



Re: Clinical Characteristics and Outcomes of COVID-19–Infected Cancer Patients: A Systematic Review and Meta-Analysis

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A recent systematic review and meta-analysis of 15 studies by Zhang et al. (1) showed a statistically significantly higher fatality rate for coronavirus disease 2019 (COVID-19) patients with cancer than for COVID-19 patients without cancer. We want to point out the methodological limitations of current published studies on COVID-19 cancer patients' outcomes, mainly the lack of patient controls and inclusion of inappropriate controls, such as other cancer types. Of the studies in this meta-analysis, only 3 included noncancer controls, with pooled fatality rates of 23.4% and 5.9% for cancer and noncancer patients, and high statistical heterogeneity (87% and 85%, respectively). One of the 3 studies reported unadjusted survival rates for 13 hematological cancer patients and 11 hospitalized health-care workers (2). As expected, the health-care workers fared better than other study controls, likely because of a healthy worker effect (3). This study contributed the most extreme fatality rates for both cancer (62%) and noncancer cases (0%). A sensitivity analysis of the 2 remaining studies with matched control groups shows cancer and noncancer fatality rates of 16% and 8%, respectively; however, these studies are restricted to China and may not be generalizable elsewhere.

We want to underline the unique aspects of COVID-19–infected cancer patients that should guide the choice of appropriate controls. Cancer patients are likely to be older and male and to have more comorbidities than noncancer patients, factors consistently shown to be associated with poor COVID-19 outcomes (4); thus, appropriate matching or multivariate adjustments are critical for obtaining valid relative estimates. We recently published higher COVID-19 case fatality rates in cancer than noncancer hospitalized patients (30.6% and 24.8%, respectively) (5). However, when directly compared, after adjusting for age, sex, and comorbidities, cancer patients had statistically significantly higher odds of morbidity but no statistically significant difference in short-term mortality.

Studies need to include noncancer controls with equal COVID-19 exposure opportunity. For example, cancer patients have increased health-care interactions and, therefore, more

chances for incidental COVID-19 diagnosis; controls should be selected from similar care settings to reduce this bias. The strategy of drawing noncancer controls from the same population as cancer cases also reduces the confounding effect of the novel more transmissible or debilitating virus variants, which we know vary geographically. Furthermore, this strategy would also address the poor COVID-19 outcomes directly related to high community case rate (6) and consequent hospital strain.

Although it is urgently important to identify factors associated with poor COVID-19 outcomes and protect those most vulnerable, it is also imperative to use appropriate epidemiologic design to avoid bias and confounding to accurately quantify morbidity and mortality.

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Data Availability

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