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REVIEW

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

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Philippe Caillet[1,2]
Marie Laurent[1,2]
Sylvie Bastuji-Garin[1,3,4]
Evelyne Liuu[2]
Stephane Culine[5]
Jean-Leon Lagrange[6]
Florence Canoui-Poitrine[1,2,3,*]
Elena Paillaud[1,2,*]

[1]Laboratoire d'Investigation Clinique (LIC), Faculté de Medecine, Université Paris Est Créteil (UPEC), Créteil, Paris, [2]Unité de Coordination d'Onco-Gériatrie, Département de Médecine Interne et Gériatrie, Hôpital Henri-Mondor, Assistance Publique – Hopitaux de Paris (AP-HP), Créteil, [3]Service de Santé Publique, Hôpital Henri-Mondor, AP-HP, Créteil, [4]Unité de Recherche Clinique, Hôpital Henri-Mondor, AP-HP, Créteil, [5]Service d'Oncologie Médicale, Hôpital Saint-Louis, AP-HP, Paris, [6]Service de Radiotherapie, Hôpital Henri-Mondor, AP-HP, Créteil, France

*These authors contributed equally to this work

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

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

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

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

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

Introduction

The management of older cancer patients has become a major public health concern in Western countries because of the aging of the population and the steady increase in cancer incidence with advancing age. Today, over 60% of all cancers are diagnosed in patients older than 65 years in Europe and the USA. This percentage is expected to rise to 70% within the next 30 years.[1,2] The care of older patients thus constitutes an important part of everyday oncology practice. However, despite the rapid growth of the geriatric oncology population in the real-life setting, older patients are underrepresented in the clinical trials that set the standards of care in oncology.[3] As a result, there is a lack of evidence on the risk/benefit ratio of cancer treatments in older patients. Comorbidities

Correspondence: Elena Paillaud
Unité de Coordination d'Onco-Gériatrie, Département de Médecine Interne et Gériatrie, Hôpital Henri Mondor,
51 rue de Marechal de Lattre de Tassigny, 94010 Créteil Cedex, France
Tel +331 4981 3074
Email elena.paillaud@hmn.aphp.fr

and disabilities become increasingly prevalent with advancing age and are associated with treatment-related side effects and poorer outcomes.[4–7] Thus, a major issue for oncologists treating older cancer patients is determination of the intensity of cancer treatment best suited to each patient. There is considerable heterogeneity among patients of the same age, so that chronologic age alone provides little information regarding an individual's tolerance to cancer treatments.

Identifying comorbid conditions and aging-related, organ-specific physiologic changes that increase the risk of toxicities may allow oncologists to better assess the risk/benefit ratio in individual patients, to develop customized treatment adjustments, and to implement interventions designed to decrease the risk of toxicity. The Comprehensive Geriatric Assessment (CGA) is one approach developed for this purpose. The CGA was designed by geriatricians as a multidimensional assessment of general health status based on validated geriatric scales and tests that produce an inventory of health problems, allowing the development of an individualized geriatric intervention program. Since the mid-1990s, oncologists and geriatricians have worked to integrate CGA approaches into oncologic practice. The International Society of Geriatric Oncology created a task-force to determine the best CGA format for use in oncology.[8] Independent of these recommendations, the feasibility and effectiveness of the CGA in managing older cancer patients and the evidence of its usefulness in everyday oncology practice deserve consideration. Only two systemic reviews have focused on the CGA in older cancer patients.[9–11]

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

Materials and methods

Data sources

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

Study eligibility criteria

We used four eligibility criteria to select studies for our review: a focus on older patients (65 years or older) with solid cancer (excluding hematologic malignancies) who were seen in oncology or surgery or geriatric-oncology clinics (as outpatients or inpatients); prospective data collection and observational or interventional design; a sample size of at least 100 patients; and assessment of at least five CGA domains (from nutrition, cognition, mood, functional status, mobility and falls, polypharmacy, comorbidities, and social environment). We excluded editorials, case studies, studies published as abstracts, and review articles other than the two most recent systematic reviews of the CGA in geriatric oncology.[9–11]

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

We designed a specific algorithm for each objective:

1) Algorithm 1 to assess the usefulness of the CGA in assessing health problems (Figure 1): ("Neoplasms" [Mesh] OR "cancer" [Text Word]) AND ("Geriatric Assessment" [Mesh] OR "Comprehensive Geriatric Assessment" [Text Word]);
2) Algorithm 2 to assess the usefulness of the CGA in predicting outcomes (Figure 2): ("Geriatric Assessment" [Mesh] OR "Comprehensive Geriatric Assessment" [Text Word]) AND ("Neoplasms" [Mesh] OR "cancer" [Text Word]) AND ("Epidemiologic Studies" [Mesh] OR "Epidemiologic Research Design" [Mesh] OR "Survival" [Mesh] OR "Mortality" [Mesh] OR "toxicity" [Subheading] OR "Morbidity" [Mesh] OR "Treatment Outcome" [Mesh]);
3) Algorithm 3 to assess the usefulness of the CGA in developing a coordinated program of tailored geriatric interventions (Figure 3): ("Geriatric Assessment-based intervention" [Mesh] OR "Comprehensive Geriatric Assessment-based intervention" [Text Word]) AND ("tumor" [Text Word] OR "cancer" [Text Word] OR "neoplasms" [Mesh]) AND ("clinical trial" [Mesh] OR "trial" [Mesh] OR "randomized trial" [text Word]).

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

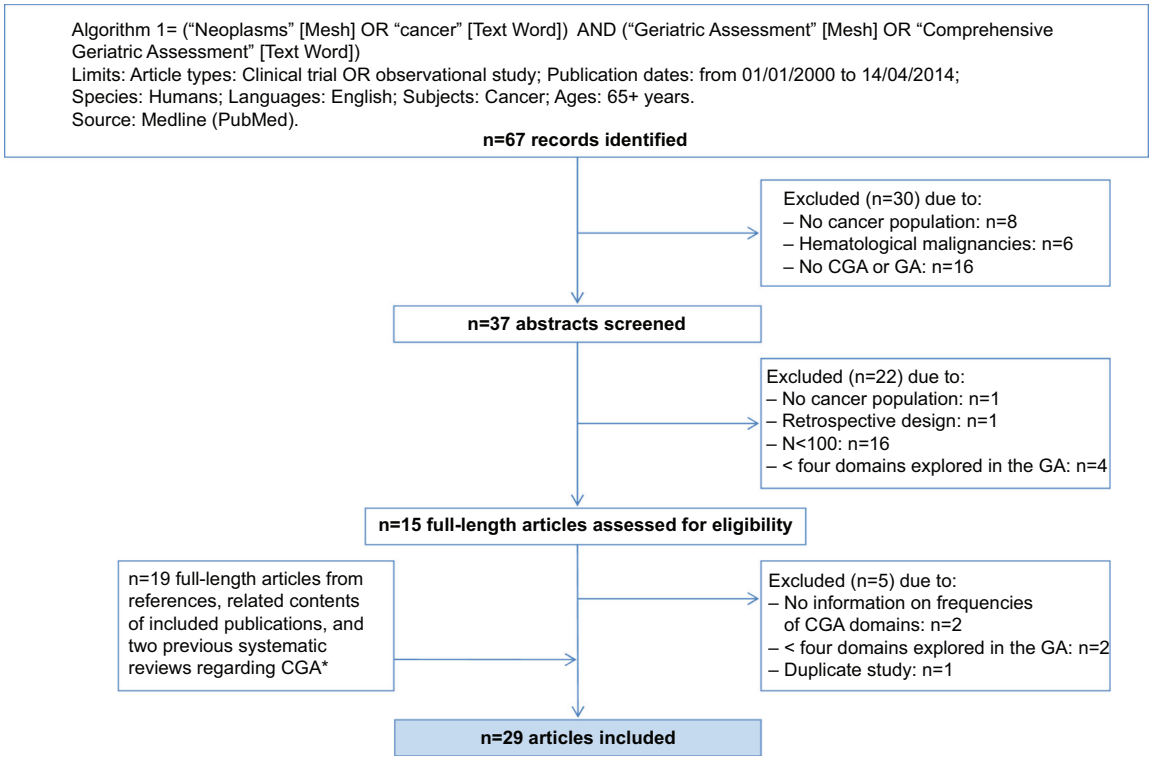

Figure 1 Search results and study selection for ability of the CGA to detect health problems in elderly patients with solid malignancies.
Notes: N, number of patients; n, number of articles. *Data from Hamaker et al[9] and Puts et al.[10,11]
Abbreviations: CGA, Comprehensive Geriatric Assessment; GA, Geriatric Assessment.

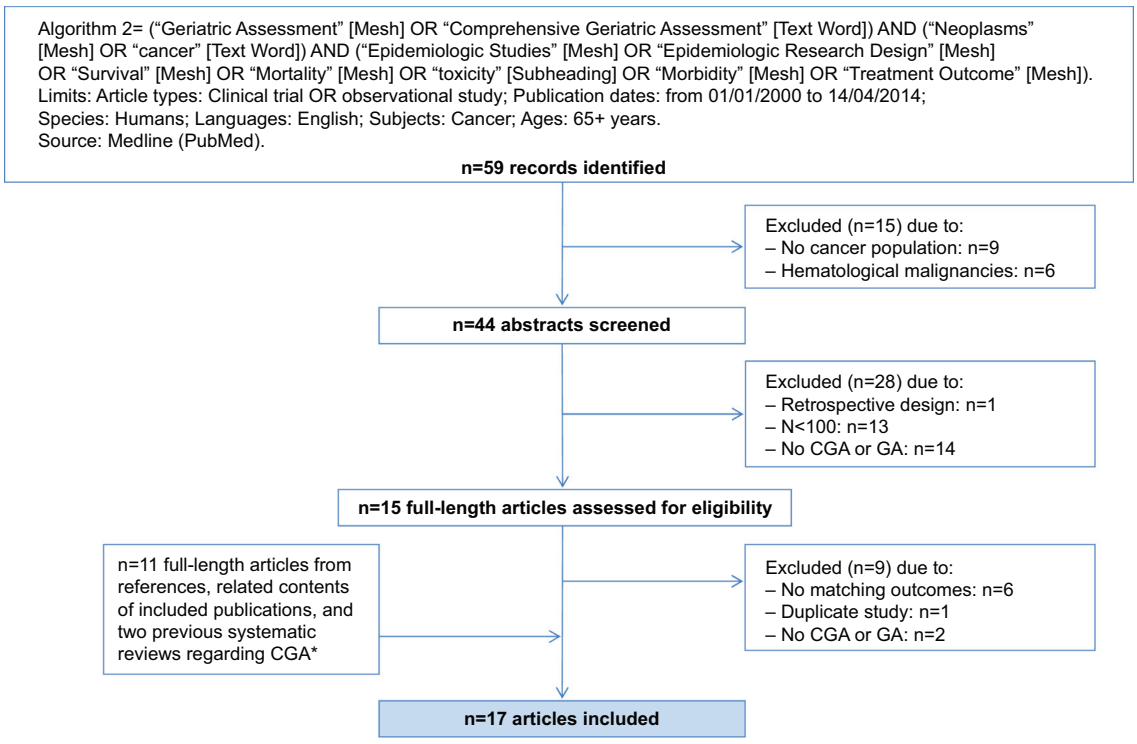

Figure 2 Search results and study selection for usefulness of the CGA in predicting outcomes in elderly patients with solid malignancies.
Notes: N, number of patients; n, number of articles. *Data from Hamaker et al[9] and Puts et al.[10,11]
Abbreviations: CGA, Comprehensive Geriatric Assessment; GA, Geriatric Assessment.

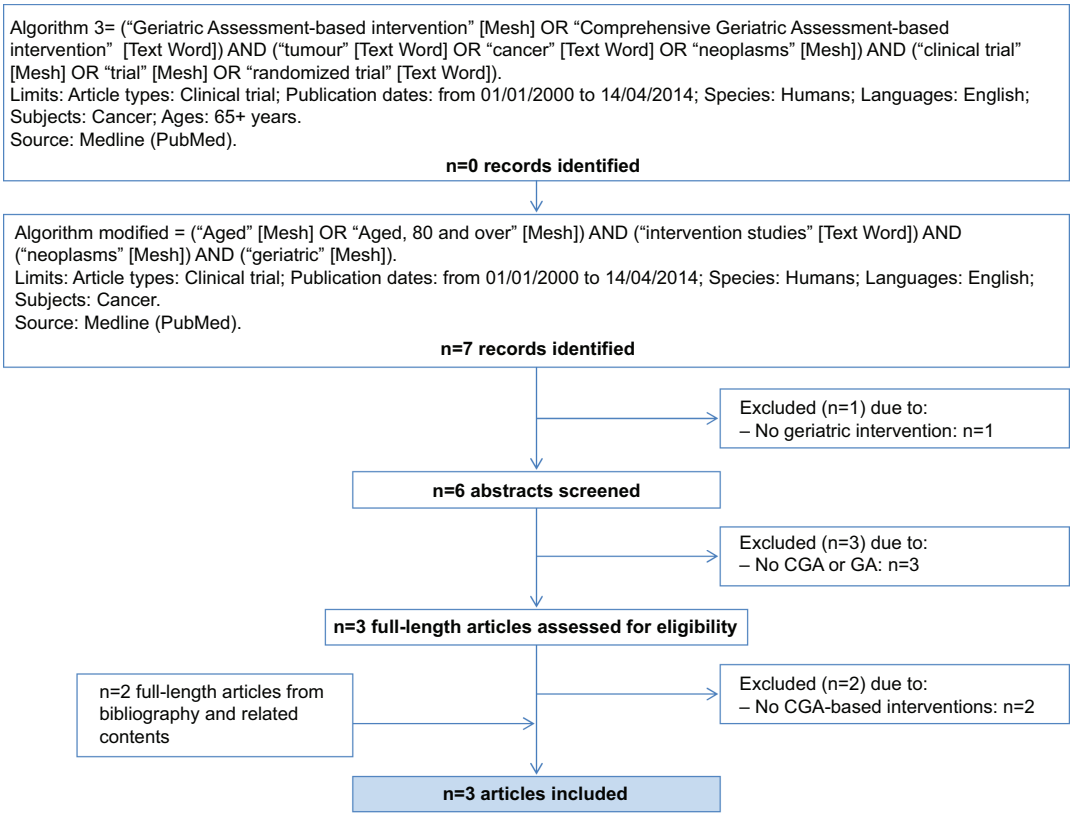

Figure 3 Search results and study selection for usefulness of the CGA in developing a coordinated program of tailored geriatric interventions.
Abbreviations: CGA, Comprehensive Geriatric Assessment; GA, Geriatric Assessment.

Study selection

Articles were selected initially by three senior medical doctors specialized in geriatric oncology (PC, FCP, and EP), based on the titles and abstracts and on the eligibility criteria described above. When one or more of these three investigators were uncertain about whether the article fulfilled the eligibility criteria, the abstract was included and the full-length article was analyzed by the same three investigators. Disagreements were resolved by consensus. We also reviewed the reference lists of all selected articles, related contents of the Medline search, and reference lists of the three above-mentioned reviews[9–11] to look for relevant articles.

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

What is the CGA?

Definition

The CGA was defined in 1988 as

> [...] a multidisciplinary evaluation in which the multiple problems of older persons are uncovered, described, and explained, if possible, and in which the resources and strengths of the person are catalogued, need for services assessed, and a coordinated care plan developed [...][12]

CGA components and assessment tools

The core components of the CGA are functional status, cognition, mood and emotional status, social support, financial concerns, nutritional status, comorbidities and polypharmacy, geriatric syndromes (fall risk, confusion, urinary incontinence, visual or hearing impairments), goals of care, and advance care planning.[8] The CGA uses validated geriatric scales and tests to produce an inventory of health problems, which can then serve to develop an individualized geriatric intervention plan. The content of the assessment varies with the care setting (eg, home, clinic, hospital, or nursing home). In many settings, the CGA process relies on a core team consisting of a physician, a nurse, and a social worker, who obtain assistance as needed from other health care professionals (eg, nutritionist, physical therapist, and/or psychologist).

The effects of implementing a CGA-based approach have been evaluated in a number of controlled studies conducted in inpatients and community-dwelling

outpatients. A meta-analysis of 28 controlled trials comprising 4,959 patients who underwent one of five CGA types and 4,912 controls[13] showed that the CGA, when used to guide management decisions and combined with long-term follow-up, detected a greater number of health problems and improved survival, functional status, and unplanned admissions in older patients with nonmalignant diseases, compared with usual care. However, the effect size was greater for inpatients than for community-dwelling patients. A meta-analysis of 21 trials with 10,315 patients indicated that the CGA increased the likelihood of patients being alive and in their own homes 6 months after an emergency admission.[14]

Conducting the CGA in oncology

To help oncologists select the best treatment for older patients, the US National Comprehensive Cancer Network, International Society of Geriatric Oncology, and European Organisation for Research and Treatment of Cancer recommend a CGA-based approach for elderly cancer patients.[8,15] However, the best CGA type and implementation method for cancer patients in everyday practice remain to be defined. Limitations to the widespread use of the CGA in everyday practice are the considerable time and human resources needed to conduct the assessment and the failure of some health insurance systems to reimburse it. The abundance of studies investigating the effectiveness of the CGA or using CGA components supports the feasibility of this assessment in geriatric oncology. Only one large prospective multicenter study[16] carried out in ten hospitals in Belgium, including 1,967 older cancer patients, has specifically addressed the feasibility of the CGA. In this study, the high inclusion rate involving 71% of patients indicated that the implementation of a geriatric assessment was very feasible. Nevertheless, this study showed that the information revealed by the CGA did not always reach treating physicians and efforts were needed to improve the interaction between the oncologist, geriatrician, and trained health care worker.

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

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

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

Influence of CGA on treatment decisions

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

A prospective study[16] of 1,967 older cancer patients (87.2% with solid malignancies and 12.8% with hematologic malignancies) evaluated the prevalence of changes in treatment decisions based on CGA findings. The oncologists were aware of the CGA results at the time of treatment decision-making for only 61.3% of patients and, among these, 25.3% had changes in the final treatment decision in response to the CGA results. This study did not assess relationships between individual CGA parameters and cancer treatment decisions.

Table 1 Studies of health problem identification using Comprehensive Geriatric Assessment

References	Study design	Sample size	Cancer type and metastatic status	Age, mean ± SD or median (range)	Dependency	Mobility impairment – fall risk
Laurent et al[17]	P	385	CRC 28.6%, breast 23.1%, GI non-CRC 19.2%, urinary tract 13.2%, prostate 10.9%, other 4.9% M+ 47.0%	78.9±5.4	21% ADL 40.2% PS ≥2	34.5% walking problems 47.2% fall risk
Pottel et al[18]	P	100	HNC 100% 69% stages III–IVb	72 (65–86)	10.2% ADL 59.2% IADL	26.5% (Tinetti)
Kanesvaran et al[19]	P	803	Lung 32.1%, CRC 21.0%, breast 7.2%, prostate 2.1%, other 37.5% M+ 56.3%	72 (65–94)	29.4% ADL 63.7% IADL	NR
Kenis et al[20]	P	937	Breast 40.4%, CRC 20.6%, lung 7.8%, ovarian 6.3%, prostate 9%, hematologic malignancies 15.9% M+ 51.8%	76 (70–95)	51.4% ADL 57.4% IADL 27.7% PS ≥2	3.7% ≥2 falls without injury 11.2% ≥2 falls with injury
Decoster et al[21]	P	937	Breast 40.4%, CRC 20.6%, lung 7.8%, ovarian 6.3%, prostate 9%, hematologic malignancies 15.9%	76 (70–95)	51.4% ADL 57.4% IADL 27.7% PS ≥2	3.7% ≥2 falls without injury 11.2% ≥2 falls with injury
Aaldriks et al[22]	P	143	CRC (colon 83%, rectum 17%)	75 (70–92)	2% PS ≥2	NR
Hoppe et al[23]	P	299	NHL 31.8%, colon 25.8%, stomach 11.4%, lung 10.0%, pancreas 5.7%, prostate 5.4%, bladder 4.7%, ovary 4.0%, primary unknown 1.3% M+ 37.5%	77.35 (70–93)	31.8% ADL 72.9% IADL 21.7% PS ≥2	22.4% TGUG
Bouzereau et al[24]	P	111	Lung 26.1%, GI 18%, HNC 12.6%, genitourinary tract 6.3%, breast 9.9%, gynecologic 5.4%, prostate 4.5%, hematologic malignancies 10.8%, skin 4.5%, other 1.9%	80.6 (65–96)	33.3% ADL 58.6% IADL	NR
Falandry et al[25]	P	111	Ovarian cancer 100% M+ 35%	79 (71–93)	55% ADL 69% IADL	NR
Kenis et al[16]	P	1,967	Breast 40.5%, CRC 21.5%, lung 12.0%, ovary 5%, prostate 8.2%, hematologic malignancies 12.8% M+ 44.9%	76 (70–96)	56.5% ADL 64.5% IADL 29.6% PS ≥2	4.4% ≥2 falls without injury 13.7% ≥2 falls with injury
Beitar A et al[26]	P	170	Urinary tract 29%, digestive tract 19%, HNC 16%, breast 15%, lung 11%, others 11% M+ 57%	77 (66–97)	33% ADL 52% IADL	35% TGUG
Soubeyran et al[7]	P	348	Colon/stomach 37.1%, NHL 30.7%, other 32.2% M+ 81.3%	77.45 (70–99)	18.1% ADL 73.0% IADL 27.3% PS ≥2	24.1% TGUG
Bellara et al[27]	CS	364	NHL 30%, colon 28%, stomach 10%, lung 10%, pancreas 6%, prostate 6%, bladder 5%, ovary 4%, unknown primary 1% M+ 53%	77 (70–99)	17% ADL 72% IADL	23% TGUG

Malnutrition	Cognitive impairment	Depression	Comorbidities	Polypharmacy	Social difficulties	Frailty
41.8% MNA	12.3% MMSE	27.9% GDS-4	% NR (CIRS-G)	% NR (number of drugs/day)	36.1% living alone 30.9% home services	NR
46.9% risk of MNA	22.4% MMSE	20.4% GDS	69.4% ≥1 comorbid condition (CIRS-G)	NR	NR	75% vulnerable Vulnerability: 38.8% by VES-13 69.4% by G8 61.2% by VES-13 + G8
25.4% with 25% food intake reduction in last week	% NR (QLQC30)	% NR (QLQC30)	55.4% ≥3 comorbidities	28.4% ≥3 drugs/day	8.7% living alone	NR
63.7% MNA-SF	10.6% MMSE	20.6% GDS-15	29.1% CCI ≥2	% NR	30.2% living alone	NR
63.7% MNA-SF 83% MNA	10.6% MMSE	20.6% GDS-15	29.1% CCI ≥2	53.1% ≥5 drugs/day	30.2% living alone	73.5% geriatric risk
27.3% MNA	13.3% IQCODE 7.7% MMSE	NR	49% ≥2 comorbid organ systems CCI	50% ≥4 drugs/day	NR	24% GFI
10.7% BMI <19 kg/m² 63.2% MNA 23.8% albumin <35 g/L	17.1% MMSE	44.5% GDS-15	39.1% grade 3 or 4 comorbidities by CIRS-G	NR	NR	NR
70% weight loss	42.2% MMSE	46.7% GDS-4	58.6% ≥2 comorbidities CCI	NR	24.3% social worker	37% fit 37% vulnerable 26% frail
21% BMI <21 kg/m² 61% albumin <35 g/L	29% MMSE	36% GDS-15 37% HADS	24% ≥3 comorbidities	68% ≥4 drugs/day	17% home care	NR
80.4% MNA-SF 83% MNA	13.2% MMSE	60.9% GDS-4	33.8% ≥2 comorbidities CCI	% NR (number of drugs/day)	35.2% living alone	70.7% geriatric profile by G8
53% MNA	9% MMSE	24% GDS-30	35% ≥1 grade 3 or 4 comorbidities by CIRS-G	NR	20% MOS-SSS	47% vulnerable (GFI)
34.9% MNA	19.0% MMSE	44.0% GDS-15	38.2% ≥1 grade 3 or 4 comorbidities by CIRS-G	NR	NR	NR
64% MNA	17% MMSE	45% GDS-15	39% ≥1 grade 3 or 4 comorbidity by CIRS-G	NR	NR	82% impaired G8 score

(*continued*)

Table 1 (*Continued*)

References	Study design	Sample size	Cancer type and metastatic status	Age, mean ± SD or median (range)	Dependency	Mobility impairment – fall risk
Biesma et al[28]	P	181	Lung 100% Stages III–IV, M+ 68%	74 (70–87)	23.0% ADL 47.5% IADL	14% TGUG
Caillet et al[29]	P	375	GI 58.7%, including 58.6% CRC, breast 16.3%, prostate and urinary tract 18.4%, lung 1.6%, others 5.1% M+ 54.6%	79.6±5.6 (70–99)	31.5% ADL 49.9% PS ≥2	45.1% walking problems 29.9% falls in the past 6 months 54.9% fall risk
Chaïbi et al[30]	P	161	CRC 33%, GI non-CRC 17%, breast 19%, lung 9%, gynecologic 7%, other 15% Advanced or M+ 53%	82.4 (73–97)	32% ADL 60% IADL	20% TGUG
Hurria et al[5]	P	500	Breast 11%, lung 29%, prostate, GI 27%, gynecologic 17%, urinary tract 10%, others 6% M+ 61%	73±6.2 (65–91)	21% KPS <70% % NS (ADL, IADL)	80% ≥1 fall in last 6 months % NS (TGUG, mobility limitation)
Hamaker et al[31]	P	292	CRC 14%, GI non-CRC 34.2%, hematologic malignancies 17.8%, breast 6.2%, lung 6.2%, prostate 5.5%, bladder 4.8%, other 11.3% M+ 43.2%	74.9 (65–96)	38.1% ADL 76.9% IADL	47.9% mobility limitation 12.7% ≥2 falls in past 3 months
Owusu et al[32]	CS	117	Breast 59%, other 41% 41% stages II–IV	73 (69–80)	19% ADL 45% IADL 28% PS ≥2 38% KPS ≤80	23% fall risk (≥2 falls in past 6 months, TGUG)
To et al[33]	CS	200	GI 32%, lung 24%, genitourinary 13%, breast 13%, other 18% M+ 63%	76.7±4.9 (70–92)	45% ADL 41% IADL 35% KPS <70	22% ≥1 falls in past 6 months
Luciani et al[34]	CS	419	Lung 32%, CRC 29%, breast 8.4%, HNC 2.7%	76±5 (70–97)	30% ADL 25% IADL 5.5% PS ≥2	36% mobility problems by VES-13
Kristjansson et al[35]	P	178	CRC (colon 71%, rectum 29%) M+ 12%	79.6±5.7 (70–94)	15.7% Barthel Index, NEADL	NR
Kellen et al[36]	CS	113	Prostate 32%, lung 11%, breast 15%, colon 15%, other 27%	77±4	61% ADL 77% IADL	NR
Hurria et al[37]	CS	245 214 analyzed	Breast 41%, NHL 9%, gynecologic or genitourinary tract 17%, GI 19%, other 14% M+ 36%	76±7 (65–95)	45.8% IADL 17.3% KPS ≤60	20.1% ≥1 fall in past 6 months

Malnutrition	Cognitive impairment	Depression	Comorbidities	Polypharmacy	Social difficulties	Frailty
NR	7.5% MMSE	27.5% GDS	% NR (CIRS-G, CCI)	NR	NR	% NR (GFI)
57.5%	27.1% MMSE	28.3% GDS-4	% NR (CIRS-G)	66.9% ≥5 drugs/day	17.6% inappropriate social environment 40.1% living alone	% NR (number of altered CGA parameters)
65% MNA	26% MMSE	34% GDS-15	46.5% ≥1 grade 3 or 4 comorbidity by CIRS-G	NR	NR	NR
12% BMI 38% unintentional weight loss >5% in last 6 months % NR (albumin)	Blessed Orientation Memory Concentration test	% NR (HADS)	90% ≥1 comorbid condition	NR	21% living alone % NR (assistance for housework, decrease in social activities)	NR
46.0% SNAQ and/or BMI	15.1% IQCODE-SF 21.5% CAM	65.3% GDS-2	% NR (CCI)	48.0% ≥5 drugs/day	5.0% not living independently	91.1% ≥1 geriatric condition
NR	6% MMSE	12% GDS-15	36% CCI ≥2	9% ≥10 drugs/day	42% living alone 27% inadequate social support (MOS support scale)	43% ≥2 geriatric abnormalities
34% >5% weight loss	22% self-reported memory problems	17.5% psychologic distress	19% >4 comorbidities 17% CCI >2	38% >5 drugs/day	30% living alone 39% support service	28% fit 60% vulnerable 13% frail
% NR (MNA-SF)	% NR (MMSE)	NR	81% ≥3 comorbid condition (CIRS-G)	57% ≥3 drugs/day	8.8% no caregiver	28% CGA impairment 53.7% vulnerable by VES-13 score
9.0% MNA	6.7% MMSE	10.1% GDS-30	23.0% severe comorbidities by CIRS-G	6.2% ≥8 drugs/day	26% help from relatives or friends 20% public help	57.3% not frail 42.7% frail
NR	14% MMSE	30% GDS	76% ≥1 comorbidity	NR	34% living alone	68% ≥5 altered CGA domains 31% vulnerable by GFI 49% vulnerable by VES-13
32.2% weight loss in past 6 months % NS (BMI)	NR	% NR (MOS emotional)	50.0% ≥3 comorbidities	% NR (number of drugs/day)	32.7% living alone 15.0% support service	NR

(*continued*)

Table 1 (*Continued*)

References	Study design	Sample size	Cancer type and metastatic status	Age, mean ± SD or median (range)	Dependency	Mobility impairment – fall risk
Mohile et al[38]	CS	2,349	Lung 5.1%, colon 14.0%, breast 25.6%, uterus 11.6%, prostate 22.3%, bladder 5.2%, ovarian 3.6%, other 25.7% (some patients with more than one cancer)	76.2	Self-reported 31.9% ADL 49.5% IADL	25.9% with self-reported falls
Girre et al[39]	CS	105	Breast 60.9%; lung 5.7%; CRC 6.7%; gynecologic 7.5%, prostate 1.9%, hematologic malignancies 1.9%; others 15.1% M+ 57.1%	79 (70–97)	42% ADL 54% IADL 39.6% PS ≥2	19.8% ≥2 falls in past year
Marenco et al[40]	P	571	CRC 29.9%, GI non-CCR 16.3%, kidney and bladder 14.2%, lung 10%, breast 6%, prostate 10%, others 13.6% M+ 42.7%	78.0±4.8	28.2% ADL % NS (IADL, KPS)	NR
Wedding et al[41]	CS	200	% NR (hematologic malignancies, GI, lung, breast, ovary, prostate, bladder, pancreas, liver, skin, larynx)	75.9 (70–94)	50% ADL 46% IADL	23% fall risk (Tinetti)
Hurria et al[42]	CS	250	Breast 41%, NHL 9%, gynecologic or genitourinary 17%, GI 19%, others 15% M+ 36%	76±7 (65–95)	49% IADL 26% KPS ≤60%	21% with history of falls

Note: This table lists only prospective studies with 100 or more patients and assessment of at least four CGA domains.

Abbreviations: CGA, Comprehensive Geriatric Assessment; CS, cross-sectional study; P, prospective observational study; CRC, colorectal cancer; GI, gastrointestinal cancer; GI non-CRC, gastrointestinal cancer other than colorectal cancer; HNC, head and neck cancer; NHL, non-Hodgkin lymphoma; M+, metastatic spread at time of CGA; ADL, activities of daily living; IADL, instrumental activities of daily living; KPS, Karnofsky performance status; NEADL, Nottingham Extended Activities of Daily Living scale; PS, performance status; TGUG, Timed Get-Up-and-Go test; BMI, body mass index; MNA, Mini-Nutritional Assessment; MNA-SF, Mini-Nutritional Assessment Short Form (12 items); SNAQ, Simplified Nutritional Appetite Questionnaire; CAM, Confusion Assessment Method; IQCODE, Informant Questionnaire on COgnitive Decline in the Elderly; IQCODE-SF, IQCODE Short Form; MMSE, Mini-Mental State Examination; SPMSQ, Short Portable Mini-mental State Questionnaire; QLQC30, Quality of Life Questionnaire; GDS, Geriatric Depression Scale; HADS, Hospital Anxiety and Depression Scale; CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics; SRC score, Satanario and Ragland Comorbidity score; MOS, Medical Outcomes Study; MOS-SSS, Medical Outcomes Study - Social Support Survey; GFI, Groningen Frailty Indicator; VES-13, Vulnerable Elders Survey 13; G8, G8 screening tool; NR, not reported; % NR, percentage not reported; SD, standard deviation.

Two studies used univariate analyses to investigate associations between CGA parameters and treatment decisions. In a prospective study of 105 older cancer patients (98.1% with solid malignancies),[39] the treatment plan was modified after CGA in 38.7% of cases. By univariate analysis, body mass index ≤23 and absence of depression were associated with treatment changes. In another prospective study of 161 patients with solid malignancies,[30] the CGA influenced cancer treatment decisions in 49% of cases. Chemotherapy intensity was diminished in 21% of patients (by using less intensive regimens in 18% and by delaying treatment initiation in 3%) and augmented in 28% of patients.

Only two prospective studies involved multivariate analyses to identify CGA parameters associated with treatment decisions. In 571 older patients with solid malignancies,[40] factors independently associated with receiving supportive care only were older age, living alone, ADL impairment, and low body mass index, whereas a higher instrumental ADL score was associated with receiving active cancer treatment. The other study[29] included 375 older patients with solid malignancies, of whom 20.8% had CGA-based changes in their treatment plan, which consisted of decreased treatment intensity in 81% of cases. By multivariate analysis, factors independently associated with treatment changes were a lower ADL score and malnutrition.

Malnutrition	Cognitive impairment	Depression	Comorbidities	Polypharmacy	Social difficulties	Frailty
NR	Self-reported 11.5%	Self-reported 26.1%	24.2% with 2 self-reported comorbidities 50.5% ≥3 comorbidities	NR	NR	45.8% vulnerability by VES-13 79.6% frail (Balducci criteria)
45.6% BMI 7.7% weight loss ≥10% in last 3 months 60% albumin	NR	53.1% GDS-4	33.3% ≥2 comorbidities	74% ≥3 drugs/day	16.9% without caregiver	NR
17.7% BMI	40.8% SPMSQ	NR	60% ≥3 comorbidities % NR (CIRS)	NR	24.3% living alone	23.3% ineligible for active cancer treatment 39.2% eligible for active cancer treatment 37.5% referred for palliative care
43% poor nutritional status or at risk	8% MMSE	NR	23.4% 1 comorbidity by CCI 16.1% ≥2 comorbidities by CCI	78.7% ≥1 drug/day	NR	25% fit 25.5% vulnerable 49.5% frail
20% BMI 26% weight loss	NR	NR	94% ≥1 comorbidity	% NR (number of drugs/day)	17% living alone	NR

These five studies suggest that some CGA parameters may influence treatment decisions. Function and nutritional status may have the strongest effect.

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

Determining the optimal therapeutic strategy is a major challenge in older cancer patients. An important goal of the CGA is prediction of mortality and cancer treatment toxicities. Table 2 shows the findings from 17 studies reporting associations that link CGA components to cancer treatment outcomes, functional decline, and mortality in elderly patients with solid malignancies.[5–7,17,23,25,28,35,43–52] Four studies[5,6,25,44] investigated relationships between CGA components and chemotoxicity. Dependency as indicated by impaired instrumental ADL or ECOG-PS values, mobility impairment, cognitive dysfunction, malnutrition, social difficulties, and polypharmacy were significantly associated with chemotoxicity. Nine studies[7,25,45,47–52] assessed the ability of CGA components to predict mortality. Dependency assessed by instrumental ADL and/or ECOG-PS, mobility impairment, cognitive dysfunction, depressive mood, malnutrition, and

Table 2 Effectiveness of CGA components in predicting cancer treatment outcomes, functional decline, morbidity, and mortality in older patients with solid malignancies

CGA components	Treatment outcomes				
	Postoperative complications	**Chemotherapy feasibility**	**Chemotoxicity**	**Functional decline disability**	**Death**
Dependency	Audisio et al[43]: (460 patients, mixed tumor sites), IADL and ECOG-PS were associated with 1-month postsurgical complications	Biesma et al[28]: (181 patients, NSCLC) better ADL, IADL, and QLQC30 associated with greater likelihood of chemotherapy completion Laurent et al[17]: (385 patients, mixed solid malignancies), better ADL (or ECOG-PS) associated with greater likelihood of chemotherapy completion Falandry et al[25]: (111 patients, ovarian cancer), GVS including ADL and IADL associated with greater likelihood of chemotherapy completion	Extermann et al[6]: (518 patients, mixed tumor sites), altered IADL associated with hematologic toxicity and altered ECOG-PS with nonhematologic toxicity Hurria et al[5]: (500 patients, mixed cancer sites), need for assistance in taking medications associated with severe chemotoxicity Aparicio et al[44]: (123 patients, metastatic colorectal cancer), altered IADL associated with severe chemotoxicity Falandry et al[25]: (111 patients, ovarian cancer), geriatric vulnerability score (GVS) including ADL and IADL associated with severe chemotoxicity	Hoppe et al[23]: (364 patients, mixed tumor), IADL $\leq$7 associated with loss of 0.5 point ADL or more between beginning of chemotherapy and 2nd cycle	Maione et al[45]: (566 patients with advanced NSCLC), altered IADL, ECOG-PS, and QLQC30 associated with overall survival Falandry et al[25]: (111 patients, ovarian cancer), geriatric vulnerability score (GVS) including ADL and IADL associated with overall survival
Mobility impairment, falls	Makary et al[46]: (594 patients, 60% operated for solid tumor), frailty assessed by Fried criteria-associated postoperative complications		Hurria et al[5]: one or more falls and unable to walk one block were associated with severe chemotoxicity		Soubeyran et al[7]: (348 patients, mixed tumor sites and stages, first-line chemotherapy): long TGUG associated with early death (<6 months)
Malnutrition			Extermann et al[6]: altered MNA score associated with nonhematologic toxicity Falandry et al[25]: (111 patients, ovarian cancer), geriatric vulnerability score (GVS) including albuminemia associated with severe chemotoxicity		Soubeyran et al[7]: low MNA associated with early death
Depression					Kanesvaran et al[47]: (249 patients, mixed cancer sites), GDS associated with overall survival Giantin et al[48]: (160 patients, mixed cancer sites), GDS associated with 6-month and 12-month survival

Cognitive impairment		Extermann et al[6]: decreased MMSE score associated with nonhematologic toxicity Aparicio et al[44]: MMSE ≤27 associated with severe chemotoxicity	Giantin et al[48]: (160 patients, mixed cancer sites), MMSE associated with 6-month and 12-month survival
Comorbidities/ polypharmacy/ number of CGA components	Kristjansson et al[35]: (176 patients, colorectal cancer surgery), CGA-based frailty predicted postoperative complications	Hurria et al[5]: severe renal insufficiency and anemia associated with chemotoxicity	Clough-Corr et al[49]: (660 patients, breast cancer), ≥3 deficient CGA components associated with all-cause mortality at 5 and 10 years Kim et al[50]: (141 patients, mixed tumor sites), cumulative impairments of CGA components associated with postsurgical adverse outcomes (in-hospital death or post-discharge institutionalization) Bo et al[51]: (294 patients, 52% cancer surgery), altered CIRS score associated with 1-month postsurgical death Tougeron et al[52]: (109 patients with esophageal cancer), CCI score ≥2 associated with overall survival Giantin et al[48]: (160 patients, mixed cancer sites), CIRS-G associated with 6-month and 12-month survival
Social difficulties		Hurria et al[5]: decreased social activities associated with chemotoxicity	

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

Abbreviations: CGA, Comprehensive Geriatric Assessment; GVS, geriatric vulnerability score; NSCLC, non-small cell lung carcinoma; ADL, activities of daily living; IADL, instrumental activities of daily living; ECOG-PS, Eastern Cooperative Oncology Group-Performance Status; MMSE, Mini-Mental State Examination; QLQC30, Quality of Life Questionnaire; TGUG, Timed Get-Up-and-Go test; BMI, body mass index; MNA, Mini-Nutritional Assessment; GDS, Geriatric Depression Scale; CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale for Geriatrics.

Table 3 Ongoing randomized controlled trials of geriatric interventions in older patients with solid malignancies registered with the US National Institutes of Health

Clinical trial identifier Sponsor/country	Study title
NCT01321658 Oslo University Hospital, Norway	Geriatric intervention in frail elderly patients with colorectal cancer
NCT02054741 University of Rochester, MN, USA	Geriatric assessment intervention in reducing chemotherapy toxicity in older patients with advanced cancer
NCT01915056 University of Rochester, MN, USA	A geriatric assessment intervention for older cancer patients receiving chemotherapy
NCT01416168 H Lee Moffitt Cancer Center and Research Institute, FL, USA	Pilot study of a geriatric intervention after colorectal and lung cancer surgery
NCT02025062 Assistance Publique Hôpitaux de Paris, France	Comprehensive geriatric assessment and head and neck elderly cancer patients: Protocol for a Multicentre Randomized Controlled Trial (EGeSOR)
NCT02000011 Assistance Publique Hôpitaux de Marseille, France	Interest of a geriatric intervention plan associated to a comprehensive geriatric assessment on autonomy, quality of life and survival of patients aged 70 years old and more surgically treated for a resectable cancer (thoracic, digestive, or urologic). Randomized multicenter study (EPIGAC)
NCT01329107 University of Aarhus, Denmark	Multimodal Rehabilitation Program to Bladder Cancer patients (MRPBC)

comorbidities was associated with mortality independently from cancer parameters. Finally, each CGA domain was associated with chemotoxicity and survival in at least one study. The domains most often reported as predicting mortality and chemotoxicity were functional impairment, malnutrition, and comorbidities.

CGA-based individually tailored coordinated care plans

An important aim in conducting a CGA is to develop and implement individually tailored geriatric interventions. Few studies have described the interventions carried out based on CGA results in older patients with cancer. In one study, a geriatrician performed a CGA, then suggested multidisciplinary interventions based on the results in 375 patients referred to a geriatric oncology unit.[29] The interventions involved social support for 172 (46%) patients, physiotherapy for 157 (41%), changes in current chronic medications for 115 (31%), nutritional care for 262 (70%), a memory evaluation for 79 (21%), and psychologic care for 135 (36%). Similar findings were obtained in a study[30] of 161 patients, among whom 122 (76%) received CGA-based interventions, including nutritional care (43%), treatment of depression (19%), a memory evaluation (18%), changes in chronic medications (37%), and/or social support (20%). In a recent large cohort study[16] of 1,967 patients, the results of CGA led to intervention plans targeting all CGA domains in 25% of patients.

Very few randomized trials have assessed the potential effect on patient outcomes of CGA-based management and follow-up of health problems in older cancer patients (Figure 3). Two randomized trials in older post-surgical cancer patients showed significant survival gains with home care by advanced practice nurses[53] or improved appropriateness of treatment strategies with nurse case management.[54] A secondary subset analysis of data from a randomized 2×2 factorial trial comparing care in a geriatric inpatient unit, geriatric outpatient clinic, both, and neither in frail older cancer inpatients showed that inpatient geriatric assessment and management significantly improved quality of life but not 1-year survival.[55] In a recent randomized trial in older patients undergoing elective surgery for solid cancer, an individualized geriatric intervention plan based on patient-related risk factors for delirium failed to decrease the occurrence of postoperative delirium, other complications, or death.[56] We urgently need randomized controlled trials of patient outcomes after CGA-based geriatric interventions. The available data suggest that these trials will demonstrate significant improvements, thus helping to convince health authorities that geriatric oncology teams must receive strong support. Seven such trials are ongoing and are registered on clinicaltrials.gov (Table 3).

Conclusion

All CGA types detect numerous unrecognized health problems that may interfere with cancer treatment and/or compete with cancer as a cause of death. CGA results affected

treatment decisions in 21%–49% of patients in available studies. The results of 17 studies with large sample sizes and multivariate analyses indicate independent associations linking functional impairment, malnutrition, depressive symptoms, and comorbidities to chemotoxicity and/or overall survival. Only three randomized trials of the effectiveness of CGA-based interventions have been published. Further research to produce high-level evidence about the effects of CGA on patient outcomes are needed.

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