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Original Article

The Added Challenges of Bone Metastases Treatment in Elderly Patients☆

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Abstract

Most cancers occur in those older than the age of 65 years. As the population of the world ages and life expectancies continue to increase, it is important to address treatment challenges for elderly patients. This narrative review details the challenges of palliative radiotherapy treatment for elderly patients with bone metastases. We begin with the definition of elderly and its appropriateness, outlining recent demographic data of patients with cancer. The current status of elderly participation in clinical trials is discussed by reviewing the recent literature and clinical trial data. Factors affecting enrolment of the elderly are assessed, with a focus on palliative radiotherapy trials, and what we can do to improve accrual in this data-driven setting. At present, there is a lack of level 1 evidence that evaluates the optimal treatment for elderly patients with bone metastases. Therefore, a review of safety and efficacy is given based on previously published reports. Palliative radiotherapy for elderly patients is a worthwhile treatment and should be recommended regardless of age, as supported by available evidence. Patient, family and physician concerns about physical burden may be reduced as single treatments (that often can be done in a single visit) are as beneficial as multiple treatments for painful bone metastases. In elderly patients, radiotherapy may even be the best treatment for these cases as opioid-related adverse events are amplified in this group and often dosages are more difficult to titrate. Clinicians should continue to encourage the enrolment of elderly patients on to clinical trials as these data form the basis of optimal treatment guidelines. Radiation oncologists are encouraged to reduce the physical burden for elderly patients by offering single treatments where appropriate and completing consultation, treatment simulation and treatment in a single clinical visit.

Key words: Bone metastases; clinical trials; elderly; radiotherapy

Introduction

The Canadian Cancer Society estimates that 186 400 new cases of cancer and 75 700 deaths from cancer will occur in Canada in 2012 [1]. Of these cases, those older than 60 years will constitute over 70% of the new cases and 83% of cancer deaths. This number is expected to grow due to increasing global life expectancy and especially in North America, where large groups of baby-boomers are aging. Yancik *et al.* [2] estimate that by 2030, about one in five in the USA will be older than 65 years.

At present there is no general consensus on the criteria required to be defined as an elderly person. According to the World Health Organization, the most well-developed nations have accepted a rather arbitrarily set cut-off of 65 years for the definition of an elderly person [3]. Although the World Health Organization details a definition based on a numerical value, there is the question as to whether one's chronological or numerical age truly matters, or whether one's biological age is of more importance (defined as the loss of role along with physical decline). Furthermore, the life span of the elderly changes with location (Figure 1) and time even at the same location (Figure 2). Regardless of the definition of elderly, the care of older patients is complicated by physiological and additional comorbid conditions, and as such, it is important to address potential treatment challenges for these patients. The purpose of this paper is to review the enrolment of elderly patients on clinical trials and to determine the evidence for radiotherapy treatment of elderly patients with painful bone metastases.

Elderly Patients and Clinical Trials

In the ideal world, we would practice evidence-based medicine with data presented from randomised clinical

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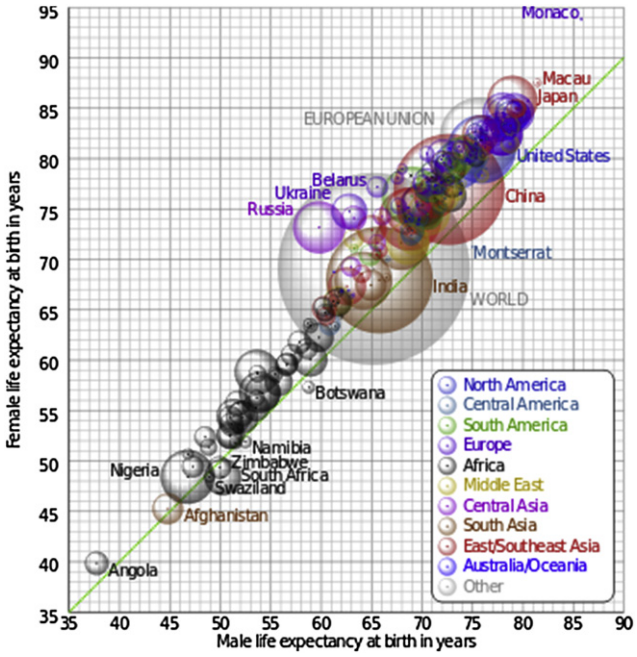

Fig 1. Global life expectancies as estimated by the Central Intelligence Agency with 2012 data: https://www.cia.gov/library/publications/the-world-factbook/fields/2102.html.

trials. Unfortunately for elderly patients, their lack of representation in these trials may result in treatment guidelines that may not be most applicable to their care. Analyses of data from three large oncology trial groups have shown markedly lower participation of elderly patients compared with their expected enrolment based on the incidence of disease in this age group [4–6]. Overall, the underrepresentation of elderly patients enrolled in clinical trials was consistent across all tumour sites, and not confined to one group of patients.

Hutchins *et al.* [6] analysed data from 16 396 patients enrolled in 164 Southwest Oncology Group trials from 1993 to 1996 and compared this with the elderly proportion of the general population with cancer from the 1990 United States Census and Surveillance Epidemiology and End Results 1992–1994. Overall, the authors found that patients ≥65 years of age were underrepresented overall in trials (25% in trials versus 63% of the patients with cancer in this age group; $P < 0.001$). Similarly, in National Cancer Institute (NCI)-sponsored co-operative group trials, an analysis of 59 300 patients enrolled between 1997 and 2000 with similar methodology showed the same low enrolment of elderly patients (32% versus 61%; $P < 0.001$) [4]. Not limited to the USA, data from Canada have shown similar, where Lee *et al.* [5] showed a significant disparity when elderly patients enrolled on to clinical trials were compared with those with cancer (22% versus 58%; $P < 0.0001$) when analysing 4174 patients in 69 National Cancer Institute of Canada (NCIC) trials between 1993 and 1996. Even in supportive care trials, the elderly made up only 21% of patients. Multiple groups have hypothesised that there are three main factors that are the cause of low accrual of elderly patients: physician-related, patient-related, and logistical [7–9].

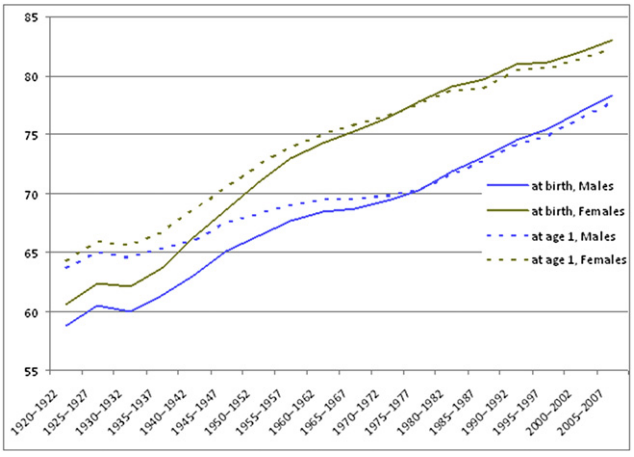

Fig 2. Statistics Canada data on life expectancy in Canada over time: http://www.statcan.gc.ca/pub/82-624-x/2011001/article/chart/11427-02-chart2-eng.htm.

Physician-related Factors

Townsley *et al.* [7] recently conducted a systematic review of barriers to the recruitment of elderly patients on clinical trials and identified two studies involving surveys of physicians involved with NCI or NCIC clinical trials [10,11]. Although it was realised that the reluctance to enrol elderly patients was multifactorial, the most common issues cited as barriers to enrolment by physicians were comorbid conditions and potential toxicities of treatment. In addition, less common factors were also identified (Table 1).

Table 1
Issues affecting elderly enrolment to clinical trials as identified by physicians participating in two surveys in cancer co-operative groups in Canada and the USA [10,11]

Issues affecting elderly enrolment to clinical trials
Comorbid conditions
Toxicity of treatment
Lack of support for older patients to manage side-effects at home
Patient preference
Influence of family
Transportation needs
Patient difficulty in understanding trials
Excessive time required to enrol patients
Not meeting study eligibility criteria
Lack of coverage for health care costs related to participation
Physician's personal bias that one arm of trial was not effective or unacceptable
Perceptions that the best treatments for their patients were not included in the trial
Life expectancy too short to justify participation
Likelihood of success was low
Geographic inaccessibility
Trials not being offered by physicians
Physicians unaware of such trials
Concerns about additional investigations