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Elderly patients with brain metastases: new support for the balancing act in treatment decision making

Brigitta G. Baumert and Gianfranco Angelo Pesce

Cantonal Hospital Graubünden, Institute for Radiation-Oncology, Chur, Switzerland (B.G.B.); Radiation Oncology Clinic, Ospedale San Giovanni, Bellinzona, Switzerland (G.A.P.)

Corresponding Author: Brigitta G. Baumert, MD, PhD, MBA, Cantonal Hospital Graubünden, Institute for Radiation-Oncology, Loestr. 170, CH-7000 Chur, Switzerland (BrigittaGertrud.Baumert@ksgr.ch).

See the article by Lamba et al in this issue pp. 661–676.

Elderly patients are underrepresented in clinical trials[1] with 25% despite the fact that the majority, two-thirds of the cancer patients is older than 65 years.[2] Reported outcomes from clinical trials can therefore not fully translated into daily clinical practice. As the population is aging, a need for specific knowledge, investigation, and corresponding adapted treatment recommendations has been identified.

The latter is important as the group of elderly patients represents a heterogeneous population consisting of frail individuals at the one end and physically and mentally fit individuals at the other end. Treatment decision making is a balancing act between a choice of treatment and its related toxicities and the potential prognosis and quality-of-life outcome. This is the more important as elderly patients may face unconscious discriminating bias because of their age and the perception that they may not tolerate treatments as well younger patients.[3,4]

In this volume, Lamba et al present an investigation of real-life data concerning elderly patients with brain metastases on a population-based level.[5] A large number of nearly 10 000 patients was included. Overall, results revealed a general poorer prognosis as shown by prognostic indices (Recursive Partitioning Analysis [RPA] and the Diagnosis Specific-Graded Prognostic Assessment [DS-GPA]) using the same prognostic criteria. The aim was to contribute to the knowledge of these indices, as their outcome may not be generalizable to older patients due to the facts cited above: elderly patients represent a minority in clinical randomized trials where these indices originate from.

The median survival observed was 3–4 months for all primary tumor sites except ovarian cancer. Subgroup analysis for non-small lung cancer and melanoma patients with mutation-driven treatment had much longer survival. Also, local treatment as stereotactic radiotherapy, neurosurgical resection, and systemic therapy were associated with longer survival compared with nonstereotactic radiation like whole-brain radiation.

Another pooled analysis of 3 large randomized trials on stereotactic radiosurgery (SRS) with or without whole-brain radiation therapy (WBRT) for patients with 1–4 brain metastases found that for patients older than 50 years of age an increasing mortality and increasing distant brain failure was observed with increasing age, whereas no survival disadvantage was observed with SRS alone.[6] It should however be noted that patient numbers evaluated were quite small with about 300 patients in the older group above 50 years of age.

The improved survival with stereotactic radiotherapy observed by Lamba et al[5] maybe due to a lower metastatic burden as stereotactic radiotherapy (and neurosurgical resection) is often given for patients with few brain metastases and for patients usually in a better performance status. This should however be weighed against the fact that stereotactic radiotherapy has a low toxicity profile and a high local control of the metastasis and as such a high probability of symptom control. A significant increased toxicity with grades 1–4 has been reported for WBRT compared to SRS in elderly and very elderly patients with brain metastases in a retrospective review of patients aged 70 years or older.[7] A quite low toxicity profile with the Karnofsky performance score remaining stable in nearly 100% of the patients was reported by a single centre study who also treated patients with up to 8 brain metastases in 1 session with SRS.[8]

The QUARTZ trial, randomizing patients with brain metastases from a non-small lung cancer unsuitable for surgical resection or stereotactic radiotherapy between dexamethasone and best supportive care versus WBRT found no difference in survival and quality of life between the 2 groups.[9] Median age was 66 years and most patients were localized in RPA class II and III with a low performance status. Only younger patients below 70 years of age had a benefit from WBRT. A low performance status, which was not reported in the population database,[5] could have also contributed to the low median survival.

The real-life data extracted from a large population database contribute to a better understanding and prognostication of elderly patients harboring brain metastases. Prognosticators as number of brain metastases, performance status, or systemic disease were not part of this database. Therefore, a treatment of brain metastases should be discussed interdisciplinary in order to estimate the prognosis of individual patients, taking

into account the age of the patient, performance status, tumor load, characteristics of the primary tumor, possibility of preferable targeted therapies or immunotherapy often being less toxic than chemotherapy, and other relevant prognostic markers. Stereotactic radiotherapy should be preferred if radiotherapy is recommended.

Potential benefits should be weighed against potential toxicity, especially for elderly patients. This could also mean to restrain from treatment of brain metastases and provide appropriate palliative supportive care.

For the future prospective trials also integrating specific geriatric assessment tools beside biomarkers for this heterogeneous patient group are needed in order to identify the right treatment.

Conflict of interest statement. None declared.

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