



Paul Gauguin. *Three Tahitians*, 1899. Oil on canvas.

Geriatric assessments can help define the prognosis of older individuals with cancer and may influence treatment choices and outcomes.

Studies of Comprehensive Geriatric Assessment in Patients With Cancer

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Background: *The comprehensive geriatric assessment (CGA) has been developed to individually assess the health status of older patients.*

Methods: *This article reviews the findings regarding the impact of a comprehensive geriatric assessment (CGA) on treatment and outcomes in patients with cancer.*

Results: *Several geriatric variables have been linked with the prognosis of older cancer patients, thus challenging the role of ECOG performance status in this population. A CGA may detect multiple untreated or undertreated problems in cancer patients. Although results are preliminary, some studies suggest that CGA may influence cancer treatment decisions and have a prognostic impact on patients with this disease.*

Conclusions: *More work is needed to simplify such assessments to make them more feasible and to determine when they should be used during a patient's clinical course.*

Introduction

The health status of older patients is variable; some elderly individuals experience few age-related limitations in their daily lives, while others are faced with

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multiple comorbidities, reduced resources, and social isolation. To globally assess the health status of their patients, geriatricians have devised the comprehensive geriatric assessment (CGA), including an interdisciplinary intervention, to comprehensively address the patient's clinical, psychologic, and social problems. The design and impact of the CGA are discussed in the previous article in this issue; this article reviews the value and results from CGA in elderly patients who have cancer. Although patients with cancer have been included in the population of most geriatric studies of CGA, they rarely have been analyzed separately, and if so, the investigation was done only in a retrospective subgroup analysis.¹ As oncologists approach the care of

their elderly patients with specific therapeutic issues in mind, a legitimate question is how the findings of a CGA can influence and guide cancer treatment.

Prevalence of Geriatric Problems in Older Cancer Patients

In the early 1990s, older cancer patients seen in academic centers were often perceived as a select group of particularly healthy elderly individuals (other than their cancer). Some support for this perception can be found. Oncologists often use the Eastern Cooperative Oncology Group (ECOG) performance status to characterize the functional status of their patients. In an academic service, 80% of patients aged 70 and older had an ECOG performance status of 0 or 1.² Some prospective cohort data also indicate that cancer patients have less comorbidity than their noncancer counterparts. Repetto et al³ assessed cohorts of younger and older cancer patients, as well as older noncancer patients, and reported that 44% of cancer patients aged 70 or more had more than two comorbidities, compared with 90% of the noncancer elderly and 43% of younger cancer patients. Functionally, 82% of the older cancer patients had an ECOG performance status of 0 or 1, compared with 31% and 97% for the noncancer elderly patients and the younger patients, respectively. However, further analysis using more sensitive geriatric evaluation tools such as Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), Geriatric Depression Scale (GDS), or Mini-Mental State Examination (MMS) may reveal a different picture. In fact, the incidence of health problems in older cancer patients is high, and this figure is stable across different settings (Table 1).

The prevalence of functional limitations in older cancer patients is actually twice as high as that reported in large cohorts of community-dwelling elderly.^{2,7} This high prevalence represents a significant benefit from screening since many geriatric problems may be undetected by the usual medical or oncologic examinations. For example, a standard medical examination recognizes dementia in less than half of patients with the disorder.⁸ In a study by Passik et al⁹ of 1,109 cancer patients who completed the Zung Self-Rating Depression Scale, 159 patients rated themselves as moderately to severely depressed, while 78 of them were classified by their oncologists as having no symptoms of depression. Only 20 patients were appropriately classified as to the severity of their depression. As more results from geriatric oncology studies become available, it is becoming apparent that the health status of older cancer patients seen in oncology practices is similar to that in an age-matched general population.

Impact of a Comprehensive Geriatric Assessment in Cancer Patients

To date, three aspects have been explored in studies that have addressed the effect of a CGA in cancer patients: (1) the detection of geriatric problems, (2) the prognostic value of geriatric variables, and (3) the therapeutic impact of a CGA.

The first aspect, the detection of geriatric problems, is also the best documented. In the general geriatric setting, four randomized, controlled trials all found that CGAs detected multiple previously unknown or suboptimally treated problems, compared to the control arm of regular care.¹⁰⁻¹³ Table 1 presents profiles of geriatric problems in targeted oncology populations as assessed by various CGAs.^{4,6} The more specific question is, "How many of these problems would have been otherwise unaddressed?" At our institute, we conducted a pilot study of a CGA intervention in older patients (median age = 79 years) with early breast cancer.¹⁴ Patients were assessed every 3 months with a CGA by a multidisciplinary team, and they received a monthly telephone call from the team's nurse practitioner. In addition, specific follow-up by the team was implemented, according to the problems detected. This intervention detected an average of six unaddressed or underaddressed

Prevalence of Geriatric Problems in Older Patients With Cancer

| | Extermann and Aapro ⁴ | Repetto ⁵ | Ingram et al ⁶ |
|-----------------------------|----------------------------------|-------------------------|---------------------------|
| Age (yrs) | 75 (median) | 72.7 (mean) | 67.7 (mean) |
| ECOG performance status 0-1 | 83.2% | 68% | |
| ADL independent | 78.8% | 83.2% | 31% |
| IADL independent | 43.8% | 62% (or 1 dependent) | 42% |
| GDS positive | 26% | 44.6% | HADS 14%-26% |
| MMS <26 | 25% | 33.3% (<24) | |
| Charlson scale = 0 | 64% | | |
| CIRS-G = 0 | 6% | | |

ECOG = Eastern Cooperative Oncology Group performance status
 ADL = Activities of Daily Living
 IADL = Instrumental Activities of Daily Living
 GDS = Geriatric Depression Scale
 MMS = Mini-Mental State Examination
 CIRS-G = Cumulative Illness Rating Scale-Geriatric
 HADS = Hospital Anxiety and Depression Scale

problems at the initial examination and an average of three new problems over the following 6 months. Examples of such problems are shown in Table 2.

The second aspect is the prognostic value of geriatric variables in cancer patients.¹⁵⁻¹⁷ In a French cooperative prospective trial of older patients with ovarian cancer, predictors of toxicity included depression, lack of autonomy, and ECOG performance status of 2 or worse. Shorter survival was associated with depression, polypharmacy, and stage IV according to the International Federation of Gynecology and Obstetrics (FIGO) staging system.¹⁶ In this study, polypharmacy may have been a surrogate indicator of comorbidity. An Italian cooperative study examined whether IADL and ADL measures added to the predictive ability of ECOG performance status in older cancer patients.¹⁷ In a multivariate model adjusting for ECOG performance status (among others measures), patients with dependence in ADL had a hazard ratio of dying of 1.96 (95% confidence interval [CI]: 1.33–2.94); with dependence in IADL, the ratio was 1.49 (95% CI: 1.09–2.04). In a prospective pilot study conducted at our institute, patient parameters that were associated with toxicity

from chemotherapy included polypharmacy, elevated diastolic blood pressure, bone marrow invasion, previous chemotherapy, elevated lactate dehydrogenase level, and high body mass index.¹⁵ Interestingly, no functional measure was predictive in this small sample of 60 patients. Thus, several of these studies suggest that despite its well-established predictive record in oncology, ECOG performance status may be suboptimal as a predictor of outcomes in the elderly.

Emerging reports are beginning to address the third issue: the therapeutic impact of a CGA in cancer patients. The largest trial, and to our knowledge the only randomized trial, was published in 2000 by McCorkle et al.¹⁸ Three hundred seventy-five cancer patients aged 60 to 92 years undergoing surgery for various types of tumors were randomized to either usual postoperative care or a 1-month geriatric intervention consisting primarily of three home visits and five telephone calls by geriatric nurse practitioners. Both the patients and their families received CGAs. Survival analysis was stratified by stage of cancer (localized vs advanced). Overall, the specialized home care intervention group lived longer ($P=.002$). Patients with early-stage disease showed no survival difference between the two arms, whereas patients with advanced-stage disease in the intervention group lived longer (Figure). The 2-year survival for the late-stage intervention group was 67% compared with 40% among control cases. It is noted that there was an imbalance against the intervention arm since more patients with advanced-stage disease were randomly allocated to this arm. In a Cox regression model, treatment group, stage of disease, and length of initial hospital stay were associated with survival, whereas age, race, depressive symptoms, symptom distress, and enforced social dependency were not.

Bernardi et al¹⁹ recently described the preliminary results of an ongoing trial using CGA to tailor the treatment of patients with lymphoma. Patients aged 70 and older who were not considered frail were stratified into two arms: those with an ADL and IADL score of at least 5 received normal treatment, and those 80 years of age and older or whose IADLs were below 5 received 75% of the planned dose. To date, the investigators have treated 23 patients with reasonable efficacy and toxicity. None of 19 fully evaluable patients had grade 4 toxicity, and 79% had complete responses. In a retrospective subgroup analysis of a large randomized study of 99 cancer patients in 11 Veterans Affairs medical centers,²⁰ Rao et al¹ identified a significant effect on pain management in older cancer patients who received care in a GEM unit, with a sustained effect at repeated assessments over 1 year. Length of hospitalization and costs were no different than with

Table 2. — Types of Active Problems Requiring Team Intervention Encountered in 11 Elderly Breast Cancer Patients*

| Problem | Number** |
|--|----------|
| Functional (dependence, including significant fatigue) | 6 |
| Mental (cognitive, depression, anxiety, insomnia) | 10 |
| Social support, financial | 8 |
| Medications (dosage, schedule, adverse drug events) | 21 |
| Nutritional, including supplements (malnutrition, fluid intake, constipation) | 18 |
| Medical, noncancer | 21 |
| Cancer | 11 |

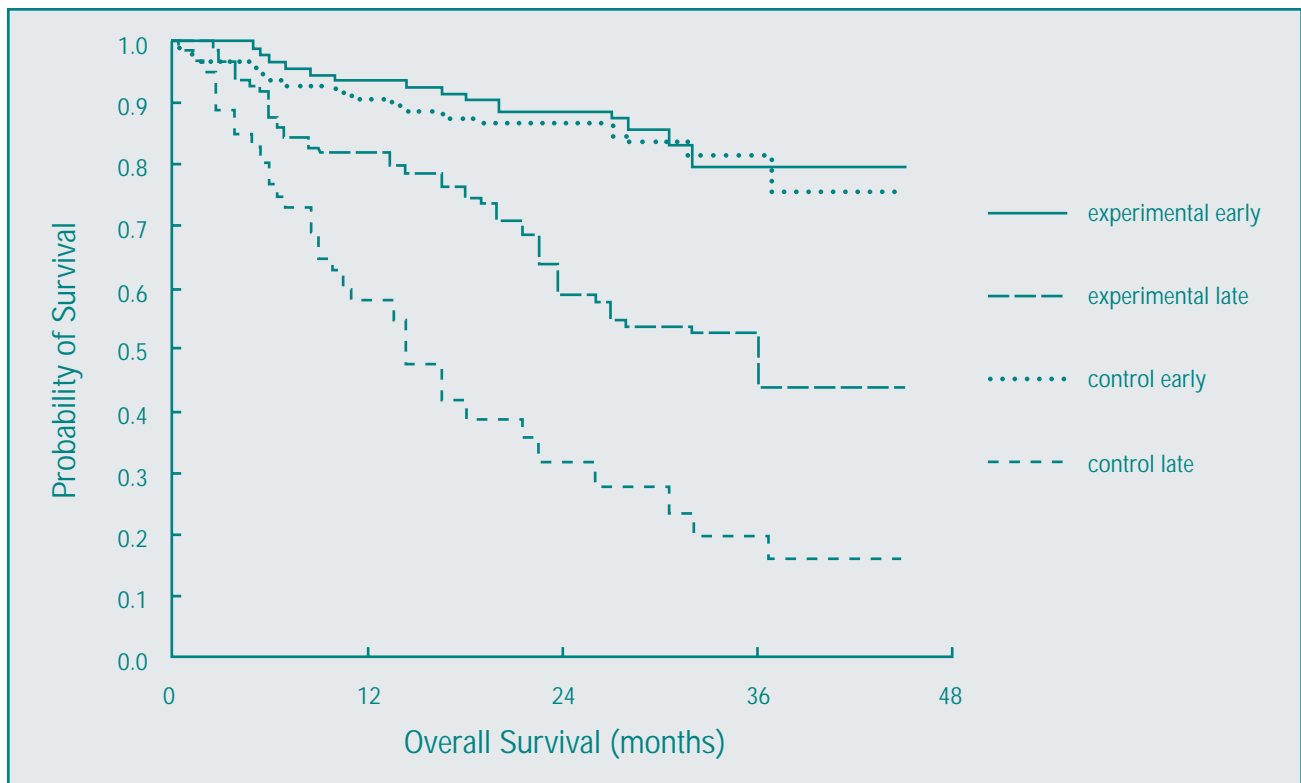
Examples of intervention results:

- Modification in chemotherapy decision in an 83-year-old patient with memory problems
- Detection of incorrect filling of paroxetine prescription (4 × planned dose)
- Increase in compliance with adjuvant hormonal therapy (including 1 patient on study)
- Family counsel to control medications, with subsequent improvement in mental status

* Problems already satisfactorily addressed were not counted (eg, correctly treated comorbidity).

** Some patients had more than one disorder.

From Extermann M, Meyer J, McGinnis M, et al. Comprehensive geriatric intervention detects multiple problems in older breast cancer patients. *Crit Rev Oncol Hematol*. Epub July 9, 2003. Reprinted with permission by Elsevier Science.



Impact of a geriatric intervention (experimental arm) on the survival of older patients with early- or late-stage cancer. From McCorkle R, Strumpf NE, Nuamah IF, et al. A specialized home care intervention improves survival among older post-surgical cancer patients. *J Am Geriatr Soc.* 2000;48:1707-1713. Reprinted with permission by Blackwell Publishing.

usual care. Mortality was unaffected, which is consistent with results in the overall trial.

Our own program¹⁵ also evaluated interventions to address the problems detected by CGA. Over a 6-month period, patients underwent an average of 17 team interventions that varied from simple counseling to complex interventions that included the entire patient family. In 4 of 11 patients who had complete follow-up, the intervention influenced the oncologic treatment itself (Table 2).

Although these studies are small, they suggest a potential for interaction between a CGA and oncologic treatment. Thus, it seems appropriate to continue efforts to implement geriatric interventions in the oncology setting.

Experience Using a Comprehensive Geriatric Assessment in Older Cancer Patients

Pioneer groups in geriatric oncology have implemented a CGA in different ways.^{6,18,21} Since 1994, our institute has implemented a multidisciplinary geriatric assessment of every new patient age 70 and older seen in the Senior Adult Oncology Program outpatient clinic.²¹

The patient is seen by the primary nurse, a nurse practitioner who administers the core geriatric assessment, a dietitian, a social worker, and a pharmacist. The case is summarized for the oncologist, who then meets with the patient. A weekly team meeting allows a more thorough interdisciplinary review and completes the treatment plan. In the last year, we have assessed screening tools that would allow extending access to the geriatric assessment to other services within our institute. The primary nurse administers a short screening. If positive, the nurse practitioner proceeds with a more detailed CGA and, if necessary, refers the patient for a team consultation in the Senior Adult Oncology Program.

Ingram et al⁶ tested a different approach to CGA by mailing a set of questionnaires to the homes of 266 male oncology outpatients at the Durham Veterans Affairs Medical Center. The questionnaires addressed functional status, comorbidity, pain, financial and social issues, emotional status, spiritual issues, and quality of life. Three quarters of the patients kept their clinic appointments. Of these, 76% returned the questionnaires. The profile of this population is shown in part in Table 1. In the randomized trial by McCorkle et al,¹⁸ geriatric nurse practitioners conducted in-home CGAs to patients who had been treated surgically. The intervention included three home visits and five telephone calls over 1 month.

At the Centre Léon Bérard, Lyon, France, a geriatrician administers a screening CGA in the oncology clinic for every new older patient at first visit. If the screening is positive, the patient undergoes a full outpatient geriatric evaluation by the geriatric service (Catherine Terret, personal communication, August 2003). In Italy, several centers are utilizing a core oncogeriatric assessment set administered by a physician.²² Numerous other programs in both Europe and North America are now attempting to implement at least partial CGAs.

Several geriatric oncology programs have recently explored screening models that might allow community usage. Our group tested the Lachs screening tool proposed in the guidelines of the National Comprehensive Cancer Network (NCCN).²³ Although this includes some screening for nutritional problems and, to some degree, for psychosocial problems, it is insensitive for functional limitations and has not allowed us to effectively engage the geriatric team. We are now studying an internally designed tool to determine whether team involvement can be improved. At the Institut Paoli-Calmettes in Marseille, France, a short screening is administered by the clinic staff. If the screening is "moderately positive," the patient is seen by a geriatrician in consultation in the clinic. If the screening is "strongly positive," the patient is referred to the geriatric department for a complete evaluation. Patients at risk receive a comprehensive geriatric preparation by the geriatricians prior to their chemotherapy (Anne-Chantal Braud, MD, personal communication, August 2003).

A key aspect in the effectiveness of a CGA intervention is follow-up,²⁴ an area that needs further development in geriatric oncology. The intervention by McCorkle et al¹⁸ included a twice-weekly intervention for 1 month. In our pilot study, we used a repeated interdisciplinary evaluation and telephone phone calls. While this approach detected several problems and helped in implementation of the recommendations,¹³ it proved burdensome in an oncology setting. The challenge is to develop an effective follow-up system that is leaner and more feasible. Implementing such a system of CGA will necessarily increase staff time, but several geriatric studies have shown a CGA to be cost-effective, even in an HMO setting.²⁵ To our knowledge, no specific cost-effectiveness study of CGA has been conducted solely in cancer patients.

Experience From Cooperative Study Groups

Geriatric instruments and parameters have been successfully incorporated into cooperative trials. These instruments usually include a detailed functional assess-

ment, depression and dementia screening tools, and recording of comorbidity, and they often include assessment of nutritional status and quality of life. Some studies are already published,^{16,22,26,27} and others are in progress. A study by the Radiation Oncology Cooperative Group (RTOG 0213), for example, is targeting lung cancer patients who are unable to tolerate combined chemoradiation therapy. They receive celecoxib and radiation therapy and are screened for IADLs, comorbidity, depression, mental status, and nutrition. Similar parameters are also being assessed in an adjuvant trial (CALGB 49907) for older patients with breast cancer in which capecitabine is being compared with doxorubicin and cyclophosphamide or with cyclophosphamide, methotrexate, and fluorouracil. Several other studies are being designed in Europe and the United States.

What Does the Future Hold?

As oncologists and geriatricians have become more convinced of the feasibility and potential impact of a CGA in oncology, the need for a thorough review of evidence from that perspective arose. The International Society of Geriatric Oncology has created a CGA task force composed of 4 oncologists and 4 geriatric specialists to systematically review the evidence along four key questions: (1) Are there definitions or stages of aging that could be helpful for the oncologist? (2) What does a CGA detect that is not detected by a regular oncological/medical assessment? (3) What is the evidence that CGA changes outcomes in the geriatric population and in older cancer patients, and what are the keys to its effectiveness? (4) What is the validity of proposed shorter screening tools and alternative assessments compared with a full multidisciplinary CGA? A report answering these questions is expected soon.

Results from the cooperative group trials previously mentioned not only will contribute to our knowledge of the various issues that determine the prognosis of our elderly patients, but also should facilitate the transfer of the results to the general population of older cancer patients.²⁶

Another direction of research is the development of a screening tool to help the oncologist easily conduct an initial categorization of patients. A screening strategy has proven successful even in busy settings such as emergency departments.^{28,29} This augurs well for the design of a similar approach for patients with cancer.

As cancer in the elderly represents a major epidemiological issue, funding agencies have developed several initiatives to provide research funds in this area. Several grant-funding opportunities from the National

Institutes of Health (<http://www.nia.nih.gov/data/fundbrowse.asp>) include PA-02-169 (Integrating Aging and Cancer Research), PA-00-001 (Aging Women and Breast Cancer), PAR-03-056 (National Institute on Aging Pilot Research Grant Program). A planning grant (P20) has also been issued that encourages comprehensive cancer centers to develop geriatric oncology programs. In Europe, similar targeted grants are proposed by the European Union, the French Association pour la Recherche contre le Cancer, the Swiss Bridge program, and others.

Conclusions

Specific information on the comprehensive assessment of older cancer patients has begun to appear in recent years. A CGA has the potential to directly affect cancer care and is being included in several multicenter trials. Its integration in the clinical oncology setting should be actively pursued. Presently, the CGA format is often dependent on the available staff resources structure. As evidence accumulates, other assessment models and guidelines designed specifically for the cancer population will become available.

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