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## COMORBIDITY, POLYMORBIDITY, POLYPHARMACY

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The elderly population (and the oldest old above all) is the fastest growing segment of the world population. There are significant differences in the disease pattern in adulthood and in old age. Geriatric patients are special patients, with a high rate of comorbidity (presence of a primary or index disease associated with other concurrent conditions), multimorbidity (sum of conditions, without a specific primary or index disease), and a frequent association with nutritional problems, anemia, sarcopenia, falls, polypharmacy, and functional loss (cognitive/physical/mood/socio-economic areas).

Advancing age is associated with increased vulnerability to chronic health problems. Many chronic diseases are common with age and may complicate the prognosis in geriatric patients such as anemia, diabetes mellitus, hypertension, ischaemic heart disease, cardiac insufficiency, renal dysfunction, COPD, osteoporosis, joint disease, gastrointestinal illness, cerebrovascular disease, malignancies and neurodegenerative disorders (Alzheimer's disease, Parkinson's disease). Comorbidities, as well as frailty, functional and cognitive impairment, and physical disability, increase the risk for adverse outcomes.

Although the two terms "comorbidity" and "multimorbidity" are often used interchangeably, they have different meanings, as discussed above. Thus, comorbidity refers to the presence of an index disease (e.g., cancer, Parkinson's disease, diabetes) associated with the co-occurrence of other age-related health conditions (e.g., disability, anemia, functional impairments, urinary incontinence) or diseases (e.g., diabetes, heart disease, hypertension). Conversely, multi-morbidity refers to the presence of two or more diseases or active health conditions that may or may not be linked by a causal relationship or with no consistent dominant index disorder

With advancing age, a reduction of homeostasis and decreased physiological organs reserve may predispose to chronic diseases. Health problems tend to accumulate and complicate individuals' health status and quality of life. Functional decline and impairments, and geriatric syndromes, such as incontinence, falls, disability, bed rest, delirium, pressure ulcers, malnutrition, and depression, are commonly associated with comorbidity and ageing.

Strictly related to comorbidity and multimorbidity is polypharmacy, since the presence of different diseases in different organs lead to the prescription of an alarming number of multiple medications. Polypharmacy is even more common when the patient, and especially the older patient, is under the care of multiple and uncoordinated specialists. Multiple prescriptions, especially in a frail elderly patient are often associated with side effects, increased risk of drug-drug interactions and iatrogenic illnesses.

In the evaluation of an older patient, it is important to take into account the fitness status (physiologic age) which is, at least in part, the reflection of a normal loss of body reserves, with a very large variability among individuals of the same age. Thus, ageing is associated with a large functional heterogeneity (fitness gap), with some people who are functionally independent (fit elderly) and others of the same age who are frankly frail or disabled (i.e. at the same age of 80 years, you can find robust and frail subjects, although there are intermediate stages, where evaluation may be even harder).

Frailty is a multifactorial condition of poor health predisposing old people to comorbidity, geriatric syndromes, latrogenic diseases, institutionalization and mortality. The concept of frailty has changed in recent years and there are now mainly two different approaches to estimate frailty. The first is called "the frail phenotype" and was developed by Linda Fried from the Cardiovascular Health Survey. It is based on physical signs, including weight loss, weakness, decreased physical activity, exhaustion and slow gait speed, all independent of disease or disability. The second approach is called the deficit accumulation approach, developed by Rockwood from the Canadian National Health and Population survey, in which the accumulation of multiple deficits are used to calculate a "frailty index". Frail patients and older patients with comorbidities have been traditionally excluded from most of intervention trials. This phenomenon has led to a major underrepresentation of elderly frail patients in cooperative studies. Few data are therefore available to clinicians on how to adapt the results from the trials to single elderly patients with complex comorbidity. Patients may also have multiple combinations of concurrent morbid conditions, and the occurrence and impact of specific combinations of comorbidities has not been studied extensively, as well as the impact of comorbidity on the outcome of treatment.

Traditional medicine based on the treatment of each single disease do not respond to the needs of the frail elderly patient, with multiple chronic disease that often cannot be healed, that have multiple causes, and that are often complicated by one or more geriatric syndromes. There is not a disease to treat, but a patient to take care of, in the best possible way, preferably in his own familiar context.

Thus, frailty should be considered as a separate entity to be identified, distinct from the diseases that may precede disability and functional impairment. Its identifications may help in the risk assessment for the development of organ failures or disability during treatment of malignancies or other severe conditions. The Comprehensive Geriatric Assessment (CGA) is important in the evaluation and identification of frail subjects with comorbidity. The CGA is a multidimensional, multidisciplinary diagnostic instrument designed to collect data on the medical, psychosocial and functional capabilities and limitations of elderly patients. The geriatric assessment differs from a standard medical evaluation in three general ways: 1) it focuses on elderly individuals with complex problems and comorbidities, 2) it emphasizes functional status and quality of life, and 3) it frequently takes advantage of an interdisciplinary team of providers. Whereas the standard medical evaluation works reasonably well in most other populations, it tends to miss some of the most prevalent problems faced by the elder patient. These challenges, often referred to as the "Five I's of Geriatrics", include intellectual impairment, immobility, instability, incontinence and iatrogenic disorders. Possible advantages of CGA in geriatric oncology include identification of frail subjects, better estimation of life expectancy, better identification and treatment of other health problems and concomitant conditions (comorbidity, functioning, depression, polypharmacy), better evaluation of the toxicity risks of chemoterapy, prevention and treatment of malnutrition, better identification of social problems, recognition of patient preferences, and better quality of survival.