Perspectives

Complicated and complex: Helping the older patient with cancer to exit the labyrinth

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The myth of the Minotaur is more than 4000 years old. Yet it offers a cogent metaphor of the complexity of modern cancer treatment. Like cancer, the Minotaur with the head of the bull and the body of a man was a biological aberration. Like many cancers, the Minotaur originated from the interaction of the human body with a foreign substance that perverts the normal body function (think of cigarette smoking or other environmental carcinogens). The monster was the product of the adulterine intercourse of Pasiphae, King Minos's spouse with a bull. Like cancer, the Minotaur was a cannibal. Perhaps the most relevant part to the story concerns the dwelling of the Minotaur. His stepfather enclosed him in a labyrinth. Even if he succeeded in killing the Minotaur, the brave warrior would have remained imprisoned in the labyrinth and starved to death.

To find the exit from the labyrinth is the dilemma of most forms of cancer treatment: how to eliminate the cancer without hurting the patient. This is particularly true of older patients with cancer. The value of antineoplastic treatment is minimized in persons with a limited life-expectancy and increased risk of therapeutic complications.

The practitioners managing older patients have become aware that aging is a complex situation. The substitution of the term comorbidity with "polymorbidity" reflects this awareness. Comorbidity implies a major disease threatening to the life and function of the patient, whose management is "complicated" by other diseases. Polymorbidity implies that multiple diseases conspire to compromise a patient's survival and independence. The management of a single disease may not improve and may even worsen the overall outcome. It is not enough to kill the Minotaur. It is necessary to exit the labyrinth!

The assessment tools used in geriatrics mirror the complexity of the clinical situation. They are utilized for three purposes: to assess clinical needs, to estimate the risks of
mortality, and to evaluate loss of independence. Biological markers, such as the concentration of inflammatory markers in the circulation, the length of lymphocytic telomeres, and the expression of p16INK4a in normal cells, have been proposed to assess the physiologic age of a person, but they lack specificity. The same may be said of single tests of functional assessment, including the “timed get up and go” test or the clinical definition of frailty.

The most useful tools in estimating needs and prognosis of the individual patient take into account the complexity of the situation by examining multiple domains, as is done in the comprehensive geriatric assessment (CGA). The CGA may be used to estimate risk of mortality and functional decline and, along with other instruments, predict the risks of surgical and medical complications of cancer treatment.

The estimate of the risk of mortality and therapeutic complications is just a step, albeit an important one, in the approach to the complex interactions of aging and cancer. This step represents a post sign around which to construct a decisional road map.

The first step of this pathway assesses the prognosis of the disease itself. In addition to the clinical and standard pathologic assessment, molecular and genomic biomarkers should allow one to identify diseases that are rapidly lethal from those that may be safely observed.

The second step is the geriatric evaluation, which provides an estimate of therapeutic risks and benefits. This includes the benefits of antidotes to treatment toxicity. For example, age is a risk factor for neutropenia and neutropenic infections with regimens that may be well tolerated by younger people. Prophylactic growth factors ameliorate this risk and allow the administration of chemotherapy in full doses.

The third step is perhaps the most critical one, and involves the art of medicine, one of the situations where a physician is still asked to act as a “doctor” rather than as a provider. From the Latin “docere” or “to teach”, to be a doctor means to provide counseling based on one’s knowledge, experience and most of all care. This step includes the communication of prognosis, and the exploration of the patient’s goals. In addition to the hope of a cure and symptom relief, these goals may include prolongation of survival up to a specific landmark (a wedding, a graduation), a pain-free death, and the prolongation of “active life expectancy”. The loss of independence is the major threat to the quality of life of older individuals.

The fourth step involves monitoring of the treatment, which includes readjustment of goals according to the antineoplastic effectiveness, the patient direct experience of complications, and the emergence of unexpected toxicity.

The fifth step is outcome assessment and identification of previously unrecognized predictive factors. The diversity of the older population may be harnessed by the prospective study of the outcome of older individuals receiving different forms of cancer treatment. Instruments to predict the risk of complications of cancer treatment were initially developed in this way and may be progressively refined. Electronic health records may facilitate such endeavors in two ways: 1) uniform assessment of function, morbidity, and social needs of older patients; and 2) an enlarging data base necessary to make predictions of benefits and risks more accurately.

Classical clinical trials play an important role for older individuals. Randomized phase III trials provide proofs of principles, such as the benefits of adjuvant chemotherapy when indicated in patients age 65 and older with breast cancer. Phase II studies allow investigators to explore the pharmacokinetics and pharmacodynamics of new drugs in the elderly. These trials have very selective enrollment criteria and offer little help in assessing individual prognosis in a population whose hallmark is diversity.

Complexity is with us. The approach to complexity represents an important clinical challenge with the aging of the population. In this paper we have described the nature of complexity and proposed a five-step roadmap through it. The pathway is far from perfect and many more older patients will not be able to exit the labyrinth. In the meantime, we have offered a blueprint for building more and more reliable assessment instruments able to maximize the benefits and minimize the risks of cancer treatment in older individuals.

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