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Supportive Care in Older Adults with Cancer: Across the Continuum

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Abstract

Supportive care is an essential component of anti-cancer treatment regardless of age or treatment intent. As the number of older adults with cancer increases, and supportive care strategies enable more patients to undergo treatment, greater numbers of older patients will become cancer survivors. These patients may have lingering adverse effects from treatment and will need continued supportive care interventions. Older adults with cancer benefit from geriatric assessment (GA)-guided supportive care interventions. This can occur at any stage across the cancer treatment continuum. As a GA commonly uncovers issues potentially unrelated to anti-cancer treatment, it could be argued that the assessment is essentially a supportive care strategy. Key aspects of a GA include identification of comorbidities, assessing for polypharmacy, screening for cognitive impairment and delirium, assessing functional status, and screening for psychosocial issues. Treatment-related issues of particular importance in older adults include recognition of increased bone marrow toxicity, management of nausea and vomiting, identification of anemia, and

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prevention of neurotoxicity. The role of physical therapy and cancer rehabilitation as a supportive care strategy in older adults is important regardless of treatment stage or intent.

Keywords

Supportive care; Geriatric oncology; Older adults; Cancer; Geriatric assessment-guided intervention; Survivorship

Introduction—What Is Supportive Care?

The National Cancer Institute define supportive care as follows:

Care given to improve the quality of life of patients who have a serious or life-threatening disease. The goal of supportive care is to prevent or treat as early as possible the symptoms of a disease, side effects caused by treatment of a disease, and psychological, social, and spiritual problems related to a disease or its treatment. Also called comfort care, palliative care, and symptom management [1].

The Multinational Association for Supportive Care in Cancer (MASCC) uses a slightly different definition that potentially goes beyond just the cancer and its treatment.

Supportive care in cancer is the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer experience from diagnosis through treatment to post-treatment care. Supportive care aims to improve the quality of rehabilitation, secondary cancer prevention, survivorship, and end-of-life care [2].

Supportive Care and Survivorship in the Older Adult with Cancer

Cancer and cancer treatment may result in long-term and late effects that can have a major impact on patient quality of life [3, 4]. Cancer survivorship and supportive care initiatives point us to the importance of the physical, functional, and psychosocial needs for patients and their caregivers from the time of the cancer diagnosis for the remainder of their life [5]. This definition of survivorship has been acknowledged by leading authorities [6] and stresses the importance of supportive care throughout the continuum of the patients' illness.

Survivorship care is particularly important for older cancer survivors who may have baseline vulnerability or frailty. This decrement in functional status potentially heightens the possibility of experiencing cancer and treatment-related toxicity that can further increase the risk for lasting adverse effects. It is especially important for the older person that clinicians take into account the patient's physiological reserve starting at the time of diagnosis and continuing through treatment decision-making, planning, and surveillance. In addition, older cancer patients are to be closely monitored for the development of signs and symptoms of toxicity, allowing for early intervention such as modification of cancer therapy and/or institution of supportive care. The opportunities to intervene with supportive care strategies

occur at all time points along the cancer journey. This review provides a comprehensive outline and practical guidance for age-appropriate survivorship and supportive care.

Geriatric Assessment As a Supportive Care Strategy

Multiple chronic health conditions, functional disabilities, and geriatric syndromes impact prognosis and treatment outcomes in older patients with cancer [7]. Older patients are more vulnerable to treatment side effects [8]. Treatment toxicity can worsen underlying chronic health conditions and may potentiate functional dependence and geriatric syndromes such as depression, dementia, falls, and malnutrition [8]. Supportive care management of older patients with cancer requires an approach that systematically assesses health status, functional abilities, and evaluation of geriatric issues unique to the individual.

Geriatric assessment (GA) is a multidimensional assessment of an older patient's health, functional status, and geriatric syndromes. A GA-guided supportive care process can be used as a strategy to identify evidence-based interventions for specific issues that may interfere with treatment and impact quality of survival [9•]. GA is comprised of validated tools to assess areas of health referred to as domains [7]. Potential domains include the following: (1) medical: evaluation of co-morbidity, polypharmacy, and nutritional status; (2) mental health: evaluation of cognition, depression, and delirium; (3) functional status: assessment of activities of daily living (ADL) [10]; instrumental activities of daily living (IADL) [11]; physical performance (mobility); and falls and (4) social: evaluation of environment, resources, and social support [12].

Implications of the Findings of a Geriatric Assessment for Supportive Care

The findings from a comprehensive geriatric assessment can be used to guide supportive care interventions and an individualized supportive care management plan [9•]. Key domains in this assessment include the following:

Comorbidity

Comorbidity increases with age [13]. Care management decisions must include a careful consideration of the likely impact of chronic conditions on cancer and cancer treatment as well as the possible effect of treatment on underlying comorbidity. For example, increased incidence of treatment-related cardiomyopathy is associated with older age, baseline cardiomyopathy, and history of hypertension in patients treated with anthracyclines and trastuzumab [14]. Patients with existing neuropathy may be at increased risk from falls when given neurotoxic chemotherapy [15]. Baseline renal function must be assessed in older adults prior to commencing potentially nephrotoxic or renally excreted drug therapy [16]. In addition to a simple assessment of the number, type, and severity of comorbidities, the Charlson Comorbidity Index [17] and the Cumulative Illness Rating Scale for Geriatrics [18] are validated tools to characterize comorbidity burden.

Polypharmacy

In addition to having a high comorbidity burden, older adults with cancer are likely to see multiple specialists and receive multiple additional medications for symptoms related to

cancer and its treatment [19, 20]. A high-quality GA should therefore include a full medication reconciliation and individualized evaluation of appropriateness of a patient's entire medication regimen; both prescription and non-prescription including supplements and complementary and alternative medicines (CAM). Complementary and alternative medicine use is a potential source of polypharmacy and drug-drug interactions [21]. Moreover, several cross-sectional studies in geriatric oncology have demonstrated that older patients with cancer are routinely exposed to polypharmacy, or excess medication use, and unnecessary and inappropriate medications, defined as medications with a high risk to benefit ratio [19, 22, 23, 24, 25]. Several tools can be used to identify medications that are considered inappropriate in older adults; the most widely used being the Screening Tool for Older Peoples' Prescriptions (STOPP) and the American Geriatrics Society Beers Criteria [26, 27]. In addition, for patients who have advanced disease or a limited life expectancy, tools exist that incorporate frailty, functional status, life expectancy, and goals of care into treatment decisions around discontinuing medications [28–30]. Addressing polypharmacy is an important part of a multidisciplinary supportive care strategy in older adults with cancer.

Nutrition

Malnutrition is associated with poor outcomes in older adults [31] and can have multiple unintended consequences. Chemotherapy-induced nausea/vomiting, anemia, and fatigue can potentiate poor nutrition, and likewise, poor nutrition can worsen fatigue. The Mini Nutritional Assessment (MNA) [32] is a six-item questionnaire that can be used to identify patients at risk for malnutrition. Interventions for patients at risk of malnourishment include the following: (1) referral to dietician for nutritional assessment and advice; (2) assessment for depression, access to food, and social support; and (3) implementation of community services such as home-delivered meals and support for meal preparation and shopping [33].

Cognition/Delirium

Patients with preexisting cognitive impairment are at particular risk of complications such as delirium during cancer treatment. It is important to identify cognitive impairment as part of a GA-guided supportive care management plan [9]. The Mini Mental Status Exam (MMSE) [34] and Montreal Cognitive Assessment (MoCA) [35] are available screening tools for cognitive impairment. Patients with cognitive impairment require further evaluation for reversible causes, capacity evaluation, assessment of ADL and IADL, and support for monitoring of toxicity (i.e., home health care). Older patients with cancer are at risk for delirium due to polypharmacy, anemia, dehydration, and electrolyte disturbances. Assessment for delirium is important with acute changes in mental status. Delirium can be diagnosed with high sensitivity and specificity with the Confusion Assessment Method [36].

Depression

Depression is often undertreated and underrecognized in older adults [8]. Anhedonia can impede the ability to adhere to treatment. Late life depression can be effectively treated with antidepressants or psychotherapy [37]. Treatment with pharmacotherapy can be complex and referral to psychiatry is warranted as few older adults receive adequate treatment [38]. Structured psychosocial interventions that include behavioral activation and problem-solving have been shown to be effective management in older adults with cancer [39]. Validated

questionnaires for depression include the Hospital Anxiety and Depression Scale (HADS) [40], the Center for Epidemiologic Studies on Depression (CESD-20) [41], the Beck Depression Inventory (BDI) [42], and the Geriatric Depression Scale (GDS) [43]. Clinicians caring for older adults with cancer can initiate pharmacotherapy, assess for risk factors for suicide, evaluate for underlying conditions that can contribute to depression such as anemia and thyroid disorders, review medications, and assess for psychosocial factors (ensure adequate social support, caregiver stress, financial burden) that can contribute to depressive symptoms [8].

Functional Status, Mobility, and Falls

Functional impairment is common in older patients with cancer [44]. Functional status includes the ability to complete tasks of basic self-maintenance (ADL) and skills necessary to live independently in the community (IADL). These tasks are evaluated by the Katz ADL Index [10] and Lawton IADL scale [11]. Depression and impairment in IADL predict functional decline following the first cycle of chemotherapy [45]. Longer hospitalization, fatigue, and IADL dependence are found in older patients with functional impairment prior to cancer surgery [46]. Referral to physical and occupational therapy and assessment of social support and cognition are important next steps in the evaluation of functional impairment.

Mobility and fall risks are assessed by physical performance tests. Older patients with cancer are particularly at risk for falls secondary to treatment side effects and advanced stage [47]. Patients with history of falls within the last 6 months should be assessed for gait impairment, balance, and vitamin D level. The Timed Up and Go (TUG) [48] and Short Physical Performance Battery (SPPB) [49] are physical performance assessments for gait, strength, and balance. Early interventions for patients with a history of falls include the following: (1) medication review, (2) addressing vision impairment, (3) physical therapy and exercise programs with goals to strengthen muscles and improve balance, (4) Vitamin D repletion, and (5) home safety evaluation and implementation of emergency response system for patients who live alone [50].

Social

Assessment of social supports including presence of a caregiver, financial status, and availability of transport is a key component of a GA-based supportive care strategy [9]. A basic question to ask the patient is “who is available to help in case of an emergency?” Informal care-givers can provide support to older cancer patients to compensate for the impact of functional and cognitive decline. They also provide emotional and social support which is essential to the well-being and quality of life of cancer patients [51]. A social worker in a supportive care team can help review resources and available supports. The older patient with cancer may also be a caregiver for others; thus, particular attention is needed to the whole social situation.

Prediction of Toxicity

GA domains can be predictive of chemotherapy toxicity. The Cancer and Aging Research Group (CARG) developed a risk model that includes geriatric factors predictive of grades 3–

5 chemotherapy toxicity. Impairment in IADL, mobility, hearing, falls, and decrease in social activities predicted grades 3–5 chemotherapy toxicity [52]. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) model predicts severe hematologic and non-hematologic toxicity. In this model, impairment in IADL predicted hematologic toxicity; malnutrition and abnormal cognition predicted non-hematologic toxicity [53]. Similarly, nutrition, impaired function, and comorbidity predicted interruption of chemotherapy in older patients with solid malignancies receiving chemotherapy [54]. Thus, geriatric assessment at diagnosis and at the initiation of treatment can be used to identify patients with higher risks of toxicity and to guide treatment modifications and supportive care interventions to avoid this toxicity.

Supportive Care for Treatment-Related Issues

Older patients may be at risk of certain treatment-related toxicities. Supportive care strategies are particularly important in the following areas:

Bone Marrow Toxicity

(a) Neutropenia and infection—It is generally accepted that the risk of hematological toxicity is increased in older adults (> 65 years) undergoing myelosuppressive chemotherapy. Older adults are at risk of febrile neutropenia (FN) and life-threatening infections that may in turn lead to reduced dose intensity and decreased effectiveness of treatment. Prophylaxis with granulocyte colony-stimulating factors (G-CSFs) serves to reduce the rate of neutropenic infection and improve dose intensity [55].

Clinical guidelines from the American Society of Clinical Oncology (ASCO) [56], the National Comprehensive Cancer Network (NCCN) [57], and the European Society of Medical Oncology (ESMO) [58] recommend that primary G-CSF prophylaxis be given to all patients over the age of 65 if they are receiving chemotherapy which confers a >20 % risk of febrile neutropenia. The 2010 update of the EORTC guidelines for CSF use include a detailed analysis of factors in addition to age which may further increase risk of FN [59]. The use of growth factors may be indicated in older adults with these comorbidities even if the FN risk of a particular chemotherapy regimen is cited as between 10 and 20 %.

This use of prophylactic growth factors is particularly relevant to older patients receiving anthracycline-based regimens as curative treatment for non-Hodgkin's lymphoma [60]. A recent analysis of 5884 patients over age 65 using SEER data found that clinicians' adherence to guidelines recommending primary G-CSF prophylaxis in elderly patients with NHL receiving anthracycline-based chemotherapy now approaches 70 % in the USA [61]. Primary prophylaxis reduced the risk of outpatient encounters for fever or infection but did not have an impact on inpatient encounters or deaths during cycle 1 of chemotherapy.

The MASCC febrile neutropenia risk score can be used to potentially identify patients with established FN who may be at increased risk of complications [62, 63]. It has been used to identify "low risk" patients who could be managed as outpatients. This index uses age over 60 years as a risk factor for FN complications (Table 1) [62].

(b) Anemia—The assessment of anemia is an important part of any supportive care strategy in older adults with cancer as the incidence and prevalence of anemia increases with age. Screening for anemia and the investigation of possible causes is recommended as part of pretreatment assessment. Anemia is a risk factor for chemotherapy-related toxicity and has been associated with functional dependence, falls, cardiac failure, cognitive impairment, and dementia [12].

Causes of anemia in the older adult are often multifactorial [64], but correction of reversible causes such as iron deficiency should be pursued and addressed as a matter of urgency. The NCCN guidelines for management of cancer and chemotherapy-induced anemia include management algorithms that apply to patients regardless of age [65].

Once the cause of anemia has been ascertained, a number of treatment strategies are available. The new formulations of IV iron are associated with fewer side effects and better efficacy than oral iron. There is a suggestion that IV iron may reduce the need for transfusions in some settings [66].

The utility of erythropoietin-stimulating agents (ESAs) in patients with cancer remains contentious and is generally not recommended due to the increased risk of adverse events such as thrombosis and the evidence of possible decreased survival in patients receiving these agents.

Judicious use of red blood cell transfusions remains the mainstay of treatment of symptomatic anemia in older patients with cancer. Transfusions are not generally recommended for asymptomatic patients unless the hemoglobin level is between 7 and 8 g/dL [65].

Treatment-Induced Nausea and Vomiting—Antiemetics

Although chemotherapy-induced nausea and vomiting (CINV) is less common in older adults [67], the risk of adverse consequences such as dehydration and renal impairment is higher due to the increased likelihood of comorbidities. Supportive care guidelines for the prevention of CINV are applicable to patients of all ages [68, 69], and with modern therapy, vomiting can be completely prevented in 70–89 % of cases [70, 71]. Antiemetic therapy is highly effective in older adults but care needs to be taken in specific circumstances. The potential for drug-drug interactions with some agents is a theoretical problem that rarely arises in practice. More of a concern is the increased likelihood of unstable diabetes and insomnia with the use of corticosteroids and the increased risk of constipation with 5HT3 antagonists [72]. Careful counseling on the use of laxatives around the time of chemotherapy is an important supportive care strategy.

Treatment-Induced Neurotoxicity and Falls

The evidence for an increased incidence of neurotoxicity in older adults is conflicting and dependent upon the chemotherapy drug in question [73]. While there is no evidence that older patients are at increased risk from platinum-agents such as oxaliplatin, there is some evidence of an increased risk of clinically significant peripheral neuropathy due to paclitaxel in older women with ovarian cancer [74, 75]. There are currently no recommendations for

dose modification of taxanes in older patients, but caution needs to be exercised in patients with preexisting neuropathy.

A recent systematic review of falls in patients with cancer identified 31 studies exploring this topic [76]. The authors reported that falls are more common in older patients with cancer than in community-dwelling older adults without cancer. A number of factors increasing the risk of falls included pain and chemotherapy type. The risk of falls increased with the administration of doublet vs single-agent neurotoxic chemotherapy and with increasing number of cycles of these agents [47, 77]. Other established risk factors for falls in the general population such as prior history of falls and dependence in ADLs are also risk factors in older adults with cancer [76].

Cancer Rehabilitation for the Older Adult

Physical supportive care strategies are important in older adults regardless of the timing and intent of anticancer treatment. Older adults who have cancer are at a higher risk of reporting that they are in poor or fair health, higher levels of disability, increased number of falls, and higher levels of functional decline [78–81]. The ultimate goal of cancer rehabilitation is to improve the quality of life of people with cancer and can be provided at any age and stage of cancer continuum [82]. The cancer rehabilitation team usually consists of occupational and physical therapists who work together and in parallel with other supportive care services. Occupational and physical therapists strive to improve function, decrease disability, decrease risk of falling, and improve quality of life, yet referral to cancer rehabilitation has been underutilized [83, 84]. Improving access to these services can occur through detection of need via a GA or even a simple question about previous falls [85].

Occupational therapy assists people across the lifespan to engage in activities to improve quality of life [86]. Occupational therapists use meaningful activity therapeutically to restore abilities or, through an adaptive model, modify the environment or the activity to allow for participation [86]. For older adults with cancer, participation in ADL and IADL is vital to improved survival and quality of life [87]. Examples of interventions occupational therapists may provide include the following: self-care management, environmental adaptation, cognitive rehabilitation, fall risk prevention, medication management, upper extremity mobility and exercise, lymph-edema care, and management of peripheral neuropathy and of cancer-related fatigue [88, 89].

Exercise can improve overall quality of life [90, 91]. Physical therapy can provide individualized exercise programs to those with a variety of comorbid conditions, physical limitations, or gait and balance disturbances [92]. Physical therapists individualize exercise and mobility treatment plans in order to maintain function and slow down or prevent future disability. Through increasing exercise and physical mobility, physical therapy can also decrease pain and improve balance to decrease fall risk [93–96].

Both physical and occupational therapy can be provided at any stage of the cancer care continuum including pretreatment. Pretreatment can include exercise and endurance training prior to surgery [97] to provide education about the potential impact of treatment, how to

preserve ability to complete daily activities, and the importance of physical activity and mobility after surgery. Furthermore, *prehabilitation* can provide patients with education on how to maintain range of motion and provide specific exercises and fittings for adaptive devices as needed [82, 98].

Supportive Care in the Older Adult with Cancer at the End of Life

In patients of any age with advanced illness end of life supportive care is critical in addressing untreated symptoms that diminish function and quality of life. Symptoms such as pain, fatigue, functional dependence, and delirium are not unique to older patients, but can be more prevalent and challenging to treat in this population [99]. A Swedish study identified older age as a risk factor for poor end-of-life quality in cancer patients because younger patients were routinely informed more often about imminent death, more systematically assessed for pain and other symptoms, and more likely to be assessed by a formal palliative care service. In addition, the families of younger patients were more likely to be informed about imminent death and to be offered support in bereavement [100]. As is the case earlier in the disease trajectory, supportive care strategies need to be individualized to the patient's physiologic and social reserve. Certain medications may be higher risk in older patients due to physiologic changes, altered pharmacokinetics, comorbidity burden, and polypharmacy. While non-pharmacological approaches are thus very important, it should be acknowledged that older patients are also at risk of undertreatment of symptoms due to fear of toxicity. Optimal treatment requires a more cautious approach to initiation and titration, with a commitment to continuing to increase medication use as appropriate to alleviate symptoms. Adequate supportive care at the end of life must also focus on the caregivers [99, 101]. Family and carers are often unaware of the changes that occur at the very end of life and education can serve to alleviate panic and distress [99]. Although prediction of death itself is not possible, providers can educate family members about the signs and symptoms of the terminal phases of death. Helping caregivers to anticipate this can help to lessen the anxiety and stress of the approach of death [102]. Delirium can be present during the dying process and is more likely to happen if the patient has experienced delirium prior to the end of life. It is key to educate families about the potential causes of and interventions for terminal delirium [103]. When patients experience terminal delirium, a shift toward providing comfort through use of sedatives may be appropriate, even if patients become less alert as a result [104]. Elderly patients may present differently in these stages, and close monitoring of symptoms is imperative to ensure the greatest reduction of patient suffering.

Conclusion

Care of the older adult with cancer relies upon adequate assessment as a guide for appropriate treatment. A multidimensional geriatric assessment with guided intervention is a vital part of this strategy. As many of the issues uncovered by a GA are unrelated to treatment of the cancer, it can be argued that a GA is actually a sophisticated approach to providing optimal supportive care. The provision of supportive care is crucial to reduce morbidity and enhance wellbeing throughout the survivorship trajectory: from diagnosis to

end of life. Multidisciplinary teams including oncologists, geriatricians, nurses, pharmacists, social workers, and physical therapists need to work together to achieve this aim.

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Table 1

MASCC febrile neutropenia risk score

Characteristic	Weight
Burden of illness: no or mild symptoms	5
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumor or no previous fungal infection	4
No dehydration	3
Burden of illness: moderate symptoms	3
Outpatient status	3
Age <60 years	2

A total score of 21 identified patients at low risk of complications from febrile neutropenia. Points attributed to the variable “burden of illness” are not cumulative. The maximum theoretical score is therefore 26. From Klastersky J., Paesmans M., The Multinational Association for Supportive Care in Cancer (MASCC) risk index score: 10 years of use for identifying low-risk febrile neutropenic cancer patients. *Support Care Cancer*. 2013;21(5):1487–95. doi:10.1007/s00520-013-1758-y, with permission of Springer