

The Older Cancer Patient

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Introduction

Cancer is a common problem in the older adult population and the second leading cause of death for both men and women. More than half of cancers occur in adults over the age of 65 years. The biologic, psychological, and social aspects of the aging process must be considered for optimal screening, diagnosis, and treatment to occur in this population. The growing number of older adults facing a cancer diagnosis in conjunction with other acute and chronic conditions makes it imperative for primary care physicians, geriatricians, oncologists, surgeons, radiation oncologists, and virtually all specialists to consider the merits of geriatric assessment and treatment for optimal management. Of course cancer is not one disease but many. Rather than address even a short list of common cancers, this article focuses on aspects of the aging process that impact cancer development, progression, and treatment, along with principles that can be applied to the care of older patients who have cancer.

Principles of aging in the care of older adult patients who have cancer

Understanding what makes the older adult patient who has cancer different from the middle-aged patient who has cancer, apart from comorbid

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illness, which can be a burden in both groups, is an important place to start conceptualizing appropriate care for this group of individuals (Table 1).

Decreasing homeostatic reserve

Aging results in a steady decline in physiologic reserve capacity in most organ systems and dysregulation in others. These changes are related to the passage of time and are not the result of disease processes but do increase the vulnerability to disease. These changes generally are imperceptible at rest or in the individual's steady state but become apparent under stress of the system. Important changes that result in decreased reserve capacity include impaired glucose tolerance, decreased FEV₁ and FVC, decreased creatinine clearance and glomerular filtration rate, decreased muscle mass (sarcopenia), decreased bone mass, decreased brain blood flow and impaired autoregulation of blood flow, decreased dark adaptation of vision, decreased odor detection, and loss of high-frequency auditory tones, to name only a few. An example of decreased bone marrow reserve is evident in higher rates of neutropenia among older patients treated with full-dose chemotherapeutic regimens for non-Hodgkin lymphoma [1]. As aging advances the loss of reserve capacity progresses and becomes evident even in a steady state; this advanced stage of absent reserves and dysregulation is being defined as the syndrome of frailty.

Heterogeneity in aging

Despite these predictable age-related changes that decrease reserve capacity and increase the vulnerability of older adults to progressively

Table 1
Selected aspects of aging and their impact on older adults who have cancer

Aging process	Impact on older adult patient who has cancer
Decreasing homeostatic reserve	<ul style="list-style-type: none"> • Decreased ability to tolerate cancer treatment without adverse events or complications • Assessment is needed to measure functional reserves (eg, creatinine clearance, cognitive screening)
Heterogeneity	<ul style="list-style-type: none"> • Assessment parameters other than chronologic age will best characterize an individual patient's ability to undergo cancer-specific treatment with acceptable levels of toxicity, and quality of life (eg, comorbidities, functional status) • A particular patient may exhibit adequate reserves in some organ system and more limited reserves in others
Declining adaptability	<ul style="list-style-type: none"> • Prolonged recovery and rehabilitation • Increased sensitivity to drug effects
Altered pharmacokinetics	<ul style="list-style-type: none"> • Potential for poor drug absorption, higher peak concentrations, and prolonged half-life because of altered excretion
Altered pharmacodynamics	<ul style="list-style-type: none"> • Increased sensitivity to toxicity of drugs (eg, higher rates of neutropenia, higher rates of mucositis)

smaller and smaller stresses, there is an amazing degree of heterogeneity that is evident in the aging population. This heterogeneity is most evident when comparing older adults to one another but it is also evident in the variability of age-related changes within organ systems of a given individual. For example, in the Baltimore Longitudinal study glomerular filtration rate on average declined 1 mL/min/y. But as many as 30% of individuals experienced no decline, whereas others experienced a decline of up to 2 mL/min/y [2]. In addition to presumed genetic differences that influence aging rates, behavioral factors, such as diet and exercise, play an important role.

Slowing of the adaptive response

Older adults adapt more slowly to environmental stressors. Aging has been defined as a progressive loss of adaptability of an individual organism as time passes. This loss is compellingly demonstrated in the marathon records by age group published by the US Corporate Athletic Association [3]. By this listing men aged 30 to 34 currently hold the best time of 2:19:04; however, the record for men aged 65 to 99 is 3:26:38, more than an hour longer. Although it is great news that men of this age are capable of completing marathons at a pace that would outdo many younger marathon runners, clearly older men do not possess the same degree of adaptability in this sport. In a perhaps more immediately relevant example, a slower (less vigorous) adaptive response may explain in part the increased susceptibility with age of normal tissues to chemotherapy. Mucosa, hemopoietic cells, the heart, and the nervous system are more susceptible to chemotherapy. For example, in patients who have cancer of the colon age is an independent risk factor for the development of mucositis induced by fluorinated pyrimidines [4].

Alterations in pharmacokinetics and pharmacodynamics of antineoplastic therapy

Aging has a profound impact on the pharmacokinetics and pharmacodynamics of antineoplastic therapy [5]. Pharmacokinetics is what the body does to the drug in terms of absorption, distribution, metabolism, and excretion. With increasing age absorption may be reduced by decreased gastrointestinal motility, decreased secretion of gastric enzymes, and mucosal atrophy. Drug distribution is a function of body composition and the concentration of plasma proteins. In older adults body fat increases and water content decreases; this translates into a larger volume of distribution for fat-soluble drugs and reduced volume of distribution for water-soluble drugs, which lead to changes in peak concentration and alterations in half-life. Metabolism mainly occurs in the liver and is not affected strongly by aging processes but can be altered by surgical stress and illness [6,7]. Excretion is most affected by the gradual decline in glomerular filtration rate.

Pharmacodynamics refers to what the drug does to the body, primarily referring to alterations in sensitivity that may lead to adverse events. For example, the plasma concentration of midazolam at which 50% of patients will be nonresponsive to the stimulus of verbal command decreases steadily with patient age [8]. It is more difficult to study pharmacodynamics because of the confounding effects of pharmacokinetics, which may appear to increase sensitivity when in actuality drug levels are elevated above typical levels because of alterations in distribution, metabolism, or excretion.

The geriatrics adage, "start low, go slow," means start with a low dosage and advance the dosage slowly. This simple yet effective approach has become a mainstay for avoiding problems because of altered pharmacokinetics and pharmacodynamics. It may not be as applicable for cancer-specific treatment as it is for symptom-specific treatment, however, because lower dosages of chemotherapy may rob older adults of the benefits of desired treatment effects while minimizing toxicity.

Aging biology in the development of cancer

The biologic basis of cancer development is multidimensional. Disruption of genetic integrity is a cornerstone of this process. Alterations in the cellular environment also are important. These factors lead to the multistep process of cellular changes that result in neoplasia. The relationship between cancer biology and aging biology is beginning to unfold. The general increase in frequency of cancer with age makes the relationship between aging and cancer biology somewhat intuitive, but not all cancers increase in incidence with age. The incidence of breast, colon, and prostate cancers increase with age, whereas cervical cancer does not. The influence of aging on cancer biology remains uncertain. Some cancers appear more aggressive in advanced age, such as acute myelogenous leukemia, Hodgkin disease, and non-Hodgkin lymphoma, whereas other cancers, such as breast and prostate cancer, may become more indolent with advanced age. The linkage between aging and cancer biology may differ by cancer type and is influenced by environmental exposures and lifestyle choices. At a basic level aging provides the necessary time for chemical mutagens, radiation, and free radicals to promote genetic damage and aged cells may be more susceptible to these carcinogens. Cellular senescence is an important link between aging and cancer. This theory holds that nonmalignant cells have a finite replicative potential that is governed largely by telomere shortening. Telomeres, specialized regions of reiterative DNA at the ends of chromosomes, gradually shorten with successive replicative cycles. This shortening leads to the accumulation of senescent cells with age. Malignant cells overcome telomere shortening by upregulating production of telomerase [9]. Research regarding this linkage between aging and cancer is quickly accelerating our understanding of the interplay between cancer biology and aging biology, but other linkages

are coming to light also, such as decreased ability to repair DNA, oncogene activation or amplification, decreased tumor suppressor gene activity, microenvironment alterations, and decreased immune surveillance [10].

Comprehensive geriatric assessment for patients who have cancer

Because chronologic age is not an adequate indicator of response to cancer treatment and tolerance of toxicity, other factors need to be identified that characterize a “functional age,” assist in developing the most appropriate treatment plan, and further our understanding of what factors do influence outcomes. In the last 10 years there has been a growing recognition of the potential for comprehensive geriatric assessment (CGA) to improve the care of older adults who have cancer [11]. The International Society of Geriatric Oncology recommends the use of CGA in the evaluation of older patients who have cancer to detect unaddressed problems and improve functional status and, possibly, survival [12]. Components of the geriatric assessment are outlined in Table 2 along with screening tools, examples of detailed test components, and additional resources. CGA is “a multi disciplinary evaluation in which the multiple problems of older adults 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 to focus interventions on the person’s problems” [13].

Geriatric assessment has been studied in various settings that include specialized hospital units, hospital consultation services alone or with outpatient followup, clinic-based services, and in-home assessments. CGA has been shown to have positive effects on various health outcomes, such as prevention of disability progression, reduction of fall risk, rates of hospitalization, and nursing home admission. CGA is most effective when programs have control over implementation of recommendations and extended followup. Meta-analyses have suggested an impact on mortality [14,15], but more recent multi-institutional randomized controlled trials show no impact on mortality [16,17]. The results of studies of cost-effectiveness have been varied but generally favorable [17,18].

Specific trials of geriatric assessment outcomes in the oncologic setting are lacking. Some studies have suggested promise for the approach, however. One study using hospital inpatient geriatric care units for older adults who have cancer has shown improvements in psychologic status and pain management compared with usual care [19]. Another approach that has been implemented successfully has been to use primarily self-report components [20,21]. A pilot study of CGA by Extermann and colleagues in older women with breast cancer identified multiple undiagnosed problems [22]. Several studies indicate that when important predictors of mortality, such as cancer stage at diagnosis and age, are controlled, the burden of comorbid

Table 2
Comprehensive geriatric assessment

Dimension	Screen	Detailed assessment	Resources
Medical			
Nutrition	Height, weight, serum albumin, cholesterol	BMI, Mini Nutritional Assessment	Dietician, speech therapist
Vision	“Describe any visual limitations.”	Snellen Eye Chart	Ophthalmologist, optometrist
Hearing	“Do you have any trouble with your hearing?” Finger rub test	Audioscope	Audiologist
Mobility/balance	Observed standing up, ambulation, and sitting down	Timed Get Up and Go [58], measured gait speed	Physical therapist, medically supervised exercise programs
Urinary incontinence	Screening questions	Urodynamic testing, urinalysis and urine culture	Urologist, gynecologist, geriatrician
Comorbidities	Review of systems, medical record	Activity, severity, stability	Primary care physician, specialists
Medications	Review medication by having the patient bring all medication bottles to the visit	Ask patient to explain regimen, reason for each drug, and potential adverse effects	Pharmacist Primary care physician
Cognitive	“Do you have any memory or thinking problems?” Get permission to ask the same question of family members, Minicog	Mini Mental Status Exam	Neuropsychological testing, referral to geriatrician, psychiatrist, neurologist
Affective	Clinical observation, “Do you often feel sad or blue?”	Geriatric Depression Scale Koenig Depression Screen	Psychiatrist, psychologist, social worker
Functional status	ADL	Katz ADL and IADL scale	Physical therapist, occupational therapist, speech therapist

	Do you need help using the bathroom, bathing, dressing eating?		
	IADL		
	“Can you use the telephone, pay your bills, shop, drive a car?”		
Social support	“Who would help you in an emergency?”	Detailed assessment of caregiver involvement and extended social support	Social worker, home health services, hospice
Economic	“Do you have the financial resources to meet your current and future needs?”	Health insurance Drug coverage	Social worker
Environment	Home safety checklist	Home visit	Occupational therapist, physical therapist, home health nurse
Advance directives	“Do you have an advanced directive?”	Detailed discussion	Social worker

Abbreviations: ADL, activities of daily living; BMI, body mass index; IADL, instrumental activities of daily living.

Adapted and modified from Balducci L, Extermann M. Management of cancer in the older person: a practical approach. *Oncologist* 2000;5:224–37 and Reuben DB. Geriatric assessment in oncology. *Cancer* 1997;80:1311–6.

illness is an important predictor of mortality [23,24]. Specific comorbidities, especially depression and cognitive impairment, are under-recognized in the oncology setting [25,26]. Comorbidity and functional status are independent predictors in older adult patients who have cancer and both need to be assessed [27]. Traditional oncologic measures of function, such as Karnofsky and Eastern Cooperative Oncology Group, are incomplete predictors in the elderly [27,28]. Ultimately, CGA should evaluate not only comorbidities and functional status but also stages or states of aging along with functional and coping (psychosocial) reserves that accurately predict therapeutic outcomes and improve outcomes through tailored treatment strategies.

In this vein CGA may be used to recognize frailty, a developing concept of a phenotype that is strongly predictive of falls, disability, hospitalization, and mortality [29]. This phenotype is not synonymous with comorbidity or disability. Comorbidity is likely causative and disability should be considered an outcome. Frailty is attributable to underlying processes of aging and may be particularly useful in uncovering limited or absent reserve capacity associated with advanced aging. Recognizing older adults who appear stable and functional but have limited ability to recover from the stressors associated with cancer treatment may be extremely helpful in tailoring treatment plans [30]. At present there are competing definitions of frailty. Balducci and colleagues define frailty as one or more of the following: dependence in at least one activity of daily living (ADL), three or more serious comorbid conditions, and one or more geriatric syndromes [31]. Fried and colleagues define frailty by the presence of three of the following criteria: involuntary weight loss $\geq 10\%$ of body weight over 1 year, fatigue, weakness (grip strength), slow walking speed, and low physical activity [29].

To date it seems that few specialists caring for older patients who have cancer use CGA on a regular basis, despite a general acknowledgment that age alone is not an adequate means of making treatment decisions [32,33]. This lack of assessment may be in large part because of a perceived impracticality of adopting a potentially time-consuming procedure with still unclear benefits for patient care. Cancer specialists are beginning to do the hard work of determining how to make CGA practical in usual care settings, however. There are several potential answers to this dilemma. Using primarily self-report components may optimize data gathering while minimizing staff time, but this may be less practical for more impaired individuals or diverse patient populations with limited literacy or English proficiency. Using hospital inpatient geriatric care units for older adults who have cancer may be a viable option in locations where these are available. In academic settings cancer specialists may be able to work in conjunction with geriatricians to manage more complicated older adult patients who have cancer. Also, cancer specialists should consider partnering with other clinical professionals in the implementation of CGA. Nurses, social workers, and midlevel practitioners can and should be part of the geriatric assessment process. A team approach to care has already been implemented to bring

together the various cancer specialists to ensure that treatment modalities, including chemotherapy, radiation, and surgery, are implemented seamlessly; such programs can incorporate geriatric assessment into this team management framework. Screening tools may be another way of limiting time commitments, reserving full-blown CGA to those most likely to benefit from it. Screening tools may be informal, such as the screening questions outlined in [Table 2](#). Alternatively, the Vulnerable Elders Survey 13 (VES-13) represents a formal means of predicting functional decline and death that also may be a viable screening tool ([Fig. 1](#)) [34]. The incorporation of CGA into clinical trials is of critical importance if we are to better delineate which patients with functional and cognitive limitations are appropriate for specific treatment regimens. This methodology will allow for comparison of patient characteristics across studies.

Tailoring treatment

CGA also can facilitate the process of tailoring treatment for individual patients ([Table 3](#)). The information collected should be used to establish goals of care; direct cancer-specific and symptom-specific treatment in light of comorbidities, functional status, psychological and social resources; and begin or review advanced planning (eg, living will, health care power of attorney, use of feeding tube).

Cancer-specific treatment

When carefully selected, older adult patients who have cancer undergoing the range of cancer treatment modalities experience similar responses to those seen in younger patients. Surgeons have been able to select carefully older adults who successfully undergo curative and palliative surgical procedures. Careful preoperative assessment, management of comorbidities, appropriate anesthesia management, and meticulous postoperative care have produced outcomes similar to those experienced by younger patients [35]. Radiation therapy is successful in older adults who have cancer and has developed its technical specificity for curative and palliative application with improved tolerability for older adults. Hormonal therapy is effective in older adult patients who have cancer of the breast, uterus, and prostate. With the advent of effective supportive therapy for the toxicity associated with chemotherapy more physicians have been willing to extend this treatment option to older patients, even those with some functional limitations and comorbidities. Growth factors, such as granulocyte colony-stimulating factor, modify or eliminate immunosuppressant effects. Cytoprotective agents, such as dexrazoxane, modify the cardiotoxic effects of doxorubicin. Newer antiemetics and improved techniques of chemotherapy administration also have opened the door of effective treatment to a wider range of older adult patients who have cancer. Important studies, such as the recent study of

Table 3
CGA-based cancer treatment plan

Treatment type	Components
Cancer-specific treatment	Surgery Chemotherapy Hormonal therapy Radiation therapy
Symptom-specific therapy	Example: pain relief Medication, exercise, heat/cold, alternative therapies (eg, acupuncture), relaxation techniques, nerve blocks
Supportive therapy	Dietary support Exercise prescription Support groups
End-of-life care	Address advance directives Periodically review goals of care

information regarding likely outcomes, adverse effects, and a description of the usual experience of treatment participation (frequency and length of procedures, usual recovery period, and so forth). If the treating physician is aware of functional limitations, cognitive impairment, or limitations of social support through the process of CGA, this allows for a more productive discussion of treatment options with the ability to anticipate and plan for how these issues may impact the treatment process and outcomes. For example, older adults who have cognitive impairment are at increased risk for developing delirium during hospitalization. Recognizing this potential complication can allow for interventions, such as family members staying with the patient around the clock, to be anticipated and planned. Many older adults rely heavily on close family members to assist them in treatment decisions. The physician can facilitate this process by inviting and encouraging the patient to bring family members to appointments.

Treatment goals should be established clearly between the physician and patient. These goals should be reassessed periodically depending on factors that may precipitate change, such as a lack of response to therapy or a significant change in functional status. Communication helps to ensure that the goals of care are reflected in the course of treatment [37].

Symptom-specific treatment

Whether or not patients decide to undergo cancer-specific treatment, symptom-specific treatment should be part of the treatment plan from diagnosis until death. Cancer specialists are becoming more and more adept at recognizing and treating cancer-related and treatment-related symptoms [38]. For example, fatigue is a particularly common symptom, especially in advanced stages of cancer. Treatment modalities include education, exercise, treatment of anemia, antidepressants, and psychostimulants.

Pain is a common symptom experienced from early to late stages of cancer. Pain should be systematically assessed. Options include a visual descriptor scale containing a set of numbers with words representing different levels of pain. A visual analog scale typically uses a 10-cm line marked “no pain” on the left and “worst possible pain” on the right. The pain thermometer is a visual scale that allows patients to place their pain on a vertical scale that resembles a thermometer. The Faces pain scale provides a series of faces depicting various degrees of facial grimacing. Perhaps most frequently, patients are asked without a visual device such as those just described to rate their pain on a scale of 0 to 10, with 0 being no pain and 10 being the worst possible pain. The American Geriatrics Society guidelines for persistent pain management are helpful in developing a comprehensive treatment plan that is based on anticipatory treatment of pain with scheduled dosing rather than dosing as needed. This topic is addressed thoroughly elsewhere in this volume.

Depression is fairly common among older adults who have chronic illness. Rates in patients who have cancer have been estimated at 17% to 33% [39,40]. Women who have severe illness, poor functional status, and advanced cancer are most at risk [40,41]. Multiple validated screening tools are available and should be used routinely, given the high prevalence of depression among patients who have cancer [42–44]. Treatment options include antidepressants, counseling, and electroconvulsive therapy.

Supportive care

Efforts currently are underway to assess the impact of diet and exercise prescriptions on the trajectory of functional decline and quality of life in newly diagnosed older adult patients who have cancer. Such efforts signal an acknowledgment of the motivation among patients who have cancer to make lifestyle changes and the potential for supportive interventions in addition to cancer-specific and symptom-specific treatments to improve the functional status and quality of life [45,46]. In another study, older patients who had cancer who also had mouth or tooth problems making it hard for them to eat experienced lower quality of life, poor emotional health, lower levels of physical functioning, and greater pain than patients without these problems [47]. This study emphasizes the impact that comorbid conditions can have on patients who have cancer, especially if they are not optimally identified and treated. In addition to comprehensive medical care, psychosocial interventions for the patient and caregiver can be extremely important. Supportive care needs to continue long term for cancer survivors who report a greater degree of disability than their counterparts without a history of cancer [48].

Psychosocial support is extremely important for the patient who has cancer, because the psychosocial demands of the illness course make an independent contribution to survival outcomes [49]. Support also should be

available for the caregiver, because despite the many benefits of caregiving, such as greater intimacy, satisfaction, and gaining meaning and purpose in life, there are also substantial mental, physical, social, and economic costs [50].

End-of-life care

End-of-life care should begin as early as possible in the course of a life-threatening illness. An important initial step is asking about advanced directives, such as living will and health care power of attorney. If patients are unfamiliar with such documents, their usefulness should be explained and written information provided. It is important for patients to understand that choosing a less aggressive treatment plan does not mean they will forgo the involvement of a physician. The phrase “nothing more can be done” should not be used; physicians need to convey a willingness to stay involved with care and symptom management up until the moment of death [51]. Ideally the patient’s goals should be elicited at every stage of treatment and should be reflected in the course of treatment that is provided [37]. End-of-life care is thoroughly covered elsewhere in this volume.

The emergence of geriatric oncology

Although 61% of new cases of cancer occur among the elderly they represent only 32% of participants in phase II and III clinical trials [52]. When comorbidities are controlled, age remains a strong predictor of whether or not a patient who has cancer will be offered a clinical trial, but when offered older adults respond with willingness to participate at similar rates [53]. Physicians may have good reasons for not offering clinical trials to older adults, such as protocol requirements that are onerous and not easily appreciated on enrollment, treatment-specific issues, including toxicity, and older patients’ medical and cognitive characteristics that may not exclude them but will hinder compliance with study requirements [54]. Insufficient enrollment of older adults in clinical trials is only one example of the inadequacies of current research to meet the needs of this growing population of patients who have cancer. There is an urgent need for further research at the interface of aging and cancer [55]. The lack of sufficient research makes it difficult to answer many of the questions that arise about cancer in older adults. Geriatric oncology represents a viable means of meeting the clinical and research needs of older adults who have cancer [56]. With the help of the John A. Hartford Foundation, gero-oncology training programs have been initiated and leaders are beginning to call for a new subspecialty of gero-oncology. Given the magnitude of the issue of appropriately caring for a growing number of older adults who have cancer, this seems to be a prudent course to pursue [57].

Summary

Providing effective and tolerable cancer treatment for the growing number of older adult patients who have cancer will require an understanding of the role of aging, comorbidity, functional status, and frailty on treatment outcomes. The incorporation of CGA into the care of older patients who have cancer will ensure that the heterogeneity of this population is considered in the development of treatment plans. It also may improve outcomes by identifying and optimally treating comorbid conditions and functional impairments. Optimal treatment of the older adult patient who has cancer starts with careful delineation of goals through conversation. The treatment plan should be comprehensive and address cancer-specific treatment, symptom-specific treatment, supportive treatment modalities, and end-of-life care.

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