TECHNIQUES: PROTONS

Comparative Effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for Locally Advanced Cancer.

Baumann BC, Mitra N, Harton JG, Xiao Y, Wojcieszynski AP, Gabriel PE, Zhong H, Geng H, Doucette A, Wei J, O'Dwyer PJ, Bekelman JE, Metz JM.

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Importance:

Concurrent chemoradiotherapy is the standard-of-care curative treatment for many cancers, but it is associated with substantial morbidity. Concurrent chemoradiotherapy administered with proton therapy might reduce toxicity and achieve comparable cancer-control outcomes compared with conventional photon radiotherapy by reducing the radiation dose to normal tissues.

Objective:

To assess whether proton therapy in the setting of concurrent chemoradiotherapy is associated with fewer 90-day unplanned hospitalisations (Common Terminology Criteria for Adverse Events, version 4 [CTCAEv4], grade ≥3) or other adverse events and similar disease-free and overall survival compared with concurrent photon therapy and chemoradiotherapy.

Design, Setting, and Participants:

This retrospective, non-randomised comparative effectiveness study involved 1483 adult patients with non-metastatic, locally advanced cancer. They were treated with concurrent chemoradiotherapy with curative intent from 1 January, 2011, to 31 December, 2016, at a large academic health system. A total of 391 patients received proton therapy and 1092 received photon therapy. Data were analysed from 15 October, 2018, to 1 February, 2019.

Interventions:

Proton vs photon chemoradiotherapy.

Main Outcomes and Measures:

The primary end-point was 90-day adverse events associated with unplanned hospitalisations (CTCAEv4 grade ≥3). Secondary end-points were: decline in performance status according to the Eastern Cooperative Oncology Group (ECOG) standard during treatment; 90-day adverse events of at least CTCAEv4 grade 2 that limited instrumental activities of daily living; and disease-free and overall survival. Data on adverse events and survival were gathered prospectively. Modified Poisson regression models with inverse propensity-score weighting were used to model adverse event outcomes, and Cox proportional-hazards regression models

with weighting were used for survival outcomes. Propensity scores were estimated using an ensemble machine-learning approach.

Results:

Of the 1483 patients whose results were analysed (935 men [63.0%]; median age, 62 [range, 18-93] years), those who received proton therapy were significantly older (median age, 66 [range, 18-93] vs 61 [range, 19-91] years; P < .01). They also had less favourable Charlson-Deyo comorbidity scores (median, 3.0 vs 2.0; P < .01), and had lower integral radiation dose to tissues outside the target (mean [SD] volume, 14.1 [6.4] vs 19.1 [10.6] cGy/cc × 107; P < .01). Baseline grade ≥2 toxicity (22% vs 24%; P = .37) and ECOG performance status (mean [SD], 0.62 [0.74] vs 0.68 [0.80]; P = .16) were similar for the two cohorts. In propensity-score weighted analyses, proton chemoradiotherapy was associated with a significantly lower relative risk of 90-day adverse events of at least grade 3 (0.31; 95% CI, 0.15-0.66, P = .002), 90-day adverse events of at least grade 2 (0.78; 95% CI, 0.65-0.93, P = .006), and decline in performance status during treatment (0.51; 95% CI, 0.37-0.71; P < .001). There was no difference in disease-free or overall survival data.

Conclusions and Relevance:

In this analysis, proton chemoradiotherapy was associated with significantly reduced numbers of acute adverse events that caused unplanned hospitalisations, with similar disease-free and overall survival figures. Prospective trials are warranted to validate these results.