Handbook of Geriatric Oncology
Handbook of Geriatric Oncology

Practical Guide to Caring for the Older Cancer Patient

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Foreword

The *Handbook of Geriatric Oncology* arrives at an optimal time for the practicing physician, as the number of older adults with cancer is on a steep rise globally. This growth in the number of older adults with cancer, which is a result of aging of the worldwide population and the association of cancer with aging, coincides with an anticipated workforce shortage in both oncology and geriatrics. Hence, care of the older patient with cancer is now the “bread and butter” of not only oncologists and geriatricians, but also primary care providers, subspecialists, and members of the multidisciplinary team. However, training in geriatric oncology is often not a standard component of medical education. Nevertheless, health care providers need to be armed with the latest data on how to optimize and embrace the complexity of care in the older cancer patient. Dr Beatriz Korc-Grodzicki (geriatrician) and Dr William Tew (medical oncologist), leading experts in the field of geriatric oncology, join forces to address this need by providing a *Handbook of Geriatric Oncology* that serves as a key reference for oncologists, geriatricians, and other health care providers caring for an aging population with cancer.

One might ask, “What makes care of older adults with cancer different from any other patient?” The answers to that question are clearly elucidated in this book, which weaves together the best practices from geriatrics and oncology in order to optimize the care of older adults with cancer. First, this *Handbook* describes how to assess the older adult and gain a better understanding of the patient’s “functional age” rather than just the chronological age. Second, it provides insight into these patients’ unique areas of physiologic, functional, and social vulnerability, and suggests interventions to help the patient. Third, this *Handbook* summarizes cutting-edge data that inform best practices in the care of older adults with cancer. Last, and most important, this *Handbook* suggests how to communicate these findings to a patient. In addition, this integration of knowledge and skill sets results in a collaborative informed decision that is in line with the patient’s goals and preferences, maximizing the benefits and minimizing the risks of cancer therapy.

The critical need for education and training in geriatric oncology has been recognized by the Institute of Medicine and the American Society of Clinical Oncology. Drs Tew and Korc-Grodzicki have brought together world experts who address this need by providing a concise reference that can be used in daily practice, covering topics ranging from how to assess the older adult with cancer, to treatment of specific cancers in older adults, to key issues regarding survivorship, palliative care, and
integrative medicine. Caring for older adults with cancer is a gratifying, personally rewarding experience that brings together the complexity of medicine with the most touching and meaningful aspects of the human condition.

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Handbook of Geriatric Oncology: Practical Guide to Caring for the Older Cancer Patient
1 Introduction to Geriatric Oncology

Stuart M. Lichtman

INTRODUCTION

Age is the single most important risk factor for developing cancer, with 60% of all newly diagnosed malignant tumors and 70% of all cancer deaths occurring in persons 65 years or older. It has been estimated that by the year 2030, 20% of the U.S. population (70 million people) will be older than age 65 years. The median age range for diagnosis for most major tumors is 68 to 74 years, and the median age range at death is 70 to 79 years. The mortality rate is disproportionately higher for the elderly population. There are several potential reasons for this, including more aggressive biology, competing comorbidity, decreased physiologic reserve compromising the ability to tolerate therapy, physicians’ reluctance to provide aggressive therapy, and barriers in the elderly person’s access to care (1). The elderly patient with cancer often has an elderly caregiver, or is socially isolated. The older patients have not been participants in clinical trials and the data necessary to help clinicians care for these patients is lacking. All of these factors contribute to the difficulty of caring for these complex, heterogeneous, and vulnerable patients (2). The field of geriatric oncology has become increasingly recognized as an important component of cancer care and cancer research. This introductory chapter explores the major issues confronting clinicians, which are assessment and aging physiology.

GERIATRIC ASSESSMENT (GA) IN ONCOLOGY

The identification of problems in older patients is critical in prognostication and decision making. Researchers in geriatric oncology have demonstrated that the traditional method of routine history and physical is inadequate in determining elder-specific issues (3,4). Clinicians have not been trained to ask the appropriate questions and interpret the available data. Medical oncologists have used performance status scales such as the Karnofsky and Eastern Cooperative Oncology Group (ECOG) scales to help stratify patients for treatment and as part of clinical trial eligibility. This has been a valuable tool and, for the general oncology population, has been helpful and has withstood the test of time. However, this simple approach is not adequate in the complex, heterogeneous older population. These performance status scales often do not reflect the functional status of older patients (4). Clinicians will appropriately refer to published clinical trials and established national and international guidelines to assist in decision making and evaluating treatment options.
Unfortunately, older patients have been grossly under represented in clinical trials, and data reporting has been inadequate (5,6). This includes registration trials for new drugs (7,8). When they do participate, they are an exceptional group of elders who have passed the often stringent eligibility requirements and usually have minimal to no comorbidity and an excellent performance and functional status. Therefore, the available data usually do not reflect the average patient seen in practice. The result is that there is a paucity of data with which to make true evidence-based decisions.

To obtain this important information, researchers in geriatric oncology have been developing GA scales appropriate for the oncology patient. There is a need to assess basic information. Functional assessments (see Chapter 13) include activities of daily living (toileting, feeding, dressing, grooming, ambulation, bathing) and instrumental activities of daily living (using the telephone, shopping, food preparation, housekeeping, laundry, transportation, and ability to take medication accurately). Dependence in these areas has shown to be a prognostic factor for poor outcomes and treatment-related toxicity (9–11). The presence of geriatric syndromes (delirium, dementia, incontinence, falls, pressure ulcers, malnutrition, osteoporosis, hearing and vision difficulties, and sleep disorders) also has a negative impact (12). The study of the overall evaluation of the older patient has been an extrapolation of the established comprehensive geriatric assessment (CGA), an interdisciplinary diagnostic process focusing on the medical, psychosocial, and functional capabilities of the patient, in order to develop a coordinated and integrated plan for treatment and follow-up (13). It is recognized that a CGA as performed by geriatricians is not practical in the usual outpatient oncology setting. Researchers are trying to streamline the approach by determining the most important questions in terms of oncologic care and then validating this approach in various settings. A position paper published by the International Society of Geriatric Oncology (SIOG) highlighted the issues in this field and discussed the domains that needed to be evaluated and the important questions to be addressed (13).

There is a significant clinical rationale for performing GAs. A GA can provide relevant clinical information beyond that captured in a standard history and physical examination. It can help predict oncology treatment-related complications and overall survival. Data is emerging that it is helpful in making oncology treatment decisions. There are questions concerning what components of the GA should be incorporated in oncology-related assessments and how the problems which are detected can be addressed.

In terms of predictive models, one area that has developed a significant amount of important data is the risk of therapy-related toxicity. Two models have been developed and are described in detail in Chapter 13. The Cancer and Aging Research Group (CARG) score has been shown to be predictive for significant (grade 3+) hematologic toxicity (10). The power of this model is that it has been shown to be better than clinical judgment in predictive value. The study also demonstrated that those older patients with the lowest scores (0–3) still had a 25% risk of ≥ grade 3 toxicity. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score is able to distinguish several risk levels of severe toxicity. It predicts separately hematologic and nonhematologic toxicity (14). Oncology-specific geriatric screening
tools are also being developed to predict other outcomes (15,16) and are discussed in Chapter 14.

Another important consideration is recognizing frailty (see Chapter 14). The frail patient can be thought of an individual who has a higher susceptibility to adverse outcomes, such as mortality and institutionalization. From an oncology perspective, the “frail” label often indicates a patient who is dependent on others for basic activities and if given standard therapies will often not complete the treatment, have excessive toxicity, and therefore will not benefit. Clinicians need to recognize this group to avoid excessive toxicity and suffering (17,18). Predictors of mortality can be helpful to clinicians to weigh the risk versus benefits of therapy, particularly adjuvant treatment. The website e-prognosis (www.eprognosis.com) is one such example. Gait speed has been shown to be a powerful predictor of survival (19) and is clearly simple to evaluate. GA can also be helpful in predictions of delirium (11). These scales and predictive models have been shown not to be time-consuming to the medical staff, are often self-administered by the patient or can be done by nursing. Newer technologies are beginning to be utilized to capture and evaluate this information (20).

PHYSIOLOGY OF AGING AND DRUG THERAPY

A number of physiological changes accompany aging (21,22). Drug compliance is an important issue, particularly with the marked increase in oral anticancer therapies which compound the problem of polypharmacy (23–25). Studies have emphasized that obesity is a significant problem in the elderly population and should be considered in trials (26–28). Other variables to be considered are the effect of age and diet, and genetic polymorphisms (29). Polypharmacy can also affect metabolism due to the potential of drug–drug interactions. There is an age-related reduction in glomerular filtration rate which is not reflected by an increase in serum creatinine levels, because of the simultaneous loss of muscle mass that occurs with age. It should be noted that many older patients who have a serum creatinine in the normal range for a particular laboratory have renal insufficiency (30). Dosing recommendations for older patients and those with renal insufficiency have been published (22,31–35). Appropriate dose modifications can foster safe and effective outcomes (36). The study of the pharmacokinetics of chemotherapy in older patients has truly been lacking. Future study is required.

RESEARCH

Research in geriatric oncology is being performed by a growing number of investigators. The SIOG, founded in the year 2000, fosters the mission of developing health professionals in the field of geriatric oncology, in order to optimize treatment of older adults with cancer, through education, clinical practice, and research. The Society’s publication, the *Journal of Geriatric Oncology*, is the first journal devoted solely to the field. The Cancer and Leukemia Group B (now the Alliance
for Clinical Trials in Oncology) Cancer in the Elderly Committee has supported furthering research in geriatric oncology through clinical trials and secondary data analyses (37,38). The CARG initiated and supported trials in different clinical settings and, most importantly, mentors junior investigators in geriatric oncology and studies novel clinical trial designs (39). The Gynecologic Oncology Group Elderly (now NRG Oncology) task force is supporting the first prospective trial in older women with ovarian cancer and planning further studies in other diseases and modalities. The American Society of Clinical Oncology (ASCO) also fosters a number of initiatives in geriatric oncology. These include a Geriatric Oncology Issue Exploration Team, educational materials including ASCO University, sessions at the annual meeting including a geriatric oncology track, the B. J. Kennedy Award for Excellence in Geriatric Oncology, articles in the ASCO Post, and a geriatric oncology component of the Cancer Education Committee. ASCO has also published a position paper encouraging research in older patients to increase the available evidence-based data (1). One area of great interest is rethinking clinical trial design. It is important that clinical trials prospectively obtain important patient data such as baseline functional status. Eligibility, appropriate endpoints, and toxicity evaluation should be reconsidered for older patients (40,41). Data analysis and clinical trial reporting also have to be adapted for appropriate evaluation and interpretation. These issues are imperative to obtain quality data so clinicians have the ability to make meaningful decisions.

The care of the older cancer patient is a complex endeavor. It requires careful thought and evaluation. Goals of therapy must be carefully considered. A multidisciplinary approach is preferred. Geriatric oncology ought to move to the forefront of oncology care. These vulnerable patients should be the focus of our endeavors.

**TAKE HOME POINTS**

1. Older patients comprise the majority of cancer patients in both incidence and mortality.
2. Geriatric-specific assessment is required to evaluate these patients.
3. GA adds to the routine history and physical exam, uncovering problems not previously recognized.
4. Oncology-specific prediction tools are available to help in this geriatric evaluation.
5. Aging physiology must be considered before deciding upon and dosing anticancer therapy.

**REFERENCES**


INTRODUCTION

Every year about 140,000 patients are diagnosed with colorectal cancer (1). Older cancer patients are disproportionately affected by it. About 29% and 43% of deaths related to colorectal cancer occur in men and women older than age 80, respectively (2). Although individuals older than age 65 are minority compared to the whole population, 60% of colorectal cancer cases are diagnosed in this age group (2). Although the incidence and mortality from colorectal cancer have decreased in the aging population, due to colorectal cancer screening and surgical treatment of localized cancer, the number of older colorectal cancer patients requiring treatment still remains very high (2).

Treatment of older colorectal cancer patients presents different challenges than treatment of younger patients. In general, as patients become older, they develop more comorbid conditions, take more medications, lose their independence, and become more socially isolated. As a result, applying standard of care without addressing these issues may cause more harm rather than achieving benefit.

In this chapter, we briefly discuss the concept of frailty as it impacts chemotherapy decision making, and review some of the most common challenges that may be faced by medical oncologists taking care of older colorectal cancer patients.

INTERSECTION OF FRAILTY AND AGING-RELATED PHYSIOLOGICAL CHANGES (FIGURE 17.1)

- Geriatric assessment (GA) is a multidimensional assessment of older patients that captures their functional activity, psychosocial well-being, cognitive function, polypharmacy, and nutritional status.
- Patients with more deficits based on GA are considered to be frail.
- Less time-consuming screening versions of GA are available (3).
- Cancer treatment decision making will be based on GA and organ function of older colorectal cancer patients.

ADJUVANT TREATMENT FOR LOCALIZED COLORECTAL CANCER (FIGURE 17.2)

1. **Assessment of frailty/fitness:** Various definitions and screening tools for fitness/frailty assessment exist. In a broad definition, a **fit patient** is a patient with no or just
one comorbid condition who is independent in basic and instrumental activities of
daily living (see Chapters 3 and 13).

2. **Assessment of patient’s life expectancy**: Older patients are more likely to die
from noncancer causes than younger patients (4). Consider administering adju-
vant chemotherapy in patients with life expectancy of greater than 5 years or in
those with high lymph node involvement. A comorbidity-adjusted life expectancy
table (5) is useful in this assessment. Other useful methods for calculating life
expectancy are the Schonberg mortality index (6), and e-prognosis (7).

3. **Chemotherapy toxicity calculators for older adults with cancer**: At least two
chemotherapy toxicity prediction models have been validated among older cancer
patients. In the Cancer and Aging Research Group (CARG) calculator (8), the
toxicity is assessed by aging-related deficits, hemoglobin and kidney function, and
the number of chemotherapy agents. In the Chemotherapy Risk Assessment Scale
for High-Age Patients (CRASH) calculator (9), the risk is assessed by aging-related
deficits, diastolic blood pressure, lactate dehydrogenase (LDH), and the toxicity
risk associated with certain chemotherapy agents and regimens. The CRASH cal-
culator estimates hematological and nonhematological toxicity risk, whereas the
CARG calculator provides only one risk score.

4. **Capecitabine versus fluorouracil (5-FU)**: A—5-FU and capecitabine have similar
efficacy in improving patient outcomes (10). B—The decision for choosing 5-FU
versus capecitabine should be based on their toxicity profiles and ease of use based
on the patient’s overall status. C—About 30% of patients only receive 1 to 4 months

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**FIGURE 17.1** The impact of frailty and organ dysfunction on treatment
decision making.
of adjuvant chemotherapy (11). These patients are two times more likely to die compared to those who complete the adjuvant chemotherapy. This emphasizes the importance of the proper selection of older colon cancer patients for adjuvant chemotherapy, proper decision making on single versus doublet chemotherapy and 5-FU versus capecitabine, and providing support for older colon cancer patients.

**FIGURE 17.2** Treatment decision making for older cancer patients with localized colorectal cancer.

5-FU, fluorouracil.
5. **Use of oxaliplatin:** A—oxaliplatin has limited benefits in improving outcomes of older patients with colon cancer. The probability of 5-year survival was 75.8% for patients who received 5-FU and oxaliplatin compared to 76.1% for patients who only received 5-FU/Leucovorin (LV) (12). B—Despite lack of solid benefit, in the community, 50% of patients age 70 to 79, 33% of patients age 80 to 84, and 13% of patients older than age 85 have received oxaliplatin as a part of their adjuvant treatment (13). C—Strongly consider omitting oxaliplatin in patients with diabetes and/or diabetic neuropathy, with history of multiple falls, or with other sensory deficits (e.g., poor vision).

**METASTATIC COLORECTAL CANCER; TREATMENT DECISION MAKING (FIGURE 17.3)**

1. Refer to chemotherapy toxicity calculators for older adults with cancer in the previous section.
2. For selecting between single-agent 5-FU versus capecitabine or irinotecan, refer to Table 17.1.
3. For making decisions on administering oxaliplatin, refer to point 5 of the previous section.
4. One study showed that among patients unfit for standard-dose chemotherapy, starting with 80% dose-reduced chemotherapy is an acceptable option leading to less toxicity and no significant change in overall survival (14).

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**Chemotherapy Risk Calculator**

- Fit + adequate organ function
- Fit + inadequate organ function
- Frail + adequate organ function
- Frail + inadequate organ function

**POUNTS WORTH CONSIDERING:**

1. Single agent vs. FOLFOX vs. CAPEOX vs. FOLFIRI
2. Starting with dose-reduced chemotherapy
3. Intermittent vs. continuous treatment
4. Number of chemotherapy lines
5. Biologic agents

**FIGURE 17.3** Treatment decision making for older patients with metastatic colorectal cancer.
5. Two studies showed that stopping treatment after 12 weeks of treatment, and restarting the treatment after the disease progressed, does not impact patients’ outcome and may lead to better quality of life (15,16).

6. A study on older patients with metastatic colon and rectal cancer who received treatment between the years 2000 and 2009 showed that the addition of three or more lines of treatment led only to an additional month of survival for patients older than age 75. For those 65 to 74 years of age, the increased survival was 6 months for colon cancer patients and 10 months for rectal cancer patients (17).

7. Adding bevacizumab to the first line of treatment leads to an increase in progression-free survival of approximately 3 months in older patients with metastatic colorectal cancer. Patients receiving bevacizumab are at higher risk for arterial thromboembolic events, gastrointestinal perforation, slower wound healing, and increase in blood pressure (18). As a result, it is important to evaluate comorbid conditions of older patients with metastatic colorectal cancer very carefully. Cetuximab and panitumumab are antibodies toward epidermal growth factor receptors. Patients with metastatic colorectal cancer with wild-type V-Ki-ras2 Kristen rat sarcoma (KRAS) status benefit from addition of cetuximab or panitumumab to combination chemotherapy (19,20). For those who progress on previous lines of chemotherapy, cetuximab or panitumumab can be used as single agent if patients have not received them before. In this setting, their benefit is about prolonging life by about 1.5 months (21) or not at all, partially explained by a crossover study (22). These agents can cause skin rash, diarrhea, and fatigue (23). In our experience, we use triplet treatment as the first line of treatment for metastatic colorectal cancer patients if they are fit and have low volume of metastatic disease; surgery is considered curative following chemotherapy.

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**TABLE 17.1 Barriers and Benefits of Capecitabine, 5-FU, and Irinotecan**

<table>
<thead>
<tr>
<th></th>
<th>Capecitabine</th>
<th>5-FU</th>
<th>Irinotecan</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main side effect</strong></td>
<td>Hand and foot syndrome</td>
<td>Neutropenia</td>
<td>Diarrhea, hair loss</td>
</tr>
<tr>
<td><strong>Advantage</strong></td>
<td>May require fewer office visits given the 3-wk schedule</td>
<td>Patients with polypharmacy are not required to take additional chemotherapy pills</td>
<td>No need for port placement</td>
</tr>
<tr>
<td><strong>Not very helpful in</strong></td>
<td>Patients with cognitive impairment, patients already suffering from polypharmacy</td>
<td>Inability to maintain port hygiene/patients with lack of proper access for chemotherapy infusion every 2 wk</td>
<td>Patients concerned about hair loss</td>
</tr>
<tr>
<td><strong>Dose adjustment</strong></td>
<td>Kidney failure</td>
<td>Liver failure</td>
<td>Liver failure</td>
</tr>
</tbody>
</table>

5-FU, fluorouracil.
TAKE HOME POINTS

1. Assess older colorectal cancer patients’ fitness level and organ function in order to make treatment decisions.
2. Frail older patients with inadequate organ function should receive surveillance and best supportive care. If these patients have metastatic disease, they should also be offered palliative care.
3. Be cautious about the use of oxaliplatin in the adjuvant setting (limited benefit) and in metastatic disease, especially if the patient suffers from neuropathy.
4. Utilize chemotherapy toxicity calculators when deciding on number and dose of agents.
5. Administering more than two lines of chemotherapy to metastatic colorectal cancer patients older than age 75 has extremely limited benefit. Consider discussing goals of care in this setting.

REFERENCES


