

# Real-World Scenario of Patients With Lung Cancer Amid the Coronavirus Disease 2019 Pandemic in the People's Republic of China



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## ABSTRACT

**Introduction:** The coronavirus disease 2019 (COVID-19) outbreak throughout the world has affected millions of people in many ways, putting a huge burden on the health care system. The ongoing outbreak of this respiratory disease has posed critical challenges to public health, research, and medical communities around the world. This study aimed at evaluating the impact of COVID-19 pandemic on patients with lung cancer in the People's Republic of China.

**Methods:** We collected data on 397 inpatients from a single center during 4 weeks of the pandemic (2020 group) and that of 2504 inpatients during the same period (4 wk) in the past 5 years (2015–2019 group). A questionnaire was used to investigate the medical demands of 803 patients with lung cancer at 65 hospitals in 20 provinces in the People's Republic of China during the pandemic. We evaluated the incidence data of COVID-19 in Guangdong to analyze the tendency of the pandemic and compared it with inpatient data.

**Results:** The number of hospitalizations and lung cancer-related operations had steadily increased from 2015 to 2019 but reduced by an average of 26.72% (133.8) and 57.18% (45.4) in 2020. The hospital capacity decreased by 28.00% (35 inpatient beds) during the pandemic period of

infection with severe acute respiratory syndrome coronavirus 2. The pandemic caused a greater impact on medical work related to lung cancer after the Chinese New Year holiday. Patients were most concerned about long waiting times for outpatient services, inpatient beds, physical ex-

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Drs. Fu and Wu contributed equally to this work.

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aminations, or operations (406; 50.56%); the possibility of infection with the novel coronavirus (359; 44.71%); and the difficulties in getting to a hospital owing to transportation outages (279; 34.74%). Patients in stage I and II revealed having less fear about disease progression (14 [18.18%] and four [14.81%], respectively), had lower proportions of delayed medical arrangement (15 [19.48%] and six [22.22%], respectively), and complained less about complex treatment procedures (12 [15.58%] and five [18.52%], respectively). Patients in the high-infected area (345, 56.74%) complained more frequently about longer booking periods than those in the low-infected area (61, 31.28%).

**Conclusions:** The treatment of patients with lung cancer has been affected by the pandemic to some extent. We provide suggestions on both clinical diagnosis and treatment strategies for lung cancer to optimize the process, given the urgency of the current circumstances. The demand for medical support among patients with lung cancer or other life-threatening diseases should be given sufficient attention, especially during the current COVID-19 outbreak.

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**Keywords:** Coronavirus disease 2019; Severe acute respiratory syndrome coronavirus 2; Pandemic; Lung cancer

## Introduction

Two months ago, a novel coronavirus surfaced in the People's Republic of China and spread across the whole country, causing tens of thousands of infections and thousands of deaths.<sup>1</sup> Its basic reproduction number (R0) ranged from 2 to 3.58, indicating its potential for high infectivity.<sup>2,3</sup> The WHO on March 11, 2020 declared coronavirus disease 2019 (COVID-19) a pandemic.<sup>4</sup> Whereas 80,991 laboratory-confirmed cases had been identified in the People's Republic of China as of March 13, 2020, a total of 51,767 cases had been confirmed in 122 other countries or territories.<sup>5</sup> We must realize that the pandemic threatens the survival of 7.8 billion people on the planet.

Cancer, as one of the leading causes of death worldwide, accounted for approximately 4,292,000 new cases per year in the People's Republic of China.<sup>6</sup> Recently published data revealed that 1.3% of patients with COVID-19 were also diagnosed with a variety of cancer.<sup>7</sup> Among all types, lung cancer is the malignancy with the highest morbidity and mortality worldwide.<sup>8</sup> Patients with lung cancer are also immunocompromised, making them more vulnerable to contracting COVID-19.<sup>7</sup> In addition, older patients with comorbidities are at

increased risk of death.<sup>9</sup> Delayed treatment, especially for patients in the advanced stages of the disease may lead to serious consequences. The sudden outbreak of COVID-19 has caused a huge consumption of medical supplies and requisition of medical staff, which has had an enormous effect on the treatment of other life-threatening diseases. Having said that, an intensive understanding of the real-world scenario for patients with lung cancer could help improve the clinical management of patients to ensure the timely delivery of treatment.

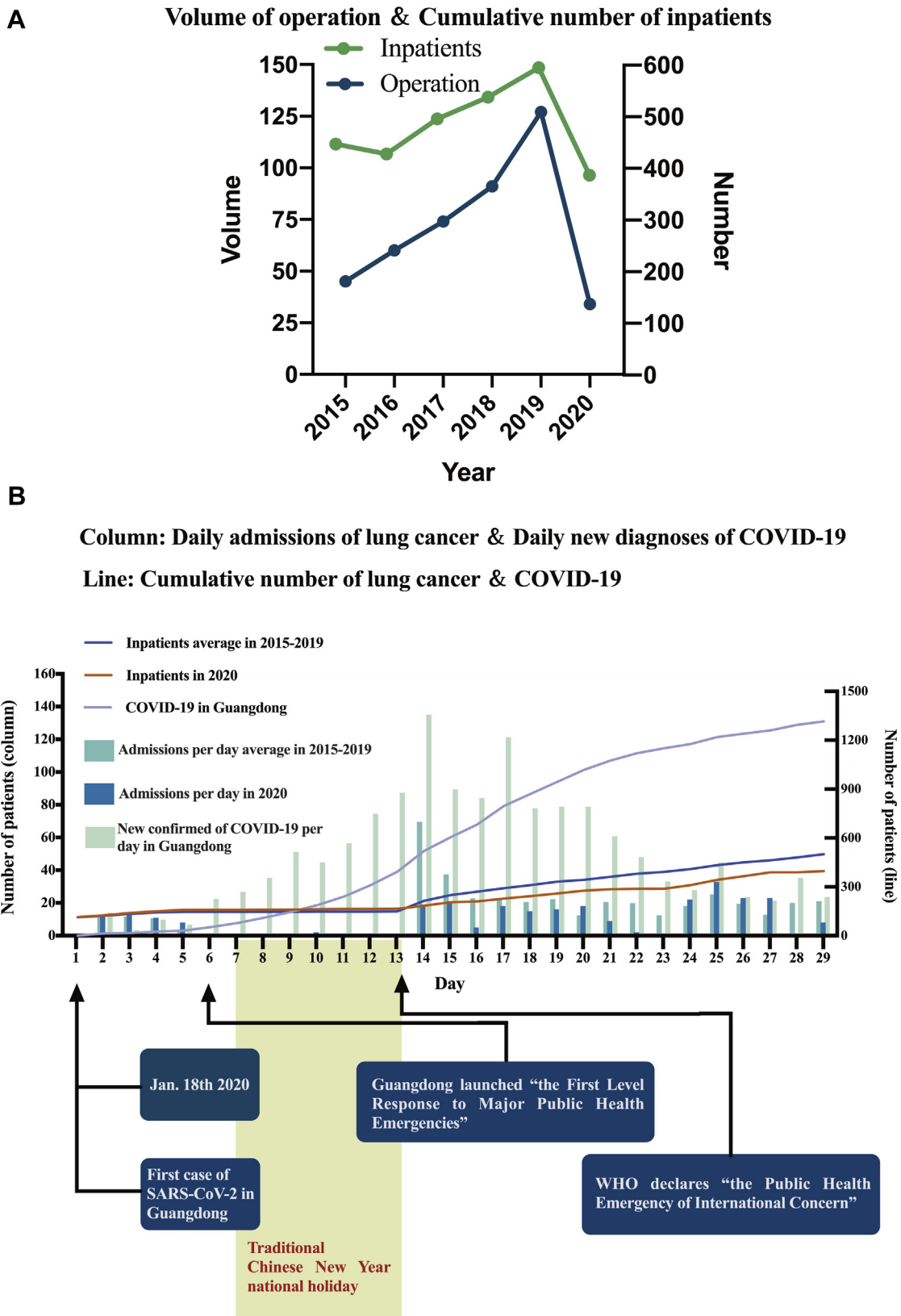
## Material and Methods

### Participants

We determined that the vulnerable time for patients with lung cancer in Guangdong province during the COVID-19 outbreak was during the 4 weeks between January 18, 2020 and February 15, 2020. The province launched the first-level response to major public health emergencies on January 23, 2020. The first COVID-19 case in the province was diagnosed on January 18, 2020, which was 6 days before the Chinese New Year holiday, and February 15, 2020 is the 16th day after the holiday. The same period from 2015 to 2019 was also evaluated (peer-years), which was also 4 weeks starting from 6 days before the Chinese New Year. The Chinese New Year holiday usually lasts 7 days every year. The flowchart in [Appendix 1](#) summarizes the entire process.

We collected data of inpatients from a single center between January 18, 2020 and February 15, 2020 (the 2020 group) and those hospitalized during the same period from 2015 to 2019 (2015–2019 group). Detailed information, including their sex, age, TNM stage (eighth edition), pathologic diagnosis, date of admission, date of discharge, and the volume of operation was retrospectively collected. We then analyzed the tendency of the pandemic in Guangdong (matching COVID-19 pandemic information with inpatient data) and identified the time point in which it started to interfere with the daily work of the medical staff. Guangdong province's pandemic data can be accessed at the official website of the Health Commission of Guangdong Province.<sup>10</sup> This study was approved by the hospital's Research Ethics Committee.

The survey was conducted on patients with lung cancer in February 2020 at 65 hospitals in 20 provinces nationwide using a self-administered questionnaire. All patients received the questionnaire survey at the hospital clinic. Through the interviews, we collected their age, sex, pathological diagnosis, TNM stage, the current plan of treatment, the purpose of visit, and difficulties in lung cancer diagnosis and treatment during the pandemic. We also subdivided the surveyed patients into high-infected area group (n = 608, 10 provinces) and low-infected area group (n = 195, 10 provinces) on the



**Figure 1.** (A) Inpatient data of patients with pulmonary tumors during the COVID-19 pandemic in 2020 and during the same period from 2015 to 2019. (B) The number of patients infected with SARS-CoV-2 or lung cancer in Guangdong province. Column: Daily admissions of lung cancer and the daily new diagnosis of COVID-19. Line: Cumulative number of lung cancer and COVID-19 cases. Before the end of the traditional Chinese New Year holiday, the frequency of the number of cumulative inpatients with lung cancer is almost the same as that in the previous 5 years; however, a notable difference was seen when the holiday was over. COVID-19, coronavirus disease 2019; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2.

basis of the People's Republic of China's national registry on the cumulative number of patients with COVID-19.<sup>5</sup> The provinces in the top 11 pandemic areas infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were considered as the high-infected areas. The primary outcome was the main difficulty that patients faced during the outbreak. All the patients provided written informed consent.

### Statistical Analysis

Continuous variables were expressed as median (interquartile range) and compared using the Mann-Whitney *U* test. Categorical variables were expressed as number (%) and comparisons between the 2015 to 2019 and 2020 groups were made using Pearson's chi-square test. Cramer's *V* coefficient was used to measure the degree of correlation between two categorical variables. Statistical analyses were performed using SPSS version 25.0 software (SPSS, Inc., Chicago, IL). A two-sided  $\alpha$  of less than 0.05 was considered statistically significant.

### Results

The clinical characteristics of inpatients with lung cancer are presented in [Supplementary Table 1](#). There were no significant differences ( $p > 0.05$ ) in age and sex between the two groups. The groups revealed significant differences in pathological diagnosis and distribution of TNM stages ( $p < 0.05$ ). The values of Cramer's *V* indicate an effect of small magnitude between groups and pathological diagnosis (0.16) or TNM stage (0.10).

Because most rooms were occupied for quarantine purposes and for treating patients with COVID-19, the hospital capacity for patients with lung cancer reduced by 35 beds (28.00%)—from 125 beds originally between 2015 and 2019 to 90 beds in 2020. From 2015 to 2019, the number of patients with pulmonary tumor and lung cancer-related operations increased year after year but declined sharply in 2020 ([Fig. 1A](#)) by an average of 133.8 (26.72%) and 45.4 (57.18%) patients, respectively. The number of patients with lung cancer who were hospitalized and the number of daily admissions from the start of the pandemic to the end of the Chinese New Year holiday in 2020 remained almost the same as those during the corresponding period from 2015 to 2019. However, a notable difference between the two groups was observed after the holiday ([Fig. 1B](#)). This change was in line with the increasing trend in the number of new COVID-19 cases diagnosed in a day in the province.

A total of 803 patients with pulmonary tumors from 65 hospitals in 20 provinces of the People's Republic of China received our questionnaire forms. Most of them

(530, 66.00%) came from hospitals in Guangdong and Hunan provinces ([Fig. 2A](#)) where the number of COVID-19 cases was high (the provinces were ranked first and fourth, respectively, when not taking into account the cases in the Hubei province). The clinical characteristics of the patients are presented in [Supplementary Table 1](#), and the overall results of the questionnaire are illustrated in [Figures 2B](#) and [3A](#). More than a quarter of the participants (209, 26.03%) complained that they had to delay doctor's appointments and treatment or examination schedules owing to the coronavirus outbreak. Moreover, 241 patients (30.01%) were worried about disease progression or tumor relapse without proper management during the pandemic. Most interviewees (406, 50.56%) believed that the waiting time for hospitalization, outpatient services, or radiologic examination took much longer than earlier. In addition, 359 (44.71%) patients were concerned about possible infection with SARS-CoV-2. Patients also reported greater inconvenience in transportation (279, 34.74%) and more difficulty in getting a doctor's appointment (128, 15.94%). A minority of participants (51, 6.35%) indicated that they had a shortage of tumor-related medications.

Subgroup analysis revealed a notable difference between high- and low-infected area groups regarding longer booking periods. ([Fig. 3B](#)). More patients with lung cancer in the high-infected area group (345, 56.74%) complained about longer booking periods than in the low-infected area group (61, 31.28%). Moreover, patients in stage III and IV seemed to face more difficulties than those in stage I and II ([Fig. 4A](#)). More than half of the patients in stage III expressed concern about the long waiting time (71, 60.17%). Patients in stage I and II revealed having less fear about disease progression (14 [18.18%] and four [14.81%] patients, respectively), experienced delayed medical arrangement in lower proportions (15 [19.48%] and six [22.22%] patients, respectively), and had fewer complaints about complex treatment procedures (12 [15.58%] and five [18.52%] patients, respectively).

### Discussion

We report the predicament of patients with lung cancer in a real-world setting amid the COVID-19 pandemic. Several aspects, such as medicine, operations, radiologic examinations, and consultation of the patients, were affected. The medical demands of patients with lung cancer are being compromised by the pandemic. Being threatened by two extremely dangerous diseases at the same time, these patients are likely to endure more psychological pressure compared with others. Over 30,000 physicians and nurses around the country went to the Hubei province for providing

medical support, and nonhealth professionals were advised to stay home owing to the risk of SARS-CoV-2 infection. Therefore, the major problem for patients with cancer has been the inability to receive necessary medical services.

In this study, we found that, in addition to the “clifflike drop” in the number of hospitalizations and the number of operations performed, the clinical characteristics in the pathological diagnosis and TNM stages were also different from the same period in the last 5 years. They may be related to the delay in routine medical examination or treatment arrangement for some patients. The reduced number of inpatient admissions and operations was because rooms used for patients with early- or advanced-stage lung cancer before the outbreak were repurposed to quarantine and treat patients with COVID-19 during the pandemic. Elective admissions for operation, radiotherapy, chemotherapy, and immunotherapy and emergency admissions to manage toxicities of cancer-related symptoms were also mainly influenced by room occupancy. In the People’s Republic of China, another factor influencing the admissions process was that every nonemergent patient and their accompanying relatives had to be tested for SARS-CoV-2 nucleic acid two or three times before admission. This was an effective measure to prevent a COVID-19 outbreak in the hospital; however, 2 to 3 days are required to obtain the result. Moreover, the patient’s attitude toward daily medical treatment became more cautious during the COVID-19 pandemic. Traffic control and the risk of exposure in hospitals prevented people from going to hospitals; though beneficial for pandemic control, this can also be problematic for those with other diseases that need to be diagnosed and treated. In addition, the sudden COVID-19 outbreak has led to insufficient supplies of protective equipment and a reduction in the number of blood donors. Medical staff in different positions were recruited to support the diagnosis, treatment, and prevention of COVID-19. The lack of medical resources made the medical staff more conservative in their daily work. Therefore, the allocation of scarce resources in a pandemic should be on the basis of maximizing health benefits.<sup>11</sup> At this time, a special guideline for the diagnosis, treatment, and follow-up of patients with lung cancer during the SARS-CoV-2 pandemic could help ensure the orderly conduct of daily medical work.<sup>12</sup>

At the same time, the patient’s subjective feelings should not be ignored, especially during this crisis. According to our study, most of their concerns during the pandemic include longer waiting times for outpatient services, inpatient beds, examinations, or operations (406, 50.56%). Other concerns included the possibility of being infected with the novel coronavirus (359, 44.71%) and difficulty in going to the hospital owing to

transportation outages (279, 34.74%). In addition, 209 patients (26.03%) indicated that their treatment was delayed owing to the current COVID-19 outbreak. Subgroup analysis suggested that patients in stage III and IV faced more difficulties than those in stage I and II. That is understandable because patients with locally advanced and advanced lung cancer with a higher tumor burden are of advanced age, have shorter periods of absent treatment windows, and worse prognosis than those in the early stage. Some of them are immunocompromised, making them more vulnerable to SARS-CoV-2 infection. Aside from this, more patients with lung cancer living in high-infected areas complained of longer appointment periods, which may be related to the mobilization of more resources in these areas toward tending to COVID-19 cases. Long waiting periods, along with delayed diagnosis and treatment, may lead to lung cancer progression and interfere with the best treatment outcomes.

The European Society for Medical Oncology proposed guidelines for the management of patients with lung cancer during the COVID-19 pandemic.<sup>13</sup> The guideline established priority groups for patients with different stages and medical purposes. For every group, it sets out three priority levels (high, medium, and low). In addition, the American Society of Clinical Oncology recommends developing a fair and consistent prioritization and allocation policy.<sup>11</sup> These documents should supplement and not supersede applicable local, regional, or national allocation plans.<sup>11</sup> Here, we have provided supplementary suggestions for both clinical diagnosis and treatment strategies for lung cancer, given the urgent circumstances, on the basis of our institutional implementation (Fig. 4B).

First, for those patients with findings of ground-glass opacities, it is crucial to determine whether it is caused by COVID-19 or a lung tumor, as they may share identical appearances at the beginning. Surgical indication under such circumstances should be held off temporarily, and surveillance intervals should be extended in consideration of the slow-growing tumor biology and the possibility of benign disease. Second, for patients with locally advanced lung cancer and N2 positive status, which is highly heterogeneous, neoadjuvant-targeted therapy has been proven safe and effective in patients harboring activating mutations in oncogenes such as *EGFR* and *ALK*.<sup>14,15</sup> Multiple ongoing clinical trials incorporating checkpoint inhibitors into neoadjuvant therapy for NSCLC have revealed encouraging findings of high response rates in major pathologic characteristics.<sup>16–18</sup> Therefore, neoadjuvant-targeted therapy or immunotherapy is an option to be considered when medical supply is limited and immediate operation is not available. For patients with advanced disease, the hospital medical policy should allow outpatient services to

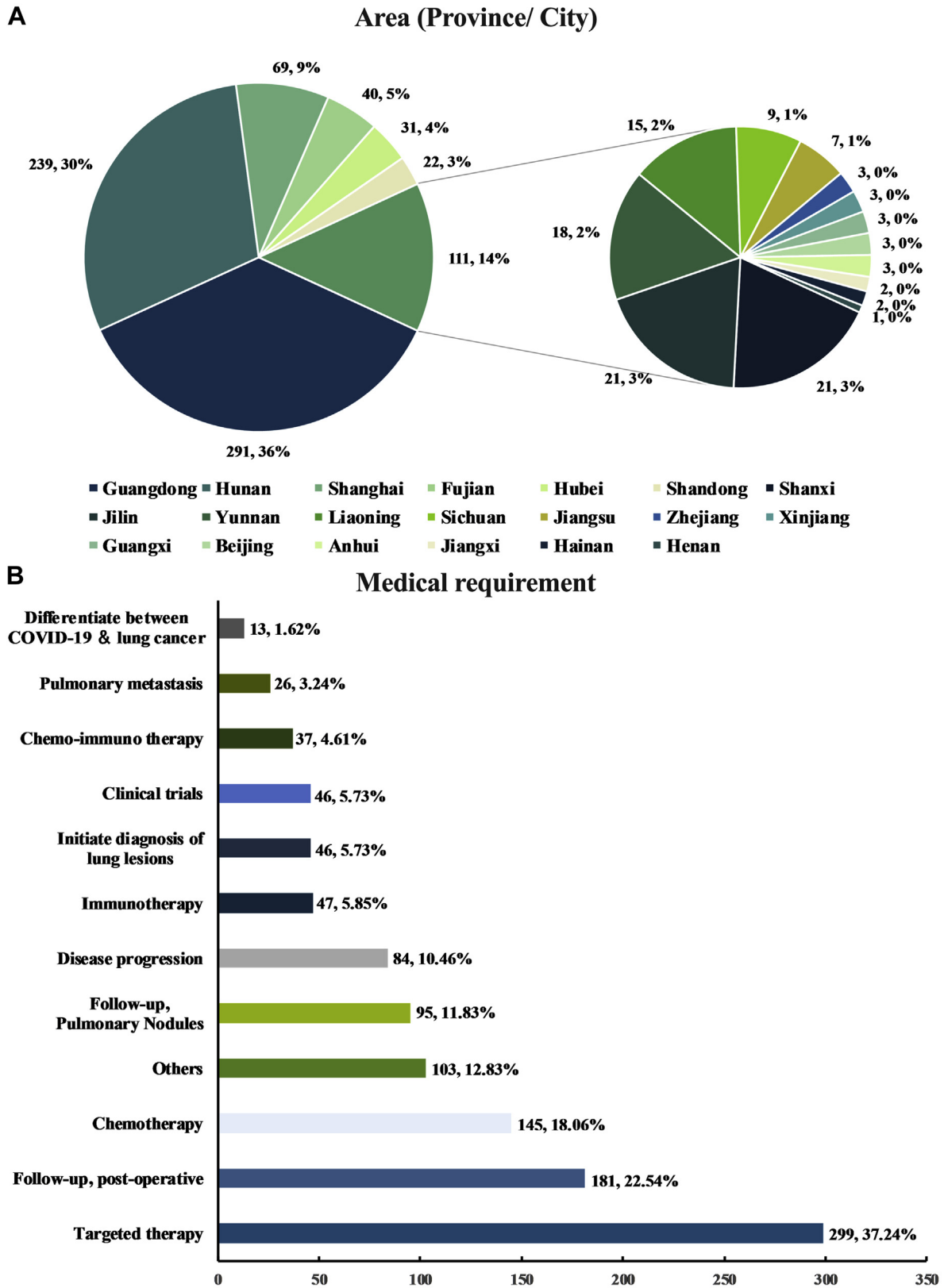
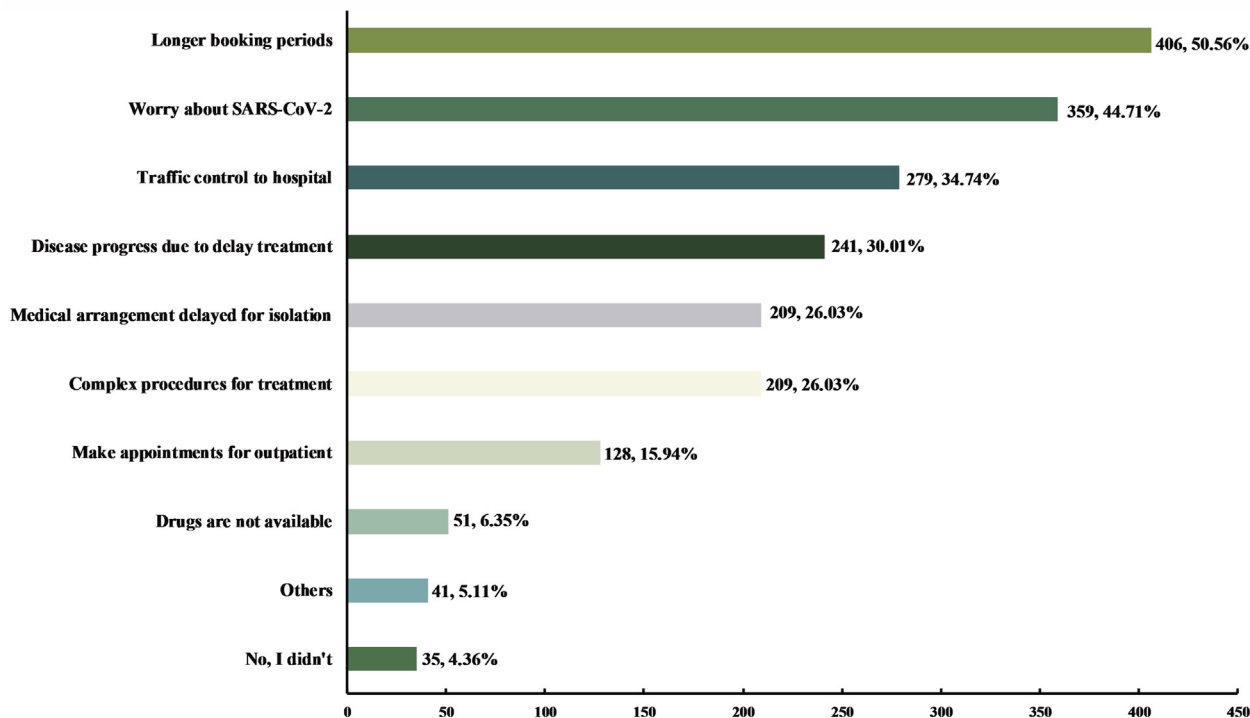


Figure 2. (A) Area and (B) medical requirements of participants. COVID-19, coronavirus disease 2019.

**A** The difficulties of pulmonary tumors during SARS-CoV-2 epidemic



**B**

The difficulties between high-infected area and low-infected area

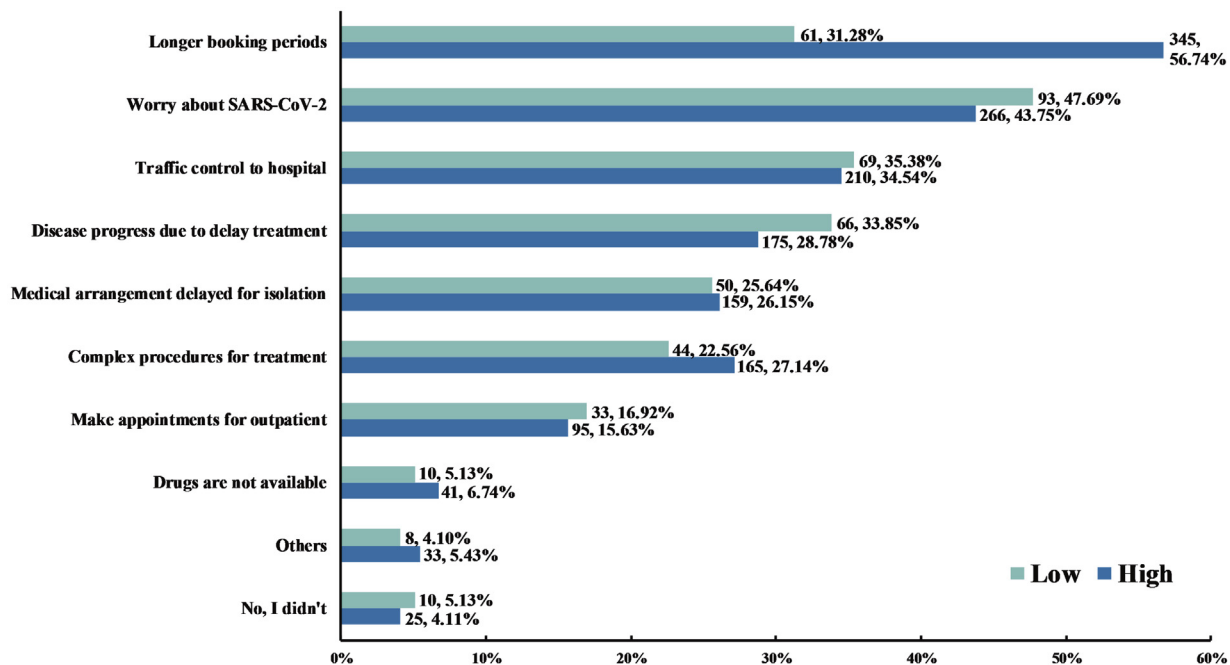
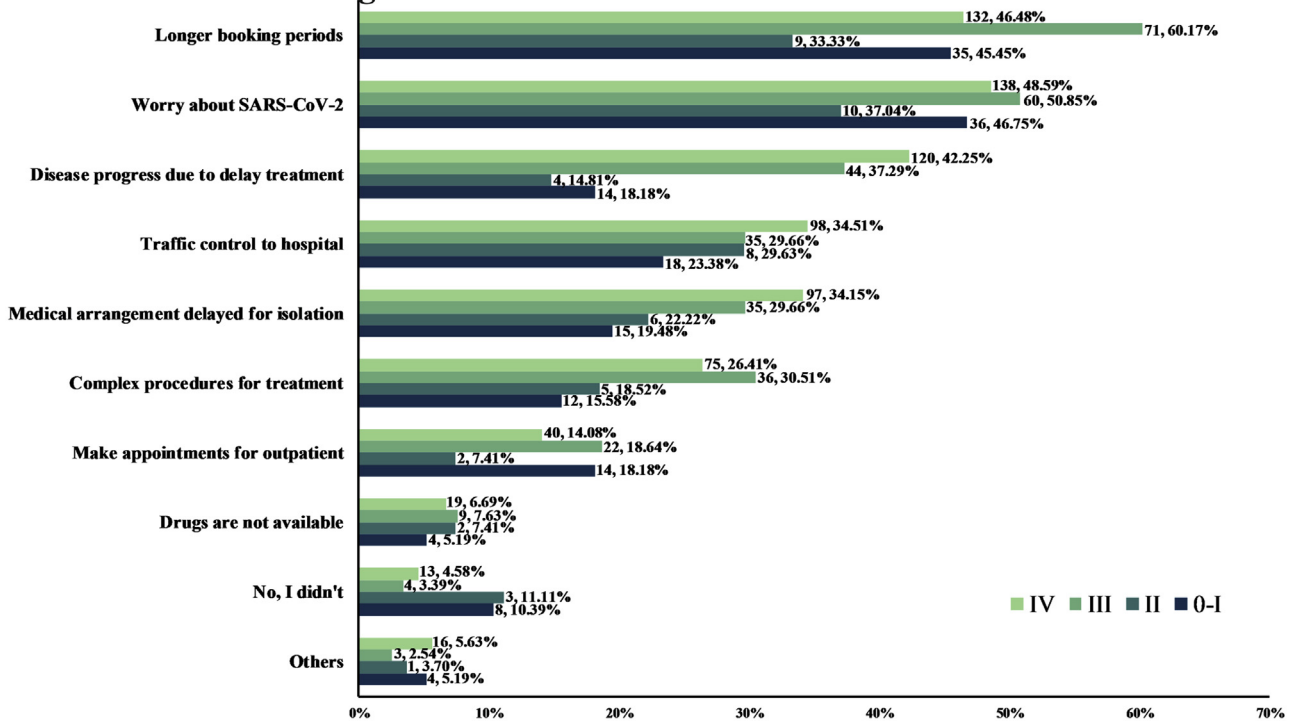


Figure 3. (A) Difficulties encountered by the patients during the pandemic and (B) subgroup analysis between high- and low-infected area groups. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

A

### The difficulties of patients with different stages



B

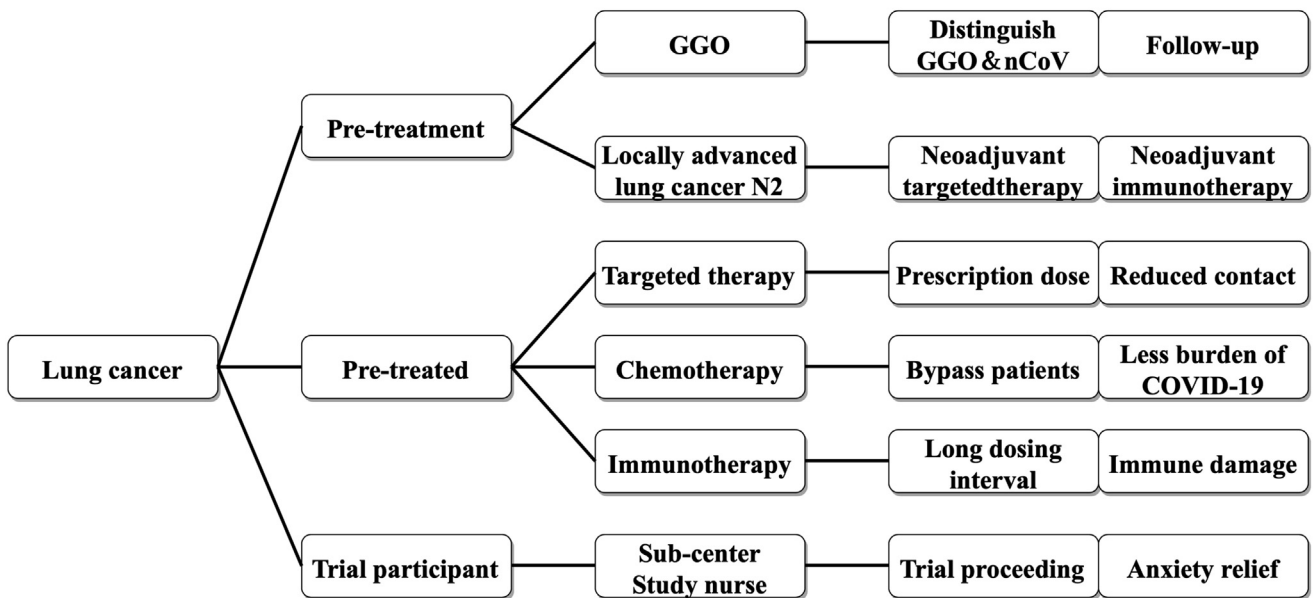


Figure 4. (A) The difficulties and (B) supplementary clinical strategies of patients with different stages during the COVID-19 pandemic. COVID-19, coronavirus disease 2019; GGO, ground-glass opacity; nCoV, novel coronavirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.



provide medication prescription that covers a longer duration of intake to avoid repeated trips just to get the prescriptions. In contrast, patients who need to return for immunotherapy or chemotherapy could be referred to the local hospitals that had a lesser clinical burden of COVID-19. The safety and efficacy are similar for patients transitioning from nivolumab 3 mg/kg every 2 weeks to 480 mg every 4 weeks<sup>19</sup> or from pembrolizumab 2 mg/kg every 3 weeks to 400 mg every 6 weeks,<sup>20</sup> and long dosing intervals decrease the frequency of visits to the hospital and have the potential to reduce the risk of exposure to COVID-19. Both immunotherapy and chemotherapy could notably influence the host immune system, which may interact with SARS-CoV-2 and cause extra damage. Therefore, we should stay vigilant for patients with possible SARS-CoV-2 infection receiving antitumor treatment in case of disease deterioration. Finally, for patients involved in ongoing trials for lung cancer before the COVID-19 pandemic, delayed administration of medication might influence drug efficacy and also violate the study protocol. Affiliated centers should take advantage of their ability to proceed with treatment for those who had injectable medications like immunotherapy or chemotherapy. In addition, study nurses should keep a close (online) follow-up of participants to help ease up their anxiety.

Though it would seem that COVID-19 does not affect oncologists, in the end, physicians and patients are still in the same environment and are equally vulnerable to the disease. As of February 11, 2020, over 3000 physicians have been reported to be infected in their clinical practice even after maintaining constant vigilance. Considering the relatively long latency period and lack of classic symptoms of COVID-19, it is crucial to reduce the chances of infection among patients with cancer. Throughout the COVID-19 pandemic, providing solutions to immediate problems and prevention of future problems are two equally important responsibilities for every leader globally.<sup>21</sup> The People's Republic of China's experience in pandemic prevention could help governors and medical staff in other countries address COVID-19. In the fast-rising period of the pandemic, some medical problems might be temporarily suppressed or ignored owing to the focus on COVID-19. However, as the pandemic continues, other medical problems will gradually be exposed, and lung cancer is one of them. This study could, thus, serve as a reference on how lung cancer or other life-threatening diseases can be managed during the COVID-19 pandemic.

This study also has several limitations. Inadequate surveillance prevented us from identifying any potential influences on the prognosis of patients with cancer. Another limitation is that the patients surveyed were mainly from the Guangdong and Hunan provinces. Therefore, the results may not be sufficiently

representative of other places. From January 18, 2020 to April 18, 2020, only one inpatient (1 of 24) was found to have both lung cancer and COVID-19 in our center. He was a 57-year-old man with mild COVID-19 and advanced pulmonary adenocarcinoma. He had received treatment with EGFR tyrosine kinase inhibitors, chemoimmunotherapy, and chemotherapy. He had fever as the initial and only symptom after he came back from Wuhan. As per the local policy, he underwent SARS-CoV-2 testing, was quarantined in our hospital and then transferred to an infectious disease hospital for further treatment soon after he tested positive. However, we could not determine the outcome given that the patient had been transferred.

In these desperate times, we, as a community with a shared future, should coordinate for socioeconomic development and stand together not only against the COVID-19 pandemic but also against other critical illnesses. Enhancing humanistic care, expanding online consultations, and cutting down resource consumption could achieve a new balance between pandemic isolation and social development.

In summary, we used the hospital data from a single center and simultaneously collected data using a self-administered questionnaire at multiple centers to evaluate the impact of the COVID-19 outbreak on the diagnosis and treatment of patients with lung cancer. We have provided suggestions for both clinical diagnosis and treatment strategies of lung cancer to optimize the process, given the urgency of current circumstances. The demand for medical support among patients with lung cancer or other life-threatening diseases should be given sufficient attention, especially during the current COVID-19 outbreak.

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## Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *Journal of Thoracic Oncology Clinical and Research Reports* at [www.jtocrr.org](http://www.jtocrr.org) and at <https://doi.org/10.1016/j.jtocrr.2020.100053>.

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