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Review of the literature

Report

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Report

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A complete review of oncogeriatric literature on the use of screening tools, geriatric assessment and geriatric interventions was performed, in collaboration with the International Society of Geriatric Oncology (SIOG) leading to the proposition of guidelines for daily practice.

In this report a summary of the literature review is given, including recommendations for the daily practice in Belgium.

Published papers for the screening tools and geriatric assessment review are added in the appendix.

1. Screening tools

A review on the use of screening tools in older patients with cancer was performed by the UZ Brussel team and was published in in the *Annals of Oncology* in June 2014[1].

1.1 Definition of screening tool

A screening tool is a brief assessment conducted to help the clinician to identify those patients in need of further evaluation by geriatric assessment (GA), which may provide a better insight into the patients' general health and individual probability of survival and allow directed interventions. Screening tools may also have prognostic and/or predictive value for important outcome measures such as treatment-related toxicity, functional decline and overall survival.

Screening tools should be simple and fast with high sensitivity and negative predictive value as the most important characteristics. Additionally, a high specificity is also at interest in order to limit the number of fit patients who unnecessarily undergo GA.

1.2 Studies included

A total of 50 citations were included: 22 original papers, 22 conference abstract and six reviews. These articles and abstracts reported on the use of 17 screening tools in older patients with cancer in 44 studies. Five tools were specifically developed for the older cancer population (G8, Oncogeriatric Screen (OGS), abbreviated CGA (aCGA), Senior Adult Oncology Program (SAOP)-2) and for the Flemish version of the Triage Risk Screening Tool (fTRST) the cut-off value was lowered.

1.3 Screening tools in older patients with cancer

1.3.1 Comparison of screening tools with GA

Twenty-two studies compared a total of 14 screening tools with GA and reported on sensitivity and specificity (see table 1). However, comparison of the results of these studies is difficult due to variations between the number and type of items used in the GA as well as the cut-off for impairment.

The three most studied tools in older patients with cancer are: G8 (*n*=3816), VES-13 (*n*=2776) and fTRST (*n*=1077). Of these the highest sensitivity was observed with the G8 (>80% in 6/8 studies) and fTRST (>80% in 2/2 studies). Eleven studies directly compared two or more screening tools. In these studies the G8 consistently demonstrated a good sensitivity. Results were more heterogeneous for the VES-13. In two comparisons between G8 and fTRST, both tools were equally sensitive.

1.3.2 Prognostic and predictive value of screening tools

Twelve studies reported the relationship between seven screening tools with outcome (functional status, treatment-related toxicity and survival) (table2).

a. <u>Functional decline</u>

   Both G8 and fTRST demonstrated high sensitivity for functional decline on Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) but low specificity. This means that older patients with normal score on G8 or fTRST have low risk for functional decline.

b. <u>Treatment-related toxicity</u>

   For patients treated with chemotherapy, four tools were predictive for the occurrence of severe toxicity (G8 1/2 studies, VES-13 1 study, Groninger Frailty Index (GFI) 1 study and ECOG Performance Status 1 study).

For patients treated with surgery only the Timed Up and Go test (TUG) was predictive for 30-day morbidity (1/2 studies).

c. Overall Survival

Six screening tools were associated with overall survival: G8, VES-13, fTRST, GFI, Fried Frailty criteria, handgrip strength.

1.4 Recommendations

Although we have a large amount of screening performance data in older patients with cancer, it is clear that screening tools do not replace GA. However, in a busy clinical practice the use of such a tool is recommended to identify patients in need of further evaluation by GA. The performance of different tools may depend on the clinical situation and treatment type.

Although the international expert panel did not come to a consensus in recommending one single tool for the use in daily practice, we currently think that data with G8 are the most robust (both for efficacy in detecting problems on GA and for prognostic/predictive value).

Recently the Elderly Task Force of the EORTC has proposed to measure G8 in all patients ≥70 years in future EORTC trials. The G8 was also the screening tool of choice in France.

However, in Belgium, we need to come to a consensus with geriatric efforts on the use of screening tools. The interRAI may be of interest but so far there has been no report on its use in older patients with cancer.

2. Geriatric assessment

A review on the use of geriatric assessment (GA) in older patients with cancer was performed by the UZ Leuven team and was published in in the *Journal of Clinical Oncology* in August 2014[2].

2.1 Implementation of GA in geriatric oncology.

The aim was to synthesize the evidence and provide a consensus on key questions on GA in geriatric oncology.

2.1.1 What is the rationale for performing GA?

- Important reasons to perform GA in older patients with cancer are: detection of unidentified problems and risk for which targeted interventions can be applied, prediction of adverse outcomes, estimation of life expectancy and lethality of the malignancy in the context of competing comorbidities and general health problems.
- The main goal of GA is to provide a comprehensive health appraisal to guide targeted geriatric interventions and appropriate cancer treatment selection. GA has the potential to evaluate the balance of benefits and harms of performing or omitting specific oncologic interventions.
- Many oncological studies have used age ≥70 years as the age for implementing GA.

2.1.2 What information is provided by GA beyond that captured in a standard history and physical exam?

- Deficits in GA domains are frequent in older patients with cancer (approximately 50%).
- Assessment of all domains is relevant because GA can potentially identify deficits across domains.
- GA reveals deficits that are not routinely captured in a standard history and physical examination.

2.1.3 What is the ability of GA to predict oncology treatment-related complications?

- GA items are predictive of the risk of severe treatment-related toxicity in a variety of diseases and treatment settings.
- The optimal geriatric parameters to predict severe treatment toxicity or modify therapeutic approach have not yet been established for different cancer types or treatment options.

2.1.4 What is the association between findings and overall survival (OS)?

- GA items independently predict OS in a variety of oncological diseases and treatment settings.
- Prognostic models for geriatric oncology are needed, including both cancer- and geriatric-related prognostic factors.

2.1.5 What is the impact of GA findings on oncology treatment decisions?

- GA can influence treatment decisions in older patients with cancer. Oncology teams should integrate GA findings into treatment decisions.

2.1.6 What should a GA comprise, including domains and tools?

- Important domains in GA are functional status, fatigue, comorbidity, cognitions, mental health status, social support, nutrition and geriatric syndromes. Various tools are available to investigate these domains and the superiority of one tool over another has not been proven (see table 3).

2.1.7 How should GA be organized and implemented in clinical care?

- There are several ways of implementing GA in geriatric oncology (see table 4). All models have advantages and disadvantages and preference should be given to models that fit with the local health care structure and setting. Interaction with multidisciplinary geriatric teams is highly recommended.

2.2 Recommendations

Implementation of GA in the standard care of older patients with cancer is recommended based on the presence of information demonstrating that GA detects general health care problems that are routinely under-recognized in general oncology and that GA has shown to predict treatment-related complications.

A GA should include functional status, fatigue, comorbidity, cognition, mental health status, social support, nutrition and geriatric syndromes. The use of a uniform assessment is advised in order to allow transfer of the assessment results to other health care settings such as primary and residential care. This would improve continuity of care.

A uniform approach for Belgium would be advisable, preferably integrating the current efforts into the present geriatric consultations team.

3. Geriatric interventions

A review on the implementation of geriatric interventions in older patients with cancer was performed by the UCL team. The article will be submitted in the future.

3.1 Introduction

Geriatric interventions are specialized care or strategies aimed to improve or palliate impairments in older persons. Geriatric impairments may affect several aspects of the patient's condition (autonomy, nutritional status, cognition, social situation, etc.) and may be revealed and evaluated by a multidimensional geriatric assessment.

Therefore geriatric interventions are part of a comprehensive management of the older patient and of a personalized geriatric care plan whose main objectives are autonomy, quality of life and survival.

In the general geriatric population, programs linking geriatric assessment with interventions are effective for improving functional status and survival of the patients. As a condition, an extended follow-up of the interventions implementation appears to be essential.

The benefit of geriatric interventions in older patients with cancer is still unclear. The goal of this review is to analyse the available data on geriatric interventions in older patients with cancer and to propose recommendations for their implementation.

3.2 Methods

A systematic literature review was performed from January 2000 to August 2015. Full text published articles were included when they described controlled clinical trials evaluating the impact of geriatric interventions (exercise, nutrition support, education, case management, etc.) in patients with a mean age of 60 years and older with a well-defined primary objective.

A level of evidence (I to V) was assigned to each item and recommendations (grade A to D) have been proposed and validated using the Delphi consensus method (including 3 steps involving two groups of experts).

3.3 Results and recommendations

Thirty-five articles were selected of which a majority of clinical trials phase 3. Ten articles focused specific on older patients (all included patients aged 60 and older in the described study).

In summary, in older patients with cancer, geriatric interventions are effective in improving the physical condition (grade A recommendation), adherence to the proposed cancer treatment plan (grade A recommendation) and nutritional parameters (grade B recommendation). However, there is no consistent evidence for a significant impact of geriatric interventions on quality of life, fatigue and patient survival.

3.4 Discussion

This review has some limitations. Several included studies are not specifically dedicated to older patients. In addition, the data are heterogeneous. Various interventions (type and duration) were studied in different patient populations with different objectives and measurement tools. This makes it difficult to compare studies.

In the future, new randomized trials are needed, designed to allow better interpretation of data. Therefore, a selection of patients likely to benefit most from interventions, consensus on intervention methods and identification of the most relevant clinical endpoints for this patient population are warranted.

4. References

Screening tools

- Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older patients with cancer: an update on SIOG recommendations. Annals of oncology: official journal of the European Society of Medical Oncology / ESMO. 2015;26(2):288-300.

Geriatric assessment

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Geriatric interventions

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  To be submitted.

Table 1: Results of 22 studies comparing screening tools with Geriatric Assessment

Screening tool First author (reference)	N pts	% 'abnormal' on screening tool	% 'non-fit' on GA	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95%CI)	NPV (%) (95%CI)
G8							
Soubeyran	*1425*	68	80	77 (74-79)	64 (59-70)	NR	NR
Kenis	*937*	74	74	87 (84-89)	59 (53-65)	86 (83-88)	61 (55-68)
Liuu	*518*	80	84	87 (83-90)	60 (48-70)	NR	NR
Bellera	*364*	82	94	85 (81-89)	65 (41-85)	NR	NR
Luce	*211*	80	NR	65 NR	3 NR	44 NR	8 NR
Baitar	*170*	76	64	92 (85-96)	52 (39-65)	78 (70-84)	78 (63-88)
Kenis	*140*	NR	79	80 NR	40 NR	83 NR	35 NR
Pottel	*51*	67	69	86 (72-94)	75 (52-91)	88 NR	71 NR
VES-13							
Soubeyran	*1425*	60	80	69 (66-71)	74 (69-79)	NR	NR
Luciani	*419*	54	28	87 (81-92)	62 (56-68)	NR	NR
Biganzoli	*259*	47	66	62 (54-69)	81 (71-88)	86 (79-92)	52 (44-61)
Monfardini	*150*	NR	44	68 NR	71 NR	65 NR	74 NR
Owusu	*117*	35	43	88 NR	69 NR	68 NR	88 NR
Kellen	*113*	49	68	61 (49-72)	78 (61-90)	85 (73-93)	48 (35-62)

Falci	*93*	43	43	60 NR	70 NR	60 NR	70 NR
Molina-Garrido	*58*	35	88	39 NR	100 NR	100 NR	18 NR
Pottel	*51*	39	69	57 (42-71)	100 (83-100)	100 NR	52 NR
Mohile	*50*	50	60	73 NR	86 NR	89 NR	67 NR
Molina-Garrido	*41*	29	56	55 NR	100 NR	100 NR	66 NR
G8+VES-13							
Soubeyran	*1425*	NR	80	87 NR	53 NR	NR	NR
Pottel	*51*	NR	69	91 (79-98)	94 (74-100)	97 NR	83 NR
fTRST							
Kenis	*937*		74				
Cut off 1		82.5		91 (89-93)	42 (36-48)	81 (78-84)	63 (56-71)
Cut off 2		54.7		67 (64-71)	80 (74-85)	90 (87-93)	47 (42-52)
Kenis	*140*		79				
Cut off 1		NR		92 NR	50 NR	87 NR	63 NR
Cut off 2		NR		64 NR	100 NR	100 NR	43 NR
GFI							
Baitar	*170*	47	64	66 (89-75)	87 (76-94)	90 (82-95)	59 (49-69)
Kenis	*140*	NR	79	57 NR	87 NR	94 NR	36 NR
Kellen	*113*	31	68	39 (28-51)	86 (70-95)	86 (70-95)	40 (29-51)
SOF index							

Luciani	*400*	67	68	89 (85-93)	81 (73-88)	NR	NR
KPS							
Luce Owusu	*211* *117*	86 38	NR 43	29 NR 78 NR	44 NR 91 NR	39 NR 87 NR	34 NR 85 NR
Fried criteria							
Biganzoli Molina-Garrido	*259* *58*	75 35	66 88	87 (81-92) 37 NR	49 (38-60) 86 NR	77 (70-82) 95 NR	66 (53-77) 16 NR
Barber							
Molina-Garrido Molina-Garrido	*173* *41*	68 42	47 56	74 (65-83) 59 NR	39 (28-49) 79 NR	58 (49-67) 77 NR	56 (43-69) 63 NR
ISAR							
Luce	*211*	79	NR	70 NR	10 NR	47 NR	22 NR
OGS							
Valéro	*126*	89	89	88 (80-93)	44 (28-63)	85 (77-91)	50 (31-69)
ECOG-PS							
Owusu	*117*	66	43	94 NR	55 NR	61 NR	93 NR
aCGA							
Kellen	*113*	NR	68	51 (39-62)	97 (85-100)	97 (87-100)	48 (36-60)
Gerhematolim							
Fargeas	*104*	NR	NR	95 (87-99)	87 (72-96)	93 (84-98)	92 (78-98)
SAOP2							

Extermann	*31*	NR	84	100 NR	40 NR	90 NR	100 NR

Legend: CI: Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value; NR: Not reported

*Sensitivity, Specificity, PPV and NPV indicate the value of the screening tool for detecting predefined abnormal geriatric assessment

Table 2: Screening tools as a prognostic/predictive marker

Tool	Outcome	First author (reference)	Population (*N*)	N	Conclusion
G8	Functional decline	Kenis	Various cancers	937	High sensitivity and NPV for functional decline on ADL (84% and 91% respectively) and IADL (76% and 70% respectively) but low specificity (31% both for ADL and IADL). Older patients with normal G8 have low risk for functional decline in ADL and less pronounced in IADL. Patients with an abnormal G8 need further evaluation during follow-up.
	Treatment-related toxicity	Stokoe	Various cancers treated with chemotherapy	185	Abnormal G8 was associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment): 65% versus 47% (p=0.025).
		Dubruille	Hematological malignancies	85	Abnormal G8 was not predictive for intolerance to chemotherapy (*p=0.905*)
	Survival	Kenis	Various cancers	937	G8 showed a significant prognostic value for OS (median survival 31.8 months for abnormal G8 versus not reached for normal G8 (HR 0.38 (95%CI 0.27-0.52; *p<0.001*). Older patients with normal G8 had 62% less chance of dying after a median follow up of 18.95 months.
		Dubruille	Hematological malignancies	85	Abnormal G8 was not predictive for one-year survival (*p=0.388*)
		Liuu	Various cancers	518	Abnormal G8 associated with 6-month death in multivariate analysis (HR 6.68; 95% CI 1.63-27.35; *p=0.001*)
VES-13	Treatment-related toxicity	Stokoe	Various cancers treated with chemotherapy	185	Abnormal VES-13 was associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment): 76% versus 54% (*p=0.015*).
		Papis	Hepato-pancreato-biliary cancers treated with surgery	20	In uni-variate analysis VES-13 was not predictive for 30-day morbidity (*p=1*), mortality (*p=1*) and hospital stay (*p=0.8*).
		Huisman	Various cancers treated with surgery	345	In a univariate logistic regression analysis VES-13 was not associated with 30-day morbidity (OR 1.63; 95% CI 0.85-3.11; *p=0.14*)
	Survival	Kitamura	Gastrointestinal, hepato-biliary and pancreatic cancers treated with chemotherapy	21	VES-13 was significantly correlated with overall survival (HR 1.243; 95%CI 1.048-1.480; *p<0.0014*)

fTRST(1)	Functional decline	Kenis	Various cancers	937	High sensitivity and NPV for functional decline on ADL (91% and 92% respectively) and IADL (86% and 73% respectively) but low specificity (21% for ADL and 22% for IADL). Older patients with normal fTRST(1) have low risk for functional decline in ADL and less pronounced in IADL. Patients with an abnormal fTRST(1) need further evaluation during follow-up.
	Survival	Kenis	Various cancers	937	fTRST(1) showed a significant prognostic value for OS (median survival 36.7 months for abnormal G8 versus not reached for normal G8 (*p<0.001*).
GFI	Treatment-related toxicity	Papis	Hepato-pancreato-biliary cancers treated with surgery	20	In uni-variate analysis GFI was not predictive for 30-day morbidity (*p=0.6*), mortality (*p=0.3*) and hospital stay (*p=0.08*).
		Van Fraeyenhove	Various cancers treated with chemotherapy	21	Normal GFI was predictive for the absence of a serious adverse event after the first chemotherapy, defined as hospitalization or death: sensitivity 86%, NPV 50%
		Huisman	Various cancers treated with surgery	345	In a univariate logistic regression analysis GFI was not associated with 30-day morbidity (OR 1.52; 95% CI 0.81-2.87; *p=0.20*)
	Survival	Aaldriks	Various cancers treated with chemotherapy	202	Abnormal GFI was associated with an increased mortality (HR 1.80; 95%CI 1.17-2.78; *p=0.007*)
		Aaldriks	Breast cancers treated with chemotherapy	55	Abnormal GFI was associated with increased mortality with a mean follow up of 16 months (HR 3.4; 95% CI 1.62-7.10; *p=0.001*).
Fried frailty criteria	Treatment-related toxicity	Kristjansson	Colorectal cancer treated with surgery	176	Abnormal Fried frailty criteria screening was not predictive for any complication (*p=0.18*) nor for severe complications (grade 2 or higher) (*p=0.23*)
	Survival	Kristjansson	Colorectal cancer treated with surgery	176	Abnormal Fried frailty criteria screening was associated with worse survival: HR for pre-frail patients 2.33 (95%CI 1.16-4.67;*p=0.018*) and HR for frail patients 2.67 (95%CI 1.11-6.83; *p=0.29*).
ECOG-PS	Treatment-related toxicity	Stokoe	Various cancers treated with chemotherapy	185	ECOG-PS ≥2 was not associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment) (*p=0.318*).
Handgrip strength	Survival	Kanesvaran	Various cancers	249	Handgrip strength was significantly associated with overall survival: HR 0.97 (95%CI 0.97-0.99) in univariate analysis.
Timed Up & Go		Huisman	Various cancers treated by surgery	345	In multivariate logistic regression analysis, TUG was predictive for 30-day morbidity (OR 3.16; 95%CI 1.20-8.31; *p=0.020*)

	Treatment-related toxicity	Papis	Hepato-pancreato-biliary surgical patients	20	In uni-variate analysis TUG was not predictive for 30-day morbidity (*p=0.5*), mortality (*p=1*) and hospital stay (*p=0.9*).

Legend: N: Number; NPV: Negative Predictive Value; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; HR: Hazard Ratio

Table 3: Domains and instruments used in GA*

Domain	Tool (References)
Demographic data and social status	Questions on living situation, marital status, educational level, safety of environment, financial resources. Medical Outcomes Study Social Activity Survey Caregiver burden; Medical Outcomes Study Social Support Survey: Emotional/Information and Tangible Subscales Summary of some criteria (e.g. availability of family support, appropriateness of social environment)
Comorbidity	Charlson Comorbidity Index CIRS (Cumulative Illness Rating Scale) CIRS-G (Cumulative Illness Rating Scale-Geriatrics) NYHA (New York Heart Association) Number of comorbid conditions Simplified Comorbidity Score Summary of comorbidities Hematopoietic Cell Transplantation Comorbidity Index Physical Health Section (subscale of OARS; Older Americans Resources and Services)
Functional status	ADL (activities of daily living): Katz index IADL (instrumental activities of daily living): Lawton scale Performance status index Barthel Index (any version) Lawton-Brody IADL Scale Nottingham Extended Activities of Daily Living Scale Activities of Daily Living (subscale of Medical Outcomes Study Physical Health) Instrumental Activities of Daily Living (subscale of OARS; Older Americans Resources and Services) Pepper Assessment Tool for Disability Visual and/or hearing impairment, regardless of use of glasses or hearing aids Medical Outcomes Study physical Health (any version) Mobility Problem (requiring help or the use of a walking aid) Timed Get Up and Go Hand grip strength Short Physical Performance Battery One-leg standing balance test Walking problems/gait assessment/gait speed Eastern Cooperative Oncology Group Performance Status Karnofsky Self-Reported Performance Rating Scale Karnofsky Health Care Professional-Rated Performance Rating Scale
Cognition	Mini Mental State Examination (any version) Informant Questionnaire on Cognitive Decline in the Elderly (any version) Modified Mini-Mental State Examination Clock-drawing test Blessed Orientation-Memory-Concentration Test
Depression	Geriatric Depression Scale (any version) Center for Epidemiologic Studies Depression Scale Hospital Anxiety and Depression Scale Mental Health Index Presence of depression (as a geriatric syndrome) The distress thermometer
Nutrition	Body Mass Index (weight and height) Weight loss (unintentional loss in 3 or 6 months)

	Mini Nutritional Assessment (any version) Short nutritional assessment questionnaire DETERMINE nutritional index
Fatigue	MOB-T Mobility Tiredness Test
Polypharmacy	Beers criteria§ STOP and START criteria§
Geriatric syndromes**	Dementia Delirium Incontinence (fecal and/or urinary) Osteoporosis or spontaneous fractures Neglect or abuse Failure to thrive (Self-reported number of falls (within different time frames) Constipation Polypharmacy Pressure ulcus Sarcopenia§

* For studies published before November 16, 2010, see review Puts et al.

**** Some studies have reported geriatric syndromes which overlap with other domains.

§ Although this tool was not used in the newfound articles, it is mentioned because of high relevance in geriatrics.

Table 4: GA models in general geriatric medicine and geriatric oncology

General geriatrics	
CGA models	***Definition*** **Effectiveness**
GA ward models - GEMU - ACE	*A specific ward with a specialized geriatric care team that applies GA and …* - *… delivers both acute and rehabilitation care to inpatient.(GEMU).* - *… only delivers acute care.(ACE). Patients in ACE are transferred to long term care facilities for rehabilitation program.* Six meta-analyses show that the *GEMU* is the most effective way of caring for geriatric patients with lower mortality, less institutionalization and less functional decline compared to standard (non-GEMU) care for the same patients
GCT	*A specialized geriatric team that applies GA on non-GA wards on as consultative basis.* A recent meta-analysis could not show a consistent effect of *IGCT* interventions in non-GEMUs on mortality, readmission, length of stay, or functional status. Absence of effect is mainly due to a low adherence rate to the IGCT's recommendation.
CMM	*Joint geriatric and specialized care (e.g. orthogeriatric beds/units).* Individual studies of CMMs, mainly operationalized as ortho-geriatric beds to date, show promising results and advantages.
Geriatric oncology	
GA models	***Definition*** **Advantages (+) / disadvantages (-)**
Geriatric oncology unit	*A specific ward with a team specialized in caring for older patients with cancer that applies GA based on the GEMU or the ACE model.* (+) centralization of geriatric expertise and treatment options (-) potential patient withdrawal from familiar treating oncologist (-) financial incentives might drive general oncologists not to refer patients (-) only a limited number of patients can be reached (-) General geriatric oncologists might miss the detailed rapidly evolving knowledge of the broad field of oncology
GCT	*A specialized geriatric team that applies GA on non-GA wards or in other settings on a consultative basis.* (+) patients remain under the supervision of their treating oncologist (+) this model can reach a large majority of older patients with cancer (+) Interaction between oncologists and geriatric teams is feasible (-) decentralization of geriatric expertise has logistic and practical (e.g. staffing) challenges. (-) several factors may lead to low compliance of treating physicians to (I)GCT's advices: GA results may be unknown at time of treatment decision making, treating physicians might not know what to do with GA results, onset of geriatric interventions or treatment adjustment depends of local possibilities. (-) patients who need referral to specific geriatric care programs, might encounter waiting lists

Geriatric expertise Not nearby	*GA in stand-alone comprehensive cancer centers without geriatric department or private practice oncology clinic.* (+) patients remain under the supervision of their treating oncologist (+) validated methods can easily be used to target high-risk patients and introduce geriatric care (+) a large majority of older patients with cancer can be reached (-) realization of interaction between oncologists and geriatric teams is difficult (-) there is no gold standard to screen high-risk patients (-) interrater reliability and interpretation of results can be a problem (-) patients who need referral, might encounter waiting lists

(C)GA = comprehensive geriatric assessment; GEMU = geriatric evaluation and management unit; ACE = acute care for elders; GCT = geriatric consultation team; CMM = co-management model

Appendix I

Screening tools

- Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older patients with cancer: an update on SIOG recommendations. Annals of oncology: official journal of the European Society of Medical Oncology / ESMO. 2015;26(2):288-300.

Appendix II

Geriatric assessment

- Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, … Kenis C et al. International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2014;32(24):2595-603.

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Screening tools for multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendations†

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Background: Screening tools are proposed to identify those older cancer patients in need of geriatric assessment (GA) and multidisciplinary approach. We aimed to update the International Society of Geriatric Oncology (SIOG) 2005 recommendations on the use of screening tools.

Materials and methods: SIOG composed a task group to review, interpret and discuss evidence on the use of screening tools in older cancer patients. A systematic review was carried out and discussed by an expert panel, leading to a consensus statement on their use.

Results: Forty-four studies reporting on the use of 17 different screening tools in older cancer patients were identified. The tools most studied in older cancer patients are G8, Flemish version of the Triage Risk Screening Tool (fTRST) and Vulnerable Elders Survey-13 (VES-13). Across all studies, the highest sensitivity was observed for: G8, fTRST, Oncogeriatric screen, Study of Osteoporotic Fractures, Eastern Cooperative Oncology Group-Performance Status, Senior Adult Oncology Program (SAOP) 2 screening and Gerhematolim. In 11 direct comparisons for detecting problems on a full GA, the G8 was more or equally sensitive than other instruments in all six comparisons, whereas results were

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mixed for the VES-13 in seven comparisons. In addition, different tools have demonstrated associations with outcome measures, including G8 and VES-13.

Conclusions: Screening tools do not replace GA but are recommended in a busy practice in order to identify those patients in need of full GA. If abnormal, screening should be followed by GA and guided multidisciplinary interventions. Several tools are available with different performance for various parameters (including sensitivity for addressing the need for further GA). Further research should focus on the ability of screening tools to build clinical pathways and to predict different outcome parameters.

Key words: screening tools, older cancer patients, geriatric assessment

introduction

The older cancer population is heterogeneous with respect to overall health status due to differences in co-morbidities, functional status, geriatric syndromes and socioeconomic aspects resulting in decreased physical reserve. In addition, cancer and its treatment may further decrease this physical reserve.

In 2005, the International Society of Geriatric Oncology (SIOG) published recommendations on the approach of older cancer patients, recommending the performance of geriatric assessment (GA) [1]. Recent reviews [2, 3] state that the use of GA in older cancer patients may identify health and functional status issues and that several domains of GA are associated with oncological outcomes.

Ideally, all older cancer patients should be evaluated by GA followed by interventions and follow-up. However, this approach is resource-consuming and not necessary in all patients. Therefore, the use of a screening tool has been proposed to identify patients in need of GA and multidisciplinary approach. In 2005, SIOG recommended the use of screening tools in cancer patients aged 70 years or older, but in the absence of tools tested in this population, no specific tool was recommended [1]. Since 2005, research on screening tools in older cancer patients has grown exponentially.

In order to update the 2005 SIOG recommendations, four SIOG task forces were established, covering different domains: screening, GA [3], geriatric interventions and frailty. The aim of the current SIOG paper is to review the use of screening tools in older cancer patients, leading to a consensus statement.

definition of screening tool

A screening tool in older cancer patients is a brief assessment, conducted to help the clinician to identify those patients in need of further evaluation by GA, which may provide a better insight into the patients' general health and individual probability of survival, and allow directed interventions.

Screening tools might also have prognostic/predictive value for important outcome measures such as treatment-related toxicity, functional decline and survival.

Screening tools should be simple and take a few minutes, while full GA may take much longer. High sensitivity and negative predictive value (NPV) are the most important characteristics for screening tools in order to identify all patients at risk for adverse outcomes. In addition, a high specificity is of interest in order to limit the number of fit patients who unnecessarily undergo GA.

methods

The screening tools task force was composed of a writing committee of geriatricians and medical oncologists, and a reference committee of geriatricians, medical and surgical oncologists, and two geriatric nurse practitioners (supplementary Appendix A, available at *Annals of Oncology* online for composition).

A systematic literature review was carried out by LDC and KVP (supplementary Appendix B, available at *Annals of Oncology* online for detailed description of methodology). A review by Hamaker included 14 studies comparing screening tools with GA and was considered as the starting point [4].

For the current review, a publication was eligible for inclusion if it reported on older cancer patients and the use of screening tools for detection of impairments on GA. Articles and abstracts published up to December 2013 were considered.

A quality score of the retrieved studies was carried out by LDC and KVP using the methodological index for nonrandomized studies (supplementary Appendix C, available at *Annals of Oncology* online) [5].

Based on the results of the literature search, a first draft was written by the writing group and presented to the entire task force. The data were discussed, leading to a consensus statement.

results

included studies

The literature search yielded 1937 citations. After exclusion of duplicates, studies not reporting on results in oncology patients or on screening tools and abstracts not reporting any results, a total of 50 citations were included [4, 6–54]: 22 original papers, 22 conference abstracts and 6 reviews. The articles and abstracts reported the results of 44 studies on the use of 17 screening tools in older cancer patients (supplementary Appendix D, available at *Annals of Oncology* online for description of tools).

Twenty-two studies compared a total of 14 screening tools with GA and reported on sensitivity and specificity [6–27]. Tables 1 and 2 summarize, respectively, the characteristics and the results of these studies. The number of domains included in the GA, used as reference procedure, varied between 5 and 10 and the cutoff for impairment between ≥1 and ≥2 deficiencies. Eleven studies directly compared screening tools (Table 3) [6, 7, 10–13, 15, 17, 18, 20, 22].

The other 22 studies reported on various aspects of different screening tools but did not report on sensitivity and specificity compared with GA [28–54].

Table 1. Characteristics of 22 studies comparing screening tools with Geriatric Assessment

First author (reference)	Publication type (years)	Number of patients	Study population	Age cutoff Median age (years)	Screening tool	Cutoff for the screening tool to be 'abnormal'	Number of GA items	Cutoff for the number of deficits assessed by GA, to classify as 'nonfit'
Soubeyran [6]	A (2011)	1425	Various cancer types	≥70 78	G8 VES-13	≤14 ≥3	7	≥1
Kenis [7]	FP (2013)	937	Various cancer types	≥70 76	G8 fTRST	≥1 or ≥2 ≤14	7	≥2
Liuu [8]	A (2012)	518	Various cancer types	≥70 80	G8	≤14	7	≥1
Bellera [9]	FP (2012)	364	Various cancer types	≥70 77	G8	≤14	7	≥1
Luce [10]	FP (2012)	211	Various cancer types	>70 78	G8 ISAR KPS	<15 ≥2 <80	10	≥1
Baitar [11]	FP (2013)	170	Various cancer types	≥65 77	G8 GFI	≥4 ≤14	8	≥2
Kenis [12]	A (2009)	140	Various cancer types	≥70 77	G8 fTRST GFI	≥1 or ≥2 ≤14 ≥4	7	≥2
Pottel [13]	FP (2012)	51	Head and Neck	≥65 72	G8 VES-13	≥3 ≤14	7	≥2
Luciani [14]	FP (2010)	419	Various cancer types	≥70 76	VES-13	≥3	8	≥1
Biganzoli [15]	FP (2013)	259	Various cancer types	≥70 77	VES-13 Fried	≥3 ≥1	5	≥1
Monfardini [16]	A (2010)	150	Breast cancer	≥70 76	VES-13	≥3	NR	NR
Owusu [17]	FP (2011)	117	Various cancer types	≥65 73	VES-13 ECOG-PS KPS	≥3 ≥1 ≤80	10	≥2
Kellen [18]	FP (2010)	113	Various cancer types	≥70 77	VES-13 aCGA GFI	≥1 ≥3 ≥4	5	≥2 or cognitive impairment
Falci [19]	A (2009)	93	Various cancer types	≥70 76	VES-13	≥3	NR	NR
Molina-Garrido [20]	A (2011)	58	Various cancer types	≥70 NR	VES-13 Fried criteria	≥3 ≥3	NR	≥2
Mohile [21]	FP (2007)	50	Prostate cancer	≥70 78	VES-13	≥3	7	≥2
Molina-Garrido [22]	FP (2011)	41	Breast cancer	≥65 75	VES-13 Barber test	≥1 ≥3	7	≥2
Luciani [23]	FP (2012)	400	Various cancer types	≥70 77	SOF	≥2	6	≥2

Molina-Garrido [24]	A (2012)	173	Various cancer types	≥70 79	Barber test	≥1	≥NR	≥2	
Valéro [25]	FP (2011)	126	Various cancer types	≥75 78	OGS	≥1	5	≥1	
Fargeas [26]	A (2009)	104	Hematological	≥70 79	Gerhematolim	NR	NR	NR	
Extermann [27]	A (2009)	31	Various cancer types	≥68 NR	SAOP2	NR	6	≥1	

GA, geriatric assessment; FP, full paper; A, abstract; NR, not reported.

Twelve studies reported the relationship between seven screening tools with outcome (functional status, treatment-related toxicity and survival) [7, 8, 29, 30, 33–38, 41, 49] (Table 4).

The six reviews all discussed different screening tools [4, 50–54], but only the paper by Hamaker et al. [4] was a systematic review.

screening tools in older cancer patients

G8. The G8 is an eight-item screening tool, developed for older cancer patients. The tool covers multiple domains usually assessed by the geriatrician when performing the GA and takes ∼5 min [6]. A score of ≤14 is considered abnormal [9].

Since the G8 was developed for the cancer population, there are no data available on its use in the general older population.

The G8 was compared with GA in eight studies, which cumulatively included 3816 patients [6–13] (Tables 1 and 2). Sensitivity ranged from 65% to 92% and was more than 80% in six studies. Specificity ranged from 3% to 75% and was more than 60% in four studies.

In 1967 Belgian patients, G8 was considered a feasible screening tool both in academic and nonacademic hospitals [28].

In four studies, G8 was compared with outcome measures [7, 8, 29, 30] (Table 4). G8 showed high sensitivity and NPV for functional decline but low specificity [7]. In various cancers, G8 was predictive for chemotherapy-related toxicity ($P = 0.025$) [29], but this was not observed in hematological malignancies ($P = 0.905$) [30]. Finally, G8 was prognostic for survival in two studies in various cancer types [7, 8] but not in hematological malignancies [30].

Vulnerable Elders Survey-13. The Vulnerable Elders Survey-13 (VES-13) is a 13-item self-administered tool, developed for identifying older people at increased risk of health deterioration in the community [55]. A score of ≥3 identified individuals as vulnerable, defined as increased risk of functional decline or death over 2 years [55]. Time to complete VES-13 is 5 min [6, 16, 21].

In older persons in the community, abnormal VES-13 was associated with functional decline, survival and health outcomes [55, 56].

In two studies in older cancer patients, self-completion of VES-13 was often troublesome [16, 31] with 36.7% of breast cancer patients unable to complete VES-13 autonomously [16].

In 11 studies including 2776 older cancer patients, VES-13 was compared with GA [6, 13–22] (Tables 1 and 2). Sensitivity ranged from 39% to 88% and was more than 80% in 2 of 11 studies, while specificity ranged from 62% to 100%. When compared with subparts of GA, VES-13 showed a high sensitivity for functional status but not for comorbidity [14, 32]. Patients older than 85 years old are at the cutoff value only because of age [21].

VES-13 was compared with treatment-related toxicity in three studies [29, 33, 34] (Table 4). In patients with various cancers, VES-13 was predictive for the occurrence of severe chemotherapy toxicity ($P = 0.015$) [29]. In older surgical patients, VES-13 was not predictive for postoperative morbidity [33, 34] and mortality [33]. In patients with digestive cancers treated with chemotherapy, VES-13 was associated with survival ($P < 0.0014$) [35].

Table 2. Results of 22 studies comparing screening tools with geriatric assessment

Screening tool First author (reference)	Number of patients	% 'Abnormal' on screening tool	% 'nonfit' on GA	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
G8							
Soubeyran [6]	1425	68	80	77 (74–79)	64 (59–70)	NR	NR
Kenis [7]	937	74	74	87 (84–89)	59 (53–65)	86 (83–88)	61 (55–68)
Liuu [8]	518	80	84	87 (83–90)	60 (48–70)	NR	NR
Bellera [9]	364	82	94	85 (81–89)	65 (41–85)	NR	NR
Luce [10]	211	80	NR	65 (NR)	3 (NR)	44 (NR)	8 (NR)
Baitar [11]	170	76	64	92 (85–96)	52 (39–65)	78 (70–84)	78 (63–88)
Kenis [12]	140	NR	79	80 (NR)	40 (NR)	83 (NR)	35 (NR)
Pottel [13]	51	67	69	86 (72–94)	75 (52–91)	88 (NR)	71 (NR)
VES-13							
Soubeyran [6]	1425	60	80	69 (66–71)	74 (69–79)	NR	NR
Luciani [14]	419	54	28	87 (81–92)	62 (56–68)	NR	NR
Biganzoli [15]	259	47	66	62 (54–69)	81 (71–88)	86 (79–92)	52 (44–61)
Monfardini [16]	150	NR	44	68 (NR)	71 (NR)	65 (NR)	74 (NR)
Owusu [17]	117	35	43	88 (NR)	69 (NR)	68 (NR)	88 (NR)
Kellen [18]	113	49	68	61 (49–72)	78 (61–90)	85 (73–93)	48 (35–62)
Falci [19]	93	43	43	60 (NR)	70 (NR)	60 (NR)	70 (NR)
Molina-Garrido [20]	58	35	88	39 (NR)	100 (NR)	100 (NR)	18 (NR)
Pottel [13]	51	39	69	57 (42–71)	100 (83–100)	100 (NR)	52 (NR)
Mohile [21]	50	50	60	73 (NR)	86 (NR)	89 (NR)	67 (NR)
Molina-Garrido [22]	41	29	56	55 (NR)	100 (NR)	100 (NR)	66 (NR)
G8 + VES-13							
Soubeyran [6]	1425	NR	80	87 (NR)	53 (NR)	NR	NR
Pottel [13]	51	NR	69	91 (79–98)	94 (74–100)	97 (NR)	83 (NR)
fTRST							
Kenis [7]							
Cut off 1	937	82.5	74	91 (89–93)	42 (36–48)	81 (78–84)	63 (56–71)
Cut off 2		54.7		67 (64–71)	80 (74–85)	90 (87–93)	47 (42–52)
Kenis [12]							
Cut off 1	140	NR	79	92 (NR)	50 (NR)	87 (NR)	63 (NR)
Cut off 2		NR		64 (NR)	100 (NR)	100 (NR)	43 (NR)
GFI							
Baitar [11]	170	47	64	66 (89–75)	87 (76–94)	90 (82–95)	59 (49–69)
Kenis [12]	140	NR	79	57 (NR)	87 (NR)	94 (NR)	36 (NR)
Kellen [18]	113	31	68	39 (28–51)	86 (70–95)	86 (70–95)	40 (29–51)
SOF index							
Luciani [23]	400	67	68	89 (85–93)	81 (73–88)	NR	NR
KPS							
Luce [10]	211	86	NR	29 (NR)	44 (NR)	39 (NR)	34 (NR)
Owusu [17]	117	38	43	78 (NR)	91 (NR)	87 (NR)	85 (NR)
Fried criteria							
Biganzoli [18]	259	75	66	87 (81–92)	49 (38–60)	77 (70–82)	66 (53–77)
Molina-Garrido [20]	58	35	88	37 (NR)	86 (NR)	95 (NR)	16 (NR)
Barber							
Molina-Garrido [24]	173	68	47	74 (65–83)	39 (28–49)	58 (49–67)	56 (43–69)
Molina-Garrido [22]	41	42	56	59 (NR)	79 (NR)	77 (NR)	63 (NR)
ISAR							
Luce [10]	211	79	NR	70 (NR)	10 (NR)	47 (NR)	22 (NR)
OGS							
Valéro [25]	126	89	89	88 (80–93)	44 (28–63)	85 (77–91)	50 (31–69)
ECOG-PS							
Owusu [17]	117	66	43	94 (NR)	55 (NR)	61 (NR)	93 (NR)
aCGA							
Kellen [18]	113	NR	68	51 (39–62)	97 (85–100)	97 (87–100)	48 (36–60)

Continued

Table 2. *Continued*

Screening tool First author (reference)	Number of patients	% 'Abnormal' on screening tool	% 'nonfit' on GA	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
Gerhematolim Fargeas [26]	104	NR	NR	95 (87–99)	87 (72–96)	93 (84–98)	92 (78–98)
SAOP2 Extermann [27]	31	NR	84	100 (NR)	40 (NR)	90 (NR)	100 (NR)

Sensitivity, specificity, PPV and NPV indicate the value of the screening tool for detecting predefined abnormal geriatric assessment.
CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; NR, not reported.

Combination of VES-13 and G8. Two studies investigating both VES-13 and G8 suggested that a combination of both tools would be a sensitive screening tool in older cancer patients [6, 13]. Soubeyran et al. found that an abnormal test on either G8 or VES-13 demonstrated a sensitivity of 86.6% and a specificity of 53.2% for detection of patients unfit on GA [6]. In the study of Pottel et al. [13], VES-13 + (17-G8) ≥5 demonstrated a sensitivity of 91.4% and a specificity of 93.8%. The combination of both tools was significantly better than the G8 or VES-13 alone ($P = 0.024$ and $P = 0.0237$).

Flemish version of the Triage Risk Screening Tool. The original Triage Risk Screening Tool (TRST) was developed to identify older patients at risk for failed discharge home from the emergency department, defined as return to the emergency department, admission to the hospital or admission to a nursing home within 30 to 120 days after discharge [57, 58]. The tool is composed of five yes/no questions and a score of ≥2 is considered as at risk. This tool takes two minutes to complete [57].

In the older population presenting at the emergency department TRST correlates with functional decline at baseline and at follow-up [57, 58].

The performance of Flemish version of the Triage Risk Screening Tool (fTRST) was compared with GA in two studies including 1077 older cancer patients [7, 12] (Tables 1 and 2). When using the validated cutoff of ≥2, the fTRST(2) led to sensitivity of, respectively, 64% and 67% and specificity of 100% and 80%. Lowering the cutoff to ≥1 [fTRST(1)) resulted in an increased sensitivity (92% and 91%) but a decreased specificity (42% and 50%)].

Both fTRST(1) and fTRST(2) were predictive for functional decline with fTRST(1) demonstrating the highest sensitivity [7] (Table 4). They also demonstrated prognostic value for overall survival ($P < 0.001$ for both) [7]. Compared with G8, the latter demonstrated a higher discriminatory power: hazard ratio (HR) 0.38 for G8 and 0.67 for fTRST(2), while fTRST(1) was not retained in the stepwise regression.

Groningen Frailty Indicator. The Groningen Frailty Indicator (GFI) is composed of 15 questions addressing various domains and was developed in people aged 65 years and over, including hospital inpatients, nursing home residents and community-dwelling elderly [59]. A score of ≥4 indicates a risk for physical, social and/or psychological impairment.

In community-dwelling elderly, an abnormal GFI correlated more strongly with a decline in self-management abilities than chronological age [60].

In older cancer patients, GFI was compared with GA in 423 patients with various cancers in three studies [11, 12, 18] (Tables 1 and 2). Sensitivity ranged from 39% to 66% and specificity from 86% to 87%. Lowering the cutoff to ≥3 resulted in a sensitivity of 87% and a specificity of 70% [11].

Five studies investigated the correlation of GFI with outcome measures [33, 34, 36–38] (Table 4). In patients with various cancers, GFI was predictive for chemotherapy-related toxicity [36]. In two studies in older surgical cancer patients, GFI was not associated with postoperative morbidity [33, 34] and mortality [34]. In two studies in patients treated with chemotherapy (one in various cancers and one in breast cancer), GFI correlated with survival [37, 38].

Study of Osteoporotic Fractures Index. The Study of Osteoporotic Fractures (SOF) index is a three-item tool designed to measure 'prefrailty' and 'frailty'. Patients presenting one of the items were considered to be in a prefrailty status and patients with more than one item were considered 'frail'.

In women older than 69 years [61] and in men older than 67 years [62] without cancer, a score of ≥2 was associated with higher risk of recurrent falls, disability, fractures and death.

In 400 patients with various cancers, this screening tool demonstrated a sensitivity of 89% and a specificity of 81% when compared with GA (Tables 1 and 2) [23].

Karnofsky Performance Status and Eastern Cooperative Oncology Group-Performance Status. Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group-Performance Status (ECOG-PS) are tools frequently used by oncologists to classify the performance status of their patients [63, 64].

The KPS was compared with GA in 328 patients in two studies [10, 17], resulting in a sensitivity and specificity of, respectively, 29% and 44% for a cutoff value of <80 [10] and 78% and 91% for a cutoff value of ≤80 [17] (Tables 1 and 2).

The ECOG-PS cutoff value of one resulted in a sensitivity of 94% and a specificity of 55% [17] (Tables 1 and 2). The correlation between ECOG-PS and functional scales such as ADL and IADL was moderate [39, 40].

In one study [29], ECOG-PS was not predictive for chemotherapy-related toxicity in older cancer patients (Table 4).

Table 3. Studies with a direct comparison between screening tools

First author (reference)	Number of patients	Tools	% abnormal	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
Soubeyran [6]	1425	G8	68	77 (74–79)	64 (59–70)	NR	NR
		VES-13	60	69 (66–71)	74 (69–79)	NR	NR
Kenis [7]	937	G8	74	87 (84–89)	59 (53–66)	86 (83–88)	61 (55–68)
		fTRST(1)	83	91 (89–93)	42 (36–48)	81 (78–84)	63 (56–71)
		fTRST(2)	55	67 (64–71)	80 (74–85)	90 (87–93)	47 (42–52)
Biganzoli [15]	259	VES-13	47	62 (54–69)	81 (71–88)	86 (79–92)	52 (44–61)
		Fried Frailty Criteria	75	87 (81–92)	49 (38–60)	77 (70–82)	66 (53–77)
Luce [10]	211	G8	80	65 (NR)	3 (NR)	44 (NR)	8 (NR)
		ISAR	79	70 (NR)	10 (NR)	47 (NR)	22 (NR)
		KPS <80	86	29 (NR)	44 (NR)	39 (NR)	34 (NR)
Baitar [11]	170	G8	76	92 (85–96)	52 (39–65)	78 (70–84)	78 (63–88)
		GFI	47	66 (56–75)	87 (76–94)	90 (82–95)	90 (82–95)
Kenis [12]	140	G8	NR	80 (NR)	40 (NR)	83 (NR)	35 (NR)
		GFI	NR	57 (NR)	87 (NR)	94 (NR)	36 (NR)
		fTRST(1)	NR	92 (NR)	50 (NR)	87 (NR)	63 (NR)
		fTRST(2)	NR	64 (NR)	100 (NR)	100 (NR)	43 (NR)
Owusu [17]	117	VES-13	35	88 (NR)	69 (NR)	68 (NR)	88 (NR)
		KPS ≤80	38	78 (NR)	91 (NR)	87 (NR)	85 (NR)
		ECOG-PS	66	94 (NR)	55 (NR)	61 (NR)	93 (NR)
Kellen [18]	113	VES-13	49	61 (49–72)	78 (61–90)	85 (73–93)	48 (35–62)
		GFI	31	39 (28–51)	86 (70–95)	86 (70–95)	40 (29–51)
		aCGA	NR	51 (39–62)	97 (85–100)	97 (87–100)	48 (36–60)
Molina-Garrido [20]	58	VES-13	35	39 (NR)	100 (NR)	100 (NR)	18 (NR)
		Fried Frailty Criteria	35	37 (NR)	86 (NR)	95 (NR)	16 (NR)
Pottel [13]	51	G8	67	86 (72–94)	75 (52–97)	88 (NR)	71 (NR)
		VES-13	39	57 (42–71)	100 (83–100)	100 (NR)	52 (NR)
Molina-Garrido [22]	41	VES-13	29	55 (NR)	100 (NR)	100 (NR)	66 (NR)
		Barber	41	59 (NR)	79 (NR)	77 (NR)	63 (NR)

Sensitivity, specificity, PPV and NPV indicate the value of the screening tool for detecting predefined abnormal geriatric assessment.
CI, confidence interval; PPV, positive predictive value, NPV, negative predictive value; NR, not reported.

Fried Frailty Criteria or physical frailty phenotype. The Fried Frailty Criteria include five items: weight loss, handgrip strength, gait speed, exhaustion and physical performance and a score of ≥3 indicates 'frailty'.

In the general older population, the physical frailty phenotype predicts risk of falls, disability, fracture and death [61, 62].

When compared with GA in 317 older cancer patients in two studies [18, 20], the Fried Frailty Criteria resulted in a sensitivity of 37% and 87% and a specificity of 86% and 49% (Tables 1 and 2).

In a subgroup analysis, wide variations in specificity were observed [18]: 60% in early breast cancer versus 19% in early gastrointestinal cancer.

In colon cancer patients, the Fried Frailty Criteria failed to predict complications after surgery, in contrast to GA, but was associated with survival [41] (Table 4).

Barber Questionnaire. The Barber Questionnaire was developed to identify older persons at risk for dependence in the community [65]. It consists of nine yes/no questions and patients with a score of ≥1 are considered candidates for further evaluation through GA.

The Barber questionnaire was compared with GA in two studies [22, 24] (Tables 1 and 2). In patients with various cancers, sensitivity was 74% and specificity 39% [24]. In breast cancer patients, the sensitivity was lower (59%) but specificity higher (79%) [22].

In a small breast cancer population, the reliability of the tool was 67% and all patients classified as fit by the Barber test were also considered fit by GA [42]. In 41 breast cancer patients, the Barber test was moderately predictive for identifying a deficit on ≥2 tests of GA [43].

Identification of Seniors At Risk. The Identification of Seniors At Risk (ISAR) is a six-item, self-administered tool developed for the emergency department [66]. A score of two or more categorizes patients as at risk for adverse outcome.

For older patients presenting at the emergency department, ISAR correlates with baseline functional impairment and with functional decline at 6 months [66].

ISAR was compared with GA in 211 older cancer patients resulting in a sensitivity and specificity of, respectively, 70% and 10% [10] (Tables 1 and 2).

Table 4. Screening tools as a prognostic/predictive marker

Tool	Outcome	First author (reference)	Population (*N*)	Conclusion
G8	Functional decline	Kenis [7]	Various cancers (937)	High sensitivity and NPV for functional decline on ADL (84% and 91%, respectively) and IADL (76% and 70%, respectively) but low specificity (31% both for ADL and for IADL). Older patients with normal G8 have low risk for functional decline in ADL and less pronounced in IADL. Patients with an abnormal G8 need further evaluation during follow-up.
	Treatment-related toxicity	Stokoe [29]	Various cancers treated with chemotherapy (185)	Abnormal G8 was associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment): 65% versus 47% ($P = 0.025$).
		Dubruille [30]	Hematological malignancies (85)	Abnormal G8 was not predictive for intolerance to chemotherapy ($P = 0.905$).
	Survival	Kenis [7]	Various cancers (937)	G8 showed a significant prognostic value for OS (median survival 31.8 months for abnormal G8 versus not reached for normal G8 [HR 0.38; 95% CI 0.27–0.52; $P < 0.001$). Older patients with normal G8 had 62% less chance of dying after a median follow-up of 18.95 months.
		Dubruille [30]	Hematological malignancies (85)	Abnormal G8 was not predictive for 1-year survival ($P = 0.388$).
		Liuu [8]	Various cancers (518)	Abnormal G8 associated with 6-month death in multivariate analysis (HR 6.68; 95% CI 1.63–27.35; $P = 0.001$).
VES-13	Treatment-related toxicity	Stokoe [29]	Various cancers treated with chemotherapy (185)	Abnormal VES-13 was associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment): 76% versus 54% ($P = 0.015$).
		Papis [33]	Hepato-pancreato-biliary cancers treated with surgery (20)	In univariate analysis, VES-13 was not predictive for 30-day morbidity ($P = 1$), mortality ($P = 1$) and hospital stay ($P = 0.8$).
		Huisman [34]	Various cancers treated with surgery (345)	In a univariate logistic regression analysis, VES-13 was not associated with 30-day morbidity (OR 1.63; 95% CI 0.85–3.11; $P = 0.14$).
	Survival	Kitamura [35]	Gastrointestinal, hepatobiliary and pancreatic cancers treated with chemotherapy (21)	VES-13 was significantly correlated with overall survival (HR 1.243; 95% CI 1.048–1.480; $P < 0.0014$).
fTRST	Functional decline	Kenis [7]	Various cancers (937)	High sensitivity and NPV for functional decline on ADL (91% and 92%, respectively) and IADL (86% and 73%, respectively) but low specificity (21% for ADL and 22% for IADL). Older patients with normal fTRST(1) have low risk for functional decline in ADL and less pronounced in IADL. Patients with an abnormal fTRST (1) need further evaluation during follow-up.
	Survival	Kenis [7]	Various cancers (937)	fTRST(1) showed a significant prognostic value for OS [median survival 36.7 months for abnormal G8 versus not reached for normal G8 ($P < 0.001$)]. HR for fTRST (2) (normal versus abnormal) 0.67 (95% CI 0.53–0.85). fTRST(1) was not retained in the stepwise regression.

Continued

Table 4. *Continued*

Tool	Outcome	First author (reference)	Population (*N*)	Conclusion
GFI	Treatment-related toxicity	Papis [33]	Hepato-pancreato-biliary cancers treated with surgery (20)	In univariate analysis, GFI was not predictive for 30-day morbidity ($P = 0.6$), mortality ($P = 0.3$) and hospital stay ($P = 0.08$).
		Van Fraeyenhove [36]	Various cancers treated with chemotherapy (21)	Normal GFI was predictive for the absence of a serious adverse event after the first chemotherapy, defined as hospitalization or death: sensitivity 86%, NPV 50%.
		Huisman [34]	Various cancers treated with surgery (345)	In a univariate logistic regression analysis, GFI was not associated with 30-day morbidity (OR 1.52; 95% CI 0.81–2.87; $P = 0.20$).
	Survival	Aaldriks [37]	Various cancers treated with chemotherapy (202)	Abnormal GFI was associated with an increased mortality (HR 1.80; 95% CI 1.17–2.78; $P = 0.007$).
		Aaldriks [38]	Breast cancers treated with chemotherapy (55)	Abnormal GFI was associated with increased mortality with a mean follow-up of 16 months (HR 3.4; 95% CI 1.62–7.10; $P = 0.001$).
Fried Frailty Criteria	Treatment-related toxicity	Kristjansson [41]	Colorectal cancer treated with surgery (176)	Abnormal Fried Frailty Criteria screening was not predictive for any complication ($P = 0.18$) nor for severe complications (grade 2 or higher) ($P = 0.23$).
	Survival	Kristjansson [41]	Colorectal cancer treated with surgery (176)	Abnormal Fried Frailty Criteria screening was associated with worse survival: HR for prefrail patients 2.33 (95% CI 1.16–4.67; $P = 0.018$) and HR for frail patients 2.67 (95% CI 1.11–6.83; $P = 0.29$).
ECOG-PS	Treatment-related toxicity	Stokoe [29]	Various cancers treated with chemotherapy (185)	ECOG-PS ≥2 was not associated with higher occurrence of severe chemotherapy toxicity (grade 3/4 toxicity, dose reduction, unplanned hospitalization, treatment discontinuation or death within 30 days of treatment) ($P = 0.318$).
Handgrip strength	Survival	Kanesvaran [49]	Various cancers (249)	Handgrip strength was significantly associated with overall survival: HR 0.97 (95% CI 0.97–0.99) in univariate analysis.
Timed Up and Go	Treatment-related toxicity	Huisman [34]	Various cancers treated by surgery (345)	In multivariate logistic regression analysis, TUG was predictive for 30-day morbidity (OR 3.16; 95% CI 1.20–8.31; $P = 0.020$).
		Papis [33]	Hepato-pancreato-biliary surgical patients (20)	In univariate analysis, TUG was not predictive for 30-day morbidity ($P = 0.5$), mortality ($P = 1$) and hospital stay ($P = 0.9$).

N, number; NPV, negative predictive value; ADL, activities of daily living; IADL, instrumental activities of daily living; HR, hazard ratio; CI, confidence interval; OR, odds ratio.

Oncogeriatric screen. The oncogeriatric screen (OGS) was developed for oncology patients aged 75 years or over [25]. The tool consists of 10 yes/no questions exploring five items. Patients are considered in need of GA if at least one response for an item was positive. The OGS is a tool to be filled in by the treating oncological specialist.

In 126 older patients with various cancers, patients presenting with one to three risks were considered 'vulnerable' and patients with four or five risks were considered frail using the Balducci classification ('fit', 'vulnerable' and 'frail') [50]. In this study, the sensitivity of OGS was 88% and the specificity 44% [25] (Tables 1 and 2).

Abbreviated Comprehensive Geriatric Assessment. The abbreviated comprehensive geriatric assessment (aCGA) is a screening tool developed in older cancer patients [44, 45] and consists of the 15 items of the full GA that correlated the most with the findings of the GA. Time to complete aCGA was ∼5 min.

Kellen et al. [18] compared the aCGA with full GA in a heterogeneous group of older cancer patients and observed an overall sensitivity of 51% and specificity of 97% (Tables 1 and 2). The sensitivity was high for functional impairment (97% for ADL and 92% for IADL) but low for cognitive impairment (23% for MMSE <24).

Gerhematolim. Gerhematolim is a tool containing 27 questions and biological data and was developed for older patients with a hematological malignancy [46].

In 104 patients with hematological malignancies [26], this tool resulted in a sensitivity of 95% and a specificity of 87% compared with GA (Tables 1 and 2).

Senior Adult Oncology Program 2 screening. The SAOP2 screening tool was developed for older cancer patients to determine when a multidisciplinary approach was indicated.

The tool was compared with GA in 31 patients aged 65 years or older with various cancers and demonstrated a sensitivity of 100% and a specificity of 40% [27] (Tables 1 and 2). Of note, specificity was defined as impairment in the same domain as the screening question (e.g. if a loss of appetite turned out on GA to be in fact a depression, this was considered a specificity failure).

Physical Performance test. The physical performance test (PPT) was designed in older outpatients [67]. It is an objective measure of physical function based on seven timed items. Each item was scored on a five-point Likert scale (0–4) with the best score being 28. Patients were classified in three classes: no health impairment (PPP >20), moderate impairment (10 < PPT < 21) and severe impairment (PPT <11). The PPT takes 5 min.

When compared with KPS, the PPT seems to be a more accurate measure of impairment in older cancer patients [47]: 83% of patients with a KPS 60%–80% had a PPT <20. Further validation is necessary.

Handgrip test. The handgrip test measures the maximal strength of the dominant hand using a hydraulic hand dynamometer.

In the general older population, handgrip strength is predictive for functional decline [68].

The result of this test in older cancer patients was significantly higher for fit patients and lower for frail patients according to both the impression of the oncologist and the VES-13 [48]. In 249 older cancer patients, handgrip strength was significantly associated with survival (HR 0.97) [49].

Timed Up and go. The timed up and go (TUG) is a test of balance and requires a person to stand up, walk 3 m, turn, walk back and sit down. Time to complete the test is correlated with functional mobility [69] in hospitalized older persons.

In patients undergoing surgery for solid tumors, the TUG was predictive for morbidity. TUG was as predictive as GA in identifying patients at high risk of complications [odds ratio (OR): TUG 3.16 and GA 3.25; $P = 0.020$] [34] (Table 4). This was not observed in a smaller cohort of surgical patients [33].

direct comparisons. Eleven studies directly compared two or more screening tools [6, 7, 10–13, 15, 17, 18, 20, 22] (Table 3). Ten tools were included in the comparisons: G8, VES-13, fTRST, GFI, KPS, ECOG-PS, Fried Frailty Criteria, Barber questionnaire, ISAR, aCGA.

The most frequently compared tool is the VES-13 (seven studies) [6, 13, 15, 17, 18, 20, 22], followed by the G8 (six studies) [6, 7, 10–13]. In the two direct comparisons of these tools, the G8 was significantly more sensitive [nonoverlapping 95% confidence interval (CI)] [6, 13]. The G8 was more sensitive than the GFI in two studies [11, 12] and the VES-13 tended to be more sensitive than the GFI as well [18]. In two comparisons between the G8 and the fTRST(1) [7, 12], both tools were equally sensitive. The G8 and the ISAR were more sensitive than the KPS <80 [10], whereas the VES-13 was as sensitive as ECOG-PS ≥1 and KPS ≤80 [17]. In two comparisons between the VES-13 and the Fried Frailty Criteria, the sensitivity was equally low in one [22], whereas the Fried Frailty Criteria were more sensitive in another [15].

discussion

Since the 2005 SIOG GA guidelines [1], a significant amount of work has been done on screening tools. A total of 17 different tools have been studied in 44 different studies. Five tools were specifically developed for the older cancer population (G8, OGS, aCGA, SAOP2, Gerhematolim) and, for fTRST, the cutoff value was lowered.

Most studies ($n = 22$) have focused on the comparison of screening tools with GA. However, there is a variation between the number and type of items used in the GA as well as the cutoff for impairment, making interstudy comparison difficult.

The three most studied screening tools in older cancer patients are G8 ($n = 3816$), VES-13 ($n = 2776$) and fTRST ($n = 1077$). Of these, the highest sensitivity was observed with G8 (>80% in six of eight studies) and fTRST (>80% in two of two studies).

Further insight can be gained from the subgroup of 11 studies that made direct comparisons between instruments. In these, the G8 consistently demonstrated a good sensitivity. Results are more heterogeneous for the VES-13. The GFI appears to be underperforming as a screening tool, although this should not be taken as a critique of its role as a frailty index. More comparisons are needed for the other indexes.

Comparing sensitivity and specificity to GA has the advantage of feasibility in a study. It, however, only indirectly addresses the question of how useful the tool is for selecting patients who will truly benefit from GA for the management of their cancer and general health. Assessing this aspect would warrant more sophisticated study designs, accounting for feedback of a GA team as to the appropriateness of the referral, whether interventions followed, and whether these interventions went beyond standard oncology care. Attention should be paid to significant geriatric issues that would have been missed as well. It is likely that randomized studies of screening tools will be impossible due to confounding issues between arms. Outcome measures comparing centers using screening tools and those who do not in terms of service utilization, geriatric referrals, complications, functional independence and survival variables might provide good clues. However, a good sensitivity and NPV is a prerequisite for a good performance on these more sophisticated end points. In that sense, progress has been made since 2005.

A point of serious debate in the geriatric oncology community is whether one can rely on a screening tool alone for decision-making or whether a full GA is needed, following an abnormal screening. The arguments in favor of requiring its use only in combination with a GA is that all the studies that have demonstrated outcome improvements in geriatrics have used full GA. In addition, as mentioned in the parallel SIOG task force article on GA [3], interventions modifying oncology treatment have been based on GA as well. It is thus difficult to dissect the effect of the screening tool from the subsequently carried out GA (in patients with abnormal screening test) on outcome. While it is acknowledged that the ideal is to have a GA in all patients, most oncology practices do not have access to a geriatric team nor the time to do full GA. Moreover, some studies have

demonstrated an association of screening tools with outcomes. Both G8 and fTRST have shown to be predictive for functional decline [7]. G8, VES-13 and GFI were associated each in one trial with chemotherapy-related toxicity [29, 36] and TUG was predictive for postoperative morbidity [34]. Six screening tools were associated with overall survival: G8, VES-13, fTRST, GFI, Fried Frailty Criteria and handgrip strength [7, 8, 30, 35, 37, 38, 41, 49]. Based on such data, the argument is that raising awareness to potential GA deficits would improve the tailoring of oncology care. While the argument makes general intuitive sense, evidence of effectiveness is still lacking. On the other hand, if a sensitive screening tool is used, it may identify fit older patients who should be treated with standard treatments. Since many population studies have demonstrated a general tendency to undertreat older cancer patients, this by itself is an argument for recommending using even a simple screening tool alone in all oncology practices.

All the reviewed screening studies have focused on one time point, often the initial visit or an initial treatment decision. No data are available to guide the frequency at which such screening should be repeated. Yet, general geriatric data identify repeated GAs as a key component of effective geriatric interventions. Therefore, this point needs to be addressed in future geriatric oncology studies.

consensus statement

Although we now have a large amount of screening performance data, screening tools in older cancer patients should not replace GA. However, in a busy clinical practice, the use of a screening tool is recommended to identify patients in need of further evaluation by GA. Currently, G8 data seem the most robust (extensively studied, high sensitivity with acceptable specificity and prognostic/predictive for outcome measures). However, the performance of different screening tools may depend on the setting and the preferred screening tool may depend on the clinical situation. For this reason, no specific screening tool can be recommended or discouraged. Future research should focus on the outcomes of integrating tools in geriatric oncology clinical practice, the impact of the multidisciplinary management approach they trigger and patient-tailored screening. In addition, while geriatric studies point to the effectiveness of repeated screening and intervention, there are no data on repeated screening in older cancer patients and this should be targeted by future research.

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disclosure

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Rare Cancers Europe (RCE) methodological recommendations for clinical studies in rare cancers: a European consensus position paper

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While they account for one-fifth of new cancer cases, rare cancers are difficult to study. A higher than average degree of uncertainty should be accommodated for clinical as well as for population-based decision making. Rules of rational decision making in conditions of uncertainty should be rigorously followed and would need widely informative clinical trials. In principle, any piece of new evidence would need to be exploited in rare cancers. Methodologies to explicitly weigh and combine all the available evidence should be refined, and the Bayesian logic can be instrumental to this end. Likewise, Bayesian-design trials may help optimize the low number of patients liable to be enrolled in clinical studies on rare cancers, as well as adaptive trials in general, with their inherent potential of flexibility when properly applied. While clinical studies are the mainstay to test hypotheses, the potential of electronic patient records should be exploited to generate new hypotheses, to create external controls for future studies (when internal controls are unpractical), to study effectiveness of new treatments in real conditions. Framework study protocols in specific rare cancers to sequentially test sets of new agents, as from the early post-phase I development stage, should be encouraged. Also the compassionate and the off-label settings should be exploited to generate new evidence, and flexible regulatory innovations such as adaptive licensing could convey new agents early to rare cancer patients, while generating evidence. Though validation of surrogate end points is problematic in rare cancers, the use of an updated notion of tumor response may be of great value in the single patient to optimize the use of therapies, all the more the new ones. Disease-based communities, involving clinicians and patients, should be regularly consulted by regulatory bodies when setting their policies on drug approval and reimbursement in specific rare cancers.

Key words: rare cancers, clinical trials, research methodology

introduction

These recommendations were worked out through a multidisciplinary and multistakeholder consensus process, promoted by 'Rare Cancers Europe' (RCE). They are proposed to the health and research communities as a contribution to improve clinical studies about rare cancers, given the peculiar difficulties they pose. The ultimate goal is to make sure that rare cancer patients are not discriminated against because of the rarity of their diseases.

Having regard to the area of clinical research, they expand Political Recommendations on rare cancers (http://www.rarecancerseurope.org) selected in 2008 as the founding basis for RCE. RCE is a multistakeholder initiative dedicated to putting rare cancers firmly on the European policy agenda, advancing the way rare cancer patients are diagnosed and treated

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REVIEW ARTICLE

International Society of Geriatric Oncology Consensus on Geriatric Assessment in Older Patients With Cancer

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ABSTRACT

Purpose
To update the International Society of Geriatric Oncology (SIOG) 2005 recommendations on geriatric assessment (GA) in older patients with cancer.

Methods
SIOG composed a panel with expertise in geriatric oncology to develop consensus statements after literature review of key evidence on the following topics: rationale for performing GA; findings from a GA performed in geriatric oncology patients; ability of GA to predict oncology treatment–related complications; association between GA findings and overall survival (OS); impact of GA findings on oncology treatment decisions; composition of a GA, including domains and tools; and methods for implementing GA in clinical care.

Results
GA can be valuable in oncology practice for following reasons: detection of impairment not identified in routine history or physical examination, ability to predict severe treatment-related toxicity, ability to predict OS in a variety of tumors and treatment settings, and ability to influence treatment choice and intensity. The panel recommended that the following domains be evaluated in a GA: functional status, comorbidity, cognition, mental health status, fatigue, social status and support, nutrition, and presence of geriatric syndromes. Although several combinations of tools and various models are available for implementation of GA in oncology practice, the expert panel could not endorse one over another.

Conclusion
There is mounting data regarding the utility of GA in oncology practice; however, additional research is needed to continue to strengthen the evidence base.

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INTRODUCTION

More than half of patients newly diagnosed with cancer are age ≥ 65 years.[1] Although this number is expected to increase as the world population ages, there is less evidence on which to base treatment decisions for older patients with cancer, because this group is underrepresented in clinical trials.[2] Furthermore, there is heterogeneity in the aging process, which further contributes to the complexity of treatment decisions. These factors contribute to age-related variations in treatment patterns and outcomes, potentially resulting in increased likelihood of under- or overtreatment, which can influence both risk of treatment toxicity and survival.[3,4] Because chronologic age alone is a poor descriptor of heterogeneity in the aging process, a systematic and evidence-based way of describing the heterogeneity is needed to guide oncology treatment decisions. A comprehensive geriatric assessment (CGA) can fill this knowledge gap.[5,6] CGA is defined as a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up.[7] In the general (noncologic) geriatric population, CGA-guided treatment plans have been shown in some, but not all, studies to improve overall survival (OS), quality of life, and physical function and decrease the risk of hospitalization and nursing home placement.[8-10] However, these benefits have primarily been noted in acute geriatric care units.[8,11] Data on the utility of GA in the older (often ambulatory) cancer population have emerged only more recently.[12] Because CGA research specifically in the oncology setting has

mainly studied the diagnostic process/assessment and has not yet thoroughly focused on geriatric interventions, we decided to use the term geriatric assessment (GA) rather than CGA.

The International Society of Geriatric Oncology (SIOG) established recommendations on GA in older patients with cancer in 2005.[13] Numerous publications have emerged during the subsequent years. To synthesize this evidence and provide consensus opinion from individuals with expertise in geriatric oncology, SIOG established four multidisciplinary task forces consisting of individuals with international expertise in CGA in oncology practice. The aim of this article is to synthesize the evidence and provide geriatric oncology consensus on key questions on GA in geriatric oncology: (1) What is the rationale for performing GA? (2) What information is provided by a GA beyond that captured in a standard history and physical exam? (3) What is the ability of GA to predict oncology treatment–related complications? (4) What is the association between GA findings and OS? (5) What is the impact of GA findings on oncology treatment decisions? (6) What should a GA comprise, including domains and tools? (7) How should GA be organized and implemented in clinical care?

METHODS

A review by Puts et al,[12] relevant to questions 2 to 5, which included published or in-press data through November 16, 2010, was considered as the starting point for our review. Retrieved articles from a systematic literature search by P.H. (Appendix Table A1, online only, provides detailed information on methodology) were interpreted and discussed by the multidisciplinary group of experts, who could add relevant publications.

A quality score of the retrieved studies was performed by P.H. and C.K. using the methodologic index for nonrandomized studies (Appendix, online only).[14] After a first draft by the writing team, seven expert workgroups (for seven questions) were created (Appendix, online only). For all recommendations, data from the review by Puts et al,[12] as well as the newly selected publications, were used. Table 1 and Appendix Tables A2 to A6 (online only) list the recent publications; the review by Puts et al provided the older data. Finally, a task group consensus was developed. The Oxford 2011 levels of evidence (Appendix Table A7, online only) were used to grade the quality of evidence and strength of recommendations.[15]

RESULTS

Question 1

What is the rationale for performing GA?

Key evidence. GA can fill a significant knowledge gap, as described in the Introduction. Many publications have made statements on the rationale for performing GA in older patients with cancer. Key concepts are summarized in the Appendix Table A2 (online only), and most of these concepts are discussed in more detail in the questions 2 to 5 of this article.

Interpretation of key evidence. Important reasons to perform GA in older patients with cancer are: detection of unidentified problems and risks for which targeted interventions can be applied (question 2); prediction of adverse outcomes (eg, toxicity, other relevant items such as functional or cognitive decline, postoperative complications; question 3); and better estimation of residual life expectancy and lethality of the malignancy in the context of competing comorbidities and general health problems (question 4; level 5).

The main goal of GA is to provide a comprehensive health appraisal to guide targeted geriatric interventions and appropriate cancer treatment selection (question 5). GA has the potential to evaluate the balance of benefits and harms of performing or omitting specific oncologic interventions (level 5).

Which patients would benefit from GA is an area of controversy. Many oncologic studies have used age $\geq$ 70 years as the age for implementing GA, but other age cutoffs have been proposed. An active area of research is to identify whether a shorter geriatric screening tool can identify which older patients with cancer would benefit from more comprehensive GA (level 5).

Question 2

What information is provided by a GA beyond that captured in a standard history and physical exam?

Key evidence. The literature from 2010 to 2013 was reviewed to identify research studies summarizing the findings from GA performed in an oncology patient population. A comprehensive review of these study findings is summarized in the Appendix Table A3 (online only). Literature from previous years is summarized in an article by Puts et al.[12]

GA identifies age-related problems not typically identified by a routine history and physical examination in approximately half of older patients with cancer.[16,17] Only one (large) study[15] reported the percentage of patients per domain in whom GA had identified new problems, with the most frequent problems being fatigue (36.6%), nutritional issues (37.6%), and functional impairments (40.1%). Several studies reported only the percentage of patients with at least one deficit, with percentages varying between 90.4% and 92.6%.[24,32] Comparison of the different studies is difficult because of the use of different populations, regions, tools, and cutoffs.

Interpretation of key evidence. Deficits in GA domains are frequent in older patients with cancer (level 3). Assessment of all domains is relevant because GA can potentially identify deficits across domains (level 3). GA reveals deficits that are not routinely captured in a standard history and physical examination (level 3).

Question 3

What is the ability of GA to predict oncology treatment–related complications?

Key evidence. GA has the potential to predict several relevant treatment-related complications (eg, postoperative complications, toxicity related to systematic treatment, and so on; Appendix Table A4, online only).[12,19,25,39-42] Because newfound articles on this topic (not discussed in Puts et al[12] review) only focused on severe toxicity (generally defined as grade 3 to 5 adverse events[43]) related to systemic treatments, we refer to the Puts et al review for predictive capabilities of GA for other outcomes.

Most previously published studies on prediction of chemotherapy toxicity were retrospective, small in size, and underpowered to discover clinically relevant changes.[12] Some studies found no predictive value of GA variables for treatment toxicities, whereas other studies did. Two large prospective studies—CARG (Cancer and Aging Research Group)[20] and CRASH (Chemotherapy Risk Assessment Scale for High-Age Patients)[41]—clearly identified parameters of GA capable of predicting severe chemotherapy-related complications in a heterogeneous cancer population. Both studies attempted to correct for differences in treatment characteristics (CRASH: MAX-2 index;

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Table 1. Domains and Instruments Used in GA*

Domain	Tool
Demographic data and social status	Questions on living situation, marital status, educational level, safety of environment, financial resources[15-18]
	MOS Social Activity Survey[19-21]
	Caregiver burden[22]
	MOS Social Support Survey (Emotional/Information and Tangible Subscales)[19-21]
	Summary of some criteria (eg, availability of family support, appropriateness of social environment)[16,17,23,24]
Comorbidity	Charlson comorbidity index[18,23,24,25,26,27]
	CIRS[28,29]
	CIRS-G[16,17,29-31]
	NYHA[31]
	No. of comorbid conditions[21]
	Simplified comorbidity score[24]
	Summary of comorbidities[16]
	Hematopoietic cell transplantation comorbidity index[32]
	Physical Health Section (subscale of OARS)[19,20]
Functional status	ADLs (Katz index)[15-17,22-24,27,30-33]
	IADLs (Lawton scale)[15,17,22-24,26,27,31-33]
	PS index[27]
	Barthel index (any version)[25,28]
	Lawton-Brody IADL Scale[25]
	Nottingham Extended ADL Scale[28]
	ADLs (subscale of MOS Physical Health)[20,21]
	IADLs (subscale of OARS)[19-21]
	Pepper assessment tool for disability[32]
	Visual and/or hearing impairment, regardless of use of glasses or hearing aids[17,22,23,]
	MOS Physical Health (any version)[18,19]
	Mobility problem (requiring help or use of walking aid)[22]
	Timed Get Up and Go[16,19,20,26,27,33]
	Hand grip strength[32]
	Short Physical Performance Battery[32]
	One-leg standing balance test[16,27]
	Walking problems, gait assessment, and gait speed[16,17,23]
	ECOG PS[23,25,26]
	Karnofsky self-reported performance rating scale[19-21]
	Karnofsky health care professional-rated performance rating scale[19-21]
Cognition	Mini Mental State Examination (any version)[15-17,23-28,30,31,33,34]
	Informant Questionnaire on Cognitive Decline in the Elderly (any version)[22,34]
	Modified Mini Mental State Examination[32]
	Clock-drawing test[23,26]
	Blessed Orientation-Memory-Concentration Test[19,20]
Depression	Geriatric Depression Scale (any version)[15-17,22-29,31,33]
	Center for Epidemiologic Studies Depression Scale[32]
	Hospital Anxiety and Depression Scale[19,20]
	Mental health index[18]
	Presence of depression (as geriatric syndrome)[30]
	Distress thermometer[32]
Nutrition	Body-mass index (weight and height)[16-23,26]
	Weight loss (unintentional loss in 3 or 6 months)[16,17,19-21,23,24]
	Mini Nutritional Assessment (any version)[15,16,25,27,28,33,34]
	Short Nutritional Assessment Questionnaire[22]
	DETERMINE Nutritional Index[26]
Fatigue	MOB-T[15]
Polypharmacy	Beers criteria[35]†
	STOPP and START criteria[36]†
Geriatric syndromes‡	Dementia[24,26,29,30]
	Delirium[24,26,29,30]
	Incontinence (fecal and/or urinary)[16,17,22-24,26,29,30]
	Osteoporosis or spontaneous fractures[22,24,26,29,30]
	Neglect or abuse[24,26,29,30]
	Failure to thrive[26,29]

(continued on following page)

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Table 1. Domains and Instruments Used in GA* (continued)

Domain	Tool
	Self-reported No. of falls (within different time frames)[15-17,19-23,26,27,29,30]
	Constipation[22]
	Polypharmacy[15-17,19,22,23,26,28]
	Pressure ulcus[22]
	Sarcopenia[37]†

Abbreviations: ADL, activity of daily living; CIRS, Cumulative Illness Rating Scale; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; DETERMINE, Disease, Eating poorly, Tooth loss/mouth pain, Economic hardship, Reduced social contact, Multiple medicines, Involuntary weight loss/gain, Needs assistance in self-care, Elder years > 80; ECOG, Eastern Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; MOB-T, Mobility Tiredness Test; MOS, Medical Outcomes Study; NYHA, New York Heart Association; OARS, Older Americans Resources and Services; PS, performance status; START, Screening Tool to Alert Doctors to Right Treatment; STOPP, Screening Tool of Older Person's Prescriptions.

*For studies published before November 16, 2010, see review by Puts et al.[12]

†Although this tool was not used in newfound articles, it is mentioned because of high relevance in geriatrics.

‡Some studies reported geriatric syndromes that overlap with other domains.

CARG: poly- *v* monochemotherapy and standard *v* reduced dose), but these categorizations do not fully capture the diversity of specific chemotherapy drugs and schedules. The predictive ability of these models remains moderate at the individual level, and they require further validation and optimization.

Aparicio et al[39] and Falandry et al[42] studied more-homogenous populations of patients with untreated metastatic colorectal cancer and patients with metastatic breast cancer who received first-line chemotherapy, respectively. The specific GA variables predictive for toxicity differed in most studies; however, the factors most consistently associated with toxicity were functional status[12,25,41] and comorbidity.[12] Other identified risk factors were cognitive problems,[12,39,41] lack of social support,[12] hearing difficulties,[20] falls,[20] nutritional status,[41] poor grip strength,[12] and GA group allocation (ie, fit, vulnerable, or frail).[12]

Interpretation of key evidence. GA items are predictive (independent from classic oncologic predictors) of the risk of severe treatment-related toxicity in a variety of diseases and treatment settings (level 3). The optimal geriatric parameters (including cutoff points) to predict severe treatment toxicity or modify therapeutic approach (including dose or regimen adaptations and/or GA-guided interventions to decrease risk of toxicity) have not yet been established for different cancer types or treatment options (level 4).

Question 4

What is the association between GA findings and OS?

Key evidence. There is emerging evidence in the literature regarding the association between factors captured in GA and OS, with several new studies from 2010 to 2013 (Appendix Table A5, online only). However, a majority of studies were small in size (< 100 patients) and/or included patients with heterogeneous diseases, treatments, and tumor stages, which could independently have had an impact on overall mortality. Most, but not all, studies identified geriatric parameters that were independent predictors of mortality.[12,22,44-44b] Besides age strata, factors most consistently associated with OS were functional status,[12,24,26] nutritional status,[12,24,26,33,34] overall fitness,[12,28,30,31] and mental health.[12,24,26] Most studies performed multivariable analyses correcting for some general aspects, but the generally heterogeneous populations in terms of oncologic prognosis (independent of age) were a major weakness. Prognostic models based on GA parameters have been developed in the general geriatric population (eg, Lee score,[45] Porock scale,[46] and other scales available at the Eprognosis Web site[47]), allowing prediction of prognosis depending on geriatric parameters at the individual level, but they have not yet been studied specifically within the oncology population. Prognostic indices specifically focusing on older patients with cancer are needed; however, the ideal specificity of these instruments remains unclear. A validated GA for every disease and situation seems impossible to achieve. Because the cancer prognosis competes with other (age-related) causes of death, distinction between deaths resulting from cancer and other causes should be established whenever possible.[48]

Interpretation of key evidence. There is clear evidence that GA items independently predict OS in a variety of oncology diseases and treatment settings (level 4). Poorer OS in older patients with cancer and deficits identified in geriatric domains might potentially be explained by several factors (eg, increased risk of death resulting from causes other than cancer, increased death resulting from cancer because of less aggressive treatment, or death resulting from complications of cancer treatment). Therefore, disease-specific survival and OS should both be reported in trials of older patients with cancer (level 4). Several prognostic models for OS in the general geriatric population are available; however, these have not been specifically validated in older patients with cancer. Prognostic models for geriatric oncology are needed, including both cancer- and geriatric-related prognostic factors (level 4).

Question 5

What is the impact of GA findings on oncology treatment decisions?

Key evidence. We identified six new studies[15,16,23,27,39,49] conducted after 2010 that examined how GA results can affect oncology treatment decisions (Appendix Table A6, online only). The impact of GA on altering treatment choice varied significantly between the different available studies, ranging from 0% to 83.0%. The GA results more commonly led to a decrease in the aggressiveness of treatments, especially with regard to systemic therapies. It might sometimes be difficult to distinguish the effect of clinical impression (without GA) versus the independent effect of GA on treatment decision. One study[27] compared a treatment recommendation before GA was performed versus treatment recommendations after knowledge of GA results and found that GA did influence oncology treatment decisions (ie, lowering amount of prescribed drugs, reducing chemotherapy

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intensity, or initiating supportive care) in 44.9% of patients. Decoster et al[49] found that patient age and clinical impression of the physician altered treatment choice in 45% of patient cases, whereas the addition of information provided by GA further changed treatment choice in only 5.0%, including both a decreased intensity of therapy (omission of treatment or dose reduction) as well as an increased intensity of therapy (standard therapy instead of dose reduction). GA also allowed pretreatment patient optimization, when remediable problems were unmasked.[23]

Interpretation of key evidence. Age by itself and clinical impression lead to treatment changes in a significant proportion of older patients with cancer, although the appropriateness of this judgment is underdocumented (it might lead to overtreatment or, more frequently, undertreatment)[3,4] (level 4). GA can additionally influence treatment decisions in older patients with cancer, either by decreasing or increasing treatment intensity (level 4). GA can inform key parts of the decision-making process to tailor treatment and trigger targeted GA-driven interventions (level 4). Oncology teams should integrate GA findings into treatment decisions (level 4).

Question 6

What should a GA comprise, including domains and tools?

Key evidence. Important domains in a GA are functional status, comorbidity, cognition, mental health status, nutrition, social status and support, fatigue, and assessment for polypharmacy and presence of geriatric syndromes, and various tools are available for assessing these domains. An overview of the different tools that were used in retrieved articles to assess the different domains of a GA in older patients with cancer is provided in Table 1. Classical oncology tools of functional status assessment like Eastern Cooperative Oncology Group or Karnofsky performance status have been shown to poorly reflect functional impairment in older patients with cancer.[50,51] Nearly all geriatric tools were developed in the general geriatric population and are subsequently being used in the geriatric oncology population. Tools describing polypharmacy and potentially inappropriate medications in older adults (eg, Beers criteria[35] and STOPP [Screening Tool of Older Person's Prescriptions] and START [Screening Tool to Alert Doctors to Right Treatment] criteria[36]) and sarcopenia[37] as a geriatric syndrome were added to the list of domains and tools because of their high relevance in geriatric care. Assessment of spirituality and religion is also relevant to both geriatric and oncology care.[52]

Most oncology teams and research groups use fixed combinations of tools in the original or adapted form; most of these are first- (eg, collection of single-domain, individually validated instruments) and second-generation instruments (eg, GA-introduced, health setting–specific comprehensive assessments).[53] Examples are the European Organisation for Research and Treatment of Cancer minimal data set[54]; Multidimensional Prognostic Index[55]; short, primarily self-administered GA tool developed by the Cancer and Leukemia Group B (Alliance)[19]; Mini Geriatric Assessment[56]; and National Comprehensive Cancer Network Senior Adult Oncology Guidelines,[57] which summarize various tools for assessing older patients with cancer. The online InterRAI-tool[58] is a standardized and internationally validated tool for assessing geriatric patients with different levels of clinical complexity across all health care settings (eg, home care, nursing homes, and acute hospitals). However, this more comprehensive tool is time consuming and has not been validated in oncologicy patients. The InterRAI Consortium[59] is in the process of developing a tool specifically for older patients with cancer.

Interpretation of key evidence. Important domains in GA are functional status, fatigue, comorbidity, cognition, mental health status, social support, nutrition, and geriatric syndromes (eg, dementia, delirium, falls, incontinence, osteoporosis or spontaneous fractures, neglect or abuse, failure to thrive, constipation, polypharmacy, pressure ulcers, and sarcopenia)[19] (level 5). Various tools are available to investigate these domains, and the superiority of one tool over another has not been proven. Choice of instrument might rely on local preference, aim of the tool, or resources present (level 5).

Question 7

How should GA be organized and implemented in clinical care?

Key evidence. Table 2 describes major models for implementation of GA in general geriatric medicine and in geriatric oncology, as well as the potential advantages and disadvantages of each approach. Three major models were identified. The first model is the creation of geriatric oncology units[60,66] within selected general oncology hospitals. This has the major advantage that geriatric expertise is centralized; however, the disadvantage is that this model can only reach a limited number of patients who are willing and able to travel to the geriatric oncology unit for consultation. Another model is to bring geriatric consultation teams[15,67] to patients who remain under the supervision of their treating oncologists. This model is possible in settings where oncology clinics are located within general hospitals with physician and multidisciplinary geriatric expertise. There is synergy in the care of this patient population, and therefore, this model has the potential advantage of reaching a large proportion of older patients with cancer. The crosstalk between oncology and geriatric teams allows for cross-fertilization of oncology and geriatric principles. Selected patients can also be referred to appropriate specific geriatric programs, such as a geriatric day care center, fall clinic, or memory clinic. The third model occurs in settings where geriatric expertise is not nearby (eg, stand-alone cancer centers without geriatric department or private practice oncology clinics). In these settings, GA can be performed to identify high-risk patients who could be referred to geriatricians outside of the cancer center (consultation or even electronic consulting[68]) or to members of a multidisciplinary team within the cancer center. Some comprehensive cancer centers have created nurse practitioner–led clinics to increase accessibility of care in regions with long distances to specialist care and/or long waiting lists resulting from a lack of geriatric staff in general hospitals.[69] Additional research is needed regarding the effectiveness of these models among patients with cancer.

Interpretation of key evidence. There are several ways of implementing GA in geriatric oncology (level 4). All models have advantages and disadvantages (Table 2), and preference should be given to models that fit with the local health care structure and setting. An assessment of outcomes should be built into the model and reported (level 5). Interaction with multidisciplinary geriatric teams (for selected patients) is highly recommended (level 5).

DISCUSSION

This article summarizes the review and interpretation of key evidence related to GA in geriatric oncology by the SIOG GA task force. We performed quality assessment of included studies. Because no randomized studies were available, and because of inconsistencies among

Table 2. GA Models in General Geriatric Medicine and Geriatric Oncology

CGA Model	General Geriatrics: Definition	General Geriatrics: Effectiveness
GA ward	Specific ward with specialized geriatric care team that applies GA and:	Six meta-analyses show that GEMU is most effective way of caring for geriatric patients with lower mortality, less institutionalization, and less functional decline compared with standard (non-GEMU) care for same patients[7,9,11,61-63]
GEMU	Delivers both acute and rehabilitative care to inpatients[11]	
ACE	Only delivers ACE; patients in ACE are transferred to long-term care facilities for rehabilitation programs[60]	
GCT	Specialized geriatric team that applies GA in non-GA wards on consultative basis	Recent meta-analysis[64] could not show consistent effect of IGCT interventions in non-GEMUs on mortality, readmission, length of stay, or functional status; absence of effect is mainly because of low adherence rate to IGCT recommendations
CMM	Joint geriatric and specialized care (eg, orthogeriatric beds or units)	Individual studies of CMMs, mainly operationalized as orthogeriatric beds to date, show promising results and advantages[65]

GA Model	Geriatric Oncology: Definition	Advantage	Disadvantage
Geriatric oncology unit	Specific ward with team specialized in caring for older patients with cancer that applies GA based on GEMU or ACE model[60,66]	Centralization of geriatric expertise and treatment options	Potential patient withdrawal from familiar treating oncologist; financial incentives might drive general oncologists not to refer patients; only limited No. of patients can be reached; general geriatric oncologists might miss detailed, rapidly evolving knowledge of broad field of oncology
GCT	Specialized geriatric team that applies GA in non-GA wards or in other settings on consultative basis[15,67]	Patients remain under supervision of their treating oncologists; can reach large majority of older patients with cancer; interaction between oncologists and geriatric teams is feasible	Decentralization of geriatric expertise has logistic and practical (eg, staffing) challenges; several factors may lead to low compliance of treating physicians to GCT advice; GA results may be unknown at time of treatment decision making; treating physicians might not know what to do with GA results; onset of geriatric intervention or treatment adjustment depends on local possibilities; patients who need referral to specific geriatric care programs might encounter waiting lists
Geriatric expertise not nearby	GA in standalone comprehensive cancer centers without geriatric department or private practice oncology clinic	Patients remain under supervision of their treating oncologists; validated methods can easily be used to target high-risk patients and introduce geriatric care; large majority of older patients with cancer can be reached	Realization of interaction between oncologists and geriatric teams is difficult; no gold standard to screen high-risk patients; inter-rater reliability and interpretation of results can be problem; patients who need referral might encounter waiting lists

Abbreviations: ACE, acute care for elders; CGA, comprehensive geriatric assessment; CMM, comanagement model; GA, geriatric assessment; GCT, geriatric consultation team; GEMU, geriatric evaluation and management unit; IGCT, inpatient geriatric consultation team.

some study results, the levels of evidence supporting the recommendations from this expert consensus panel were generally low.

Nevertheless, abundant information is present demonstrating that GA detects general health care problems in older patients with cancer that routinely are under-recognized in clinical oncology care. However, prevalence rates of geriatric conditions in any population correlate positively with the number of conditions evaluated for and strongly depend on selected tools, cutoffs for defining impairment, and the time points of evaluation.[70] There is general agreement regarding the domains of a GA; however, there are several different tools used to evaluate these domains, making cross-study comparison difficult. Therefore, future research should focus on standardization of assessment tools. Furthermore, there is a need to standardize interventions usng expertise from a multidisciplinary geriatric and oncology team. Performance capacity of various GA tools and the efficacy of interventions in different settings should also be considered. GA results should be documented in patients' medical records so that these results are available when treatment decisions are being made. This will require the development of algorithms for scoring and interpretation of the results for treating physicians. Future research should explore how problems detected by the GA and subsequent interventions interact with cancer care. Specifically, research is needed regarding the optimal way to communicate the information to the clinical team and how referrals for the implementation of GA-guided interventions should be organized.

GA has been shown to predict the risk of treatment-related complications (eg, chemotherapy toxicity or surgical risk), but toxicity prediction at the individual level remains moderate. This is likely because individual treatment toxicity is dependent on a variety of factors, including general host factors (eg, age, genetic predisposition, and capacity for metabolizing drugs), factors identified in a GA (eg, functional status, comorbidity, and others described in our article), treatment-related aspects (eg, choice of

therapy, including different regimens and drug-drug interactions), and tumor characteristics (ie, tumor aggressiveness affecting host). Although no causal relations could be determined, several general risk factors for treatment toxicity in older patients with cancer have been described. Further research should investigate if there are additional or specific risk factors among patients with specific diseases receiving specific treatment types. This should be investigated broadly for systemic therapies in addition to surgery, radiotherapy, or combined treatment modalities, leading to concise risk assessment models that can be implemented in everyday clinical practice. Similar trial design should be promoted, allowing cross-trial comparison in different settings. Biologic phenomena like genetic predisposition, drug metabolism, and drug-drug interactions can also have a major impact on the toxicity of specific drugs. Models should be built integrating both biologic and clinical aspects as well as geriatric parameters, which might predict toxicity better than each of these alone. Studies have generally focused on severe toxicity, mostly defined as grade 3 to 5. It should be recognized that specific grade 2 toxicities can also be associated with significant morbidity in older patients with cancer, and these drug-specific adverse effects should also be captured in study designs.[71]

The prognostic capacity for survival of existing GA-based models such as Eprognosis[47] should be explored in older cancer populations. Given the major impact of cancer-specific characteristics like tumor type, stage, and treatment, it is preferable to study this in uniform cancer populations where oncologic differences are small. The emerging big data systems combining patient and treatment information from electronic medical records present a unique opportunity for generating these data that should be harnessed. OS and treatment efficacy can also be significantly influenced by tumor biology, independent of the ageing process. For instance, similar tumors treated with identical therapy might respond differently because of differences in drug sensitivity. Personalized medicine for the tumor attempts to find the right drug and treatment for the right tumor, but personalized medicine should also titrate treatment to the host capacity to tolerate treatment. Future models should integrate biologic and GA aspects to further optimize the prognostic models.

Randomized trials comparing GA-guided therapy versus no GA are generally lacking in the oncology field. A fundamental question is whether level I evidence is required for incorporating GA in treatment decision making for older patients with cancer. Is it acceptable to omit GA in clinical trials, knowing that identified problems and subsequent interventions can influence important outcomes independent of treatment, as shown in the geriatric (nononcologic) literature? The effects of GA by itself are limited, unless followed by geriatric interventions, follow-up GA, and adaptation of care planning.[61] Measurement of blood pressure, weight, and blood count have also never been proven in randomized trials to be beneficial, but they are generally considered standard parameters essential for the basic evaluation of patients. Conversely, the geriatric world has been able to perform randomized GA trials and showed outcome benefit, so all efforts in this domain are encouraged.[7,9,11,61-63,71a]

Because local health care structures and settings can differ, various models for the implementation of GA in geriatric oncology are necessary. Governments should stimulate national or international implementation projects precluding every center from developing its own model. The use of uniform assessment is advised and encouraged, because it would allow benchmarking of patient or hospital data and would also allow transfer of the assessment results to other health care settings, such as primary and residential care. This has the potential for improving continuity of care and creating a uniform language for geriatric care problems and syndromes.[72] Further research also needs to focus on cost effectiveness of GA-directed intervention models in older patients with cancer with regard to key outcomes such as decreasing treatment toxicity, hospitalization, and readmissions.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Methodology

Because geriatric assessment (GA) is a wide-ranging topic, the task force agreed for this recommendation article to select seven important and relevant questions upfront after input from all members. Unfortunately, other relevant topics (eg, prognostic capacity for maintenance of independence or quality of life) did not fall within the scope of this article.[71a]

A study was eligible for inclusion if it:

(1) Reported on older patients (mean or median age of study participants, ≥ 65 years) diagnosed with cancer (any type of cancer, including hematologic malignancies) and being seen in oncology clinics (outpatient oncology or hematology clinics or inpatient oncology or hematology units)
(2) Reported on cross-sectional, longitudinal, observational, or interventional studies focusing on GA and answering one of the seven questions on GA in geriatric oncology that we identified
(3) Was written in English, French, Dutch, or German
(4) Was published after November 16, 2010, and not included in systematic review by Puts et al[12] on GA

Excluded were editorials, case studies, reviews, expert opinion papers, and studies published as abstracts only. Studies investigating new drugs or treatment regimens were not included, because these addressed GA from another perspective and in preselected patient groups.

Data Sources

Our databank including PubMed, Embase, CINAHL, Medline (Ovid-SP), PsycInfo, and the Cochrane Library. Included articles were published between November 16, 2010, and March 7, 2013. We used keywords cancer and geriatric assessment.

Process From Study Selection to Final Draft

First study selection was based on titles and abstracts and performed by P.H. using the inclusion and exclusion criteria. In total, 1,204 titles and abstracts were reviewed. In case of indecision about the eligibility of a study, the article was considered as potentially relevant and proceeded to the full-text review stage. Nineteen studies remained after the full-text review stage.

A data abstraction form was predesigned by P.H. with Excel software. Abstracted information by P.H. included first author, year, study design, aim, location, sampling method, sample size, participant inclusion criteria, characteristics of included study participants, and results relevant to the seven questions.

Obscurities during full-text review by P.H. were discussed and clarified in consensus with H.W. The reference list of all selected studies was reviewed to obtain additional relevant articles. This added two articles. Retrieved articles were interpreted and discussed by experts, who could add relevant publications.

H.W., P.H., C.K., K.M., and A.H. established a first draft for each of the seven questions. Seven expert workgroups (for seven questions) were created to obtain concrete task force input. For all recommendations, data from the review by Puts et al,[12] as well as the newly selected publications, were used. Table 1 and Appendix Tables A2 to A6 summarize the recent publications, and we refer to the review by Puts et al[12] for the older data. After consensus within every workgroup was accomplished, a first integral draft was developed and sent to all task force members. Their suggestions were used to make new drafts until task group consensus was realized, with H.W. as the moderator. The Oxford 2011 levels of evidence[38] were used to grade the quality of evidence and strength of recommendations (Appendix Table A7).

Quality Assessment

The methodologic quality of included studies was separately evaluated by P.H. and C.K. using the methodologic index for nonrandomized studies.[14] We only performed a quality assessment on the studies that were initially retrieved by our literature search. Discrepancies between the scores were resolved by H.W. Results of quality assessment are listed in Appendix Table A1.

International Society of Geriatric Oncology Task Group on GA in Geriatric Oncology

Writing group. Hans Wildiers, Pieter Heeren, Cindy Kenis, Koen Milisen, and Arti Hurria.

Workgroup 1: What is the rationale for performing GA? Johan Flamaing, Riccardo Audisio, Lazzaro Repetto, and Eva Topinkova.

Workgroup 2: What information is provided by a GA beyond that captured in a standard history and physical exam? Theodora Karnakis and Martine Extermann.

Workgroup 3: What is the ability of GA to predict oncology treatment–related complications? Riccardo Audisio, Maryska L.G. Janssen-Heijnen, Supriya Mohile, Lazzaro Repetto, and Andrew Artz.

Workgroup 4: What is the association between GA findings and overall survival? Maryska L.G. Janssen-Heijnen, Claire Falandry, Barbara Van Leeuwen, Martine Extermann, and Etienne Brain.

Workgroup 5: What is the impact of GA findings on oncology treatment decisions? Supriya Mohile, Claire Falandry, Barbara Van Leeuwen, and Etienne Brain.

Workgroup 6: What should a GA comprise, including domains and tools? Martine Puts, Theodora Karnakis, Eva Topinkova, and Andrew Artz.

Workgroup 7: How should GA be organized and implemented in clinical care? Johan Flamaing and Martine Puts.

Table A1. Quality Assessment of Included Studies Using Methodologic Index for Nonrandomized Studies

Study	1 Clearly Stated Aim	2 Inclusion of Consecutive Patients	3 Prospective Collection of Data	4 End Points Appropriate to Aim of Study (+ ITT*)	5 Unbiased Assessment of Study End Points	6 Follow-Up Period Appropriate to Aim of Study	7 Loss to Follow-Up < 5%	8 Prospective Calculation of Study Size	9 Adequate Control Group	10 Contemporary Groups	11 Baseline Equivalence of Groups	12 Adequate Statistical Analysis	Total
Observational transversal													12
Aliamus et al[27]	2	2	NA	1	0	NA	2	0	NA	NA	NA	NA	7
Horgan et al[23]	2	1	NA	2	0	NA	0	0	NA	NA	NA	NA	5
Hurria et al[19]	2	1	2	2	0	NA	NA	1	NA	NA	NA	NA	8
Observational longitudinal													16
Kenis et al[15]	2	1	2	2	0	0	0	0	NA	NA	NA	NA	7
McCleary et al[21]	2	1	2	2	0	2	1	1	NA	NA	NA	NA	11
Aaldriks et al[34]	2	2	2	1	0	2	1	0	NA	NA	NA	NA	10
Soubeyran et al[33]	2	1	2	2	0	1	1	0	NA	NA	NA	NA	9
Klepin et al[32]	2	1	2	2	0	0	1	0	NA	NA	NA	NA	8
Hamaker et al[22]	1	2	2	1	0	2	1	0	NA	NA	NA	NA	9
Kanesvaran et al[26]	2	2	1	1	0	2	1	0	NA	NA	NA	NA	9
Hurria et al[20]	2	2	2	2	0	1	2	1	NA	NA	NA	NA	12
Clough-Gorr et al[18]	2	1	2	2	0	2	1	0	NA	NA	NA	NA	10
Caillet et al[16]	2	1	2	2	0	0	0	1	NA	NA	NA	NA	8
Shin et al[25]	2	2	2	1	0	2	1	0	NA	NA	NA	NA	10
Gironés et al[24]	2	2	2	1	0	2	0	0	NA	NA	NA	NA	9
Kristjansson et al[28]	2	1	2	2	0	2	1	0	NA	NA	NA	NA	10
Lazarovici et al[17]	2	2	1	1	0	0	0	0	NA	NA	NA	NA	6
Extermann et al[41]	1	1	2	2	0	2	1	1	NA	NA	NA	NA	10
Gironés et al[44]	1	2	2	1	0	2	1	0	NA	NA	NA	NA	9
Interventional													24
Spina et al[31]	2	2	2	1	0	2	1	0	0	0	0	0	10
Olivieri et al[30]	2	1	2	1	0	2	1	0	0	0	0	0	9

NOTE. Index is as follows: 0, not reported; 1, reported but inadequate; and 2, reported and adequate.
*Only considered in interventional studies.
Abbreviations: ITT, intention to treat; NA, not applicable.

Table A2. Reasons to Perform GA Based on Statements in Former Publications

Literature Search Results
GA can reveal/detect previously unknown and potentially reversible geriatric problems not found by routine oncology care[15,22,23,25,28,32-34,44]
GA can predict toxicity/adverse effects from cancer treatment or decrease in QOL, enabling more targeted use of preventive measures[15,18-21,23,25,32,41]
GA has important prognostic information that can be helpful in estimating life expectancy, which is of paramount importance when making treatment decisions[15,18,19,22-24,26,28-34,44,75]
GA can influence/improve treatment decisions[15,16,21,23,25,27,32]
GA allows targeted interventions, which can improve QOL and compliance with therapy[15,23,22,32]
GA is a systematic procedure to appraise objective health, including multimorbidity and functional status, which interfere with cancer prognosis and treatment choices in older patients[15,22,30]

Abbreviations: GA, geriatric assessment; QOL, quality of life.

Table A3. Problem Detection Through GA (global and per domain)*

Study	Year	Sample Size/Population	Age (years)	Patients in Whom GA Detected Problem (%)	GA Domain (%)							
					Demographic Data and Social Status	Functional Status	Presence of Fatigue	Presence of Comorbidities	Cognitive Problems	Depression	Nutritional Problems	Presence of Geriatric Syndromes†
Kenis et al[15]	2013	1,967 patients; six tumor types	Median, 76	NR 51.2‡	NR 10.2‡	37.7-56.5 30.5-40.1‡	69.4 36.6‡	— —	13.2 19.0‡	60.9 27.2‡	83.0 37.6‡	— —
Hurria et al[20]	2011	500 various patient cases of cancer	Mean, 73	NR	32.0-44.0	17.0-50.0	—	NR	NR	NR	34.0-60.0	Falls, 18.0; hearing, 25.0
Caillet et al[16]	2011	375 consecutive older patients with various cancers	Median, 79.6	NR	17.6	29.9-54.9	—	NR	27.1	28.3	57.5	Incontinence, 15.9; polypharmacy, 66.9
Soubeyran et al[33]	2012	348 patients; eight tumor types or cancers of unknown primary origin	Median, 77.45	NR	—	18.1-73.0	—	—	19.0	44.0	64.9	—
Hamaker et al[22]	2011	292 patients with known or first diagnosed cancers admitted to general medicine or oncology ward	Median, 74.9	91.1	43.8	26.0-76.9	—	—	15.1	65.3	46.0	Polypharmacy, 48.0; pain, 64.8; constipation, 22.1; incontinence, 25.2; decubitus, 1.4; delirium, 21.5
Kanesvaran et al[26]	2011	249 older patients with various cancers	Median, 77	NR	—	47.3-88.0	—	65.0	31.5-53.8	28.1	73.1	60.6
Gironés et al[24]	2012	83 patients with lung cancer	Median, 77	90. 4	NR	48.2-69.9	—	94.0-100.0§	26.4	31.3	44.6	Geriatric syndromes, 48.2; dementia, 26.4; falls, 22.9
Lazarovici et al[17]	2011	65 patients scheduled for colorectal cancer surgery	Median, 82.4	NR	NR	27.6-66.1	—	66.1	45.3	47.6		Incontinence, 20.0
Shin et al[25]	2012	64, newly diagnosed solid tumor except leukemia	Median, 71	NR	—	10.9-23.4	—	23.4	56.3	40.6	81.3	—
Aaldriks et al[34]	2013	55, advanced breast cancer	Mean, 76	NR	—	—	—	—	9.0-8.0	—	42.0	—
Klepin et al[32]	2011	54 patients with acute myelogenous leukemia	Mean, 70.8	92.6	—	40.7-53.7	—	46.3	31.5	38.9-53.7	—	—
Horgan et al[23]	2012	30 patients lung or GI cancer	Median, 78	NR 70.0‡	13.0 NR‡	20.0-53.0 NR‡	— —	60.0 60.0‡	NR NR‡	33.0 NR‡	37.0 NR‡	NR NR‡

Abbreviations: GA, geriatric assessment; NR, not reported.
*For studies published before November 16, 2010, see review by Puts et al.[12]
†Some studies have reported geriatric syndromes that overlap with other domains.
‡Data reporting on new detected problems (previously unknown to treating physician).
§Patients with at least one comorbidity.

Table A4. Predictive Value of GA (treatment complications)*

Study	Year	Trial Design	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Treatment Complications
Extermann et al[41]	2012	Prospective observational	Multivariable logistic regression model	Yes; forward-selection approach with predictors selected based on $P < .1$; adjustments for toxicity of regimen	518 patient cases of various cancers; 64% of patients experienced severe toxicity; 32% had grade 4 hematologic toxicity; 56% had grade 3 or 4 nonhematologic toxicity	In univariable analysis, diastolic blood pressure, IADL, aspartate aminotransferase, lymphocytes, and LDH were associated with grade 4 hematologic toxicity; ECOG PS, hemoglobin, creatinine clearance, albumin, MMS, self-rated health, and MNA were correlated with grade 3 to 4 nonhematologic toxicity; best performing model for hematologic toxicity included diastolic blood pressure, IADL, and LDH along with chemotoxicity (c-statistic, 0.76); best performing model for nonhematologic toxicity included ECOG PS, MMS, MNA, and chemotoxicity (c-statistic, 0.66); combination of two subscores (counting chemotoxicity only once) yielded model with c-statistic of 0.65; model established on first 331 patients and validated on subsequent 187 patients
Hurria et al[20]	2011	Prospective observational	Multivariable logistic regression model	Yes; variables with $P < .1$ in univariable analyses and clinically relevant variables (chemotherapy dosing [standard *v* dose reduced], No. of drugs [mono- *v* polychemotherapy], chemotherapy duration, and receipt of primary prophylaxis with WBC growth factor) examined in multivariable analysis	500 patient cases of various cancers; 53% of patients experienced ≥ one grade 3 to 5 toxicity (grade 3, 39%; grade 4, 12%; grade 5, 2%)	Predictors of severe chemotherapy complications: age (OR, 1.85; 95% CI, 1.22 to 2.82), cancer type (GI or GU; OR, 2.13; 95% CI, 1.39 to 3.24), chemotherapy dosing (OR, 2.13; 95% CI, 1.29 to 3.52), polychemotherapy (OR, 1.69; 95% CI, 1.08 to 2.65), hemoglobin (OR, 2.31; 95% CI, 1.15 to 4.64), creatinine clearence (OR, 2.46; 95% CI, 1.11 to 5.44), hearing (OR, 1.67; 95% CI, 1.04 to 2.69); falls (≥ one in past 6 months; OR, 2.47; 95% CI, 1.43 to 4.27), MOS (limited in walking one block; OR, 1.71; 95% CI, 1.02 to 2.86)
Aparicio et al[39]	2013	Prospective Randomized trial	Multivariable logistic regression model	Yes; variables with $P < .20$ in univariable analysis were tested using multiple logistic regression analysis	123 patient cases of metastatic colorectal cancer; 71 patients (58%) had grade 3 to 4 toxicity	Significant predictive factors for grade 3 to 4 toxicity: irinotecan arm (OR, 5.03; 95% CI, 1.61 to 15.77; $P = .006$), impaired cognitive function (OR, 3.84; 95% CI, 1.24 to 11.84; $P = .019$), impaired autonomy (OR, 4.67; 95% CI, 1.42 to 15.32; $P = .011$)
Badgwell et al[40]	2013	Prospective observational	Multivariable logistic regression model	Yes; variables significant ($P < .05$) in univariable analysis were included in multivariable analysis	111 patients undergoing abdominal cancer surgery; grade 1 to 2, 3 to 4, and 5 complications occurred within 90 days of surgery in 36%, 18%, and 3% of patients, respectively; because some patients experienced multiple complications, overall 90-day morbidity rate was 48% (n = 53)	No variables associated with morbidity
Shin et al[25]	2012	Prospective observational	Multivariable logistic regression model	Yes; variables with $P < .30$ in univariable analysis were tested using multiple logistic regression analysis; analyses adjusted by age, primary tumor type, treatment intent, relative dose-intensity, and MAX-2 index; association between significant toxicity and change in each GA parameter analyzed by repeated-measure analysis of covariance	64 patient cases of various cancers; significant toxicity noted in 16 patients (25.0%): 27.4% (three of 11 patients) in curative setting and 24.5% (13 of 53 patients) in palliative setting	ECOG PS ≥ 2 was only independent predictive factor for chemotherapy toxicity (OR, 38.52; 95% CI, 1.25 to 1191.97; $P = .037$); risk of significant toxicity was not significantly different according to frailty category; postchemotherapy changes in GA parameters were not associated with occurrence of significant toxicity
Falandry et al[42]	2013	Observational trial	Multivariable logistic regression model	Yes; covariates significantly associated in univariable analysis ($P < .1$) were included in multivariable analyses	60 older patients with metastatic breast cancer; No. of hematologic and nonhematologic toxicities was 60 and 59, respectively; No. of grade 3 and 4 toxicities was 65 and 13, respectively	Considering death, unplanned hospital admissions, and grade 3 to 4 toxicities, risk factors significantly associated by univariable and multivariable analyses were creatinine clearance ≤ 50 mL/min and living in nursing homes (no empiric data); only age ≥ 80 years (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$) was related to nonhematologic grade 3 to 4 events

Abbreviations: ECOG, European Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; LDH, lactate dehydrogenase; MMS, Mini Mental Health Status; MNA, Mini Nutritional Assessment; MOS, Medical Outcome Study; OR, odds ratio; PS, performance status.
*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A5. Prognostic Value of GA*

Study	Year	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Age (years)	Mortality
Prospective						
Clough-Gorr et al[18]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjusted models validated using stepwise and backward regression analyses; adjustments made for age, stage, and education and marital status (fully adjusted)	660 patient cases of stage I to IIIa breast cancer only; events NR	≥ 65	All-cause and breast cancer–specific death rate at 5 and 10 years was consistently approximately 2× higher in women with ≥ three GA deficits (all cause, fully adjusted: 5-year HR, 1.87; 95% CI, 1.36 to 2.57; 10-year HR, 1.74; 95% CI, 1.35 to 2.15; breast cancer, fully adjusted: 5-year HR, 1.95; 95% CI, 1.18 to 3.20; 10-year HR, 1.99; 95% CI, 1.21 to 3.28)
Soubeyran et al[33]	2012	Logistic regression	Yes; variables significant in univariable analysis at 5% level selected for inclusion in multivariable model; forward-ascending stepwise selection procedure used; model adjusted for treatment site	348 patient cases of various cancers; within 6 months, 56 patients (16.1%) had died	≥ 70	
Hamaker et al[22]	2011	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; factors with $P < .20$ in univariable analysis and with < 20% missing data were included in multivariable analysis; backward selection procedure applied, accepting $P < .05$	292 patient cases of various cancers; mortality rate was 64% at 12 months	≥ 65	No GA-related parameters retained, but metastatic disease (HR, 1.67; 95% CI, 1.23 to 2.29) and tumor-related reason for admission (HR, 1.57; 95% CI, 1.12 to 2.21) were independent predictors of mortality
Kristjansson et al[28]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjustments made for cancer stage and age	176 patients cases of CRC only; events NR	≥ 70	GA frailty (HR, 3.39; 95% CI, 1.82 to 6.29), age, and cancer stage were independent predictors of mortality
Falandry et al[44a]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; geriatric variables reaching $P < .2$ and considered clinically relevant were included in Cox model to identify optimal combined set of geriatric risk factors, termed geriatric vulnerability parameters; these were used to predict survival by calculating GVS	109 patients with advanced ovarian cancer; of 27 patients who discontinued early, eight died; at last follow-up, 75 patients (68%) had died; median OS was 17.4 months (95% CI, 13.3 to 21.4)	≥ 70	Among patients with GVS ≥ 3, HR for premature death was 2.94 (95% CI, 1.79 to 4.84; $P < .001$) in univariable analysis (median survival, 21.7 *v* 11.5 months) and 2.89 (95% CI, 1.74 to 4.78; $P < .001$) in multivariable analysis after adjustment for FIGO stage (stage IV: HR, 2.19; 95% CI, 1.34 to 3.58; $P = .002$)
Spina et al[31]	2012	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; variables significant in univariable analysis at 5% level selected for inclusion in multivariable model; additional adjustments were not conducted	100 patient cases of DLBCL only; 5-year OS rate was 60% (95% CI, 50% to 69%); at time of writing, 65% of fit patients, 34% of unfit patients, and 31% of frail patients were alive ($P = .006$), with 5-year OS rates of 76%, 53%, and 29% ($P = .001$), respectively	≥ 70	Geriatric group (unfit: HR, 1.96; 95% CI, 1.04 to 3.70; frail: HR, 2.55; 95% CI, 1.14 to 5.73) and IPI score (2 or 3: HR, 1.95; 95% CI, 1.04 to 3.66; 4 or 5: HR, 4.93; 95% CI, 1.55 to 15.64) were independent predictors of death
Olivieri et al[30]	2011	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; following parameters were evaluated: sex, age, stage, IPI score, and group allocation; rituximab use and comorbidities were not evaluated, because of collinearity with group; variables reaching statistical significance at 90% level ($P < .1$) on univariable analysis were included in regression model for multivariable analysis	91 patient cases of DLBCL only; median follow-up of 57 months (range, 6 to 78 months); 42 patients were alive (31 fit patients, seven with comorbidities, and four frail patients)	Median, 74.4	Univariable analysis revealed age > 70 years and treatment group allocation to be significant factors predicting OS, but on multivariable analysis, group allocation was only independent factor

(continued on following page)

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Table A5. Prognostic Value of GA* (continued)

Study	Year	Type of Statistical Analysis Used	Multivariable Analysis Conducted? Adjustments Used?	Sample Size/No. of Events	Age (years)	Mortality
Gironés et al[24,44]	2011, 2012	Log-rank test, Wilcoxon test, Kaplan-Meier method	NA	83 patient cases of lung cancer only; 59 patients had died at time of final follow-up	≥ 70	Factors related to survival (univariable): ECOG PS ($P <$ .001), IADLs ($P <$ .001), weight loss (P = NR), delirium (P = NR), incontinence (P = NR), dementia (P = .02), and depression ($P <$ .001); frailty was related to survival, but this finding was not statistically significant (P = .07); neither CCI nor SCS was related to survival (log-rank P = .47 and .24, respectively); stage significantly associated with survival (log-rank $P <$ .001)
Falandry et al[42]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; covariates significantly ($P <$ .1) associated in univariable analysis (hypoalbuminemia, living in residential homes) were included in multivariable analyses	60 patients with hormone-resistant metastatic breast cancer; eight patients died during treatment	> 70	Factors related to survival (univariable): hypoalbuminemia ≤ 30 g/L (HR, 12.5; 95% CI, 1.4 to 112; P = .024) and living in residential homes (HR, 0.95; 95% CI, 1.59 to 9.8; $P <$ .004); latter was only significant predictor of premature death in multivariable analysis (no empiric data of multivariable analysis were published)
Aaldriks et al[34]	2013	Cox regression analysis, log-rank test, Kaplan-Meier method	Yes; adjustment for age and comorbidities	55 patient cases of advanced breast cancer only; 41 (75%) of 55 patients had died after mean follow-up of 16 months	≥ 70	Inferior MNA (HR, 3.05; 95% CI, 1.44 to 6.45; P = .004) and GFI scores (HR, 3.40; 95% CI, 1.62 to 7.10; P = .001) associated with increased HR for mortality
Retrospective						
Kanesvaran et al[26]	2011	Cox regression analysis	Yes; reduced model selection carried out using backward stepdown by applying stopping rule of Akaike's information criterion among those significant parameters by means of univariable analysis; additional adjustments not conducted	249 patient cases of various cancers; events NR	≥ 70	Age (OR, 1.04; 95% CI, 1.01 to 1.07), abnormal albumin level (OR, 1.97; 95% CI, 1.23 to 3.15), poor ECOG PS (≥ $v <$ 2: OR, 1.77; 95% CI, 1.15 to 2.72), abnormal GDS (OR, 1.81; 95% CI, 1.29 to 2.56), advanced-stage cancer (OR, 1.71; 95% CI, 0.98 to 2.95), or moderate (moderate v low risk: OR, 1.59; 95% CI, 1.02 to 2.50) or high malnutrition risk (high v low risk: OR, 1.84; 95% CI, 1.17 to 2.87) tended to have shorter survival

Abbreviations: CCI, Charlson comorbidity index; CRC, colorectal cancer; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Obstetricians and Gynecologists; GA, geriatric assessment; GFI, Groningen frailty indicator; GVS, geriatric vulnerability score; HR, hazard ratio; IADL, instrumental activity of daily living; IPI, International Prognostic Index; MNA, Mini Nutritional Assessment; NA, not applicable; NR, not reported; OR, odds ratio; OS, overall survival; PS, performance status; SCS, simplified comorbidity score.

*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A6. Impact of GA on Cancer Treatment Decision Making or Prediction of Cancer Treatment Delivery*

Study	Year	Sample Size	Impact of GA
Kenis et al[15]	2013	1,967	GA led to geriatric intervention in 286 patients (25.7%); for 282 patients (25.3%), treating physician stated that GA results influenced treatment decision in some way; GA results did not always reach treating physician before treatment decision was made
Decoster et al[49]	2013	902	In 42.2% of patients, clinical assessment led to different treatment decision compared with younger patients without comorbidities; in 56% of patient cases, treating physician consulted GA results before final treatment decision; in these patients, treatment decision was influenced by clinical assessment in 44.2%; in 31 (6.1%) of 505 patients, GA further influenced treatment, mostly concerning chemotherapy or targeted therapy; in eight patients, GA influenced physician to choose more aggressive chemotherapy; these patients had breast cancer and were age 70 to 82 years
Caillet et al[16]	2011	375	After GA, initial cancer treatment plan was modified for 20.8% of patients (95% CI, 16.8 to 25.3), usually to decrease treatment intensity (63 [80.8%] of 78 patients); by univariable analysis, cancer treatment changes were associated with ECOG PS $\geq$ 2 (73.3% in group with changes *v* 41.1% in group without; $P < .001$), dependency for $\geq$ one ADL (59.0% *v* 24.2%; $P < .001$), malnutrition (81.8% *v* 51.2%; $P < .001$), cognitive impairment (38.5% *v* 24.9%; $P = .023$), depression (52.6% *v* 21.7%; $P < .001$), and greater No. of comorbidities (mean, 4.8; SD, 2.9 *v* mean, 4.0; SD, 2.6; $P < .02$); by multivariable analysis, factors independently associated with cancer treatment changes were lower ADL score (OR, 1.25 per 0.5-point decrease; 95% CI, 1.04 to 1.49; $P = .016$) and malnutrition (OR, 2.99; 95% CI, 1.36 to 6.58; $P = .007$)
Aparicio et al[39]	2013	123	Dose reduction analyzable in 122 patients; 41 patients (33%) had reduction in dose-intensity > 33% during first 4 months after starting treatment; in multivariable analysis, significant independent predictive factors for reduction in dose-intensity > 33% were irinotecan arm (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$) and alkaline phosphatase > 2× ULN (OR, 3.32; 95% CI, 0.99 to 11.20; $P = .022$)
Aliamus et al[27]	2011	49	GA led to changes in 44.9% of initial treatment plans; only 16.7% of these modifications occurred in frail patients (Balducci classification), whereas 60% occurred in vulnerable patients; treatment of vulnerable patients was significantly more frequently changed compared with fit or frail patients (OR, 4.9; 95% CI, 1.3 to 18.6; $P = .02$); principal treatment modifications in vulnerable patients were: change of chemotherapy, one drug instead of two (27.3%), chemotherapy dose adaptation (13.6%), supportive care (13.6%), confirmation of standard treatment without modification (22.7%); by univariable analysis, cancer treatment changes in vulnerable patients were associated with lowered MMSE and IADLs; multivariable analysis indicated lowered MMSE score (< 26) as only independent predictor for treatment modification in vulnerable patients
Horgan et al[23]	2012	30	When treatment plan was decided before GA (n = 24), it altered final decision in only one patient (4%); for those for whom treatment plan was undecided (pending further investigation and patient decision), findings on GA affected final plan in five patients (83%); only 60% of recommendations made for management of additional problems identified were implemented

Abbreviations: ADL, activity of daily living; ECOG, Eastern Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; MMSE, Mini Mental State Examination; OR, odds ratio; PS, performance status; SD, standard deviation; ULN, upper limit of normal.
*For studies published before November 16, 2010, see review by Puts et al.[12]

Table A7. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1)*	Step 2 (Level 2)*	Step 3 (Level 3)*	Step 4 (Level 4)*	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances†	Local nonrandom sample†	Case series†	NA
Is this diagnostic or monitoring test accurate? (diagnosis)	Systematic review of cross-sectional studies with consistently applied reference standard and blinding	Individual cross-sectional studies with consistently applied reference standard and blinding	Nonconsecutive studies or studies without consistently applied reference standards†	Case-control studies or poor or nonindependent reference standard†	Mechanism-based reasoning
What will happen if we do not add therapy? (prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case series, case-control studies, or poor-quality prognostic cohort studies†	NA
Does this intervention help? (treatment benefits)	Systematic review of randomized trials or n-of-one trials	Randomized trials or observational studies with dramatic effect	Nonrandomized controlled cohort/follow-up studies†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning
What are common harms? (treatment harms)	Systematic review of randomized trials, systematic review of nested case-control studies, n-of-one trials with patient about whom you are raising question, or observational studies with dramatic effect	Individual randomized trials or (exceptionally) observational studies with dramatic effect	Nonrandomized controlled cohort/follow-up studies (postmarketing surveillance) provided there are sufficient numbers to rule out common harm (for long-term harms, duration of follow-up must be sufficient)†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning
What are rare harms? (treatment harms)	Systematic review of randomized trials or n-of-one trials	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (screening)	Systematic review of randomized trials	Randomized trials	Nonrandomized controlled cohort/follow-up studies†	Case series, case-control studies, or historically controlled studies†	Mechanism-based reasoning

NOTE. Data adapted.[38]
Abbreviations: NA, not applicable; PICO, patients, intervention, comparator, outcomes.
*Level may be graded down on basis of study quality, imprecision, or indirectness (study PICO does not match question PICO); because of inconsistency between studies; or because absolute effect size is very small. Level may be graded up if there is large or very large effect size.
†Systematic review is generally better than individual study.

KPC_24_B_026

Review of the literature

Summary in Dutch and French

KPC_24_B_026

Literatuurreview

Samenvatting

Auteurs:

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1. Geriatrische screening

Inleiding:

Het gebruik van geriatrische screeningsinstrumenten wordt aangeraden om die oudere patiënten met kanker te identificeren die het meeste nood hebben aan een geriatrische evaluatie (GE) en een multidisciplinaire benadering. Deze publicatie heeft als doelstelling de aanbevelingen van de 'International Society of Geriatric Oncology' (SIOG) uit 2005 betreffende het gebruik van screeningsinstrumenten te vernieuwen.

Methode:

SIOG stelde een groep van experten samen om de literatuur over het gebruik van screeningsinstrumenten bij oudere patiënten met kanker te beoordelen, te interpreteren en te bespreken. Een systematische review werd uitgevoerd en besproken door deze groep experten, leidend tot een consensus over het gebruik van screeninginstrumenten.

Resultaten:

Vierenveertig studies aangaande 17 verschillend screeningsinstrumenten bij oudere patiënten met kanker werden geïdentificeerd. De meest onderzochte screeningsinstrumenten in oudere patiënten met kanker zijn: G8, Geriatrisch Risicoprofiel (GRP) en Vulnerable Elders Survey-13 (VES-13). Binnen deze studies werd de hoogste sensitiviteit waargenomen bij: G8, GRP, Oncogeriatric screen, Study of Osteoporotic Fractures (SOF), Eastern Cooperative Oncology Group (ECOG) - Performance Status, Senior Adults Oncology Program (SAOP2) screening en Gerhematolim. In 11 directe vergelijkende studies ter detectie van problemen op een GE, bleek de G8 meer of even sensitief dan andere screeningsinstrumenten in alle zes vergelijkingen, terwijl de resultaten eerder wisselend waren voor de VES-13 in zeven

vergelijkingen. Daarenboven vertoonden verschillende screeningsinstrumenten waaronder de G8 en de VES-13 een correlatie met belangrijke uitkomsten.

Conclusie:

Screeningsinstrumenten kunnen geen GE vervangen, maar worden aangeraden in een drukke praktijk ten einde die patiënten te identificeren die het meeste baat hebben bij een GE. Indien het resultaat abnormaal is, moet het screeningsinstrument gevolgd worden door een GE en gerichte multidisciplinaire interventies. Verschillende screeningsinstrumenten zijn beschikbaar met verschillende resultaten op gebied van verschillende uitkomsten (inclusief sensitiviteit voor de nood aan verdere GE). Verder onderzoek moet zich richten op de mogelijkheden van screeningsinstrumenten om klinische paden uit te bouwen en om verschillende belangrijke uitkomsten te voorspellen.

Kernwoorden:

Screeningsinstrumenten, oudere patiënten met kanker, geriatrische evaluatie

2. Geriatrisch assessment

Doel:

Deze studie heeft als doelstelling de aanbevelingen van de International Society of Geriatric Oncology (SIOG) uit 2005 over geriatrische evaluatie (GE) in oudere patiënten met kanker te vernieuwen.

Methode:

SIOG stelde een groep experten in de geriatrische oncologie samen om een consensus uit te werken na literatuurreview betreffende volgende vraagstellingen: de beweegreden voor het verrichten van een GE; de bevindingen van een GE in oudere patiënten met kanker; het vermogen van een GE om nevenwerkingen / complicaties te voorspellen gerelateerd aan de kankerbehandeling; de relatie tussen GE bevindingen en algemene overleving; de impact van GE bevindingen op oncologische therapiebeslissingen; de samenstelling van een GE inclusief geriatrische domeinen en meetinstrumenten; en methodes om GE te implementeren in de dagdagelijkse oncologische praktijk.

Resultaten:

GE is waardevol in de dagdagelijkse oncologische praktijk omwille van volgende redenen: detectie van geriatrische problemen die door standaard anamnese en klinisch onderzoek niet geïdentificeerd worden; de mogelijkheid om ernstige behandelingsgerelateerde nevenwerkingen / complicaties te voorspellen; de mogelijkheid om algemene overleving te voorspellen bij oudere patiënten met verschillende oncologische aandoeningen en met verschillende soorten behandeling; en mogelijkheid om therapiekeuze en intensiteit te beïnvloeden.

De experten groep raadt aan dat de volgende domeinen worden geëvalueerd in een GE: functionele status, comorbiditeiten, cognitie, mentale status, vermoeidheid, sociale situatie / ondersteuning, voedingsstatus en de aanwezigheid van geriatrische syndromen. Hoewel verschillende combinaties van meetinstrumenten en verschillende modellen beschikbaar zijn voor de implementatie van GE in de oncologische praktijk, bleek het voor de groep experten niet mogelijk om hieromtrent een aanbeveling te doen.

Conclusie:

Er is een groeiende hoeveelheid data betreffende de meerwaarde van een GE in de dagdagelijkse oncologische praktijk, hoewel bijkomend onderzoek noodzakelijk is om de evidentie verder uit te bouwen.

3. Geriatrische interventies

Inleiding:

Geriatrische interventies zijn gespecialiseerde zorgen of strategieën met als doel om beperkingen van oudere personen op bepaalde geriatrische domeinen (zelfredzaamheid, voedingsstatus, cognitie, sociale situatie, enz.) te corrigeren of te verminderen. In de algemene geriatrische populatie leidt een multidimensionele GE, gevolgd door geriatrische interventies en gerichte opvolging, tot een verbetering van de zelfredzaamheid en overleving van de patiënten.

Doelstelling:

Het doel is om de beschikbare literatuur aangaande geriatrische interventies bij oudere patiënten met kanker te analyseren en aanbevelingen voor te stellen voor implementatie.

Methode:

Een systematische review van de literatuur werd uitgevoerd. De artikels werden gerangschikt volgens het niveau van evidentie. In de werkgroep werd een consensus gezocht om aanbevelingen voor te stellen.

Resultaten:

In totaal werden 21 artikels geselecteerd aangaande de impact van verschillende interventies (fysieke inspanning, nutritionele ondersteuning, educatie, case management, enz.) op verschillende aspecten van de gezondheid van de patiënt (levensverwachting, levenskwaliteit, zelfredzaamheid, vermoeidheid, enz.). Verschillende studies stellen dat geriatrische interventies een significante impact kunnen hebben op de gezondheidstoestand en de

toekomst van oudere patiënten met kanker. In het bijzonder, kunnen de lichamelijke conditie (graad A aanbeveling), de levenskwaliteit (graad B) en de levensverwachting (graad C) verbeterd worden. Het aantal studies is echter zeer beperkt en de gegevens zijn heterogeen. Verscheidene interventies werden bestudeerd met betrekking tot verschillende beperkingen, in verschillende populaties van verschillende patiënten, met verschillende doelstellingen. Dit alles bemoeilijkt een vergelijking van deze studies.

Conclusie:

Geriatrische interventies kunnen een significante impact hebben op de gezondheidstoestand en de toekomst van de oudere patiënt met kanker, net zoals in de algemene geriatrische populatie. Een gepaste selectie van de patiënten, van het type interventies en van het tijdstip van de interventies blijkt essentieel. De gegevens zijn echter te beperkt en te heterogeen om algemene aanbevelingen te formuleren. Nieuwe gerandomiseerde studies zijn noodzakelijk, ten einde het mogelijk te maken om de gegevens beter te interpreteren, om patiënten die het meest nood hebben aan geriatrische interventies te selecteren en om een duidelijke evaluatie te kunnen maken van de reële voordelen van deze interventies.

4. Referenties

Screeningsinstrumenten

- Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older patients with cancer: an update on SIOG recommendations. Annals of oncology: official journal of the European Society of Medical Oncology / ESMO. 2015;26(2):288-300.

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Geriatrische interventies

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Revue de la littérature

Résumé

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1. Dépistage gériatrique

Introduction:

Les outils de dépistage gériatrique ont été développés dans le but d'identifier les personnes âgées atteintes de cancer où une évaluation gériatrique (EG) et une approche multidisciplinaire seraient nécessaires. Notre but était de mettre à jour les recommandations de la Société Internationale d'Oncologie Gériatrique (SIOG) concernant les outils de dépistage.

Méthode:

La SIOG a formé un groupe de travail pour revoir, interpréter et discuter les niveaux d'évidence dans l'utilisation des outils de dépistage chez les patients âgés cancéreux. Une revue systématique a été exécutée et examinée par un groupe d'experts, menant à un consensus concernant leur utilisation.

Résultats:

Quarante-quatre études concernant l'utilisation de 17 outils de dépistage différents chez les personnes âgées atteintes de cancer ont été identifiées. Les outils les plus étudiés chez les personnes âgées cancéreuses sont le G8 , la version flamande du 'Triage Risk Screening Tool (fTRST)' et le 'Vulnerable Elders Survey-13' (VES-13). A travers toutes les études, la plus haute sensibilité a été observée pour : le G8, le fTRST, le 'Oncogeriatric screen', le 'Study of Osteoporotic fractures', l' 'Eastern Cooperative Oncology Group-Performance Status' (ECOG-PS), le 'Senior Adult Oncology Program (SAOP) 2 screening' et le 'Gerhematolim'. Dans 11 comparaisons directes pour la détection de problèmes sur base d'une évaluation gériatrique complète, le G8 était supérieur ou égal en matière de sensibilité aux autres instruments dans toutes les 6 comparaisons, alors que les résultats pour le VES-13 étaient variables dans 7

comparaisons. De plus, différents outils, notamment le G8 et le VES-13, ont démontré des associations avec des mesures de résultats.

Conclusion:

Les outils de screening ne remplacent pas l'EG, mais leur utilisation est recommandée pour identifier les patients qui devraient bénéficier d'une évaluation gériatrique multidimensionnelle. Si le résultat est anormal, le dépistage devrait être suivi par une EG et par des interventions multidisciplinaires spécifiques. Plusieurs outils avec des performances différentes par rapport à des paramètres variables (incluant la sensibilité à détecter la nécessité de réaliser une EG) sont disponibles. Des recherches supplémentaires devraient cibler la capacité des outils de screening à construire des trajets cliniques et à prédire certains paramètres de résultat.

Mots clés:

Outils de dépistage, patients âgés atteints de cancer, évaluation gériatrique

2. Evaluation gériatrique

Objectif:

Mettre à jour les recommandations 2005 de la Société Internationale d'Oncologie Gériatrique concernant l'évaluation gériatrique (EG) chez les patients âgés atteints de cancer.

Méthode:

La SIOG a désigné un groupe d'experts en oncogériatrie pour développer des consensus à partir d'une revue de littérature sur les niveaux d'évidence dans les sujets suivants: le raisonnement pour exécuter les EG; les résultats provenant d'une EG réalisée chez des patients oncogériatriques; la capacité de l'EG à prédire des complications liées au traitement oncologique; le lien entre les résultats de l'EG et la survie générale (SG); l'impact des résultats de l'EG sur les décisions concernant le traitement oncologique; composition de l'EG, incluant les domaines et les outils; et les méthodes pour implémenter l'EG dans la pratique clinique.

Résultats:

L'EG peut être précieux dans la pratique oncologique pour les raisons suivantes : détection de problèmes non identifiés dans l'anamnèse ou lors de l'examen clinique, capacité de prédire des toxicités sévères liées au traitement, capacité de prédire la SG dans une variété de configurations tumorales et thérapeutiques, et la capacité d'influencer le choix du traitement et son intensité.

Le groupe d'experts a recommandé que les domaines suivants soient évalués lors de l'EG: l'état fonctionnel, les comorbidités, l'état cognitif, la santé mentale, la fatigue, l'état social et le soutien, la nutrition, et la présence de syndromes gériatriques. Bien que différentes compilations d'outils et des modèles variables soient disponibles pour l'implémentation de

l'EG dans la pratique oncologique, le groupe d'experts n'a pas pu en privilégier un en particulier plutôt qu'un autre.

Conclusion:

Il y a énormément de données sur l'utilité de l'EG dans la pratique oncologique; cependant, des recherches supplémentaires sont nécessaires pour continuer à renforcer les preuves scientifiques.

3. Interventions gériatriques

Introduction:

Les interventions gériatriques sont des soins spécialisés ou des stratégies visant à corriger ou à pallier les fragilités qui affectent les sujets âgés dans différents domaines (autonomie, nutrition, état cognitif, situation sociale, etc). Dans la population gériatrique générale, les programmes de soins associant une évaluation gériatrique multidimensionnelle, des interventions gériatriques et un suivi prolongé du patient, ont fait la preuve de leur efficacité pour améliorer l'autonomie et la survie des patients.

Objectifs:

Le but est d'analyser les données disponibles concernant les interventions gériatriques chez les patients âgés atteints de cancer et de proposer des recommandations pour leur mise en œuvre.

Méthode:

Une revue systématique de la littérature a été réalisée. Les articles ont été classés selon le niveau d'évidence. Un consensus a été recherché au sein du groupe de travail pour formuler des recommandations.

Résultats:

Vingt-et-un articles ont été sélectionnés concernant des essais contrôlés évaluant l'impact de différentes interventions (exercice physique, support nutritionnel, éducation, case management, etc) sur différents aspects de la santé des patients (espérance de vie, qualité de vie, autonomie, fatigue, etc).

Plusieurs études suggèrent que des interventions gériatriques peuvent avoir un impact significatif sur l'état de santé et le devenir des patients âgés atteints de cancer. En particulier, la condition physique (recommandation de grade A), la qualité de vie (grade B) et l'espérance de vie (grade C) peuvent être améliorées.

Cependant les études sont peu nombreuses et les données sont hétérogènes. Des interventions variées sont étudiées, visant des fragilités différentes, dans des populations de patients différentes, avec des objectifs différents. Ceci rend la comparaison des études difficile.

Conclusion:

Les interventions gériatriques peuvent avoir un impact significatif sur l'état de santé et le devenir des patients atteints de cancer comme dans la population gériatrique générale. Une sélection appropriée des patients, du type d'intervention et du moment de leur mise en œuvre apparait essentielle. Cependant, les données sont trop limitées et trop hétérogènes pour formuler des recommandations générales. De nouveaux essais randomisés sont nécessaires, conçus pour permettre une meilleure interprétation des données, une sélection des patients susceptibles de bénéficier le plus des interventions, une évaluation claire du bénéfice réel des interventions, avec les objectifs les plus pertinents.

4. Références

Dépistage gériatrique

- Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for multidimensional health problems warranting a geriatric assessment in older patients with cancer: an update on SIOG recommendations. Annals of oncology: official journal of the European Society of Medical Oncology / ESMO. 2015;26(2):288-300.

Evaluation gériatrique

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Interventions gériatriques

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