Assessing the Older Cancer Patient

By Martine Extermann, MD, PhD

ABSTRACT

As the American population ages, an increasing number of cancers will touch elderly patients. Already more than half of cancers occur in people over the age of 65. The health status of elderly patients can be highly variable, and the challenge for the oncologist is to reach an integrated understanding of each patient in order to design the most appropriate oncologic treatment. This article outlines several instruments and evaluation sets that can be used in the assessment of an older cancer patient, including one recently suggested by the National Comprehensive Cancer Network. It also describes the potential beneficial effects of comprehensive management on patient outcomes.

Oncology Spectrums 2001;2(6):395-403

INTRODUCTION

Aging is multidimensional, and changes in medical conditions, function, cognition, nutrition, and emotional and social support may influence the prognosis and treatment of cancer. Because these changes are often subtle and difficult to recognize, it is suggested that older individuals be screened for them routinely. The importance of a multidimensional assessment for older cancer patients is increasingly recognized, given the high prevalence of interrelated problems in this population.^{1,2} In an academic setting, 94% of patients aged 70 and over presented at least one comorbidity as measured by the cumulative illness rating scale-geriatric (CIRS-G), and 56% presented with a dependence in instrumental activities of daily living (IADL). This is often not captured by an Eastern Cooperative Oncology Group performance status (ECOG PS), since 80% of that same population had an ECOG PS of 0 or 1 (Table 1).3 In another study, women aged 70 and older with early breast cancer presented an average of six other problems requiring team intervention, and three more problems developed over a period of 6 months. Because such patients may be considered "lowrisk" oncologic patients, it may indicate that the prevalence of geriatric problems in the general cancer population is even higher. Hence, geriatric oncology focuses on a population whose general problems may interfere significantly with oncologic decision-making.

IMPORTANCE OF A MULTIDIMENSIONAL ASSESSMENT

A multidimensional assessment that screens for abnormality in multiple domains is key to the approach of older cancer patients. Comorbidity,⁵ functional status,⁶⁸ depression,^{69,10} cognitive impairment,⁶ nutritional status,¹¹ and insufficient social support¹² have all been demonstrated to affect survival of elderly and/or cancer patients, with relative risks of death often in the two- to fourfold range. Their impact on other variables such as treatment toxicity is less known and a subject of ongoing study (see below).

Geriatric problems are often underdetected without systematic screening. In a recent American study, an in-home yearly comprehensive geriatric assessment (CGA) detected at least one major problem that was unrecognized or suboptimally treated in 76.7% of older subjects. 13 An additional problem was detected in one third of the subjects every year after. New therapeutic or preventive recommendations were made each year in 11.5% of the subjects. As mentioned, older cancer patients can also have a significant number of concomitant geriatric problems.4 Geriatric studies have also shown that the various dimensions mentioned above interact to influence the prognosis and management of older patients. Interventions along multiple axes have better chances of success than interventions limited to one or two elements.14 Properly conducted geriatric interventions have produced thought-provoking results (Table 2). To be a good

EDUCATIONAL OBJECTIVE

Understand the importance of a comprehensive geriatric assessment of older cancer patients, and become familiar with the tools available to conduct such assessments, including the National Comprehensive Cancer Network guidelines.

TALKING POINTS Physicians Pharmacy Formulary Cancer Nurses

The guidelines for the assessment and management of older cancer patients recently published by the National Comprehensive Cancer Network are a useful resource for geriatric oncology.

Older cancer patients are at high risk of polypharmacy.

The problems encountered in geriatric oncology may interfere significantly with oncologic decision making.

A multidisciplinary team approach can aid in the detection of multiple problems in older cancer patients.

Dr. Extermann is assistant professor of oncology and medicine at the University of South Florida in Tampa. Acknowledgments: The authors report no financial, academic, or other support of this work.

basis for intervention, a multidimensional assessment needs to be done with reliable tools. We will review next a series of well-

CAOD patients (0/)

tested instruments that can be used. This is not an exhaustive review, but presents a set of instruments that are simple and reliable for use in geriatric oncology.

TABLE 1. PROFILE OF THE PATIENTS IN THE SENIOR ADULT ONCOLOGY PROGRAM AT H. LEE MOFFITT CANCER, A TERTIARY ACADEMIC CENTER

eristics SAOP patients (%		
_		

SAOP=Senior Adult Oncology Program; CIRS-G=cumulative illness rating scale-geriatric; ECOG PS=Eastern Cooperative Oncology Group performance status.

Extermann M. Oncology Spectrums. Vol 2. No 6. 2001.

TABLE 2. COMPARISON OF THE EFFECT OF COMPREHENSIVE GERIATRIC ASSESSMENT (CGA) WITH TWO WELL-ACCEPTED INTERVENTIONS

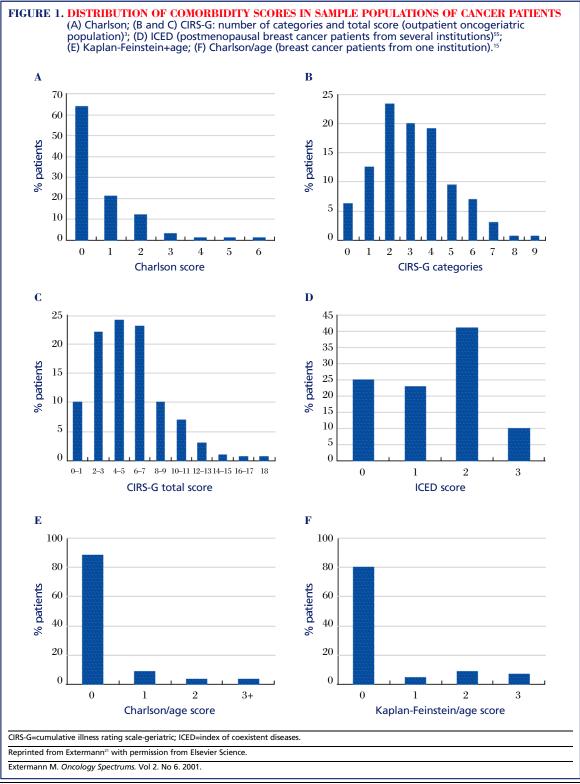
Setting, Intervention/Outcome of Interest	Risk Reduction
Elderly, CGA/not living at home	26%
Breast cancer, adjuvant chemotherapy/relapse	23.5%
Myocardial infarction, beta-blocker/new infarction	27%
Setting, Intervention	Mortality Reduction
Elderly, CGA	14%
Breast cancer, adjuvant chemotherapy	15.3%
Myocardial infarction, beta-blocker	22%
Note: All results are from long-term, statistically significant m Overall study results are presented.	ieta-analyses. ^{38,52,53}
Extermann M. Oncology Spectrums. Vol 2. No 6. 2001.	

COMORBIDITY

Comorbidity should be distinguished from functional status. Comorbidity is the ensemble of physical and psychological diseases that a patient has besides cancer. Functional status refers to a patient's ability to perform daily tasks. In several geriatric studies, functional status and comorbidity have had a low level of correlation.3 This is also the case for older cancer patients. Our group addressed this issue in a study of 203 older cancer patients who underwent a comprehensive geriatric evaluation by the senior adult oncology program (SAOP) at the H. Lee Moffitt Cancer Center.3 Comorbidity was measured with the Charlson comorbidity index15 and the CIRS-G.16 Functional status was measured with the ECOG PS,17 Katz's activities of daily living (ADL),18 and Lawton's IADL.19 Correlations between comorbidity and functional status were ranging from P=0.10 to P=0.27. Since tumor stage does not appear to correlate strongly with functional status either (P=0.13-0.20), function seems to reflect an independent or multifactorial aspect of a patient's health. Both comorbidity and function may independently affect the outcome and tolerance of chemotherapy in older cancer patients.

For example, in a recent cooperative Italian study, 59% of older lung cancer patients with an ECOG PS of 2 discontinued chemotherapy early, compared with 31% of patients with an ECOG PS of 0 or 1. Eighty-two percent of patients with a Charlson score of >2 discontinued treatment early, compared with 30% of those with a Charlson score of 2.20 Therefore, comorbidity and functional status need to be measured separately.

Measuring comorbidity is a complex, multidimensional task. The choice of the summary instrument has important quantitative and qualitative consequences on the measured prevalence of comorbidity. For example, in one of our studies, 36% of the patients had a comorbidity when assessed with the Charlson index, whereas 94% had a comorbidity on the CIRS-G scale (43% grade 3–4) (Fig. 1).21 The most frequent comorbidities, when assessed with the CIRS-G, were locomotive/tegumental problems (43%), vascular conditions (36%), genitourinary



"The Charlson scale focuses on a short list of selected diseases, and is aimed at simplicity. The CIRS-G is aimed at comprehensiveness, and allows ratings of all diseases encountered."

diseases (31%), cardiac conditions (30%), and breast and endocrine diseases (29%). On the Charlson index, the most frequent diseases were second tumor (10%) and diabetes (7%). Figure 1 also illustrates the wide variation in number of diseases and their severity among geriatric oncology patients.²¹

At the present time, studies comparing various comorbidity indexes and their predictive ability are few, especially in cancer patients.5 Further research using validated indexes is needed to allow meaningful comparisons. Our group has reviewed the most commonly used indexes in clinical studies, detailing their construction, clinical experience, metrological performance, ease of use, cross-compatibility, and preservation of data.21 These are the Charlson comorbidity index, the cumulative index rating scale, the Kaplan-Feinstein index, and the index of coexistent diseases. Some other indexes are being tested in an oncologic setting. Piccirillo and his group developed recently an extended version of the Kaplan-Feinstein index, the ACE 27, that warrants further testing.22 The Cancer and Leukemia Group B has been using the comorbidity list of the older Americans rating scale, which has been used in geriatric studies. However, the interrater and test-retest performance of this subscale appears somewhat lower than for the other indexes mentioned above.

Our group chose to test the performance of the Charlson scale and the CIRS-G in an academic oncogeriatric outpatient clinic. 3,23,24 These scales were selected because they are well defined and validated. Both have been used in several settings, with reliable results, and they represent two different approaches to comorbidity. The Charlson scale focuses on a short list of selected diseases, and is aimed at simplicity. The CIRS-G is aimed at comprehensiveness, and allows ratings of all diseases encountered. Both the Charlson and the CIRS-G scales showed very good interrater and test-retest reliability in oncogeriatric patients.²¹ For a trained rater, the Charlson takes 5 minutes to rate, while the CIRS-G takes 5-10 minutes, according to the number of comorbidities. In addition, the Charlson can be extracted from the CIRS-G, allowing concomitant rating in a few seconds more than rating the CIRS-G alone.

Although the global impact of comorbidity on survival is well demonstrated,⁵ much less is known on the relative impact of specific diseases or combinations of diseases on survival, treatment tolerance, and decision making in older cancer patients. Some data are available about the impact of specific conditions on certain drugs, such as renal clearance of carboplatin or methotrexate. Dutcomes such as treatment tolerance or quality of life are poorly amenable to retrospective study but they can be studied prospectively with well-validated tools. Diven the diversity of older cancer patients, progress can only be made if we prospectively gather coherent comorbidity data across studies that will be amenable to later crossstudy comparison and meta-analysis.

FUNCTIONAL STATUS

The ECOG or the World Health Organization PS score¹⁷ and the Karnofsky score²⁶ are the most widely used functional scores in oncology. The Karnofsky index has 11 levels while the ECOG PS has only 5, but both indexes appear to offer similar predictive performance.²⁷ Both scores have been effective predictors of outcome in multiple oncology studies. However, as shown in Table 1, their application to older cancer patients may be problematic and may underrepresent their degree of functional impairment. Geriatricians prefer to rate functional status by a patient's ability to perform specific tasks.

The most widely used scales are Katz's basic ADL (bathing, dressing, going to the bathroom, shifting position, and feeding),18 and Lawton's IADL (ability to use the telephone, shop, prepare food, keep house, do handyman work, do laundry, comply with a medication regimen, and handle finances).15 Lawton updated his scale because the initial shorter version had an important gender bias. Therefore the nine-items version should be used.19 The correlation between ECOG PS and ADL (P=0.51) or IADL (P=0.61) is moderate but not sufficient to allow substitution in cancer patients.3 Other well-validated scales of functional status in older people are the OARS functional scale 19,28 and the SF-36 PF/10.29 Geriatricians have studied multiple adaptations in the pooling and scoring of functional activities mentioned above, but none has gained wide acceptation. Our group uses Katz's six-item ADL and Lawton's nine-item IADL.

DEPRESSION

Oncologists misdiagnose depression about half of the time, usually by missing it,

especially if affective symptoms such as tears or expression of negative feelings are absent.30 Therefore, a screening tool is warranted. Several short tools have been tested in older patients.³¹ The geriatric depression scale (GDS) is a widely used one. In its short form, it comprises 15 yes or no questions that the patient answers.32 The GDS performs well in detecting major depression and it is the one we use in our program.³¹ It also has prognostic validity.6 Some other available instruments tested in the elderly are the longer 30-item original GDS, which is slightly more sensitive and specific, 31,33 the Center for Epidemiologic Studies Depression Scale (CES-D), $^{\scriptscriptstyle 31.34}$ the $\check{\rm B}{\rm eck}$ depression inveninvent tory,35 and the Zung self-rated depression scale.30,36 These scales are screening tools only, and, if positive, should be completed by an evaluation using standard psychiatric criteria (eg, the Diagnostic and Statistical Manual of Mental Disorders, 4th edition).

Mental Status

Like depression, cognitive disorders are underdiagnosed without screening. The assessment of mental status can be affected by several variables such as education, stress, etc. Therefore, the assessment needs to be done in two steps: a short, sensitive screening tool; and then a more elaborate battery of tests. The most commonly used screening tool in a general medical setting is Folstein's Mini Mental Status exam (MMS), which has a good ability to discriminate between depression and cognitive disorders.37 In our program, about one fifth of the patients screen positive for cognitive disorders (Table 1). If the screening is positive, we offer the patient the services of our psycho-oncology team for further evaluation. Given the availability of newtreatments for Alzheimer's disease, referral of patients to a memory disorders clinic or a geriatrician is important, especially if these disorders are minor and the cancer has a good prognosis. Also, supportive measures can greatly enhance the cognitive functioning of the patient and subsequently compliance.38

MEDICATIONS

A careful assessment of medications needs to be done, and a very effective method is to ask the patients to come in with their medication bottles. The prevalence of polypharmacy in the elderly is very high: 29% of our patients are taking seven or more different medications (Table 1).

These patients often have multiple physicians, and prescribing of two medications of the same class is frequent (eg, benzodiazepines, analgesics). Concomitant medications can significantly alter the outcome of chemotherapy.39 The interaction of allopurinol and 6-mercaptopurine is well known. Fluconazole increases the area under the curve of the tyrosine-kinase inhibitor STI 571 by 40%. The impact of medications, such as calcium channel blockers at a usual pharmacologic dosage, on multidrug resistance (MDR)-sensitive chemotherapy regimen's effectiveness and toxicity is not known. A careful review of dosage adjustments for renal function, based on calculated creatinine clearance, is warranted. A recent Canadian survey in older long-term care residents disclosed that, based on c reatinine clearance, 42.3% had received at least one inappropriate prescription.40

NUTRITION

The prevalence of malnutrition is high in older patients, and even higher in cancer patients (Table 1).41 It is often a topic of great concern for the patients and their caregivers. Nutritional status and dietary habits should be screened to prevent unwarranted complications of treatment with appropriate dietary advice or support structures. Specific screening tools can be used, such as the Mini-Nutritional Assessment (MNA), that performs well in geriatric populations. 42 In these patients, the MNA score has been correlated with several indicators, such as nutritional intake and anthropometric and biologic parameters of nutrition. 43 Close attention should be paid to maintaining good hydration during treatment. Due to a decreased thirst reflex, older patients are more likely than younger ones to experience dehydration secondary to nausea, vomiting, or diarrhea, especially if they have no close support.

SOCIAL SUPPORT

Older cancer patients are often partially dependent on a caregiver or are themselves caregivers for a dependent spouse or sibling. The impact of dependence in IADL, affecting 60% of older cancer patients, is highly modulated by the availability of close support from a personal or professional caregiver (transportation, meals, medications). For marned patients, notably, the spouse's health status can greatly alter the patient's ability to comply with treatment. For single patients,

"A recent Canadian survey in older long-term care residents disclosed that, based on creatinine clearance, 42.3% had received at least one inappropriate prescription."

support can be more problematic, especially in an era where family relatives, such as children, often live a long distance away. Recognizing early potential problems can lead to effective prevention measures and help maintain patients in an independent community setting. At the present time, the assessment of the quality of social support is essentially a qualitative assessment and there is no widely accepted tool for clinical practice that would allow evaluation of the "effectiveness" of a social support network.

PRACTICAL SUGGESTIONS TO EVALUATE OLDER CANCER PATIENTS

An overview of three approaches to consider for the assessment of older cancer patients in various clinical settings will conclude this review. For everyday practice in oncology, the National Comprehensive Cancer Network (NCCN) recently published a set of practical general guidelines for older patients with cancer.² A proposed screening panel is reproduced in Table 3. If the screening is positive, the patient can be referred to a

Realm	Screening	Confirmatory Test
Mental status	Serial 3: Tell patient "I am going to name three objects (pencil, truck, book) and I am going to ask you to repeat them now and a few minutes from now."	Folstein Mini-Mental Status If score <24, institute work-up for dementia
Emotional status/depression	Ask patient, "Do you often feel depressed or sad?"	Geriatric depression scale If positive (score >10), work-up for depression
Activities of daily living	Can you dress yourself? Do you need help going to the bathroom? Do you wet yourself? Can you eat without help? Can you move from one place to another without help? Do you need help taking a bath or a shower?	Formal Katz activities for daily living scale
Instrumental activities of daily living	Do you drive? Are you able to use public transportation? Do you prepare your own meals? Do you go shopping? Do you do your own checking? Can you call somebody with the telephone? Do you remember to take your medications?	Formal IADL scale
Home environment	Do you have trouble with stairs inside and outside the house? Do you trip often on rugs?	
Social support	Who would be able to help you in case of emergency?	If no caregiver, try to arrange for a caregiver; if the caregiver is a spouse, a sibling, or a friend of the same age as the patient, assess independence of the caregiver
Comorbidity	Evaluate the presence of the following conditions from ROS: congestive heart failure, coronary artery disease, valvular heart disease, chronic lung disease (obstructive or restrictive), cerebrovascular disease, peripheral neuropathy, chronic renal insufficiency, hypertension, diabetes, coexisting malignancies, collagen vascular disease, incapacitating arthritis	Confirm the presence of the condition and grade the seriousness
Nutrition	Weigh patient, measure height, inquire about weight loss	Mini-Nutritional Assessment
Polypharmacy	Review number and type of medications	If >3 medications, look for duplications, interactions, and compliance
NCCN=National Comprehensive Ca	ancer Network; IADL=instrumental activities of daily living; ROS=revie	ew of systems.
significant data becomes available treatment. Any clinician seeking circumstances to determine any pa ing their content, use or applicatic	ates' with permission and the following. "These guidelines are a variance. The NCCN guidelines are a statement of consensus of its authors regoon apply or consult any NCCN guideline is expected to use indepetient's care or treatment. The National Comprehensive Cancer Netwo and disclaims any responsibility for their application or use in any all rights reserved. These guidelines and illustrations herein may not be	jarding their views of currently accepted approaches to ndent medical judgment in the context of individua rk makes no warranties of any kind whatsoever regard way. These quidelines are copyrighted by the Nationa

geriatrician, if available, or the work-up can be extended. A complete history and physical examination should be done, including psychiatric history, as well as a formal assessment of orientation in time and space, short-term memory (three items recall), and visual and hearing problems. Special attention should be paid to nutrition and medications, including nonprescription drugs. Creatinine clearance should be measured and drug doses adjusted if necessary. Before any chemotherapy, creatinine clearance should be recorded on the patient's chart because numerous chemotherapy agents have to be modified according to renal clearance (Table 4). A detailed assessment of the patient's social resources should also be done. The opinion of the patient, even when suffering from dementia, should be sought when feasible, as proxy evaluation by family or physicians has a low correlation.44-47

Another approach is cooperative research. Cooperative groups have long been looking for better ways to integrate older patients into their studies.48 As pointed out, ECOG PS is a poor indicator of an older patient's health and functioning: 80% of them score 0 or 1, whereas more than 90% have comorbidities. Also, less than half are independent per the IADL. Cooperative studies have so far provided few clues as to how valid their results are in patients in suboptimal health. To obviate this, cooperative groups have been working on integrating more elaborate measures of function and comorbidity in the assessment of their elderly patients. Ideally, some standard package should be developed, that would allow cross-study comparisons. This package should offer a wide-spectrum overview of the patient's health, take approximately 15 minutes to administer, and be easily manageable by research nurses. Such a package would also help us learn more on the interactions of comorbidity with cancer treatment.

The last suggestion, for centers with the ability and the will to develop a full geriatric oncology program, is to set up a multidisciplinary CGA. In geriatrics, a CGA including a follow-up intervention can improve both detection of a significant number of geriatric problems and function, cognition, and survival. 38 Although we do not know how fully these results transfer to cancer patients, geriatric results certainly warrant further investigation (Table 2). As we have shown, the potential for intervention in cancer patients

is high.4 Our team uses a nurse, a dietician, a pharmacist, a social worker, a nurse practitioner, and an oncologist.49 Nurse practitioners are often key persons in CGAs. The complete initial visit lasts 2.5 hours, which is usually well tolerated provided the patients are advised in advance of the duration. In our opinion, several 15-minute assessments with different team members are much better tolerated than a long visit with one person. Another possible model is the one used in Lyon, France, where a geriatrician sees the patient in the oncology clinic for a screening assessment. If the patient warrants further geriatric testing, he/she is given an appointment with the geriatric hospital for a full multidisciplinary assessment. This kind of approach is, however, limited to major cancer centers or centers cooperating with a geriatric division. It should include a strong element of research, since a multidimensional assessment can only be done prospectively, and its detailed impact on cancer treatment is still largely unexplored.

TABLE 4. MODIFICATIONS OF CHEMOTHERAPY DRUGS DOSAGE ACCORDING TO RENAL CLEARANCE (% REGULAR DOSE)

	CrCl (mL/min)		
	60	45	30
Renal Excretion			
Bleomycin	0.70	0.60	NR
Carboplatin	Calvert's formula		
Carmustine	0.80	0.75	NR
Cisplatin	0.75	0.50	NR
2-CDA	NE		
Cytarabine*	0.60	0.50	NR
Dacarbazine	0.80	0.75	0.70
Fludarabine	0.80	0.75	0.65
Hydroxyurea	0.85	0.80	0.75
Idarubicin	NE		
Ifosfamide	0.80	0.75	0.70
Melphalan	0.65	0.50	NR
Methotrexate	0.85	0.75	0.70

Hepatic Excretion

Doxorubicin

Daunorubicin

Epirubicin

Vinca alkaloids

Taxanes

Mixed Excretion

Epipodophyllotoxins Mitomycin-C

*High-dose cytarabine.

CrCl=creatinine clearance; NR=not recorded; NE=not established

Reprinted from Cancer. 1997;80(7):1317-1322, with permission from Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc. © 1997 American Cancer Society.

Extermann M. Oncology Spectrums. Vol 2. No 6. 2001.

"...as the oncologic population ages, oncologists will have to become increasingly familiar with the integration of geriatric tools in the multidimensional evaluation and treatment of their patients."

RESEARCH ISSUES

Given its potential for improving independence and survival (Table 2), as well as its cost-effectiveness in the geriatric setting. CGA should be thoroughly investigated in cancer patients. Geriatric studies have shown that to be truly effective, the CGA needs to be more than a "one-time" intervention, and has to integrate a comprehensive follow-up. 14,38,50 The best way of implementing such an approach in cancer patients is being explored. The early results of our research have shown that patients present numerous problems that need to be addressed in a comprehensive way.4 A better identification of patients at risk of complications is also a primary research goal. Several approaches are under investigation, such as pharmacology during the first cycle, body composition analysis, and predictive scores for toxicity of chemotherapy. These may be integrated in the future into the assessment of older patients.

In conclusion, as the oncologic population ages, oncologists will have to become increasingly familiar with the integration of geriatric tools in the multidimensional evaluation and treatment of their patients. The integration of elements such as comorbidity status can significantly influence treatment choices, eg, in the adjuvant setting for early breast cancer patients. The NCCN guidelines mentioned above constitute a practical starting point to be developed as research progresses.

REFERENCES

- Yancik R, Wesley MN, Ries LA, et al. Comorbidity and age as predictors of risk for early mortality of male and female colon carcinoma patients: a population-based study. Cancer. 1998;82:2123-2134.
- Balducci L, Yates J. General guidelines for the management of older patients with cancer. NCCN Proceedings. Oncology. 2000;14:221-227.
- Extermann M, Overcash J, Lyman GH, Parr J, Balducci L. Comorbidity and functional status are independent in older cancer patients. J Clin Oncol. 1998;16:1582-1587.
- Balducci L, Extermann M, Meyer J, et al. Comprehensive follow-up for older breast cancer patients: a pilot study [abstract 3008]. Proc Ann Mtg Am Soc Clin Oncol. 2001
- Extermann M. Measurement and impact of comorbidity in older cancer patients. Crit Rev Oncol/Hematol. 2000;35:181-200.
- Inouye SK, Peduzzi PN, Robison JT, Hughes JS, Horwitz RI, Concato J. Importance of functional measures in predicting mortality among older hospitalized patients. JAMA. 1998;279:1187-1193.
- Finkelstein DM, Ettinger DS, Ruckdeschel JC. Longterm survivors in metastatic non-small cell lung cancer: an Eastern Cooperative Oncology Group Study. J Clin

- Oncol. 19864:702-709.
- Keller BK, Potter JF. Predictors of mortality in outpatient geriatric evaluation and management of clinic patients. J Gerontol. 1994;49:M246-M251.
- Murphy E, Smith R, Lindesay J, Slattery J. Increased mortality rates in late-life depression. Br J Psychiatry. 1988:152:347-353.
- Ganzini L, Smith DM, Fenn DS, Lee MA. Depression and mortality in medically ill older adults. J Am Geriatr Soc. 1997:45:307-312.
- Lobato-Mendizabal E, Ruiz-Arguelles GJ, Marin-Lopez A. Leukemia and nutrition I: malnutrition is an adverse prognostic factor in the outcome of treatment of patients with standard-risk acute lymphoblastic leukemia. *Leuk* Res. 1989;13:899-906.
- Ell K, Nishimoto R, Mediansky, Mantell J, Hamovitch M. Social relations, social support and survival among patients with cancer. J Psychosom Res. 1992;36:531-541.
- Alessi CA, Stuck AE, Aronow HU. The process of care in preventive in-home comprehensive geriatric assessment. *J Am Geriatr Soc.* 1997;45:1044-1050.
- Gillepsie LD, Gillepsie WJ, Cumming R, Lamb SE, Rowe BH. Interventions to reduce the incidence of falling in the elderly. *The Cochrane Database of Systematic Reviews*. 1998;3. Accessed at: http://www.cochrane.co.uk
- Charlson ME, Pompei P, Ales K, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis.* 1987;40:373-383.
- Miller MD, Paradis CF, Houck PR, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. *Psychiatry Res.* 1992.41:237-248.
- Zubrod CG, Schneiderman M, Frei E III, et al. Appraisal of methods for the study of chemotherapy in man: comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. J Chron Dis. 1960;11:7-33.
- Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardzed measure of biological and psychosocial function. JAMA. 1963;185:94-99.
- Lawton MP. Scales to measure competence in everyday activities. Psychopharmacol Bull. 1988;24(4):609-614,789-791.
- Frasci G, Lorusso V, Panza N. Gemeitabine plus vinorelbine versus vinorelbine alone in elderly patients with advanced non-small-cell lung cancer. J Clin Oncol. 2000;18:2529-2536.
- Extermann M. Measuring comorbidity in older cancer patients. Eur J Cancer. 2000;36:453-471.
- Bang D, Piccirillo J, Littenberg B, Johnston A. The Adult Comorbidity Evaluation-27 (ACE-27) test—a new comorbidity index for patients with cancer. Proc Am Soc Clin Oncol. 2000:19:434a.
- Extermann M, Chen H, Cantor AB. Predictors of toxicity from chemotherapy in older patients: a prospective pilot study. Abstract 2430: American Society of Clinical Oncology, New Orleans, La: May 2000. ASCO virtual meeting: http://www.conference-cast.com/ asco/vm2000/post_2403_2452.htm
- Overcash J, Extermann M, Parr J, Perry J, Balducci L. Validity and reliability of the FACT-G scale for use in the older person with cancer. Am J Clin Oncol. In press.
- Cova D, Beretta G, Balducci L. Cancer chemotherapy in the older patient. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. 2nd ed. Amsterdam, Netherlands: Hardwood Academic Publishers; 1998:429-442.

- Karnofsky DA, Abelmann WH, Craver LF, et al. The use of the nitrogen mustards in the palliative treatment of carcinoma. Cancer. 1948;1:634-656.
- Buccheri G, Ferrigno D, Tamburini M. Karnofsky and ECOG performance status scoring in lung cancer: a prospective, longitudinal study of 536 patients from a single institution. Eur J Cancer. 1996;32A:1135-1141.
- Fillenbaum GG. Screening the elderly. A brief instrumental activities of daily living measure. J Am Geriatr Soc. 1985;33:698.
- Ware JE, Sherbourne CD. The MOS-36 items Short Form Health Survey (SF-36): I. Conceptual framework and item selection. Med Care. 1992;30:473-483.
- Passik SD, Dugan W, McDonald V, Rosenfeld B, Theobald DE, Edgerton S. Oncologists' recognition of depression in their patients with cancer. J Clin Oncol. 1998;16:1594-1600.
- Lyness JM, Noel TK, Cox C, King DA, Conwell Y, Caine ED. Screening for depression in elderly primary care patients. A comparison of the Center for Epidemiologic Studies-depression scale and the geriatric depression scale. Arch Intern Med. 1997:157:449-454.
- Sheikh JJ, Yesavage JA. Geriatric depression scale (GDS): recent evidence and development of a shorter version. In: Brink TL, ed. Clinical Gerontology: A Guide to Assessment and Intervention. New York, NY: Haworth Press; 1986:165-173.
- Yesavage J, Brink T, Rose T, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res. 1983;7:37-49.
- Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Ann Psychol Measure. 1992;7:343-351.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry. 1961:4:53-63.
- Zung WW, Richards LB, Short MJ. Self-rating depression scales in an outpatient clinic: further validation of the SDS. Arch Gen Psychiatry. 1965;13:508-515.
- Folstein MF, Folstein SE, McHugh PR. "Mini Mental State." A practical method for grading the cognitive status of patients for the clinician. J Psychiatr Res. 1975;12:189-198.
- Stuck AE, Siu AL, Wieland D, Adams J, Rubenstein IZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. *Lancet.* 1993;342:1032-1036.
- Relling MV, Pui CH, Sandlund JT, et al. Adverse effect of anticonvulsivants on efficacy of chemotherapy for acute lymphoblastic leukemia. *Lancet.* 2000;356:285-290.
- Papaioannou A, Clarke JA, Campbell G, Bédard M. Assessment of adherence to renal dosing guidelines in longterm care facilities. J Am Geriatr Soc. 2000;48:1470-1473.
- Hudson J. Nutrition, cancer and aging. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. 2nd ed. Amsterdam, Netherlands: Harwood Academic Publishers; 1998:301-306.

- Guigoz Y, Vellas B, Garry PJ. Mini Nutritional Assessment: a practical assessment tool for grading the nutritional state of elderly patients. Facts Research and Intervention in Geriatrics 1997. Serdi Publishing Company; 1997(suppl):15-60.
- Vellas B, Guigoz Y, Baumgartner M, Garry PJ, Lauque S, Albarede JL. Relationships between nutritional markers and the Mini-Nutritional Assessment in 155 older persons. J Am Geriatr Soc. 2000;48:1300-1309.
- Robinson BE, Balducci L. Breast lump in an 85-year old woman with dementia: a decision analysis. J Am Geriatr Soc. 1995;43:282-285.
- Slevin ML, Plant H, Lynch D, Drinkwater J, Gregory WM. Who should measure quality of life, the doctor or the patient? Br J Cancer. 1988;57:109-112.
- Pearlman RA, Uhlman RF. Quality of life in chronic diseases: perceptions of elderly patients. J Genotol. 1988;43:M25-M30.
- Tsevat J, Cook EF, Green ML, et al. Health values in the seriously ill. Ann Intern Med. 1994;122:514-520.
- Hutchins LF, Unger JM, Crowley JJ, Coltman CA, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med. 1999;341:2061-2067.
- Overcash J. The case for a geriatric oncology program in a cancer center. In: Balducci L, Lyman GH, Ershler WB, eds. Comprehensive Geriatric Oncology. 2nd ed. Amsterdam, Netherlands: Harwood Academic Publishers; 1998:813-824.
- Reuben D, Franck J, Hirsch S, McGuigan K, Maly R. A randomized clinical trial of outpatient Comprehensive Geriatric Assessment (CGA) coupled with an intervention to increase adherence to recommendations. J Am Geriatr Soc. 1999;47:269-276.
- Extermann M., Balducci L, Lyman GH. What threshold for adjuvant therapy in older breast cancer patients? *J Clin Oncol*. 2000;18:1709-1717.
- Early Breast Cancer Trialists' Collaborative Group.
 Polychemotherapy for early breast cancer: an overview of the randomised trials. *Lancet*. 1998;352:930-942.
- Yusuf S, Wittes J, Friedman L. Overview of results of randomized clinical trials in heart disease. *JAMA*. 1988:260:2088-2093.
- Balducci L, Extermann M. Cancer chemotherapy in the older person: what the medical oncologist needs to know. *Cancer*. 1997;80:1317-1322.
- Greenfield S, Blanco D, Elashoff RM, Ganz P. Patterns of care related to age of breast cancer patients. *JAMA*. 1987:257:2766-2770.