Chapter 01 – Introduction

Defining the Elderly

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

Biology of Ageing and Changes in Organ Function

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

- Ageing with pathology and disability
- Normal ageing with some disability
- Successful ageing with minimal disability

The heterogeneity of the ageing process has practical consequences for the assessment of older cancer patients: patients need individualised assessments to determine their biological age. Biological age is believed to reflect a person’s remaining life expectancy and functional reserves, and will influence treatment decisions and predict treatment tolerance. There is no simple way to assess biological age, and one of the best clinical tools available to date is the comprehensive geriatric assessment (described in chapter 3 of 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 disease, and organ disease along with the ageing 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, for example during surgery or chemotherapy treatment.

Within oncology, decreased organ function in older patients may complicate treatment. For example, impairments in renal, hepatic, and bone marrow function increase drug toxicity. However, dose adjustments are usually not straightforward because there is a lack of accurate measurements of function or reserve capacity. Comorbidities and polypharmacy 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 generalisations 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 can seriously impact cancer care and treatment. It is important to keep in mind that in some cases formal cognitive testing is the only way to identify cognitive dysfunction, especially in early stages of disease when the patient has preserved language function or if the caregiver does most of the talking.

Pre-treatment counselling often involves complicated decision-making, involving weighing the cost and benefit of different treatment options, and it is paramount for the counselling physician to assess the patient´s decision-making capacity.

For surgical procedures, the risk of post-operative 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 warrants concern regarding the patient's understanding of important signs of toxicity, such as fever or bleeding, and arranging more intensive surveillance may be necessary. As both surgery under general anaesthesia 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 Ageing

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, the incidence of cancers levels off beyond age 80. The link between cancer and ageing is complex, and most of the fundamental questions remain unanswered. In some instances, such as cellular senescence or telomere shortening, strategies that protect us from cancer may increase our rate of ageing. However, cancer and ageing also seem to share common aetiologies, 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 ageing. Another explanatory model views cancer and ageing as stem cell diseases, where cancer represents the effect of growth promoting mutations within a given stem cell while ageing represents the natural exhaustion and depletion of the stem and progenitor pool.

A common misconception among the general population and some doctors is that all cancers grow slowly in older patients. This is true for some cancers, such as certain types of breast cancer and lung cancer, but the opposite is true for other cancers such as acute

leukaemias, brain tumours, and ovarian cancer, which may be more aggressive in older patients.

Clinical Aspects

Since older 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, older 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, an older 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 important that these symptoms are not interpreted as “normal ageing”; ageing does not happen overnight. The physician must search systematically for an underlying cause whenever there is an abrupt change in the functional or cognitive state of an older patient.

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

When cancer is diagnosed, treatment decisions will often be more complicated in the older 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 along with transportation and caregiver issues need to be addressed. In addition, the heterogeneity of this population complicates the development 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 alertness/attention.
- 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/her will reveal 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, benzodiazepine withdrawal and sensory impairment.

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

It is essential to keep in mind the atypical presentation of diseases in older patients during the search for the underlying cause of delirium. 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 administered) is usually the agent of choice, at a dose 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 behaviour. Symptoms should last for at least six months, with normal consciousness.

The most common cause of dementia is Alzheimer's disease, followed by vascular dementia. Recent research has documented that the combination of Alzheimer's 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 behavioural control.

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

Falls

An estimated one-third of people over the age of 65 fall each year, and about half of these people 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, sleep medication, and antidepressants. A history of falls in the last six months has been shown to predict both chemotherapy toxicity and post-operative morbidity after surgery.

Anticancer therapy often leads to an increased fall risk, examples being surgical treatment involving prolonged bed rest (which 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. Therefore, it is important to ask the patient and caregiver about falls and to assess balance and gait speed.

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 older patients are undertreated for many conditions, examples being atrial fibrillation and hypertension. On the other hand, a higher number of drugs increases 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 chemo- toxic agents or other anticancer drugs increases the risk of drug-drug interactions.

Further Reading

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