

Letter to the Editor

In regard to Kabarriti et al

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In a recent analysis, Kabarriti et al¹ reported an association between increasing prior mean radiation therapy (RT) lung dose and worse mortality in 107 patients with cancer and 2019 coronavirus disease (COVID-19) infection. The study was accepted as a preprint and the manuscript draft was promoted on social media (since deleted). Pulmonary toxicity associated with RT is an important issue, but we have several concerns about the methodologies and conclusions of this study.

Notably, socioeconomic and clinical factors linked with worse outcomes in patients infected with COVID-19, including smoking history and comorbidities²⁻⁴ such as diabetes or chronic obstructive pulmonary disease, were not included. Several oncologic factors that have a substantial effect on mortality also were unaccounted, including cancer stage and recurrence status, treatment intent (ie, definitive or not), or other recent cancer treatment, which is associated with a higher risk of a severe event with infection than without recent treatment.⁵ Furthermore, a recent comprehensive COVID-19 study⁶ of 105 and 536 age-matched patients with and without cancer, respectively, found a higher risk of severe events in patients treated with recent surgery or immunotherapy, but not RT. Additionally, results from both the COVID-19 and Cancer Consortium (CCC19)⁴ and TERA-VOLT8⁷ registry of thoracic malignancies show no increased risks associated with RT, albeit with small numbers.

Another major issue is the uncontrolled confounding variable of cancer diagnosis. The authors note that both a

lung cancer diagnosis and a mean lung dose (MLD) of >4 Gy were significantly associated with mortality; however, they declined to perform a multivariate analysis owing to a high correlation between the 2 variables. However, of the listed histologies, only locally advanced lung cancer would be expected to generate a MLD of >4 Gy. The lack of reporting of these known confounding factors and the failure to complete multivariate modeling makes interpreting the relationship between MLD and mortality impossible. Such a severe limitation on interpreting the study results should at least be mentioned in the discussion.

From a patient perspective, the study may have unintended negative consequences. Some patients with lung cancer who were not alerted to the significant limitations and conflicting findings with earlier studies contemplated cancelling their scheduled RT because of the perceived tremendous risk of death if they contracted COVID-19. Others, having already completed RT, were frightened to leave their house, even if medically necessary.

In summary, we applaud the authors for their effort in raising awareness to a potential negative prognostic factor for patients infected with COVID-19; however, we feel that the significant omissions noted herein limit the applicability of this analysis. We urge caution in overstating the results in the manuscript as well as on social media to avoid potential distress to vulnerable patient populations.

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