
Jimmy T. Efird, PhD, MSc; Tarun Podder, PhD; Tithi Biswas, MD

Comparative effectiveness studies offer an important validation of clinical research. In the new study by Tabrizi et al., 1 COVID-19 risk was simulated using data from 8 randomized clinical trials of patients receiving radiation therapy with the aim of identifying an optimal fractionation schedule. The results of their analysis are both informative and transformational in the treatment setting. 1

In various regions of the world, such as Australia and New Zealand, hypofractionated radiotherapy is a well-recognized and accepted mode of treatment for many cancers, contingent on age, pathological stage, histological grade, or clear surgical margins. 2, 3 Evaluation of the high α/β ratio, such as in prostate cancer, offers increasing support of fewer, larger fractions that can be delivered safely with modern technology. It also points to a comparative effectiveness with conventional 2-Gy fractions, providing that the overall radiation dose is correctly reduced to compensate for toxic effects associated with larger daily fractions. When appropriate, a hypofractionated regimen is resource-efficient and better-suited to patients needs in terms of convenience and time constraints (ie, as fewer fractions are required, the treatment window is considerably shorter). In the COVID-19 era, time constraints are especially salient, given the increased risk of infection to staff and patients when treatment times are longer.

The study by Tabrizi et al. 1 addresses a timely and important topic, as SARS-CoV-2 infection rates continue to soar throughout the United States and globally. 1 Using a stochastic simulation approach, they have examined dynamic changes in COVID-19 risk to assess the impact of treatment changes. In a high COVID-19–risk setting, convincing model evidence of preexisting patient data are provided to suggest that suitable fractionation adjustment (hypofractionation) was associated with decreased mortality. This is congruent with the important concept of modeling mortality, as expressed by Selby and Fireman, 4 “Persons at greater risk have the most to gain from treatment.”

As is true for any model, the level of complexity needs to be carefully balanced against its practical utility. In this respect, Tabrizi et al. 1 have achieved a sensible and meaningful model. Nevertheless, avenues of further development might include incorporating antineoplastic therapies, such as immune checkpoint inhibitors targeting programmed cell death 1 and programmed cell death ligand 1, into their model, given that these agents can cause dilemma in diagnosis, have controversial effects on COVID-19 disease and severity, and are now frontline treatment for many cancers in marker-appropriate populations. 5 Additionally, examining the differential effect of epidemiological factors, such as obesity and smoking, both of which appear to be associated with mortality in patients with COVID-19, would be an important addition. 6, 7
Reserve University, Case Comprehensive Cancer Center, Cleveland, Ohio (Biswas).

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REFERENCES


