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Geriatric Oncology

The Value of Geriatric Assessments in Predicting Treatment Tolerance and All-Cause Mortality in Older Patients With Cancer

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LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Describe the predictive value of geriatric assessments for survival in older cancer patients.
2. Describe the predictive value of geriatric assessments for treatment tolerance (such as toxicity of chemotherapy and perioperative complications) in older cancer patients.
3. Explain the concept of frailty compared to individual geriatric conditions.

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ABSTRACT

Background. **Awareness of the use of geriatric assessments for older patients with cancer is increasing. The aim of this review is to summarize all available evidence on the association between geriatric assessments and relevant oncologic outcomes.**

Method. **A systematic search was conducted in Medline and Embase of studies on geriatric assessment in oncology, focusing on the association between baseline assessment and outcome.**

Results. **The literature search identified 2008 reports; 51 publications from 37 studies were selected for inclusion in the review. The quality of studies was heterogeneous and generally poor. A median of five geriatric conditions were assessed per study (interquartile range: 4–8). Little consistency was found in the results of the studies. Furthermore, different tools appear to be predictive depending on the outcome measure: frailty, nutritional status, and comorbidity assessed by the Cumulative Illness Rating Scale for Geriatrics were predictive for all-cause mortality; frailty was predictive for toxicity of chemotherapy; cognitive impairment and activities of daily living impairment were predictive for**

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chemotherapy completion; and instrumental activities of daily living impairment was predictive for perioperative complications.

Conclusion. **Although various geriatric conditions appear to be of some value in predicting outcome in elderly patients with cancer, the results are too inconsistent to guide treatment decisions. Further research is needed to elucidate the role of geriatric assessments in the oncologic decision-making process for these patients.** ***The Oncologist*** 2012;17:1439–1449

INTRODUCTION

Although malignant tumors occur at all ages, cancer disproportionately strikes individuals aged 65 years and older [1]. In addition, the number of elderly patients with cancer will increase substantially in the coming decades as a result of increasing life expectancy and aging of the population. Oncologists are faced with the challenge of determining the optimal treatment for these patients, with their heterogeneity in comorbidity, physical reserve, disabilities, and geriatric conditions. In this context, a myriad of editorials and review articles have been published, endorsing the use of a comprehensive geriatric assessment (CGA) in geriatric oncology [2–9]. A CGA is a systematic procedure used to objectively appraise the health status of older people, focusing on somatic, functional, and psychosocial domains [2] and aimed at constructing a multidisciplinary treatment plan. Its value in geriatric medicine has been proven extensively [10], but outside this field, the evidence is more scarce.

Oncology studies comparing treatment choices in patients that are considered fit or frail on the basis of a CGA have shown that frail patients receive less intensive treatment or receive no treatment at all [11, 12]. Although this shows that standard medical assessment overlaps in part with geriatric assessment, an additional value of the latter is its ability to identify previously unrecognized but potentially modifiable health issues, such as depressive symptoms, cognitive or functional impairment, and malnutrition [4, 5, 7]. In addition, some studies are now using CGA to assess patients for trial eligibility or to allocate them to alternative treatments regimens [13, 14]. However, the legitimacy of such decision-making protocols has been insufficiently proven thus far. It remains unclear how to translate data from the CGA to clinical practice: Should geriatric assessment only be used to classify patients as fit, vulnerable, or frail, or do individual geriatric conditions have predictive value for relevant patient outcomes?

Therefore, the aim of this systematic review is to summarize all available evidence on the association between CGA (its individual domains as well as the summarized assessment of vulnerability) and clinically relevant outcomes, such as all-cause mortality, chemotherapy toxicity, chemotherapy completion, perioperative complications, and radiotherapy tolerance.

METHODS

Search Strategy and Article Selection

Our aim was to identify cohort studies that investigated the association between baseline geriatric assessment and outcome in patients with cancer, independent of age, cancer type, or stage of disease. For this purpose, a geriatric assessment was defined as an assessment using validated assessment tools composed of two or more of the following distinct domains: cognitive function, mood/depression, nutritional status, activities of daily living (ADL), instrumental activities of daily living (IADL), comorbidity, polypharmacy, mobility/falls, and frailty. Studies only using nonvalidated assessment tools or nonvalidated subscales of validated assessment tools were excluded. We also excluded studies that included other patient groups in addition to patients with cancer, as well as studies using a treatment protocol in which the outcome of the geriatric assessment determined treatment choice. For outcome, the following items were defined: all-cause mortality, toxicity of chemotherapy, chemotherapy completion, perioperative complications, and radiotherapy completion and toxicity.

We performed the following search in both Medline and Embase on February 15, 2012: ((“Geriatric Assessment” [Mesh]) OR (geriatric assessment*[tiab])) AND ((“Neoplasms”[Mesh]) OR (neoplasm*[tiab] OR cancer*[tiab] OR tumour[tiab] OR tumours[tiab] OR tumor[tiab] OR tumors[tiab] OR oncolog*[tiab] OR malignan*[tiab])) (Mesh indicates medical subheading; tiab, title/abstract). No limits in age, language, or publication date were applied to the search.

In addition, conference abstracts for the 2007–2011 scientific meetings of the American Society of Clinical Oncology, European Society of Medical Oncology, International Society of Geriatric Oncology, American Geriatric Society, and European Geriatric Medicine Society (EUGMS) were handsearched for studies on geriatric assessments in patients with cancer to identify additional eligible studies.

The titles and abstracts of all studies retrieved by the search were assessed by one investigator (M.H.) to determine which were eligible for further investigation. All potentially relevant articles were subsequently screened as full text by two authors (M.H. and A.V.). In case only an abstract was available, we attempted to find a final report of the study by searching Embase and Medline using the names of first, second, and/or final authors as well as key words from the title. Also, in case of insufficient data in the original manuscript, the authors were contacted for additional information (e.g., about the tools used in the geriatric assessment). Finally, references of included publications were cross-referenced to retrieve any additional relevant citations.

Data Extraction

Data regarding study design and results were independently extracted by two investigators (M.H. and A.V.) for each eligible study. Items that were extracted included the type of study, study setting, study population (cancer type, cancer stage, cancer treatment), content of geriatric assessment and assessment tools used, outcome measures examined, methods of statistical

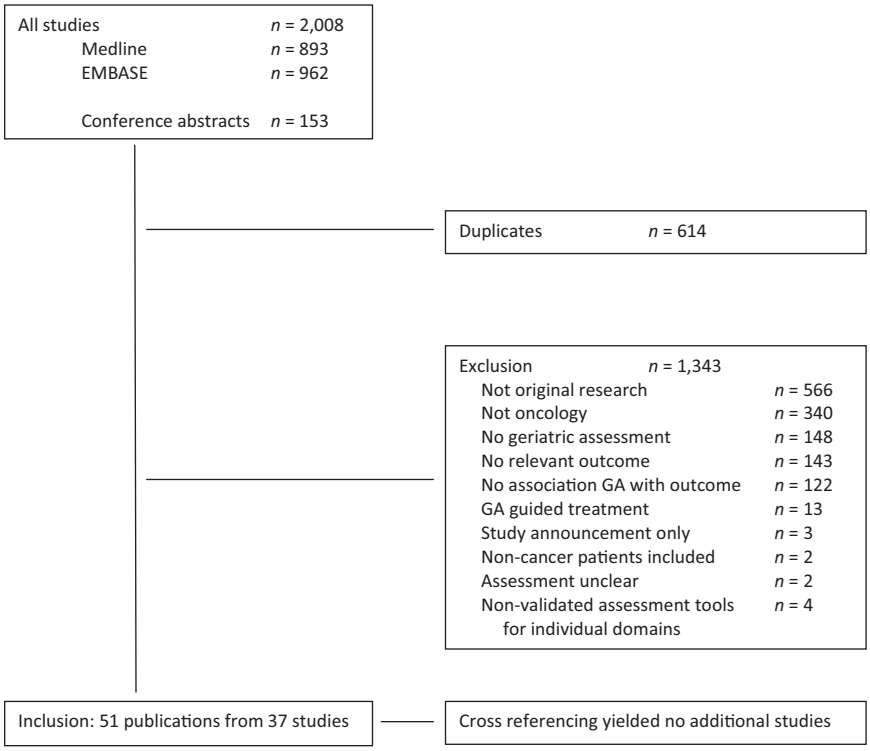

Figure 1. Search results and study selection.

analysis, and the reported results on the association between geriatric assessments and the outcome measures.

Quality Assessment

The methodological quality of each of the studies was independently assessed by two reviewers (M.H. and A.V.). Disagreements among the reviewers were discussed during a consensus meeting; in case of persisting disagreement, the assistance of a third reviewer (B.v.M.) was enlisted. We used a standardized list of 16 criteria to assess the methodological quality of the included studies. This list was a modified version of the checklist used by Kuijpers et al. [15] based on the theoretical considerations and methodological aspects described by Altman [16] (supplemental online Appendix 1a).

Data Synthesis and Analysis

As a result of heterogeneity in study designs, diversity of patient populations, and the wide variety in content of the geriatric assessment, a formal meta-analysis was not possible. Therefore, we summarized the study results to describe our main outcomes of interest. If necessary, reciprocal odds ratios or hazard ratios were calculated for optimizing comparability of data. When applicable, subgroup summaries were made based on the tools used in the assessment of the geriatric conditions.

Results

Study Characteristics

The literature search identified 1,855 citations (893 from Medline and 962 from Embase), of which 61 were duplicates. Hand-searching of conference abstracts yielded another 153 potentially relevant publications. Details on the search and reasons for exclusion can be found in Figure 1. After exclusion of 1,343 publications, 51 publications from 37 studies were included in this review [17–67]. Cross-referencing yielded no additional results.

The characteristics of these 37 studies are summarized in Table 1. The first publication is from 2002, but more than half of the studies were published in the last 2 years [17–67]. All but one study consisted of prospective cohorts [24]. The median sample size was 152 patients (range 20–1,130 patients) [17–67]. Study populations were heterogeneous, with only half focusing on a specific type of cancer [19, 20, 23, 25–27, 30–35, 45–46, 49–52, 56, 58–59, 61–63], of which eleven also focused on a specific cancer stage (30% of all studies) [19, 20, 23, 30, 32–35, 45, 52, 59, 61–63]. Furthermore, although 26 studies focused on chemotherapy (70%) [17–20, 23–36, 39–41, 45–46, 52–53, 56, 58–60, 62–66] and four studies focused on surgery (11%) [22, 47–51, 54–55], seven studies included patients receiving multiple treatment modalities (19%) [21, 37, 38, 42–44, 57, 61, 67].

The median number of geriatric conditions that were assessed was five (interquartile range: 4–8, Table 1) [17–67]. Table 2 gives an overview of the geriatric conditions included in the studies and the method of assessment [68–93]; a more detailed overview per study can be found in supplemental online Appendix 2. Ten studies summarized results of geriatric assessment in a summary score (27%) [21, 23–24, 28–30, 32–33, 49–51, 57, 63–64]: two of these studies used the cumulative number of geriatric conditions [57, 64] as a summary and

Table 1. Characteristics of included studies

Study	Publication year	Setting	Study population	Types of treatment	Number of patients	Age, median yrs (range)	Number of assessed conditions	Summary score used	Outcome measures examine
Aaldriks et al. [17, 18]	2010, 2011	Medical oncology department	Various	CT	202	77.2 (71–92)	3		All-cause mortality, chemotherapy completion
Aparicio et al. [19, 20][a]	2011	Medical oncology/ gastroenterology departments	Metastatic colon cancer	CT	123	80 (75–91)	4		Chemotherapy completion, chemotherapy toxicity
Arnoldi et al. [21]	2007	Various	Various	Various	153	76 (70–91)	5	Yes	All-cause mortality
Audisio et al. [22]	2003	Surgical oncology department	Various	Surgery	72	77 (70–92)	5		Surgery
Bamias et al. [23]	2007	Clinical therapeutics department	Irresectable bladder cancer	CT	32	75.5 (57–84)	4	Yes	All-cause mortality
Basso et al. [24]	2008	Medical oncology ward	Various	CT	117	75 (70–92)	7		All-cause mortality, chemotherapy completion
Biesma et al. [25–27]	2007, 2009, 2011	Medical oncology department	NSCLC	CT	182	74 (70–87)	8		All-cause mortality, chemotherapy completion, chemotherapy toxicity
Brunello et al. [28, 29][a]	2010, 2011	Medical oncology department	Various	CT	1,038	77 (70–92)	6	Yes	All-cause mortality
Brunello et al. [30][a]	2008	Medical oncology department	Metastatic renal cell cancer	CT	28	73.6 (70–81)	7	Yes	Chemotherapy toxicity
Castagneto et al. [31]	2004	Oncology department	Bladder cancer	CT	25	76 (71–87)	3		All-cause mortality
De Wit et al. [32, 33][a]	2009, 2010	Medical oncology department	Metastatic breast cancer	CT	152	61 (22–85)	4	Yes	All-cause mortality, chemotherapy completion, chemotherapy toxicity
Extermann et al. [36]	2011	Medical oncology department	Various	CT	518	75.5 (70–92)	6		Chemotherapy toxicity
Freyer et al. [34]	2005	Medical oncology department	Advanced ovarian cancer	CT	83	76 (70–90)	3		All-cause mortality, chemotherapy toxicity
Freyer et al. [35]	2004	Medical oncology department	Metastatic breast cancer	CT	26	70+	6		All-cause mortality
Hamaker et al. [37]	2011	General medicine ward	Various	Various	292	74.9 (65–96)	8		All-cause mortality
Honecker et al. [38][a]	2009	Internet-based registry	Various solid tumors	Various	1,130	76.3 (69–95)	7		All-cause mortality
Hurria et al. [39, 40]	2010, 2011	Medical oncology department	Various solid tumors	CT	500	73 (65–91)	5		Chemotherapy toxicity
Hurria et al. [41]	2006	Medical oncology department	Breast/lung/ prostate cancer	CT	20	75 (66–84)	4		Chemotherapy toxicity
Kanesvaran et al. [42–44]	2010, 2011, 2011	Geriatric oncology clinic	Various	Unclear	249	77 (70–94)	8		All-cause mortality
Karampeazis et al. [45][a]	2011	Medical oncology department	Advanced NSCLC	CT	131	74 (65–92)	5		Chemotherapy toxicity
Klepin et al. [46][a]	2011	Medical oncology department	Acute myologenous leukemia	CT	74	70 (±6.2)	4		All-cause mortality
Kothari et al. [47, 48]	2010, 2011	Thoracic surgery department	Various	Surgery	60	76 (Unknown)	5		Surgery
Kristjansson et al. [49–51]	2008, 2010, 2010	Surgery department	Colorectal cancer	Surgery	182	80 (70–94)	7	Yes	All-cause mortality
Maione et al. [52]	2005	Medical oncology department	Advanced NSCLC	CT	566	74 (70–84)	3		All-cause mortality
Marinello et al. [53]	2009	Geriatric/oncology unit	Lung/colon/ breast cancer	CT	110	75 (70–87)	4		All-cause mortality, chemotherapy completion, chemotherapy toxicity
Audisio et al. [54, 55]	2006, 2008	Surgical oncology department	Various	Surgery	460	76.9 (70–95)	5		Surgery
Pilnik et al. [56][a]	2010	Medical oncology department	Lung cancer	CT/CTRT	130	Unknown	4		Chemotherapy toxicity
Poon et al. [57][a]	2009	National cancer center	Various	Various	233	77 (70–93)	7	Yes	All-cause mortality
Ramsdale et al. [58][a]	2011	Oncology department	Colorectal cancer	CT	38	72 (65–89)	5		All-cause mortality, chemotherapy completion
Sostelly et al. [59][a]	2011	Medical oncology department	Metastatic breast cancer	CT	60	Unknown	4		Chemotherapy toxicity
Soubeyran et al. [60][a]	2006	Medical oncology department	Various	CT	364	77.5 (70–99)	7		All-cause mortality

(continued)

Table 1. (Continued)

Study	Publication year	Setting	Study population	Types of treatment	Number of patients	Age, median yrs (range)	Number of assessed conditions	Summary score used	Outcome measures examine
Tahir et al. [61][a]	2010	Breast cancer clinic	Early breast cancer	Unclear	124	82 (70–94)	5		All-cause mortality
Tredan et al. [62]	2006	Medical oncology department	Advanced ovarian cancer	CT	155	75.5 (70–90)	5		All-cause mortality
Tucci et al. [63]	2009	Medical oncology department	Diffuse large cell lymphoma	CT	84	73 (66–89)	3	Yes	All-cause mortality
v Fraeyenhove et al. [64][a]	2010	Medical oncology department	Various	CT	21	71.2 (66–86)	8	Yes	Chemotherapy toxicity
Wedding et al. [65, 66]	2007, 2010	Medical oncology ward	Various	CT	427	Unknown (18–80+)	3		All-cause mortality
Zagonel et al. [67][a]	2002	Medical oncology department	Various	Various	252	72 (65–94)	2		All-cause mortality

[a]Abstract.
Abbreviations: CT, chemotherapy; CTRT, chemoradiation; NSCLC, non-small cell lung cancer.

eight defined patients as frail if they were ADL-dependent, had 3 or more comorbidities (or one severe comorbid conditions), or one or more geriatric conditions. [21, 23–24, 28–30, 32–33, 49–51, 63].

The association between geriatric assessment and all-cause mortality was assessed in 25 out of 37 studies (68%, Table 1) [17, 18, 21, 23–29, 31–35, 37–38, 42–44, 46, 49–53, 57–58, 60–67], chemotherapy toxicity in 13 (35%) [19, 20, 25–27, 30–36, 39–41, 45, 53, 56, 59, 64], and chemotherapy completion in seven (19%) [17–20, 24–27, 32–33, 53, 58]. Four studies focused on the association between geriatric assessment and perioperative complications (11%) [22, 47–51, 54–55]. No studies were found on geriatric assessment in relation to radiotherapy.

Study Quality

The quality of the studies was heterogeneous, with a median score of 9 out of the 16 items on the quality checklist (interquartile range: 7–11). Reviewer agreement was >95% for all aspects. Inclusion and exclusion criteria and patient population were clearly described in 22 and 26 studies, respectively. The participation rate (i.e., the percentage of potential participants that received a geriatric assessment) was only described in nine studies. Although 21 studies listed the duration of follow-up, only eight described the number of patients lost to follow-up or compared completers with noncompleters. Only 13 studies described the completeness of data. Outcome reporting was of better quality, with 28 studies providing data from univariable analyses for the association of geriatric assessments with outcome measures and 24 presenting some form of prognostic model. However, reporting of associations differed notably between studies, with some presenting odds ratios, others hazard ratios, and others only *p* values to indicate a statistical significance without reporting on the actual odds/hazard ratio or confidence interval. This complicated any comparison of data and hindered combining data for a formal meta-analysis. Furthermore, three studies did not appear to have sufficient numbers for their multivariable analyses. Full results for the quality assessment can be found in supplemental online Appendix 1b.

All-Cause Mortality

The predictive value of geriatric assessments for all-cause mortality was reported in 25 studies (Table 3). Six studies addressed the association of a summary score with mortality: all six found that frail patients showed poorer overall survival (100%) [21, 23–24, 28–29, 57, 63]. In these studies, median survival was between 1.6 and 3.7 times longer for fit patients compared to frail subjects. Likewise, frailty assessed with a formal frailty screening tool was found to be associated with mortality in three out of four studies (75%) [17, 18, 23, 25, 58]. Nutritional status was found to be associated with mortality in all four studies in which it was assessed (100%) [17, 18, 42, 50, 58, 60]. For comorbidity, initial analysis revealed that only 6 out of 16 studies found an association with mortality (38%). However, when subdividing according to the assessment method used, only one out of five studies using the Charlson comorbidity index [38] and none of the four studies using the number of comorbid conditions found an association, while four out of five studies using the Cumulative Illness Rating Scale for Geriatrics (CIRS-G) found comorbidity to be associated with mortality (80%) [33, 50, 53, 60, 65]. For one study, the results for comorbidity were not clearly reported. Of the 14 studies addressing cognitive function, only two found an association between cognition and mortality [38, 61]. Only 4 out of 14 studies found an association between ADL impairment and mortality (29%) [25, 38, 46, 61, 67], and 6 out of 16 reported finding an association for IADL impairment (38%) [25, 33, 38, 46, 52, 67]. Results for mood/depression, mobility, and polypharmacy were inconclusive, with approximately equal numbers of studies that did and did not find an association. All of these results were not altered when correcting for the assessment tool that was used.

Toxicity of Chemotherapy

Results for toxicity of chemotherapy and chemotherapy completion are listed in Table 4. For toxicity, the score summarizing geriatric assessment was found to be associated with toxicity of chemotherapy in two out of three studies (66%), but these only reported univariable results [33, 64]. Similarly, two

Table 2. Content of geriatric assessments in included studies

Assessment tool used for assessing condition	*n* of studies assessing condition	*n* of studies using tool
Instrumental activities of daily living	32 (86%)	
Lawton & Brody [68]		30
NEADL [69]		1
PAT-D [93]		1
Comorbidity	32 (86%)	
Charlson [70]		12
CIRS-G [71]		12
Satariano [72]		2
n of conditions		7
Activities of daily living	31 (84%)	
Barthel [73]		6
Katz [74]		22
OARS [76]		1
PAT-D [93]		1
Unclear		1
Cognition	26 (70%)	
MMSE [75]		23
IQcode [77]		2
Blessed [78]		1
SPMSQ [79]		1
Mood/depression	24 (65%)	
GDS [80]		18
HADS [81]		4
PANAS [82]		1
SCID [84]		1
CES-D [91]		1
Polypharmacy	13 (35%)	
n of pills		12
Nutritional status	9 (24%)	
MNA [83]		6
Determine [85]		1
SNAQ [86]		1
NHI NHC		1
Mobility	9 (24%)	
TUG [90]		7
SPPB [92]		2
Frailty screening	6 (16%)	
GFI [87]		3
VES-13 [88]		2
Fried [89]		1

Some studies used more than one tool to assess the domain.
Abbreviations: CES-D, Centre for Epidemiologic Studies-Depression; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Index; HADS, Hospital Anxiety and Depression Scale; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; NEADL, Nottingham Extended Activities of Daily Living; NHI NHC, National Health Initiative Nutritional Health Checklist; OARS, Older American Resources and Services; PAT-D, Pepper Assessment Tool for Disability; SCID, Structured Clinical Interview for DSM IV; SNAQ, Short Nutritional Assessment Questionnaire; SPMSQ, Short Portable Mental Status Questionnaire; SPPB, Short Physical Performance Battery; TUG, Timed Get-Up-And-Go; VES-13, Vulnerable Elders Scale-13.

out of three studies found an association between toxicity and a frailty screening tool [56, 64]. For all other geriatric conditions, results were quite variable across studies. Polypharmacy was associated with toxicity in two out of four studies [33, 56]. Comorbidity was associated with toxicity of chemotherapy in only 3 out of 10 studies [53, 56, 59]. The method of assessing for comorbidity did not influence results. Toxicity of chemotherapy was associated with impaired cognition in 17% of studies, depressed mood in 13%, impaired mobility in 33%, ADL impairment in 0%, and IADL impairment in 18%, respectively (Table 4).

Chemotherapy Completion

For completion of chemotherapy, impaired cognitive function was found to be associated with less completion or the need for dose reduction in two out of three studies (66%, Table 4) [17–20]. ADL impairment showed similar results, with association in two out of three studies [25, 58]. Furthermore, three out of five studies [33, 53, 58] found that comorbidity was predictive of lower completion rates (60%). Two of these used the CIRS-G and one the Charlson comorbidity index to assess comorbidity; the two studies that did not find an association both used the Charlson comorbidity index. One study addressed nutritional status and found an association in the multivariable analysis [17, 18]. Data was inconclusive for the summary score (association in one of two studies, 50%) and negative for depressed mood, impaired mobility, IADL impairment, and the presence of frailty (Table 4).

Perioperative Complications

Four studies addressed the association between geriatric assessment and perioperative complications (Table 4). Only one study assessed the association of a summary score and found it to be associated with perioperative complications (100%) [49]. This association was found for IADL impairment in three out of the four studies [47, 49, 54]. For depressed mood, results were inconclusive, with only two out of four studies finding an association [47, 49]. For ADL impairment, polypharmacy, nutritional status, cognitive function and comorbidity, no or little association was found. None of the studies used a frailty screening tool.

Radiotherapy Toxicity/Completion

No studies were identified that addressed the association between geriatric assessments and toxicity or completion of radiotherapy. One study assessed patients receiving chemotherapy or chemoradiation, but did not report separately on the latter group [56].

Discussion

In this review on the value of geriatric assessments in predicting treatment tolerance and all-cause mortality in older patients with cancer, little consistency was found between the results of the various studies. Interestingly, different geriatric conditions appear to be predictive for the primary outcome measures: frailty, nutritional status, and comorbidity (when measured with CIRS-G) for all-cause mortality; frailty for toxicity of chemotherapy; cognitive function and ADL impairment for chemotherapy completion; and IADL impairment for

Table 3. Association of geriatric assessment with all-cause mortality

Study	*n* of patients	Cancer type	Summary score	Cognition	Mood/ depression	Mobility	ADL	IADL	Nutritional status	Frailty screening	Comorbidity	Polypharmacy
De Wit et al. [32, 33]	152	Breast						+ +			+ +	− −
Freyer et al. [35]	26	Breast		−	−	−		−			−	−
Tahir et al. [61]	124	Breast		+ +	− −		+ +	− −			− −	
Kristjansson et al. [49–51]	182	Colorectal		− −	− −		− −	− −	+ +		+ +	− −
Ramsdale et al. [58]	38	Colorectal		− −	− −		− −			+ +	− −	
Biesma et al. [25–27]	182	Lung		− −	+ +	+	+ +	+ +		+ +	?	
Maione et al. [52]	566	Lung					− −	+ +			− −	
Tucci et al. [63]	84	Lymphoma	+									
Klepin et al. [46]	74	AML			− −	++	− −	++				
Bamias et al. [23]	32	Bladder	+							−		
Castagneto et al. [31]	25	Bladder			−		−	−				
Freyer et al. [34]	83	Ovarian		− −							− −	+ +
Tredan et al. [62]	151	Ovarian		− −	+ +			− −			±	− −
Aaldriks et al. [17, 18]	202	Various		− −					+ +	+ +		
Arnoldi et al. [21]	153	Various	+									
Basso et al. [24]	117	Various	+									
Brunello et al. [28, 29]	1,038	Various	+ +									
Hamaker et al. [37]	292	Various		−		− −	− −	− −			− −	− −
Honecker et al. [38]	1,130	Various		+	+	+	+	+			+	+
Kanesvaran et al. [42–44]	249	Various		− −	+ +		− −	− −	+ +		− −	− −
Marinello et al. [53]	110	Various		− −			− −	− −			+ +	
Poon et al. [57]	233	Various	+ +	±								
Soubeyran et al. [60]	364	Various		− −	− −	− −	− −	− −	+ +		− −	
Wedding et al. [65, 66]	437	Various					− −	±			+ +	
Zagonel et al. [67]	252	Various					+ +	+ +				

Abbreviations: +, significant in univariable analysis: no multivariable analysis performed or factor not included in multivariable analysis; ++, significant in multivariable analysis: there was little uniformity across studies in the confounders and variables included in these analysis; −, no association in univariable analysis: no multivariable analysis performed or factor not included in multivariable analysis; − −, no association in multivariable analysis: there was little uniformity across studies in the confounders and variables included in these analysis; ?, association not described in the publication; ±, association only present in subgroup of patients but not all patients; ADL, activities of daily living; AML, acute myelogenous leukemia; IADL, instrumental activities of daily living.

perioperative complications. However, the only truly consistent finding was the association between a summary score of the geriatric assessment and mortality.

The studies included in this systematic review were heterogeneous in design, content, and reported outcomes. In addition, reporting was frequently too inadequate to assess potential sources of bias. It was often unclear whether outcome of geriatric assessment was known to the treating physician, allowing differences in overall survival to be caused by the reception of suboptimal oncologic treatment based on the outcome of geriatric assessment (and subsequently the assumption that patient would not be able to tolerate standard treatment). Another potential bias is that the patients participating in studies focusing on chemotherapy and surgery were already preselected as suitable for this treatment by their physician. Thus, although many geriatric conditions were not predictive of toxicity, one cannot conclude that patients should receive chemotherapy irrespective of their cognitive status or IADL score, for example.

These factors limited our possibilities of performing a formal meta-analysis and drawing definitive conclusions. One method to solve some of these issues would be to perform an individual patient data analysis using the original data of included studies. A second limitation of this review is that it fo-

Table 4. Association of geriatric assessment with treatment complications/completion

Outcome	Study	Cancer type	Number of patients	Summary score	Cognition	Mood/ depression	Mobility	ADL	IADL	Nutritional status	Frailty screening	Comorbidity	Polypharmacy
Chemotherapy toxicity	De Wit et al. [32, 33]	Breast	152	+			−		−			−	+
	Sostelly et al. [59]	Breast	60			−−		−−	−−		++	++	
	Aparicio et al. [19, 20]	Colorectal	123		++	−−			++			−−	
	Biesma et al. [25–27]	Lung	182			++	−−	−−	−−		−−	−−	
	Karampeazis et al. [45]	Lung	131		−	−		−	−			−	
	Pilnik et al. [56]	Lung	130					−	−			+	+
	Brunello et al. [30]	Renal cell	28	−									
	Freyer et al. [34]	Ovarian	83		−−							−−	−−
	Castagneto et al. [31]	Bladder	25			−		−	−				
	Extermann et al. [36]	Various	518		±	−−			±	±		−−	−−
	Hurria et al. [39, 40]	Various	500		−−	−−	++		++			?	
	Hurria et al. [41]	Various	20			−		−	−			−	
	Marinello et al. [53]	Various	110		−−			−−	−−			++	
	Van Fraeyenhove et al. [64]	Various	21	+							+		
Chemotherapy completion	De Wit et al. [32, 33]	Breast	152	−			−		−			+	−
	Aparicio et al. [19, 20]	Colorectal	123		++	−−			−−			−−	
	Ramsdale et al. [58]	Colorectal	38			−−	++	++	?		−−	++	
	Biesma et al. [25–27]	Lung	182			−−	−−	++	++		−−	−−	
	Aaldriks et al. [17, 18]	Various	202		++					++	−−		
	Basso et al. [24]	Various	117	+									
	Marinello et al. [53]	Various	110		−−			−−	−−			++	
Perioperative complications	Kristjansson et al. [49–51]	Colorectal	182	++	−−	++		−−	++	−−		++	−−
	Audisio et al. [22]	Various	72		−	−		+	−			−	
	Kothari et al. [47, 48]	Various	60			+		−	+	−			
	Audisio et al. [54]	Various	460		−−	−−		−−	++			−−	

Abbreviations: +, significant in univariable analysis: no multivariable analysis performed or factor not included in multivariable analysis; ++, significant in multivariable analysis: there was little uniformity across studies in the confounders and variables included in these analysis; −, no association in univariable analysis: no multivariable analysis performed or factor not included in multivariable analysis; −−, no association in multivariable analysis: there was little uniformity across studies in the confounders and variables included in these analysis; ?, association not described in the publication; ±, association only present for a particular type of toxicity but not all toxicities; ADL, activities of daily living; IADL, instrumental activities of daily living.

cuses on studies assessing multiple geriatric conditions. Studies focusing on single conditions or including multiple conditions but not identified as geriatric assessment would not have been selected from Medline or Embase with our search strategy. Despite these limitations, this review does provide a thorough overview of the currently available evidence on the value of geriatric assessment for predicting relevant outcomes in older patients with cancer.

The results of this review have several clinical implications. First of all, although various geriatric conditions appear to have some predictive value for each of the four outcome measures, the lack of consistency in the findings does not support excluding patients from certain treatment options based solely on their score on a geriatric assessment tool.

A second clinical implication of this review is that although current geriatric assessments used in oncology primarily focus on cognitive function, mood/depression, and functional limitations, less frequently examined geriatric conditions, such as malnutrition and polypharmacy, appear to be of similar or even greater predictive value and are potentially modifiable; there-

fore, their assessment should not be omitted. Also, it appears that assessment of comorbidity without including a measure for the severity of these conditions is not useful; therefore, we recommend using the CIRS-G rather than the Charlson comorbidity index, despite that fact that the former is more time-consuming [71, 94]. Interestingly, assessment of mobility (which is one of the cornerstones of geriatric medicine) is rarely included. Given its predictive value in the general geriatric population, this element of CGA deserves further exploration [95].

Several factors may have contributed to the variation in the results of the included studies. First of all, it appears that the choice of assessment tool influences outcome, as was clearly illustrated in the assessment of comorbidity. Heterogeneity in patient populations will also have contributed to the variation in study outcomes: not only do different elements of the CGA appear to be predictive depending on the outcome measure that is examined, but it is possible that the specific characteristics and prognosis of a malignancy will also affect the predictive value of various geriatric syndromes. All of these factors mean that finding that one optimal assessment tool that will be predictive of all outcome measures in all patient populations in a broad scope of treatment settings may not be feasible.

On the other hand, the results of our systematic review suggest that in predicting outcome, it may be more important to determine whether or not a patient is frail than to determine what makes him or her frail. This fits with the definition of frailty as the final common pathway of aging [96], in which the presence of deficits in geriatric domains is the determinative factor while the particulars of each deficit are of secondary importance. If this is the case, a short frailty screening tool could potentially suffice in allocating a patient to standard treatment of tailored care and the time-consuming process of a formal geriatric assessment could be avoided [40, 47, 97]. This does require that the tool has a high sensitivity for frailty, allowing the assessor to trust that those patients deemed fit actually are fit [88]. Patients who are not fit should then receive further assessment to ascertain their ability to tolerate treatment. However, there is still much debate on the precise definition of frailty and how it should be measured; as yet, there is insufficient evidence on the quality of the various screening tools in predicting fitness in this particular setting to endorse one tool over the others [98].

Ultimately, in limiting the use of a systematic geriatric assessment in oncology practice to a decision-making tool, the potential benefit of using the CGA to optimize care for elderly patients with cancer is overlooked. For example, although a cognitive disorder does not necessarily predict chemotherapy toxicity, it potentially means that a patient may not respond adequately in case of complications or will not take oncologic or supportive medication as prescribed; these patients may require extra monitoring or home health care. Similarly, addressing previously undiagnosed depressive symptoms or malnutrition can improve a patient's resilience when undergoing treatment. A geriatric assessment could thus be seen as a starting point for further treatment and care, for improving not only the outcomes addressed in this review but also quality of life or functional capacity. However, because a formal comprehensive geriatric assessment is time consuming and a geriatric consultation is often a scarce commodity, it may be useful to develop screening tools that are particularly suitable for finding those patients at high risk for having geriatric conditions that are modifiable or require intervention [99].

In conclusion, this systematic review shows that although different geriatric conditions appear to be predictive for each of the major outcome measures, currently available evidence is too inconsistent to guide clinical decision-making. Many questions remain unanswered and will require further exploration. To elucidate the impact of the various geriatric conditions on treatment tolerance and outcome for older patients with cancer, future clinical research should use broad geriatric assessments that address all geriatric conditions and include geriatric outcome measures, such as functional capacity, in addition to standard oncologic outcomes. Furthermore, research should focus on validating screening tools that predict fitness rather than frailty and applying geriatric assessment as an intervention aimed at optimizing a patient's resilience during treatment, rather than as a decision-making tool only.

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