GERIATRIC PRINCIPLES FOR PATIENTS WITH CANCER

Princípios geriátricos para pacientes com câncer

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ABSTRACT

Cancer is primarily a disease of older persons. Given the heterogeneity of aging, physiological age, rather than chronological age, better expresses the cumulative effect of environmental, medical, and psychosocial stressors, which modifies life expectancy. Comprehensive geriatric assessment, a tool that helps ascertain the physiological age of older individuals, is the gold standard for assessing older adults with cancer. Several international organizations recommend using the geriatric assessment domains to identify unrecognized health problems that can interfere with treatment and predict adverse health-related outcomes, aiding complex treatment decision making. More recently, it has been shown that geriatric assessment-guided interventions improve quality of life and mitigate treatment toxicity without compromising survival. In this review, we discuss the role of comprehensive geriatric assessment in cancer care for older adults and provide the reader with useful information to assess potential treatment risks and benefits, anticipate complications, and plan interventions to better care for older people with cancer.

KEYWORDS: neoplasms; aged; geriatric assessment.

RESUMO

O câncer é principalmente uma doença de pessoas idosas. Diante da heterogeneidade do envelhecimento, a idade fisiológica expressa, melhor do que a idade cronológica, o efeito cumulativo dos estressores ambientais, médicos e psicossociais que modificam a expectativa de vida. A avaliação geriátrica ampla é uma ferramenta que ajuda a determinar a idade fisiológica de um indivíduo idoso e o padrão ouro para avaliar idosos com câncer. Diversas organizações internacionais recomendam considerar os domínios da avaliação geriátrica a fim de identificar problemas de saúde não reconhecidos capazes de interferir no tratamento, e prever resultados adversos relacionados à saúde, auxiliando na complexa tomada de decisão do tratamento. Mais recentemente, intervenções direcionadas com base na avaliação geriátrica também demonstraram melhorar a qualidade de vida e mitigar a toxicidade do tratamento, sem comprometer a sobrevida. Nesta revisão discutimos o papel da avaliação geriátrica ampla no tratamento do câncer para idosos e fornecemos ao leitor informações úteis para avaliar os riscos e benefícios potenciais do tratamento, antecipar complicações e intervir para melhor cuidar dos idosos com câncer.

PALAVRAS-CHAVE: neoplasias; idoso; avaliação geriátrica.

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INTRODUCTION

Cancer is primarily a disease of older persons; by 2035, the estimated annual number of new cancer cases in older individuals is expected to increase to 13.7 million.¹ Given the heterogeneity of aging,² chronological age does not always reflect “physiological” age. Whereas chronological age is based on time, physiological age expresses the cumulative effect of environmental, medical, and psychosocial stressors, which modify life expectancy.¹

Comprehensive geriatric assessment (CGA) is a tool that helps ascertain the physiological age of an older adult.³ CGA is a multidisciplinary evaluation of geriatric syndromes and medical, cognitive, psychosocial, functional, and nutritional domains that detects impairments not identified by routine examination and predicts severe treatment-related toxicity,⁴ early treatment interruption, functional decline,⁵ and overall survival (OS).⁶ Although CGA is the gold standard for assessing older adults with cancer,⁷ a lack of expertise in some practice settings limits its application. In such settings, geriatric oncology screening tools may help identify patients in need of a multidisciplinary approach.⁸

The identification of each patient’s vulnerabilities influences the therapeutic approach by limiting treatment in vulnerable patients and preventing undertreatment in those who are fit.⁹ Furthermore, targeted interventions may improve treatment tolerance and completion,¹⁰ as well as other outcomes such as physical function and quality of life (QoL).¹¹

The aim of this review is to summarize the available evidence about CGA and other tools in the evaluation and management of older adults with cancer. Cited articles were retrieved from various libraries and search engines, including EMBASE, Google Scholar, PubMed, Science Direct, and Scopus. Using free-text term searches, the search syntax was adapted for different databases. The articles included in each section were selected according to the authors’ discretion.

WHAT IS THE USEFULNESS OF CGA FOR OLDER ADULTS WITH CANCER?

The American Society of Clinical Oncology recommends evaluating functional status, physical performance, falls, comorbidities, cognitive performance, social networks, and nutritional and mental status (all part of CGA) in all older adults diagnosed with cancer to identify unrecognized health problems that could interfere with treatment.^{12,13}

Using CGA, patients can be classified according to vulnerability to determine treatment strategy, as well as to predict OS, treatment-related toxicity, treatment discontinuation, and/or unplanned hospitalizations.¹⁴⁻¹⁸ Additionally, CGA has

been associated with improved pain control, mental health, well-being, and patient satisfaction with patient-physician communication.¹⁹

WHICH PATIENTS SHOULD UNDERGO CGA?

Screening tools

Tools traditionally used to assess functional status in oncology, such as the Karnofsky Performance Score and the Eastern Cooperative Oncology Group performance status, are not appropriate for evaluating physiological age. In scenarios where CGA is not feasible, the guidelines recommend using screening tools for all older adults with cancer. Although screening tools do not replace CGA, they have the advantage of being quick, easy to apply tests that can properly identify patients who could benefit from full CGA before starting treatment. Several tools have been developed, and while expert panels do not endorse one over another, the most common are the G8 and the Vulnerable Elders Survey-13.^{7,20}

Domains to be assessed in older adults with cancer

Functional status

In patients with cancer, functional status is classically assessed through subjective scales, such as the Eastern Cooperative Oncology Group performance status or the Karnofsky Performance Score. However, these scales tend to overestimate functional status in older adults, and assessments such as the Katz index and the Barthel scale for activities of daily living (ADL), and the Lawton scale for instrumental activities of daily living (IADL) are frequently used to gather additional information.¹² Current American Society of Clinical Oncology guidelines for geriatric oncology recommended assessing IADL function,¹² although ADL are also an essential part of CGA. Briefly, ADL include self-care activities such as bathing or toileting, while IADL are tasks required for independent living in the community. Both ADL and IADL are correlates of various health-related outcomes in older adults with cancer. For instance, both are associated with OS; in addition, ADL performance is associated with changes in treatment decisions^{21,22} and major postoperative complications,²³⁻²⁵ while IADL performance is predictive of early treatment discontinuation²⁶ and postoperative delirium.²⁷

Furthermore, some IADL are included in tools designed to estimate chemotherapy toxicity risk in older adults, such as the Cancer and Aging Research Group calculator (CARG)¹⁸

and the Chemotherapy Risk Assessment Scale for High-Age Patients score (CRASH).⁴

Rehabilitation services could be essential for improving ADL performance in older adults.²⁸ It has been demonstrated that exercise programs improve functional status in men with prostate cancer during radiation therapy and androgen deprivation therapy.²⁹ Moreover, some studies have shown that physical function improves in older patients undergoing prehabilitation³⁰ compared to usual care before surgery, although the impact of prehabilitation on postoperative clinical outcomes is still unclear.³¹

Objectivized physical performance

Various objective physical performance tests, including gait speed, the Timed Up and Go test and the Short Physical Performance Battery, have proven helpful in treatment decision-making in older adults with cancer (treatment regimen and aggressiveness, safety surveillance, and physical rehabilitation prior to treatment).³² In older adults with nonmetastatic cancer, faster gait speed has been associated with improved OS and lower 2-year progression to disability.

Falls

Between 28–35% of people aged >65 years fall every year,³³ and 20–30% of these falls lead to serious injuries that can negatively impact functional status.³⁴ Besides age- and comorbidity-related changes that predispose older adults to falling, such as functional and cognitive impairment,^{35,36} older patients with cancer show additional risk factors, including chemotherapy-induced sensory impairment, brain metastases,³⁷ and cancer-related pain.³⁸ Moreover, these patients have a higher prevalence of osteoporosis and malnutrition, leading to a 3-fold increase in fracture risk.³⁹ Falling is also a risk factor for severe chemotherapy toxicity in older people with cancer.¹⁸

Since falls are multifactorial in origin, CGA and the ensuing interventions, including ophthalmologic evaluation, occupational therapy, physical therapy, home safety, and medication evaluation, should be used to minimize the risk of falling.^{40,41}

Nutrition

Malnutrition and weight loss are frequent in older patients with cancer and can increase the risk of complications and impact health-related outcomes, such as treatment response and tolerance, QoL, and mortality.¹ Risk factors for malnutrition include poor appetite, difficulty chewing or swallowing, limited access to food,⁴² and tumor-associated changes such as malabsorption, obstruction, diarrhea, and vomiting, which lead to anorexia and impaired metabolism.⁴³ Systematic

screening using validated tools, such as the Mini Nutritional Assessment, body mass index, and % of unintentional weight loss in the past 6 months, should always be performed initially and during follow-up visits to determine interventions aimed at preventing nutritional deficiencies, maintaining healthy weight, and avoiding complications.^{1,42,43} It should be pointed out that clinicians consider nutritional status one of the most relevant factors when modifying oncological treatment,²² probably due to its predictive power (eg, the Mini Nutritional Assessment) for non-hematological toxicity among older adults receiving chemotherapy.⁴

The concept of comorbidity and competing comorbidity

Comorbidities, defined as medical conditions that exist along with an index condition, become more frequent with age. In older adults, they can interfere with cancer progression, affect survival and modify the risks and benefits of cancer treatments. This concept is known as “competing risk”.

To assess competing risks, the patient’s age, performance, and functional and comorbid status must be considered, and these factors must be weighed against tumor characteristics. Incorporating competitive risks aids complex decision-making and decreases the risk of overtreating patients who have significant competing risks and of undertreating patients who have tolerable competing risks.

The Charlson Comorbidity Index,⁴⁴ the Cumulative Illness Rating Scale-Geriatrics⁴⁵ and the Index of Co-Existing Diseases are some validated comorbidity indices.

Polypharmacy

Polypharmacy is a well-established problem in older adults with cancer.^{46–48} Although the term lacks a universal definition, the most prevalent is intake of ≥ 5 medications per day.⁴⁹ Depending on the definition used, the prevalence can be $\geq 80\%$ in older adults with cancer and reach a mean of 9.1 medications, most of which are for comorbidities.^{47,48,50–53}

Polypharmacy is associated with an increased risk of adverse events, drug-drug interactions, geriatric syndromes, and nonadherence.⁵⁴ Additionally, in patients with cancer, it is related to greater functional decline, increased treatment toxicity, and higher mortality.^{46,55,56} Therefore, medication reconciliation should be an essential part of CGA, with an emphasis on prescribing suitable drugs for the patient’s goals and life expectancy.^{47,48}

Multiple tools, such as the AGS Beers Criteria, have been developed to avoid prescribing potentially inappropriate drugs, improve selection, and reduce adverse events.^{57,58} Although useful in patients with cancer, these criteria have not been validated for individuals receiving palliative care.^{57,58}

Sensory impairment

Visual and hearing impairments are common among older adults.⁵⁹⁻⁶¹ In patients with solid tumors who are beginning a new chemotherapy regimen, 36% reported hearing or visual impairment, and 7% reported both.⁶² Additionally, older cancer survivors are at higher risk of these impairments.⁶³

Visual and hearing impairments have been associated with mobility restrictions, ADL and IADL disability, cognitive impairment, social isolation, depression, anxiety, and mortality.^{60,62,64-68}

Self-reported hearing impairment has also been linked to an increased risk of chemotherapy-related toxicity.¹⁸ Furthermore, mild visual impairment is associated with inadequate performance in self-care activities. Community-dwelling older adults with normal vision have better performance in self-care tasks and fewer errors complying with multi-drug regimens.⁶⁹

Structured assessment and correction of sensory impairments might reduce disability, thus improving QoL and therapeutic outcomes.^{63,70}

Cognition

Since the risk of minor and major cognitive disorders increases with age, a formal cognitive assessment, including patient observation, accounts from caregivers, and cognitive screening tests, should be performed in older patients with cancer.¹ Cognitive impairment may impact the patient's decision-making ability, especially in complex circumstances such as those expected in cancer treatment planning, and could increase the risk of adverse events and chemotherapy toxicity due to a decreased understanding of treatment instructions.

Furthermore, aging is associated with biological changes⁷¹ which are exacerbated by cancer⁷² and its treatment,⁷³ such as DNA damage, oxidative stress, inflammation, and decreased telomere length.⁷⁴ These mechanisms, together with cancer-related psychological distress⁷⁵ and fatigue,⁷⁶ may lead to cognitive decline.⁷⁷ Most frequently, a neuropsychological frontal-subcortical profile has been demonstrated in patients with cancer/chemotherapy-related cognitive impairment,⁷⁸ which affects a number of domains, including executive function, learning and memory, verbal function, and language skills.⁷⁹

Cognitive screening tests such as the Montreal Cognitive Assessment,⁸⁰ the clock drawing test, the MiniCog,⁸¹ or the Mini-Mental State Examination⁸² are useful for identifying patients who would benefit from further neuropsychological testing.⁸³

Detecting cognitive impairments can help identify individuals with difficulty following medical advice, those needing help with daily activities,⁸⁴ and those needing further assessment of decision-making capacity.⁸⁵

Mood disorders

The most common psychological issues among older adults with cancer are depression, distress, and anxiety, which can lead to impaired QoL and functional decline.^{1,42} Compared with younger patients, older adults with cancer frequently present with unspecific clinical features that can mask the symptoms of depression. For example, sadness is less often expressed,^{86,87} and somatic symptoms, such as asthenia, sleep disturbances, and weight loss, can easily be confused with cancer-related symptoms or treatment toxicity, leading to underdiagnosis.⁸⁸ Although anxiety is less prevalent in older adults than in their younger counterparts, as many as 20% of older people with cancer show significant anxiety.⁸⁹ Therefore, the systematic use of validated screening tools, such as the Geriatric Depression Scale, the Hospital Anxiety and Depression Scale, or the Distress Thermometer is recommended.^{42,86,90} Psychological state affects cancer therapy, since older patients with depression tend to receive less definitive cancer treatment and have worse OS.

The concept of frailty in geriatric oncology

Frailty is a complex, multidimensional, and reversible state of diminished physiologic reserve that results in decreased resilience and adaptive capacity, and increased vulnerability to stressors.⁹¹ Although several working definitions of frailty are available, none is universally accepted. There are over 70 different tools for measuring frailty, although only a few have been validated. They differ in extent, intended purpose (eg, screening tools, risk-stratification tools, and formal assessment for guiding treatment) and scope (multidimensional vs. risk-stratification), and might have overlapping features.

One of these definitions, phenotypic frailty, focuses on five criteria (weight loss, strength, gait speed, exhaustion, and activity) and has been used as a risk stratification tool for postoperative complications;⁹²⁻⁹⁴ whereas the frailty index,⁹⁵ based on a cumulative deficit model, has also been used as a postoperative complication risk stratification tool.⁹⁶⁻¹⁰⁰

Perhaps the most frequently used tool for defining frailty in geriatric oncology is CGA itself. By using principles similar to the cumulative deficit model, a given number of affected domains (usually ≥ 3) is used to define frailty. The CGA-based definition of frailty has been associated with poor postoperative outcomes,^{94,101,102} worse OS, and severe chemotherapy-related toxicity,¹⁰³⁻¹⁰⁵ etc.

The CGA-based definition of frailty can guide therapy decisions for older patients with different types of cancer.

The Elderly Selection on Geriatric Index Assessment was a randomized clinical trial of older adults with advanced non-small cell lung cancer who were assigned to CGA-tailored treatment vs. standard care.¹⁰⁶ Patients whose treatment was determined by CGA results experienced less chemotherapy toxicity and had less toxicity-associated treatment failure (without compromising OS) than those whose treatment was selected through standard care.

Social and financial networks

Evaluating social and financial domains is an essential part of CGA. In the Nurses' Health Study, patients diagnosed with breast cancer who were socially isolated had a 66% increased risk of all-cause mortality, and a two-fold increased risk of mortality from breast cancer compared

with women with better social support.¹⁰⁷ Since there is no universally accepted definition of a proper socioeconomic support network or consensus about how to approach this domain,¹⁰⁸ several different strategies have been proposed, including subjective and objective measures based on the number of relatives, patient perception, availability of a caregiver, financial resources, living conditions, and/or marital status.^{42,109} In any case, the involvement of a social or financial worker should always be considered. Table 1 summarizes some of the tools available for CGA in older adults with cancer.

Patient's preferences and advance directives

Current medical laws and ethics value and protect autonomy and individuality. Thus, it is essential to inquire about

Table 1. Frequently used tools in the comprehensive geriatric assessment of older patients with cancer.

Selected tools	Tool Characteristics	Proposed cut-off points
Comorbidities		
Charlson Comorbidity Index ⁴⁴	Assesses 19 conditions, weighted 1 to 6 <ul style="list-style-type: none"> • Scores ≥ 1: associated with mortality¹¹⁰ • Scores ≥ 2: associated with early chemotherapy discontinuation¹¹¹ 	Weighted comorbidity classes <ul style="list-style-type: none"> • 0 = low • 1–2 = medium • 3–4 = high • ≥ 5 = very high
Cumulative Illness Rating Scale-Geriatrics ⁴⁵	<ul style="list-style-type: none"> • Assesses 14 organ system categories • Each rated 0–4, weighted by the physician's judgment • Includes some geriatric syndromes 	<ul style="list-style-type: none"> • No specific cut-off established • Higher scores indicate more comorbidities
Polypharmacy		
	Total number of medications (prescription, over the counter, supplements, etc.)	<ul style="list-style-type: none"> • Variable • Generally ranges from 5–10¹¹²
Functional status		
Activities of daily living	<ul style="list-style-type: none"> • Self-care activities such as bathing, dressing, grooming, toileting, continence, and feeding • Included in the abbreviated CGA 	<ul style="list-style-type: none"> • Katz index ≤ 5 indicates disability • Barthel index ≤ 95 indicates disability
Instrumental activities of daily living	<ul style="list-style-type: none"> • Abilities needed to live in the community (shopping, transportation, using the telephone, financial calculation, managing medications, doing housework, and cooking) • Included in the abbreviated CGA and in the CRASH tool 	<ul style="list-style-type: none"> • Lawton index (8-item version) < 8 indicates disability
Objectivized physical performance		
Timed Up and Go	Assesses sitting balance, transfers, gait characteristics, ability to turn and lower extremity strength	<ul style="list-style-type: none"> • ≥ 10 seconds associated with grade 3–5 chemotherapy toxicity • ≥ 12 seconds associated with overall survival • ≥ 20 seconds associated with overall survival, major postoperative complications and functional decline during chemotherapy¹¹³
Short Physical Performance Battery	Assesses standing balance, 4-meter gait speed, balance, and lower extremity strength (ability)	<ul style="list-style-type: none"> • < 12 is associated with adverse drug reactions and mortality (12 months) • < 10 is associated with major postoperative complications, functional decline, discharge to rehabilitation facility • < 9 is associated with overall survival¹¹³

Continue...

Table 1. Continuation.

Selected tools	Tool Characteristics	Proposed cut-off points
Falls		
	<ul style="list-style-type: none"> Self-report during the previous 6 or 12 months This domain is included in the CARG tool 	<ul style="list-style-type: none"> ≥ 1 is associated with the risk of chemotherapy toxicity
Nutritional Status		
Body mass index	Body mass divided by height squared	$< 20 \text{ kg/m}^2$ – high sensitivity for diagnosing severe malnutrition in older patients with cancer ¹¹⁴
% of unintentional weight loss in the previous 6 months	Self-reported or obtained from medical records	$> 5\%$ of usual body weight over 6 to 12 months
Mini-Nutritional Assessment (MNA) and its short form (MNA SF) ¹¹⁵⁻¹¹⁷	<ul style="list-style-type: none"> Easy to administer Does not require a trained dietitian 	<ul style="list-style-type: none"> MNA: Malnutrition < 17, malnutrition risk 17–23.5 MNA SF: Malnutrition < 8, malnutrition risk 8–11
Cognition		
Mini Mental State Examination (MMSE) ⁸²	<ul style="list-style-type: none"> Assesses temporal and spatial orientation, memory encoding and recall, attention/concentration, language and visuospatial function Included in the CRASH tool 	<ul style="list-style-type: none"> Different cutoff points have been used ≤ 23 commonly regarded as abnormal
Montreal Cognitive Assessment ¹¹⁸	<ul style="list-style-type: none"> Assesses delayed word recall, visuospatial/executive function, language, attention/concentration, and orientation Designed to detect mild cognitive impairment Less data on older patients with cancer than MMSE¹¹⁹ 	<ul style="list-style-type: none"> $\leq 25/30$ $\leq 24/30$ for patients with ≤ 12 years of formal education
Mini-Cog ⁸¹	<ul style="list-style-type: none"> Rapid assessment tool Free recall and a version of the clock drawing test Good sensitivity and low specificity for dementia Performs less well for minor neurocognitive disorder 	Impaired if patients are unable to recall any of the words or if they recall only 1-2 words and have an abnormal clock drawing test
Mood disorders		
Geriatric Depression Scale-15 ¹²⁰	<ul style="list-style-type: none"> Self-report screening instrument Validated in multiple settings 	<ul style="list-style-type: none"> Diverse cut off points exist Most popular > 5
Patient Health Questionnaire-9 ¹²¹	<ul style="list-style-type: none"> Screens depression Developed for primary care settings Useful to assess response to treatment¹²² 	<ul style="list-style-type: none"> 5 to 9: mild 10 to 14: moderate 15 to 19: moderately severe ≥ 20: severe
Hospital Anxiety and Depression Scale (HADS) ¹²³	<ul style="list-style-type: none"> Screening in non-psychiatric settings Self-report questionnaire Consists of two subscales (HADS-A and HADS-D) 	In patients with cancer: > 9 units for the HADS-A, > 7 units for the HADS-D
Distress thermometer	<ul style="list-style-type: none"> 10-point Likert scale resembling a thermometer 0 (no distress) to 10 (extreme distress) Self-report over the past week 	Further screening if ≥ 4 ^{124,125} or ≥ 3 during the first month of a new cancer diagnosis
Social support		
Medical outcomes study social support survey ¹²⁶	<ul style="list-style-type: none"> 19 items, self-administered Includes 4 subscales (emotional/informational support, tangible support, affectionate support, positive social interaction) 	Two ways to calculate scale and index scores: averaging non-missing items and transforming the resulting scores to 0–100 scales

CARG: Cancer and Aging Research Group calculator; CGA: comprehensive geriatric assessment; CRASH: Chemotherapy Risk Assessment Scale for High-Age Patients score

patient preferences regarding medical decision-making, including their desired degree of involvement.¹²⁷⁻¹²⁹ In order to better individualize treatment, the physician must know the amount and type of information patients desire. Several situational factors can modify patient preferences over time, including disease severity, time since diagnosis, and type of decision.^{127,130,131} Importantly, both the amount of information received about treatment consequences and the probability of various outcomes can influence the patient's final decision. Since some decisions involve a great deal of information, it follows that patients will not come to an immediate conclusion.^{132,133}

Preferences, beliefs, and desires concerning end-of-life care should also be considered. Even among patients with poor cognitive function, this information could be obtained by giving hypothetical situations as examples and asking patients about their priorities.^{134,135}

Specific assessment tools and additional evaluation

Life expectancy estimation

Appraising life expectancy is an essential part of shared decision-making, and failure to take into account overall life expectancy may lead to under- or overtreatment.¹³⁶ For cancer treatment decision-making, estimated life expectancy should be weighed against the risk of relapse and death during the projected time period. Several tools for predicting life expectancy are available online at the e-Prognosis website. It should be pointed out that although these tools are useful for day-to-day clinical activity, they are non-disease-specific prognostic indices, and most of them were developed and validated for older people living in high-income countries.

Estimating treatment benefits

When offering potentially curative treatment to older adults with cancer, it is paramount to assess the risk of cancer-related mortality against other potential causes of death to better understand the possible benefits. Several tumor-specific prediction tools are available, including Adjuvant! Online¹³⁷ and PREDICT¹³⁸ for breast cancer, Adjuvant! Online¹³⁹ and Numeracy!¹⁴⁰ for colon cancer, and the MSKCC pre-radical prostatectomy nomogram¹⁴¹ and the Roswell Park Prostate cancer calculator for prostate cancer.¹⁴²

Cancer treatment toxicity risk assessment

Since older cancer patients on chemotherapy are at higher risk of treatment toxicity than their younger counterparts,¹⁴³ various models for predicting toxicity in this

population have been developed. Two of the most widely used models, the CARG and the CRASH tools, will be briefly discussed here. Both provide clinicians with additional information often useful in the decision-making process and both are available online.

The CRASH⁴ model was validated in a sample of 518 older adults with hematological and solid tumors. CRASH can predict the risk of grade 4 hematological toxicity and grade 3-4 non-hematological toxicity. It considers the specific chemotherapy regimen, blood pressure, IADL, lactic dehydrogenase levels, the Eastern Cooperative Oncology Group performance status, and the Mini-Mental State Examination and Mini Nutritional Assessment results.

On the other hand, the CARG model¹⁸ was validated in a population of 500 older adults with solid tumors, and it can predict the risk of grade 3-5 chemotherapy-related toxicity. The CARG model considers clinical, CGA, cancer, and treatment-associated variables to classify patients into low, intermediate, and high toxicity risk groups. The CARG tool outperforms the clinician-assessed Karnofsky Performance Score at predicting toxicity. Ongoing studies are modifying the CARG tool for specific tumors.

Postoperative complications risk assessment

Several CGA domains are useful for assessing surgical risk in older adults with cancer. The Preoperative Assessment of Cancer in the Elderly, a tool consisting of individual assessments of fatigue, performance status, and functional status, predicts the risk of mortality, postoperative complications, and length of hospital stay in patients undergoing elective cancer surgery.¹⁴⁴ Another example is the modified frailty index,¹⁴⁵ which was originally developed in a population of patients undergoing colectomy for various reasons. It is based on the cumulative deficit model and is calculated as the proportion of the following 11 items present in the patient's medical history: non-independent functional status, history of diabetes mellitus, history of chronic obstructive pulmonary disease or pneumonia, history of congestive heart failure, history of myocardial infarction, history of percutaneous coronary intervention, cardiac surgery or angina, hypertension requiring the use of medications, peripheral vascular disease or rest pain, impaired sensorium, transient ischemic attack or cerebrovascular accident without residual deficit, and cerebrovascular accident with a residual deficit. A higher modified frailty index is associated with a higher risk of complications that require intensive care unit care or result in death in older patients with cancer. Table 2 outlines some of the geriatric oncology resources available online.

Immunotherapy in older adults with cancer

Immunotherapy has improved many types of cancer treatment. Clinical trials have shown that in older adults immunotherapy has reasonable toxicity and adequate efficacy compared to cytotoxic agents, including no differences in OS. Although current guidelines do not recommend against using immunotherapy in older patients, it should be pointed out that most immunotherapy studies do not include subanalyses by age group and vastly underrepresent patients aged ≥ 75 years. Since aging causes complex changes in the immune system, studies focusing on the efficacy and safety of immunotherapy in older adults are needed to reach sound conclusions. Patients using immunotherapy should be monitored closely, and a high level of suspicion for adverse effects is required. The most commonly affected sites are the skin and the digestive, endocrine, musculoskeletal, renal, nervous, hematologic, and ocular systems.

Table 2. Online resources for geriatric oncology.

ePrognosis Life expectancy calculators for older people in various settings http://eprognosis.ucsf.edu
WHO Global Health Observatory Life tables for 194 countries http://www.who.int/gho/mortality_burden_disease/life_tables/life_tables/en/
ConsultGeri Website of the Hartford Institute for Geriatric Nurses Several geriatric assessment tools are available in this site https://consultgeri.org/
Cancer and Aging Research Group (CARG) geriatric assessment tools Contains the CARG geriatric assessment tool and the CARG chemotherapy toxicity calculator http://www.mycarg.org/tools
Senior Adult Oncology Program Tools, Moffitt Cancer Center Contains several geriatric assessment tools and the Chemotherapy Risk Assessment Scale for High-Age Patients score calculator http://moffitt.org/for-healthcare-providers/clinical-programs-and-services/senior-adult-oncology-program/senior-adult-oncology-program-tools/
International Society of Geriatric Oncology Contains geriatric oncology guidelines, publications and selected geriatric assessment tools http://www.siog.org/
National Cancer Comprehensive Network (NCCN) Guidelines section Contains diverse guidelines for supportive care including survivorship https://www.nccn.org/professionals/physician_gls/default.aspx#survivorship

Radiation therapy in older adults with cancer

Radiation therapy is a key part of treatment in older adults, especially when surgery or chemotherapy represent a greater risk. Although there is only limited evidence from clinical trials regarding radiotherapy toxicity in older adults, it appears to be well tolerated, and novel radiotherapy techniques, such as hypofractionation, brachytherapy, and stereotactic techniques, may be more suited for older patients.

Current guidelines recommend considering four age-related factors before starting radiotherapy:

- **Loco-regional tumor behavior:** certain tumors are more indolent or aggressive depending on age. These variations affect the treatment benefit;
- **Competing risks:** the patient's projected life expectancy can affect the overall gain from radiotherapy and the relevance of long-term radiation toxicity. Radiotherapy could also worsen underlying comorbidities;
- **Functional reserve assessment:** it is crucial to determine the patient's ability to complete the duration and dose of the treatment (usually several weeks) and to anticipate the need for supportive care to manage toxicity;
- **Treatment goal:** curative or palliative radiation treatment.^{146,147}

Geriatric interventions and cancer-specific outcomes

While a large amount of data support the use of CGA to identify geriatric syndromes and predict mortality and chemotherapy toxicity, little evidence has been compiled regarding its effects on cancer-specific outcomes, such as survival or QoL.⁵⁹ However, at least three recent randomized clinical trials have shown that CGA-guided interventions may improve QoL and mitigate treatment toxicity without compromising survival¹⁴⁸⁻¹⁵⁰ (Table 3).

The GAP-70 trial allocated patients to CGA-guided intervention or usual oncologist-directed care.¹⁴⁸ A set of CGA-guided recommendations were provided to oncologists in practices randomized to the intervention arm. There was a 20% absolute reduction in severe toxicity in the intervention arm compared to usual care (50 vs. 71%), which may have been due to the fact that intervention patients were more likely to receive a reduced dose of chemotherapy in cycle 1 (49 vs. 35%). Despite the dose reductions, similar 6-month survival was observed between the arms, which indicates that the CGA intervention reduced toxicity without decreasing survival.

The Australian INTEGERATE trial allocated patients with cancer aged ≥ 70 years to integrated geriatric oncology

Table 3. Randomized trials exploring cancer specific outcomes of geriatric interventions.

Reference	Intervention	Design	Patients	Outcomes
GAP-70 ¹⁴⁸	CGA-based recommendations for treating oncologists	Cluster RCT conducted across 41 practices in the USA	<ul style="list-style-type: none"> • Age > 70 • > 1 impaired GA domain • Incurable solid tumors or lymphoma • Starting new treatment 	<ul style="list-style-type: none"> • 21% decrease in severe chemotherapy toxicity • No effect on 6-month survival
INTEGRATE ¹⁴⁹	Co-management by a geriatrician during oncological treatment.	RCT conducted at three Australian hospitals	<ul style="list-style-type: none"> • Age ≥ 70 • Solid tumors and lymphoma • Candidates for systemic therapy 	<ul style="list-style-type: none"> • Improved quality of life at 6 months • 41% fewer hospitalizations
GAIN ¹⁵⁰	Multidisciplinary CGA-based interventions	RCT conducted at single academic center in the USA	<ul style="list-style-type: none"> • Age ≥ 65 • Any functional status • Solid tumors • All stages • Starting chemotherapy 	<ul style="list-style-type: none"> • 10% decrease in grade 3–5 chemotherapy toxicity • 14% increase in advance directive completion

CGA: comprehensive geriatric assessment; RCT: randomized clinical trial.

care or usual care.¹⁴⁹ Patients underwent CGA followed by standardized interventions, while patients in the control arm were managed by their treating oncologist alone. At 24 weeks of follow-up, patients receiving integrated care had better QoL scores, significantly lower healthcare utilization, and fewer unplanned hospitalizations.

The GAIN trial randomized patients aged ≥ 65 years with solid tumors who were beginning chemotherapy to a multidisciplinary geriatric intervention or usual care.¹⁵⁰ There was a significant reduction of grade 3–5 chemotherapy toxicity among patients randomized to the CGA intervention compared to usual care (50 vs. 60%). Additionally, patients randomized to the intervention were more likely to complete advance directives (70 vs. 59%).

These studies show that geriatric interventions may improve oncological outcomes for older adults with cancer in different settings.⁷ Importantly, while patients who were co-managed with CGA were less likely to get full-dose chemotherapy, this did not result in reduced survival in the GAP-70 trial.¹⁴⁸ That being said, it is still necessary to determine which components of the interventions had the greatest effect on outcomes, and the results of full trials are eagerly awaited. Furthermore, systemic barriers to the implementation of geriatric interventions in cancer care must be overcome, and implementation research is a necessary step toward making geriatric oncology accessible to everyone worldwide.^{151–153}

CONCLUSIONS

Cancer is primarily a disease of older persons. Given the heterogeneity that characterizes aging, chronological age does not always imply physiological age. CGA can

help determine the physiological status of older patients. This comprehensive appraisal includes evaluation of geriatric syndromes and medical, cognitive, psychosocial, functional, and nutritional domains through a multidisciplinary perspective. In an attempt to improve outcomes, several medical societies currently recommend assessing most CGA domains in older patients with cancer to identify unrecognized health problems that might interfere with treatment.

As we have shown in this review, CGA can identify patients at risk of poorer outcomes, since it evaluates factors that affect treatment efficacy and outcomes. Furthermore, CGA-based geriatric interventions may improve oncological outcomes for older adults with cancer across different settings.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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AUTHORS' CONTRIBUTION

APNR: conceptualization, writing — original draft, writing — review & editing. KAM: writing — original draft. JG-C: writing — original draft. YJC: writing — original draft. ACTP: writing — original draft. DJCP: writing — original draft. JPN-N: writing — original draft, writing — review & editing. ESPC: writing — original draft, writing — review & editing.

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