Factors affecting COVID-19 outcomes in cancer patients: A first report from Guy's Cancer Centre in London

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Abstract

Background: There is insufficient evidence to support clinical decision-making for oncology patients diagnosed with COVID-19 due to the lack of large studies.

Methods: We used data from a large UK Cancer Centre to assess demographic/clinical characteristics of 106 cancer patients with a confirmed COVID-19 diagnosis between 29 February-15 April 2020. Logistic/Cox proportional hazards models were used to identify which demographic and/or clinical characteristics were associated with COVID-19 severity/death.

Results: 87 (82%) presented with mild/moderate COVID-19 and 19(18%) with severe disease. Age, sex, ethnicity, SES, and current cancer treatment were not associated with COVID-19 severity. Initial diagnosis of cancer >24m before COVID-19 (OR:3.01 (95%CI: 1.02-8.58)), presenting with fever, dyspnoea, gastro-intestinal symptoms, or higher levels of CRP and ferritin were linked with greater COVID-19 severity. During median follow-up of 17.5d, 14 patients had died of COVID-19(13%).

Conclusions: Low SES, hypertension and non-malignant lung disease were common in cancer patients with COVID-19. A longer-established diagnosis of cancer was associated with increasing severity of infection, possibly reflecting effects of more advanced malignant disease on impact of this infection. Advanced age and comorbidities may be associated with an increased risk of COVID-19-related death in cancer patients, as has been reported for general populations without cancer.
Background

In the context of cancer, the COVID-19 pandemic has led to challenging decision-making (1). Patient visits to the cancer clinic increase the potential risk of infection when the alternative is self-isolation at home, and some cancer treatments may predispose patients to moderate or severe harmful effects of COVID-19 (2, 3). Current precautionary management decisions being made for cancer patients are based on assumptions that are supported by limited evidence, based on small case series from China (4-8). As a result of their limited sample sizes, these studies were not able to distinguish between the effects of age, cancer, and other comorbidities on COVID-19 outcomes (9, 10). Recently published prognostic studies in COVID-19 positive patients have been judged to be at high risk of bias, mainly due to non-representative selection of control patients, exclusion of patients who had not experienced the event of interest by the end of the study, high risk of model overfitting, and limited information on model building strategies used (11).

The intersection between COVID-19 and cancer is even more complex. It can be difficult to confidently diagnose COVID-19 symptoms in cancer patients, as presenting features of the infection are often similar to cancer symptoms and treatment-related adverse events (9, 12). This may result in a delayed or missed COVID-19 diagnosis, which may lead to late interventions for more life-threatening disease (13). In addition, COVID-19 may be a barrier to dignified and humane end-of-life cancer care (9). Finally, the pandemic is causing huge service reconfiguration for both curative and palliative oncology care, resulting in fewer clinic visits due to social distancing (14), cessation of screening, and delays or changes in treatments that will inevitably have serious impacts on cancer-related mortality and morbidity (9,
13). Our recent systematic review reported there is currently no definitive evidence that specific cytotoxic drugs are contraindicated in cancer patients infected with COVID-19 (15).

Larger studies are urgently warranted to further explore this intersection of COVID-19 and cancer in terms of clinical outcomes, so as to inform oncological care during this outbreak and potential future pandemics (16). Guy’s Cancer Centre in South-East London, which treats approximately 8,800 patients annually, including 4,500 new diagnoses, is one of the largest Comprehensive Cancer Centres in the UK and is currently at the epicentre of the UK COVID-19 epidemic.

Methods

Study population

Guys’ Cancer Cohort is a Health Research Authority approved research database (Reference: 18/NW/0297) of all routinely collected clinical data of cancer patients at Guy’s and St Thomas’ NHS Foundation Trust (GSTT) and forms the basis of this observational study (17). It received a favourable opinion on the 15th May 2018 from the North West- Haydock Research Ethics Committee. The database contains routinely collected prospective and retrospective demographic/clinical data on all cancer patients treated at Guy’s Cancer Centre. We have an established clinical database for all cancer patients tested for COVID-19 either in outpatient clinics or ward setting since 29 February 2020. Using the unique hospital number, these databases were merged prior to anonymization for research purposes. We assessed outcomes included in the core outcome sets currently being developed for COVID-19 to ensure all relevant information is collected in our COVID specific database (18).
The latter was populated through linkages with existing hospital software and managed by various Oncologists.

For this first report we have included any Guy’s Cancer patient who received a diagnosis of COVID-19, from a positive PCR test, between 29th February-15th April 2020. A COVID-19 test was ordered for cancer patients if they presented with symptoms necessitating hospitalization or if they were scheduled to undergo a cancer-related treatment. Cancer-specific information was collected for any patient who underwent active treatment within the last 24-months. On average, our Cancer Centre sees about 375 new cancer patients monthly. During the last six months this ranged from 314 to 379. In March 2020, the number of new cancer diagnoses was 331. A total of 462 patients were tested between 29 February and 15 April 2020, of whom 143 had COVID-19 (31%). We report data on the first 106 of these COVID-19 positive cancer patients to inform the oncology community whilst data entry for more complex studies is ongoing.

**Statistical methods**

For this first analysis of our data we had three aims:

1) To describe demographic and clinical characteristics of COVID-19 positive cancer patients, in terms of their COVID-19 and cancer diagnoses.

2) To identify which demographic and/or clinical factors were associated with COVID-19 severity in cancer patients.

3) To identify which demographic and/or clinical factors were associated with COVID-19 death in cancer patients.
Descriptive statistics were used to address the first aim. Most variables had several categories for the purpose of these descriptive analyses, but were collapsed for the purpose of regression analyses due to the sample size of our cohort. Socio-economic status (low, middle, high) was determined based on the English Indices of Multiple Deprivation for postcodes (19). Lymphocyte count ($x10^9$) was categorized as $\leq$0.5, 0.6-0.8, 0.9-1.2, and >1.2 based on the Common Terminology Criteria for Adverse Events v.5 (CTCAE). For the other laboratory variables, we created tertiles instead of clinical cut-offs due to cancer patients already having abnormal values for most of these blood markers (Ferritin, C-reactive protein, eGFR, and albumin).

For the second aim, we conducted logistic regression analyses. Mild/moderate COVID-19 was defined as mild/severe pneumonia and/or sepsis (i.e. those patients managed on the ward), whereas severe COVID-19 was defined as acute respiratory distress syndrome (ARDS) or septic shock (i.e. those patients managed in the Intensive Care Unit). These definitions were based on the WHO COVID-19 classification (20). The models used to quantify the association between each factor and COVID-19 severity were defined through a directed acyclic graph (DAG) (Figure 1 in Appendix) whereby each factor was individually set as the main exposure variable in a model with the same conditional independencies. An overview of the minimal adjustments for each factor is shown in Table 1 in the Appendix.

The third research aim was addressed with Cox proportional hazards regression analyses, whereby the models were defined as above (Table 1 in Appendix). Follow-up was defined from date of COVID testing until death or 15 April 2020. We also generated Kaplan Meier curves.
All statistical analyses were conducted with STATA version 15.1.

Results

Demographic and clinical characteristics of COVID-19 positive cancer patients

87 patients (82%) presented with mild/moderate COVID-19 and 19 patients (18%) with severe COVID-19 (Table 1). More patients were male (55%) and aged 60+ (70%; median age: 67). However, 14% of the cancer population was aged <50 years (n=15; median age: 41). When stratified by COVID grade, more male cancer patients presented with severe disease (74%). Most patients were from a lower socio-economic background (82%). With respect to ethnicity, the majority of patients were White, though about a quarter of patients were of Black origin (n=26) and 6 patients were of Asian origin – this distribution was similar when stratified by COVID grade. Hypertension was by far the most commonly reported comorbidity (51%), followed by diabetes mellitus (22%), renal impairment (22%) and cardiovascular disease (20%). However, benign lung conditions were more commonly reported for those who presented with severe COVID-19 (32% vs 13% in those with mild COVID-19). A total of 40% of cancer patients with the infection reported being never-smokers.

The most frequently reported tumour types were urological/gynaecological (34%), followed by haematological (18%) and breast (15%) (Table 2). Of all cancer patients tested for COVID-19, 51 tested positive after their cancer-related hospital admission (48%), of which 38 were solid tumours (75%) and 13 were haematological cancers (25%). All 51 patients had nosocomial infection and tested positive >48 hours after hospital admission (range: 3-137 days). When stratified by COVID-19 severity, the distribution of tumour types was comparable. A large proportion of patients had
advanced cancer (37% stage IV) and were diagnosed with their malignancy in the last 12 months (49%). However, those with severe COVID-19 were more likely to have been diagnosed more than 24 months before development of their infection (58% vs 31%). A total of 43% of patients were receiving palliative treatment, 34% were receiving radical treatment and 11% were treatment naive. Treatment distributions were fairly comparable between COVID-19 severity groups. Table 2 provides further details on the cancer characteristics.

58% of the cancer patients diagnosed with COVID-19 in this cohort presented with a cough and 54% had a fever. The majority of patients were molecularly diagnosed within 7 days of their initial symptoms (63%) (Table 3). More patients in the severe COVID-19 group presented with C-reactive protein (CRP) values in the highest tertile (53 vs 22% for mild/moderate disease). Similarly, they had a lower lymphocyte count (53 vs 27% in the lowest category (≤0.5)) and lower albumin levels (47 vs 23% in the lowest tertile).

*Factors associated with COVID-19 severity in cancer patients*

The odds ratios (21) for the associations between the various demographic and clinical factors and COVID-19 severity status are shown in Table 4. Those patients who were diagnosed with cancer more than 24 months ago were at a higher risk of presenting with severe COVID-19 as compared to those diagnosed during the last 24 months (OR: 3.01 (95%CI:1.02-8.58)).

With respect to symptom presentation, those presenting with a fever, dyspnea, or gastro-intestinal symptoms were also at a higher risk of having severe COVID-19 as
compared to those without these symptoms (OR: 7.22 (1.55-33.53), 2.54 (0.77-8.38), and 5.34 (1.58-17.99), respectively). Both ferritin and CRP were also associated with higher odds of severe COVID-19 (OR for T3 as compared to T1: 8.57 (0.83-89.04) and 15.93 (0.084-302.46), respectively).

Factors associated with COVID-19 death in cancer patients

During a median follow-up of 17.5 days (IQR:9-24), 14 cancer patients had died of COVID-19 (13%). Given the small number of events, limited analyses could be conducted (Appendix Table 2). However, there was a non-statistically significant positive association for age and number of comorbidities with risk of COVID-19 death (HR for age >60 as compared to ≤60: 2.80 (95%CI:0.63-12.53) and HR for ≥3 comorbidities as compared to none: 5.23 (95%CI:0.61-44.78; p for trend: 0.065) (Figure 1). It is noteworthy that despite there being no HR estimate for socio-economic status, 12/14 deaths occurred in those with a lower socio-economic status.

Discussion

This study reports on the largest cohort of COVID-19 positive cancer patients to date and also the first cohort outside China. Low SES, hypertension and non-malignant lung disease were common in cancer patients with COVID-19. Age, sex, ethnicity, SES, and current cancer treatment were found to not be associated with severity of COVID-19 infection in cancer patients. However, having had a cancer diagnosis more than 24 months previously (as compared to within 24 months) and presenting with fever, dyspnoea, or gastro-intestinal symptoms was linked with higher odds of developing severe illness as compared to mild/moderate COVID-19. Higher levels of
CRP and ferritin were also associated with more severe COVID-19 disease in infected cancer patients. Despite our follow-up being limited to 17.5 days, a non-statistically significant positive association could be seen for age, comorbidities, and risk of death from COVID-19 in cancer patients.

Demographic and cancer characteristics

Three retrospective cohort studies based on data from hospitals situated in Wuhan, China have reported on the clinical characteristics of COVID-19 positive cancer patients. Zhang et al (4) reported on 28 patients, Yu et al (7) on 12 patients and Du et al (5) on 85 fatal cases. The median ages reported in each of these small studies was similar to our study: 65, 66, and 66 years, respectively. Both Zhang and Du also reported a higher proportion of male patients. Lung cancer was the most commonly reported cancer in the Zhang (4) and Yu (7) studies (25 and 59%), but only accounted for 11% in our patient population. Zhang et al. (4) estimated that in their cohort 29% of patients tested positive for COVID-19 following hospital admission, whereas this was estimated at 48% in our cohort. Interpretation of this statistic is difficult given the latency between exposure and manifestations of infection, so that patients diagnosed after admission may have been infected outside hospital. Du et al (5) also noted that hypertension, diabetes and coronary heart disease were the most commonly reported comorbidities irrespective of the presence of a cancer diagnosis.

A nationwide report from China, which was based on data from 2007 COVID-19 positive patients from 575 hospitals in 31 provincial administrative regions identified a small subgroup of 18 cancer patients (8). Like other published Chinese case series, in this report lung cancer was also the most commonly reported cancer type (28%).
Our cancer cohort is similar in distribution of age, sex, and comorbidities to the smaller case series reported in China. The ethnicity and SES of our COVID-19 positive cancer patients are most likely a reflection of the catchment area of our Cancer Centre in South-East London (22), covering more deprived Boroughs (Lambeth and Southwark). Based on the number of cancer patients treated at our Cancer Centre in 2019, about 49% of patients are of a White ethnic background. Differences observed with the Chinese data for cancer type, stage, and treatment may be a reflection of clinical practice (e.g., intensity of treatment and frequency of hospital visits), of relative cancer incidence, or of extent of treatment changes introduced as mitigation in the face of the emerging pandemic. For example, the most recently reported age-standardized lung cancer incidence rates for males and females in Wuhan are 54.1 and 19.1 per 100,000, whereas these are estimated to be 37.5 and 24.3 per 100,000 in London (23). Careful and early modification and prioritization of treatment was introduced at our centre, compatible with now-published guidance (24).

**COVID-19 characteristics**

Comparably to our study, both the Zhang and the Du studies also reported fever, cough, shortness of breath and dyspnea as common clinical features (4, 5). If we consider the Chinese cohort of 85 fatal cases to be similar to our cohort who presented with severe COVID-19, it is observed that the laboratory findings are comparable: decreased lymphocytes, increased CRP, and decreased albumin (5).

**COVID-19 severity and death**
Severe events were reported for 54% of the study population and mortality for 29% in the Zhang study, as compared to 18% and 13% in our cohort. Zhang et al. also reported that recent treatment within 14 days was associated with an increased risk of developing severe events (28 days) (4). This difference with our observations may be attributed to different definitions of severe events, as it was not entirely clear how these were defined by Zhang et al. As highlighted by Wynants et al in their assessment of current statistical models published for COVID-19 (11), there is a need for consistent use of outcome definitions.

The study by Yu et al. reported 3 deaths (25%) (7). The nationwide report from China, based on 18 cancer patients, also evaluated how chemotherapy or surgery in the last month were associated with clinically severe events and identified a positive association (OR: 5.34, 95%CI: 1.80-16.18) (8). In addition, they identified age as a risk factor for severe events (OR: 1.43, 95%CI: 0.97-2.12). No difference in probability of severe events was observed by cancer type. Given the limited information published to date on very small case series, it is difficult to compare our study with these earlier findings. It is, however, interesting that SES and ethnicity did not have an effect on severity or death from COVID-19 in our cancer population. This is in contrast to the emerging role for ethnicity in disease severity in the UK population (25). To our knowledge, no study to date has specifically looked at COVID-19 severity at presentation in COVID-19 positive cancer patients and hence our observation of an association with time since cancer diagnosis and presenting symptoms needs further validation in other large cohorts. However, it is possible that time since cancer diagnosis is also a reflection of extent of disease and progression along the palliative patient pathway from diagnosis to death.
We did observe a non-statistically significant positive association between age and COVID-19 death, which may be in line with the notion of an increased risk of development of severe events with age by Liang et al (8).

Strengths and limitations
Whilst this is the largest COVID-19 positive cancer cohort to date, sample size is still relatively modest and hence confidence intervals for some statistically significant observations are still wide. No firm conclusions in terms of prognostic modelling can be drawn as of yet (11). Current analyses were aimed at hypothesis generation about patient or tumour characteristics indicative of severity of or death from COVID-19 in the cancer context. Our data for some of the patient characteristics is limited, for example smoking status was missing for 29% of patients and hence likely underestimates the proportion of ever smokers. COVID testing in the UK has only been implemented gradually during the period of our data collection, and there is selection bias in favour of patients being tested as inpatients. Our analysis is likely to have missed cancer outpatients under our care diagnosed with COVID-19 at other hospitals. It is a strength of our study that we used clearly defined definitions of COVID-19 severity as well as a DAG to develop the different models, as to date very limited knowledge is available regarding the intersection between COVID-19 and cancer (11). Detailed information on our modelling will help comparison with future studies with larger sample sizes and longer follow-up.
Conclusion

Our analysis of the largest series of COVID-19 positive cancer patients to date confirms a similar distribution of age, sex, and comorbidities as reported for other COVID-19 populations, irrespective of cancer diagnosis. This first analysis suggests that patients who have lived longer with their cancer are susceptible to a greater infection severity, possibly reflecting the effect of more advanced malignant disease on the impact of this infection. Older age and presence of comorbidities may be associated with increased risk of death in COVID-19-infected cancer patients, as has been reported for general populations without cancer. Further validation will be provided from other large case series, as well as from those including ours with longer follow-up, to provide more definite guidance for oncological care.
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Ethics approval and consent to participate: Guy’s Cancer Cohort, a research ethics committee approved research database (Reference number: 18/NW/0297) of all routinely collected clinical data of cancer patients at Guy’s and St Thomas’ NHS Foundation Trust (GSTT), forms the basis of this observational study.

Consent for publication: N/A

Data availability: Data can be obtained by researchers via an application to the Access Committee of Guy’s Cancer Cohort. An application form can be obtained via charlotte.moss@kcl.ac.uk

Conflict of interest: None to be declared.

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| Tables and Figures |
|-------------------|
| **Total (n=106)** | **WHO COVID Grade** |
|                  | Mild/Moderate (n=87) | Severe (n=19) |
| n     | %   | n     | %   | n     | %   |
| Sex |
| Male | 58  | 54.70 | 44   | 50.60 | 14  | 73.70 |
| Female | 48  | 45.30 | 43   | 49.40 | 5   | 26.30 |
| Age |
| <50  | 15  | 14.20 | 14   | 16.10 | 1   | 5.30 |
| 50-59 | 17  | 16.00 | 13   | 14.90 | 4   | 21.10 |
| 60-69 | 33  | 31.10 | 26   | 29.90 | 7   | 36.80 |
| 70-79 | 25  | 23.60 | 20   | 23.00 | 5   | 26.30 |
| ≥80  | 16  | 15.10 | 14   | 16.10 | 2   | 10.50 |
| Mean (SD) | 65 (14.22) | 65 (14.91) | 67 (10.62) |
| SES |
| Low  | 87  | 82.08 | 72   | 82.80 | 15  | 78.90 |
| Medium | 1  | 0.90  | 1    | 1.20  | 0   | 0.00 |
| High | 9   | 8.50  | 7    | 8.00  | 2   | 10.50 |
| Missing | 9  | 8.50  | 7    | 8.00  | 2   | 10.50 |
| Ethnicity |
| White British | 47  | 44.30 | 37   | 42.50 | 10  | 52.60 |
| White Other | 9   | 8.50  | 7    | 8.00  | 2   | 10.50 |
| Black Caribbean | 6  | 5.70  | 5    | 5.70  | 1   | 5.30 |
| Black African | 12  | 11.30 | 11   | 12.60 | 1   | 5.30 |
| Black Other | 8   | 7.50  | 6    | 6.90  | 2   | 10.50 |
| Asian | 6   | 5.70  | 4    | 4.60  | 2   | 10.50 |
| Mixed | 1   | 0.90  | 1    | 1.10  | 0   | 0.00 |
| Other | 2   | 1.90  | 1    | 1.10  | 1   | 5.30 |
| Unknown | 15  | 14.20 | 15   | 17.20 | 0   | 0.00 |
| Comorbidities |
| Hypertension | 54  | 50.90 | 46   | 52.90 | 8   | 42.10 |
| Diabetes Mellitus | 23  | 21.70 | 19   | 21.80 | 4   | 21.10 |
| Lung Conditions | 17  | 16.00 | 11   | 12.60 | 6   | 31.60 |
| Renal Impairment | 23  | 21.70 | 19   | 21.80 | 4   | 21.10 |
| Liver Conditions | 1   | 0.90  | 1    | 1.10  | 0   | 0.00 |
| CVD | 21  | 19.80 | 16   | 18.40 | 5   | 26.30 |
| Frailty | 8   | 7.50  | 7    | 8.00  | 1   | 5.30 |
| Chronic Steroid Use | 5   | 4.70  | 5    | 5.70  | 0   | 0.00 |
| No. of Comorbidities |
| 0 | 24  | 22.60 | 19   | 21.80 | 5   | 26.30 |
| 1 | 34  | 32.10 | 29   | 33.30 | 5   | 26.30 |
| 2 | 26  | 24.50 | 22   | 25.30 | 4   | 21.10 |
| 3+ | 22  | 20.80 | 17   | 19.50 | 5   | 26.30 |
| Smoking history |
| Never | 42  | 39.60 | 35   | 40.20 | 7   | 36.80 |
| Current | 7   | 6.60  | 6    | 6.80  | 1   | 5.30 |
| Ex-smoker | 26  | 24.50 | 22   | 25.30 | 4   | 21.10 |
| Unknown | 31  | 29.20 | 24   | 27.60 | 7   | 36.80 |
| Medications |
| Polypharmacy | 43  | 40.60 | 35   | 40.20 | 8   | 42.10 |
| NSAIDs | 17  | 16.00 | 13   | 14.90 | 4   | 21.10 |
| ACE/ARB | 24  | 22.60 | 19   | 21.80 | 5   | 26.30 |
| Beta-blockers | 18  | 17.00 | 14   | 16.10 | 4   | 21.10 |

**Table 1:** Demographic characteristics of COVID-19 positive cancer patients.
| Cancer type               | n  | %    | WHO COVID Grade                  | n  | %    | Severe (n=19) |
|--------------------------|----|------|----------------------------------|----|------|---------------|
|                          |    |      | Total (n=106)                    | Mild/Moderate (n=87) |      |               |
|                          |    |      |                                  | n  | %    | n  | %    |               |
| Cancer type              |    |      | Urological/Gynae                 | 36 | 34.00 | 29 | 33.30 | 7  | 36.80 |
|                          |    |      | Hematological                    | 19 | 17.90 | 14 | 16.10 | 5  | 26.30 |
|                          |    |      | Breast                           | 16 | 15.10 | 13 | 14.90 | 3  | 15.80 |
|                          |    |      | Lung                             | 12 | 11.30 | 10 | 11.50 | 2  | 10.50 |
|                          |    |      | Gastro-intestinal                | 12 | 11.30 | 11 | 12.60 | 1  | 5.30  |
|                          |    |      | Central Nervous System           | 6  | 5.70  | 6  | 6.90  | 0  | 0.00  |
|                          |    |      | Skin/Head and neck               | 5  | 4.70  | 4  | 4.60  | 1  | 5.30  |
| Cancer stage             |    |      | I                                | 17 | 16.00 | 17 | 19.50 | 0  | 0.00  |
|                          |    |      | II                               | 19 | 17.90 | 17 | 19.50 | 2  | 10.50 |
|                          |    |      | III                              | 17 | 16.00 | 14 | 16.10 | 3  | 15.80 |
|                          |    |      | IV                               | 39 | 36.80 | 30 | 34.50 | 9  | 47.40 |
|                          |    |      | Missing                          | 14 | 13.20 | 9  | 10.30 | 5  | 26.30 |
| Treatment Paradigm       |    |      | Treatment naive                  | 12 | 11.30 | 12 | 13.80 | 0  | 0.00  |
|                          |    |      | Neoadjuvant                       | 5  | 4.70  | 5  | 5.70  | 0  | 0.00  |
|                          |    |      | Adjuvant                          | 5  | 4.70  | 5  | 5.70  | 0  | 0.00  |
|                          |    |      | Radical                           | 26 | 24.50 | 21 | 24.10 | 5  | 26.30 |
|                          |    |      | Palliative                        | 46 | 43.40 | 36 | 41.40 | 10 | 52.60 |
|                          |    |      | Watch and wait                    | 2  | 1.90  | 2  | 2.30  | 0  | 0.00  |
|                          |    |      | Surveillance                      | 8  | 7.50  | 6  | 6.80  | 2  | 10.50 |
|                          |    |      | Missing                           | 2  | 1.90  | 0  | 0.00  | 2  | 10.50 |
| Systemic Treatment (N=58)|    |      | Systemic chemotherapy             | 25 | 23.60 | 21 | 24.10 | 4  | 21.10 |
|                          |    |      | Immunotherapy                     | 5  | 4.70  | 3  | 3.40  | 2  | 10.50 |
|                          |    |      | Biological                        | 8  | 7.50  | 6  | 6.80  | 2  | 10.50 |
|                          |    |      | Targeted Therapy                  | 14 | 13.20 | 10 | 11.50 | 4  | 21.10 |
|                          |    |      | Combination Therapy               | 6  | 5.70  | 5  | 5.70  | 1  | 5.30  |
| Time since cancer diagnosis |    |      | <3 months                         | 31 | 29.20 | 29 | 33.30 | 2  | 10.50 |
|                          |    |      | 3-12 months                       | 21 | 19.80 | 16 | 18.40 | 5  | 26.30 |
|                          |    |      | 12-24 months                      | 16 | 15.10 | 15 | 17.20 | 1  | 5.30  |
|                          |    |      | >24 months                        | 38 | 35.80 | 27 | 31.00 | 11 | 57.90 |
| Performance status       |    |      | 0                                 | 16 | 15.10 | 13 | 14.90 | 3  | 15.80 |
|                          |    |      | 1                                 | 39 | 36.80 | 33 | 37.90 | 6  | 31.60 |
|                          |    |      | 2                                 | 23 | 21.70 | 19 | 21.80 | 4  | 21.10 |
|                          |    |      | 3                                 | 17 | 16.00 | 15 | 17.20 | 2  | 10.50 |
|                          |    |      | 4                                 | 5  | 4.70  | 3  | 3.40  | 2  | 10.50 |
|                          |    |      | Missing                           | 6  | 5.70  | 4  | 4.60  | 2  | 10.50 |

Table 2: Tumour characteristics of COVID-19 positive cancer patients.
| Symptoms                      | Total (n=106) | WHO COVID Grade               |
|-------------------------------|--------------|--------------------------------|
|                               | n | % | n | % | n | % |
| Cough                         | 61 | 57.50 | 50 | 57.50 | 11 | 57.90 |
| Fever                         | 57 | 53.80 | 41 | 47.10 | 16 | 84.20 |
| Dyspnoea                      | 38 | 35.80 | 29 | 33.30 | 9  | 47.40 |
| Gastro-intestinal symptoms    | 17 | 16.00 | 10 | 11.50 | 7  | 36.80 |
| Time between first symptom and diagnosis |
| <7 days                       | 67 | 63.20 | 54 | 62.10 | 13 | 68.40 |
| 7-14 days                     | 19 | 17.90 | 15 | 17.20 | 4  | 21.10 |
| >14 days                      | 6  | 5.70  | 4  | 4.60  | 2  | 10.50 |
| Missing                       | 14 | 13.20 | 14 | 16.10 | 0  | 0.00 |
| Care setting                  |               |                                |
| Outpatient                    | 25 | 23.60 | 25 | 28.70 | 0  | 0.00 |
| Inpatient                     | 69 | 65.10 | 60 | 69.00 | 9  | 47.40 |
| ITU                            | 10 | 9.40  | 0  | 0.00  | 10 | 52.60 |
| Missing                       | 2  | 1.90  | 2  | 2.30  | 0  | 0.00 |
| Laboratory values*            |               |                                |
| Ferritin (ug/L)               |               |                                |
| T1 (80-793)                   | 13 | 12.30 | 12 | 13.80 | 1  | 5.30 |
| T2 (891-1442)                 | 12 | 11.30 | 7  | 8.00  | 5  | 26.30 |
| T3 (1596-5938)                | 12 | 11.30 | 7  | 8.00  | 5  | 26.30 |
| Missing                       | 69 | 65.10 | 61 | 70.10 | 8  | 42.10 |
| CRP (mg/L)                    |               |                                |
| T1 (3-41)                     | 30 | 28.30 | 27 | 31.00 | 3  | 15.80 |
| T2 (42-117)                   | 30 | 28.30 | 24 | 27.60 | 6  | 31.60 |
| T3 (126-508)                  | 29 | 27.40 | 19 | 21.80 | 10 | 52.60 |
| Missing                       | 17 | 16.00 | 17 | 19.50 | 0  | 0.00 |
| Lymphocytes (x10⁹)            |               |                                |
| ≤0.5                          | 29 | 27.40 | 19 | 21.80 | 10 | 52.60 |
| 0.6-0.8                       | 25 | 23.60 | 20 | 23.00 | 5  | 26.30 |
| 0.9-1.2                       | 20 | 18.90 | 19 | 21.80 | 1  | 5.30 |
| >1.2                          | 18 | 17.00 | 15 | 17.20 | 3  | 15.80 |
| Missing                       | 14 | 13.20 | 14 | 16.10 | 0  | 0.00 |
| Albumin (g/L)                 |               |                                |
| T1 (20-32)                    | 29 | 27.40 | 20 | 23.00 | 9  | 47.40 |
| T2 (33-38)                    | 29 | 27.40 | 23 | 26.40 | 6  | 31.60 |
| T3 (39-57)                    | 26 | 24.50 | 24 | 27.60 | 2  | 10.50 |
| Missing                       | 22 | 20.80 | 20 | 23.00 | 2  | 10.50 |

*Distribution shown in tertiles (T).

Table 3: COVID-19 presentation of COVID-19 positive cancer patients.
|                  | OR*  | 95% CI          |
|------------------|------|-----------------|
| **Sex**          |      |                 |
| Male             | 1.00 | Ref             |
| Female           | 0.37 | (0.12-1.10)     |
| **Age**          |      |                 |
| ≤60              | 1.00 | Ref             |
| >60              | 1.26 | (0.41-3.85)     |
| **SES**          |      |                 |
| Low              | 1.00 | Ref             |
| Middle           | NA   |                 |
| High             | 1.71 | (0.24-12.16)    |
| **Ethnicity**    |      |                 |
| White            | 1.00 | Ref             |
| Black            | 0.67 | (0.19-2.31)     |
| Asian            | 1.83 | (0.30-11.24)    |
| Other            | 1.83 | (0.15-21.98)    |
| **Number of comorbidities** |      |                 |
| 0                | 1.00 | Ref             |
| 1                | 0.29 | (0.04-2.25)     |
| ≥2               | 0.28 | (0.04-2.10)     |
| >3               | 0.32 | (0.04-2.43)     |
| P for trend      | 0.402|                 |
| **Smoking History** |     |                 |
| Never            | 1.00 | Ref             |
| Ever             | 0.83 | (0.16-4.37)     |
| **Cancer Type**  |      |                 |
| Solid            | 1.00 | Ref             |
| Hematological    | 1.00 | (0.15-6.68)     |
| **Treatment Paradigm** |  |                 |
| No active treatment | 1.00 | Ref             |
| Radical/Curative | 1.94 | (0.18-21.08)    |
| Palliative       | 1.14 | (0.15-8.58)     |
| **Time since cancer diagnosis** |  |                 |
| ≤24 months       | 1.00 | Ref             |
| >24 months       | 3.01 | (1.05-8.58)     |
| **Performance Status** |  |                 |
| 0-2              | 1.00 | Ref             |
| 3+               | 0.33 | (0.05-2.21)     |
| **Symptoms**     |      |                 |
| Cough            | 0.91 | (0.32-2.61)     |
| Fever            | 7.22 | (1.55-33.53)    |
| Dyspnoea         | 2.54 | (0.77-8.38)     |
| GI symptoms      | 5.34 | (1.58-17.99)    |
| **Time between first symptom and diagnosis** |  |                 |
| <7 days          | 1.00 | Ref             |
| 7-14 days        | 1.11 | (0.31-3.90)     |
| >14 days         | 2.08 | (0.34-12.59)    |
| **Ferritin (ug/L)** |  |                 |
| T1 (80-793)      | 1.00 | Ref             |
| T2 (891-1442)    | 8.57 | (0.83-89.04)    |
| T3 (1596-5958)   | 8.57 | (0.83-89.04)    |
| **CRP (mg/L)**   |      |                 |
| T1 (3-41)        | 1.00 | Ref             |
| T2 (42-117)      | 2.26 | (0.14-35.92)    |
| T3 (126-508)     | 15.93| (0.84-302.46)   |
| **Lymphocytes (x10^9)** |  |                 |
| ≤0.5             | 1.00 | Ref             |
| 0.6-0.8          | 0.42 | (0.05-3.76)     |
| 0.9-1.2          | 0.14 | (0.01-2.16)     |
Table 4: Odds Ratios and 95% Confidence intervals for COVID-19 severity in cancer patients.

*Adjustment as defined by the DAG (Table 1 Appendix)

| eGFR (mL/min)                  | Odds Ratio | 95% CI       |
|--------------------------------|------------|--------------|
| >1.2                           | 0.54       | (0.02-12.96) |
| T1 (2-52)                      | 1.00       | Ref          |
| T2 (59-89)                     | 0.05       | (0.00-1.03)  |
| T3 (90-234)                    | 0.21       | (0.01-3.00)  |

| Albumin (g/L)                  | Odds Ratio | 95% CI       |
|--------------------------------|------------|--------------|
| T1 (20-32)                     | 1.00       | Ref          |
| T2 (33-38)                     | 0.85       | (0.11-6.69)  |
| T3 (39-57)                     | 0.23       | (0.02-3.36)  |
Figure 1: Kaplan Meier curve for COVID-19 death in cancer patients who tested positive for COVID-19 based on age (A) and number of comorbidities (B).
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