

Chapter 2

Health Status Evaluation of Elderly Patients with Genitourinary Tumors

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Abstract In addition to accurate cancer evaluation, aging people require geriatric assessment that explores non-cancer-related parameters with significant impact on the cancer treatment decision-making process and patient's outcomes. Emphasis should put specifically on the patient's performances in functional, cognitive, physical domains, as well as on his comorbidity and socio-environmental situation. To date, different kinds of geriatric assessment tools have been developed from the gold standard that is the comprehensive geriatric assessment approach to elementary screening tools. This chapter first reviews components, methods, and objectives of geriatric assessment in geriatric oncology. Then, we focus on areas that should be more specifically explored in older patients with genitourinary tumors according to the treatment option, surgery, radiation therapy, and/or medical therapy. This chapter provides additional tools, which could significantly improve the value of geriatric assessment in this setting.

Keywords Geriatric assessment • Screening tools • Cancer in the elderly
Genitourinary cancer • Comorbidity • Functional status

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Introduction

Aging is a highly individual process which largely influences older people's health status. Age-linked physiological declines variably evolve among aging individuals. Furthermore, extrinsic factors, such as diet, exercise, personal habits, and psychosocial factors, heighten discrepancy between older persons [1]. Standard medical evaluations have failed to adequately approach the complexity of an aging individual's health status. Based on the work of Marjory Warren, geriatricians have progressively built appropriate evaluation and management of the elderly population [2].

Bladder tumors, prostate, and renal cancers mainly affect aging people. Incidence peaks around 75–80 years of age, except for bladder cancers which incidence increases continuously as a function of age. Active cancer treatments, particularly in early disease stages, involve various procedures with potential risks of adverse events. Consequently, cancer treatment decision making in such tumor types requires accurate assessment of individual's health status and survival likelihood.

Geriatric assessment in older patients with genitourinary tumors comprises core components corresponding to the main geriatric domains usually explored in every instrument. Additional investigations may be added depending on tumor types and projected cancer management plan

Common Geriatric Assessment Components

Comorbidity and Polypharmacy

Comorbidity has been defined as the coexistence or occurrence of any health-related condition or disease in reference to an index disease [3, 4]. Aging people are at risk of developing concomitant chronic conditions. Diabetes, respiratory diseases, cancer, cardiovascular problems, arthritis, hypertension are frequently encountered in older persons. Different measurement tools have been proposed depending on the population and research issues. Comorbidity instruments integrate data on different origins, medical record, and patient self-report, administrative database. Data collection represents a crucial step, in which errors can occur, especially in cognitively impaired patients who can underreport conditions [5]. The Charlson index weighs 19 conditions that significantly affect survival [6]. However, many diseases like hypertension are not rated although they may interfere with treatment regimen including targeted therapies. The Cumulative Illness Rating Scale for Geriatrics (CIRS-G) lists nonlethal diseases by organ system affected and rates them according to their severity and level of control by treatment [7]. The two indices have already been validated in older cancer patients with comparable prognostic performances [8].

Comorbidity impact has been largely studied in patients with localized bladder cancer [9–13] and prostate cancer [14, 15]. This index is also an appropriate prognostic tool for predicting postoperative complications [16].

Sensory impairments frequently lead to functional decline, increase risk for falls, and they worsen quality of life in older persons. As they may also interfere with patients' decisional capacity, they should be systematically screened in older cancer patients. Hearing loss may be easily detected with simple tests like the whispered-voice test [17]. Screening for vision disorders could lead to effective treatments that correct or prevent vision loss [18].

Older patients frequently receive medications prescribed by different physicians, leading to polypharmacy and increased risks of drug interactions. Therefore, patients' complete medication lists should be reviewed, as well as their observance. In case of potential severe drug adverse effect, treatment requires adaptation, including dosage changes and drug discontinuation.

Malnutrition

Malnutrition is a well-known indicator of poor health status and a strong prognostic factor for adverse outcomes [19, 20]. Older people with weight loss are twice likely to die than well-nourished people, regardless of their body mass index [21]. Nutritional disorders are frequently observed in elderly people, and up to 40 % of hospitalized cancer patients are at risk of malnutrition, if not already malnourished [22]. They originate from the combination of aging changes including reduced appetite, mouth dryness, tooth loss, dysgeusia, and cancer-related factors, like anorexia and treatment side effects. Cancer is probably the major cause of protein–calorie malnutrition in older patients

The Mini Nutritional Assessment developed in 1989 [23] is commonly used to evaluate older cancer patient's nutritional status. The test is composed of anthropometric parameters (weight, height, body mass index – BMI, and weight loss), brief questions related to lifestyle, medication, mobility, dietary questionnaire (number of meals, food, and fluid intake, and autonomy of feeding), and patient's self-perception of health and nutrition. It can be completed in less than 10 min. The MNA score distinguishes between elderly patients with adequate nutritional status, $MNA \geq 24$; protein–calorie undernutrition, $MNA < 17$; and at risk for malnutrition, MNA between 17 and 23.5. MNA was found to be predictive of length of hospital stay and costs and of overall survival [24].

More generally, nutrition disorders, defined as weight loss, low body mass index, and low serum albumin level (< 37 g/L), significantly predicted 90-day mortality and overall survival in bladder cancer patients undergoing radical cystectomy [25]. Similar results were shown in patients surgically treated for renal cell carcinoma [26].

Cognition

Cognitive impairment is increasingly encountered among aging patients. Since dementia causes disability and shortens patient's lifespan, the cancer treatment decision-making process must involve assessment of cognitive status. Cognitive

decline actually interferes with the diagnosis step, reduces the spectrum of available treatment options, promotes treatment nonadherence, and increases the risks of severe adverse events. In geriatric oncology, assessment of decisional capacity defined as a person's abilities to understand, appreciate reason, and make a choice appears a mandatory step before cancer treatment decision making.

Detection of cognitive disorders frequently appeals to the Mini Mental State Examination. This 30-item interviewer-administered assessment explores several areas of cognitive functioning [27]. However, oncologists must keep in mind that MMSE is only a simple screening tool. Low scores do not always indicate a diagnosis of dementia, nor do normal results exclude the possibility of cognitive decline. Whenever a cognitive deterioration is suspected, patients may undergo further neuropsychological evaluation to confirm and precise the disorder.

A recent study showed that the diagnosis of prostate cancer was associated with a decreased survival of patients with preexisting dementia [28]. Demented patients were more likely to be diagnosed at an early or unknown stage of cancer. Approximately 28.5 % of patients with dementia and 4.3 % of nondemented patients died within 6 months of prostate cancer diagnosis. Dementia increased the risk of dying from all causes, predominantly from noncancer causes, whereas cancer stage did not substantially influence cancer-related or all-cause mortality, emphasizing the negative impact of dementia.

Affective Status

Mood disorders are commonly observed in the elderly population. The prevalence of depression in older patients ranges from around 40 % in hospitalized patients to 8–15 % in community settings [29, 30]. Chronic conditions like stroke, sensory impairment, cardiac disease, or chronic lung disease were risk factors for increased depression [31]. The occurrence of cancer psychologically affects elderly patients because it may cause disability and reduced lifespan. An appropriate assessment may reveal preexisting psychological and/or psychiatric disorders behind the additional distress brought about by the cancer itself. The 30-item Geriatric Depression Scale (GDS) was developed to facilitate the quick identification of depressive symptoms in older people without considering physical complaints [32]. A score between 0 and 10 indicates adequate emotional status, whereas a score higher than 10 suggests depression. This form has been validated in several settings worldwide. Among various shorter versions, the GDS-15 and GDS-4 forms are considered as adequate screening tools for depressive symptoms [33]. However, the reduction of items limits the clinical significance of the shortest version in terms of illness severity. Many other screening tools have been developed to detect depressive symptoms.

In patients with prostate cancer, studies showed that depressive symptoms significantly and consistently increase with age [34]. Similarly, patients with bladder cancer undergoing radical cystectomy frequently experience psychological distress during the perioperative period [35].

Psychological disorders in this population influence health-related quality of life.

Physical Capacities

Gait and balance disorders dramatically impact the general health of an individual since they are associated with a substantial increase in the risk of falls and of fall-related injuries (fractures, fear of falling, functional decline). Falls occur in 30–60 % of older adults each year, and 10–20 % of these result in injury, hospitalization, and/or death [36]. Various instruments are available that assess balance and gait. The Timed Up and Go test (TUG) is a timed measure of the patient's ability to rise from an arm chair, walk 3 m, turn, walk back, and sit down again; when time completion exceeds 20 s, patients deserve further evaluation [37]. The Performance-Oriented Assessment of Mobility instrument is a standardized instrument that measures gait and balance [38]. An aspect that is closely related to the emergence of balance and gait disorders is the safety of home environment. Hazard checklist may evaluate the risk of falls of older people [39].

Studies have shown a higher risk of falls and physical impairment in older prostate cancer patients treated with hormonal therapy [40].

Social Situation and Environment

The key component of social situation in geriatric oncology is the existence of effective support. It includes informal resources like family, friends, and neighborhood, as well as formal support like healthcare professionals. Social support may refer to reliance on relatives providing both emotional support and tangible aid in activities of daily living [41]. The availability of assistance from caregivers may influence cancer treatment decision making, cancer care strategy, and adverse events monitoring, especially in older people with cognitive impairment. It is worthy to identify the human resources available in case of sudden functional decline or difficulties to remain safely at home.

Two environment dimensions should also be assessed, the safety of home layout and the patient's accessibility to adequate personal and medical services, particularly for those with impaired physical capacities.

Functional Status

Functional status is a key indicator of health status. The patient's ability to perform routine tasks best describes the joint impact of individual's morbid conditions and age-related decline. In geriatric oncology, functional status provides useful prognostic information, but it is also increasingly considered as a major treatment outcome, even more relevant than survival in aging people whom lifespan might not be prolonged. Cancer care plan should integrate functional status assessment and targeted intervention to improve any impairment. Functional status can be evaluated in at

least two areas. Basic activities of daily living (BADL) assess the patient's ability to perform basic self-care tasks (bathing, dressing, toileting, transferring, continence, and feeding) [42]. Instrumental activities of daily living (IADL) evaluate patient's competences to remain independently at home (i.e., meal preparation, groceries shopping, housework and/or handyman work, laundry, handling finances, taking medications, driving or using public transportation, and using the telephone) [43].

Geriatric Assessment Methodology

Comprehensive Geriatric Assessment (CGA)

The best biological and clinical markers for use in senior adult cancer patients are unknown. Geriatricians have developed a comprehensive geriatric assessment (CGA) tool to appraise the objective health status of elderly people.

Comprehensive geriatric assessment (CGA) is a multidisciplinary approach aiming at assessing and managing reserves and needs of aging people [44]. This instrument explores different key domains in geriatric medicine: cognition, comorbidity and pharmacy, mood, functional independence, nutrition, social and economic status, and environmental conditions. From this assessment, patient's resources and needs are carefully listed; recommendations and interventions are generated and integrated into an individualized care plan. It is noteworthy that the dynamic process of CGA involves also periodic reevaluation and adaptation of the care plan.

CGA has been performed in various settings from specific hospital wards called geriatric evaluation and management units (GEMU) to community-based locations like home assessment services (HAS). Randomized trials and meta-analysis demonstrated the positive effects of CGA on various outcomes, on mortality, living location, and on patients' physical and cognitive status [45–48]. A meta-analysis published in 1993 showed a 35 % decrease of 6-month mortality for GEMU and a 14 % decrease of 3-year mortality for HAS and an increased probability of living at home at 6 months [45]. This meta-analysis highlighted that CGA programs' effectiveness depended on the addition of proactive recommendations, implementation, and ambulatory follow-up. A second meta-analysis reported that older patients undergoing inpatient CGA were more likely to be alive at home after hospital admission as an emergency admission [46]. In a recent systematic review, CGA in GEMU provided lower rate of institutionalization and of functional decline than usual care [47], whereas effectiveness of preventive home visit programs appears dependent on the use of multidimensional geriatric assessment and follow-up [48].

The International Society of Geriatric Oncology (SIOG) published recommendations on the use of CGA-based instruments in geriatric oncology [49]. Experts advocate the integration of such instrument, with or without screening and with follow-up, in all cancer patients older than 70 years in order to detect unaddressed

problems to improve their functional status and possibly also improve their survival. Recent studies showed that unsuspected conditions, mainly malnutrition, functional impairment, and depression, induced changes in cancer treatment decision making [50, 51]. Based on geriatric parameters, published indices may help estimate life expectancy or risk of morbidity and/or mortality related to cancer treatment [52–56].

Multidimensional Geriatric Assessment Instruments (MGA)

A geriatric assessment has been recommended as a basis for planning the treatment of older cancer patients [49]. The objectives of such an evaluation slightly differ in oncology in comparison with the general geriatric population. Geriatricians aim their process to determine comprehensive plans and long-term follow-up including interventions focused on the patient's problems, whereas oncologists have been looking for an instrument capable of discriminating older patients whose health problems may interfere with cancer treatment planning and monitoring.

Hence, multidimensional assessment tools (MGA) that exploit the CGA, first step of identification and description of patients' health problems, emerge as an appropriate approach in the geriatric oncology setting. However, most instruments consist of a set of different screening tools (i.e., MNA, MMSE, GDS,...). Though instruments generally cover similar domains, the screening tools they are composed of might differ from a study to another. Nevertheless, several studies showed that MGA instruments provide suitable data on older patients' noncancer health problems [50, 51, 57–62]. They may consequently constitute adequate tools in clinical research [62].

However, oncologists should keep in mind that those instruments do not provide accurate diagnosis and their results should be cautiously considered while they are not balanced by a geriatrician's judgment. Since MGA instruments were firstly developed in the geriatric setting, they optimally require specific resources such as a trained interdisciplinary team and geriatric skills that can hardly be available in conventional oncology units. Thus, the approach has been once again simplified with the implementation of a preliminary screening step before undertaking geriatric assessment.

Screening Tools

Screening instruments aim to help oncologists differentiate older cancer patients whose problems might interfere with cancer treatment and who require in-depth geriatric assessment. These tools share similar characteristics; they must be simply administered and quickly completed, without requiring geriatric resources or skills. Consequently, they provide basic information, and positive results indicate that

patients need a geriatric evaluation. They should be considered as a preliminary step, and their results cannot be assimilated to those obtained with in-depth geriatric assessment.

Screening tools may be distributed in two groups. On the one hand, patients are asked to fill questionnaires up, sometimes with the assistance of a healthcare professional [63–66]. Items refer to common geriatric domains; they sometimes derive from longer validated screening tools. On the other hand, scoring systems have been evaluated in older cancer patients. For example, the Vulnerable Elderly Survey, the VES-13 tool was originally designed to identify vulnerable elderly people. Vulnerability is defined by the risk of functional decline or death over a 2-year period. A score greater than 3 corresponds to a high risk of vulnerability [67]. A pilot study has evaluated the performances of the VES-13 for identifying older prostate cancer patients at risk for impairment in the oncology clinic setting [68]. The investigators have found that the VES-13 tool is feasible in the oncology setting and predictive in identifying impairment when compared to a MGA procedure. Recently, a prospective trial, the ONCODAGE project, compared two screening tools (G8 and VES-13) to a standardized MGA instrument in France. The G8 scale incorporates seven items from the MNA test and age; it was initially aimed to identify older cancer patients with increased risks of death within a 6-month period after treatment initiation [69]. Preliminary data showed that G8 scores higher than 14 correctly distinguish patients with at least one impaired dimension in the MGA approach [70]. The ONCODAGE trial enrolled more than 1,500 cancer patients aged 70 years and older and confirmed these findings; G8 displayed sensitivity and specificity higher than 76 and 64 %, respectively [71].

Geriatric Evaluation Objectives

Treatment recommendations should balance, for each individual patient, the risk of cancer-related death against the risk of treatment adverse outcomes and the competing risks patients face from other causes.

Comprehensive geriatric assessment provides detailed evaluation of a given person's health status and an estimation of his/her expected lifespan. Such thorough procedure should be highly recommended in older patients with urological tumors when they are candidates to major surgery or complex combined treatment plan; i.e., when cancer treatment options impact on both patient's survival and quality of life and their balance between benefits and risks should be carefully determined.

On the other hand, simplified instruments, either MGA, or screening tools aimed to classify patients into health status groups in order to facilitate treatment decisions. Such instruments help developing clinical research dedicated to older cancer patients, allowing comparison between predefined age groups. SIOG guidelines for elderly prostate cancer patients provided an example of such classification effort (Table 2.1) [72]:

Table 2.1 SIOG classification for chemotherapy decision making in older prostate cancer patients [108]

Group	Characteristics	Treatment
Fit	Comorbidity (CIRS-G): grade 0, 1, or 2 IADL independency Adequate nutritional status (MNA > 23.5)	Standard regimen
Vulnerable (reversible problem)	Comorbidity (CIRS-G): at least one grade 3 Dependent in ≥ IADL At risk for malnutrition	Standard regimen after improvement of reversible conditions
Frail	Comorbidity (CIRS-G): several grade 3 or at least one grade 4 Dependent in ≥ IADL Severe malnutrition	Adapted regimen and targeted geriatric intervention plan
Too sick	Bedridden Life-threatening diseases Severe cognitive impairment	Palliative care

1. Patients considered fit, i.e., fully independent in IADL without any severe comorbidity or nutritional disorder. They should be offered cancer standard treatment.
2. Patients called “vulnerable,” i.e., dependent in at least one IADL, or with at least one severe condition, or at risk for malnutrition. Appropriate geriatric interventions should improve reversible altered conditions, authorizing standard cancer treatment administration.
3. Patients called “frail,” i.e., dependent in one or more IADL, or with two or more serious conditions, or one life-threatening comorbid condition, or severe malnutrition. Care plans should encompass targeted geriatric interventions and adapted cancer therapy options.
4. Patients called “too sick,” i.e., impairments in several major health domains, without any possibility of long-lasting rehabilitation. Palliative and best supportive care is commonly offered to patients belonging to this group.

Screening tools may serve pedagogical purposes by alerting oncologists on possible health problems in their aging patients that they would not have suspected without screening tools.

Geriatric Evaluation in Older Patients with Urological Cancer

Core components of geriatric assessment remain relevant in urological cancers, regardless of the cancer type and treatment plan and intent. However, additional dimensions might be sometimes explored, using extra investigations or measurement tools, depending on the selected treatment plan.

Assessment Before Surgery

Surgery with curative intent in elderly people always raises the key issue of prognosis. Since aging people may die from various causes of death, accurate assessment of patient's potential lethal morbid conditions appears mandatory to establish a hierarchical listing and then to estimate the mortality risks of a given patient. Among mortality prediction indices developed in the geriatric setting, several tools exhibit potential advantage in geriatric oncology, exploring short- or longer-term outcome. Carey et al. developed a 2-year mortality index based on self-reported functional status, age, and gender [52]. The validation study determined six independent risk factors for 2-year mortality, male gender, age over 75 years, dependence in bathing and shopping, difficulty walking several blocks, and moving heavy objects. Points assigned to each item provide scores ranging from 0 to 10; patients were distributed to three risk groups according to their scores. Mortality rates varied between 5 % in the low-risk group (0–2 points), to 36 % in the high-risk group (7–10 points), and 12 % in the intermediate group (3–6 points). Another prognosis index including 12 variables, not only age, gender, and functional disability (bathing, managing money, walking several blocks, and moving heavy objects) but also morbid conditions (diabetes, cancer, lung disease, heart failure, current tobacco use, and body mass index less than 25), helps estimate 4-year mortality risk of older community-dwelling people [53]. Scores were associated with 4-year mortality that ranged from 4 % in older people with 0–5 points to 64 % in those with 14 or more points. Analogous 11-item index may predict 5-year mortality [54]. Because the benefits of treatment of early-stage bladder cancer or kidney tumor are not reached for 5 years, surgeons call for targeting surgical options to individuals with an expected lifespan of at least 5 years.

Conversely, guidelines recommend definitive therapy for localized prostate cancer in patient with survival likelihood of at least 10 years. Recent studies have shown that radical prostatectomy provides to older men gains in life expectancy comparable to those in younger men [73]. The ability of several instruments to predict 10-year mortality has been studied. The Charlson comorbidity index has been the most widely used, though this tool was developed in the 1980s and it does not involve recent progress in cardiovascular mortality control and updated disease definition. Because gait speed requests contribution from multiple organ systems, involving cardiovascular, respiratory and locomotor systems, as well as energy expenditures, it has been associated with older people survival and adverse outcomes in different studies [74–76]. Since cutoff turns around 0.8 m/s, older people with faster gait speeds may live longer than average life expectancy of their generation and gender. Conversely, persons with gait speeds lower than 0.6 m/s are more likely to develop functional decline and disability. Gait speed measure may be easily implemented in daily practice; it can be assessed by nonprofessional staff using a 4-m walkway and a stopwatch [76].

Besides survival probability, geriatric assessment helps determine risk factors for postoperative complications. The Physiological and Operative Severity Score for

the Enumeration of Mortality and Morbidity (POSSUM) and the Portsmouth POSSUM were designed to evaluate risks for morbidity and mortality, respectively [77, 78]. These scores take into account 12 physiological variables, including white blood cell count and hemoglobin level, electrolytes, cardiovascular and respiratory signs, and 6 operative parameters (operation type, severity and presentation, number of procedures, blood loss). A new score was recently developed to specifically predict mortality and morbidity in elderly patients undergoing major colorectal surgery [79].

Delirium frequently occurs in older patients undergoing surgery with an incidence ranging widely from 8 to 70 %. Risk factors include low albumin level, anemia, functional decline cognitive impairment, and above all preexisting cognitive impairment [80]. A recent study showed that 3–4 ASA (American Society of Anesthesiologists) scores, impaired mobility (TUG > 20 s), and postoperative tramadol administration were independent risk factors for delirium after major abdominal surgery [81]. Postoperative delirium increases patient's risk of short- and long-term mortality. Adverse outcomes also include prolonged hospital stay, increased medical care costs, and early institutionalization. Previous history of delirium and hypotension episodes during surgery have been predictive variables for postoperative delirium in older patients undergoing urological surgery [82]. However, as surgery for urological tumor is generally an elective procedure, contributing factors like anemia, dehydration, hormonal disorders, psychoactive drugs, and opioids can be assessed and resolved before surgery.

Functional impairment increases the risk for postoperative complications [83]. Dependence in ADL was associated with postoperative complications in older patients undergoing thoracic surgery [84]. Impairment in IADL significantly increased postoperative complications in a sample of 460 older candidates to cancer surgery [85].

Cardiovascular complications are important causes of morbidity with major non-cardiac procedures in aging patients [55]. A cohort study aimed to validate an index for risk of major cardiac complications after noncardiac elective surgery. Six factors with approximately equal prognostic importance were identified: high-risk surgery procedure, history of ischemic heart disease or of congestive heart failure, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative serum creatinine > 2.0 mg/dL. The presence of two or three and more of these factors identified patients with moderate (7 %) and high (11 %) complication rates, respectively.

Pulmonary complications represent a large part of postoperative morbidity, especially in older patients [86]. They include pneumonia, respiratory failure, and bronchospasm. Preoperative geriatric assessment may focus on patient-related factors include chronic obstructive pulmonary disease (COPD), recent cigarette use, high ASA scores, functional impairment. Clinical assessment may be completed with chest radiograph and laboratory tests investigating renal function and serum albumin level. Pulmonary function tests including spirometry might be recommended in patients with respiratory symptoms like cough or dyspnea or those who have COPD or asthma.

Specific attention should be paid to older patients undergoing surgery for bladder cancer as smoking is a well-known risk factor for this type of cancer [87] and for cardiovascular or pulmonary chronic conditions. Furthermore, studies have found that current smokers are two to six times more likely than noncurrent smokers to develop postoperative pulmonary complications as well as cardiovascular morbidity [88].

The burden of chronic kidney disease (CKD) increases with aging. Renal function should be then carefully assessed in older patients undergoing surgery for renal cancer [89]. A recent study determined that older age, tumor size, and baseline glomerular filtration rate (GFR) were significantly associated with postoperative onset of renal insufficiency. Another recent publication reported results of a comparative analysis of postoperative renal function after either radical nephrectomy (RN) or nephron-sparing surgery (NSS) in young and older patients with kidney cancer [90]. Around half of older patients, the older age group underwent decrease in GFR, regardless of the surgical procedure; 24 and 51 % of elderly patients developed new CKD after NSS and RN, respectively.

Hence, preoperative geriatric assessment should involve GFR estimation using adequate formula, like the Cockcroft–Gault (CG) and the Modification of Diet in Renal Disease (MDRD) formulas [91, 92]. It is noteworthy that these formulas may provide different GRF estimates depending on age, BMI, and serum creatinine level [93]. The measure of differential renal function by renal scintigraphy before nephrectomy may help treatment decision, especially in case of $\text{GFR} < 60 \text{ mL/min/1.73 m}^2$ [94].

Radiation Therapy

Radiation therapy (RT) is frequently administered to older patients with urological cancer. Definitive RT represents a relevant curative option for older patients with localized prostate cancer, with similar local control than for younger patients. RT also plays a crucial role in palliating symptoms in elderly patients due to progressive local and metastatic disease, especially painful bone metastasis.

Effectiveness of RT in older patients raises two key issues, technical feasibility and social resources [95].

Safe administration of RT implies repeated patient's immobilization in various positions, mainly in dorsal position, sometimes in ventral position, that may be totally unfeasible in some older patients. Chronic conditions like osteoarticular or neurological disorder and heart or lung disease may limit correct RT delivery. Immobilization devices may help patients to remain correctly positioned during sessions as far as they are able to endure them. Furthermore, RT requires adequate collaboration between patient and professionals who must be informed of existing cognitive decline or sensory impairment that may alter patient's ability to understand and respect instructions.

Social situation may also influence patient's availability to attend RT centers. Burden of travel, difficulties of living in accommodation, or financial concerns may negatively impact patient's willingness to undergo RT [96].

Concomitant comorbidity, nutritional disorders, physical and functional limitations might benefit from additional supportive care plan during RT, allowing its completion in adequate conditions.

Medical Treatment

Hormonal Therapy

Androgen deprivation therapy (ADT) remains the standard option of hormone-sensitive metastatic prostate cancer. However, adverse events should be carefully monitored in older patients [97]. Castration, regardless of its modality, induces several side effects. Baseline geriatric assessment aims to evaluate preexisting conditions that may promote or increase the prevalence of such side effects.

Surgical or chemical castration provokes weight gain and increased body fat mass, leading to increased risks of cardiovascular adverse events and diabetes [98]. Moreover, androgen suppression significantly increases the risk of loss of bone density and of fracture which have significant morbidity and mortality implications [99]. Dual-energy X-ray absorptiometry (DEXA) represents the most common way of evaluating bone mineral density. In a cross-sectional study, 35.4 % men had osteoporosis before starting ADT [100]. Low BMI, alcohol or tobacco use, thyroid dysfunction, liver disease, and long-term corticosteroid therapy should be investigated before starting ADT. Effective preventive interventions include calcium and vitamin D supplementation and regular exercise program [101, 102]. Medical options include bisphosphonates and denosumab, a newly approved human recombinant monoclonal antibody that inhibits bone resorption by inhibiting osteoclast formation, function, and survival [103, 104].

Chemotherapy

Chemotherapy, regardless of the intent, exposes older patients to an increased risk of hematological and nonhematological side effects that may compromise their quality of life. Patients with urological tumors should undergo a geriatric assessment before starting treatment. Geriatricians should be informed of the selected regimen, its potential adverse events, and goals in order to adequately evaluate candidates to such therapy.

Geriatric assessment provides variables that have been recently correlated with the risk of severe toxicity [56, 57]. Two scoring models are now available: the Chemotherapy Risk Assessment Scale for High-age patients (CRASH) test and the

Cancer and Aging Research Group (CARG) model. Both of them integrate geriatric variables, MMS, MNA, and IADL scores on one hand [56], and hearing impairment, falls, difficulties in walking one block or taking medications, and decreased social activity on the other hand [57]. Furthermore, anemia (hemoglobin level <110 g/L for male; <100 g/L for female) and renal dysfunction (creatinine clearance <34 mL/min, according to Jelliffe formulae using ideal weight [105]) have also been integrated in the CARG model. Anemia has already been associated with increased risks for death in the elderly population [106]. Furthermore, anemia influences pharmacokinetics of drugs that are bound to red blood cells like epipodophyllotoxins, anthracyclines, and camptothecins with increased free plasma concentrations and enhanced drug effects, especially myelosuppression. Renal function alteration exposes older patients to increased toxicity linked to drugs that are renally excreted [107].

Variables from geriatric assessment have also shown their influence on the probability to complete chemotherapy in older patients [108]. Preexisting malnutrition (MNA score < 23.5) and cognitive decline (MMSE \leq 24) were significantly associated with the risk of early chemotherapy discontinuation in a sample of 200 cancer patients aged 70 years and older.

In early-stage urological tumors, chemotherapy may be offered only in patients with bladder cancer in the neoadjuvant setting [109]. However, effectiveness of such treatment option has not been yet validated in people older than 75 years. Nevertheless, chemotherapy with curative intent only applies for those with a survival probability higher than risks of early recurrence [110]. Mortality indices, such as previously described, may help define candidates with expected lifespan long enough to observe benefits from chemotherapy. Neoadjuvant chemotherapy includes cisplatin-based regimen that requires adequate renal function (i.e., GFR higher than 60 mL/min) and cardiac function. Consequently, older bladder cancer patients should be carefully evaluated before receiving such regimen.

Moreover, in all patients with metastatic bladder cancer, renal function is the first factor limiting the administration of active chemotherapy regimens. Since chemotherapy generally has limited activity, the treatment of these patients should be at best palliative with specifically adapted chemotherapy and best supportive care. At present, the standard chemotherapy for patients with GFR > 60 mL/min and no frailty risk factors is the combination of gemcitabine and cisplatin; in patients with lower GFR and/or with geriatric disability, gemcitabine alone is considered to be the standard regimen. Prospective controlled trials should be conducted, based on accurate geriatric assessment, to define which regimen provides survival and quality of life outcomes with adequate toxicity profile. When palliative chemotherapy cannot be safely administered, patients should receive only symptom management and end-of-life care.

The International Society of Geriatric Oncology (SIOG) has already published guidelines on the use of chemotherapy in older patients with prostate cancer [72]. Experts recommended evaluation of three major geriatric domains, nutrition, functional status, and comorbidity. Based on a geriatric screening procedure, patients are distributed in four groups depending on their characteristics: fit, vulnerable, frail, and too sick patients (Table 2.1). Standard regimen of docetaxel given every 3 weeks may be offered to the two first groups. SIOG recommended proposing adapted

regimen to frail patients i.e. suggesting weekly docetaxel, whereas palliative care will be considered in too sick patients.

Conclusions

Aging patients increasingly attend oncology clinics, jostling usual practice and conventional cancer treatment guidelines. Physicians face patients with multiple simultaneous health problems, and ordinary management shows limitations when applied to this heterogeneous population. Collaboration with professionals dealing daily with the geriatric population has been progressively developing worldwide. More and more oncologists acknowledge the need of accurate evaluation of older individual's resources and weaknesses and of comprehensive coordination of care enclosing cancer treatment plan. Interdisciplinary training will help both geriatric and oncology care providers to better collaborate, build up, and institute adequate standards of care in geriatric oncology.

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