

Introduction

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Defining the Elderly

There is no universally accepted age cutoff defining “elderly.” This reflects the fact that chronological age itself is less important than biological events in driving the aging process within an individual. However, chronological age is a simple and practical way of defining a target population, and 70 years is the most commonly used cutoff for defining patients as elderly within the field of geriatric oncology.

Biology of Aging and Changes in Organ Function

Almost all age-related changes lead to reduced function. However, the elderly population is characterized by a marked variability in the rate of functional deterioration, both between individuals and within individuals. Three different trajectories of aging have been described.

- Aging with pathology and disability
- Normal aging with some disability
- Successful aging with minimal disability

The heterogeneity of the aging process has practical consequences for the assessment of elderly cancer patients: patients need individualized assessments to determine their *biological age*. Biological age is believed to reflect a person’s remaining life expectancy and functional reserves. This will influence treatment decisions and predict treatment tolerance. There is no simple way to assess biological age, and the best tool available to date is a *comprehensive geriatric assessment* described in a separate chapter in this book.

Traditionally, within gerontology and geriatrics, natural age-dependent changes in structure or function of organs have been distinguished from age-related pathologies. This distinction is perhaps less useful from a practical point of view. Furthermore, normal age-dependent changes are believed to be associated with the prevalence of age-related pathologies, and disease in organs along with the aging process will exert synergistic effects on each other.

Another important characteristic of organ function and age is the close relation between supply and demand: cardiac output and respiratory function *at rest* remain largely unchanged with increasing age, but marked age effects appear when the systems need to perform under stress.

Within oncology, decreased organ function in the elderly may complicate treatment; impairments in renal, hepatic, and bone marrow function will increase drug toxicity. However, dose adjustments are usually not straightforward because of the lack of accurate measurements of reserve capacity. Comorbidities may be associated with an increased risk of side effects and drug interactions. Again, because of the broad physiological variations seen among the elderly, valid generalizations are difficult to offer.

Changes in Cognition

Age is a risk factor for developing cognitive dysfunction. The prevalence of dementia in some studies is about 1% in 65- to 69-year-olds compared with 41% in those aged 90 and over. The presence of dementia or cognitive dysfunction seriously impacts cancer treatment. It is important to keep in mind that in some cases formal cognitive testing is the only way to identify cognitive dysfunction, especially if the patient has preserved language function or if the caregiver does most of the talking.

Pretreatment counseling often involves complicated decision-making weighing cost and benefit of different treatment options, and it is paramount for the counseling physician to know whether the patient understands these issues.

For surgical procedures, the risk of postoperative acute confusional state (known as *delirium*) is markedly increased in the presence of preoperative cognitive dysfunction. Delirium can be prevented, as described below. When a patient is treated with chemotherapy, cognitive dysfunction raises

issues regarding the patient's understanding of important signs of toxicity such as fever or bleeding, and arrangements of more intensive surveillance may be necessary. As both surgery under general anesthesia and chemotherapy treatment may alter cognitive function, it is important to consider whether the treatment places the patient at risk for being transferred from an independent to a dependent life situation.

Cancer and Aging

Increasing age is one of the strongest risk factors for cancer development. There is a marked increase in epithelial carcinomas from ages 40 to 80 years. Interestingly, beyond age 80 the incidence of cancers levels off. The link between cancer and aging is complex, and most of the fundamental questions still remain unanswered. In some instances, such as cellular senescence or telomere shortening, strategies that protect us from cancer may increase our rate of aging. However, cancer and aging also seem to share common etiologies such as genomic instability and reduced rate of autophagy.

We still do not know whether DNA damage is the ultimate stimulus to both cancer and aging. Another explanatory model views cancer and aging as stem cell diseases where cancer represents the effect of growth promoting mutations within a given stem cell, while aging represents the natural exhaustion and depletion of the stem and progenitor pool.

A common misconception among the general population as well as some doctors is that all cancers grow slowly in the elderly. This is true for some cancers, such as certain types of breast cancer and lung cancer, but the opposite is, for instance, true for acute leukemias, brain tumors, and ovarian cancer, which may be more aggressive in elderly patients.

Clinical Aspects

Because elderly patients often have reduced reserves in several organ systems, stress such as surgery, chemotherapy, or an acute infection may lead to general symptoms rather than organ-related symptoms. Thus, elderly patients often have occult or atypical presentations of disease; they may lack fever during an infection and pain in the case of a myocardial infarction. Instead, the elderly patient may present with general symptoms and signs such as delirium, falls, incontinence (with sudden start or rapid

deterioration), or reduced intake of fluids leading to dehydration. It is most important that these symptoms are not interpreted as “normal aging”; aging does not happen overnight, and whenever there is an abrupt change in the functional or cognitive state of elderly patients, one must search systematically for an underlying cause.

Symptoms of cancer may be more difficult to interpret in the elderly because of comorbidity, and sometimes this leads to delayed diagnosis. Bone pain caused by a tumor may be interpreted as exacerbation of osteoarthritis, a brain tumor may be interpreted as dementia, and changes in bowel function are interpreted as constipation. In a patient with dementia who is not able to express pain or other problems distinctly, diagnosing cancer is even more difficult.

When cancer is diagnosed, treatment decisions will often be more complicated in the elderly patient because of several factors, such as reduced remaining life expectancy, the competing risks from comorbidities, reduced treatment tolerance, and potential drug interactions in the presence of polypharmacy. The impact of treatment on the patient’s functional status as well as transportation and caregiver issues need to be addressed. In addition, the heterogeneity of this population complicates the creation of “one size fits all” evidence-based guidelines.

Delirium

Delirium is an acute (hours to days) decline in attention and cognition and is reported to occur in 20% to 80% of cancer patients. Delirium is an underdiagnosed condition associated with functional decline, increased morbidity and mortality, as well as increased health care costs. Two core features separate delirium from dementia.

- First, in delirium the cognitive failure develops rapidly, whereas in dementia it develops gradually.
- Second, delirium, but not dementia, is associated with impaired or fluctuating consciousness.
- Moreover, delirium is associated with an altered psychomotor activity.
 - When the psychomotor activity is increased (hyperactive delirium), the patient is agitated, sometimes with hallucinations, with a marked motor hyperactivity, and may be difficult to manage.

- In the case of decreased psychomotor activity (hypoactive delirium), the patient is usually lying silently in his bed, but an attempt to communicate with him will reveal a severe confusion.

Most delirious patients fluctuate between hyperactive and hypoactive periods during the day. A general characteristic of delirium is its fluctuating course, making the condition difficult to diagnose.

The cause of delirium is multifactorial. If the patient is vulnerable because of cognitive impairment or several comorbidities, delirium could be triggered by a small event such as the introduction of a sleeping pill. Conversely, if the patient has few risk factors for delirium, the precipitating factors leading to delirium need to be more extreme such as surgery or major infections. Examples of risk factors for delirium are chronic cognitive dysfunction, high age, serious comorbidity, malnutrition, and sensory impairment.

Common precipitating factors are infections, dehydration, myocardial infarction, pulmonary embolism, urinary retention, renal failure, electrolyte disturbances, and the introduction of anticholinergic drugs. The introduction of opioid analgesics may also precipitate delirium, but pain and insufficient analgesia seem to be a more common precipitating factor.

During the search for the underlying cause of delirium, it is essential to keep in mind the atypical presentation of diseases in the elderly. A review of the patient's medications is mandatory. The most important therapeutic measure is to diagnose and treat the precipitating cause(s) if at all possible.

- Nonpharmacological interventions include the use of orienting influences such as a clock, regular reorienting communication, encouraging normal wake-sleep cycles, and involving family members in care.
- Pharmacological treatment may be necessary if the patient is a danger to himself or others, and haloperidol (orally or intravenously administered) is usually the agent of choice with doses of 0.5 to 1.0 mg twice daily with additional doses every four hours when necessary. An important side effect of haloperidol is extrapyramidal symptoms, and the use of this drug must be reduced to a minimum. Haloperidol is contraindicated in patients with dementia with Lewy bodies or Parkinson's disease.

In these patients, short-acting sedatives like oxazepam may constitute an alternative.

Dementia

According to the ICD-10 operational criteria, all the following must be fulfilled to make a diagnosis of dementia: there must be impairment in memory and at least one other cognitive function (e.g., language, visuospatial function, or logical reasoning). This impairment must be to a degree that interferes with the person's daily functioning. There must also be impairment of mental functions such as emotional control, motivation, or social behavior. The duration of the symptoms must be at least six months, and the consciousness must be normal.

The most common cause of dementia is Alzheimer disease, followed by vascular changes. Recent research has documented that the combination of Alzheimer and vascular pathology is more common than formerly believed. Other causes of dementia are Lewy body disease, with pronounced motor symptoms in addition to the cognitive failure and a marked intolerance for antipsychotic drugs, and frontotemporal dementia with dominating loss of emotional and behavioral control.

Most cases of dementia progress over several years from a mild impairment, which does not interfere with the person's ability to give an informed consent or to follow up cancer treatment, to severe stages making the person totally helpless in which palliative care should be prioritized.

Falls

An estimated one-third of persons over the age of 65 fall each year, and about half of the cases experience recurrent falls. Approximately 1 in 10 falls leads to a serious injury such as hip fracture or head injury. As seen in other geriatric syndromes, the risk of falls is multifactorial, and some of the most common risk factors include muscle weakness, history of falls, gait deficits, and balance deficits. Medications that may increase the fall risk include benzodiazepines, opioid analgesics, sleeping medication, and antidepressants.

Anticancer therapy often leads to an increased fall risk, examples being surgical treatment involving prolonged bed rest, which again leads to

muscle loss and orthostatic hypotension, neurological side effects of chemotherapy, and pain treatment with opioid analgesics.

Two relevant clinical points are that patients often forget that they have fallen, and that they rarely volunteer the information about a fall even if they do remember it. It is thus important to ask the patient and caregiver about falls and to assess balance and gait when indicated.

Polypharmacy

Polypharmacy is most commonly defined as the regular use of five or more drugs but may also be defined as using medications that are not clinically indicated. Among home-dwelling persons over the age of 65, 39% use five or more drugs. Polypharmacy is not a bad thing per se. It has been documented that elderly patients are undertreated for many conditions, examples being atrial fibrillation and hypertension. On the other hand, a higher number of drugs increase the risk of interactions and adverse drug reactions.

A diagnosis of cancer will often necessitate a critical revision of the patient's drug list. For example, cancer may bring about changes in life expectancy that will deem some preventive drugs unnecessary, and the use of chemotoxic agents or other anticancer drugs increases the risk of drug-drug interactions.

Declaration of Interest:

Dr Kristjansson has reported no conflicts of interest.

Dr Wyller has reported that he has given lectures on different geriatric topics sponsored by Pfizer, Lundbeck and Roche.

Further Reading

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