MEETING REPORT

Advances in caring for the older cancer patient: a report from the 2015 conference of the International Society of Geriatric Oncology

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ABSTRACT

A paradox in cancer research is that the majority of patients enrolled in clinical trials are relatively young and fit while typical patients in daily practice are elderly and have comorbidities and impaired organ function. Given these differences, many major studies provide an imperfect guide to optimizing the treatment of the majority of patients. Since cancer incidence is highly correlated with age, and since the world’s population is rapidly ageing, this problem can only increase. For this reason, oncologists and geriatricians need to collaborate in developing tools to systematically assess the health status of elderly patients and their fitness to receive cancer therapies of various intensity. Tailoring anti-cancer treatments and supportive care to individual needs should be seen as part of the move towards personalized medicine. Achieving this goal is as much of a challenge to developing and middle-income countries as it is to western nations. The 2015 annual conference of the International Society of Geriatric Oncology (SIOG) held in Prague, Czech Republic, November 2015 and had a global focus on advancing the science of geriatric oncology and supportive care. Central to this approach is the systematic assessment of life expectancy, independent functioning, and the physical and psychological health of older cancer patients. The assumption behind comprehensive geriatric assessment is that elderly cancer patients have complex needs. The implication is that effective intervention will require a multidisciplinary team. Examples of effective geriatric assessment, multidisciplinary working and supportive care were presented at the SIOG conference.

KEYWORDS

Geriatric oncology; supportive care; elderly; geriatric assessment; quality of life; comorbidities

Introduction

Along with many countries, China is undergoing rapid changes in demography and epidemiology. Between 1990 and 2013, average life expectancy improved in all provinces, with the increase ranging from 4.0 years in Hebei to 14.2 years in Tibet. Over the same period, the leading cause of years of life lost shifted from infections of the lower respiratory tract and the complications of pre-term birth to cardiovascular disease (CVD). When measured in disability-adjusted life years, cancer was second in impact only to CVD.

The burden of cancer is increasing, and the age distribution of the population is shifting towards the elderly. Given that cancer is predominantly a disease of aging, China—along with other middle income and developing countries—is as threatened as western nations by what has been termed the "cancer tsunami". The most prevalent tumors—as the breast, colon and rectum (CRC), lung, stomach, liver and oesophagus—account for 56% of the cancer burden. Their overall peak incidence is in people aged 80-84 years. The incidence and mortality of CRC rise steeply after the age of 55, and in both men and women are highest in the 75-84 age group. For a less common cancer, that of oral cavity, the pattern is similar: in the elderly, the peak incidence for both sexes is double that in people aged 35-60 years.

Globally, there is a paradox at the heart of clinical cancer research: while most patients with the disease are elderly and many are frail, the great majority of those involved in clinical studies are relatively young and—if their cancer is excluded—in good health. It is therefore difficult to extrapolate from trial-derived efficacy and toxicity data to the wider population of cancer patients seen in routine practice. In the case of those who care for cancer patients in non-western countries, this problem is compounded by the fact that most pivotal trials are conducted in predominantly Caucasian patients.

Such patients may differ from those in Asia in disease characteristics (mutation status in lung cancer is a notable...
example), gene polymorphisms and pharmacokinetics\(^6\). Even so, the essential questions are the same in patients of any ethnicity. How do we best match the intensity of therapy to the risk posed by the tumor, given its clinical and biological characteristics? And, in seeking to balance the risk of the cancer against the risks of treatment, how do we adapt therapy-including vital supportive care-to the aims and circumstances of individual elderly patients who may be compromised by declining physiological reserves, comorbidities and a life expectancy limited by factors other than cancer?

Assessing the mortality risk posed by competing morbidities is perhaps a particularly difficult area. Nevertheless, tailoring anti-cancer treatments and supportive care to individual needs should be seen as part of the welcome move towards personalized medicine\(^7\). At its 2015 annual conference, the International Society of Geriatric Oncology (SIOG) had a global focus on advancing the science of geriatric oncology and supportive care. Central to this approach is the systematic assessment of life expectancy, independent functioning, and the physical and psychological health of older cancer patients.

### Geriatric assessment and multidisciplinary working

In the case of each elderly patient, choice of therapy should be based not on chronological age, which is uniform and relentless, but on biological age, which is highly variable. Health status makes a considerable difference to the individual case. Thus, in the United States for example, a 70-year old in the healthiest 25% of his peers can expect to live 18 years, while for a man in the frailest 25% life expectancy is only 7 years\(^8\). Evaluation of health status is therefore vital to the appropriate management of elderly patients. Assessment of the social situation of the patient is also important in geriatric oncology and can usefully include whether or not a family care-giver is present, the individual’s financial resources, and the extent of access to social and other healthcare services. A further factor, of course, is patient preference, both in relation to the goals of therapy and the means of attaining them.

SIOG has developed guidelines for the systematic assessment of health status. The cornerstone of management is systematic and comprehensive geriatric assessment (CGA). This has to be done using tools that are practical in centers that are not highly specialised.

A rational approach is to start with screening, using a tool such as the G8, developed specifically for older cancer patients, and which can be completed in less than five minutes\(^9-11\). Although there are limitations (as with all such tools), its eight components cover food intake, weight loss, body mass index, mobility, neuropsychological problems, polypharmacy, self-perceived health status and age. In a prospective non-interventional study of almost a thousand men aged 70 or older, an abnormal score on the G8 (14 or less on a scale of 0-17) strongly predicted mortality over three years and hence the need for comprehensive assessment\(^12\).

Following studies from the US and Europe showing the G8 to be a good way of identifying older cancer patients requiring a CGA, the European Organization for Research and Treatment of Cancer (EORTC) has now made G8 screening compulsory for all patients aged 70 years and older who are included in the organization’s trials.

Individual items may require modification for the Asian context. Compared with western nations, the population distribution of body mass index, for example, may be different. Patterns of family care and provisions for social support are also likely to vary according to culture. The proportion of people with various degrees of fitness may differ, as may perceptions of what constitutes optimum treatment and outcome. However, what we have in common—as people and as patients—is more important than what sets us apart.

The CGA itself includes data on demographic, social, functional, nutritional, cognitive, and mental health status; and the presence of fatigue, comorbidities and geriatric syndromes such as osteoporosis and sarcopenia. It has demonstrated value in predicting survival and chemotherapy toxicity, identifying reversible conditions, and in determining the patients’ capacity to make decisions and their values and goals of treatment\(^13\). Part of the CGA involves administration of two scales that measure dependency, whether caused by the cancer itself or by comorbid conditions. Although relatively simple, these scales Activities of Daily Living (ADL) and the Instrumental Activities of Daily Living (IADL)-have been used to determine the need for social and healthcare interventions and have prognostic value. The Cumulative Illness Score Rating-Geriatrics (CISR) is used to assess comorbidity. In relation to comorbidity, it is helpful to ascertain the stage and potential reversibility of the condition, its history, and the risk of acute organ failure.

The assumption behind CGA is that elderly cancer patients have complex needs. The implication is that effective intervention will require a multidisciplinary team. Practical aspects of implementing geriatric assessment and facilitating multidisciplinary working were a major theme at the SIOG conference.
Local initiatives reflecting a global problem

Martine Puts (University of Toronto, Toronto, Canada) outlined steps in the process: first, identify patients who should have a CGA, and at which point in the course of their cancer management; then decide on relevant domains and tools; conduct the assessment, discuss with the patient and family their priorities for treatment and the implications of the results of the CGA; and communicate these to the multidisciplinary team which develops the care plan. To “close the loop”, it is then essential to evaluate interventions by monitoring changes in patient health status and function.

The Cancer Institute of Sao Paulo, Brazil, is among the hospitals that have been putting CGA into practice. Theodora Karnakis, of the Sao Paulo Institute, described the criteria that determine referral to an oncogeriatric team. These criteria are age of 80 or older, or presence of one or more of the following: neuropsychiatric or neurodegenerative disease, loss of two or more activities of daily living, a history of falls, and three or more comorbidities.

Preliminary data from Sao Paulo suggest that in breast cancer patients 45% of treatment plans were changed as a result of CGA. For assessment to have this degree of influence, oncologists should have quick access to its results, which requires effective channels of communication. This is also true for communication with patients and carers since the involvement of many different health care professionals may result in confusion about who is in charge of the overall care plan.

Locally advanced head and neck cancer is often treated with concurrent chemoradiotherapy, an intensive intervention that poses a major challenge to frail elderly patients with multiple comorbidities. Ronald Maggiore (Health Science University, Oregon, USA) explained how treatment is being tailored to the circumstances of individual patients through a combined oncogeriatric approach, assessment of life expectancy, and optimization of agents and drug dose using tools to predict chemotherapy-associated toxicity. Long-term survivors face complex problems and require the support, among others, of therapists expert in speech, swallowing, hearing and nutrition.

Research in progress will provide further information on the impact of CGA on treatment decisions, and whether treatment decisions based on CGA improve patient outcome—measured as broadly as possible, from quality of life to preventing avoidable hospital admissions. SIOG is encouraging the inclusion of endpoints that are particularly relevant to elderly patients in pivotal trials. This is especially important in geriatric oncology where treatment is frequently palliative in intent and the enhancement of quality of life and maintenance of independent function are often the goals most desired by the patient.

In this context, decisions patients make in advance about resuscitation and end-of-life care should of course be obtained and respected. Consideration of cognitive state is a highly relevant factor when assessing patients’ competence to make such decisions, and this area was reviewed by Beatriz Korc Grodzicki (Memorial Sloan Kettering Cancer Center, New York, USA). By the age of 85, almost half of us will show some signs of dementia. Progress in prevention and treatment is proving frustratingly slow. However, there is much that can be done to prevent and reverse delirium. Risk factors include malnutrition, bladder catheterisation, visual impairment, electrolyte disturbance, and over-use of steroids, benzodiazepines and opioids.

Supportive care

Depending on the patient, the cancer and the treatment, supportive care ranges from myeloid growth factors, parenteral nutrition, anti-infectives, antiemetics and bisphosphonates to yoga and mindfulness. At its best, supportive care makes it possible for elderly or frail patients to tolerate potentially curative or life-prolonging cancer therapy which they would not otherwise be able to endure. Appropriate assessment yields appropriate treatment and, because morbidity and cancer-related disability result from an accumulation of events over time, assessments may have to be repeated. Reviewing supportive care, Christopher Steer (Wodonga, Victoria, Australia) presented examples of factors that predict the need for intervention, and the range of support that may be required.

In the year after cancer diagnosis (breast or colorectal), elderly patients show increasing levels of depression and cognitive impairment. Psychosocial problems are predicted by changes in functional status (ADL and IADL) and by baseline depression, cognitive impairment and fatigue. Multivariate analysis of factors associated with clinical depression in elderly patients with cancer (mean age 80
years) found significant effects of inadequate social support, impaired mobility, cognitive impairment, polypharmacy and cancer-related pain. Functional deficits increase in frequency with age, comorbidities and lower level of education but, even when identified, may not result in an appropriate intervention. In this single-institution study, 65% of patients had a potentially modifiable deficit, but only 9% of them received occupational or physical therapy within 12 months of it being noted.

Historically, nutrition for elderly cancer patients that has been relatively neglected. Yet poor nutrition is common among the elderly. This area was reviewed by Matti Aapro (Clinique de Genolier, Switzerland) and Florian Strasser (St Gallen, Switzerland). Sarcopenia due to age and comorbidities such as chronic heart and renal failure and chronic obstructive pulmonary disease is compounded by muscle loss accompanying chemotherapy and radiotherapy. Decreased food intake due to self neglect and physical factors (ranging from poor dentition to physical obstruction in gastrointestinal cancers) is exacerbated by decreased nutrient absorption caused by vomiting and diarrhoea. Deficiencies of vitamin D and calcium are also common, and can exacerbate bone loss from endocrine therapies in breast and prostate cancer.

For all of these reasons, elderly cancer patients should be screened for nutritional status at diagnosis and during treatment and recovery. The G8 screening tool described above contains questions about nutrition, weight loss and body mass index (BMI). And data from the Mini-Nutritional Assessment are among the clinical factors included by Extermann et al. in the CRASH score that predicts toxicity from cancer therapy. Superimposed on sarcopenia, the hypercatabolic state induced in advanced cancer by inflammatory mediators causes depletion of fat and muscle reserves that is resistant to conventional nutritional interventions.

We therefore have a complex picture in which there is inadequate intake of calories, protein and nutrients; the gut-brain axis, as well as cognitive and emotional factors, suppress appetite and voluntary food intake; muscle state and function is impaired by reduced physical activity; and inflammatory processes and tumor dynamics exacerbate loss of body mass. In this context, emerging anti-cachexia drugs (melanocortin receptor 4-antagonists, ghrelin and analogues such as anamorelin, selective androgen receptor modulators, and anti-myostatin agents that act on muscle pathways) may provide new opportunities for intervention.

## De-escalation options for elderly patients

Factors predicting the non-feasibility of full-dose chemotherapy in elderly patients—due to toxicity—include low hemoglobin, reduced creatinine clearance and hypoalbuminemia, but also self-rated depression. Individualization of chemotherapy to reflect the circumstances of older cancer patients was discussed by Ravindran Kanesvaran (National Cancer Center, Singapore) who drew attention to two recent SIOG Task Forces addressing the issue. Use of single-agent oral chemotherapy (principally with capecitabine and vinorelbine) may be somewhat less active than using the intravenous route, and could be associated with problems of compliance. However, oral agents are preferred by many elderly patients and may be better tolerated. The same is true for metronomic chemotherapy.

Diffuse large B-cell lymphoma has been under-treated in the elderly, because of toxicity concerns. As in younger patients, the overall and progression-free survival of elderly patients is improved by the R-CHOP regimen. But there are now alternative regimens involving dose-reductions and the substitution of less toxic agents and formulations (accompanied by more frequent toxicity monitoring) for patients with cardiovascular morbidity or other frailties.

In radiotherapy, improved technology allows better identification of target volume, avoiding organs at risk and maintaining quality of life; and, at least in certain settings, efficacy can be maintained with a reduced number of fractions. Lorenzo Livi (Carregi Hospital, Florence, Italy) told the meeting. In glioblastoma, for example, five fractions results in overall and progression-free survival similar to that achieved with fifteen fractions. In breast cancer, it may be possible to reduce use of whole breast radiotherapy in some elderly women (aged 65 and above) who undergo breast conserving surgery and adjuvant endocrine treatment and are at low risk of local recurrence.

The conference was reminded that potential adverse effects of treatment are not confined to interventions aimed at the tumor itself. Polypharmacy is prevalent among elderly cancer patients who frequently have multiple comorbidities, and is encouraged by the "prescribing cascade": an adverse event with one drug is interpreted as a new medical condition and leads to prescription of a second drug, and so on. Around 20% of patients take 10 or more drugs and 10%-30% experience an adverse drug event in the course of a year. In around 4%, there is a life-threatening drug-drug interaction. Altered physiology and drug handling, comorbidities and co-medications (which frequently include non-prescription and herbal agents) interact to affect pharmacokinetics and pharmacodynamics. Polypharmacy is associated not only with risk of adverse events but with
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**Discussion**

Aging populations, and the growing burden of cancer that results, are a pressing problem in low and middle-income nations and have led to urgent calls to action. As described at the conference by Gouri Shankar Bhattacharyya (Kolkata, India), the situation has been one in which global attention has been focused on maternal and child health, with little attention paid to the elderly and palliative care. In many countries, the problem is compounded by the fact that cancer is still a stigma, by fatalism, by reliance on traditional medicine and, for doctors, by lack of reimbursement. However, even with sociocultural and financial constraints, much could relatively easily be done. This is exemplified in India and Africa by the legal and bureaucratic restrictions on the medical use of opiates. If these were rationalized and relaxed, even practitioners who were not specialized in geriatric oncology have global application: how can we best treat older patients, many of whom are frail, in a way that optimizes the chances of managing their cancer while maintaining quality of life?

SIOG’s aims include, for medical oncologists, the development of general principles of management, central among them being the need for systematic geriatric assessment. Geriatricians are encouraged to apply the principles of good cancer treatment to the elderly, using supportive care measures as needed. SIOG aims to stimulate reciprocal sharing of information between these two major disciplines, and with other specialties. Young health professionals will be the messengers for an integrated approach and build bridges in their own institutions. They are therefore being encouraged to attend SIOG’s advanced courses and to participate in the Society’s Task Forces and guideline development. Given the global nature of cancer and of the demographic changes that are increasing its incidence, the other crucial element of outreach is to expand SIOG’s international efforts. A regional event was held in Singapore in 2014 and another is planned for Sao Paulo in 2016.

**Conflict of interest statement**

No potential conflicts of interest are disclosed.

**References**


