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"Promoting access to innovation and clinical research for frail old persons"

Evaluation of frailty in cancer aged patients:

Clinical interest and tools

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Introduction

Due to the aging population and the increased cancer incidence related to age, clinicians should expect that they will have to care for an ever growing number of elderly cancer patients. Over 60% of cancers and more than 70% of cancer deaths occur in people over 65. Today, significant improvements in terms of increased access to screening (resulting in earlier diagnosis), and more effective therapies lead to an increased cure rate. Consequently, more than 60% of adults with cancer are surviving 5 years from diagnosis. All these data indicate the need for concerted and optimal management of cancer in the elderly.

Duality between cancer heterogeneity and patient heterogeneity

A multitude of host- and cancer-related factors influence decision making in geriatric oncology. Cancer-related factors include tumor histology, site, extension and biologic features, which often determine tumor responsiveness and the intensity and type(s) of antineoplastic therapy. Some cancer will be definitively cured after a single treatment, others will require sequential combination of therapies, all of them adding their cumulative toxicities. Therapy for cancer has become more complex over the past few years. Newer targeted therapies are now widely available, and join surgery, chemotherapy, hormonal therapy, and radiation in the armamentarium against cancer. In oncology, antineoplastic treatment is usually standardized: each type of cancer requires a particular combination of treatments, protocol, and order, etc. This relative standardization does not always apply to elderly patients. All individuals do not age in the same way or at the same speed. Some patients suffer from multiple co-morbidities; others have none. Some patients are completely dependent, while others retain complete autonomy, even in old age. Co-morbidities, disability, cognitive impairment, depression, mobility impairment, malnutrition, polypharmacy, and social context can directly impact the treatment decision. For example, parameters such as malnutrition interfere directly with the pharmacokinetic of the chemotherapy and require an adaptation to reduce the risk of toxicities. The presence of severe neuropathy or gait disturbance can indicate that a platinum-based chemotherapy should be avoided, etc… Most of the available treatments for cancer are potentially toxic. Therefore, the therapeutic window between meaningful, positive effects and unacceptable side effects is narrow. Finding the right balance between cancer burden and patient's health status remains the main priority of oncologists and geriatricians who treat cancer in old adults. We should not treat slowly evolving tumors that will never become symptomatic in patients whose life expectancy is already limited by co-morbidities or impaired functional status. On the other hand, to underestimate the potential impact of cancer and life expectancy can expose an elderly patient to a high risk of loss of autonomy and of deterioration in the quality of life that could have been preserved longer had we decided to control the tumor at diagnosis.

Detection of vulnerability in older cancer patients

Choosing the most sensitive tools to accurately assess health status is a major issue in geriatric oncology. The International Society of Geriatric Oncology (SIOG) and numerous literature reviews propose the use of a Comprehensive Geriatric Assessment (CGA) to determine optimal oncologic care, on the basis of the patient's health status rather than empirically. However, several recent literature reviews, have questioned the real value of the CGA in older cancer patients as CGA seems to have a ceiling effect in detecting vulnerability in this population[i,ii]. According to the literature data, 70%-80% of patients referred to oncology are independent for ADL (domestic activities of daily living); 50% are independent for IADL (instrumental activities of daily living); half have no co-morbidity; and 60% have a normal cognitive status. The older cancer patients represent a population that differs from the traditional geriatric patients: they have fewer co-morbidities and good functional and underlying health status at the time of diagnosis. Consequently, there is a need for more sensitive tools that will identify vulnerable patients who appear healthy but are susceptible to complications in response to aggressive cancer treatments.

Frailty is a syndrome resulting from cumulative declines across multiple physiologic systems and represents a state of reduced homeostasis and resistance to stress leading to increased vulnerability and risk of adverse outcomes such as falls, disability, hospitalization, and death. The few studies which have used frailty markers in oncology have shown that older cancer patients had a high prevalence of frailty markers (mostly malnutrition and impaired mobility) (iii) and some of them were predictive to cancer treatment toxicities. In a pilot study, Puts et al showed that low grip strength predicted 3 months treatment toxicity as none of the CGA measures did (iv). In a study including more than 300 patients with surgical procedure for cancer, Markary et al showed that preoperative frailty markers was associated with an increased risk for postoperative complications, length of stay and discharge to a skilled or assisted-living facility (v). Therefore, in older cancer patients, the concept of frailty may be a useful approach to detect vulnerability.

When assessing frailty in older cancer patients

In oncology, many factors can interfere with the results of the assessment. The patient should ideally be evaluated right after the diagnosis of cancer and before any treatment. It is also important to consider the impact of the cancer on the health of the patient at the time of assessment as patients with diseases that mimic the features of frailty may be erroneously considered as frail. For example, the classification of a patient suffering rapid weight loss, marked fatigue, loss of mobility related to aggressive or advanced cancer, as a "frail patients" can conceivably change with optimal cancer treatment. The patient should, therefore, not be refused an aggressive cancer treatment. In the case of a patient who suffers progressive loss of weight and mobility during the year preceding the cancer, the results of assessment will reflect the alteration of the reserves prior to the onset of the illness. This patient is considered vulnerable before the diagnosis of cancer, and there are risks of major toxicities with aggressive therapies.

Future direction

It is to be hoped that, in the future, a specific oncologic geriatric assessment "SOGA", will be developed, specifically tailored to older cancer patients, and adjustable according to the type of cancer and proposed treatment, with varying implications in terms of management. Frailty markers could be used not lead to denying treatment but rather to modulating the interventions proposed so as to prevent or minimize complications. Frailty markers can also help the oncologist to design studies which compare the effectiveness and side effects of cancer treatments in homogenous groups of patients (frail or not frail), to help to predict treatment toxicities and to predict life expectancy (in particular for adjuvant chemotherapy).

Conclusion

In geriatric oncology, optimal management of older cancer patients is challenging as the estimation of the underlying vulnerability guides decision making. The few studies which have used frailty markers in oncology have shown that older cancer patients had a high prevalence of frailty markers and some of them were predictive to adverse outcomes and treatment toxicities. Today, recommending the use frailty markers to detect vulnerability on older cancer patients is too premature. Studies are warranted to precise their use in geriatric oncology.

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