Integrating Geriatric Oncology into Clinical Pathways and Guidelines

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Abstract

Cancer is a disease of the elderly, and more research is needed to improve geriatric oncology care. The complexity of older cancer patients requires clinicians to consider a declining organs' function and competing comorbidities to balance pros and cons of every treatment choice within the context of estimated life expectancy.

A comprehensive geriatric assessment (CGA) is helpful and mandatory to establish an appropriate care plan as research demonstrated it can detect issues that would remain otherwise neglected and improve the care of older cancer patients. Predictive tools for chemotherapy toxicity may also help complete the assessment for patients eligible for anticancer therapy. Nevertheless, CGA may be time-consuming, and several screening tools have been developed and validated to identify potential candidates for a full assessment.

Due to the underrepresentation of older patients in clinical trials and the shortage of studies specifically addressing this population, a solid evidence base for the management of cancer in this setting is currently lacking. However, less robust levels of evidence may be

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used to inform treatment decisions. Therefore, the guidelines available can provide clinicians with the tools to pilot the care of older adults with cancer, yet more specific research in the field is awaited.

Introduction

Cancer Burden in the Elderly

Age is the most important risk factor for cancer. Sixty percent of the incidence of cancer and 70 percent of its mortality occur in patients aged 65 years and older (Ries et al. 2003). By 2030, in the United States, new cancer cases in older patients aged over 65 are expected to increase by 67 percent compared to 11 percent in younger adults (Smith et al. 2009). In Western countries up to 30 percent of the population will be aged 65 or older by 2050, and individuals aged 80 and overrepresent its fastest growing part; worldwide one in six people will be aged over 65 (WHO 2002). Geriatric oncology accounts for a relevant part of the everyday practice for the medical oncologist and is expected to be increasingly important. More research in geriatric oncology is needed in order to improve cancer prevention, its early detection and specific therapies addressing elderly patients, since a solid amount of evidence in the field is still lacking. Developing an appropriate management approach for vulnerable patients is key for oncology care (Thompson and Dale 2015). The American Geriatrics Society's guidelines propose the following: 1) assessing patient preferences, 2) interpreting the available evidence, 3) estimating prognosis, 4) considering treatment feasibility, and 5) optimizing therapies and care plans (American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity 2012). Applying these recommendations to oncology is crucial for optimizing the care of older adults with cancer.

Complexity of Older Cancer Patients

Chronological age alone cannot fully depict the complex care an older cancer patient requires, including special attention to treatment toxicities, quality of life, estimated life expectancy, age-related organ function decline, and competing medical comorbidities.

Aging correlates with a loss of physiologic reserve in critical organs' function, and older individuals are at risk of decompensation upon exposure to stresses such as surgery or chemotherapy. Table 1 enlists some of the specific challenges in elderly cancer patients and their clinical implications. Nevertheless, chronological age may not correlate with functional status due to the heterogeneity of older cancer patients. Older patients are as willing to try anticancer therapies such as chemotherapy as their younger counterparts but less keen on enduring severe treatment-related adverse events (Yellen et al. 1994), and quality of life always needs to be considered in the decision-making process (Sanoff et al. 2007). Prior to treatment initiation, an evaluation is helpful for assessment of the many domains that can affect cancer care in older adults including comorbidities; polypharmacy; functional, nutrition, and cognitive status; social support; and psychological status. Predictive tools including tools to determine expected life expectancy are available online to support decision-making with regard to cancer care in this patient population (ePrognosis n.d.; Walter and Covinsky 2001).

Comprehensive Geriatric Assessment

There is a continuum ranging from functional independence to frailty (Hamerman 1999), with some older patients without any significant limitations and minimal or no reduction in functional reserve, with others who are more vulnerable and suffer from decreased functional reserve. The oncologist is faced with the task of differentiating between the fit older individual who is likely to benefit from and tolerate standard therapy and the frail elderly patient who is prone to experience treatment-related side effects and requires

Table 1 Specific challenges in elderly cancer patients and clinical implications (Sawhney et al. 2005; Sehl et al. 2005; Peterson et al. 2016; Rolland et al. 2009)

Organ system	Aging-related changes	Implications
Liver	Hepatic volume decline Hepatic blood flow decline	Decreased drug metabolism Decreased drug elimination Increased treatment toxicities
Kidney	Decreased glomerular filtration rate	Volume depletion Decreased drug elimination Increased treatment toxicities
Muscles	Sarcopenia	Decreased mobility Impaired functional status Increased risk of falls
Bone marrow	Decreased bone marrow reserve	Increased treatment toxicities
Bone	Osteopenia and osteoporosis	Increased risk of fractures Decrease mobility Impaired functional status
Central nervous system	Neurons loss Reduced brain blood flow	Impaired cognition and dementia Increase risk of falls Increased susceptibility to benzodiazepines
Gastrointestinal	Poor motility Decreased acid production	Poor drug absorption
Cardiovascular	Decrease ventricular compliance Diastolic dysfunction Increased wall thickening	Increase risk with cardiotoxic drugs Higher risk of arrhythmias
Lungs	Decreased lung compliance Decreased sensitivity of the respiratory center Decreased mucociliary function	Decreased pulmonary capacity Higher risk of pulmonary infections Limitation on options for lung surgery/radiation

different treatment options. Moreover, some apparently fit patients are found to have deficiencies that would have become evident after treatment initiation upon thorough evaluation. A comprehensive geriatric assessment (CGA) evaluating all the factors that may potentially influence the treatment outcomes is particularly useful.

A CGA can predict treatment complications and survival (Ramjaun et al. 2013), aid in therapeutic decision-making (Kenis et al. 2013), detect subtle problems at baseline which are not recognized by routine consultation (Extermann et al. 2004), and improve mental health and pain control (Rao et al. 2005). Despite the recommendations by the National Comprehensive Cancer Network (NCCN) (VanderWalde et al. 2016) and the International Society of Geriatric Oncology (SIOG) guidelines (Extermann et al. 2005), its routine use is limited, likely due to time constraints and challenges of implementation into a busy oncology practice. Hence, screening tools have been developed that can identify patients who will benefit

from an extensive CGA (Decoster et al. 2015) such as the abbreviated CGA (Overcash et al. 2005), the Vulnerable Elders Survey-13 (VES-13) (Saliba et al. 2001), the G8 tool (Bellera et al. 2012), the modified G8 (Petit-Moneger et al. 2016), and the Flemish version of the Triage Risk Screening Tool (fTRST) (Braes et al. 2009).

The domains tested by CGA and some useful instruments to evaluate them are enlisted in Table 2. Compared to their counterparts without a history of cancer, older cancer patients have been found to have a statistically significant higher prevalence of limitations in activities of daily living (ADLs) (31.9% versus 26.9%), limitations in instrumental activities of daily living (IADLs) (49.5% versus 42.3%), geriatric syndromes (60.8% versus 53.9%), low self-rated health (27.4% versus 20.9%), a score above 3 on the VES-13 (45.8% versus 39.5%), and satisfying criteria for frailty (79.6% versus 73.4%) (Mohile et al. 2009). Functional disability is common in elderly cancer patients, with 17 percent of them

Table 2 CGA domains and available tools

Domain	Tools	Importance in oncology
Demographic data and social status	History regarding living situation, marital status, educational level, safety of environment, financial resources Caregiver burden	Support in the community
Comorbidity	Charlson comorbidity index (Charlson et al. 1994) CIRS-G	High score correlates with decreased OS and increased chemotherapy toxicity
Functional status	ADLs (Katz index) IADLs (Lawton scale) Visual and/or hearing impairment (glasses, hearing aids) Mobility difficulty (requiring help or use of walking aid) Timed get up and go Hand grip strength ECOG/Karnofsky PS Self-reported no. of falls	Poor functional status correlates with survival, quality of life, treatment toxicity
Cognition	Mini-mental state examination Clock-drawing test Montreal cognitive assessment	Poor cognitive function is a predictor of poor survival. May affect decision-making capacity
Depression	Geriatric depression scale Hospital anxiety and depression scale Presence of depression (as geriatric syndrome) Distress thermometer	Poor quality of life and compliance to treatment
Nutrition	Body mass index (BMI) Weight loss (unintentional loss in 3 or 6 months) Mini nutritional assessment	Increased morbidity and mortality with low BMI
Fatigue	Mob-T	Poor symptom control and compliance to treatment
Polypharmacy	Beers criteria STOPP and START criteria	Risk of drug interactions with chemotherapy
Geriatric syndromes	Dementia Delirium Incontinence (fecal and/or urinary) Osteoporosis or spontaneous fractures Neglect or abuse Failure to thrive Constipation Polypharmacy Pressure ulcers Sarcopenia	

Abbreviations: ADL, activity of daily living; CIRS-G, Cumulative Illness Rating Scale-Geriatrics; ECOG, Eastern Cooperative Oncology Group; GA, geriatric assessment; IADL, instrumental activity of daily living; MOB-T, Mobility-Tiredness Test; PS, performance status; START, Screening Tool to Alert Doctors to Right Treatment; STOPP, Screening Tool of Older Person's Prescriptions

reporting limitations for ADLs and 58 percent for IADLs (Serraino et al. 2001), with impact survival, quality of life, and rates of chemotherapy toxicity (Maione et al. 2005; Extermann et al. 2012; Hurria et al. 2011). Studies have shown that performance status scores as determined by care providers underestimate the degree of functional impairment in older patients (Repetto et al. 2002; Jolly et al. 2015), while the use of validated scales provides a more precise evaluation (Hoppe et al. 2013). The history of falls in an important item (Sattar et al. 2016) and their prior occurrence are consistent predictors of subsequent functional disability among older patients.

Comorbidities and cognitive function are an independent CGA domains and are considered independent prognostic markers (Extermann et al. 1998) (Charlson et al. 1987) (Miller et al. 1992; Williams et al. 2016) (Neale et al. 2001). Comorbidities impact life expectancy and treatment outcomes and correlate with poorer survival (Satariano and Ragland 1994; Asmis et al. 2008; Hines et al. 2009). Cognitive function has direct influence on the decision regarding both cancer diagnosis and treatment with regard to capacity and compliance (Gupta and Lamont 2004; Wolfson et al. 2001; Gorin et al. 2005). As such it should always be evaluated at baseline prior to any cancer treatment and ensure the compliance to the therapeutic recommendations and capacity to make treatment decisions. Nutritional status is also crucial, since weight loss and low body mass index (BMI) increase mortality for older adults (Newman et al. 2001) and impact on survival, performance status, and chemotherapy tolerance (Dewys et al. 1980). Nutritional issues are heterogeneous and may include weight loss during anticancer therapy, malnutrition during advanced disease, and obesity during survivorship (Presley et al. 2016).

A regular and comprehensive review of all medications should be performed in order to remove any unnecessary or potentially inappropriate medications and to assess potential drug interactions (Lichtman and Villani 2000; Vestal 1997). Among elderly cancer patients, medication errors and use of potentially inappropriate medication are more frequent (Coleman et al. 2005; Nightingale et al. 2015). One example is the high sensitivity of older adults to benzodiazepines, that increase the risk of falls and cognitive impairment (Schroeck et al. 2016). This class of drugs should be avoided in favor of alternative medications and approaches (Hurria et al. 2014a). There are also a number of potentially dangerous interactions of some medications with chemotherapy (e.g., warfarin and capecitabine).

Psychological distress is experienced by one third of elderly cancer patients and frequently implicates depression (Kua 2005), especially in the context of inadequate social support, higher risk of functional decline, and increased

utilization of healthcare resources (Penninx et al. 1998). Social support should always be evaluated in conjunction with treatment planning (Stuck et al. 1993; Cohen 2002). Also, it should be considered whether the patient is a caregiver for someone else or if there is anybody available to take on such role (Klepin et al. 2015). Caregivers may be exposed to stress and depression, to neglect their own health (Germain et al. 2016) (Navaie-Waliser et al. 2002). Cultural, social, psychological, and behavioral variables should be considered when evaluating the individual situation (Baider and Surbone 2014).

A number of interventions can address the issues detected in each domain of CGA (Mohile et al. 2015), including physiotherapy and occupational therapy, caregiver involvement, reducing polypharmacy, social work and home safety assessment, counseling, oral care, and nutrition consult. CGA should also be repeated throughout the continuum of cancer care, since the needs may be different in different times and settings.

Lack of External Validity of the Current Evidence

A solid amount of evidence is needed in support of the optimal management in this specific patient population. However, older patients are underrepresented in clinical trials (Hutchins et al. 1999; Lewis et al. 2003). Strict trial eligibility criteria, competing comorbidities, and logistic barriers limit enrolment of older patients (Trimble et al. 1994; Kemeny et al. 2003; Yee et al. 2003). As a result 11 percent of elderly cancer patients are excluded from clinical trials a priori on the basis of their age (Javid et al. 2012) despite evidence showing that treatment tolerance in clinical trials is similar across various age groups (Javid et al. 2012; Giovanazzi-Bannon et al. 1994; LoConte et al. 2010; Townsley et al. 2005). An additional factor hindering accrual of older patients on clinical trials is physicians' fear of toxicity, resulting in clinical trial options being discussed less frequently with elderly patients (Javid et al. 2012; Foster et al. 2010). Other potential barriers to trial enrolment of older patients include lack of

autonomy over treatment choice (Townsley et al. 2006), concerns about potential adverse events, relatives opposing participation (Javid et al. 2012), different literacy rates (Townsley et al. 2006), ambiguities in the trust in physicians (Jenkins et al. 2013), and perception of the efficacy of a trial (Jenkins et al. 2013). Nonetheless, altruism remains a powerful incentive to facilitate participation of older patients in clinical trials (Jenkins et al. 2013).

The underrepresentation of older individuals in clinical trials supporting the current available guidelines limits their applicability in the elderly population (Battisti et al. 2015). Therefore, eligibility criteria should be less restrictive to allow for enrollment of real-world patients. Furthermore, research specifically addressing older people are needed and have been proved to be feasible (Cunningham et al. 2013; Muss et al. 2009). Such trials might also inform treatment options for younger patients who are not fit for more intensive treatment. Novel study approaches and methodologies, for example, mandating certain percentages of older subjects on registration studies that would resemble the proportion of elderly patients in the real-world population, can certainly advance this field and improve the evidence base to guide the management of older cancer patients (Hurria et al. 2014b; Hurria et al. 2015). The assessment of vulnerable older patients is the ideal setting to test patient-reported outcomes. There is a consistently high risk of underreporting of subjective toxicities by physicians, even when these data are prospectively collected within randomized studies (Di Maio et al. 2015). Therefore, the incorporation of patient-related outcomes into clinical trials is strongly encouraged.

Integration of Geriatric Oncology into Clinical Pathways

Geriatricians developed and validated CGA as a holistic approach to assess older patients in 1999 (Reuben et al. 1999; Cohen et al. 2002). Following a first attempt to adapt the CGA for use in oncology (Monfardini et al. 1996), its efficacy was prospectively assessed in a large population

of elderly cancer patients at the end of last century (Repetto et al. 2002; Repetto and Balducci 2002). During the early 2000s, its importance was validated in routine oncology practice (Monfardini and Balducci 1999; Extermann and Hurria 2007). Some landmark studies demonstrated that CGA domains are associated with poor tolerance to cancer therapies, that they can predict mortality and influence treatment decisions, thus potentially leading to further tailoring care and improving older patients' quality of life (Clough-Gorr et al. 2010; Decoster et al. 2013; Freyer et al. 2005; Pottel et al. 2014). During the last decade, research has focused on the optimization of CGA in routine multidisciplinary cancer care (Sattar et al. 2014), on the most optimal screening tool to detect patients requiring a CGA (Kenis et al. 2013; Soubeyran et al. 2014), and on the proposal and validation of new tools for use within the assessment (Ketelaars et al. 2013; Lycke et al. 2014).

New models have been recently developed and validated to predict chemotherapy toxicity based upon geriatric assessment items. The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) score has been designed by Extermann et al. to anticipate the risk of chemotherapy-related hematologic and non-hematologic toxicity in older adults (Extermann et al. 2012). It takes into account the specific chemotherapy regimens to be used as well as clinical and laboratory values including blood pressure, creatinine, albumin, hemoglobin, lactate dehydrogenase and liver function tests, and assessment of functional, mental, and nutritional status including ECOG Performance Status, Mini-Mental Health Status (MMS), and Mini Nutritional Assessment (MNA). Hurria et al. developed the Cancer and Aging Research Group (CARG) model in order to predict which patients are at increased risk of developing severe or fatal toxicity from chemotherapy (Hurria et al. 2011; Hurria et al. 2016). It is based upon a number of parameters accounting for age, type of cancer, the proposed chemotherapy regimen, renal and hematologic function, hearing, and activity levels (ability to take medications, physical activity, social support), and it has been shown to be superior to

the Karnofsky Performance Status. Finally, European investigator showed that advanced disease, a low MNA score, and a long Timed Get Up And Go test are associated with a higher risk of early death (within 6 months) after initiation of first-line chemotherapy (Soubeyran et al. 2012).

A recent analysis demonstrated that a web-based symptom reporting system for adults aged 26 to 91 undergoing chemotherapy resulted in better health-related quality of life, fewer emergency room admissions, fewer hospitalizations, a longer duration of palliative chemotherapy, and a superior quality-adjusted survival (Basch et al. 2016). CGA can also be conducted in an outpatient setting also using a self-reported format, and this approach has been reported as highly reliable and may be more feasible in a busy oncology practice (Ingram et al. 2002). Along with the mailing of a questionnaire, such an approach may save a substantial portion of clinic time. Nevertheless, the use of patient self-assessment tools may be time-consuming and challenging for patients with cognitive impairment. In addition, elderly cancer patients are more likely to perceive symptoms as inevitable and as a consequence of cancer and their treatment; therefore, underreporting can still be an issue in this setting. Hence, patient self-assessment is feasible in the geriatric cancer population, yet further research is needed to allow for its wide spread adoption.

Models of Care in Geriatric Oncology

The proportion of older cancer adults is increasing, and this required more collaborative training in geriatric principles and cancer care. Nevertheless, there are insufficient geriatricians and even less geriatric oncologists to address the unique needs of this population of patients. It has been documented that in North America there are 0.5–1.5 geriatricians per 10,000 adults aged 65 and older (Hsu 2016). Therefore, these low figures make it more difficult for oncologists to refer patients for appropriate geriatric management, and they often have to act as geriatricians themselves despite having received limited training in the principles of older adults'

care (Maggiore et al. 2016). The use of appropriate geriatric oncology guidelines can be helpful in such a difficult setting (Hurria et al. 2014a). Three different models of geriatric oncology care have been tested and established in different environments, as shown in Table 3: the consultative model, the shared care model, and the comprehensive care model (Magnuson et al. 2014).

In the consultative model, the oncologist refers older cancer patients to a geriatric oncology/geriatric team in order to request a geriatric assessment and consequent recommendations and to inform treatment recommendations. The geriatrician performs a CGA in a multidisciplinary setting. The advantages include the specific geriatric oncology/geriatric expertise of the team that provide guidance based on a variety of different competencies. On the other hand, this model requires a referral from a physician, and it more frequently implies a one-time visit without any possibility of longitudinal follow-up, and the interventions are often left to the treating team. Moreover, as the visits are usually long, the number of patients per clinic session may be limited. Moreover, frequently patients have to attend multiple clinical appointments, and this may be challenging for older adults. In addition, some institutions do not have a full-time geriatrician or geriatrics service.

According to the shared care model, the oncologist will refer the patient for a geriatric assessment and subsequent interventions or treatment recommendations. A CGA is performed by a geriatrician or a geriatric oncologist, and its results as well as the care plan are reviewed within an interdisciplinary meeting. Then, the geriatric oncology team collaborates with the treating oncologist and provides concurrent care across the disease trajectory. The advantages of this model include a collaborative care through the course of the disease, a geriatric expertise, and the possibility to implement interventions and recommendations over time. Nevertheless, visits may not be centralized, and patients might require extra consultations, and again this model requires a referral from a physician. Both the shared care and the consultative model require routine and strong communication

Table 3 Models of care in geriatric oncology

Model of care	Pathway	Advantages	Challenges
Consultative	• Oncologist refers patient • Reasons: CGA and intervention recommendations, treatment recommendations • CGA performed by geriatrician and multidisciplinary team	• Geriatric/geriatric oncology expertise • Recommendations from a multidisciplinary team	• Physician buy-in need to refer • One time visit • No longitudinal follow-up • Interventions often left to treating team • Long visits: Limit no. of patients per clinic session • Multiple visits and physicians for patients • Need to maintain good communication in the team
Shared care	• Oncologist refers patient • Reasons: CGA and intervention recommendations, treatment recommendations • CGA performed by geriatrician/ geriatric oncologist and multidisciplinary team • Interdisciplinary meeting to review the results and care plan • Geriatric oncology team collaborates with treating oncologist and provides concurrent care across the disease trajectory	• Collaborative care through disease trajectory • Geriatric/geriatric oncology expertise • Interventions and multidisciplinary recommendations can be implemented over time	• Physician buy-in need to refer • Visits may not be centralized • Shortage of geriatricians • Extra visits for the patient
Comprehensive	• Geriatric oncologist is the treating oncologist throughout the patient's disease trajectory • No need for additional referrals. • GA performed • Results and recommendations are reviewed with the patient • Referrals to the multidisciplinary team	• Geriatric oncology expertise throughout the treatment trajectory • Convenience: One-stop shopping (geriatrics and oncology)	• Shortage of geriatric oncologists • Complex patient population (limited no. of patients can be seen)

Abbreviation: CGA, comprehensive geriatric assessment

between the oncology and geriatric team, which may be a challenge.

In the comprehensive care model, the geriatric oncologist is the patient's treating oncologist throughout the disease trajectory. No referral is needed since this is a one-stop shop and the full care is provided by the geriatric oncologist. CGA results and the subsequent recommendations are reviewed with the patient, and referrals may be made to the multidisciplinary team accordingly. The advantages include the benefit of a continuous geriatric oncology expertise and the convenience of combining geriatrics and oncology qualifications. However, there is a shortage of geriatric oncologists, and the number of patients that can be seen may be limited due to the complexity of this population. Therefore, oncologists should be enabled to become familiar with geriatric assessment and be able to perform it following appropriate screening to identify patients requiring a more intense geriatric evaluation. A slightly different version of the comprehensive model has been developed in some centers which involves a combined geriatric oncology clinic where patients are seen by the oncologist and immediately afterward by the geriatrician or up front by a geriatric

oncologist. In these clinics the patients can be offered additional services such as physical therapy, nutrition, and psychiatry based on deficiencies identified in the assessment.

Currently the most relevant challenges across these different models include limitation of resources in terms of space, personnel, and funding. The need for buy in and champions willing to endorse such an activity and the fact that the demand may be greater than the capacity of a geriatric oncology service, due to the demographic changes are the most important challenges. As a geriatric oncology, multidisciplinary team usually involve different professionals including geriatricians and/or geriatric oncologists, nurses, social workers, pharmacists, psychiatrists, physician assistants, nutritionists, rehabilitation services, case managers, and visiting nurses. Certainly a business, financial model, and institutional resources are needed, along with more education and more research in the field. However, the biggest challenge involves choosing the right model for the right setting.

For example, in a community clinic, separate geriatrics and oncology practices may exist, possibly within a hospital-affiliated system. Therefore, the primary care doctor or the geriatrician usually consults the oncologist when a cancer is suspected or diagnosed. Patients may be already known to geriatricians, thus facilitating the use of CGA before the treatment plans. Furthermore, common electronic records may facilitate a shared care model. However, lack of communication between the two disciplines in a timely manner may be an issue and affect the decision-making process. In a setting where oncologists are familiar with geriatrics principles and geriatricians and geriatric oncologists are not available, they can directly refer patients to relevant services and professionals based on a CGA performed by themselves.

In an academic medical center, the relationship may be determined by the size of the geriatrics and oncology departments, and referrals may be made either by the geriatricians or by the oncologist according to patients' entry into the hospital system. Such an environment promotes clinical collaboration and research, although time constraints and lack of understanding between the two areas may have an impact on shared goals.

In a comprehensive cancer center, oncologists usually are the patients' primary care physicians during cancer care and a geriatric consultation may occur at any time. Screening tools can help determine which patients are at risk of increased toxicity and guide appropriate geriatrics referrals. However, the high volume of elderly cancer patients may overwhelm the capacity of a geriatrics service.

The NCCN Senior Adult Oncology guidelines (Hurria et al. 2014a) try to give the tools to the oncologists and provide guidance for the identification of patients requiring more of a multidisciplinary approach. SIOG has issued guidelines about geriatric assessment and screening tools that can provide clinicians further guidance (Decoster et al. 2015; Wildiers et al. 2014): The SIOG panel recommended the use of screening tools for busy oncology practice while emphasizing that these assessments should not replace a full geriatric assessment. In addition, there are several disease-specific guidelines issued by the SIOG regarding the management of older patients with number of cancers (Body et al. 2016; Stauder et al. 2016; Biganzoli et al. 2012; Biganzoli et al. 2016; Ghignone et al. 2016; Biganzoli et al. 2015; Morrison et al. 2015; Droz et al. 2014; Pallis et al. 2014; Papamichael et al. 2015; Aapro et al. 2011; Bellmunt et al. 2009; Launay-Vacher et al. 2007). Implementation of these guidelines in each specific disease setting would further advance and improve the care of the older population.

Survivorship Care of Elderly Cancer Patients

A cancer survivor is defined as any person diagnosed with cancer, from the time of initial diagnosis until the end of life (National Coalition for Cancer Survivorship 2016). Two thirds of all cancer survivors will be aged over 65 by 2020 (Parry et al. 2011), and they will increase to 11 million of people in the United States due to demographic changes and increased survival of older patients after cancer diagnosis. Fatigue, physical

limitations, cognitive impairment, osteoporosis, and chemotherapy-related peripheral neuropathy are cited among the clinically significant long-term outcomes of cancer in this population (Rowland and Bellizzi 2014). As the number of survivors continues to increase, guidelines specifically addressing this topic have been developed by the NCCN (Denlinger et al. 2016).

Survivorship care plans should be incorporated into clinical care and include treatment summaries, surveillance plans, and tailored lifestyle information. The older patient's needs should be assessed in the survivorship care planning process, and some of them may need a CGA in order to define those needs. Based on this, an interprofessional team can develop a plan that is individualized for each patient. It should address needs regarding exercise, nutrition, polypharmacy, comorbidities, and social support. Survivorship guidelines should always be applied to older cancer patient, who should be able to access patient-centered, non-fragmented care.

The use of survivorship care plans in elderly cancer patients may improve the quality of care and health outcomes, but the most appropriate model of care for older adults during survivorship is still debated. Models including shared care, primary care physician only, or cancer-specific survivorship clinics have been proposed. The shared care model involves different professionals whose role may vary over time based on the specific needs of each patient (Cohen 2009); nevertheless, its impact on the management of complex older patients is currently uncertain. There is considerable need for more research to understand pros and cons of survivorship care plans, as their format, timing, and outcomes are still uncertain (Mohile et al. 2016).

Unique considerations about survivorship care plans for older cancer patients include comorbidities, polypharmacy, and the heterogeneity of this population identified through the different domains for the CGA. Fatigue and weight gain may be addressed by all clinicians and prompt an appropriate referral to physical/occupational therapists for energy conservation and function

maintenance as well as nutritional services (Morgan and Tarbi 2016).

Long-term effects of chemotherapy are of paramount importance for older cancer survivors. For example, peripheral neuropathy is a debilitating toxicity associated with various chemotherapy regimens, including taxanes and platinum compounds. Taxanes have been documented to cause grade 2 to 4 neuropathy rates ranging from 15% to 23% based on different drugs, schedules, and durations of treatment (Schneider et al. 2015). This side effect which may be permanent is particularly relevant to older adults as it can severely interfere with function and result in increased risk for falls. In addition, effective therapies are lacking for its treatment and prevention (Hershman et al. 2014). Elderly patients with a history of complication from diabetes, receiving paclitaxel, and those treated with a platinum agent have an increased risk or neuropathy (Hershman et al. 2016). A variety of comorbid conditions including hypothyroidism, vasculitis, infections (herpes varicella zoster and HIV), and some medications treating hypertension and hypercholesterolemia, which are more prevalent in the older population, can increase the likelihood of developing peripheral neuropathy. Monitoring of these symptoms and interventions by the rehabilitation team may help improve the management of this long-term treatment related outcome.

Anthracyclines are effective and commonly used chemotherapy agents for both solid and hematological malignancies, but they are known to cause short- and long-term cardiotoxicity, including potentially fatal congestive heart failure (CHF) (Ewer and Lenihan 2008). Older adults with a diagnosis of hypertension or diabetes and a limited cardiac reserve may be at particular risk for these long-term complications of anticancer therapy (Barrett-Lee et al. 2009), and their life expectancy is still sufficient for potential long-term toxic effects to become apparent (Aapro et al. 2011). Doxorubicin has been associated with a 29% increase in risk of CHF in a retrospective series of older patients treated for diffuse large B-cell lymphoma (Hershman et al. 2008). In

elderly breast cancer survivors, the incidence of CHF 10 years after completion of adjuvant chemotherapy has been found to be 38% (Pinder et al. 2007). Regarding breast cancer, the risk of cardiac dysfunction may be exacerbated by the sequential use of trastuzumab after anthracyclines, as this is a known side effect of such monoclonal antibody (Denegri et al. 2016). In case of aggressive lymphomas, options are more limited than in breast cancer; the use of epirubicin rather than doxorubicin, different treatment schedules, liposomal formulations, and non-anthracycline-based regimens may be possible useful approach in this population, along with a closer cardiac function monitoring. As such cardiac monitoring as part of survivorship care should be considered specifically in older patients who received these treatment regimens.

Finally, such plans should consider the specific cultural context and the beliefs, desires, and wishes of this population. The engagement of family, friends, and caregivers is relevant, as some older adults may want to include them as part of the survivorship care process. Also, the way information is delivered is important, as some of them might prefer having a paper copy of their plan rather than going paperless.

Many older adults present a myriad of health issues, and healthcare is often provided by a fragmented group of professionals. Therefore, it is important that survivorship care is well coordinated, comprehensive, and focused on the patient's goals and preferences. Prompt communication between different members of the multidisciplinary team and especially between different specialists is key, while the primary care physician or the geriatrician should coordinate and facilitate the overarching care plan. Older cancer patients should always be at the center of all interprofessional teams, and clinicians must consider that their needs may change over time and that adjustments may need to be made accordingly. Health professionals including medical oncologists, radiation oncologists, surgeons, primary care physicians, registered and advanced practice nurses, physician assistants, psychosocial support professionals, pharmacists, dieticians, rehabilitation specialists, palliative care clinicians, and research coordinators are considered integral part of the survivorship care team, along with any other specialists possibly involved in the care of other medical conditions. Additional members might include patient navigators, nurse aides, home health and home care aides, and patient advocates. Finally, caregivers, who hold the responsibility of the care of older adults at home, have also a crucial role within the team. Each of them contributes uniquely with a broad range of skills, knowledge, and expertise and should communicate clearly, educate one another, and develop clear expectations and accountability in order to deliver and promote coordinated, patient-centered care. Across the continuum from acute cancer treatment to survivorship, the team leader may change based on the patient's conditions and needs.

Integration of Geriatric Oncology into Disease-Specific Guidelines

The underrepresentation of elderly patients in clinical trials and their exclusion from studies due to variety of reasons undermine the applicability of disease-specific guidelines for the care of an older patient (Battisti et al. 2015). Trials' subjects are a selected group of healthy and fit patients whose characteristics do not necessarily reflect those of the senior adults that an oncologist meets everyday in clinic. Due to the lack of evidence to guide therapy in this patient population, significant heterogeneity exists between key opinion leaders regarding the appropriate care, which adds additional challenge to the development of guidelines. Few studies addressing the management of cancer in older adults are available and therefore included into guidelines. When such evidence is lacking, the incorporation of less robust data, including retrospective series, meta-analyses, single-institution studies, and phase II trials, may provide some more guidance for the oncologist.

Assessing whether the expected benefits of treatment are superior to the risks in a population

with a reduced life expectancy and decreased functional reserve and tolerance to stress may be challenging. Moreover, the biology of cancer and its responsiveness to therapy are different in older adults compared to their younger counterparts (Balducci 2006). In addition, elderly patients have decreased tolerance to anticancer treatments and view the benefits of therapy differently. On the other hand, age alone should not preclude patients from receiving effective treatment potentially improving their survival and quality of life (Extermann 2004). Addressing these clinical questions is challenging via guidelines, and therefore most provide the practitioner an overview of the appropriate areas that need to be evaluated, deficiencies that should be addressed and issues that must be discussed with the patient during the continuum of cancer care. In this sense, the NCCN Older Adult Oncology guidelines (VanderWalde et al. 2016) discuss more of the assessment and treatment decision algorithm in older patients rather than specific therapeutic recommendations. For example, they provide guidance on assessing the ability to make decisions and point out specific considerations for using anticancer therapies in the elderly; they also highlight the relevance of estimating life expectancy in this setting and of the assessment of the domains of CGA. These are not specific treatment guidelines, but rather more general tools to allow the oncologist to better evaluate and manage older patients, regardless of their cancer.

In summary, specific problems related to aging formed the basis for the development of the NCCN Older Adult Oncology guidelines in order to suggest to clinicians the adequate mindset and tools and ensure an appropriate evaluation and management of older cancer patients in an individualized manner. Properly selected patients can receive effective and safe cancer therapy, whereas treatments that may potentially affect their quality of life without any significant benefit in survival should be avoided. As oncologists we are tasked with determining the best mechanism to incorporate the available assessment tools and supportive care measures, to ensure appropriate evaluation of the older cancer patient and delivery of a treatment plan that would result in the optimal outcome. Additional research is needed in this field to better inform our approach to this growing patient population.

References

Aapro M, Bernard-Marty C, Brain EG, Batist G, Erdkamp F, Krzemieniecki K, et al. Anthracycline cardiotoxicity in the elderly cancer patient: a SIOG expert position paper. Ann Oncol. 2011;22(2):257–67.

American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. Patient-centered care for older adults with multiple chronic conditions: a stepwise approach from the American Geriatrics Society: American Geriatrics Society expert panel on the Care of Older Adults with multimorbidity. J Am Geriatr Soc. 2012;60(10):1957–68.

Asmis TR, Ding K, Seymour L, Shepherd FA, Leighl NB, Winton TL, et al. Age and comorbidity as independent prognostic factors in the treatment of non small-cell lung cancer: a review of National Cancer Institute of Canada clinical trials group trials. J Clin Oncol Off J Am Soc Clin Oncol. 2008;26(1):54–9.

Baider L, Surbone A. Universality of aging: family caregivers for elderly cancer patients. Front Psychol. 2014;5:744.

Balducci L. Management of cancer in the elderly. Oncology (Williston Park). 2006;20(2):135–43. discussion 44, 46, 51-2

Barrett-Lee PJ, Dixon JM, Farrell C, Jones A, Leonard R, Murray N, et al. Expert opinion on the use of anthracyclines in patients with advanced breast cancer at cardiac risk. Ann Oncol. 2009;20(5):816–27.

Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: a randomized controlled trial. J Clin Oncol Off J Am Soc Clin Oncol. 2016;34(6):557–65.

Battisti N, Sehovic M, Extermann M. Assessment of the external validity of National Comprehensive Cancer Network and European Society for Medical Oncology guidelines for non-small cell lung cancer in a population of elderly patients aged 80 and older. J Clin Oncol. 2015;33(15_suppl (May 20 Supplement)):e20539.

Bellera CA, Rainfray M, Mathoulin-Pelissier S, Mertens C, Delva F, Fonck M, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Ann Oncol. 2012;23(8):2166–72.

Bellmunt J, Negrier S, Escudier B, Awada A, Aapro M. The medical treatment of metastatic renal cell cancer in the elderly: position paper of a SIOG taskforce. Crit Rev Oncol Hematol. 2009;69(1):64–72.

Biganzoli L, Wildiers H, Oakman C, Marotti L, Loibl S, Kunkler I, et al. Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and

European Society of Breast Cancer Specialists (EUSOMA). Lancet Oncol. 2012;13(4):e148–60.

Biganzoli L, Lichtman S, Michel JP, Papamichael D, Quoix E, Walko C, et al. Oral single-agent chemotherapy in older patients with solid tumours: a position paper from the International Society of Geriatric Oncology (SIOG). Eur J Cancer. 2015;51(17):2491–500.

Biganzoli L, Aapro M, Loibl S, Wildiers H, Brain E. Taxanes in the treatment of breast cancer: have we better defined their role in older patients? A position paper from a SIOG task force. Cancer Treat Rev. 2016;43:19–26.

Body JJ, Terpos E, Tombal B, Hadji P, Arif A, Young A, et al. Bone health in the elderly cancer patient: a SIOG position paper. Cancer Treat Rev. 2016;51:46–53.

Braes T, Flamaing J, Sterckx W, Lipkens P, Sabbe M, de Rooij SE, et al. Predicting the risk of functional decline in older patients admitted to the hospital: a comparison of three screening instruments. Age Ageing. 2009;38(5):600–3.

Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.

Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994;47(11):1245–51.

Clough-Gorr KM, Stuck AE, Thwin SS, Silliman RA. Older breast cancer survivors: geriatric assessment domains are associated with poor tolerance of treatment adverse effects and predict mortality over 7 years of follow-up. J Clin Oncol Off J Am Soc Clin Oncol. 2010;28(3):380–6.

Cohen HJ. Cancer care in the older population: physiology of aging. American Society of Clinical Oncology Curriculum. 2002.

Cohen HJ. A model for the shared care of elderly patients with cancer. J Am Geriatr Soc. 2009;57(Suppl 2): S300–2.

Cohen HJ, Feussner JR, Weinberger M, Carnes M, Hamdy RC, Hsieh F, et al. A controlled trial of inpatient and outpatient geriatric evaluation and management. N Engl J Med. 2002;346(12):905–12.

Coleman EA, Smith JD, Raha D, Min SJ. Posthospital medication discrepancies: prevalence and contributing factors. Arch Intern Med. 2005;165(16):1842–7.

Cunningham D, Lang I, Marcuello E, Lorusso V, Ocvirk J, Shin DB, et al. Bevacizumab plus capecitabine versus capecitabine alone in elderly patients with previously untreated metastatic colorectal cancer (AVEX): an open-label, randomised phase 3 trial. Lancet Oncol. 2013;14(11):1077–85.

Decoster L, Kenis C, Van Puyvelde K, Flamaing J, Conings G, De Greve J, et al. The influence of clinical assessment (including age) and geriatric assessment on treatment decisions in older patients with cancer. J Geriatr Oncol. 2013;4(3):235–41.

Decoster L, Van Puyvelde K, Mohile S, Wedding U, Basso U, Colloca G, et al. Screening tools for

multidimensional health problems warranting a geriatric assessment in older cancer patients: an update on SIOG recommendationsdagger. Ann Oncol. 2015;26(2):288–300.

Denegri A, Moccetti T, Moccetti M, Spallarossa P, Brunelli C, Ameri P. Cardiac toxicity of trastuzumab in elderly patients with breast cancer. J Geriatr Cardiol. 2016;13(4):355–63.

Denlinger CS, Ligibel JA, Are M, Baker KS, Broderick G, Demark-Wahnefried W, et al. NCCN guidelines insights: survivorship, version 1.2016. J Natl Compr Cancer Netw. 2016;14(6):715–24.

Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. Eastern cooperative oncology group. Am J Med. 1980;69(4):491–7.

Di Maio M, Gallo C, Leighl NB, Piccirillo MC, Daniele G, Nuzzo F, et al. Symptomatic toxicities experienced during anticancer treatment: agreement between patient and physician reporting in three randomized trials. J Clin Oncol Off J Am Soc Clin Oncol. 2015;33(8):910–5.

Droz JP, Aapro M, Balducci L, Boyle H, Van den Broeck T, Cathcart P, et al. Management of prostate cancer in older patients: updated recommendations of a working group of the International Society of Geriatric Oncology. Lancet Oncol. 2014;15(9):e404–14.

ePrognosis. n.d.. Available from http://eprognosis.ucsf.edu/.

Ewer MS, Lenihan DJ. Left ventricular ejection fraction and cardiotoxicity: is our ear really to the ground? J Clin Oncol Off J Am Soc Clin Oncol. 2008;26(8):1201–3.

Extermann M. Management issues for elderly patients with breast cancer. Curr Treat Options in Oncol. 2004;5(2):161–9.

Extermann M, Hurria A. Comprehensive geriatric assessment for older patients with cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2007;25(14):1824–31.

Extermann M, Overcash J, Lyman GH, Parr J, Balducci L. Comorbidity and functional status are independent in older cancer patients. J Clin Oncol Off J Am Soc Clin Oncol. 1998;16(4):1582–7.

Extermann M, Meyer J, McGinnis M, Crocker TT, Corcoran MB, Yoder J, et al. A comprehensive geriatric intervention detects multiple problems in older breast cancer patients. Crit Rev Oncol Hematol. 2004;49(1):69–75.

Extermann M, Aapro M, Bernabei R, Cohen HJ, Droz JP, Lichtman S, et al. Use of comprehensive geriatric assessment in older cancer patients: recommendations from the task force on CGA of the International Society of Geriatric Oncology (SIOG). Crit Rev Oncol Hematol. 2005;55(3):241–52.

Extermann M, Boler I, Reich RR, Lyman GH, Brown RH, DeFelice J, et al. Predicting the risk of chemotherapy toxicity in older patients: the chemotherapy risk assessment scale for high-age patients (CRASH) score. Cancer. 2012;118(13):3377–86.

Foster JA, Salinas GD, Mansell D, Williamson JC, Casebeer LL. How does older age influence oncologists' cancer management? Oncologist. 2010;15(6):584–92.

Freyer G, Geay JF, Touzet S, Provencal J, Weber B, Jacquin JP, et al. Comprehensive geriatric assessment predicts tolerance to chemotherapy and survival in elderly patients with advanced ovarian carcinoma: a GINECO study. Ann Oncol. 2005;16(11):1795–800.

Germain V, Dabakuyo-Yonli TS, Marilier S, Putot A, Bengrine-Lefevre L, Arveux P, et al. Management of elderly patients suffering from cancer: assessment of perceived burden and of quality of life of primary caregivers. J Geriatr Oncol. 2016;8(3):220–8.

Ghignone F, van Leeuwen BL, Montroni I, Huisman MG, Somasundar P, Cheung KL, et al. The assessment and management of older cancer patients: a SIOG surgical task force survey on surgeons' attitudes. Eur J Surg Oncol. 2016;42(2):297–302.

Giovanazzi-Bannon S, Rademaker A, Lai G, Benson AB 3rd. Treatment tolerance of elderly cancer patients entered onto phase II clinical trials: an Illinois cancer center study. J Clin Oncol Off J Am Soc Clin Oncol. 1994;12(11):2447–52.

Gorin SS, Heck JE, Albert S, Hershman D. Treatment for breast cancer in patients with Alzheimer's disease. J Am Geriatr Soc. 2005;53(11):1897–904.

Gupta SK, Lamont EB. Patterns of presentation, diagnosis, and treatment in older patients with colon cancer and comorbid dementia. J Am Geriatr Soc. 2004;52(10):1681–7.

Hamerman D. Toward an understanding of frailty. Ann Intern Med. 1999;130(11):945–50.

Hershman DL, McBride RB, Eisenberger A, Tsai WY, Grann VR, Jacobson JS. Doxorubicin, cardiac risk factors, and cardiac toxicity in elderly patients with diffuse B-cell non-Hodgkin's lymphoma. J Clin Oncol Off J Am Soc Clin Oncol. 2008;26(19):3159–65.

Hershman DL, Lacchetti C, Dworkin RH, Lavoie Smith EM, Bleeker J, Cavaletti G, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol Off J Am Soc Clin Oncol. 2014;32(18):1941–67.

Hershman DL, Till C, Wright JD, Awad D, Ramsey SD, Barlow WE, et al. Comorbidities and risk of chemotherapy-induced peripheral neuropathy among participants 65 years or older in southwest oncology group clinical trials. J Clin Oncol. 2016;34(25):3014–22.

Hines RB, Chatla C, Bumpers HL, Waterbor JW, McGwin G Jr, Funkhouser E, et al. Predictive capacity of three comorbidity indices in estimating mortality after surgery for colon cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2009;27(26):4339–45.

Hoppe S, Rainfray M, Fonck M, Hoppenreys L, Blanc JF, Ceccaldi J, et al. Functional decline in older patients with cancer receiving first-line chemotherapy. J Clin Oncol Off J Am Soc Clin Oncol. 2013;31(31):3877–82.

Hsu T. Educational initiatives in geriatric oncology - who, why, and how? J Geriatr Oncol. 2016;7(5):390–6.

Hurria A, Togawa K, Mohile SG, Owusu C, Klepin HD, Gross CP, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. J Clin Oncol Off J Am Soc Clin Oncol. 2011;29(25):3457–65.

Hurria A, Wildes T, Blair SL, Browner IS, Cohen HJ, Deshazo M, et al. Senior adult oncology, version 2.2014: clinical practice guidelines in oncology. J Natl Compr Cancer Netw. 2014a;12(1):82–126.

Hurria A, Dale W, Mooney M, Rowland JH, Ballman KV, Cohen HJ, et al. Designing therapeutic clinical trials for older and frail adults with cancer: U13 conference recommendations. J Clin Oncol. 2014b;32(24):2587–94.

Hurria A, Levit LA, Dale W, Mohile SG, Muss HB, Fehrenbacher L, et al. Improving the evidence base for treating older adults with cancer: American Society of Clinical Oncology statement. J Clin Oncol Off J Am Soc Clin Oncol. 2015;33(32):3826–33.

Hurria A, Mohile S, Gajra A, Klepin H, Muss H, Chapman A, et al. Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2016;34(20):2366–71.

Hutchins LF, Unger JM, Crowley JJ, Coltman CA Jr, Albain KS. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. N Engl J Med. 1999;341(27):2061–7.

Ingram SS, Seo PH, Martell RE, Clipp EC, Doyle ME, Montana GS, et al. Comprehensive assessment of the elderly cancer patient: the feasibility of self-report methodology. J Clin Oncol Off J Am Soc Clin Oncol. 2002;20(3):770–5.

Javid SH, Unger JM, Gralow JR, Moinpour CM, Wozniak AJ, Goodwin JW, et al. A prospective analysis of the influence of older age on physician and patient decision-making when considering enrollment in breast cancer clinical trials (SWOG S0316). Oncologist. 2012;17(9):1180–90.

Jenkins V, Farewell V, Farewell D, Darmanin J, Wagstaff J, Langridge C, et al. Drivers and barriers to patient participation in RCTs. Br J Cancer. 2013;108(7):1402–7.

Jolly TA, Deal AM, Nyrop KA, Williams GR, Pergolotti M, Wood WA, et al. Geriatric assessment-identified deficits in older cancer patients with normal performance status. Oncologist. 2015;20(4):379–85.

Kemeny MM, Peterson BL, Kornblith AB, Muss HB, Wheeler J, Levine E, et al. Barriers to clinical trial participation by older women with breast cancer. J Clin Oncol. 2003;21(12):2268–75.

Kenis C, Bron D, Libert Y, Decoster L, Van Puyvelde K, Scalliet P, et al. Relevance of a systematic geriatric screening and assessment in older patients with cancer:

results of a prospective multicentric study. Ann Oncol. 2013;24(5):1306–12.

Ketelaars L, Pottel L, Lycke M, Goethals L, Ghekiere V, Santy L, et al. Use of the Freund clock drawing test within the mini-cog as a screening tool for cognitive impairment in elderly patients with or without cancer. J Geriatr Oncol. 2013;4(2):174–82.

Klepin HD, Rodin M, Hurria A. Treating older adults with cancer: geriatric perspectives. Am Soc Clin Oncol Educ Book. 2015:e544–52.

Kua J. The prevalence of psychological and psychiatric sequelae of cancer in the elderly – how much do we know? Ann Acad Med Singap. 2005;34(3):250–6.

Launay-Vacher V, Chatelut E, Lichtman SM, Wildiers H, Steer C, Aapro M. Renal insufficiency in elderly cancer patients: International Society of Geriatric Oncology clinical practice recommendations. Ann Oncol. 2007;18(8):1314–21.

Lewis JH, Kilgore ML, Goldman DP, Trimble EL, Kaplan R, Montello MJ, et al. Participation of patients 65 years of age or older in cancer clinical trials. J Clin Oncol Off J Am Soc Clin Oncol. 2003;21(7):1383–9.

Lichtman SM, Villani G. Chemotherapy in the elderly: pharmacologic considerations. Cancer Control. 2000;7(6):548–56.

LoConte NK, Smith M, Alberti D, Bozeman J, Cleary JF, Setala AN, et al. Amongst eligible patients, age and comorbidity do not predict for dose-limiting toxicity from phase I chemotherapy. Cancer Chemother Pharmacol. 2010;65(4):775–80.

Lycke M, Ketelaars L, Boterberg T, Pottel L, Pottel H, Vergauwe P, et al. Validation of the Freund clock drawing test as a screening tool to detect cognitive dysfunction in elderly cancer patients undergoing comprehensive geriatric assessment. Psycho-Oncology. 2014;23(10):1172–7.

Maggiore RJ, Callahan KE, Tooze JA, Parker IR, Hsu T, Klepin HD. Geriatrics fellowship training and the role of geriatricians in older adult cancer care: a survey of geriatrics fellowship directors. Gerontol Geriatr Educ. 2016;17:1–13.

Magnuson A, Dale W, Mohile S. Models of Care in Geriatric Oncology. Curr Geriatr Rep. 2014;3(3):182–9.

Maione P, Perrone F, Gallo C, Manzione L, Piantedosi F, Barbera S, et al. Pretreatment quality of life and functional status assessment significantly predict survival of elderly patients with advanced non-small-cell lung cancer receiving chemotherapy: a prognostic analysis of the multicenter Italian lung cancer in the elderly study. J Clin Oncol Off J Am Soc Clin Oncol. 2005;23(28):6865–72.

Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. Psychiatry Res. 1992;41(3):237–48.

Mohile SG, Xian Y, Dale W, Fisher SG, Rodin M, Morrow GR, et al. Association of a cancer diagnosis with vulnerability and frailty in older Medicare beneficiaries. J Natl Cancer Inst. 2009;101(17):1206–15.

Mohile SG, Velarde C, Hurria A, Magnuson A, Lowenstein L, Pandya C, et al. Geriatric assessment-guided care processes for older adults: a Delphi consensus of geriatric oncology experts. J Natl Compr Cancer Netw. 2015;13(9):1120–30.

Mohile SG, Hurria A, Cohen HJ, Rowland JH, Leach CR, Arora NK, et al. Improving the quality of survivorship for older adults with cancer. Cancer. 2016;122(16):2459–568.

Monfardini S, Balducci L. A comprehensive geriatric assessment (CGA) is necessary for the study and the management of cancer in the elderly. Eur J Cancer. 1999;35(13):1771–2.

Monfardini S, Ferrucci L, Fratino L, del Lungo I, Serraino D, Zagonel V. Validation of a multidimensional evaluation scale for use in elderly cancer patients. Cancer. 1996;77(2):395–401.

Morgan B, Tarbi E. The role of the advanced practice nurse in geriatric oncology care. Semin Oncol Nurs. 2016;32(1):33–43.

Morrison VA, Hamlin P, Soubeyran P, Stauder R, Wadhwa P, Aapro M, et al. Diffuse large B-cell lymphoma in the elderly: impact of prognosis, comorbidities, geriatric assessment, and supportive care on clinical practice. An International Society of Geriatric Oncology (SIOG) expert position paper. J Geriatr Oncol. 2015;6(2):141–52.

Muss HB, Berry DA, Cirrincione CT, Theodoulou M, Mauer AM, Kornblith AB, et al. Adjuvant chemotherapy in older women with early-stage breast cancer. N Engl J Med. 2009;360(20):2055–65.

National Coalition for Cancer Survivorship. 12 Apr 2016. Available from http://www.canceradvocacy.org/.

Navaie-Waliser M, Feldman PH, Gould DA, Levine C, Kuerbis AN, Donelan K. When the caregiver needs care: the plight of vulnerable caregivers. Am J Public Health. 2002;92(3):409–13.

Neale R, Brayne C, Johnson AL. Cognition and survival: an exploration in a large multicentre study of the population aged 65 years and over. Int J Epidemiol. 2001;30(6):1383–8.

Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP. Weight change in old age and its association with mortality. J Am Geriatr Soc. 2001;49(10):1309–18.

Nightingale G, Hajjar E, Swartz K, Andrel-Sendecki J, Chapman A. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and potentially inappropriate medication use among ambulatory senior adults with cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2015;33(13):1453–9.

Overcash JA, Beckstead J, Extermann M, Cobb S. The abbreviated comprehensive geriatric assessment (aCGA): a retrospective analysis. Crit Rev Oncol Hematol. 2005;54(2):129–36.

Pallis AG, Gridelli C, Wedding U, Faivre-Finn C, Veronesi G, Jaklitsch M, et al. Management of elderly

patients with NSCLC; updated expert's opinion paper: EORTC elderly task force, lung cancer group and International Society for Geriatric Oncology. Ann Oncol. 2014;25(7):1270–83.

Papamichael D, Audisio RA, Glimelius B, de Gramont A, Glynne-Jones R, Haller D, et al. Treatment of colorectal cancer in older patients: International Society of Geriatric Oncology (SIOG) consensus recommendations 2013. Ann Oncol. 2015;26(3):463–76.

Parry C, Kent EE, Mariotto AB, Alfano CM, Rowland JH. Cancer survivors: a booming population. Cancer Epidemiol Biomark Prev. 2011;20(10):1996–2005.

Penninx BW, Guralnik JM, Ferrucci L, Simonsick EM, Deeg DJ, Wallace RB. Depressive symptoms and physical decline in community-dwelling older persons. JAMA. 1998;279(21):1720–6.

Peterson LL, Hurria A, Feng T, Mohile SG, Owusu C, Klepin HD, et al. Association between renal function and chemotherapy-related toxicity in older adults with cancer. J Geriatr Oncol. 2016;8(2):96–101.

Petit-Moneger A, Rainfray M, Soubeyran P, Bellera CA, Mathoulin-Pelissier S. Detection of frailty in elderly cancer patients: improvement of the G8 screening test. J Geriatr Oncol. 2016;7(2):99–107.

Pinder MC, Duan Z, Goodwin JS, Hortobagyi GN, Giordano SH. Congestive heart failure in older women treated with adjuvant anthracycline chemotherapy for breast cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2007;25(25):3808–15.

Pottel L, Lycke M, Boterberg T, Pottel H, Goethals L, Duprez F, et al. Serial comprehensive geriatric assessment in elderly head and neck cancer patients undergoing curative radiotherapy identifies evolution of multidimensional health problems and is indicative of quality of life. Eur J Cancer Care. 2014;23(3):401–12.

Presley CJ, Dotan E, Soto-Perez-de-Celis E, Jatoi A, Mohile SG, Won E, et al. Gaps in nutritional research among older adults with cancer. J Geriatr Oncol. 2016;7(4):281–92.

Ramjaun A, Nassif MO, Krotneva S, Huang AR, Meguerditchian AN. Improved targeting of cancer care for older patients: a systematic review of the utility of comprehensive geriatric assessment. J Geriatr Oncol. 2013;4(3):271–81.

Rao AV, Hsieh F, Feussner JR, Cohen HJ. Geriatric evaluation and management units in the care of the frail elderly cancer patient. J Gerontol A Biol Sci Med Sci. 2005;60(6):798–803.

Repetto L, Balducci LA. Case for geriatric oncology. Lancet Oncol. 2002;3(5):289–97.

Repetto L, Fratino L, Audisio RA, Venturino A, Gianni W, Vercelli M, et al. Comprehensive geriatric assessment adds information to eastern cooperative oncology group performance status in elderly cancer patients: an Italian Group for Geriatric Oncology Study. J Clin Oncol Off J Am Soc Clin Oncol. 2002;20(2):494–502.

Reuben DB, Frank JC, Hirsch SH, McGuigan KA, Maly RC. A randomized clinical trial of outpatient comprehensive geriatric assessment coupled with an intervention to increase adherence to recommendations. J Am Geriatr Soc. 1999;47(3):269–76.

Ries EM, Kosary CL, Hankey BF. SEER cancer statistics review: 1975–2000. Bethesda: National Cancer Institute; 2003.

Rolland Y, Lauwers-Cances V, Cristini C, Abellan van Kan G, Janssen I, Morley JE, et al. Difficulties with physical function associated with obesity, sarcopenia, and sarcopenic-obesity in community-dwelling elderly women: the EPIDOS (EPIDemiologie de l'OSteoporose) study. Am J Clin Nutr. 2009;89(6):1895–900.

Rowland JH, Bellizzi KM. Cancer survivorship issues: life after treatment and implications for an aging population. J Clin Oncol Off J Am Soc Clin Oncol. 2014;32(24):2662–8.

Saliba D, Elliott M, Rubenstein LZ, Solomon DH, Young RT, Kamberg CJ, et al. The vulnerable elders survey: a tool for identifying vulnerable older people in the community. J Am Geriatr Soc. 2001;49(12):1691–9.

Sanoff HK, Goldberg RM, Pignone MP. A systematic review of the use of quality of life measures in colorectal cancer research with attention to outcomes in elderly patients. Clin Colorectal Cancer. 2007;6(10):700–9.

Satariano WA, Ragland DR. The effect of comorbidity on 3-year survival of women with primary breast cancer. Ann Intern Med. 1994;120(2):104–10.

Sattar S, Alibhai SM, Wildiers H, Puts MT. How to implement a geriatric assessment in your clinical practice. Oncologist. 2014;19(10):1056–68.

Sattar S, Alibhai SM, Spoelstra SL, Fazelzad R. Puts MT. falls in older adults with cancer: a systematic review of prevalence, injurious falls, and impact on cancer treatment. Support Care Cancer. 2016;24(10):4459–69.

Sawhney R, Sehl M, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part I. ancer J. 2005;11(6):449–60.

Schneider BP, Hershman DL, Loprinzi C. Symptoms: chemotherapy-induced peripheral neuropathy. Adv Exp Med Biol. 2015;862:77–87.

Schroeck JL, Ford J, Conway EL, Kurtzhalts KE, Gee ME, Vollmer KA, et al. Review of safety and efficacy of sleep medicines in older adults. Clin Ther. 2016;38(11):2340–72.

Sehl M, Sawhney R, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part II. Cancer J. 2005;11(6):461–73.

Serraino D, Fratino L, Zagonel V. Prevalence of functional disability among elderly patients with cancer. Crit Rev Oncol Hematol. 2001;39(3):269–73.

Smith BD, Smith GL, Hurria A, Hortobagyi GN, Buchholz TA. Future of cancer incidence in the United States: burdens upon an aging, changing nation. J Clin Oncol. 2009;27(17):2758–65.

Soubeyran P, Fonck M, Blanc-Bisson C, Blanc JF, Ceccaldi J, Mertens C, et al. Predictors of early death risk in older patients treated with first-line

chemotherapy for cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2012;30(15):1829–34.

Soubeyran P, Bellera C, Goyard J, Heitz D, Cure H, Rousselot H, et al. Screening for vulnerability in older cancer patients: the ONCODAGE prospective multicenter cohort study. PLoS One. 2014;9(12): e115060.

Stauder R, Eichhorst B, Hamaker M, Kaplanov K, Morrison V, Osterborg A, et al. Management of Chronic Lymphocytic Leukemia (CLL) in the elderly: a position paper from an International Society of Geriatric Oncology (SIOG) task force. Ann Oncol. 2016;28(2):218–27.

Stuck AE, Siu AL, Wieland GD, Adams J, Rubenstein LZ. Comprehensive geriatric assessment: a meta-analysis of controlled trials. Lancet. 1993;342(8878):1032–6.

Thompson K, Dale W. How do I best manage the care of older patients with cancer with multimorbidity? J Geriatr Oncol. 2015;6(4):249–53.

Townsley CA, Selby R, Siu LL. Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials. J Clin Oncol. 2005;23(13):3112–24.

Townsley CA, Chan KK, Pond GR, Marquez C, Siu LL, Straus SE. Understanding the attitudes of the elderly towards enrolment into cancer clinical trials. BMC Cancer. 2006;6:34.

Trimble EL, Carter CL, Cain D, Freidlin B, Ungerleider RS, Friedman MA. Representation of older patients in cancer treatment trials. Cancer. 1994;74(7 Suppl):2208–14.

VanderWalde N, Jagsi R, Dotan E, Baumgartner J, Browner IS, Burhenn P, et al. NCCN guidelines insights: older adult oncology, version 2.2016. J Natl Compr Cancer Netw. 2016;14(11):1357–70.

Vestal RE. Aging and pharmacology. Cancer. 1997;80(7):1302–10.

Walter LC, Covinsky KE. Cancer screening in elderly patients: a framework for individualized decision making. JAMA. 2001;285(21):2750–6.

WHO. World population aging 1950–2050. Geneva: WHO, Department of Economic and Social Affairs Population Division; 2002.

Wildiers H, Heeren P, Puts M, Topinkova E, Janssen-Heijnen ML, Extermann M, et al. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2014;32(24):2595–603.

Williams GR, Mackenzie A, Magnuson A, Olin R, Chapman A, Mohile S, et al. Comorbidity in older adults with cancer. J Geriatr Oncol. 2016;7(4):249–57.

Wolfson C, Wolfson DB, Asgharian M, M'Lan CE, Ostbye T, Rockwood K, et al. A reevaluation of the duration of survival after the onset of dementia. N Engl J Med. 2001;344(15):1111–6.

Yee KW, Pater JL, Pho L, Zee B, Siu LL. Enrollment of older patients in cancer treatment trials in Canada: why is age a barrier? J Clin Oncol Off J Am Soc Clin Oncol. 2003;21(8):1618–23.

Yellen SB, Cella DF, Leslie WT. Age and clinical decision making in oncology patients. J Natl Cancer Inst. 1994;86(23):1766–70.