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## Older Adults and Cancer Treatment

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### Abstract

Approximately 60% of the cancer incidence occurs in adults age 65 and older, yet older patients often are not accorded access to treatment trials. Therefore, we remain uninformed about clinical and behavioral responses of older patients with cancer to cancer treatment. This article gives a broad overview of what some of the dimensions of cancer treatment in the elderly are, and raises issues for behavioral research. The literature is reviewed in general for cancer treatment and briefly addresses areas such as comorbidity, function, adverse events, palliation and side effects, social and psychological factors, cognition, and provider behavior. The importance to behavioral research is discussed. Challenges for behavioral researchers are discussed in the context of cancer treatment. Few studies were found specific to behavioral research. Chronological age alone is an inadequate indicator to determine responses among older patients to cancer treatment. When carefully selected, older patients can benefit from treatment or palliation. More research is needed to define clinical and behavioral criteria for the inclusion of older patients in treatment trials.

### Keywords

Cancer treatment; older adults; behavioral research; comorbidity; physical function; treatment; side effects

### Introduction

Persons 65 years of age can expect to live another 15 years and remain functionally independent. Persons 75–84 have an average of 10 years longevity while those 85 have an average of 6 years longevity<sup>1</sup>. Approximately 60% of the cancer incidence and 70% of cancer mortality occurs among adults age 65 and older. Currently, 6 million cancer survivors over 65 years of age have undergone cancer treatment. Historically, few randomized chemotherapy trials enrolled patients over the age of 65 in order to exclude those with multiple comorbid conditions<sup>2, 3</sup>. While age alone is no longer an exclusion criteria, little evidence exists describing how psycho-social and behavioral factors influence decisions to treat, the course of treatment, or the outcomes of care for older adults with cancer. Older cancer patients are physiologically, psychologically, socially, economically and culturally heterogeneous. As a result, there is a complexity in the care of older cancer patients that deserves to be addressed through research on this growing segment of the population<sup>2</sup>. Balducci and Beghe<sup>4</sup>, Muss<sup>5</sup>, Extermann<sup>6</sup>, Repetto<sup>7</sup>, and Rodin<sup>8</sup>, emphasize the critical importance of geriatric oncology to be considered for the management of the older adult with cancer. As scientists begin to unravel the science of cancer and aging<sup>9</sup>, decisions regarding the treatment and management of cancer need to begin to consider how comorbid

conditions, functional and cognitive status are related to the tolerance and benefit from the treatment<sup>10</sup>. (Duplication deleted here)

The goal of this paper is to summarize the psycho-social literature on the treatment and care of older adults with cancer. It is important to emphasize the focus of this manuscript is not on chronological age, but the importance of the interplay among the biological, psychological and social factors of aging that occur in older cancer patients. We recognize that selecting appropriate treatment protocols for the older person with cancer can be challenging, and involve a review of therapies and how they may interact with comorbid conditions, organ deterioration, geriatric syndromes or affect physical and cognitive status. The interplay of these clinical factors may be complicated by the availability of family support to maintain the patient at home, and to provide transportation necessary for access to care. We examine how psycho-social research, broadly defined, can inform treatment approaches to older patients with cancer. We argue that prior to selecting a treatment plan for the older patient, a more comprehensive screening and evaluation should be undertaken. To this end, we summarize dimensions to be evaluated and the state of the science related to these assessments.

### **Screening and early detection for the older cancer patient**

Cancer screening guidelines for older adults are not clear. General frameworks for making decisions regarding screening exist<sup>11</sup>, but for breast cancer they appear to be left to the discretion of providers or patients<sup>12</sup>. For prostate cancer rates of screening among the elderly with limited life expectancy may be too high<sup>13, 14</sup>. Following a cancer diagnosis, elderly patient should be carefully evaluated as to how comorbidity, physical function and psycho-social health may influence treatment plans.

### **Comorbid conditions and geriatric assessments as screening tools to guide treatment**

Ongoing treatment for comorbid conditions such as diabetes, pulmonary and heart disease may result in drug interactions when chemotherapy is introduced. Chronic diseases such as renal or liver disease may alter pharmacokinetics and pharmacodynamics of chemotherapeutic agents. These changes as well as alterations in drug absorption, distribution, metabolism and excretion may result in greater toxicities among older cancer patients<sup>15, 16</sup>.

As a result, older adults are less likely to receive optimal doses of chemotherapy compared with younger patients due to toxicities and complications<sup>17, 19</sup>. However, treatment trials seldom adjust for comorbid conditions or organ decrements when considering treatment modalities<sup>3, 19, 16, 20, 21</sup>. Careful assessments comorbid conditions<sup>6, 22</sup> and comprised organ function and how these factors may lead to subsequent suboptimal treatment dosages among older patients warrant further research. Under some circumstances with comorbidity and altered organ function, it is essential to consider palliation and supportive care as the best course of management for the older patient rather than suboptimal levels of curative treatment.

Geriatric oncologists propose using the Comprehensive Geriatric Assessment (CGA) to determine which older cancer patients can benefit from treatment and which patients' may benefit more from palliative care as the preferred treatment approach<sup>6, 22, 1</sup>. This multi-dimensional assessment includes an evaluation of physical functioning, including activities of daily living (ADLs) and instrumental activities of daily living [IADLs], comorbid conditions, cognitive performance, psychological and nutritional status, social support, a

review of current medications and the presence of geriatric syndromes<sup>1, 8, 19, 23, 20</sup>. The CGA identifies reversible or mutable conditions, predicts treatment toxicity and determines the amount of family support available and pairs it with what will be needed to implement the therapeutic plan. Unfortunately, few formal tests have been conducted of the CGA with treatment protocols, and research is needed to determine the predictive capacity of the CGA for guiding and monitoring treatment decisions among older cancer patients. An associated concept, frailty, also may inform the manner in which the CGA is assessed<sup>24</sup> and the relationships between comorbidity and geriatric syndromes are beginning to be evaluated<sup>25</sup>.

### **Functional status and its impact on older cancer patients**

Loss of physical function with resultant disability occurs with age. Over 60% of those ages 65–74 have some disability, 65% of those 75–79 report disability and over 76% of those 80 and over report some disabling conditions<sup>26</sup>. As a result, patients with no or few ADL or IADL limitations may be able to tolerate full doses of treatment, but should have frequent monitoring to identify potential adverse events<sup>6, 27, 28, 29</sup>. Maione and colleagues, however, documented that global quality of life, performance status, and IADL were prognostic factors for the survival of elderly patients<sup>30</sup>.

Among older cancer patients, losses in physical function and disability are associated with losses of functional reserve, which, in the presence of chemotherapy, increases the likelihood these patients will experience toxic side effects<sup>10, 16, 26</sup>. However, studies are needed to define the tolerance and response to treatment among older patients with varying levels of disability and to conduct sub-analyses describing how treatments impact patients' functional reserves and their ability to recover their levels of functioning following the end of treatment<sup>31</sup>. Finally, the interplay between function, dose delays, reductions and drug stoppages needs to be carefully assessed. Such information can help to estimate life expectancy and treatment tolerance, and establishes a common classification of physical function to be used to plan care for older adults.

### **Screening for psychological and social factors influencing treatment**

Among older patients, social factors such as the availability of a spouse to provide home care, widowhood, fixed incomes and transportation and living arrangements, such as assisted living, should be considered in developing cancer treatment plans<sup>32</sup>. Radiation therapy may be inappropriate for older patients who cannot mobilize transportation or social, emotional, or psychological support required for daily administrations. Home care may also be compromised<sup>32, 33, 34</sup>. Blanchard-Fields indicates that older adults are more focused than younger adults in solving instrumental problems, which means they can identify ways to adapt to their cancer treatment<sup>35</sup>. Depression may be associated not only with functional decline for the older adult with health status problems but with the need for more social support and family care<sup>1, 36, 37</sup>.

Maintaining physical and social function and managing symptoms through psycho-social interventions might enable older patients to receive and respond to a course of chemotherapy<sup>36, 37, 38</sup>. Future research should assess the social and psychological states of older cancer patients who are undergoing treatment and consider supportive interventions to facilitate their adherence to treatment protocols, and adjustment and participation in palliative care when curative treatment is not adequate. Patient preferences for treatment is an essential consideration for older adults. Screening and assessment of the psychosocial factors are essential when treatment plans are made.

## Cognition

Assessment of the cognitive status of older cancer patients is important in developing a cancer treatment plan. Older patients with mild cognitive deficits, may experience greater declines with treatment and recover cognitive performance more slowly. Older patients with deficits in hearing, vision, memory loss or cognitive deficits will have difficulty participating in treatment regimens, especially newer regimens that may involve oral agents. Oral agents require patients to follow complex dosing, recognize signs of toxicity, and seek help in response to early complications so that doses can be adjusted and outcomes such as hospitalizations avoided<sup>15, 39</sup>.

## Treatment and older cancer patients

Older cancer patients face both clinical and broader institutional barriers to appropriate treatment and are less likely to have their cancer staged<sup>3, 10</sup>. They may receive less aggressive treatment (i.e. sub therapeutic dosing). Older breast cancer patients are less likely to receive auxiliary lymph node dissection, adjuvant radiation therapy, or chemotherapy or hormone therapy<sup>3, 17, 40</sup>. Further, older patients may not be referred to comprehensive cancer centers or offered participation in clinical trials. Assessments such as those described above can form the basis for determining eligibility for trials and open communication as to older patients' interest in trial participation and referral to larger centers for second opinions or treatment plans<sup>41, 27</sup>.

Older patients, when selected carefully, appear to tolerate and respond well to cancer treatments<sup>42</sup>. Although evidence is limited, older patients derive benefit from adjuvant therapies provided they have a life expectancy exceeding 5 years<sup>3</sup>.

Older patients who have undergone pulmonary resection (up to the age of 80) and treatment for colorectal, breast, prostate cancer and non-Hodgkin's lymphoma all have tolerated and shown positive responses to their treatments<sup>27, 40, 43, 19, 22, 44, 45</sup>. Radiation therapy with short treatment time and reduced tissue toxicity appears beneficial for selected patients<sup>46</sup>. Older patients who are in good health status may tolerate molecular targeted therapies either alone or in combination with chemotherapy<sup>41, 47</sup>. (Duplication deleted here)

The treatment and management decisions for older cancer patients should be guided by treatments for comorbid conditions, organ function, frailty and cognitive status. The International Society of Geriatric Oncology<sup>19, 16, 48</sup> and the National Comprehensive Cancer Network<sup>23</sup> have concluded that older patients in good health status can benefit from treatment but some may require reduced dosing due to intolerance<sup>28, 49, 50</sup>. Thus, chronological age alone should not be viewed as a barrier to treatment. (Duplication deleted here)

The interactions among functional status, frailty, and cancer treatment deserves further investigation. For example, how are indicators of frailty such as anorexia, weight loss, fatigue, inactivity, sarcopenia, osteopenia, deconditioning, exacerbated by treatments such as chemotherapy or radiation<sup>10</sup>, and specifically, which protocols are more toxic and have sustained deleterious effects? Such information is needed so that older cancer patients can make informed choices regarding their treatment options. It is important to determine what level of frailty or dysfunction should be used to consider the exclusion of older patients from treatment. Future research should focus on the development of evidence to determine how treatments exacerbate these conditions, which, in turn, may extend recovery time<sup>15</sup> or lower the quality of life to the point where the consequences of treatment outweigh the benefits. The point at which palliation should be added to care should be defined. Side effects such as

pain, fatigue, nausea, insomnia or neutropenia have been less aggressively and appropriately managed in the older adult<sup>15</sup>. Supportive care medications should be prescribed and consideration given to reduced dosage or “light” treatment<sup>22, 49</sup>. Frail older patients and those with three or more dependencies in ADL, severe comorbidities, or the presence of other geriatric syndromes may not be offered therapeutic treatment but they may be offered only supportive symptom management and palliation<sup>4, 10</sup>.

For those older cancer patients who are not suited for therapeutic approaches due to health status, palliative care should be added to the care. It is essential that patients and families are guided to palliative care where they are assisted with decisions, receive support and communication between providers and patients and families are encouraged so that goals of care can be reassessed. The levels of evidence to inform such choices are not available at this time. We focus on areas to be considered when treatment plans are developed in the next section.

### **Adverse effects and side effects management**

The pattern, severity and management response of older adults to the toxic and adverse effects of treatment has not been well documented<sup>51</sup>. Few psycho-social interventions for symptom management have been described. It is important to know if age differentiates among patients according to their responses to symptom management interventions. A test of the moderating effects of neutropenia on the impact of a cognitive behavioral intervention to reduce symptom severity indicated that when age was included along with neutropenia in the model, older patients exposed to the experimental intervention reported greater symptom severity. No age effect was observed when neutropenia was not in the model. Identifying how age influences symptom severity endpoints and the moderating effects of consequences, such as neutropenia, is essential<sup>52</sup>.

In a trial of a psycho-social intervention, patients 45 years of age and younger and those greater than 75 years of age and older responded differently to cognitive behavioral interventions to manage cancer treatment side effects delivered by nurses compared with interventions delivered by either an automated voice response system or social workers. While no differences were observed among patients 46 to 75, the youngest group (<46) reported significant reductions in symptom severity using the automated voice (AVR) or the social workers, while patients over 75 years of age reported greater reductions in symptom severity when the intervention was delivered by nurses<sup>53</sup>. These differences point to the importance of understanding how, or if age influences patients’ responses to behavioral interventions for side effects due to cancer treatment.

### **Challenges for behavioral researchers**

Given the aging of the population and the limited research on the interactions between cancer treatments and the response of older patients, research needs to be completed to understand the consequences of new therapeutic regimens. If the cognitive status is altered, this may limit patients’ abilities to respond to behavioral interventions that deliver education, counseling, decision making and communication strategies<sup>39</sup>. Similarly, tests of interactions between age, comorbid conditions, physical function and treatment modalities may help to isolate how age and these conditions affect outcomes. Is it age alone or does age in the presence of one or more of these conditions pose a synergistic effect on responses to treatment? It is important to understand at what point certain comorbid conditions and compromises in physical function in the presence of different chemotherapy protocols, produce negative patient reactions. As these trials are launched, behavioral as well as clinical researchers will need to monitor pre and post treatment states; not only clinical characteristics, but the impact of these drugs on organ function, symptom experience,

physical function and cognitive performance. We need to have guidelines to determine when palliative care is the best approach for the older person<sup>15, 54</sup>.

To participate in treatments, older cancer patients may require the involvement and support of family members. Given the lack of evidence to guide treatment of older adults, providers rely on clinical impressions to make treatment decisions about older cancer patients<sup>1, 27, 43, 16, 28, 5</sup>. Behavioral research needs to examine how and when decisions are made, determine who makes treatment related decisions (patients, family, providers)<sup>32</sup> and determine the premises upon which these decisions are based. Decisions should be based on physical or cognitive health of the older patient, patient preferences, the costs of treatment, and the benefits weighed against the toxicities and side effects.

When the patient cannot tolerate treatment, care providers need to ensure that there is an adequate palliative plan of care. Patient decisions to accept palliation rather than active curative treatment also warrants further study<sup>56</sup>. A focus on palliative care is needed to ensure the best quality of life as older adults reach the end of their life. Professionals need to assist with decision making and management to establish appropriate palliative care goals and patient preferences for care. Frailty, comorbidities, and psychosocial deficits add to the complexity of palliative care<sup>57</sup>. Referral to palliative care is important at appropriate phases of care. Support and resources for patients and their caregivers to assure comfort and finally a peaceful death<sup>58, 59, 60</sup>.

## Conclusions

Geriatric oncology is an emerging field that needs to integrate clinical and psycho-social factors into comprehensive treatment plan. Cognitive and functional performance as well as the emotional affect of the older patient should be assessed and incorporated into treatment plans. As these models are examined through trials, it will be important to balance arms according to clinical, functional, and cognitive indicators. A priority research theme will be to explore how, for a site and stage of cancer, a treatment protocol of known efficacy interacts with comorbid conditions, physical function, geriatric syndromes and cognitive and psychological states to produce treatment outcomes that are acceptable to patients. We need to determine for which patients are these protocols are acceptable and for which patients are they not acceptable. Under these circumstances, older patients and their families need to be informed of risks and potential benefits that they may derive from treatment. Patients need to be actively engaged in making treatment decisions. When treatment is not recommended, patients and their families need the best guidance and support to receive maximum benefit from palliation.

Innovative techniques for use with the older patients, such as telephone based automated voice response systems or web-based approaches could be considered as a means to more frequently monitor symptoms, temperature and hematological parameters, physical function, depressive affect, cognition and, if appropriate, adherence levels to newer oral therapeutic agents. Finally, the burden that these treatments place on the family, particularly as they relate to employment, insurance coverage and other economic and social dimensions, should be determined.

One important step for future research is the development of patient reported measures that are responsive to the needs of the older patient to accompany established clinical parameters. Such measures are precise and sensitive to change to define the treatment outcomes, but also to chart the course, time and extent of recovery<sup>61, 62</sup>. Comprehensive Geriatric Assessment could be used to predict severity of toxicity and overall survival<sup>63</sup>.

Evidence from this review suggests that chronological age alone is an inadequate indicator to determine the clinical and behavioral response of older patients to cancer treatment. Each age cohort brings a wide range of comorbid conditions, depressive affect, physical, social, and cognitive limitations and other indicators of frailty and associated indications of organ decrements or geriatric syndromes. It is important to understand how variations in each of these indicators narrow with successively older cohorts of patients. Based on this review, we argue that cancer treatment, and palliative care, among older patients represents an area for close collaboration among behavioral, clinical and geriatric oncology researchers and the patients themselves.

Cancer and aging are dynamic multi-dimensional processes that pose challenges to older patients and require multi-disciplinary research teams. Concomitant with that is a need for behavioral research to partner with the clinical geriatric oncology to develop the science for the best treatment, and palliative care, and quality of life for our growing aging cancer population. (Several sentences deleted) There is much work to be completed in the treatment of the older patient with cancer and for palliative care in the final phases of care.

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