

Editorial

What is an “Elderly” oncologic patient?

Geriatric oncology is a young subspecialty with an amount of scientific knowledge still limited. About 50% of new patients presenting with cancer are over 60 years of age today and we all know that the proportion of so called elderly patients presenting with cancer will steadily rise in developed countries in the forthcoming years, since the life expectancy is increasing of 3 months every year in countries like France. The importance of increasing our knowledge is therefore paramount. *Critical Reviews in Oncology and Hematology* has taken the endeavour to gather and publish as much information as possible to help oncologists facing elderly patients. Where are we now?

Geriatricians have developed tools and scales to evaluate and quantify the frailty of elderly patients. Comprehensive Geriatric Assessment (CGA) fully captures the complexity of problems that are typical of those of older persons [1].

Balducci and Exterman [2] develop the different elements of CGA to detect frailty. They try to define the main objectives of CGA in geriatric oncology: detect comorbidity that is associated with decreased life expectancy and that is an independent prognostic factor for cancer outcome, compromising eventually the tolerance of cancer chemotherapy. A comprehensive assessment of the older person allows to detect individual problems that may affect the safety and effectiveness of treatment, and to assess the risk/benefit balance in individual situations. It helps trying to understand whether the cancer would cause symptoms or disability during the residual life span beyond what is already present or predictable by causes other than cancer itself. These tools are available for cancer patients but are not routinely used in oncology practice: many oncologists are not familiar with those tests; geriatric evaluation is time consuming (1 h per patient); oncologists have not enough time and a skilled geriatrician is not often available next door. In practice, the decision to treat and how to treat an elderly patient often relies on the experience and personal feeling of the physician.

Information on specific pharmacology of anticancer drugs (pharmacokinetics and pharmacodynamics for efficacy and toxicity) in elderly patients in particular taking in account comorbidities and/or comedication is extremely scarce. Such studies are difficult to design and perform, with numerous dropouts in part due to the frailty of the patients, and

would generate results largely heterogenous due for example to the variety and combinations of comedication. We have reliable information on competition for metabolism through the cytochrome pathway for almost every anticancer drug and information on PK variations in case of renal and hepatic insufficiency in the general population. John et al. tried to discuss specific diseases and to give recommendations for drug selection by considering limitations of saturability of absorption, patient compliance and the pharmacokinetic and pharmacodynamic changes that occur in older patients [3]. But in practice, for elderly patients, with multiple comedication or comorbidities we must take daily decisions without adequate information.

The majority of the literature on geriatric oncology deals with analyses of efficacy and tolerance among the subsets of elderly patients extracted from prospective studies and often compared to the population of younger patients from the same studies [4]. Most of these retrospective analyses conclude to similar efficacy and tolerance in “elderly” patients as compared to younger ones. In this issue of *CROH* a paper by Kulkarni et al. reports on the retrospective analysis of elderly (over 65 years of age) patients from three randomized trials comparing Pemetrexed given alone or in combination with other drugs. The authors conclude that both efficacy and tolerance are similar in elderly and younger subpopulations of these trials. It is good to know that, and it is appropriate that such data be published if the analyses are adequately performed, which is the case of the study by Kulkarni et al. But what can be questioned is the relevance of such analyses to the real problems of geriatric oncology.

Studies specifically designed to recruit only elderly patients are infrequent, often mix poor performance status with elderly patients [5,6] and often meet difficulties to fulfil their accrual objectives. The IFCT, the French cooperative group for thoracic oncology recently initiated a trial to compare mono versus doublet chemotherapy in non-operable Non-Small Cell Lung Cancer over 75 years of age. Poor accrual prompted the group to lower age limit to 70. It must be noted however that patients between 70 and 75 represent 43% of the total population of NSCLC referred to the participating centers. Can it be called the “older” population of lung cancer?

Therefore a first issue is the age cut-off. In most instances, 65 is probably irrelevant. In developed countries most patients up to 70 and often 75 are physiologically very similar to younger population. Why should they have different outcomes? A problem for the oncologist is to decide which patients should have CGA. Physical disability could be detected by the assessment utilized in the Cardiovascular Health Study, validated in approximately 8500 individuals followed for an average of 11 years [7]. But there is no validated screening test evaluated in geriatric oncology to detect when the old patient is physiologically different from younger ones. For example, in the paper from Kulkarni, patients over 65 years of age are considered as a whole and a homogeneous population. If let us say 80% of the population analysed is under 70, then the information is really of poor value. It would be at least appropriate to split the population in subgroups every 5 years and eventually analyse apart the older subsets.

The second issue relates to inclusion criteria of prospective studies including, but not exclusively, elderly patients. These criteria include likelihood to tolerate the treatment studied and therefore, even if elderly patients can be included, those eligible are likely not to represent the general population of elderly people. Extrapolating the data from those populations to "elderly cancer patients" is not valid and can be misleading. This point is adequately discussed in the discussion section of the paper by Kulkarni et al.

We believe that geriatric oncology has to move forward in several directions. First, promote geriatric evaluation as a part of the initial workup of any cancer patient over 70 or 75. Second promote studies on the pharmacology of anticancer drugs specifically in elderly patients, as is done, with great difficulties, in pediatric patients who usually have no comorbidities and few or no comedications. Finally promote clinical studies prospectively focusing on elderly patients, with whenever possible, registration of all ineligible patients and the reason for ineligibility, based for example on geriatric evaluation.

Such studies are certainly more useful to elaborate the decision making processes than retrospective analyses of subsets in general prospective trials.

References

- [1] Ferrucci L, Guralnik JM, Cavazzini C, et al. The frailty syndrome: a critical issue in geriatric oncology. *Crit Rev Oncol Hematol* 2003;46(2):127–37.
- [2] Balducci L, Extermann M. Management of cancer in the older person: a practical approach. *Oncologist* 2000;5:224–37.
- [3] John V, Mashru S, Lichtman S. Pharmacological factors influencing anticancer drug selection in the elderly. *Drugs Aging* 2003;20(10):737–59.
- [4] Pepe C, Hasan B, Winton TL, et al. Adjuvant vinorelbine and cisplatin in elderly patients: National Cancer Institute of Canada and Intergroup Study JBR 10. *J Clin Oncol* 2007;25(April 20 (12)):1553–61.
- [5] Leong SS, Toh CK, Lim WT, et al. A randomized phase II trial of single-agent gemcitabine, vinorelbine, or docetaxel in patients with advanced non-small cell lung cancer who have poor performance status and/or are elderly. *J Thorac Oncol* 2007;2(March (3)):230–6.
- [6] Hesketh PJ, Chansky K, Lau DH, et al. Sequential vinorelbine and docetaxel in advanced non-small cell lung cancer patients age 70 and older and/or with a performance status of 2: a phase II trial of the Southwest Oncology Group (S0027). *J Thorac Oncol* 2006;1(July (6)):537–44.
- [7] Fried LP, Tangen CM, Walston J, et al. Frailty in older adults. Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146–56.

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