



Cancer and Coronavirus Disease (COVID-19): Comorbidity, Mechanical Ventilation, and Death Risk

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Abstract

Background The presence of comorbidity poses a major clinical challenge in the care and treatment of COVID-19 patients. Moreover, having one or more comorbidities could be a life-threatening situation in COVID-19 patients. Cancer is substantially associated with significant morbidity and mortality in COVID-19 patients. However, there is not sufficient data to conclude that cancer patients have a higher risk of COVID-19 infection. In this study, we reviewed cancer comorbidity and risk of mechanical ventilation or death in patients with confirmed COVID-19.

Methods A comprehensive systematic search was performed on PubMed, Scopus, Web of Science, SciELO, and CNKI, to find articles published until August 01, 2020. All relevant case series, case reports, systematic and narrative reviews, meta-analyses, and prospective and retrospective studies that reported clinical characteristics and epidemiological information of cancer patients infected with COVID-19 were included in the study.

Results A total of 12 cohort studies exclusively on cancer patients with confirmed COVID-19 were selected.

Conclusions According to the findings of this study, cancer was not among the most prevalent underlying diseases in patients with confirmed COVID-19. Moreover, cancer patients infected with COVID-19 had the lowest risk of mechanical ventilation or death than the non-cancer infected patients.

Keywords COVID-19 · Cancer · Malignancy · Intensive care unit · Ventilation · Death

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first recognized in persons presenting with pneumonia of unknown etiology in Wuhan City, China, in December 2019 [1–3]. The World Health Organization (WHO) selected the official name of COVID-19 (stands for coronavirus disease 2019) for the disease [4, 5]. The new

pandemic is a source of profound morbidity and mortality which caused by a novel single-strand RNA (ssRNA) beta-coronavirus [6]. Compared with previous viral outbreaks, the COVID-19 pandemic has a relatively high mortality rate, the reasons for which are not entirely known [5, 6]. Analyzing the clinical and epidemiological data of patients with confirmed COVID-19 revealed that the presence of comorbidities increases the risk of the infection and worse prognosis of the

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disease [7]. The most common comorbidities reported in Covid-19 patients are hypertension, cardiovascular diseases, and diabetes [8]. However, a few cancer patients with confirmed COVID-19 were reported and treatment options for these patients are currently limited [9–12]. Moreover, the reported cases were heterogeneous with different clinical and biological mechanism, highly variable disease courses, and with different treatment strategies, which are not ideally representative of the whole population with cancer [13].

Cancer care services are confronted by immediate and delayed consequences of the COVID-19 epidemic [14, 15]. During the pandemic, remarkable efforts are made to understand the particularity of cancer patients and protect this vulnerable population from COVID-19 [13]. Several therapeutic challenges, guidelines, and recommendations by medical societies were announced for the management of cancer patients in order to effectively confront this terrible situation [16–18]. However, the COVID-19 pandemic has a negative effect on the conduct of cancer clinical trials and treatment, with both immediate and delayed consequences [19]. Now there is limited data on COVID-19 in immunocompromised cancer patients [9]. The incorporation of COVID-19-associated risk models into the analysis of randomized trials can help guide cancer treatment and management during this pandemic [20]. The first cancer cases provide important first opportunities to study the pathology of COVID-19 [12, 21]. However, there is not sufficient data to conclude that cancer patients have a higher risk of COVID-19 infection or mortality. Thus, in this study, we reviewed cancer comorbidity and risk of mechanical ventilation or death in patients with confirmed COVID-19.

Materials and Methods

Literature Search Strategy

An ethical approval was not required for this study, as it is a systematic review and meta-analysis. We have performed a comprehensive literature search on electronic databases including PubMed, EMBASE, Web of Science, Elsevier, Google Scholar, Cochrane Library, SciELO, SID, WanFang, VIP, Chinese Biomedical Database (CBD), and Chinese National Knowledge Infrastructure (CNKI) to identify all relevant studies published up to August 01, 2020. Combinations of the following MeSH terms and keywords were used in the search: (“Severe Acute Respiratory Syndrome Coronavirus 2” OR “Wuhan Coronavirus” OR “COVID-19” OR “COVID19” OR “Coronavirus Disease 2019 Virus” OR “SARS-CoV-2” OR “SARS2” OR “2019-nCoV” OR “2019 Novel Coronavirus”) AND (“Comorbidity” OR “Mortalities” OR “Mortality” OR “Death” OR “Intensive Care Unit” OR “Ventilation” OR “Computerized Tomography” OR “Risk”) AND (“Cancer” OR “Malignancy” OR “ OR “Lung

Cancer” OR “Gynecological Cancer” OR “Breast Cancer” OR “Ovarian Cancer” OR “Gastric Cancer” OR “Colorectal Cancer” OR “Head and Neck Cancer” OR “Thyroid Cancer”). The search was limited to human studies published in English and Chinese language. We also reviewed the reference lists of previous reviews, meta-analyses, and eligible publications to find other potential sources.

Including Criteria

Studies meeting the following criteria were included (a) studies with any design (randomized controlled trials, non-randomized controlled trials, case-control studies, cross-sectional studies); (b) case series, case reports, prospective and retrospective studies, systematic and narrative reviews, and meta-analysis; (c) studies reported data on pediatric or adult and male or female cancer patients with confirmed COVID-19; (d) studies reported results of the clinical characteristics of COVID-19 including mortality and/or intensive care unit (ICU) admission.

Results

Selected Studies

Initially, our search strategy yielded 358 possibly relevant articles. Of them, 269 publications were removed due to duplication, or were not human research. Finally, a total of 12 cohort studies exclusively on cancer patients with confirmed COVID-19 were included in the review. Of note, most of cohort studies were published in Chinese, English, and French. Most of the cancer cases with confirmed COVID-19 originated from East Asian and Europe.

Discussion

Studies have shown that still there is a high mortality rate among infected people with COVID-19 on mechanical ventilation, which demonstrated that full intensive care support and life-saving strategies still cannot overcome the poor prognosis of certain individuals with an underlying disease [22–24]. Studies have revealed that COVID-19 is a strengthen factor among people with underlying conditions [23, 25, 26]. Thus, during this pandemic, careful triaging of the people with a malignancy intended to or currently receiving palliative care is required. Early referrals, where people have not a significant symptom burden, could be temporarily avoided during the crisis [15]. Due to the high frequency of routine CT in the follow-up of people with malignancy, incidental findings of COVID-19 infections may be common [27]. Recently, some guidelines are provided to prepare the impact of COVID-19

on several malignancies such as breast, ovarian, head and neck, and urological cancer and advise on how to triage, priority, and organize diagnostic assay, surgical, radiation, immunotherapy, medical, and non-active treatments [13, 28].

To date, a few studies estimate the significance of COVID-19 infection among people with a malignancy in the literature [13]. However, it is suggested that people with underlying chronic conditions such as asthma, hypertension, diabetes mellitus, and chronic bronchitis might be more worried about strengthening the condition when infected with the COVID-19 than infected cancer patients [13, 29]. Guan et al., in a nationwide study of 1590 COVID-19 hospitalized patients from 575 Chinese hospitals between December 2019 and January 2020, revealed that the most prevalent comorbidities among infected people were hypertension (16.9%) and diabetes (8.2%) and 130 (8.2%) of them reported having two or more comorbidities. They have reported that only 18 cases (1.1%) had a history of malignancy. Their endpoint data including ICU admission, invasive ventilation, and death after adjustment by age and smoking status revealed that the history of malignancy was the fourth most common risk factor of reaching the endpoints with a HR of 3.50 (95% CI 1.60–7.64). A nationwide analysis described that severe cases were more likely to have hypertension (32.7% vs. 12.6%), cardiovascular diseases (33.9% vs. 15.3%), cerebrovascular diseases (50.0% vs. 15.3%), diabetes (34.6% vs. 14.3%), hepatitis B infections (32.1% vs. 15.7%), chronic obstructive pulmonary disease (62.5% vs. 15.3%), chronic kidney diseases (38.1% vs. 15.7%), and malignancy (50.0% vs. 15.6%) compared with non-severe cases [30]. Moreover, Wang et al., in a study including 1975 people with confirmed COVID-19, reported that the first 17 deaths were mostly elderly people (median age 75; range 48–89 years) with an underlying comorbidity or a history of a surgery. Of those 17 deaths, only an 86-year-old man had colon cancer and underwent surgery. However, the patient had two underlying conditions namely hypertension and diabetes mellitus that, along with the patient age and male gender, make him more exposed to the infection [29]. Richardson et al., in a study with 5700 people with confirmed COVID-19 who admitted to 12 hospitals in New York City within the Northwell Health system, demonstrated that the most common comorbidities among them were hypertension (56.6%), obesity (41.7%), and diabetes mellitus (33.8%). They described that only 6% of those people had a history of malignancy [31]. Zhang et al., in another study, revealed that patients recently treated with chemotherapy, radiation therapy, and/or immunotherapy in the past 2 weeks had four times increased risk of severe symptoms than those who received any treatment in the last 2 weeks [11]. Desai et al., in a meta-analysis, described the clinical courses of COVID-19 among infected people based on eleven studies. Their data demonstrated that nearly 2% of all people infected with COVID-19 had a history of malignancy. Moreover, they

described a higher risk of severe symptoms among infected people who recently received a chemotherapy or surgery in the past month, than non-cancer people with COVID-19 infection (75% vs. 43%) [32]. In another study among Chinese, Tian et al. presented two people who recently received lung lobectomies for adenocarcinoma who retrospectively found infected with COVID-19 at the surgery. Their pathologic examinations revealed that apart from the malignancies, the patient's lungs exhibited other symptoms (edema, proteinaceous exudate, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells) [12]. Kobayashi et al., in a case report, described an infected 56-year-old woman with COVID-19 who was diagnosed with a high-grade serous ovarian cancer after primary surgery. The patient at first was treated with neoadjuvant paclitaxel and carboplatin and then with paclitaxel and carboplatin with the addition of bevacizumab, and the third cycle of paclitaxel and carboplatin with bevacizumab was also given. However, due to the lack of fever and respiratory symptoms, the woman was quarantined at home, but the scheduled fourth cycle of paclitaxel and carboplatin treatment was delayed [16].

The Intensive Care National Audit and Research Centre (ICNARC) estimated that the mortality rate among infected people who underwent advanced respiratory support including noninvasive or invasive ventilation, tracheostomy, or extracorporeal respiratory support was 67.3% [33]. Zhang et al. describe a non-small-cell lung carcinoma (NSCLC) case who continued osimertinib during the COVID-19 epidemic. The case had a slight discomfort during the infection, but not required intensive care. Ultimately, the patient recovered from pneumonia following antiviral treatment with lopinavir/ritonavir [34]. Moreover, Leonetti et al. described two cases of oncogene-driven NSCLC patients suspected of having infected by COVID-19 who continued targeted therapy with ALK/ROS1 tyrosine kinase inhibitors in the presence of COVID-19 and recovered from pneumonia without treatments with specific antiviral agent [35].

The head and neck region consists of all the sites by which the COVID-19 virus may be transmitted [36]. Thus, people with head and neck malignancy may be at risk of more deleterious consequence of COVID-19 infection [37]. Evidence based on previous studies suggested that people with head and neck malignancy have higher risk of mechanical ventilation or death than people without any malignancy. Thus, studies suggested some practical steps such as the use of protective equipment, warranting access to critical drugs, telecommunications technology consultations, and wider community-based supports [15, 36–38]. In a cohort of 18 people with a malignancy described that 6% of people with head and neck malignancy had a higher risk of mechanical ventilation (39%) and death (8%) than those people without a history of any malignancy. Moreover, people with a malignancy also more rapidly

deteriorated, with a median time to a critical event (less than two weeks) than 43 days among those people without a history of any malignancy [39].

Conclusions

This study found that cancer was not among the most prevalent underlying diseases among patients with confirmed COVID-19. In addition, cancer patients with confirmed COVID-19 had a lower risk of mechanical ventilation and death than those non-cancer-infected patients. Due to the limited data, it is critical that larger and well-designed studies in various malignancies from different centers are needed to confirm our data.

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Author Contribution Mohammad Hossein Antikchi and Fatemeh Asadian are responsible as the guarantor of integrity of the entire study, study design and concepts, definition of intellectual content, and literature research. Meraj Farbod, Bahare Meibodi, and Hajar Abbasi are responsible for the clinical studies, experimental studies, data acquisition, and manuscript preparation. Ali Raei-Ezzabadi, Reza Bahrami, and Hossein Neamatzadeh are responsible for the data analysis, statistical analysis, and manuscript review. All authors have read and agreed with the final version of this manuscript.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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