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Comprehensive
Cancer
Network®

NCCN Clinical Practice Guidelines in Oncology™

Senior Adult Oncology

V.2.2007

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To find clinical trials online at NCCN member institutions, [click here: nccn.org/clinical_trials/physician.html](#)

NCCN Categories of Consensus: All recommendations are Category 2A unless otherwise specified.

See [NCCN Categories of Consensus](#)

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These guidelines are a statement of consensus of the authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no representations nor warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way. These guidelines are copyrighted by National Comprehensive Cancer Network. All rights reserved. These guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN. ©2007.

Summary of the Guidelines Updates

Summary of changes in the 1.2007 version of the Senior Adult Oncology Guidelines from the 1.2005 version include:

- Under Screening: Social work consultation was added ([SAO-1](#)).
- Special considerations, after Radiation: Hearing evaluation if ear in RT fields was added as a recommendation by the panel ([SAO-2](#)).
- Special considerations, after Neurotoxicity: Avoid cisplatin/paclitaxel combination regimens was removed ([SAO-2](#)).
- Special considerations, after Cardiac: Imaging assessment of ventricular function was revised to Assessment of ventricular function ([SAO-2](#)).
- Special considerations, after Cardiac: MUGA scan was removed as an imaging example ([SAO-2](#)).
- Special considerations, after Bone Marrow: Concurrent RT/Chemotherapy often not well tolerated, consider sequential therapy was removed as a recommendation and the link [See NCCN Myeloid Growth Factor Guidelines](#) was added after the first bullet ([SAO-2](#)).
- Special considerations, Diarrhea was added as a new consideration after chemotherapy. The panel recommends to consider early aggressive rehydration and management with sandostatin if oral preparations are ineffective ([SAO-2](#)).
- Quartiles was changed to Percentiles in the title to accurately describe the table ([SAO-A](#)).
- Disease-specific issues related to age: The heading of Clinical Problems was changed to Unresolved Issues ([SAO-C](#)).
- Comprehensive Geriatric Assessment, Socioeconomic issues: Financial counsel to discuss cost, coverage options etc. was added as an assessment ([SAO-D](#)).
- Comprehensive Geriatric Assessment, Geriatric syndrome, Falls: The quantifier > 1 per month was removed and All falls should have an assessment was added ([SAO-D](#)).
- Added the word Research to the title for clarification ([SAO-E](#)).

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SCREENING

- Estimate life expectancy based on function and comorbidity^a
- Estimate risk of morbidity from cancer:
 - Stage at diagnosis
 - Risk of recurrence and progression
 - Aggressiveness of disease
- Assessment of conditions (including geriatric syndromes) that would interfere with cancer treatment and tolerability:^{b,c}
 - Malnutrition
 - Polypharmacy
 - ◊ Check for appropriate dosing
 - Lack of social support
 - Depression
 - Dementia
 - Fall risk
- Patient’s goals of treatment
- Social work consultation

Expected to die of cancer or experience complications within lifetime

Life expectancy less than developing morbidity from cancer

ASSESSMENT^d

Geriatric assessment

- Evaluate functional dependency and comorbidity^e
- Detect and correct reversible conditions that may interfere with treatment

FINDINGS

Functionally independent (ADL and IADL independent)

Intermediate functional impairment

Major functional impairment and/or complex comorbidity^f

Not able to tolerate treatment or declines therapy

Able to tolerate treatment

Specialized precautions, individualized treatment according to patient preferences and caregiver availability

Symptom management
Supportive care
[See NCCN Supportive Care Guidelines](#)

[See Treatment \(SAO-2\)](#)

Able to tolerate treatment

Not able to tolerate treatment or declines therapy

Symptom management
Supportive care
[See NCCN Supportive Care Guidelines](#)

^a See [Histograms for age-specific future life expectancy \(SAO-A\)](#).

^b See [Specific Issues Related to the Management of Cancer in Older Patients \(SAO-B\)](#) and [Disease Specific Issues Related to Age \(SAO-C\)](#).

^c Patients with complex biomedical, functional, and psychosocial needs may benefit from a comprehensive geriatric assessment.

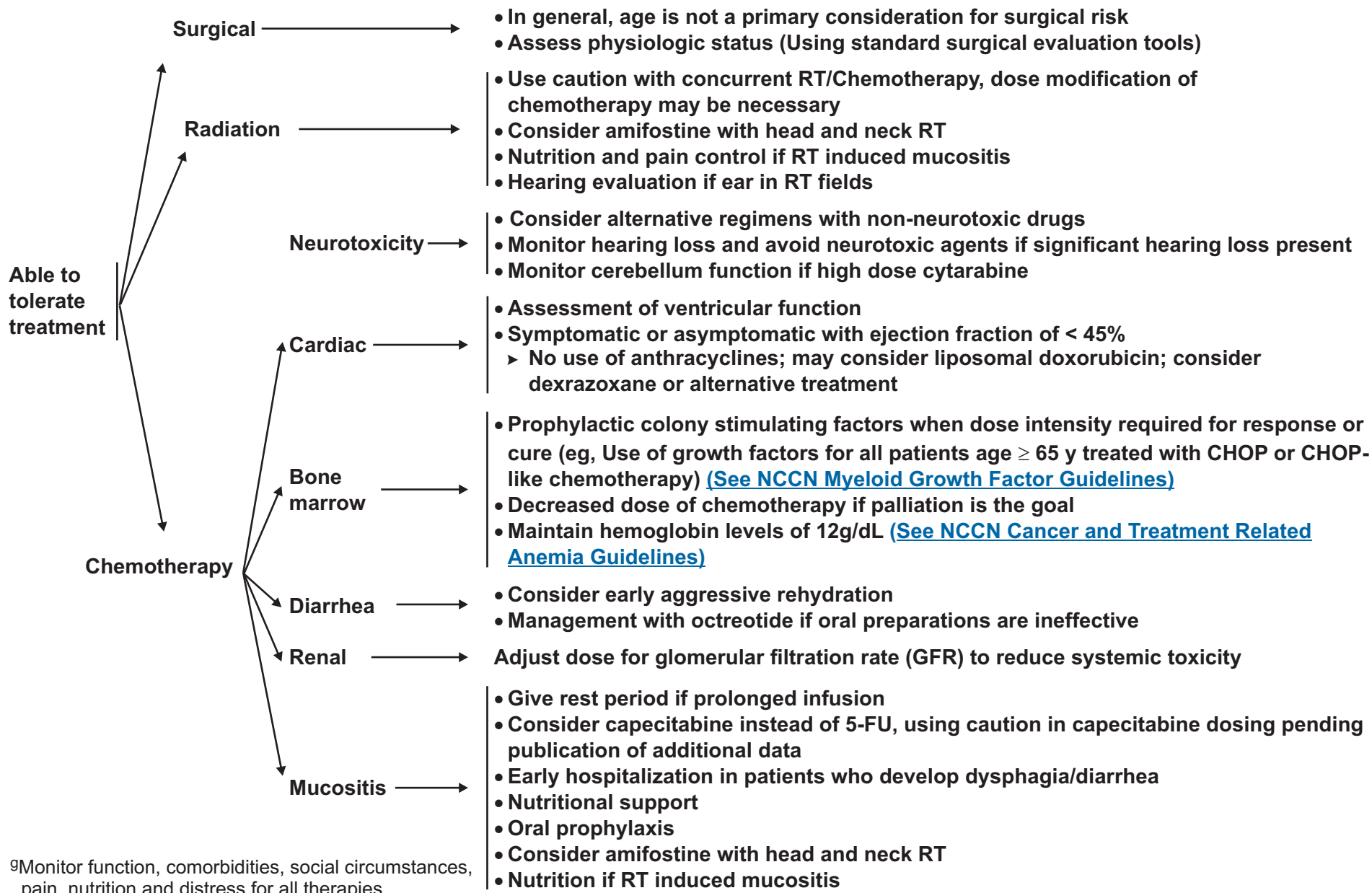
^d See [Comprehensive Geriatric Assessment \(SAO-D\)](#) and [Research Criteria Used to Define Frailty \(SAO-E\)](#).

^e See [Procedure for Functional Assessment Screening in Elderly Persons \(SAO-F\)](#) and [Vulnerable Elders Survey \(VES-13\) \(SAO-G\)](#).

^f It is expected that this will comprise 5-10% of patients.

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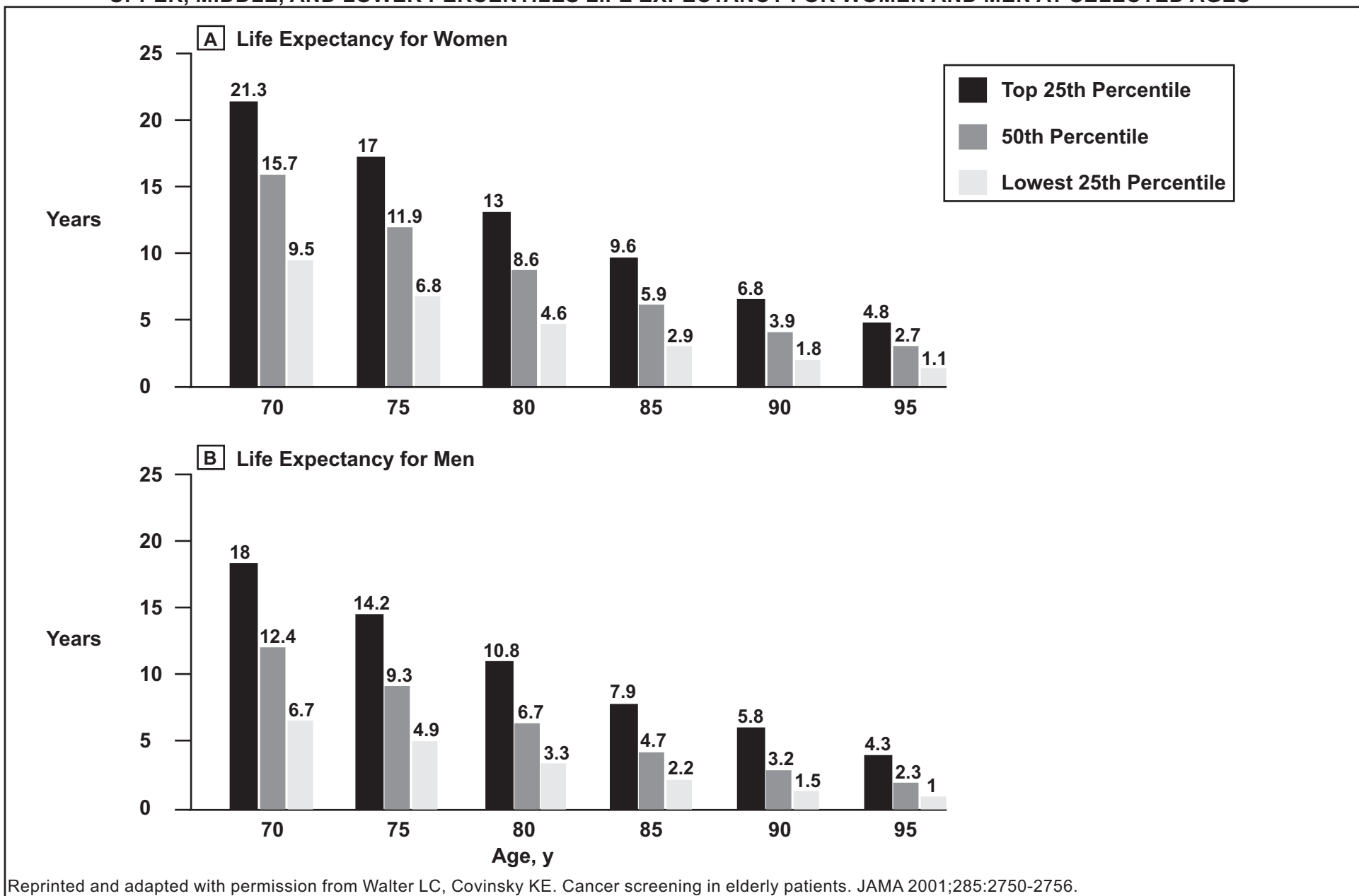
SPECIAL CONSIDERATIONS⁹



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UPPER, MIDDLE, AND LOWER PERCENTILES LIFE EXPECTANCY FOR WOMEN AND MEN AT SELECTED AGES



Reprinted and adapted with permission from Walter LC, Covinsky KE. Cancer screening in elderly patients. JAMA 2001;285:2750-2756.

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SPECIFIC ISSUES RELATED TO THE MANAGEMENT OF CANCER IN OLDER PATIENTS

- Geriatric assessment of the older individual
 - Life expectancy
 - Tolerance for treatment
 - ◊ Detect and correct reversible conditions that may interfere with treatment
 - Ability of patient to make decisions
- Amelioration of treatment complications
 - Use of hematopoietic growth factors
 - Control of anemia
 - Dose adjustment of chemotherapy agents
- Disease-specific issues ([See SAO-C](#))
 - Acute myelogenous leukemia
 - Non-Hodgkin's lymphoma
 - Breast cancer
 - Colorectal cancer
 - Lung cancer
- Management of patients unfit for standard treatment

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DISEASE-SPECIFIC ISSUES RELATED TO AGE

Disease	Age-Related Changes	Unresolved Issues
AML	<ul style="list-style-type: none"> • Decreased sensitivity to chemotherapy secondary to increased prevalence of MDR1 • Unfavorable cytogenetic profiles 	<ul style="list-style-type: none"> • Reversal of MDR1 • Role of low-dose cytarabine • Supportive care
Non-Hodgkin's lymphoma, large cells	<ul style="list-style-type: none"> • Decreased duration of complete response, possibly secondary to increased circulating levels of interleukin-6 	<ul style="list-style-type: none"> • Use of chemotherapy in higher doses • Biological treatment • Alternative regimens
Breast cancer	<ul style="list-style-type: none"> • More indolent course, secondary to higher prevalence of a well-differentiated hormone-receptor rich, slowly proliferating tumor(s) and to a hormonal and immunologic milieu that is unfavorable to the tumor(s) 	<ul style="list-style-type: none"> • Value of radiotherapy after lumpectomy (See NCCN Breast Cancer Guidelines) • Primary hormonal treatment • Value of adjuvant chemotherapy • Value of lymph node dissection • Use of epirubicin or liposomal doxorubicin in lieu of doxorubicin
Colorectal cancer	<ul style="list-style-type: none"> • Decreased tolerance of fluorinated pyrimidines 	<ul style="list-style-type: none"> • Alternative forms of adjuvant therapy
Lung cancer (non-small cell)	<ul style="list-style-type: none"> • Reduced tolerance of combined-modality treatment in stage III 	<ul style="list-style-type: none"> • Alternative approaches
Ovarian cancer	<ul style="list-style-type: none"> • Decreased response rate to cytotoxic chemotherapy 	<ul style="list-style-type: none"> • Alternative forms of treatment
AML, acute myelogenous leukemia; MDR1, multiple drug resistance gene		

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COMPREHENSIVE GERIATRIC ASSESSMENT

Parameter	Assessment
Function	<ul style="list-style-type: none"> • Activities of daily living (ADL) – Eating, dressing, continence, grooming, transferring, using the bathroom • Instrumental activities of daily living (IADL) – Using transportation, managing money, taking medications, shopping, preparing meals, doing laundry, doing housework, using telephone • Performance status
Comorbidity	<ul style="list-style-type: none"> • Number of comorbid conditions • Seriousness of comorbid conditions (comorbidity index)
Socioeconomic issues	<ul style="list-style-type: none"> • Living conditions • Presence and adequacy of caregiver • Income • Access to transportation • Financial counsel to discuss cost, coverage options etc.
Geriatric syndromes	<ul style="list-style-type: none"> • Dementia---Mini-Mental Status (MMS), other • Depression---Geriatric Depression Scale (GDS) • Delirium---For minimal infection or medication • Falls (All falls should have an assessment) • Osteoporosis (spontaneous fractures) • Neglect and abuse • Failure to thrive • Persistent dizziness
Polypharmacy	<ul style="list-style-type: none"> • Number of medications • Drug-drug interactions
Nutrition	<ul style="list-style-type: none"> • Nutritional risk-Mini-Nutritional Assessment (MNA)

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RESEARCH CRITERIA USED TO DEFINE FRAILITY

Variable	Question	Criteria
Weight loss	“In the past year, have you lost more than 10 lb unintentionally (ie, not due to dieting or exercise)?”	If yes, then subject is frail for weight loss criterion.*
Exhaustion	Using the CES depression scale, the following two statements are read. (a) I felt that everything I did was an effort. (b) I could not get going. The question is asked: “How often in the last week did you feel this way?”†	Subjects answering “2” or “3” to either of these questions are categorized as frail by the exhaustion criterion.†
Physical activity	Based on the short version of the Minnesota Leisure Time Activity questionnaire, subjects are asked about whether they do walking, chores (moderately strenuous), mowing the lawn, raking, gardening, hiking, jogging, biking, exercise cycling, dancing, aerobics, bowling, golf, singles or doubles tennis, racquetball, calisthenics, swimming.	Men: Those with physical activity < 383 Kcals/wk are frail.‡ Women: Those with physical activity < 270 Kcals/wk are frail.‡
Walk time (cutoff times are gender and height specific)	Men:¶ Height ≤ 173 cm Height > 173 cm Women:¶ Height ≤ 159 cm Height > 159 cm	Cutoff for time to walk 15 ft criterion for frailty: Men: ≥ 7 seconds ≥ 6 seconds Women: ≥ 7 seconds ≥ 6 seconds
Grip strength (cutoffs are gender and BMI specific)	Men: BMI ≤ 24 BMI = 24.1 – 26 BMI = 26.1 – 28 BMI > 28 Women: BMI ≤ 23 BMI = 23.1---26 BMI = 26.1---29 BMI > 29	Cutoff for grip strength (Kg) criterion for frailty: Men: ≤ 29 ≤ 30 ≤ 30 ≤ 32 Women: ≤ 17 ≤ 17.3 ≤ 18 ≤ 21

BMI, body mass index; CES, Center for Epidemiological Studies.

Adapted with permission from Fried L, Tangen C, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol Med Sci 2001;56A:M146-M156.

*At follow-up, weight loss is calculated as: (weight in previous year minus current measured weight)/(weight in previous year) = K. If K ≥ 0.05 and the subject does not report that he/she was trying to lose weight (ie, unintentional weight loss of at

least 5% of previous year's body weight), then subject is considered frail for weight loss.

†0 = rarely or none of the time (< 1 day); 1 = some or a little of the time (1-2 days); 2 = a moderate amount of the time (3-4 days); or 3 = most of the time.

‡Kcals/wk expended are calculated using a standardized algorithm.

¶A medium height is used.

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PROCEDURE FOR FUNCTIONAL ASSESSMENT SCREENING IN ELDERLY PERSONS

Target Area	Assessment Procedure	Abnormal Result	Suggested Intervention
Vision	Test each eye with Jaeger card while patient wears corrective lenses (if applicable)	Inability to read > 20/40	Refer to ophthalmologist
Hearing	Whisper a short, easily answered question, such as "What is your name?" in each ear while the examiner's face is out of direct view.	Inability to answer question	Examine auditory canals for cerumen and clean if necessary. Repeat test; if still abnormal in either ear, refer for audiometry and possible prosthesis.
Arm	Proximal: "Touch the back of your head with both hands." Distal: "Pick up the spoon."	Inability to do task	Examine the arm fully (muscle, joint, and nerve) paying attention to pain, weakness, limited range of motion. Consider referral for physical therapy.
Leg	Observe the patient after asking "Rise from your chair, walk 10 ft, return, and sit down." [*]	Inability to walk or transfer out of chair	Do full neurologic and musculoskeletal evaluation, paying attention to strength, pain, range of motion, balance, and traditional assessment of gait. Consider referral for physical therapy.
Urinary incontinence	Ask patient: "Do you ever lose your urine and get wet?"	Yes	Ascertain frequency and amount. Search for remediable causes including local irritations, polyuric states, and medications. Consider urologic referral.
Nutrition	Weigh the patient. Measure height.	Weight is below acceptable range for height	Do appropriate medical evaluation
Mental status	Tell the patient: "I am going to name three objects (pencil, truck, book). I will ask you to repeat their names now and then again a few minutes from now." [†]	Inability to recall all 3 objects after 1 min	Administer Folstein mini-mental status examination. If score is < 24, search for causes of cognitive impairment. Ascertain onset, duration, and fluctuation of overt symptoms. Review medications. Assess consciousness and affect. Do appropriate laboratory tests.
Depression	Ask patient: "Do you often feel sad or depressed?"	Yes	Administer Geriatric Depression Scale. If positive (normal score, 0 to 10), check for antihypertensive, psychotropic, or other pertinent medications. Consider appropriate pharmaceutical or psychiatric treatment.
ADL-IADL	Ask patient: "Can you get out of bed yourself?"; "Can you dress yourself?"; "Can you make your own meals?"; "Can you do your own shopping?"	No to any question	Corroborate responses with patient's appearance; question family members if accuracy is uncertain. Determine reasons for the inability (motivation compared with physical limitation). Institute appropriate medical, social, or environmental interventions.
Home environment	Ask patient: "Do you have trouble with stairs inside or outside of your home?"; ask about potential hazards inside the home with bathtubs, rugs, or lighting.	Yes	Evaluate home safety and institute appropriate countermeasures.
Social support	Ask patient: "Who would be able to help you in case of illness or emergency?"	...	List identified persons in the medical record. Become familiar with available resources for the elderly in the community.
<p>ADL, activities of daily living; IADL, instrumental activities of daily living. Adapted with permission from Lachs MS, Feinstein AR, Cooney LM Jr, et al. A simple procedure for general screening for functional disability in elderly patients. <i>Ann Intern Med</i> 1990;112:699-706. [*]This test is similar to the "timed up and go" (TUG) test, except that for the TUG test patients are also asked to walk 20 ft briskly. For the TUG test, a score of "one" is assigned for each of these</p>		<p>findings: (1) use of the arms to get up, (2) uncertain steps, and/or (3) more than 10 seconds to complete the activity. The higher the total score, the higher the risk of functional dependence and death. [†]This test is also referred to as the "three-item recall." It can be supplemented by the clock drawing test to assist in assessment for dementia.</p>	

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VULNERABLE ELDERLY SURVEY (VES-13)

A total score of ≥ 3 indicates that patients are vulnerable.

1. Age _____

Score: 1 point for age 75---84 years; 3 points for age ≥ 85 years

2. In general, compared to other people your age, would you say your health is:

- Poor* (1 point)
- Fair* (1 point)
- Good
- Very good
- Excellent

Score: 1 point for fair or poor

3. How much difficulty, on average, do you have with the following physical activities:

	None	A Little	Some	A Lot*	Unable to Do*
a. Stooping, crouching, or kneeling?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Lifting or carrying objects as heavy as 10 pounds?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Reaching or extending arms above shoulder level?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Writing or handling and grasping small objects?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Walking a quarter of a mile?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Heavy housework, such as scrubbing floors or washing windows?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Score: 1 point for each * response in questions 3a-f. Maximum of 2 points.

Adapted with permission from Saliba D, Elliott M, Rubenstein LZ, et al. The Vulnerable Elders Survey: a tool for identifying vulnerable older people in the community. J Am Geriatr Soc 2001;49(12):1691-1699.

4. Because of your health or a physical condition, do you have any difficulty:

a. shopping for personal items (like toilet items or medicines)?

- YES ? Do you get help with shopping?..... YES* NO
- NO
- DON'T DO ? Is that because of your health?..... YES* NO

b. managing money (like keeping track of expenses or paying bills)?

- YES ? Do you get help with managing money?..... YES* NO
- NO
- DON'T DO ? Is that because of your health?..... YES* NO

c. walking across the room?
USE OF A CANE OR WALKER IS OKAY.

- YES ? Do you get help with walking? YES* NO
- NO
- DON'T DO ? Is that because of your health?..... YES* NO

d. doing light housework (like washing dishes, straightening up, or light cleaning)?

- YES ? Do you get help with light housework? YES* NO
- NO
- DON'T DO ? Is that because of your health?..... YES* NO

e. bathing or showering?

- YES ? Do you get help with bathing or showering? YES* NO
- NO
- DON'T DO ? Is that because of your health?..... YES* NO

Score: 4 points for one or more * responses in questions 4a-e.

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NCCN Categories of Consensus

Category 1: There is uniform NCCN consensus, based on high-level evidence, that the recommendation is appropriate.

Category 2A: There is uniform NCCN consensus, based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 2B: There is nonuniform NCCN consensus (but no major disagreement), based on lower-level evidence including clinical experience, that the recommendation is appropriate.

Category 3: There is major NCCN disagreement that the recommendation is appropriate.

All recommendations are category 2A unless otherwise noted.

Overview

Cancer is the leading cause of death in women and men aged 60 to 79 years.¹ More than 60% of all cancers and 80% of cancer-related deaths in the United States occur in patients who are 65 years or older. It is estimated that 20% of the U.S. population will be 65 years or older by 2030 and 70% of cancers and 85% of all cancer-related deaths will occur in this older population. Older individuals are more prone to develop cancer than younger individuals as a result of physiological changes associated with ageing, which in turn favor the development and growth of cancer. In addition, behavior of certain neoplasms changes with patient's age. Acute myelogenous leukemia, non-Hodgkin's lymphoma (large cell and follicular lymphoma) and ovarian cancer are associated with poor prognosis in patients 60 years and older, whereas breast cancer and lung cancer are more indolent in the elderly.² Increased incidence and prevalence of cancer in elderly

people and increased lifespan of the elderly mean that cancer in older individuals is becoming an increasingly common problem.

Unfortunately, elderly cancer patients are under-represented in clinical trials for new cancer therapies.³ Advanced age alone should not preclude the use of effective cancer treatment that could improve quality of life or extend meaningful survival.⁴ Proper surgery and adjuvant treatment can decrease relapse and improve survival in some women with breast cancer who are older than 80 years.⁵ However, treatment that diminishes quality of life with no significant survival benefit should be avoided. Older patients in good performance status are able to tolerate commonly used chemotherapy regimens as well as younger patients, when adequate supportive care is provided.^{6,7,8}

The NCCN Senior Adult Oncology guidelines address specific issues related to the management of cancer in older individuals including geriatric screening and assessment, preventing or decreasing complications from therapy, accounting for disease-specific issues, and management of patients unfit for standard treatment, as well as for assessing the risks and benefits of treatment in the older patient with cancer.

Comprehensive Geriatric Assessment

Comprehensive geriatric assessment (CGA) is a multidisciplinary in-depth evaluation of elderly cancer patients to develop a coordinated plan for cancer treatment as well as appropriate interventions to the patient's problems. Older patients can be classified into three categories: (i) young old patients are 65-75 years of age; (ii) old patients are 76-85 years of age; and (iii) oldest old patients are more than 85 years of age.⁹ Proper selection of patients is the key to administering effective and safe cancer treatment. However, chronological age by itself is not reliable in estimating life expectancy, functional reserve, or the risk of treatment complications.¹⁰ This

information is best provided by a comprehensive geriatric assessment (CGA), which assesses function, comorbidity, nutrition, polypharmacy, cognition, emotional evaluation, and socioeconomic issues ([SAO-D](#)).¹¹

Evaluation of the cancer patient includes an estimate of life expectancy, functional reserve, comorbidity as well as personal and social resources.¹² Risk of tumor recurrence and progression are generally established by the stage at diagnosis and the aggressiveness of the tumor. It is also essential to determine the patient's overall goals, including whether proposed treatment is desired. CGA can identify reversible problems that may interfere with cancer treatment, such as insufficient social support, malnutrition, and reversible comorbidity.^{11,13,14} Consultation with a social worker should be encouraged. It is also important to assess whether patients are cognitively impaired. Geriatric patients with cancer who are cognitively impaired have poor performance status, higher incidence of depression, and are at greater risk for death. In addition, some cognitively impaired patients are unable to make decisions related to their treatment. Cognitively impaired patients should be cared for by an experienced multidisciplinary geriatric oncology team along with good supportive care throughout the treatment.¹⁵

Falls are one of most common geriatric syndromes. In the United States, 30-40% of adults older than 65 years fall each year. Risk factors include older age, muscle weakness and impairments in gait, balance, vision, cognition and activities of daily living.¹⁶ Evidence from a meta-analysis of randomized trials and a systematic review found that interventions are very effective preventing falls in older adults and they also reduce both the risk and rate of falling.^{17,18} CGA of elderly cancer patients should include assessment of all falls.

Life expectancy is better predicted by health status than age alone; therefore, function and comorbidity should be taken into account. Life expectancy can be estimated using life table data as suggested by

Walter and Covinsky ([SAO-A](#)).^{19,20} For example, about 25% of the healthiest 75-year-old women will live more than 17 years, 50% will live at least 11.9 years, and 25% will live less than 6.8 years.

The challenge of managing the older cancer patient is to assess whether the expected benefits of treatment are superior to the risk in a population with decreased life expectancy and decreased tolerance to stress. This assessment requires answering three questions:

- Is the patient expected to die of cancer?
- Is the patient at risk for the complications of cancer during her/his lifetime?
- Is the patient able to tolerate cancer treatment?

It is useful to assess older patients to identify those who are expected to die of cancer or experience complications within their lifetime, or those whose life expectancy is so short that they are unlikely to develop cancer-related morbidity ([SAO-1](#)). Patients in the first group can then be further assessed to estimate their fitness or desire for treatment, because some of these patients will not tolerate therapy or will decline therapy. In addition, several provisions are available to decrease the risk of treatment complications and to preserve the function of older individuals receiving chemotherapy. Patients with short life expectancy can receive symptom management and supportive care as detailed in the appropriate [NCCN Guidelines for Supportive Care](#).

Irrespective of age, a person who is totally independent and without serious comorbidity should be a good candidate for most forms of cancer treatment. However, the patient, with or without severe comorbidity, who is dependent on some instrumental activities of daily living (IADL) is at increased risk of treatment complications. For these patients with intermediate functional impairment who have milder problems (such as dependence in one or more IADL, milder comorbidity, depression, minor memory disorder, mild dementia, inadequate caregiver), treatment may still be administered with special

individualized precautions, including attempts to reverse the problem and cautious dosing of treatment ([SAO-1](#)).^{21,22}

Cytotoxic chemotherapy is generally contraindicated at full dose for patients with severe problems such as dependence on one or more activities of daily living (ADL) except for incontinence, presence of geriatric syndromes (such as severe dementia, depression, delirium, neglect and abuse, failure to thrive, multiple falls, spontaneous bone fractures, continuous dizziness), and/or presence of severe comorbidity. However, cytotoxic chemotherapy may still be used in these patients for symptom management at low doses.

Screening Tests

CGA is time-consuming and may not be practical or necessary for all patients. For this reason, several screening tests may be used as an alternative to CGA to decide which patients need either a full assessment or a more thorough assessment for a specific problem.^{14,23-27} These screening tests can be used to determine which patients may benefit from a CGA.

Frailty is a biologic syndrome of decreased reserve and resistance to stressors, causing vulnerability to adverse outcomes.²⁸ Frail patients may be at increased risk of therapeutic complications from cancer treatment; thus, it is useful to assess whether cancer patients are frail. The cardiovascular health study (CHS) has developed a screening tool to identify frail patients on the basis of five simple tests ([SAO-E](#)).²⁷ Frail patients have three or more of the following criteria: unintentional weight loss (10 pounds or more in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and/or low physical activity.²⁷ Fit, frail, and prefrail patients had different 5-year mortality rates and different risks of developing functional dependence at 3 and 7 years. Frail and prefrail patients are at risk for falling, disability, hospitalization, and death. The CHS instrument has been tested in

5317 men and women who were 65 years and older. This form of assessment is now commonly used and may be helpful to screen whether elderly cancer patients require a CGA. However, determining if someone is frail is more difficult in cancer patients, because cancer confounds the problem.

A quick screening test to assess mobility is the “timed up and go” (TUG) test. Older individuals are asked to get up from an armchair without using their arms, walk 20 feet forward briskly, turn around, walk back to the chair, and then sit down again. A score of “one” is assigned for each of these findings: (1) use of the arms to get up, (2) uncertain steps, and/or (3) more than 10 seconds to complete the activity. The higher the total score, the higher the risk of functional dependence and death.

Lachs and colleagues developed a screening assessment for elderly patients ([SAO-F](#)).²⁴ This screening test quickly assesses many areas including vision, hearing, arm/leg mobility, urinary incontinence, nutrition, mental status, depression, ADL-IADL, home environment, and social support. Lachs’ screening test is done by a physician (or office staff); it may be very useful to assess if a CGA is necessary.

A rapid screening test (ie, Distress Thermometer) to assess for distress has been specifically developed for cancer patients by the NCCN Distress Management Panel, which is one of NCCN Supportive Care Panels ([NCCN Distress Management Guideline](#)).^{29,30,31} Patients can quickly fill out this distress assessment tool before the examination; the tool can alert the physician to potential problems. This tool assesses whether cancer patients have problems of a practical (eg, housing, insurance), family, emotional (eg, depression), spiritual, and/or physical nature (eg, fatigue, pain, breathing, eating, sleep).³² There is good correlation between the NCCN Distress Thermometer and the more comprehensive Hospital Anxiety and Depression Scale (HADS).^{29,31}

Saliba and colleagues have developed a useful questionnaire called the Vulnerable Elders Survey (VES-13) that patients can quickly fill out at home or in the office ([SAO-G](#)).²⁶ A score of 3 or more on the VES-13 indicates that patients are vulnerable. They tested the questionnaire in 6205 Medicare beneficiaries aged 65 years and older. The VES-13 assesses whether elderly patients are at risk for functional decline or death. The advantage of this questionnaire is that it minimizes the amount of time required to examine patients in the office; this survey assesses age, self-rated health, limitation in physical function, and functional disabilities. The VES-13 is the official screening test for older individuals in the EORTC (European Organization for Research and Treatment of Cancer).

In the future, laboratory tests may be used to assess whether elderly patients are at risk for development of functional decline or mortality. Cohen and colleagues have demonstrated that high levels interleukin-6 and D-dimer were associated with mortality and functional dependence in home dwelling individuals aged 71 years and older.³³ In addition, cognitive decline has been found to be associated with elevated levels of D-dimer.³⁴ Thus, assessment of inflammation markers (interleukin-6 and D-dimer) may be used to predict physiologic age in elderly patients.

Amelioration of Treatment Complications

The benefits of cancer treatment include prolonged survival, maintenance and improvement of quality of life and function, as well as palliation of symptoms. Risks include complications of surgery, radiation, and/or cytotoxic chemotherapy. In older individuals, the complications of chemotherapy such as neutropenia, anemia, bleeding, mucositis, cardiac toxicity, and neurotoxicity, may precipitate functional dependence. Chemotherapy can also affect cognition, function, balance, vision, hearing, continence, and mood.²³

In terms of susceptibility to therapeutic complications, older patients appear to be at special risk for severe and prolonged myelosuppression and mucositis, increased risk of cardiomyopathy, as well as increased risk of central and peripheral neuropathy. Many cancer patients undergoing chemotherapy are at risk for infection (with or without neutropenia), dehydration, electrolyte disorders, and malnutrition either as a side effect of the chemotherapy or directly from the tumor; the combination of these complications enhances the risk of delirium in older cancer therapy receiving cytotoxic chemotherapy.²³

Cancer-related fatigue is a persistent, subjective sense of tiredness related to cancer or cancer treatment that interferes with usual functioning. In advanced cancer, the prevalence of fatigue is greater than 50-70%.³⁵ Patients perceive fatigue to be one of the most distressing symptoms associated with cancer and its treatment; fatigue is more distressing even than pain or nausea and vomiting, which can generally be managed by medication in most patients.^{36,37} In contrast to normal fatigue, cancer-related fatigue is refractory to sleep and rest, perhaps because cancer patients have aberrant sleep patterns. It is reasonable to expect that fatigue may precipitate functional dependence, especially in patients who are already dependent in IADL.³⁸

Screening for fatigue can be done using a brief screening questionnaire ([NCCN Cancer-Related Fatigue Guideline](#)): “Since your last visit, how would you rate your worst fatigue on a scale of 0 to 10 (0 = no fatigue and 10 = worst fatigue)?” Multiple factors can contribute to fatigue, including pain, emotional distress, anemia, comorbidities, and/or sleep disturbance; many of them are treatable. Certainly, the best strategy is avoidance of any fatigue that may precipitate functional dependence in older individuals. Energy conservation, exercise programs, stress management, sleep therapy, and psychostimulants are some of the interventions that have proved valuable. Cancer-related fatigue and

depression frequently occur together; therefore, patients reporting fatigue should probably be assessed for depression (eg, the Geriatric Depression Scale).^{39,40,41}

Special considerations for patients who are able to tolerate curative treatment (surgery, radiation therapy, or chemotherapy) are shown in the algorithm ([SAO-2](#)) and they are discussed below.

Surgery

In general, age is not a primary consideration for surgical risk, although the physiologic status of the patient needs to be assessed.

Performance status and comorbidities of the patient are more important factors than the age when considering surgical treatment options for elderly patients.⁴² The Surgical Task Force report from SIOG (International Society for Geriatric Oncology) reported that in many neoplasms (breast, gastric and liver) the surgical outcomes in the elderly cancer patients were not significantly different from their younger counterparts.⁴³ Preoperative Assessment of Cancer in Elderly (PACE) is an ongoing multinational study aimed at outlining the fitness of elderly cancer patients, which in turn will enable the physicians to make informed decisions about choosing the optimal treatment in the elderly.⁴⁴ According to the preliminary results of the study, performance status (PS), activities of daily living (ADL) and instrumental activities of daily living (IADL) appear to be useful in preoperative patient selection and also for predicting postoperative outcomes.⁴⁵

Radiation Therapy

Radiation therapy (RT) is beneficial to elderly cancer patients especially when surgery and chemotherapy are contraindicated. RT can be offered either in the curative or in the palliative setting.⁴⁶ External beam radiation therapy or brachytherapy are two possible modalities. Long courses of external beam RT are used for local tumor control, whereas hypofractionated regimens are used for palliation and symptom control.

Hypofractionated RT may be an alternative treatment option in patients who are unable to tolerate conventional dose RT.⁴⁷ Available data from the literature indicate that radiation therapy is highly effective, well tolerated and age is not a limiting factor in elderly cancer patients.^{48,49,50}

CGA should be performed before radiation therapy to establish baseline functional status. Concurrent chemoradiation should be used with extreme caution; dose modification of chemotherapy may be necessary to reduce toxic side effects.

Chemotherapy

Several retrospective studies have reported that the toxicity of chemotherapy is not more severe or prolonged in persons older than 70 years.^{7, 51-54} These studies are important, because they demonstrate that age, by itself, is not a contraindication to cancer chemotherapy. However, the results of these studies cannot be generalized for the following reasons:

- Only a few patients were 80 years or older; therefore, minimal information is available on the oldest patients.
- The older patients involved in these studies were highly selected by the eligibility criteria of the cooperative group protocols and were not representative of the general older population, because they were probably healthier than most older patients.
- Many of the treatment regimens used in these trials had lower dose intensity than those in current use.

In elderly patients chemotherapy should be individualized based on the nature of the disease and the performance status of the patient. CGA may be useful in the proper selection of patients when chemotherapy is considered as a treatment option.

Hematopoietic Growth Factors

Neutropenia is the major dose-limiting toxicity associated with chemotherapy, especially in older patients. Several prospective studies of older patients with large cell lymphoma have shown that the incidence of neutropenic infections may be as high as 50% in individuals aged 65 years and older treated with regimens like CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone).⁵⁵⁻⁶¹ In persons age 60 years or older receiving induction or consolidation chemotherapy for AML, the prophylactic use of growth factors is recommended on the basis of studies showing that growth factors may increase therapeutic response and improve survival. Moreover, growth factors have consistently decreased the duration of hospitalization and, thus, may be cost saving (GELoAM study).⁶²⁻⁶⁶

In addition, available data from various studies has shown that the risk of myelotoxicity increases after age 70 years.^{67,68,69} Similar conclusions were reached by Langer and colleagues in lung cancer patients treated according to the ECOG protocols.⁷⁰ Rocha Lima and colleagues found that elderly patients with lung cancer had more leukocyte toxicity after treatment.⁷¹ Neubauer and colleagues also found that elderly patients receiving weekly paclitaxel plus carboplatin for small cell lung cancer had neutropenia.⁷² At least eight prospective studies of lymphoma in older individuals revealed a higher risk of myelodepression than in younger patients.^{56-59,73,74,75}

Data from lymphoma studies indicates that:

- The risk of myelodepression increases substantially by age 65 years.
- The risk of myelodepression is decreased by 50% when using growth factors.
- In persons 70 years or older, the incidence of neutropenic infection-related mortality varies between 5% and 30%.

- Dose reductions of chemotherapeutic agents may compromise the effectiveness of treatment.
- The use of growth factors in these circumstances does not appear to be associated with increased cost and may even be cost saving if it prevents lengthy hospitalizations for neutropenic infections in older persons.

Meta-analysis of controlled clinical trials on the use of prophylactic recombinant colony-stimulating factors has confirmed their effectiveness in reducing the risk of febrile neutropenia.⁷⁶ Some concerns have been expressed that the combination of growth factors and topoisomerase II inhibitors may be associated with increased risk of acute leukemia.⁷⁷ Despite these caveats, the use of growth factors appears to be the best-established strategy to improve treatment in this group of patients.⁷⁸ The EORTC has issued similar recommendations for the prophylactic use of colony stimulating factors (G-CSF) in older patients with cancer.⁷⁹

NCCN guidelines recommend prophylactic use of hematopoietic growth factors along with CHOP or CHOP-like chemotherapy regimens in the treatment of lymphoma in patients who are 65 years or older.

Dose Reduction and Substitution

Age has been associated with pharmacokinetic and pharmacodynamic changes and with increased susceptibility of normal tissues to toxic complications. In general, all of these changes increase the risks of chemotherapy.⁸⁰⁻⁸³ Pharmacodynamic changes of interest include reduced repair of DNA damage and increased risk of toxicity. Pharmacokinetic changes of major concern include decrease in the glomerular filtration rate (GFR) and volume of distribution of hydrosoluble drugs. Although the hepatic uptake of drugs and the activity of cytochrome P450 enzymes also decrease with age, the influence of these changes on cancer chemotherapy is not clear.

Intestinal absorption may decrease with age, but it does not appear to affect the bioavailability of anticancer agents.

The pharmacokinetics of antineoplastic drugs is unpredictable to some extent; thus, drug doses should be adjusted according to the degree of toxicity that develops. However, adequate dosing is necessary to ensure the effectiveness of therapy. Extermann and colleagues have devised a convenient index (MAX2) for estimating the average per patient risk for toxicity from chemotherapy.⁸⁴

GFR decreases with age, which in turn delays elimination of many drugs. Delayed renal excretion may enhance the toxicity of drugs whose parent compounds are excreted by the kidneys (carboplatin, oxaliplatin, methotrexate, bleomycin) and drugs that are converted to active (idarubicin, daunorubicin) or toxic metabolites (high-dose cytarabine).⁹ Dose adjustment to the measured glomerular filtration rate should be considered for these drugs as well as for drugs whose parent compounds are excreted through the biliary tract, to decrease systemic toxicity. To avoid neurotoxicity, particular attention should be paid to the use of cytarabine in high doses. Older patients are particularly susceptible to the toxicity of this regimen due to decreased renal excretion of the toxic metabolite ara-uridine, and increased vulnerability of the cerebellum.

Anthracyclines are associated with increased cardiac toxicity. Risk factors include cumulative doses especially greater than 550 mg/m², hypertension, pre-existing cardiac disease and advanced age. Anthracycline induced cardiomyopathy can result in congestive heart failure (CHF). Other antineoplastic drugs may have additional effect on anthracycline-induced cardiac toxicity.⁸⁵ Pegylated liposomal doxorubicin is associated with less cardiac toxicity^{86,87} and may be a useful alternative to doxorubicin for patients 70 years or older when its efficacy is comparable to doxorubicin especially in metastatic breast cancer.⁸⁸ Dexrazoxane, an iron chelator has been shown to reduce

cardiac toxicity in randomized clinical trials.^{89,90} In addition, several agents including weekly taxanes, vinorelbine, gemcitabine, and capecitabine have a more favorable toxicity profile and may be used safely in older individuals. Capecitabine at reduced doses is particularly convenient, because the oral formulation allows home treatment.^{91,92} Furthermore, since capecitabine, prodrug of 5-fluorouracil is activated in the tumor, the normal tissues are largely spared.

NCCN guidelines recommend that any patient symptomatic for CHF, irrespective of ejection fraction and asymptomatic patients with an ejection fraction less than 45% should not receive anthracyclines. Liposomal doxorubicin, dexrazoxane or alternative treatment options should be considered for this class of patients.

Anemia

Anemia has been shown to be a risk factor for chemotherapy related toxicity and it is one of the factors responsible for reduction in volume of distribution, which may result in increased peak concentration and in increased toxicity of drugs. Evidence from at least three studies suggests that anemia is associated with enhanced myelodepression and can result in decreased distribution of water-soluble drugs.^{93,94} Anemia is also associated with cardiovascular disease, congestive heart failure, coronary death, and possibly dementia.⁹⁵⁻⁹⁸ Since the relationship between volume of distribution and red blood cells has been confirmed in a number of studies, anemia can be prevented by maintaining the hemoglobin concentration at 12 gm/dL or higher with the use of erythropoietic growth factors. The maintenance of hemoglobin levels at 12 g/dL or more is supported by studies showing that optimal relief of fatigue occurs when hemoglobin levels are between 11 and 13 g/dL.^{99,100} The use of epoetin as a treatment option for patients with chemotherapy-associated anemia who have a hemoglobin level less than 10 g/dL is recommended by both the [NCCN Cancer and Treatment-Related Anemia Guideline](#) and guidelines from

the American Society of Clinical Oncology/American Society of Hematology.¹⁰¹

It also appears beneficial to complement the administration of erythropoietin with oral or parenteral iron; although this is not specific for elderly patients, it is appropriate for any patient treated with epoetin or darbepoetin. Of concern, two randomized, double-blind placebo-controlled trials have reported that cancer patients receiving recombinant erythropoietin had decreases in survival that were statistically significant.^{102,103} These studies have been analyzed by the US Food and Drug Administration (FDA) and their industry sponsors to determine whether factors other than recombinant erythropoietin contributed to the poor outcomes; however, no firm conclusions have been drawn. In the studies in which increased mortality was reported, hemoglobin was targeted to higher levels than recommended in the prescribing information for recombinant erythropoietin.¹⁰⁴

Diarrhea

Diarrhea is a well-recognized side effect associated with a number of chemotherapeutic agents, particularly greater for regimens containing 5-fluorouracil and irinotecan. Chemotherapy-induced diarrhea (CID) can lead to discontinuation of chemotherapy and poorer clinical outcomes. Loss of fluid associated with persistent and severe diarrhea can lead to dehydration, renal insufficiency and electrolyte imbalance. There is no evidence based treatment approach for CID. Recently, ASCO published guidelines for the treatment of CID.¹⁰⁵ These guidelines recommend comprehensive evaluation at the onset of diarrhea to determine the severity. Based on the results from various clinical trials, ASCO guidelines recommend loperamide therapy for mild to moderate diarrhea; octreotide (subcutaneous or intravenous if the patient is severely dehydrated) treatment for severe diarrhea or for treatment of CID that is refractory to loperamide therapy. There is no

effective pharmacological intervention for diarrhea induced by radiation therapy.

Patients with chemotherapy-induced diarrhea should be treated with aggressive rehydration. Pharmacological management with octreotide is recommended if oral preparations are ineffective.

Mucositis

Oral and gastrointestinal mucositis are significant complications of radiotherapy and chemotherapy, especially following treatment with fluoropyrimidines. Risk of mucositis increases with age, thereby increasing morbidity and mortality associated with cancer therapy. Guidelines for preventing, evaluating, and treating oral as well as gastrointestinal mucositis have been developed by the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology.¹⁰⁶ Prevention of mucositis includes the use of oral capecitabine instead of intravenous fluorinated pyrimidines. Once mucositis has occurred, patients should be kept well hydrated with intravenous fluids and hospitalization if necessary.

Until recently, no pharmacological agents have been shown to effectively treat mucositis. In 2004, FDA approved palifermin (Kepivance[™]), human keratinocyte growth factor (KGF) for the treatment of oral mucositis in patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support.¹⁰⁷ Rosen et al have recently reported that palifermin was well tolerated and resulted in significant reduction of oral mucositis in patients with metastatic colorectal cancer treated with fluorouracil-based chemotherapy.¹⁰⁸ However, the safety and efficacy of palifermin is yet to be firmly established in non-hematologic malignancies. Recently, Saforis, a new time-released preparation of glutamine appears promising in the management of oral mucositis in breast cancer patients receiving anthracycline-based chemotherapy.¹⁰⁹

Disease-Specific Issues

Several disease-specific issues related to age have been identified ([SAO-C](#)). These issues occur partly because of the different behavior of certain cancers in older versus younger patients and partly because of the decreased tolerance of treatment by older patients. The NCCN Senior Adult Oncology Panel felt that these issues should be explored within the tumor-specific NCCN Guidelines. In view of the seriousness of the complications of AML treatment, the NCCN Senior Adult Oncology Panel recommends that older patients with AML only be treated in centers skilled in the management and supportive care of AML. Outcomes for older patients with AML have not substantively changed in the last 10 to 15 years ([NCCN Acute Myeloid Leukemia Guideline](#)). Thus, clinical trials are needed in older patients with AML (eg, trials assessing low-intensity therapy).

Summary

Because aging is highly individualized, the best guide as to whether cancer treatment is appropriate may be provided by careful assessment of the older patient ([SAO-1](#)). Screening can be used to identify patients who can benefit from a comprehensive assessment (CGA).

Chronological age is not reliable in estimating life expectancy, functional reserve, or the risk of treatment complications. Careful assessment, using the criteria described in this NCCN Senior Adult Oncology Guideline, allows oncologists to divide older patients into three groups as follows:

- patients who are functionally independent (ADL and IADL independent) and without comorbidity and, thus, are candidates for most forms of standard cancer treatment;
- patients with major functional impairment and/or complex comorbidity (dependent in one or more ADL with severe comorbidity or advanced geriatric syndromes, who are candidates only for palliative treatment;

- patients with intermediate functional impairment who cannot tolerate life-prolonging curative therapy but who may benefit from some special pharmacological approach (such as reduction in the initial dose of chemotherapy with subsequent dose escalations as tolerated);

All three groups of patients are expected to die of cancer or experience complications within their lifetimes. A fourth group of patients includes those whose life expectancy is so short that they are unlikely to develop morbidity from cancer; these patients can receive symptom management and supportive care.

Elderly patients who are able to tolerate curative treatment have special needs. In general, age is not a primary consideration for surgical risk. However, concurrent radiation therapy/chemotherapy should be used cautiously; dose modification of chemotherapy may be necessary. Chemotherapy can lead to problems such as neurotoxicity, cardiac toxicity, mucositis, that can be decreased or prevented by using specific recommendations from the NCCN Senior Adult Oncology Guidelines ([SAO-2](#)).

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