

Comorbidity assessment and radiotherapy in elderly cancer patients

F. FIORICA¹, A. STEFANELLI¹, R. FISICHELLA², U. TIRELLI³, M. BERRETTA³

¹Department of Radiation Oncology, University Hospital, Ferrara, Italy

²Department of Surgery, University of Catania, Catania, Italy

³Department of Medical Oncology, National Cancer Institute, Aviano, Italy

Abstract. – More than 60% of all cancer patients in Europe and the USA are older than 65 years at the time of diagnosis. Despite this, elderly patients are generally under-represented in clinical trials. There is a lack of clinical trials to drive evidence-based decision making in the elderly cancer patients.

In this review, we address the most important issue surrounding the treatment of older cancer patients: comorbidity assessment.

Key Words:

Elderly patients, Geriatric oncology, Radiotherapy, Radiochemotherapy.

Introduction

Radiotherapy with or without chemotherapy has become a standard treatment for many types of cancer, many trials assessed its safety and efficacy. However in elderly cancer patients there is no clear evidence of this approach.

Although more than 60% of all cancer patients in Europe and the USA are older than 65 years¹, the elderly account for only 25% of patients enrollment in randomised clinical trials², therefore data related to treatment-tolerance and results in this subset of patients are scarce. Furthermore, elderly patients are an extremely heterogeneous population as regards co-morbidity. Subjects can vary from very fit to not being able to live independently due to co-morbidities. It is not so clear whether the toxicity of treatment is justified by the level gained as measured by life prolongation and whether co-morbidities can influence the acute and late toxicities due to radiotherapy or combined treatment. One of the reasons for difference in cancer treatment of elderly patients is the fear that advanced age may be associated with a reduced tolerance of treatment. Nevertheless, patients who have reached their 80th year of life still have a mean life expectancy of seven years for men and nine years for women³. Age alone is not a sufficient reason to withhold adjuvant, neo-adjuvant, radical or pallia-

tive radio- or radiochemotherapy. Along with increasing age a decrease in physiologic reserve is observed. This is a complex process that varies in how it affects different people and even different organs. Moreover, this process is accelerated by the development of intercurrent illness.

Therapy in Geriatric Oncology

Elderly patients have a high prevalence of diseases, about 80% having three or more chronic conditions. It is likely that this population is compensated under normal condition, but when a patient is subjected to a stress, there may be inadequate functional reserve. Certainly, radiotherapy or combined radio-chemotherapy program represents a systemic and loco-regional distress. Its impact on daily functioning or its long-term impact on organ functions may be very important in many of these elderly patients. Therefore, it is essential to acquire a multidisciplinary assessment of patients in order to understand the clinical state of the individual and functional organ reserve independently from the diagnosis of cancer⁴. Evaluation of co-morbidity is very important in geriatric functional assessment, in order to recognise potentially treatable conditions, to assess functional reserve and to estimate life expectancy. Co-morbidity scores can be divided into two groups: those that have been validated in elderly people but not in malignant disease (geriatric index of co-morbidity [GIC]⁵ and those that have been developed in elderly people and validated in patients with cancer (adult co-morbidity evaluation-27 [ACE-27]⁶, cumulative illness rating scale for geriatrics [CIRS-G]⁷, and the Charlson index⁸. We have tested ACE-27 comorbidity index to analyze elderly patients with non small cell lung cancer⁹, rectal cancer¹⁰, breast¹¹ and prostate¹² cancer. Patients without or with mild co-morbidities had a significantly better survival than patients with moderate/severe co-morbidities. It's clearly demonstrated that increasing severity of co-morbidities may

sufficiently shorten the remaining life expectancy, cancel the gains obtained by radiotherapy with or without chemotherapy and increase acute toxicity. Our findings suggest the prognostic importance of co-morbidity and the potential value of including co-morbidity in clinical studies in which overall survival is relevant.

Performance Status

Another important issue, in geriatric oncology, is related to performance status (PS). PS scores are based on a patient's ability to perform daily activities and provide a measure of functional impairment¹³. Two main PS scales are routinely used in oncology: Karnofsky PS (KPS) and Eastern Cooperative Oncology Group (ECOG)PS. In all analyzed patients^{9-12,14}, included glioblastoma elderly patients¹⁵, PS represent another important prognostic factor.

After geriatric assessment, giving special attention to co-morbidities and performance, patients should be divided in fit, vulnerable, or frail. These categories of patients have different physiological reserves to tolerate a course of radiotherapy or combined radiochemotherapy¹⁶. Frail patients have a poor prognosis, present high toxicity with standard treatments, and are candidates to palliative treatments. Physiologically fit patients are able to tolerate radical treatments, and may be treated similarly to younger patients. Vulnerable patients are those with reduced functional reserve and partial limitations, and may be candidates for customized radiotherapy and chemotherapy treatment according to organ functional reserve.

That being so, elderly patients require therapeutic strategies adapted to their individual risk profile, scoring and monitoring physiological organ reserve and co-morbidities.

Whenever possible and appropriate elderly patients, correctly stratified, should be allowed and encouraged to participate in clinical studies.

References

- 1) JEMAL A, BRAY F, CENTER MM, FERLAY J, WARD E, FORMAN D. Global cancer statistics. *CA Cancer J Clin* 2011; 61: 69-90.
- 2) TALARICO L, CHEN G, PAZDUR R. Enrollment of elderly patients in clinical trials for cancer drug registration: a 7 year experience by the US Food and Drug Administration. *J Clin Oncol* 2004; 22: 4626-4631.
- 3) LICHTMAN SM. Management of advanced colorectal cancer in older patients. *Oncology (Williston Park)* 2005; 19: 597-602.
- 4) GOSNEY MA. Clinical assessment of elderly people with cancer. *Lancet Oncol* 2005; 6: 790-797.
- 5) GREENFIELD S, APOLONE G, MCNEIL BJ. Development and test of a new index of comorbidity index. *Clin Res* 1987; A35: 346.
- 6) PICCIRILLO JF, TIERNEY RM, COSTAS I, GROVE L, SPITZNAGEL JR EL. Prognostic importance of comorbidity in a hospital-based cancer registry. *JAMA* 2004; 291: 2441-2447.
- 7) MILLER MD, PARADIS CF, HOUCK PR, MAZUMDAR S, STACK JA, RIFAI AH, MULSANT B, REYNOLDS III CF. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res* 1992; 41: 237-248.
- 8) SINGH B, BHAYA M, STERN J, ROLAND JT, ZIMBLER M, ROSENFELD RM, HAR-EL G, LUCENTE FE. Validation of the Charlson comorbidity index in patients with head and neck cancer: a multiinstitutional study. *Laryngoscope* 1997; 107: 1469-1475.
- 9) FIORICA F, CARTEI F, URSINO S, STEFANELLI A, ZAGATTI Y, BERRETTA S, FIGURA S, MAUGERI D, ZANET E, SPARTÀ D, LA MORELLA C, TIRELLI U, BERRETTA M. Safety and feasibility of radiotherapy treatment in elderly non-small-cell lung cancer (NSCLC) patients. *Arch Gerontol Geriatr* 2010; 50: 185-191.
- 10) FIORICA F, CARTEI F, CARAU B, BERRETTA S, SPARTÀ D, TIRELLI U, SANTANGELO A, MAUGERI D, LUCA S, LEOTTA C, SORACE R, BERRETTA M. Adjuvant radiotherapy on older and oldest elderly rectal cancer patients. *Arch Gerontol Geriatr* 2009; 50: 54-59.
- 11) FIORICA F, BERRETTA M, URSINO S, FISICHELLA R, LLESHI A, FIORICA G, STEFANELLI A, ZINI G, TIRELLI U, ZANGHI A, CAPPELLANI A, BERRETTA S, CARTEI F. Adjuvant radiotherapy on older and oldest breast cancer patients after conservative surgery: A retrospective analysis. *Arch Gerontol Geriatr* 2012; 55: 283-288.
- 12) FIORICA F, BERRETTA M, COLOSIMO C, BERRETTA S, RISTAGNO M, PALMUCCI T, PALMUCCI S, LLESHI A, URSINO S, FISICHELLA R, SPARTÀ D, STEFANELLI A, CAPPELLANI A, TIRELLI U, CARTEI F. Safety and efficacy of radiotherapy treatment in elderly patients with localized prostate cancer: a retrospective analysis. *Arch Gerontol Geriatr* 2010; 51: 277-282.
- 13) LILENBAUM R, CASHY J, HENSING T. Prevalence of poor performance status patients in lung cancer: Implications for research. *J Thorac Oncol* 2008; 58: 71-96.
- 14) BERRETTA M, ZANET E, NASTI G, LLESHI A, FRUSTACI S, FIORICA F, BEARZ A, TALAMINI R, LESTUZZI C, LAZZARINI R, FISICHELLA R, CANNIZZARO R, IAFFAIOLI RV, BERRETTA S, TIRELLI U. Oxaliplatin-based chemotherapy in the treatment of elderly patients with metastatic colorectal cancer (CRC). *Arch Gerontol Geriatr* 2012; 55: 271-275.
- 15) FIORICA F, BERRETTA M, COLOSIMO C, STEFANELLI A, URSINO S, ZANET E, PALMUCCI T, MAUGERI D, MALAGUARNERA M, PALMUCCI S, GRASSO M, TIRELLI U, CARTEI F. Glioblastoma in elderly patients: safety and efficacy of adjuvant radiotherapy with concomitant temozolomide. *Arch Gerontol Geriatr* 2010; 51: 31-35.
- 16) GOMEZ-MILLAN J. Radiation therapy in the elderly: more side effects and complications? *Crit Rev Oncol Hematol* 2009; 71: 70-78.