Geriatric Oncology

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SECTION SUMMARY

Older adults with cancer are different from younger counterparts in ways that impact decisions and management across the cancer continuum from diagnosis to survivorship and end of life. Specifically, older adults are at higher risk for frailty and other geriatric conditions that can impact their ability to tolerate surgery, chemotherapy, and other treatments for cancer. Understanding the unique characteristics, needs, and priorities of older adults with cancer is critical to avoiding either undertreatment or overtreatment. In this chapter, we provide a framework for evaluating and managing older adults with cancer using principles of geriatric oncology, geriatric assessment (GA), and palliative care.

1. INTRODUCTION

By 2030, 70% of all new cancers will be diagnosed in older adults. Urologists are on the front line for the diagnosis and management of urinary tract cancers which are also burgeoning in older adults.[1] As a result, understanding the basic principles of geriatric oncology is increasingly important for all urologists. In this chapter, we will review demographic trends of cancer in older adults, the nuts and bolts of the cancer-specific geriatric assessment (GA), surgical and chemotherapy considerations for older adults with cancer, and the role of palliative care in geriatric oncology.

For more information see AUA Core Curriculum: **Palliative Care**.

2. EPIDEMIOLOGY & OVERVIEW OF OLDER ADULTS WITH CANCER

Cancer is the leading cause of death in older adults, and more than 70% of cancer deaths occur in individuals ages 65 years and older.[2] By 2030, approximately 70% of all new cancers will be diagnosed in older adults, a projected increase of 45%.[1] **Prostate**, **bladder**, and **kidney cancer** are among the top 10 most frequently diagnosed cancers in the United States. The incidence of all three of these common urologic cancers is expected to increase substantially in older adults over the next decade. Prostate cancer will increase by 71%, bladder cancer by 68%, and kidney cancer by 67%.[1] In particular, bladder cancer has the highest median age at diagnosis of all cancer sites (73 years), and the incidence of clinical stage Ta non-muscle-invasive bladder cancer is increasing in those over 85 years of age.[3]

Older adults with cancer are different from younger counterparts in many important ways. First, older adults

are subject to multiple conditions of aging (e.g., geriatric conditions) that may impact their ability to tolerate surgical or chemotherapeutic treatment. **Geriatric conditions include cognitive impairment, poor nutrition or weight loss, functional decline, falls, multiple chronic conditions, polypharmacy, and depression. Urinary incontinence** is also included in the spectrum of geriatric conditions and may be caused by or exacerbated by urologic cancer treatment. One study found that older hospitalized patients considered bowel and bladder incontinence to be a state worse than death and on par with requiring mechanical ventilation to live.[4]

Importantly, geriatric conditions are not counts of chronic diseases or comorbidities. Rather, **the number and severity of deficits in geriatric domains reflect an individual's physiologic reserve or frailty status**. An accumulation of deficits indicates a lack of physiologic reserve that is associated with poor outcomes following cancer treatment. Identifying geriatric conditions using screening tools and geriatric assessment at diagnosis and providing supportive care interventions prior to treatment election and initiation of chemotherapy or pursuing surgical cancer treatment is currently recommended by multiple professional societies including the American Urological Association, the American Society of Clinical Oncology, the National Cancer Control Network, the European Association of Urology, and the International Society of Geriatric Oncology.

Despite the rising incidence and prevalence of cancer in older adults, this key population continues to be excluded from clinical trials which tend to preferentially enroll younger and healthier patients. As a result, the applicability of existing clinical trial evidence to medically complex older adults may be limited in real-world oncologic practice, making treatment decisions more difficult. [5,6] **Older adults tend to value non-traditional, patient-centered outcomes such as maintaining independence, functional status, cognitive function, and quality of life in addition to usual oncologic outcomes such as recurrence, progression, and survival**.[7] Patient-centered outcomes are rarely assessed in clinical trials or the surgical literature which also limits the applicability of existing data to older adults.

Various guidelines for treatment of older adults with cancer recommend assessing goals, healthcare preferences, and values at diagnosis and at each decision point across the **cancer continuum**.[8,9] When faced with a treatment decision, older adults with serious illnesses often will not choose a treatment that would lead to functional decline or cognitive impairment.[7] **Eliciting a patient's specific preferences and priorities prior to treatment helps physicians to provide personalized, goal-aligned care to older adults**. It is also important to consider the risks of over- or undertreatment of cancer, and to take a personalized approach that accounts for tradeoffs in treatment tolerability and disease progression while recognizing our own inherent biases as physicians.[10]

Another way that older adults are different from younger counterparts is that **they often rely on informal caregivers and other social supports to manage cancer treatment**. Of note, spouse caregivers are often older adults themselves and may be synchronously managing their own medical complexity. The National Alliance for Caregiving estimates that older cancer patients are supported by an invisible workforce of over 1.4 million informal caregivers (e.g. spouses, adult children, other family members, friends).[11] Cancer is an intense care experience for informal caregivers with episodes of surgery or chemotherapy followed by recovery, surveillance for recurrence and progression, and survivorship care. Informal caregivers provide an average of 10 hours per week of caregiving support for older adults with cancer, including tasks that enable independent living at home such as activities of daily living (ADLs) and instrumental activities of daily living (IADLs) (**Table 1**).[12] Identifying informal caregivers and engaging them in decisions and treatment plans as part of the healthcare team helps to improve outcomes for older adults undergoing cancer treatment. Strong social support is consistently associated with better outcomes during cancer treatment.[13]

Table 1: Activities of Daily Living and Independent Activities of Daily Living

Activities of Daily Living[14]	Instrumental Activities of Daily Living[15]
Feeding	Using the telephone
Dressing/Grooming	Shopping
Bathing	Preparing food
Toileting/Continence	Cleaning
Transferring	Laundry
Ambulating	Medication management
	Handling finances

After cancer treatment, older adults have specialized needs in the survivorship phase of the cancer continuum due to **co-existing chronic conditions**. Two-thirds of older adults with cancer have two or more co-existing chronic conditions, or multiple chronic conditions. The prevalence of multiple chronic conditions is high among bladder and kidney cancer patients in particular, with a median of 8 co-existing chronic conditions likely due to common underlying risk factors such as smoking and obesity.[16] Cancer treatment can exacerbate existing chronic conditions, and prior research has shown that cancer survivors develop an average of two new chronic conditions following cancer treatment.[17] In addition, **cancer treatment may lead to worsening of existing geriatric conditions such as functional decline and cognitive impairment**. A tailored approach to **survivorship care** for older adults is needed and can be guided by geriatric assessment and care plan goals, all of which may evolve over the survivorship period.[18]

Overall, older adults with cancer benefit from a multidisciplinary care model that goes beyond the surgeon and medical oncologist.[19] Specialists such as geriatricians, palliative medicine, pharmacists, care managers, nutritionists, physical therapists, psychologists, and others can help older adults to better meet the challenges of cancer treatment. Multidisciplinary care models and dually trained geriatric oncologists may not be available in all care settings. However, awareness of the unique needs of older adults and utilizing tools to identify older cancer patients who may benefit from support and interventions can help urologists to guide patients and caregivers towards appropriate referrals.

3. NUTS AND BOLTS OF THE GERIATRIC ASSESSMENT (GA)

A cornerstone tool of geriatric oncology is the geriatric assessment. A **Geriatric assessment (GA) is "a systematic evaluation of areas where older adults often have deficits and includes functional status, mobility, cognition, emotional status, nutritional status, comorbidities [multimorbidity or multiple chronic conditions], polypharmacy, and social support" among other aging-related domains.**[20]

Older adults represent a heterogeneous population. Chronological age is a poor predictor of health outcomes in older adults with cancer. A **GA is better suited for characterizing an individual's physiologic reserve, providing risk-stratification, and predicting outcomes following cancer treatment.** GA can facilitate **shared decision-making** with older adults and informal caregivers, specifically providing key insights into personalized estimates of the anticipated tolerability of different cancer treatments, including surgery, radiation, and systemic therapy (e.g., chemotherapy). After identifying vulnerabilities in specific domains, the oncology care team (surgeons and/or oncologists) may place referrals or provide other interventions such as prehabilitation to optimize domains before, during, and after cancer treatment. **Table 2** shows each of the GA domains, definitions, and examples of brief screening tools for each domain.

Table 2: Examples of Brief Geriatric Assessment Tools for Point of Care or Telehealth by Domain

Domain(s)	Definition	Example Tools	Comments
Functional status	Dependence in activities of daily living (ADL) or instrumental ADLs (IADLs)	OARS IADL[15]	Can be administered by medical assistant or nurse during rooming
Mobility	Difficulty ambulating, repeated falls, assistive device use	Falls in the last 6 months	Most health systems include falls as a screening question at visits
Medical Comorbidities	≥2 concurrent chronic conditions	Chart Review OARS Comorbidity[15]	OARS Comorbidity scale is patient-reported; could be administered during check-in or rooming
Social Support	Lack of emotional or tangible physical social support	Three-question screening:[21] Social activity: In the last 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)? Social support: Who do you live with? Who is your main social support?	Could be asked by medical assistant or nurse during rooming

Cognition	Diminished cognitive or decision-making ability	Blessed Orientation-Memory-Concentration (BOMC) Test[22]	
Mental Health	Presence of depression, anxiety, or distress	PHQ-2[23] Distress Thermometer[24]	Patient-reported; could be administered during check-in or rooming
Nutritional Status	Unintentional weight loss >10%	Weight loss in last 6 months	Many health systems have a standard screening question regarding unintentional weight loss
Medications	≥5 daily prescribed medications High risk medications for interactions, side effects, delirium	Online medication interaction programs/sites: DrugBank Online Drug Interaction Checker Epocrates online or smartphone/tablet application (requires user registration) Lexicomp Drug Interactions Analysis (requires subscription, often by institution)	Could be performed by medical assistant or nurse to generate results for physician/provider
Advanced care planning	Discussion of values and treatment preferences Goals of care	Documentation in chart	Most health systems ask patients at registration for living will or advance care plan.
Online Geriatric Assessment Batteries			

Functional status Comorbidities Medications Nutritional Status Cognitive Function Psychosocial Status		Cancer and Aging Research Group (CARG) Geriatric Assessment, available at **https://www.mycarg.org**[25,26]	This resource has patient and physician/provider components; patient component could be completed during check-in or rooming

The GA has been shortened and adapted to the cancer context from a conventional comprehensive geriatric assessment (CGA). A **CGA is different in that it is a longer evaluation that is focused on diagnosis and includes the development of a personalized, coordinated treatment plan to optimize health with aging.** The cancer-specific GA can be administered using survey-based tools and adapted to a variety of settings including busy surgical clinics. The cancer-specific GA is not meant to diagnose aging-related conditions such as dementia. Rather, it is used to screen for potential impairments in each domain and alert clinicians to the need for further evaluation and attention, and perhaps referral for CGA. One example of a survey-based, cancer-specific GA was developed by the Cancer and Leukemia Group B (CALGB) and Cancer and Aging Research Group (CARG). The **CARG GA** is publicly available on the CARG website and can be administered via web-based interface or on paper (see CARG **Geriatric Assessment – Healthcare Professional Tool** and CARG **Geriatric Assessment – Patient Tool**). A free phone app called GeriKit includes tools for measuring many GA domains including cognition, depression, function, strength, falls, nutrition, and polypharmacy/**medications**.

The AUA White Paper on Preoperative Evaluation endorses evaluation of multiple geriatric domains when preparing an older adult for any type of urologic surgery. The White Paper includes recommendations regarding the following: **advance care planning, social needs assessment, functional status, frailty, cognitive impairment, aspects of multimorbidity relevant to surgery and anesthesia (e.g. pulmonary function, cardiac conditions), and medication management such as antiplatelet therapy** (**Table 3**). More specifics regarding management of older adults undergoing major cancer surgery can be found in the next section.

Table 3: Geriatric Conditions and Recommended Evaluation Tools from the AUA White Paper on Preoperative Care for Patients Undergoing Urologic Surgery

Domain	Tool(s)
Advance care planning	Wishes, goals of care Appointing health care proxy Discussion of wishes in the event of complications
Social needs assessment	Screening questions to assess food insecurity, housing instability, utility needs, financial strain, transportation, exposure to violence, socioeconomic status
Support	Identification of a support person or “health coach” who will help to manage information and health needs
Functional status	ADLs and IADLs Deficits in hearing, vision, or swallowing History of falls in the past year Timed Up and Go test
Frailty	Fried Frailty Score
Cognitive impairment	Mini-Cog Assess decision-making capacity
Nutrition	Weight loss greater than 10% within three months Near starvation for 5 or more days Nutritional Risk Screening 2002
Multimorbidity/Comorbidity	Pulmonary risk stratification Obstructive sleep apnea (Berlin or STOP Questionnaire) Cardiovascular risk (RCRI, Gupta Myocardial Infarction)
Medication management	**Antiplatelet or other anticoagulation medications** Steroids Diabetes medications Renal dosing of medications for impaired renal function

The decision to conduct a GA for an older adult following cancer diagnosis begins with the clinician. The 2021 National Comprehensive Cancer Network (NCCN) Guideline for Older Adult Oncology describes an algorithm that starts with **clinical suspicion about an older adult's ability to tolerate cancer therapy**. Even in the absence of overt concerns regarding treatment tolerability, the guideline endorses using **geriatric screening tools** to identify impairments that may not be otherwise obvious from a standard history and physical conducted during a routine clinical encounter. Screening tools and the GA can uncover previously undiagnosed geriatric conditions or other chronic conditions that may impact downstream outcomes and treatment tolerability. A variety of screening tools are available, and since most are survey-based, they are easy to implement in a busy clinical setting. In the geriatric oncology context, **the Geriatric-8** has been the most carefully studied, with a high sensitivity (85%) but lower specificity (64%) for detecting frailty on the geriatric assessment.[27] A list of selected screening tools is shown in **Table 4**.

Table 4: Selected Screening Tools for Identifying Older Adults Who May Benefit from Geriatric Assessment

Tool	Format	Scoring
Abbreviated Comprehensive Geriatric Assessment[28]	15 item clinical interview	Score Range: 0-3 ADL; 0-4 IADL; 0-8 on MMSE; 0-4 on GDS-15 Cut off: 1 ADL and IADL; ≤6 on MMSE; and ≥2 on GDS-15
Fried Frailty Criteria[29]	3 self-assessment questions, grip strength, and Timed Up and Go test	Score Range: 0-5 ≥3 criteria present identifies a frail patient
Geriatric-8 (G-8)[30]	8 item clinician administered questionnaire	Score Range: 0-17 ≤14 requires CGA
Groningen Frailty Index[31]	15 item clinician administered questionnaire	Score Range: 0-15 Score ≥4 is associated with frailty
Triage Risk Screening Tool[32]	6 item healthcare team assessment	Score: 0-5 Cut off: ≥1 to screen for risk of dependence
Vulnerable Elders Survey[33]	13 item questionnaire, self-administered	Score Range: 0-10 Cut off: Score ≥ 3 identifies a vulnerable elder

Several recent clinical trials have evaluated the impact of GA or GA-directed interventions on cancer treatment outcomes.[34] A randomized trial of 160 older adults undergoing a perioperative geriatrician-led intervention for surgical treatment of gastrointestinal cancer found that **patients who received the full intervention had decreased hospital length of stay, decreased risk of ICU admission, and improvement in symptoms**.[35]

Three other randomized controlled trials (GAIN, GAP-70, and INTEGERATE) evaluated the effects of multidisciplinary GA-directed interventions, GA-based recommendations to community oncologists, and geriatrics co-management during chemotherapy, respectively.[36,37,38,39] The GAIN trial demonstrated decreased incidence of grade 3 or higher chemotherapy toxicity with the implementation of suggested interventions based on a review of GA results by a geriatrics-trained team.[37,40] The GAP-70 cluster-randomized trial also showed decreased grade 3-5 chemotherapy toxicity, fewer falls, and more medication discontinuation in the GA-based intervention group.[36,41] The INTEGERATE trial showed improved health-related quality of life, more patients remaining on treatment, and fewer unplanned hospitalizations in the GA intervention group at 6 months and reduced hospitalizations and emergency department visits.

4. CANCER SURGERY IN OLDER ADULTS

Nearly 40% of all surgical procedures are performed in older adults ≥ 65 years and this is anticipated to increase across all surgical specialties, but particularly within urology as 65% of our procedures are performed in this population.[42,43] Earlier population-based studies identified increased age as a risk factor for postoperative complications and early mortality.[44] However, **chronological age alone is not adequate for predicting postoperative outcomes**, and in appropriately selected patients, surgical management of urologic malignancies helps to avoid the potential for undertreatment and other adverse outcomes of cancer progression.[45] **Physiologic aging, or frailty, rather than chronological age is a greater driver of postoperative outcomes**.[46] Approximately 10% of individuals over 65 years are considered frail, and the prevalence approaches 50% in older adults with cancer.[47] Surgical oncology patients have an even higher rate of frailty, with one multicenter international trial finding that over two-thirds of older adults ≥70 years had baseline frailty.[48]

Frailty is an aging-related syndrome of low physiologic reserve which reduces a patient's tolerance to stress and can lead to a pronounced decline following a stressful event . Frailty is associated with a downstream cascade of physiologic changes that can affect all organ systems (**Table 4**). While many theoretical explanations exist to explain the biologic basis of frailty, currently two models are used most frequently: frailty phenotype and deficit accumulation. Further detail regarding these models is available in this prior **AUA Update on frailty**. Frailty has known associations with postoperative outcomes. A retrospective study of 3 million patients from the National Surgical Quality Improvement Project and Veterans Affairs Surgical Quality Improvement Project found that **frailty was associated with postoperative mortality** across all non-cardiac surgical specialties.[49] Patients were stratified as normal, frail or very frail based on a Risk Analysis Index. Even minor surgical procedures carried a greater risk of mortality for very frail patients compared to high-risk procedures in non-frail patients. Another study evaluated older adults undergoing radical cystectomy for bladder cancer using an electronic rapid fitness assessment to generate an accumulated geriatric deficit score. This score was associated with **admission to the intensive care unit, 30-day mortality, and a non-home discharge**.[50]

4.1 Frailty Assessment for Cancer Surgery

Assessing for frailty prior to cancer surgery can help surgeons, patients, and families with risk stratification, surgical decision-making, and perioperative evaluation and management. In the traditional surgical model,

geriatric domains are often addressed after-the-fact during hospitalization. However, in transitioning to a geriatric-centered model of care, completing screening and assessment prior to surgery allows for proactive and individualized care.

There is no single best approach to the preoperative assessment of older adults undergoing major cancer surgery; however, multiple models are emerging that can be tailored across practice settings (**Table 5**). Historically, integration of routine frailty screening and GA into the preoperative assessment has been limited due to resource constraints.[51] However, several groups have operationalized geriatric assessment with linked interventions resulting in significant improvements in care for older adults undergoing surgery.

Table 5: Studies of Preoperative Evaluation and Inpatient Co-Management Programs for Older Adults Undergoing Major Abdominal or Cancer Surgery

POSH Initiative:[52]

- Surgeon referral and 65-84 years
- 1-2 hour preoperative geriatric assessment with care coordination
- Co-management with inpatient geriatrics team postoperatively
- Enhanced discharge planning

MSKCC Geriatric Surgery Program:[53]

- Surgeon referral and ≥75 years
- 15-minute rapid electronic survey assessment and tailored care plan/optimization based on results
- Co-management with inpatient geriatrics team postoperatively for days 1-3
- Enhanced discharge planning

Massachusetts General Hospital Program:[35]

- Randomized trial
- All older adults ≥65 years undergoing surgery for gastrointestinal cancer
- Preoperative evaluation with geriatrician
- Co-management with Geriatric inpatient team postoperatively

4.2 Perioperative Risk-Stratification and Geriatric Assessment and Co-Management Interventions

In 2013, the American College of Surgeons developed the **National Surgical Quality Improvement Program (NSQIP) Risk Calculator**. This decision support tool is based on chart-abstracted data from thousands of surgical cases from NSQIP sites and provides patient-specific information regarding the likelihood of a variety of 30-day postoperative complications.[54,55] Patient-centered and geriatric-centered outcomes in the dataset are limited; however, the outcome of discharge to non-home facility (e.g. rehab facility or nursing home) was added in 2015.[56] A subsequent update now includes prediction of pressure ulcer development, delirium, new mobility aid use, and functional decline.[57] Communicating personalized risks with patients has been associated with better patient knowledge and care satisfaction.[58]

In 2019, the ACS launched a new quality initiative to enhance hospital-based surgical care for older adults. The **Geriatric Surgery Verification (GSV) Program** provides evidence-based tools and support to help institutions to become centers of excellence in the perioperative care of older adults.[59] In parallel, comprehensive best practice guidelines were created by the ACS in collaboration with the American Geriatrics Society (AGS) for perioperative management of older adults. Preliminary results from a VA hospital study demonstrated that implementation of the GSV criteria resulted in a decreased hospital length of stay relative to matched patients from Veteran's Administration Hospitals that did not implement the program.[60] In a similar GSV implementation program at Johns Hopkins, frail older adults undergoing surgery had decreased length of stay, but also were at reduced risk of loss of independence and major complications.[61]

The **Preoperative Optimization of Senior Health (POSH)** initiative at Duke University was developed to evaluate the benefit of geriatrics involvement in the care of older patients (older than 65 years) undergoing elective abdominal surgery.[52] Eligible patients were 65-84 years old and had a diagnosis of a cognitive disorder, weight loss of more than 4.5 kg, multimorbidity, polypharmacy, visual or hearing impairment or increased perceived risk based on surgeon discretion. Enrolled patients underwent a CGA to develop a tailored, patient-centered care plan for preoperative optimization and discharge planning. Following surgery, patients were followed by the inpatient geriatrics team. Compared to historical controls, older adults enrolled in POSH had shorter lengths of stay (4 days vs. 6 days, $p < .001$), lower 30-day readmission rates (7.8% vs. 18.3%, $p=0.004$), and fewer complications (0.9 vs. 1.4, $p < .001$).

In 2015, Memorial Sloan Kettering launched a geriatric surgery program for older adults undergoing cancer surgery.[53] Older adults ≥75 years were referred at surgeon discretion and received questionnaires to screen for geriatric conditions. Preoperatively, the geriatric team provided recommendations for health optimization, discharge planning, and goal setting. Postoperatively, patients were co-managed by surgical and geriatric teams. Compared to a contemporaneous control group, co-managed patients had a reduced 90-day mortality rate (4.3% vs 8.9%, $p<0.001$). Recently, MSKCC examined the feasibility of their geriatric co-management (GERICO) program specifically in the radical cystectomy population. There was no delay in time to surgery and patients were seen a median of 13 days prior to surgery. Two patients required additional evaluation for concerns identified during the geriatric assessment and had surgery rescheduled. The GERICO program enhanced urology inpatient APP satisfaction, specifically that it enabled them to provide more well-rounded care to older adults undergoing cystectomy. These findings are impressive considering that the program was piloted from March-May 2020 during the first COVID wave in New York City and associated healthcare disruptions. [62]

Several of these programs incorporate **geriatric co-management** which involves **shared assessment and responsibility between geriatrics and surgical teams to deliver patient-centered care**. Co-management

originated in the orthopedics literature in the late 1980's and has demonstrated improvement in functional status outcomes, decreased length of stay, reduced readmissions, improved postoperative mortality rates, and higher satisfaction for older adults and health care teams.[63] These results have been consistently replicated, leading to wider adoption of co-management within orthopedic surgery and, more recently, in other surgical fields. Elective general surgery patients that were co-managed were more often discharged to home, and experienced fewer complications, shorter length of stay, and decreased readmission rates. In older adults with cancer undergoing surgery, co-management is associated with a 57% reduction in 90-day mortality.[53]

4.3 Other Perioperative Interventions: Prehabilitation and Enhanced Recovery After Surgery Programs

Prehabilitation, or "training for surgery," programs focus on **enhancing resilience and post-surgical functional recovery trajectories using a multidisciplinary approach to address domains such as physical activity, nutrition, mental health, chronic conditions, and smoking/alcohol cessation**. Data are mixed on the effectiveness of these programs in traditional post-surgical outcomes such as postoperative morbidity and mortality. However, most prehabilitation studies do not measure **functional recovery**, which is an important postoperative outcome for older adults. Some programs do show promise in certain domains. For example, the Michigan Surgical and Health Optimization Program provides a walking program, smoking cessation counseling, nutrition and stress management, and written instructions and videos for incentive spirometer use. Compared to usual care, prehabilitation was associated with reduced complications, increased intraoperative stability, and reduced hospital charges.[64] A randomized trial of a prehabilitation program for radical cystectomy patients (n=70) measured 6-minute walking tests preoperatively and at 4- and 8-weeks postoperatively. The prehabilitation program included aerobic and resistance exercise, diet therapy, and relaxation techniques. The prehabilitation group had faster recovery on the 6-minute walking test following surgery. However, the average ages of the prehabilitation and standard-of-care groups were 69 years and 66 years, and the applicability of the data to adults in higher age tiers is unknown.[65]

Enhanced Recovery After Surgery (ERAS) protocols are multimodal evidence-based perioperative pathways designed to optimize periprocedural care for complex surgeries.[46,66] These pathways were initially developed in the 1990's to address wide variation in postoperative care and outcomes in colorectal surgery. While individual pathways vary, in general, protocols are designed to increase early postoperative mobility, reduce intraoperative intravenous fluids, resume enteral nutrition earlier in the postoperative course, and decrease opioid-based analgesia. ERAS protocols recommend avoiding nasogastric tubes, bowel preparation, and prolonged NPO status. When compared to usual care, ERAS protocols result in earlier return of bowel function, decreased length of stay, and reduced complications.[46,67] For instance, in a retrospective review of 205 cystectomy patients, implementation of an ERAS protocol was associated with a significant reduction in ileus (22% to 7.3%, p =0.003) and length of stay (8 days to 4 days, p<0.001).[68] Data suggest the benefits extend to older adults as well; however, data are limited in that most existing studies do not focus on older adults and have failed to include geriatric-specific variables (e.g. frailty) or outcomes (e.g. functional recovery, time spent at home, geriatric syndromes such as delirium).[46,67]

5. SYSTEMIC THERAPY FOR CANCER IN OLDER ADULTS

Chemotherapy impacts older adults differently from younger patients. Studies have established that older age is a risk factor for increased treatment-related toxicity and **current National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines specifically recommend an assessment of older adults before initiating systemic cancer treatment**.[9,69]

5.1 Models to Predict Chemotherapy Toxicity

Predictive models have been developed and validated to estimate risk for chemotherapy toxicity in older adults.[70,71,72] Two important tools include the **Chemo-Toxicity Calculator** developed by Hurria and colleagues in the Cancer and Aging Research Group (CARG) and the **Chemotherapy Risk Assessment Scale for High-Age Patients** (CRASH) developed by Extermann et al. (**Table 6** and **Table 7**).

These models reflect early principles in geriatric oncology, the importance of integrating objective cancer-related metrics (e.g., renal function, hemoglobin, primary tumor site, number and dose of chemotherapy agents) with individual GA variables (e.g. hearing impairment, social support, ambulatory capacity, history of falls) to provide risk-stratification, manage dosing, and engage in shared decision-making. **Higher risk patients can be identified and referred for a CGA to create a treatment plan to optimize geriatric conditions and enhance treatment tolerability**.

With an evolving landscape of therapeutic options for advanced cancers, including cancers of the genitourinary tract, it is critical that we advance our understanding of how novel therapeutics impact older adults. For example, the CARG and CRASH predictive models were developed in an era before the widespread use of immunotherapy and other targeted therapies. Anti-PD-1 (e.g., Pembrolizumab, Nivolumab) and anti-PD-L1 (e.g., Avelumab, Atezolizumab, Durvalumab) checkpoint inhibitors, are now approved for multiple genitourinary malignancy settings, including **advanced/metastatic urothelial carcinoma**, BCG-unresponsive **non-muscle-invasive bladder cancer**, and **advanced/metastatic renal cell carcinoma**. Combination immunotherapy and chemo-immunotherapy regimens are emerging, and toxicities and mortality risk in older adults need to be better characterized.[73,74,75]

Table 6: CARG Chemotherapy Toxicity Calculator[72]

Variable	Responses	Score*
Patient age	≥72 years <72 years	2 0
Cancer type	GI or GU Other cancers	2 0
Planned chemotherapy dosing	Standard Reduced upfront	2 0
Number of chemotherapy drugs	Multiple Monotherapy	2 0
Hemoglobin	<11g/dL (male) or <10g/dL female ≥11g/dL (male) or ≥10g/dL female	3 0
Creatinine clearance	<34mL/min ≥34mL/min	3 0
Hearing	Fair, poor, or totally deaf Excellent or good	2 0
Number of falls in 6 months	≥1 None	3 0
Taking own medications	With some help/unable Without help	1 0
Does health limit walking 1 block?	Somewhat limited/limited a lot Not limited at all	2 0
Health interference with social activities	Limited some, most of time, all of the time Limited none or a little	1 0

* - Increasing summed score associated with increasing risk of chemotherapy toxicity.

Table 7: CRASH Chemotherapy Toxicity Calculator[70]

Predictors	0 Points	1 Point	2 Points
Hematologic Toxicity Score			
Diastolic blood pressure	≤72	>72	
IADL	26-29	10-25	
Lactate dehydrogenase	0-459		>459
Chemotherapy toxicity*	0-0.44	0.45-0.57	>0.57
Nonhematologic Toxicity Score			
ECOG Performance Status	0	1-2	3-4
Mini Mental Health Status	30		<30
Mini Nutritional Assessment	28-30		<28
Chemotherapy toxicity*	0-0.44	0.45-0.57	>0.57

* - Toxicity level of specific chemotherapeutic agents. Table in reference.

5.2 Outcomes in Older Patients with Prostate Cancer

See AUA/ASTRO/SUO Guideline **Advanced Prostate Cancer**[76,77] and AUA Core Curriculum **Prostate Cancer: Advanced Disease**.

In a pooled analysis of data from three, large randomized clinical trials (SPARTAN, ARAMIS, & PROSPER) addressing the use of second-generation anti-androgens (Apalutamide, Darolutamide, & Enzalutamide, respectively) for non-metastatic, castration-resistant prostate cancer, outcomes for men aged 80 years or older (n=1023) were compared to those younger than 80 years (n=3094). Among the older cohort (n=1023), the estimated metastasis-free survival (MFS) was 40 months (95% CI 36-41) in the androgen receptor (AR) inhibitor groups, and 22 months (18-29) in the placebo groups (adjusted HR 0.37 [0.28-0.47]). The median overall survival (OS) was 54 months (50-61) versus 49 months (43-58), respectively (adjusted HR 0.79 [0.64-0.98]). There was a higher frequency of grade 3 or higher adverse events observed in patients age ≥ 80 (55% in the AR inhibitor groups and 41% in the placebo groups) compared to patients age < 80 (44% in the AR inhibitor groups and 30% in the placebo groups). The most common grade 3-4 AEs were hypertension and fracture. Overall, the findings support the addition of an AR inhibitor (Apalutamide, Darolutamide, or Enzalutamide) to ongoing androgen deprivation therapy for non-metastatic, castration-resistant prostate cancer in older men. [78]

In another pooled analysis of three randomized clinical trials for metastatic, castration-resistant prostate cancer, where the control arms included Docetaxel chemotherapy, outcomes were evaluated for men age ≥ 75 (n=388) compared to those age < 75 (n=1212). The older patients were more likely to have any high-grade adverse effect ($p < 0.001$), any fatal adverse effect ($p=0.007$), any grade anemia ($p < 0.001$), and any neutropenia ($p < 0.001$). There was no difference in OS between the age groups over the one year follow-up period. [79]

5.3 Outcomes in Older Patients with Kidney Cancer

See AUA Core Curriculum **Renal Neoplasms.**

There are currently multiple options for systemic therapy in advanced renal cell carcinoma (RCC) including oral targeted therapies such as tyrosine kinase inhibitors (TKIs) or mTOR inhibitors and intravenous immune checkpoint inhibitors. From a geriatric oncology perspective, **important considerations concerning oral therapies include drug-drug interactions, pharmacokinetics, pharmacodynamics, adherence, and polypharmacy**. In multiple pivotal metastatic RCC trials, despite no age restrictions on enrollment, patients aged 65 years and older represented approximately a mere one-third of the population included. Importantly, this is not reflective of the actual population as approximately half of metastatic RCC occurs in older adults 65 years and older. [80]

As prospective studies dedicated to older adults are limited, we must rely on subgroup analyses and retrospective data to understand the potential role of systemic therapies in older adults. Data from the International Metastatic Renal Cell Carcinoma Database Consortium (IMDC) demonstrated that older age (≥ 60) predicts for toxicity-related treatment discontinuation (TrTD) in patients who received vascular endothelial growth factor (VEGF)-targeted therapies. [81] Older age has not been shown to affect the efficacy of VEGF agents; however, greater toxicity has been observed.[82,83] In the IMDC analysis, the hazard ratios for the risk of TrTD increased with higher age (1.8- and 3.1-fold higher for those ≥ 60 and ≥ 70 years, respectively).[81]

When novel potentially toxic systemic therapies are adapted into clinical practice, historically there have been notable reservations in treating older adults. A classic example was the utilization of high-dose interleukin-2

(IL-2) for metastatic RCC. A small single center comparative study of patients treated with high-dose IL-2 showed a lower mean number of IL-2 doses were given to older patients (age ≥ 65) during the first cycle of treatment. However, there were also higher rates of cardiac, constitutional, hematologic, metabolic, and renal toxicities observed in the younger patients (age < 65). Overall, the objective response and survival rates were not affected by age.[84] **Age alone should not be considered an absolute contraindication for systemic therapy, even with potentially toxic agents, as many times identifying vulnerable patients (at-risk for toxicity) can allow for optimization and improved tolerability of effective therapies.**

5.4 Outcomes in Older Patients with Bladder Cancer

Bladder cancer is primarily a disease of older adults, with median age at diagnosis of 73 years in the United States and median age at death of 79 years.[85] Standard of care for treatment of muscle-invasive bladder cancer (MIBC) includes neoadjuvant chemotherapy with Cisplatin-based therapy, which was established in trials enrolling predominantly younger participants.[86,87,88] The median age of participants in these landmark trials was 61 to 63 years. In older adults, renal dysfunction, hearing impairment, or other co-existing chronic conditions affect overall functional status and may preclude the use of cisplatin. Failure to provide standard of care therapy to patients in patients presenting with organ-confined and potentially curable disease is associated with a high risk of multiple hospitalizations within the year following discharge and death from bladder cancer progression with a median survival of less than one year.[89]

Curative management of MIBC consists of radical cystectomy (RC) with pelvic lymphadenectomy as appropriate. RC is a complex surgery, with high-risk for post-operative morbidity and mortality. An analysis of Surveillance Epidemiology and End Results (SEER) data from 1992-2004 compared RC to radiotherapy (RT) for MIBC stratified patients by age (< 60, 60-69, 70-79, and > 79).[90] Among the 8034 patients who underwent RC and 2773 who received RT, RC maintained an OS advantage across age groups, except for the octogenarians. There was no association between survival and RC receipt in octogenarians. A systematic review of curative intent treatment for MIBC in older adults found that most studies demonstrated decreased OS following RC with advancing age.[91] There were differences in age stratification among the studies reviewed, with cohorts arbitrarily divided at age 65, 70, 75, or 80. As discussed previously, **chronologic age should not be the sole determinant of management strategy for MIBC in older adults and decisions should consider findings from GA (e.g. functional status), quality of life, support systema, and patient's individual priorities**[8,92,93]

An alternative to RC in pT2 bladder cancer is trimodal therapy which combines a visually complete transurethral resection of the bladder with RT and concomitant radiosensitizing chemotherapy, if an older adult declines or is unfit for surgery.[94] Trimodal therapy may be better tolerated in vulnerable adults, with variable outcomes; however, randomized trials are lacking in this comparison.[95,96,97,98,39]

5.5 Integrating GA-Guided Intervention to Reduce Systemic Treatment Toxicity

As the role for GA in distinguishing the functional assessment of older adults becomes integrated into clinical practice, the need for implementation of interventions to utilize this information becomes imperative. **Randomized clinical trials specific to older adults undergoing systemic therapy with a baseline GA and subsequent GA-driven interventions have shown a reduction in grade 3 or higher toxicity without compromising survival outcomes**.[36,37,38,39]

Given increasingly prominent roles for immunotherapy in advanced kidney and bladder cancers, a recent study of the Flatiron Health database demonstrated rising rates of immune checkpoint therapy use among frail older adults with a variety of malignancies.[99] Overall, outcomes data regarding immunotherapy in older adults

with cancer are emerging. An analysis from SEER demonstrated that among patients 75 years and older, metastatic cancers the immune checkpoint era had improved overall and cancer-specific survival, except for in urothelial cancer.[100] A study from Canada evaluated the associations between age and frailty with immune-related adverse events and acute care use (emergency department visits and/or hospitalizations). The authors found that age was associated with reduced risk of immune-related adverse events; however, frailty was associated with higher acute care use.[101]

6. PALLIATIVE CARE IN GERIATRIC ONCOLOGY

Also see AUA Core Curriculum: **Palliative Care**.

6.1 Overview

Even in the current era of oncology, which is marked by rapidly advancing treatment and outcomes across urologic malignancies, many patients will still ultimately die from[2] or experience significant morbidity due to their cancer. Palliative care represents a natural extension of geriatric oncology, providing specialized care in the setting of advanced disease and at the end of life, and does not jeopardize any other care provided to older adults with cancer. While still frequently misunderstood, including by health care professionals, **palliative care is not limited to patients with incurable disease,**[102] **nor does it subvert goals of care or result in shorter life expectancy**.[103] Just as medical or rehabilitation consultations offer expertise and opportunities to address identified medical or functional deficits, **palliative care represents a guideline-concordant intervention when symptom-related, quality of life, or prognostic issues are identified for older patients with cancer**.[104] Understanding palliative care through this lens can enhance the care of patients with older adults with urologic cancers, including in the setting of curative-intent treatment.

6.2 Defining Palliative Care

The field of palliative medicine is a discipline focused on the relief of suffering for patients with serious illnesses and their families and caregivers, and is well suited to address symptoms and other impediments to patient and caregiver quality of life. [102] This field **exists on a spectrum with hospice care**, and while it is frequently conflated with hospice, it represents a distinct clinical niche. There are two general forms of palliative care: primary palliative care and specialty palliative care.[105] **Primary palliative care** includes basic supportive care that can be carried out by providers of any training or specialty, including urologists and geriatricians. Primary palliative care tasks include but are not limited to the following:

- **Uncomplicated pain or symptom management** (i.e. without severe end-organ dysfunction, superimposed substance abuse, etc.)
- Routine assessment for and initial management of **mood disorders**
- **Shared decision-making** for the therapies and/or interventions that the clinician is offering themselves (e.g. considering medical management versus TURP versus HoLEP for BPH)
- **Prognostic disclosure and/or expectation management** for the diagnoses treated by the clinician

By contrast, **specialty palliative care** is typically carried out by clinicians who have completed subspecialty training (e.g. fellowship training in Hospice and Palliative Medicine, End-of-Life Nursing Education Consortium [ELNEC] training for nurses or advance practice nurses) and provide this care in a consultative capacity through a multidisciplinary team. Specialty palliative care is ideally suited for, although is not limited to:

- **Complex pain and symptom management** (e.g. managing refractory symptoms, symptoms in medically complex or frail individuals, pain management in the setting of substance abuse)

- **Challenging** or especially nuanced **medical decision-making discussions** (i.e. circumstances in which "there is no good answer"), even if treatment may have curative intent
- **Difficult psychosocial or communication needs**
- Support of patient, caregiver, or medical team **distress**
- Care planning for patients with serious illness and a short prognosis (particularly those who may be eligible for hospice services)

Finally, specialty palliative care is supportive care intended to be concurrent with, rather than as an alternative to, conventional medical care, especially in the care of patients with greater medical frailty.[102] This is especially true in oncology, as a landmark 2010 study by Temel et al ushered in an era with multiple high-quality clinical trials demonstrating **improved patient quality of life and quality of care for patients receiving "early," meaning pre-terminal, concurrent palliative care.** Specifically, this initial study demonstrated improvement in depression and symptom control, as well as avoidance of aggressive care at the end of life for patients with advanced non-small cell lung cancer, all of which was accomplished without shortening life expectancy.[103] While not overtly designed to target the geriatric oncology patient population, this trial was conducted in patients with a mean age of approximately 65 years, demonstrating the value of palliative care in the care of older patients with cancer. Palliative care can be seen as another domain of geriatric oncology rather than an alternative to it, particularly in the setting of advanced cancer. Subsequent positive trials followed in other cancer populations, including patients with small cell lung cancer, metastatic gastrointestinal cancers, acute myeloid leukemia both with and without stem cell transplantation, and muscle-invasive bladder cancer.[106,107,108,109]

The latter of these examples, work by Rabow et al, epitomizes the intersection between specialty palliative care, geriatric oncology, and urologic oncology for patients with MIBC undergoing RC. In this trial, patients were randomized to receive perioperative specialty palliative care consultation in order to evaluate the impact of palliative care on mood, symptoms, and post-traumatic growth.[109] The study population, comprised of a majority male patients with a median age of 67 years, had improved depression, fatigue, quality of life, and post-traumatic growth compared to patients receiving standard care, thereby demonstrating the impact of identifying and managing concurrent mood disorders as part of specialty palliative care.

6.3 Differentiating Palliative Care from Hospice

The distinction between palliative care and hospice remains an ongoing challenge for the field of palliative medicine and contributes to barriers in utilization.[110] Given this, an essential task of clinicians referring patients to specialty palliative care services, particularly for older patients who are statistically more likely to have encountered hospice care for a loved one, is to draw attention to the differences and underscore the benefits that the patient may receive from this specialty medical care. Palliative care has numerous advantages for older adults, which are only accentuated in the setting of a cancer diagnosis, and therefore endorsement of this specialty care and describing potential benefit may promote patient and caregiver acceptance while avoiding misconceptions.[111] **Offering reassurance to patients about the intent of the referral should be considered a standard component of these discussions and should ideally acknowledge hospice and draw attention to some of the differences between palliative care and hospice care. Table 8** can serve as a reference for clinicians to ground their knowledge regarding the similarities and differences between palliative care and hospice and describe these distinctions with confidence.

Table 8: Understanding the Contrasts Between Palliative Care and Hospice

	Palliative Care	Hospice
Philosophy	Medical care promoting quality of life for patients with a serious illness *in conjunction with conventional medical care*	Care *focused* on comfort and dignity at the end of life, typically comprising the primary medical care delivered
Care Team	Interdisciplinary team including physicians, nurses, advanced practice providers, social workers, and sometimes chaplains and child-life specialists	Team (and hospice agency) is mandated to include physicians, nurses, social workers, and volunteers. Many agencies also include hospice aids to assist with patient personal care.
Location	Inpatient is most common, but ambulatory (especially in oncology clinics), long-term care, and home-based availability is variable	Agencies are required to be able to provide 4 levels of care: routine home services, respite, continuous care at home, and general inpatient (GIP). Routine home services are most common
Eligibility	Patients of all ages, stages, and types of serious illness; may continue disease-directed and even invasive/aggressive care	Patients of all ages and diagnoses who have a prognosis of ≤ 6 months if the illness follows a typical course. Once enrolled in hospice, patients relinquish Medicare coverage for other disease-directed or life-prolonging care affecting the terminal prognosis
Financial	Provider fees covered in accordance with the setting of care, commensurate with any other medical specialty (e.g., inpatient care is covered by Medicare part A and ambulatory care is covered by Medicare part B). Commercial payers typically follow suit.	Covered under the Medicare hospice benefit; commercial payers typically follow suit, as do state insurance programs (although coverage and structure may vary by state).

6.4 Palliative Care for the Older Adult with Urologic Cancer

High-quality care for older adults with cancer, including urologic malignancies, is a multidisciplinary pursuit and has myriad opportunities for collaboration with both geriatrics and palliative medicine. For example, data indicate that older men with prostate cancer present with more advanced disease and experience higher prostate cancer-specific mortality than younger patients, and older adults with bladder cancer have increased number and severity of co-existing conditions compared to their younger peers and consequently receive standard treatment at disproportionately lower rates.[112,113] These and other inequities between older and younger patients demand specialized care to anticipate and meet the needs of the growing older population. **When implementing geriatric oncology principles in the care of older adults with urologic cancer, palliative care should be considered an essential component of high-quality oncologic care given the differing goals and greater vulnerability of this population**. Furthermore, clinicians may consider standard referral criteria for older adults treated in their practice. Criteria may include deficits in multiple geriatric assessment domains, given that accumulating impairments predicts for worse overall survival.[114]

Unfortunately, palliative care has not had consistent uptake across the spectrum of urologic malignancies. For example, utilization of palliative care services among patients diagnosed with bladder cancer is far lower than most other solid tumors, including those with advanced renal cell carcinoma and prostate cancer, who appear to be accessing palliative care at rates commensurate with the broader advanced cancer population.[115,116,117] Despite variability in palliative care utilization among patients with urologic malignancies, there is strong evidence to support integration of palliative care into urology clinic workflows, which also underscores urologist satisfaction with palliative care services.[118,119]

7. RESOURCES

- NCCN Guideline for Older Adult Oncology: https://www.nccn.org/
- International Society of Geriatric Oncology Position Papers
  - Bladder cancer: https://pubmed.ncbi.nlm.nih.gov/32057720/
  - Prostate cancer: https://pubmed.ncbi.nlm.nih.gov/31195356/
  - Metastatic kidney cancer: https://pubmed.ncbi.nlm.nih.gov/29893263/
  - American College of Surgeons Geriatric Surgery Verification Program: https://www.facs.org/quality-programs/geriatric-surgery
  - ePrognosis calculators for estimating life expectancy: https://eprognosis.ucsf.edu/
  - GeriKit application for iPhone: https://apps.apple.com/us/app/gerikit/id1544200999
  - *Journal of Clinical Oncology* Special Issue on Geriatric Oncology: https://ascopubs.org/jco/special-series/2021/older-adults
  - Cancer and Aging Research Group (CARG): https://www.mycarg.org/

8. Podcasts

AUAUniversity Podcast Series: Episode No. 173

Presentations

Geriatric Oncology

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