nineteen studies, listed in Table 4, examined the ability of individual geriatric domains to predict systemic treatment-related outcomes. Because all studies examined the outcomes of chemotherapy treatment and no study included patients treated with anti-hormone, immune, or targeted therapy, we will therefore hereinafter call systemic treatment-related outcomes chemotherapy-related outcomes. Chemotherapy-related outcomes consisted of toxicity of chemotherapy, including dose modifications due to toxicity, early withdrawal of chemotherapy, and functional decline after the first cycle of chemotherapy.

All four studies found that physical function was predictive for chemotherapy-related outcomes (100%) [7,30,40,48].

Furthermore, eight out of fourteen studies found that malnutrition was predictive for chemotherapy-related outcomes (57%) [8,32,33,38,48–51]. Malnutrition was especially predictive for the risk of early withdrawal of chemotherapy in 86% of the studies (five out of six) [8,32,33,38,51]. For falls, one out of two studies (50%) found an association with toxicity of chemotherapy [7].

Finally, <50% of the studies found an association between toxicity of chemotherapy and social support, ADL, IADL, cognition, and mood. For fatigue and mobility, no association was found.

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## 8. Discussion

Since the SIOG's recommendation to conduct a GA, many studies were published about the predictive ability of individual GA domains for relevant oncological outcomes. However, the composition of the GA differs between studies, which makes inter-study comparison difficult. The aim of the current systematic review was to systematically evaluate which domains of the GA could predict patient-related treatment outcomes and should be included in a GA for patients with cancer. Patient-related outcomes were defined as mortality, postoperative complications of elective surgery for solid tumors, and chemotherapy-related outcomes as toxicity, completion of planned treatment, and dose modifications.

In this systematic review, eight geriatric domains were evaluated in 46 publications, namely functional status, nutritional status, cognition, mood, physical function, fatigue, social support, and falls. All of these domains were predictive for at least one of the reviewed outcomes, but the results varied between the studies. Physical function and nutritional status were the most predictive domains for mortality; physical function was the most predictive domain for postoperative complications; and for chemotherapy-related outcomes, physical function and nutritional status were the most predictive domains. In conclusion, the only truly consistent finding was that physical function was the most predictive domain of the GA for mortality, as well as for postoperative complications and for chemotherapy-related outcomes.

The reason for variation in results is the heterogeneity of the studies and study populations. First, the studies differed in study design, sample size, tumor type, and tumor stage. Second, the studies varied in the minimum age of participants: some studies also included the younger old patients (65 years or older), while other studies only included the oldest old (75 years and older). Third, the studies used different measurement tools to assess the same geriatric domain with various definitions of impairment. Finally, the studies varied in the way they reported their outcomes. Some studies reported adjusted Odds and Hazard Ratios, while others used a Chi-square test to compare the incidence of an impaired domain between the group with the outcome and the group without the outcome.

The eligible studies not only showed inconsistent results, but often also did not show a positive predictive ability of the individual domain for an oncological outcome. A reason for this null effect could be that the GA was originally not designed to predict adverse oncological outcomes but to predict functional decline and falls in an older population with cognitive and functional impairments [6]. Therefore, the used measurement tools have been validated in the traditional geriatric population instead of the oncological geriatric population. The properties of these measurement tools in oncological population may differ from

**Table 2**
Association of individual geriatric domain with mortality.

| Outcome | Study | Cancer type | Nr of patients | Functional status | | Nutrition | Cognition | Mood | Physical function | Fatigue | Social Support | Falls |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ADL | IADL | | | | | | | |
| Overall survival | Aaldriks [31] | Breast | 55 | | | ++ | -- | | | | | |
| | Aaldriks [51] | Hematological | 44 | | | -- | np | | | | | |
| | Aaldriks [8] | Various | 202 | | | ++ | -- | | | | | |
| | Aaldriks [32] | Various | 494 | | | ++ | - | | | | | |
| | Aaldriks [33] | Colorectal | 143 | | | ++ | -- | | | | | |
| | Biesma [68] | Lung | 181 | - | - | | - | - | - | | | |
| | Bila [69] | Hematological | 110 | | + | | | | | | | |
| | Clough-Gorr [41] | Breast | 660 | | | | | ++ | | | -- | |
| | Ghosn [72] | Various | 100 | - | - | - | - | - | - | | | |
| | Gírones [34] | Lung | 83 | - | + | + | + | + | | | | |
| | Goede [30] | Hematological | 75 | | - | | + | | + | | | - |
| | Hamaker [57] | Breast | 78 | | - | np | + | + | | | | |
| | Jonna [74] | Various | 803 | + | ++ | | ++ | | | | | |
| | Kanesvaran [35] | Various | 249 | + | + | ++ | + | ++ | | | | |
| | Kristjansson [36] | Colorectal | 182 | - | + | ++ | - | - | | | | |
| | Merli [76] | Hematological | 94 | + | | | | | | | | |
| | Naito [50] | Hematological | 93 | - | + | - | ++ | - | | | | |
| | Ommundsen [37] | Colorectal | 178 | - | ++ | ++ | + | - | | | | |
| | Park [38] | Hematological | 70 | | | + | - | - | | | | |
| | Spina [77] | Hematological | 100 | + | + | | | | | | | |
| | Ugolini [27] | Colorectal | 46 | - | + | - | - | - | + | - | | |
| | Wildes [78] | Breast, lung, colorectal, and lymphoma | 73 | - | - | - | - | - | | | | ++ |
| 1-year mortality | Brunello [42] | Various | 658 | -- | -- | | -- | -- | | | -- | |
| | Denewet [70] | Various | 205 | -- | ? | ? | - | ? | | | | |
| | Dubruille [71] | Hematological | 90 | -- | -- | -- | ++ | -- | | -- | | -- |
| | Ferrat [26] | Various | 993 | ++ | | + | + | + | ++ | | | |
| | Giantin [22] | Solid tumors | 160 | - | - | - | ++ | ++ | | | | |
| | Hamaker [28] | Hematological | 108 | - | - | ++ | - | - | ++ | | | |
| | Hamaker [39] | Various | 292 | + | - | - | - | - | | | - | |
| 6-monts mortality | Marinello [75] | Breast, lung, and colorectal | 110 | np | - | | np | | | | | |
| | Puts [40] | Various | 112 | ++ | - | + | - | + | - | + | | |
| | Soubeyran [29] | Various | 364 | - | - | ++ | + | - | ++ | | | |
| Nr of positive results/all st udies (%) | | | | 7/22 (32%) | 9/23 (39%) | 13/23 (57%) | 11/28 (39%) | 7/21 (33%) | 5/8 (63%) | 1/3 (33%) | 0/3 (0%) | 1/3 (33%) |

+, significant in univariate analysis: no multivariate analysis performed or factor in multivariate analysis not significant; ++, significant in multivariate analysis; -, no association in univariate analysis: no multivariate analysis performed or factor not included in multivariate analysis; --, no association in multivariate analysis; ?, results of geriatric domain not described; np, number of compromised patients was too low: statistical analysis was not possible.
Abbreviations: ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living

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**Table 3**
Association of individual geriatric domain with postoperative complications.

| Outcome | Study | Cancer type | Nr of patients | Functional status | | Nutrition | Cognition | Mood | Physical function | Fatigue | Social Support | Falls |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ADL | IADL | | | | | | | |
| Any complication <30 days | Audisio [43] | Solid tumors | 460 | ++ | + | | - | - | | + | | |
| | Badgwell [44] | Abdominal | 111 | | - | ++ | - | - | | - | | - |
| | Choi [45] | Various | 281 | - | - | + | - | - | | | | |
| | Huisman [21] | Solid tumors | 328 | ++ | -- | ++ | ++ | ++ | ++ | ++ | | |
| | Huisman [23] | Solid tumors | 263 | | | | | | ++ | | | |
| | Kenig [24] | Abdominal | 75 | ? | -- | -- | -- | -- | ++ | ? | ++ | |
| | Kristjansson [36] | Colorectal | 182 | - | ++ | - | - | - | | | | |
| | Mokutani [46] | Colorectal | 156 | ++ | -- | | ++ | -- | | | | |
| | Suh [25] | Gynaecological | 60 | - | + | - | - | - | | - | | |
| Dependence | Baier [47] | Abdominal | 200 | | -- | - | - | | - | | | |
| Nr of positive r esults/all studies (%) | | | | 3/7 (43%) | 3/9 (33%) | 3/7 (43%) | 2/9 (22%) | 1/8 (13%) | 3/4 (75%) | 2/5 (40%) | 1/1 (100%) | 0/1 (0%) |

+, significant in univariate analysis: no multivariate analysis performed or factor in multivariate analysis not significant; ++, significant in multivariate analysis; -, no association in univariate analysis: no multivariate analysis performed or factor not included in multivariate analysis; –, no association in multivariate analysis; ?, results of geriatric domain not described; np, number of compromised patients was too low: statistical analysis was not possible
Abbreviations: ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living

the traditional geriatric ones, because the oncological population may be faced with referral bias. The most vulnerable older patients with cancer are less likely to be referred to the oncologist. As a result, the population in the oncological setting has less functional and cognitive impairment than the population in which these tools were developed and tested.

Another reason for the null effects of the GA in predicting outcomes is the occurrence of other potential sources of bias. First, all patients were considered fit enough to undergo oncological treatment, and the decision whether a patient was eligible for chemotherapy or surgery had already been taken, leading to selection bias. For instance, a frequently used exclusion criterion for study participation was the presence of dementia or cognitive impairment – even in studies that aimed to assess the predictive value of cognitive impairment for oncological outcomes. Another potential bias is that often the treating physician was not blinded from the outcome of the GA. Hence, the treating physician might assume that patients with an impaired GA would not be able to tolerate standard treatment, and, consequently, he might decide to offer the patient adapted oncologic treatment based on the outcome of the GA affecting the outcome. Lastly, the ceiling effects of some

**Table 4**
Association of individual geriatric domain with chemotherapy-related outcomes.

| Outcome | Study | Cancer type | Nr of patients | Functional status | | Nutrition | Cognition | Mood | Physical function | Fatigue | Social Support | Falls |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | ADL | IADL | | | | | | | |
| Chemotherapy Toxicity | Aparicio [66] | Colorectal | 123 | | ++ | | ++ | - | | | | |
| | Baitar [67] | Various | 85 | ? | ? | ? | +[a] | ? | | | ? | |
| | Bila [69] | Hematological | 110 | | - | | | | | | | |
| | Clough-Gorr [41] | Breast | 660 | | | | | ++ | | | ++ | |
| | Extermann [49] | Various | 518 | - | | + | + | - | | | | |
| | Goede [30] | Hematological | 75 | | + | | - | | + | | | |
| | Hamaker [73] | Breast | 78 | | - | np | - | - | | | | |
| | Hurria [7] | Solid tumors | 500 | ? | ? | ? | ? | ? | + | | ? | + |
| | Marinello [75] | Breast, lung, and colorectal | 110 | np | - | | np | | | | | |
| | Naito [50] | Hematological | 93 | | - | + | - | - | | | | |
| | Puts [40] | Various | 112 | - | - | - | - | - | ++ | - | | |
| | Wildes [78] | Colorectal, lung, breast, and lymphoma | 65 | - | - | - | - | - | | | | - |
| Chemotherapy Completion | Aaldriks [31] | Breast | 55 | | | -- | -- | | | | | |
| | Aaldriks [51] | Hematological | 44 | | | ++ | -- | | | | | |
| | Aaldriks [8] | Various | 202 | | | + | + | | | | | |
| | Aaldriks [32] | Various | 494 | | | ++ | - | | | | | |
| | Aaldriks [33] | Colorectal | 143 | | | + | + | | | | | |
| | Park [38] | Hematological | 70 | | | ++ | - | - | | | | |
| Functional decline after first cycle chemotherapy | Hoppe [48] | Various | 364 | | ++ | + | + | ++ | + | | | |
| Nr of positive results/all studies (%) | | | | 1/7 (14%) | 3/11 (27%) | 8/14 (57%) | 6/17 (35%) | 2/11 (18%) | 4/4 (100%) | 0/1 (0%) | 1/3 (33%) | 1/2 (50%) |

+, significant in univariate analysis: no multivariate analysis performed or factor in multivariate analysis not significant; ++, significant in multivariate analysis; -, no association in univariate analysis: no multivariate analysis performed or factor not included in multivariate analysis; –, no association in multivariate analysis; ?, results of geriatric domain not described; np, number of compromised patients was too low: statistical analysis was not possible
Abbreviations: ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living
[a] Better cognitive function had a higher risk for a SAE

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measurements could explain the fact that only a few studies found components of the GA to be useful in predicting outcomes. The ceiling effect, as noted by Hurria et al. [52], is the effect that arises when most of the participants score the maximum score possible on a test because the test is unable to distinguish between individuals at the higher score range of the test.

This review has several strengths. We used systematic methods to select all relevant studies, and two reviewers independently assessed the selected studies on relevance and quality according to the QUIPS tool, a tool especially designed to assess the quality of prognostic studies [16,17]. In addition, no studies were excluded on the basis of quality assessment, because we have attempted to deliver a complete overview of all the current published evidence in an unbiased and reproducible way. We then provided an overview of the positive as well as the negative results. Last, we limited the selection of studies to the age cutoff of 65 years to avoid reviewing the GA domains in the "youngest old" (60–65 years) or young patients because these results may be difficult to extrapolate to our target group: the older patients with cancer (≥70 years or older).

This review also has several limitations. The scientific quality of the studies varied widely, and some quality criteria were not reported and consequently rated as having a high risk of bias. Another limitation might be the risk of publication bias. The literature is probably populated with positive studies that would not have been submitted or published had the results been different. Finally, in this systematic review we focused on studies assessing multiple geriatric domains as part of a GA. Studies focusing on single geriatric conditions or including multiple conditions but not labelled as geriatric assessment, may have been overlooked by our search strategy.

This is not the first systematic review assessing the predictive value of geriatric assessment. In 2012, Puts et al. were the first authors to conduct a systematic review of the use of geriatric assessment in oncology [53]. Since Puts' review was published, several systematic reviews have followed. To our knowledge, the most recent systematic reviews were published in 2015 and the authors performed their literature search in respectively September 2013 and June 2013 [13,14]. Thus a new systematic review was needed to obtain an overview of the most recent evidence, since more than half of the studies selected in our review were published in 2014 or later.

Moreover, some systematic reviews did not provide a complete overview of the current evidence for the predictive ability of the individual GA domains because they applied strict eligibility criteria. Caillet et al. [54] only selected the studies with a prospective study design, a sample size of at least 100 patients with a solid tumor, and in which the GA consisted of at least 5 GA domains. Similarly, Handforth et al. [13] and Ramjaun et al. [55] only included studies if they used a GA in which respectively three and six domains were assessed.

Three systematic reviews were published with the same aim, a similar literature search, and comparable inclusion criteria as our review. The first review, Puts et al. [53], concluded that ADL, comorbidity, and cognition were the domains consistently associated with mortality, postoperative complications, and chemotherapy-related outcomes. The second systematic review, Puts et al. [56], an update of Puts' first review, concluded that ADL, IADL, performance status, depression, and frailty were associated with poor health outcomes. The third review, Hamaker et al. [57], concluded that different conditions appeared to be predictive for the primary outcome measures and that the only consistent finding was the association between a summary score of the geriatric assessment and mortality. These findings differed from our findings for the following reasons: first, we made a clear distinction between domains that should be part of the geriatric assessment and domains that should be part of the routine oncological work-up (such as comorbidity and polypharmacy). In our opinion, comorbidity and polypharmacy should be explored in every patient, regardless of age, and therefore should not be considered part of the GA. Secondly, our only consistent finding was the predictive ability of physical function for mortality, postoperative complications, and chemotherapy-related outcomes, whereas Puts et al. found ADL as the consistently associated domain and Hamaker et al. did not find a consistent domain at all. These different findings could be explained by the fact that our literature search was more recent. For instance, the majority of the studies including physical function in their GA were published in 2014 or later. Another explanation could be that we only selected studies reporting predictive values of the individual domains, whereas Puts et al. and Hamaker et al. also selected studies that assessed the predictive ability of geriatric domains as part of a summary score or as part of the definition of frailty.

Interestingly, no study assessed the ability of individual geriatric domains in predicting systemic treatment-related outcomes other than chemotherapy. Other systemic antitumor treatments, such as targeted therapy or immune therapy, may lead to side effects other than chemotherapy impacting the predictive ability of the individual geriatric domains.

Based on the current systematic review, we may conclude that physical function and nutritional status are the best domains to predict mortality, postoperative complications, and chemotherapy-related outcomes in older patients with cancer and therefore should certainly be included in the GA. However, whether this means that assessing the other domains is redundant is debatable. First, the content of the GA should depend on which primary outcome one wants to predict with the GA. Every geriatric domain appears to be predictive for a different oncological outcome. For example, in almost half of the studies, an impaired ADL was significantly predictive for postoperative complications. On the contrary, no study found an association between an impaired ADL and toxicity of chemotherapy. Second, because of the heterogeneity of studies, it remains questionable whether the same geriatric impairments are relevant for patient with breast cancer undergoing surgery as for a patient with lung cancer receiving palliative chemotherapy. Still, there is no consensus regarding which assessment tools and cutoff scores should be used to identify an impaired domain.

Nevertheless, in our opinion, the aim of the GA is not only to predict various outcomes, but it should be used as a tool to develop individually tailored geriatric interventions. Interventions could be based on the identified impaired GA domains to improve tolerability of the antitumor treatment, and even more important, to maintain the quality of life and the independency as much as possible. According to a review by Hamaker et al. [58], >70% of the GAs have resulted in geriatric recommendations and interventions in older patients with cancer. In the non-cancer population, the implementation of these GA-based interventions have been shown to improve a variety of outcomes, such as decreased risk of death and a decreased risk of nursing home placement [59]. Unfortunately, there has been little investigation into the benefit of GA-based interventions for the older patient with cancer. Consequently, the few RCTs that have been performed are not generalizable to daily practice, because few have been applied in a chemotherapy setting, the studies focused on one particular domain, and the studies were conducted in older patients with just one tumor type [60–65]. To our knowledge, only one recent prospective cohort study published the impact of GA-based intervention on chemotherapy tolerance in older patients with cancer. In this study, the intervention group was more likely to complete antitumor treatment and required fewer treatment modifications compared to the control group without the interference of a geriatrician [65]. Fortunately, RCTs are currently ongoing to establish whether GA-based interventions may improve the impaired geriatric domains and may result in an improved tolerability of antitumor treatment, thereby contributing to better quality of life and maintenance of independency.

In conclusion, physical function and nutritional status should be included in the GA for older patients with cancer, especially when the GA's most important aim is predicting outcomes. Nevertheless, physical function and nutritional status have not only appeared to be the

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domains most predictive for our defined outcomes, but interventions to improve these domains may also be simple to implement, such as physiotherapy for muscle reinforcement in case of an impaired physical function, or referral to the dietician for advices on increasing dietary uptake or nutritional supplements in case of malnutrition. For the other domains, the findings are too inconsistent to draw conclusions about their inclusion in or exclusion from the GA with the aim to predict relevant outcomes. However, when the GA is used as a tool for optimizing care for older patients with cancer, a broad geriatric assessment is needed to identify all present impairments, serving as a base for a geriatric treatment plan as well as for geriatric follow-up.

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## Author Contribution

Conception and design: C.P. Bruijnen, D.G. van Harten- Krouwel, J.J. Koldenhof, M.H. Emmelot- Vonk, and P.O. Witteveen.
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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2019.02.010.

## References

[1] Surveillance, Epidemiology and End Results: SEER Cancer Statistics Review. 2009–2016 https://seer.cancer.gov/statfacts/html/all.html; 2016, Accessed date: 12 July 2016.
[2] Hurria A. Clinical trials in older adults with cancer: past and future. Oncology (Williston Park) 2007;21:351–8.
[3] Ritchie CS, Kvale E, Fisch MJ. Multimorbidity: an issue of growing importance for oncologists. J Oncol Pract 2011;7:371–4. https://doi.org/10.1200/JOP.2011.000460.
[4] Kenis C, Bron D, Libert Y, Decoster L, Van Puyvelde K, Scalliet P, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer: results of a prospective multicentric study. Ann Oncol 2013;24:1306–12. https://doi.org/10.1093/annonc/mds619.
[5] Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen MLG, Extermann M, et al. international society of geriatric oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol 2014;32:2595–603. https://doi.org/10.1200/JCO.2013.54.8347.
[6] Stuck A, Siu A, Wieland G, Rubenstein L, Adams J. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet 1993;342:1032–6. https://doi.org/10.1016/0140-6736(93)92884-V.
[7] Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol 2011;29:3457–65. https://doi.org/10.1200/JCO.2011.34.7625.
[8] Aaldriks AA, Maartense E, le Cessie S, Giltay EJ, Verlaan HACM, van der Geest LGM, et al. Predictive value of geriatric assessment for patients older than 70 years, treated with chemotherapy. Crit Rev Oncol Hematol 2011;79:205–12. https://doi.org/10.1016/j.critrevonc.2010.05.009.
[9] Chaibi P, Magne N, Breton S, Chebib A, Watson S, Duron J-J, et al. Influence of geriatric consultation with comprehensive geriatric assessment on final therapeutic decision in elderly cancer patients. Crit Rev Oncol Hematol 2011;79:302–7. https://doi.org/10.1016/j.critrevonc.2010.08.004.
[10] Freyer G, Geay JF, Touzet S, Provencal J, Weber B, Jacquin JP, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. Ann Oncol 2005;16:1795–800. https://doi.org/10.1093/annonc/mdi368.
[11] Extermann M, Aapro M, Bernabei R, Cohen HJ, Droz J-P, Lichtman S, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the international society of geriatric oncology (SIOG). Crit Rev Oncol Hematol 2005;55:241–52. https://doi.org/10.1016/j.critrevonc.2005.06.003.
[12] Sattar S, Alibhai SMH, Wildiers H, Puts MTE. How to implement a geriatric assessment in your clinical practice. Oncologist 2014;19:1056–68. https://doi.org/10.1634/theoncologist.2014-0180.
[13] Handforth C, Clegg a Young C, Simpkins S, Seymour MT, Selby PJ, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. Ann Oncol 2014:1–11. https://doi.org/10.1093/annonc/mdu540.
[14] Feng Ma, DT McMillan, Crowell K, Muss H, Nielsen ME, Smith AB. Geriatric assessment in surgical oncology: a systematic review. J Surg Res 2015;193:265–72. https://doi.org/10.1016/j.jss.2014.07.004.
[15] Moher D, Liberati A, Tetzlaff J. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12. https://doi.org/10.1016/j.jcms.2010.11.001.
[16] Hayden JA, Côté P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. Ann Intern Med 2006;144 (427–37. doi:144/6/427 [pii]).
[17] J A Hayden, Van Der Windt DA, Cartwright JL, Co P. Research and reporting methods annals of internal medicine assessing Bias in studies of prognostic factors. Ann Intern Med 2013;144:427–37. https://doi.org/10.7326/0003-4819-158-4-201302190-00009.
[18] Riley RD, Hayden JA, Steyerberg EW, Moons KGM, Abrams K, Kyzas PA, et al. Prognosis research strategy (PROGRESS) 2: prognostic factor research. PLoS Med 2013;10:e1001380. https://doi.org/10.1371/journal.pmed.1001380.
[19] Araujo SEA, de Paris Caravatto PP, de Campos FGCM, da Silva e Sousa AHJ, Nahas SC, Kiss DR, et al. Colorectal cancer among patients aged 75 years or over. Hepatogastroenterology 2007;54:427–30.
[20] Huisman MG, Veronese G, Audisio RA, Ugolini G, Montroni I, de Bock GH, et al. Poor nutritional status is associated with other geriatric domain impairments and adverse postoperative outcomes in onco-geriatric surgical patients - a multicentre cohort study. Eur J Surg Oncol 2016;42:1009–17. https://doi.org/10.1016/j.ejso.2016.03.005.
[21] Huisman MG, Audisio RA, Ugolini G, Montroni I, Vigano A, Spiliotis J, et al. Screening for predictors of adverse outcome in onco-geriatric surgical patients: a multicenter prospective cohort study. Eur J Surg Oncol 2015;41:844–51. https://doi.org/10.1016/j.ejso.2015.02.018.
[22] Giantin V, Valentini E, Iasevoli M, Falci C, Siviero P, De Luca E, et al. Does the multidimensional prognostic index (MPI), based on a comprehensive geriatric assessment (CGA), predict mortality in cancer patients? Results of a prospective observational trial. J Geriatr Oncol 2013;4:208–17. https://doi.org/10.1016/j.jgo.2013.04.008.
[23] Huisman MG, van Leeuwen BL, Ugolini G, Montroni I, Spiliotis J, Stabilini C, et al. "Timed up & go": a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A multicenter cohort study. PLoS One 2014;9:e86863. https://doi.org/10.1371/journal.pone.0086863.
[24] Kenig J, Olszewska U, Zychiewicz B, Barczynski M, Mituś-Kenig M. Cumulative deficit model of geriatric assessment to predict the postoperative outcomes of older patients with solid abdominal cancer. J Geriatr Oncol 2015;6:370–9. https://doi.org/10.1016/j.jgo.2015.03.004.
[25] Suh DH, Kim J-W, Kim HS, Chung HH, Park NH, Song YS. Pre- and intra-operative variables associated with surgical complications in elderly patients with gynecologic cancer: the clinical value of comprehensive geriatric assessment. J Geriatr Oncol 2014;5:315–22. https://doi.org/10.1016/j.jgo.2014.03.004.
[26] Ferrat E, Paillaud E, Laurent M, Le Thuaut A, Caillet P, Tournigand C, et al. Predictors of 1-year mortality in a prospective cohort of elderly patients with Cancer ; on behalf of the ELPACA study group*. J Gerontol A Biol Sci Med Sci 2015;70:1148–55. https://doi.org/10.1093/gerona/glv025.
[27] Ugolini G, Pasini F, Ghignone F, Zattoni D, Bacchi Reggiani ML, Parlanti D, et al. How to select elderly colorectal cancer patients for surgery: a pilot study in an Italian academic medical center. Cancer Biol Med 2015;12:302–7. https://doi.org/10.7497/j.issn.2095-3941.2015.0084.
[28] Hamaker ME, Mitrovic M, Stauder R. The G8 screening tool detects relevant geriatric impairments and predicts survival in elderly patients with a haematological malignancy. Ann Hematol 2014;93:1031–40. https://doi.org/10.1007/s00277-013-2001-0.
[29] Soubeyran P, Fonck M, Blanc-Bisson C, Blanc J-FF, Ceccaldi J, Mertens C, et al. Predictors of early death risk in older patients treated with first-line chemotherapy for cancer. J Clin Oncol 2012;30:1829–34. https://doi.org/10.1200/JCO.2011.35.7442.
[30] Goede V, Bahlo J, Chataline V, Eichhorst B, Dürig J, Stilgenbauer S, et al. Evaluation of geriatric assessment in patients with chronic lymphocytic leukemia: Results of the CLL9 trial of the German CLL study group. Leuk Lymphoma 2016;57:789–96.
[31] Aaldriks AA, Giltay EJ, le Cessie S, van der Geest LGM, Portielje JEA, Tanis BC, et al. Prognostic value of geriatric assessment in older patients with advanced breast cancer receiving chemotherapy. Breast 2013;22:753–60. https://doi.org/10.1016/j.breast.2013.01.011.
[32] Aaldriks AA, Maartense E, Nortier HJWR, van der Geest LGM, le Cessie S, Tanis BC, et al. Prognostic factors for the feasibility of chemotherapy and the geriatric prognostic index (GPI) as risk profile for mortality before chemotherapy in the elderly. Acta Oncol 2016;55:15–23. https://doi.org/10.3109/0284186X.2015.1068446.
[33] Aaldriks AA, van der Geest LGM, Giltay EJ, le Cessie S, Portielje JEA, Tanis BC, et al. Frailty and malnutrition predictive of mortality risk in older patients with advanced

colorectal cancer receiving chemotherapy. J Geriatr Oncol 2013;4:218–26. https://doi.org/10.1016/j.jgo.2013.04.001.
[34] Gironés R, Torregrosa D, Maestu I, Gómez-Codina J, Tenias JM, Costa RR. Comprehensive geriatric assessment (CGA) of elderly lung cancer patients: a single-center experience. J Geriatr Oncol 2012;3:98–103.
[35] Kanesvaran R, Li H, Koo K-N, Poon D. Analysis of prognostic factors of comprehensive geriatric assessment and development of a clinical scoring system in elderly Asian patients with cancer. J Clin Oncol 2011;29:3620–7. https://doi.org/10.1200/JCO.2010.32.0796.
[36] Kristjansson SR, Jordhøy MS, Nesbakken A, Skovlund E, Bakka A, Johannessen H-O, et al. Which elements of a comprehensive geriatric assessment (CGA) predict post-operative complications and early mortality after colorectal cancer surgery? J Geriatr Oncol 2010;1:57–65.
[37] Ommundsen N, Wyller TB, Nesbakken A, Jordhøy MS, Bakka A, Skovlund E, et al. Frailty is an independent predictor of survival in older patients with colorectal cancer. Oncologist 2014;19:1268–75. https://doi.org/10.1634/theoncologist.2014-0237.
[38] Park S, Hong J, Hwang I, Ahn J-Y, Cho EY, Park J, et al. Comprehensive geriatric assessment in elderly patients with newly diagnosed aggressive non-Hodgkin lymphoma treated with multi-agent chemotherapy. J Geriatr Oncol 2015;6:470–8.
[39] Hamaker ME, Buurman BM, van Munster BC, Kuper IMJA, Smorenburg CH, de Rooij SE. The value of a comprehensive geriatric assessment for patient care in acutely hospitalized older patients with cancer. Oncologist 2011;16:1403–12. https://doi.org/10.1634/theoncologist.2010-0433.
[40] Puts MTE, Monette J, Girre V, Pepe C, Monette M, Assouline S, et al. Are frailty markers useful for predicting treatment toxicity and mortality in older newly diagnosed cancer patients? Results from a prospective pilot study. Crit Rev Oncol Hematol 2011;78:138–49. https://doi.org/10.1016/j.critrevonc.2010.04.003.
[41] Clough-Gorr KM, Stuck AE, Thwin SS. Silliman R a. Older breast cancer survivors: geriatric assessment domains are associated with poor tolerance of treatment adverse effects and predict mortality over 7 years of follow-up. J Clin Oncol 2010;28:380–6. https://doi.org/10.1200/JCO.2009.23.5440.
[42] Brunello A, Fontana A, Zafferri V, Panza F, Fiduccia P, Basso U, et al. Development of an oncological-multidimensional prognostic index (Onco-MPI) for mortality prediction in older cancer patients. J Cancer Res Clin Oncol 2016;142:1069–77. https://doi.org/10.1007/s00432-015-2088-x.
[43] Audisio RA, Pope D, Ramesh HSJ, Gennari R, van Leeuwen BL, West C, et al. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. Crit Rev Oncol Hematol 2008;65:156–63. https://doi.org/10.1016/j.critrevonc.2007.11.001.
[44] Badgwell B, Stanley J, Chang GJ, Katz MHG, Lin HY, Ning J, et al. Comprehensive geriatric assessment of risk factors associated with adverse outcomes and resource utilization in cancer patients undergoing abdominal surgery. J Surg Oncol 2013;108:182–6. https://doi.org/10.1002/jso.23369.
[45] Choi J-Y, Yoon S-J, Kim S-W, Jung H-W, Kim K-I, Kang E, et al. Prediction of postoperative complications using multidimensional frailty score in older female Cancer patients with American Society of Anesthesiologists Physical Status Class 1 or 2. J Am Coll Surg 2015;221:652–60 e2 https://doi.org/10.1016/j.jamcollsurg.2015.06.011.
[46] Mokutani Y, Mizushima T, Yamasaki M, Rakugi H, Doki Y, Mori M. Prediction of postoperative complications following elective surgery in elderly patients with colorectal Cancer using the comprehensive geriatric assessment. Dig Surg 2016;33:470–7. https://doi.org/10.1159/000446709.
[47] Baier P, Ihorst G, Wolff-Vorbeck G, Hull M, Hopt U, Deschler B. Independence and health related quality of life in 200 onco-geriatric surgical patients within 6 months of follow-up: who is at risk to lose? Eur J Surg Oncol 2016. https://doi.org/10.1016/j.ejso.2016.07.013.
[48] Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc JF, Ceccaldi J, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol 2013;31:3877–82. https://doi.org/10.1200/JCO.2012.47.7430.
[49] Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, Defelice J, et al. Predicting the risk of chemotherapy toxicity in older patients: the chemotherapy risk assessment scale for high-age patients (CRASH) score. Cancer 2012;118:3377–86. https://doi.org/10.1002/cncr.26646.
[50] Naito Y, Sasaki H, Takamatsu Y, Kiyomi F, Tamura K. Retrospective analysis of treatment outcomes and geriatric assessment in elderly malignant lymphoma patients. J Clin Exp Hematop 2016;56:43–9. https://doi.org/10.3960/jslrt.56.43.
[51] a a Aaldriks, Giltay EJ, Nortier JWR, Van Geest LGM, Tanis BC, Ypma P, et al. Prognostic significance of geriatric assessment in combination with laboratory parameters in elderly patients with aggressive non-Hodgkin lymphoma. Leuk Lymphoma 2015;56:927–35. https://doi.org/10.3109/10428194.2014.935364.
[52] Hurria A, Hurria A, Zuckerman E, Panageas KS, Fornier M, D'Andrea G, et al. A prospective, longitudinal study of the functional status and quality of life of older patients with breast cancer receiving adjuvant chemotherapy. J Am Geriatr Soc 2006;54:1119–24. https://doi.org/10.1111/j.1532-5415.2006.00789.x.
[53] Puts MTE, Hardt J, Monette J, Girre V, Springall E, Alibhai SMH. Use of geriatric assessment for older adults in the oncology setting: a systematic review (provisional abstract). J Natl Cancer Inst 2012;104:1133–63. https://doi.org/10.1093/jnci/djs285.
[54] Caillet P, Laurent M, Bastuji-Garin S, Liuu E, Culine S, Lagrange J-L, et al. Optimal management of elderly cancer patients: usefulness of the comprehensive geriatric assessment. Clin Interv Aging 2014;9:1645–60. https://doi.org/10.2147/CIA.S57849.
[55] Ramjaun A, Nassif MO, Krotneva S, Huang AR, Meguerditchian AN. Improved targeting of cancer care for older patients: a systematic review of the utility of comprehensive geriatric assessment. J Geriatr Oncol 2013;4:271–81. https://doi.org/10.1016/j.jgo.2013.04.002.
[56] Puts M, Santos B, Hardt J, Monette J, Girre V, Springall E, et al. An update on a systematic review of the use of geriatric assessment for older adults in oncology. Support Care Cancer 2013;21:S200. https://doi.org/10.1007/s00520-013-1798-3.
[57] Hamaker ME, Vos AG, Smorenburg CH, de Rooij SE, van Munster BC. The value of geriatric assessments in predicting treatment tolerance and all-cause mortality in older patients with cancer. Oncologist 2012;17:1439–49. https://doi.org/10.1634/theoncologist.2012-0186.
[58] Hamaker ME, Schiphorst AH, Ten Bokkel Huinink D, Schaar C, van Munster BC. The effect of a geriatric evaluation on treatment decisions for older cancer patients - a systematic review. Acta Oncol 2013:1–8. https://doi.org/10.3109/0284186X.2013.840741.
[59] Magnuson A, Allore H, Cohen HJ, Mohile SG, Williams GR, Chapman A, et al. Geriatric assessment with management in cancer care: current evidence and potential mechanisms for future research. J Geriatr Oncol 2016;7:242–8. https://doi.org/10.1016/j.jgo.2016.02.007.
[60] Bourdel-Marchasson I, Blanc-Bisson C, Doussau A, Germain C, Blanc JF, Dauba J, et al. Nutritional advice in older patients at risk of malnutrition during treatment for chemotherapy: a two-year randomized controlled trial. PLoS One 2014;9. https://doi.org/10.1371/journal.pone.0108687.
[61] Rao a V, Hsieh F, Feussner JR, Cohen HJ. Geriatric evaluation and management units in the care of the frail elderly cancer patient. J Gerontol A Biol Sci Med Sci 2005;60:798–803. https://doi.org/10.1093/gerona/60.6.798.
[62] Goodwin JS, Satish S, Anderson ET, Nattinger a B, Freeman JL. Effect of nurse case management on the treatment of older women with breast cancer. J theAmericanGeriatrics Soc 2003;51:1252–9.
[63] McCorkle R, Strumpf NE, Nuamah IF, Adler DC, Cooley ME, Jepson C, et al. A specialized home care intervention improves survival among older post-surgical cancer patients. J Am Geriatr Soc 2000;48:1707–13.
[64] Soubeyran P, Terret C, Bellera C, Bonnetain F, Saint Jean O, Galvin A, et al. Role of geriatric intervention in the treatment of older patients with cancer: rationale and design of a phase III multicenter trial. BMC Cancer 2016;16:183–5. https://doi.org/10.1186/S12885-016-2927-4.
[65] Kalsi T, Babic-Illman G, Ross PJ, Maisey NR, Hughes S, Fields P, et al. The impact of comprehensive geriatric assessment interventions on tolerance to chemotherapy in older people. Br J Cancer 2015;112:1435–44. https://doi.org/10.1038/bjc.2015.120.
[66] Aparicio T, Jouve JL, Teillet L, Gargot D, Subtil F, Le Brun-Ly V, et al. Geriatric factors predict chemotherapy feasibility: ancillary results of FFCD 2001-02 phase III study in first-line chemotherapy for metastatic colorectal cancer in elderly patients. J Clin Oncol 2013;31. https://doi.org/10.1200/JCO.2012.42.9894 1464–70.
[67] Baitar A, Van Fraeyenhove F, Vandebroek A, De Droogh E, Galdermans D, Mebis J, et al. Geriatric screening results and the association with severe treatment toxicity after the first cycle of (radio)chemotherapy. J Geriatr Oncol 2014;5:179–84. https://doi.org/10.1016/j.jgo.2013.12.004.
[68] Biesma B, Wymenga ANM, Vincent A, Dalesio O, Smit HJM, Stigt JA, et al. Quality of life, geriatric assessment and survival in elderly patients with non-small-cell lung cancer treated with carboplatin-gemcitabine or carboplatin-paclitaxel: NVALT-3 a phase III study. Ann Oncol 2011;22:1520–7. https://doi.org/10.1093/annonc/mdq637.
[69] Bila J, Jelicic J, Djurasinovic V, Vukovic V, Sretenovic A, Andjelic B, et al. Prognostic effect of comorbidity indices in elderly patients with multiple myeloma. Clin Lymphoma Myeloma Leuk 2015;15:416–9. https://doi.org/10.1016/j.clml.2015.03.004.
[70] Denewet N, De Breucker S, Luce S, Kennes B, Higuet S, Pepersack T. Comprehensive geriatric assessment and comorbidities predict survival in geriatric oncology. Acta Clin Belg 2016;71:206–13. https://doi.org/10.1080/17843286.2016.1153816.
[71] Dubruille S, Libert Y, Roos M, Vandenbossche S, Collard A, Meuleman N, et al. Identification of clinical parameters predictive of one-year survival using two geriatric tools in clinically fit older patients with hematological malignancies: major impact of cognition. J Geriatr Oncol 2015;6:362–9. https://doi.org/10.1016/j.jgo.2015.07.006.
[72] Ghosn M, Ibrahim T, El Rassy E, Nassani N, Ghanem S, Assi T. Abridged geriatric assessment is a better predictor of overall survival than the Karnofsky performance scale and physical performance test in elderly patients with cancer. J Geriatr Oncol 2017;8:128–32. https://doi.org/10.1016/j.jgo.2016.11.002.
[73] Hamaker ME, Seynaeve C, Wymenga aNM, Van Tinteren H, Nortier JWR, Maartense E, et al. Baseline comprehensive geriatric assessment is associated with toxicity and survival in elderly metastatic breast cancer patients receiving single-agent chemotherapy: Results from the OMEGA study of the Dutch Breast Cancer Trialists' Group. Breast 2013;23:81–7. https://doi.org/10.1016/j.breast.2013.11.004.
[74] Jonna S, Chiang L, Liu J, Carroll MB, Flood K, Wildes TM. Geriatric assessment factors are associated with mortality after hospitalization in older adults with cancer. Support Care Cancer Off J Multinatl Assoc Support Care Cancer 2016. https://doi.org/10.1007/s00520-016-3334-8.
[75] Marinello R, Marenco D, Roglia D, Stasi MF, Ferrando A, Ceccarelli M, et al. Predictors of treatment failures during chemotherapy: a prospective study on 110 older cancer patients. Arch Gerontol Geriatr 2009;48:222–6. https://doi.org/10.1016/j.archger.2008.01.011.
[76] Merli F, Luminari S, Rossi G, Mammi C, Marcheselli L, Ferrari A, et al. Outcome of frail elderly patients with diffuse large B-cell lymphoma prospectively identified by comprehensive geriatric assessment: results from a study of the Fondazione Italiana

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Linfomi. Leuk Lymphoma 2014;55:38–43. https://doi.org/10.3109/10428194.2013.788176.

[77] Spina M, Balzarotti M, Uziel L, Ferreri AJM, Fratino L, Magagnoli M, et al. Modulated chemotherapy according to modified comprehensive geriatric assessment in 100 consecutive elderly patients with diffuse large B-cell lymphoma. Oncologist 2012;17:838–46. https://doi.org/10.1634/theoncologist.2011-0417.

[78] Wildes TM, Ruwe AP, Fournier C, Gao F, Carson KR, Piccirillo JF, et al. Geriatric assessment is associated with completion of chemotherapy, toxicity, and survival in older adults with cancer. J Geriatr Oncol 2013;4:227–34. https://doi.org/10.1016/j.jgo.2013.02.002.