COVID-19 infection in the cancer population: a study of emergency department imaging utilization and findings

Derek Vos1 · Daniel A. Smith1 · Sooyoung Martin1 · Sree H. Tirumani1 · Nikhil H. Ramaiya1

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Abstract

Purpose To analyze emergency department (ED) computerized tomography (CT) utilization in cancer patients with coronavirus disease 2019 (COVID-19).

Methods A retrospective chart review was performed to identify cancer patients who received COVID-19 diagnosis within the single healthcare system and presented to the ED within 30 days of COVID-19 positive date between May 1 and December 31, 2020.

Results In our 61 patients, the mean age was 72.5 years old, with 34% of patients (n = 21) on active cancer therapy and 66% (n = 40) on surveillance only. Most patients (n = 53) received their COVID-19 diagnosis within the ED, with 8 patients diagnosed prior to initial ED visit. The most common CT studies ordered within the ED were CT chest (n = 25), CT abdomen/pelvis (A/P) (n = 20), CT head (n = 8), and CT chest/abdomen/pelvis (C/A/P) (n = 7). COVID-19 findings were present on 33 scans, findings of worsening malignancy on 12 scans, and non-COVID non-cancer findings on 9 scans. Significant differences in CT severity score (p = 0.0001), indication for hospitalization (p = 0.026), length of hospitalization (p = 0.004), interventions (remdesivir, mechanical ventilation, and vasopressor support) while hospitalized (p < 0.05), and mortality (p = 0.042) were found between the prior diagnosis and ED diagnosis groups. No such differences were found between the active treatment and surveillance groups.

Conclusion ED CT imaging findings in patients with cancer and COVID-19 are predominantly related to COVID-19 infection, rather than cancer history or anti-cancer therapy status.

Keywords COVID-19 · Cancer imaging · Imaging utilization · CT severity score

Introduction

The coronavirus disease 2019 (COVID-19) global pandemic began in December 2019 with the outbreak of an unknown pneumonia within the Wuhan region of China. This unknown pneumonia was later attributed to the coronavirus SARS-CoV-2. In March 2020, the World Health Organization (WHO) declared COVID-19 to be a global pandemic and, as of June 2021, there have been over 178 million confirmed cases of COVID-19, with a death toll exceeding 3.8 million [1].

Cancer patients represent a particularly vulnerable population affected by the COVID-19 pandemic, demonstrating increased mortality and severity of disease compared to the general population [2, 3]. A meta-analysis by Yang et al. additionally revealed that the COVID-19 prevalence is increased in cancer patients compared to the general population [4]. Due to the increased prevalence of COVID-19 and increased mortality facing cancer patients, it is imperative that medical practitioners be aware of this subset of the population and the unique challenges that arise in managing their care during the COVID-19 global pandemic.

While several studies have examined the COVID-19 disease in cancer patients, there has been little discourse on the importance of emergency department (ED) utilization within this population. The ED represents the initial point of care for this vulnerable population and thus is considerably important in their management. Given the overlapping constellation of clinical and imaging findings of COVID-19,
cancer, and potential anti-cancer therapy complications, navigating the intersection of these processes within the ED is particularly challenging. Ultimately, identifying patients within this population who are at highest risk and thus warrant both ED visitation and further care may reduce the burden of the COVID-19 pandemic on the healthcare system.

In the following study, we examined the utilization of the ED in the management of cancer patients with COVID-19, focusing primarily on the role of computerized tomography (CT) imaging in their care. We additionally sought to determine whether the timing of COVID-19 diagnosis or the presence of active cancer therapy impacted ED CT utilization and subsequent clinical outcomes.

Methods

This retrospective review was approved by the institutional review board at our organization. Patients with a history of cancer who received a COVID-19 diagnosis within the single healthcare system and who presented to the emergency department (ED) within 30 days of COVID-19 positive date between May 1 and December 31, 2020, were retrospectively identified. The electronic medical records were reviewed to identify clinical and demographic data, including COVID-19 PCR positive date, cancer type, treatment status, ED utilization, and ED imaging. ED imaging was further reviewed using the picture archiving and communications system (PACS). In addition, the patient’s status at disposition was also identified. Hospitalized patients were retrospectively followed during their hospital stay to identify length of stay and disposition at discharge.

Patients who received computed tomography (CT) imaging of the chest within the ED were retrospectively identified. CT examinations of these patients were reviewed by a board-certified fellowship-trained radiologist with 22 years of experience (N.H.) and a fourth-year radiology resident (S.M.). Any initial disagreements between readers were resolved via consensus agreement. Reviewers were blinded for the patients’ treatment status and other clinical factors. The CT scoring system was based on the staging utilized for the evaluation of SARS and COVID patients described by Pan et al. and Chang et al. [5, 6]. For each lobe, a score of 0 corresponded with no involvement, a score of 1 corresponded with <5% involvement, a score of 2 corresponded with 5–25% involvement, a score of 3 corresponded with 26–49% involvement, a score of 4 corresponded with 50–75% involvement, and a score of 5 corresponded with >75% involvement. Patients who were status post lobectomy or presented with total lung collapse received a score of not applicable (N/A) within the relevant lobe.

CT findings on CT chest, CT abdomen/pelvis (A/P), and CT chest/abdomen/pelvis (C/A/P) were organized into the following categories: findings of COVID-19, findings of worsening malignancy, non-COVID, non-cancer findings, and normal scans or those containing incidental findings.

Findings of COVID-19 in the chest were based on the CT chest abnormalities with high and intermediate incidence as described by Kwee and Kwee [7]. These findings included, but were not limited to, ground-glass opacities (GGO), vascular enlargement, consolidation, linear opacity, septal thickening and/or reticulation, crazy-paving pattern, air bronchogram, pleural thickening, halo sign, bronchiectasis, nodules, bronchial wall thickening, and reversed halo sign. Chest CT findings of worsening malignancy included those where the interpreter noted concern for progression of malignancy, along with the presence of worsening tumor burden and new lesions.

CT findings in the abdomen were categorized into the previously mentioned categories used for CT chest imaging. Findings of COVID-19 in the abdomen included the previously described categorization of lung findings used in the lung bases, while abdominal findings of COVID-19 were identified based on the qualitative synthesis performed by Lui et al. [8]. These findings included, but were not limited to, bowel wall thickening, fluid-filled colon, pneumatosis, intussusception, pneumoperitoneum, and ascites.

Statistical analysis was performed to compare subgroups based on two primary categories: time of COVID-19 diagnosis (diagnosed prior to ED vs. diagnosed at ED visit) and cancer treatment status (active treatment vs. surveillance). Imaging features for these groups were compared, including imaging utilization, imaging findings, and CT chest severity scores. Clinical findings compared included age, reason for ED presentation, disposition from ED, interventions, disposition from hospital, and laboratory findings. Categorical variables were compared utilizing Fisher’s exact test or chi-squared test. Continuous variables were compared utilizing Wilcoxon or Kruskal–Wallis test. p values were based on a two-sided hypothesis, with a p value of <0.05 considered statistically significant. Statistical analyses were performed utilizing Stata® Statistical Software (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.).

Results

Patient demographics

A total of 78 COVID-19-positive cancer patients were initially identified and included within this study (Fig. 1). Out of 78 patients, 5 patients were excluded due to lack of COVID-19 PCR positivity within the EMR. An additional 12 patients were excluded due to lack of emergency department utilization within 30 days of COVID-19 diagnosis. A
A retrospective review of the electronic medical record was performed for the remaining 61 patients, including those on active anti-neoplastic treatment \((n = 21)\) and those currently on surveillance only \((n = 40)\) (Table 1). The mean age of these patients was 72.5 years old, with 57% \((n = 35)\) men and 43% \((n = 26)\) women. The cancer types among these patients included 23% breast \((n = 14)\), 21.3% prostate \((n = 13)\), 18% lung \((n = 11)\), 9.8% colon \((n = 6)\), 3.3% pancreatic \((n = 2)\), 3.3% head and neck \((n = 2)\), 3.3% renal \((n = 2)\), and numerous other malignancies at less than 2% (ovarian, bladder, lymphoma, glioma, skin, uterine, thyroid, liver, gastric, and cancer of unknown primary).

**ED presentation**

Among the 61 patients who presented to the ED, 87% \((n = 53)\) were diagnosed with COVID-19 within the ED, while the remaining 13% \((n = 8)\) were previously diagnosed with COVID-19 before presenting to the ED. The median time between COVID-19 diagnosis and presentation to the ED in the prior diagnosis group was 8 days. The most common presenting complaint in the ED was shortness of breath \((n = 25)\), followed by cough \((n = 13)\), nausea/vomiting \((n = 10)\), and abdominal pain and fever \((n = 7)\), with CT indications following a similar pattern.

**CT findings**

Patients collectively received a total of 65 CT studies performed in the ED. The most common examination ordered was CT chest \((n = 25)\), followed by CT abdomen/pelvis \((A/P) (n = 20)\), CT head \((n = 8)\), and CT chest/abdomen/ pelvis \((C/A/P) (n = 7)\). Of the 25 CT chest examinations, 10 were CT angiography (CTA) examinations ordered for concern of pulmonary embolism. IV contrast was utilized on 27 scans. The remaining CT examinations performed are summarized in Table 2.

Findings on CT chest, CT A/P, and CT C/A/P were categorized as described in the “Methods” section. COVID-19 findings were present on 63.5% of scans \((n = 33)\), with the most common findings being GGOs \((n = 24)\), atelectasis \((n = 8)\), and reticular opacities \((n = 7)\). Furthermore, findings of worsening malignancy were present on 23.1% of scans \((n = 12)\). Non-COVID, non-cancer findings were present on 17.3% of scans \((n = 9)\). Scans that represented only incidental findings or normal scans comprised 17.3% of scans \((n = 9)\).

Of the patients who received CT chest imaging, the most common findings were related to COVID-19, present on 76% \((n = 19)\) of scans. Within this subset, the most common findings of COVID-19 were ground-glass opacities (GGOs) (Fig. 2), found in 100% of scans, atelectasis in 28% of scans \((n = 7)\), and reticular opacities in 24% of scans \((n = 6)\). Following COVID-19, the major finding on CT chest imaging was pulmonary embolism, present in 2 patients. Both patients were diagnosed with pulmonary embolism on CTA examinations. Worsening tumor burden was not a major finding in this subset, with only 1 patient exhibiting the finding of progression of metastatic disease. Finally, with the exception of pulmonary embolism...
as previously discussed, none of the patients within this subset exhibited non-COVID, non-cancer findings on CT.

In the 7 patients who received CT C/A/P imaging, the most common findings were again related to COVID-19, present on 57% of scans (n = 4). As with the patients who received CT chest imaging, the predominant findings of COVID-19 on CT C/A/P were GGOs (n = 5), followed by patchy nodular densities (n = 2). Worsening tumor burden, however, was a more common finding in this subset of patient and was present on 43% of scans (n = 3). More specifically, the findings of progression of metastatic disease and new lung nodules were present on 43% and 29% of scans, respectively (n = 3 and n = 2). Non-COVID, non-cancer findings of diverticulitis and small bowel obstruction were found in 2 patients within this subset. Finally, 2 patients receiving CT C/A/P had scans which did not reveal any acute pathology.

CT chest COVID severity scoring was performed on each patient who received CT imaging of the chest, including CT chest, CTA chest, and CT C/A/P scans, following the scoring system described in the “Methods” section. In these 28 patients, a total of 32 such scans were evaluated, with a mean total severity score of 7.17. The majority of patients (n = 29) had severity scores between 1 and 15, with only 3 patients having scores greater than 15.

As with the CT chest imaging, the most common findings present on CT A/P scans were related to COVID-19, being found on 45% (n = 9) of the 20 scans. Importantly, the majority of these COVID-19 findings were present in the lung bases, with only 3 patients demonstrating COVID-19 findings in the abdomen. These findings included thickening of the bowel wall, COVID-related colitis, and fluid-filled small bowel loops. Findings suggestive of worsening malignancy were present on 35% (n = 7) of scans, while non-COVID, non-cancer findings were present on 25% (n = 5) of scans. These findings included diverticulitis, appendicitis (Fig. 3), cystitis and cholecystitis (Fig. 4), and findings consistent with UTI. A total of 4 patients (20%) within this subset demonstrated normal scans within the ED.

CT head examinations were primarily ordered due to concern for cerebrovascular accident or status/post fall. In the 8 patients who received such scans, none demonstrated any acute intracranial hemorrhage or mass. Furthermore, there was no evidence of cancer progression or new metastatic disease on any of these imaging studies.

When comparing the utilization of CT imaging or the findings of CT imaging, we did not find a statistically significant difference between those who were diagnosed with COVID-19 in the ED vs those who were diagnosed prior to initial ED visit. Importantly, however, the CT chest severity scoring was found to be worse in the prior diagnosis group compared to the ED diagnosis group. Patients who received their COVID diagnosis prior to presenting to the ED exhibited a higher total score compared to those who were diagnosed within the ED (p = 0.0001), as well as higher scores within each lobe (p < 0.05). 89.3% of patients (n = 25) who received CT imaging of the chest, regardless of severity scoring, were subsequently hospitalized. There was no significant difference between the COVID-19 severity score in patients on active treatment compared to those on surveillance only. Given the heterogeneity of cancer types within our study population and the small sample size, the relationship between cancer subtype and CT utilization or findings was not explored.
Table 2 Clinical characteristics, imaging, and outcomes—ED diagnosis vs prior diagnosis

| Characteristics                          | ED diagnosis (n = 53) (%) | Prior diagnosis (n = 8) (%) | P     |
|-----------------------------------------|--------------------------|-----------------------------|-------|
| Sex                                     |                          |                             |       |
| Male                                    | 22 (42)                  | 4 (50)                      |       |
| Female                                  | 31 (58)                  | 4 (50)                      |       |
| Age                                     |                          |                             |       |
| Mean                                    | 72.28                    | 73.63                       | 0.724 |
| Range                                   | 46–95                    | 61–84                       |       |
| Mean ED visits                          | 1.49                     | 1.25                        | 0.367 |
| ED presentation                         |                          |                             |       |
| COVID                                   | 36 (68)                  | 7 (88)                      | 0.417 |
| Other                                   | 17 (32)                  | 1 (12)                      | 0.243 |
| Disposition from ED                     |                          |                             |       |
| Discharged                              | 18 (34)                  | 3 (38)                      | 1.000 |
| Hospitalized                            | 43 (81)                  | 7 (88)                      | 1.000 |
| Mean number of hospitalizations         | 1.056                    | 0.875                       | 0.488 |
| Hospitalized for COVID                  | 33 (75)                  | 7 (88)                      | 0.658 |
| Hospitalized for cancer                 | 2 (5)                    | 1 (13)                      | 0.319 |
| Hospitalized for other                  | 30 (68)                  | 1 (13)                      | 0.026 |
| Mean length of stay (days)              | 6.792                    | 13                          | 0.004 |
| Interventions                           |                          |                             |       |
| Vasopressor support                     | 2 (4)                    | 4 (50)                      | 0.002 |
| Mechanical ventilation                  | 1 (2)                    | 3 (38)                      | 0.006 |
| Remdesivir                              | 9 (17)                   | 4 (50)                      | 0.055 |
| Disposition from hospital               |                          |                             |       |
| Home                                    | 31 (70)                  | 2 (29)                      | 0.127 |
| Death                                   | 4 (9)                    | 3 (43)                      | 0.042 |
| Imaging utilization                     |                          |                             |       |
| CT head                                 | 8                        | 0                           |       |
| CT spine                                | 2                        | 1                           |       |
| CT facial                               | 0                        | 1                           |       |
| CT upper extremity                      | 1                        | 0                           |       |
| CT chest                                | 11                       | 4                           | 0.093 |
| CTA chest                               | 9                        | 1                           | 0.699 |
| CT chest/abdomen/pelvis                | 7                        | 0                           | 1.000 |
| CT abdomen/pelvis                       | 19                       | 1                           | 0.253 |
| Contrast                                | 26                       | 1                           | 0.671 |
| Findings                                |                          |                             |       |
| COVID findings                          | 28                       | 5                           | 0.735 |
| Cancer findings                         | 12                       | 0                           | 0.275 |
| Normal/incidental findings              | 8                        | 1                           | 1.000 |
| Non-COVID, non-cancer findings          | 9                        | 0                           | 0.591 |
| CT chest severity scoring               |                          |                             |       |
| Right upper lobe                        | 1.28                     | 3.75                        | 0.0003|
| Right middle lobe                       | 1.21                     | 3.25                        | 0.0009|
| Right lower lobe                        | 1.24                     | 3.5                         | 0.0011|
| Left upper lobe                         | 1.04                     | 3.25                        | 0.0001|
| Left lower lobe                         | 1.04                     | 3.5                         | 0.0002|
| Total score                             | 5.62                     | 17.25                       | 0.0001|
Clinical features

A total of 50 patients (82.0%) were hospitalized from the ED, with a total number of 63 hospitalizations. The most common indication cited for hospitalization in the EMR was COVID-19 infection ($n=39$). However, comorbidities in addition to COVID-19 were still commonly cited as indication for hospitalization in 62% of patients ($n=31$). Importantly, worsening malignancy only accounted for a relatively small proportion of hospitalizations in both the prior diagnosis and ED diagnosis groups (14.3% and 4.7%, respectively).

Of the 50 patients who were hospitalized, 11 required re-hospitalization. There was a total of 13 re-hospitalizations, with a mean length of stay of 4.18 days. Worsening COVID-19 infection accounted for 46% of re-hospitalizations ($n=6$). The remaining indications for re-hospitalization included atrial fibrillation ($n=2$), stroke ($n=1$), urinary tract infection ($n=1$), ruptured diverticulitis ($n=1$), hypoglycemia ($n=1$), and klebsiella bacteremia ($n=1$). One patient who was re-hospitalized for worsening COVID-19 died during this hospitalization.

There was no significant difference in number of hospitalizations between the ED diagnosis group and the prior diagnosis group. Those who were previously diagnosed...
with COVID-19 were hospitalized for a mean of 13 days, while those diagnosed in the ED were only hospitalized for a mean of 6.8 days. A higher proportion of the prior diagnosis group received remdesivir while hospitalized compared to the ED diagnosis group (57.1% vs 20.9%, \( p = 0.055 \)). Additionally, those in the prior diagnosis group were more likely to require mechanical ventilation and vasopressor support during their hospitalization (42.9% vs 2.3%, \( p = 0.006 \), and 57.1% vs 4.7%, \( p = 0.0045 \), respectively).

Those who were previously diagnosed with COVID-19 experienced worse outcomes at disposition compared to those diagnosed in the ED. Of the 7 hospitalized patients in the prior diagnosis group, 3 (42.9%) died during their hospital course, while only 4 (9.3%) of the 43 patients in the ED diagnosis group died during their hospital course (\( p = 0.042 \)), with an overall in-hospital mortality of 13.7%. There was no significant difference between hospital interventions or outcomes in the active treatment vs surveillance group.

Discussion

The COVID-19 pandemic presents diagnostic and therapeutic challenges in the cancer population. COVID-19 has been identified as conveying greater risk of infection and poor prognosis in those with cancer compared to those without [9]. Additional diagnostic difficulty experienced by the cancer population during the COVID-19 pandemic may be attributed to the prevalence of nonspecific symptoms and atypical imaging features at baseline, presenting a challenge in differentiating COVID-19 from malignancy history [10, 11]. Furthermore, there is support that the extent of lung damage visible on CT in these patients represents a strong independent prognostic factor of early mortality [12]. Due to these challenges, it is imperative that radiologists be aware of the overlapping features among COVID-19 infection and malignancy.

Cancer patients have been shown to demonstrate higher mortality during the COVID-19 pandemic, requiring
additional intervention and therapy when compared to the general population. A systematic review and meta-analysis performed by Saini et al. demonstrated that the pooled mortality rate of patients with COVID-19 infection and cancer was 25.6% [2]. An additional meta-analysis and systematic review performed by Yang et al. revealed a pooled mortality rate of 14.6% in COVID-19 patients with cancer, while non-cancer COVID-19 patients demonstrated a pooled mortality rate of 3.9% [4]. Furthermore, a recent multicenter cohort study which sought to examine the differences in mortality among COVID-19-infected cancer patients, COVID-19-infected non-cancer patients, and non-COVID-19-infected cancer patients revealed that the 1-year all-cause mortality of patients with both cancer and COVID-19 infection was greater than that of non-COVID-19-infected cancer patients or COVID-19-infected non-cancer patients (30% vs 16% and 9%, respectively) [13].

As the ED represents a crucial step in the management of patients with COVID-19 and underlying cancer, our study examined the ED utilization by cancer patients during the COVID-19 pandemic, focusing on the CT imaging and clinical course of these patients. We retrospectively studied 61 cancer patients who presented to the ED within 30 days of COVID-19 diagnosis, with a total of 89 ED visits during this period. The majority of CT findings were due to COVID-19, present on 63.5% of scans (n = 33). In addition, findings of worsening malignancy were present on 23.1% of scans (n = 12). A smaller subset of patients demonstrated findings that were consistent with non-COVID, non-cancer conditions, including diverticulitis, pulmonary embolism, and other processes previously mentioned, present on 17.3% of scans (n = 9). Despite our initial suspicion that malignancy history and treatment status would be the primary driving forces behind imaging acquisition and imaging findings, it appears that COVID-19 infection is the predominant concern in this population. Importantly, patients who were diagnosed with COVID-19 prior to their first ED visit demonstrated significantly worse CT chest scoring compared to those who were diagnosed with COVID at initial ED visit.

Of the 61 patients presenting to the ED, 50 (82%) were hospitalized, with a total number of 63 hospitalizations. COVID-19 was the predominant indication for hospitalization, while worsening malignancy represented only a small proportion of hospitalizations in both the prior diagnosis and ED diagnosis groups (14.3% and 4.7%, respectively). Thus, despite the relatively high proportion of CT scans which were indicated based on the patient history of malignancy, imaging findings and hospitalizations related to malignancy were much less common than those related to COVID-19. COVID-19 interventions, including remdesivir, mechanical ventilation, and vasopressor support were far more common in the prior diagnosis group compared to the ED diagnosis group. Additionally, the overall in-hospital mortality among hospitalized patients was found to be 13.7%, with patients in the prior diagnosis group demonstrating a higher rate of mortality compared to those patients diagnosed within the ED. This mortality is slightly lower than previously described findings in the literature; however, given our small sample size, it is less surprising that this difference arose [2, 4, 13, 14]. While these findings may be attributed to the timing of disease, with patients diagnosed in the ED able to receive supportive therapy at an earlier time course compared to those diagnosed outside the ED, it is still important for radiologists and emergency physicians to be aware of these differences. Furthermore, given their higher proportion of COVID-19 findings on imaging and overall worse CT chest scoring, those patients with prior COVID-19 diagnosis may potentially be viewed as high-risk when presenting for follow-up of worsening symptoms.

Finally, we sought to elucidate whether active anti-neoplastic therapy had any impact on ED imaging or clinical features. Our results indicated a high degree of similarity among the two treatment groups, with no significant difference appreciated between these groups with respect to ED utilization, ED imaging, indications and duration of hospitalization, and mortality. These results are supported by a recent study published by Liu et al., in which antineoplastic therapy did not result in any difference in disease severity or mortality [15]. Additionally, despite the concern about treatment-related complications, our study did not reveal any imaging findings or hospitalizations attributed primarily to cancer treatment. These findings are supported by the work of Shah and Neal, in which treatment concerns represented only a small percentage of ED visitation in the lung cancer population [16].

This study is limited primarily by the small sample size, with only 61 patients demonstrating a history of active malignancy and ED utilization within 30 days of diagnosis. Furthermore, with only 8 patients belonging to the prior diagnosis group, the overall statistic power of our study was limited. As our study centered on a single hospital system, we are limited in the number of potential participants and thus our results may not be fully generalizable. Given the complex interplay between cancer and infectious disease, it may also be difficult in select cases to determine with complete certainty whether imaging findings correspond to either malignancy history or COVID-19 infection.

In conclusion, ED represents a particularly important stage in the management of COVID-19 patients with cancer. Our results indicate that the driving force behind ED utilization, CT imaging results, and hospitalizations in the cancer population during the COVID-19 pandemic is SARS-CoV-2 infection, rather than malignancy, cancer therapy, or other disease. Particular attention should be given to cancer patients who are previously diagnosed with COVID-19 before seeking care in the ED, as they may be at higher risk.
for worse outcomes. Further studies should be undertaken to compare the utilization of the ED among those with cancer and those without, to better characterize the needs of this population. In addition, larger studies which are able to effectively analyze the relationship between various cancer types and ED utilization are needed. Regardless of treatment status, ED imaging and clinical features are paramount in the diagnosis and further care of cancer patients during the COVID-19 global pandemic.

**Author contribution** All authors are responsible for the contents and have read and approved the manuscript for submission.

**Declarations**

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

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