Radiotherapy in patients with glioblastoma: does treatment delay affect survival?
A population-based analysis using data from CONCORD-3

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1. Background

- Radiotherapy is the mainstay of treatment for patients with glioblastoma.
- The American Society for Radiation Oncology (ASTRO) and the American Society of Clinical Oncology (ASCO) recommend starting radiotherapy as soon as safely permissible.
- Patients enrolled in clinical trials usually start radiotherapy 3 to 6 weeks after surgery, but for patients not in trials, the great majority, time to treatment may be longer if access to care is sub-optimal.
- The impact of treatment delay on survival is controversial; current evidence is restricted to small, retrospective, hospital-based studies.

2. Purpose of the study

- To investigate whether survival in the US varies with time to radiotherapy, using data from the third cycle of the CONCORD programme (CONCORD-3).

3. Patients and methods

- We included adults (18-70 years) diagnosed with glioblastoma (ICD-0-3 morphology codes 9440-9442) during 2000-2014 for whom the full date (day, month, year) of the first course of radiotherapy was available.
- Age was categorised as: 18-39 and 40-70 years.
- Time to radiotherapy was categorised in two ways: (1) 6 weeks or less and more than 6 weeks; (2) 6 weeks or less, 7-9 weeks, 10-12 weeks, and more than 12 weeks.
- Survival was estimated with the unbiased non-parametric Pohar Perme estimator.

4. Time to radiotherapy

- Distribution (% of time to radiotherapy)

5. Trends in two-year net survival (%) during 2000-2014 by age at diagnosis

6. Two-year net survival (%) by time to treatment (selected registries)

7. Findings

- Forty-five of 48 participating registries provided data on radiotherapy treatment.
- In 22 registries, the full data of radiotherapy was available for at least 70% of glioblastoma patients who received radiotherapy.
- The final study population comprised 28,541 individuals.
- Two-year survival was much higher in younger patients (18-39 years) than in older patients (40-70 years), and varied widely between registries.
- In many registries, especially during 2000-2004, 2-year survival was lower in patients who started radiotherapy within 6 weeks of diagnosis than those who started after 6 weeks ("delayed radiotherapy").
- Survival disparities by time to treatment persisted during the 15-year period 2000-2014, but they subsided in nearly all the 10 most populous registries from 2005 onwards.
- When delayed radiotherapy was split into 7-9 weeks, 10-12 weeks, and more than 12 weeks, two-year survival in 4 out of the 7 registries with more than 10 patients for each treatment category was similar for patients starting 7-9 weeks after diagnosis and those starting within 6 weeks.

8. Conclusions

- Disparities between states in 2-year net survival from glioblastoma are wide and persistent, both in younger and older adults, and by time to radiotherapy.
- Our findings do not allow a robust conclusion that delayed radiotherapy is associated with lower survival.
- It appears counter-intuitive that patients diagnosed 2000-2004 who received radiotherapy within the 6-week guideline had lower survival than those with longer treatment delay, but the difference was smaller from 2005 onwards.
- Possible reasons for the observed trends could be the introduction of chemotherapy in 2005, the refinement of radiotherapy techniques and the improvement of pre- and post-operative care.