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).

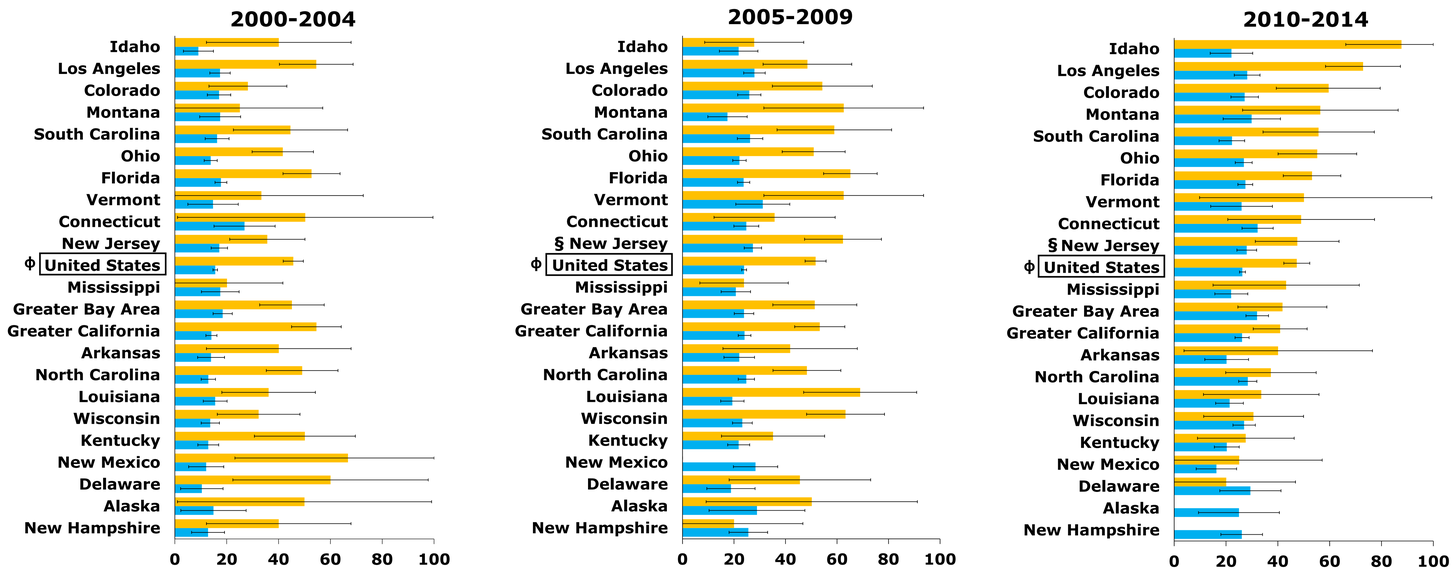
3. Patients and methods

- We included adults (18-70 years) diagnosed with glioblastoma (ICD-O-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.
- Net survival was estimated with the unbiased non-parametric Pohar Perme estimator.

4. Time to radiotherapy

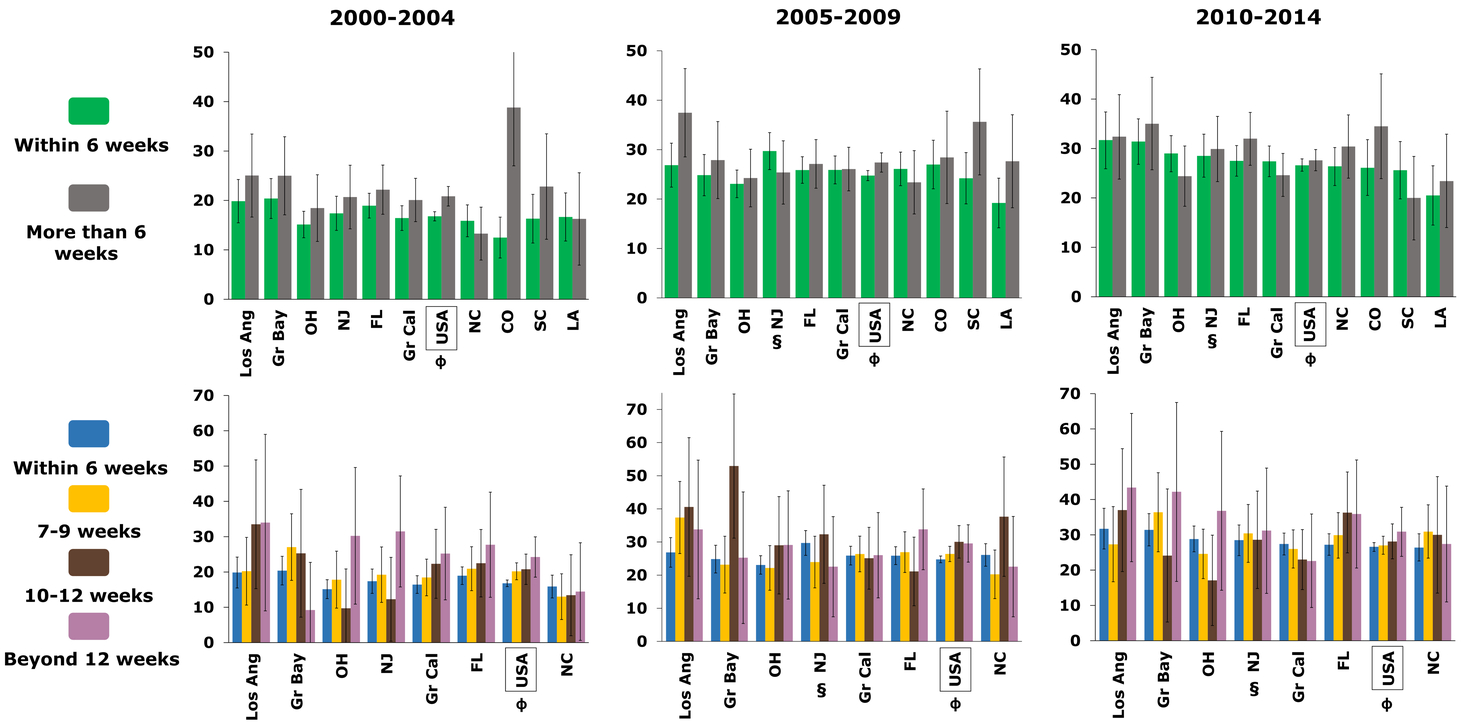
Registry	Patients	Distribution (%) of time to radiotherapy: 6 weeks or less	7-9 weeks	10-12 weeks	More than 12 weeks
Alaska	90	85.6	10.0	3.3	1.1
Arkansas	495	77.8	16.0	3.6	2.6
CA - Greater Bay Area	1,742	78.0	15.8	3.7	2.5
CA - Greater California	4,151	69.6	20.2	6.8	3.5
CA – Los Angeles	1,485	73.3	17.2	5.7	3.8
Colorado	1,049	77.3	16.0	4.1	2.6
Connecticut	768	74.9	19.0	3.1	3.0
Delaware	214	69.6	19.2	7.9	3.3
Florida	3,844	76.0	15.3	5.3	3.4
Idaho	399	84.7	12.0	2.3	1.0
Kentucky	1,195	83.4	12.1	3.2	1.3
Louisiana	929	73.6	19.6	4.0	2.8
Mississippi	605	80.5	15.2	2.0	2.3
Montana	301	85.4	11.0	1.3	2.3
New Hampshire	434	81.3	13.6	2.5	2.5
New Jersey	2,327	74.2	17.2	4.8	3.8
New Mexico	339	71.4	20.1	6.2	2.4
North Carolina	2,420	76.0	16.7	4.0	3.4
Ohio	3,054	79.9	14.2	3.6	2.3
South Carolina	1,040	75.4	17.8	5.0	1.8
Vermont	203	84.2	12.8	2.0	1.0
Wisconsin	1,457	83.7	13.3	1.8	1.2
United States	28,541	76.4	16.4	4.4	2.8

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



§ Estimates considered less reliable because 15% or more patients were lost to follow-up
ϕ USA: 22 cancer registries

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



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7. Findings

- Forty-five of 48 participating registries provided data on radiotherapy treatment.
- In 22 registries, the full date 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.
- The largest improvements in survival occurred between 2000-2004 and 2005-2009.
- 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 chemo-radiation in 2005, the refinement of radiotherapy techniques and the improvement of pre- and post-operative care.

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