Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Oncology 33 (2021) e180–e191

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Overview

Clinical Characteristics and Outcomes in Patients with COVID-19 and Cancer: a Systematic Review and Meta-analysis

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Abstract

Much of routine cancer care has been disrupted due to the perceived susceptibility to SARS-CoV-2 infection in cancer patients. Here, we systematically review the current evidence base pertaining to the prevalence, presentation and outcome of COVID-19 in cancer patients, in order to inform policy and practice going forwards. A keyword-structured systematic search was conducted on Pubmed, Cochrane, Embase and MedRxiv databases for studies reporting primary data on COVID-19 in cancer patients. Studies were critically appraised using the NIH National Heart, Lung and Blood Institute's quality assessment tool set. The pooled prevalence of cancer as a co-morbidity in patients with COVID-19 and pooled in-hospital mortality risk of COVID-19 in cancer patients were derived by random-effects meta-analyses. In total, 110 studies from 10 countries were included. The pooled prevalence of cancer as a co-morbidity in hospitalised patients with COVID-19 was 2.6% (95% confidence interval 1.8%, 3.5%, I^2: 92.0%). Specifically, 1.7% (95% confidence interval 1.3%, 2.3%, I^2: 57.6.%) in China and 5.6% (95% confidence interval 4.5%, 6.7%, I^2: 82.3%) in Western countries. Patients most commonly presented with non-specific symptoms of fever, dyspnoea and chest tightness in addition to decreased arterial oxygen saturation, ground glass opacities on computer tomography and non-specific changes in inflammatory markers. The pooled in-hospital mortality risk among patients with COVID-19 and cancer was 14.1% (95% confidence interval 9.1%, 19.8%, I^2: 52.3%). We identified impeding questions that need to be answered to provide the foundation for an iterative review of the developing evidence base, and inform policy and practice going forwards. Analyses of the available data corroborate an unfavourable outcome of hospitalised patients with COVID-19 and cancer. Our findings encourage future studies to report detailed social, demographic and clinical characteristics of cancer patients, including performance status, primary cancer type and stage, as well as a history of anti-cancer therapeutic interventions.

Key words: Cancer; COVID-19; mortality; prevalence; SARS-CoV-2; systematic review

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https://doi.org/10.1016/j.clon.2020.11.006
0936-6555/

Statement of Search Strategies Used and Sources of Information

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the study protocol was prospectively registered on PROSPERO (CRD42020182103). Searches were conducted in PubMed, EMBASE (OVID) and MedRxiv for studies published between 1 December 2019 and 24 April 2020. Finally, the citation lists of all included studies were searched for studies not identified on systematic database searches.

Introduction

Populations at risk of severe outcomes of COVID-19 are gradually being identified [1] and thus far include people with diabetes, obesity and hypertension, as well as socio-demographic risk factors, such as male sex, ethnicity and smoking status [2–5].

Patients with cancer represent a population of particular interest and are not only vulnerable to the direct impacts of COVID-19 infection, but also to the effects of healthcare reprioritisation, with subsequent delays in cancer diagnosis and treatment. Over the course of the pandemic, the UK's National Institute for Health and Care Excellence (NICE) advised clinicians to weigh up the risk of delaying in-hospital cancer care with the risk of nosocomial COVID-19 infection. However, there is still little robust data on the nature of the risks involved. Consequent post-pandemic surges in healthcare demands are expected to lead to decreased cancer survival rates [6,7].

Common immunosuppressive therapies are thought to increase vulnerability to severe outcomes of COVID-19 in cancer patients. Although recent studies of immunosuppressed patients indicate that outcomes may be less severe, larger studies of malignancy indicate an association with higher mortality rates [8,9]. These risks probably vary across specific tumour types [10,11] and therapeutic approaches [12]. Given the heterogenous nature of malignancies, determining the impact of cancer and its treatment on the presentation and prognosis of COVID-19 remains an unmet challenge.

Here we collated evidence pertaining to the manifestation of COVID-19 in patients with active malignancy. Specifically, we considered:

(i) The prevalence of cancer in hospitalised patients with COVID-19;
(ii) How COVID-19 presents in cancer patients;
(iii) Whether patients with cancer and COVID-19 are at increased risk of mortality.

Cancer heterogeneity, including pathology, treatment and service-level determinants will probably influence COVID-19 outcomes. To meaningfully answer the questions above, we therefore considered demographic, social and healthcare factors, as well as primary cancer type and stage, and recent therapeutic management. Together, this study provides an overview of the evidence and quality of data currently available, to guide future reports of larger cohort studies with regards to the prevalence, presentation and outcome of patients with COVID-19 and cancer.

Materials and Methods

Protocol

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the study protocol was prospectively registered on PROSPERO (CRD42020182103).

Inclusion and Exclusion Criteria

Patients of any age, sex, nationality and healthcare setting were included. Active malignancy was defined as current malignant disease or treatment for malignancy within the last 12 months. All study types reporting primary clinical data or original analyses of COVID-19 in patients with an existing diagnosis of active cancer in the English language were eligible for inclusion. To account for the rapid evolution of the evidence base and to minimise the effects of publication bias, preprint literature was included. Exclusion criteria were protocol-only publications, commentaries, opinion pieces and systematic reviews without original statistical analyses.

Sources and Search Strategy

We conducted searches in PubMed, EMBASE (OVID) and MedRxiv for studies published between 1 December 2019 and 24 April 2020 (see Appendix A). We subsequently manually searched the citation lists of all included studies for papers that were not identified on systematic database searches.

Study Selection

Two reviewers independently screened each title and abstract for eligibility, and an independent third reviewer resolved all disagreements. To ensure that cancer subgroups were not overlooked, abstracts without explicit mention of cancer patients were not discarded. Finally, we used the same approach to screen the full manuscripts of included studies.

Data Collection and Quality Assessment

We developed a standardised data extraction tool and used the NIH National Heart, Lung and Blood Institute's Study Quality Assessment tools to quality assess included papers. Included papers underwent single-reviewer data extraction and quality assessment, and a 30% random sample was checked by a second reviewer. Using the NIH National Heart, Lung and Blood Institute's Study Quality Assessment tools, each study was quality appraised by two reviewers and converted into 'high', 'moderate' and 'low'

risk of bias ratings through consensus between three reviewers.

Synthesis of Results

We reviewed all papers with respect to the primary questions and conducted qualitative evidence characterisation for each question. To account for variations in cancer prevalence, we categorised studies by geography into China and Western countries. We used results from the geographical subgroups to infer qualitative interpretations. We calculated (i) the pooled prevalence of co-morbid cancer in hospitalised COVID-19 patients and (ii) the pooled in-hospital mortality risk for patients with cancer and COVID-19. For the pooled analyses, we screened for studies that overlapped in terms of study site and recruitment window, in order to prevent duplication of data, i.e. double counting of the same patients within the quantitative synthesis. Where two or more studies were conducted at the same hospital with overlapping recruitment windows, the study with the longest recruitment window and/or the largest sample size of cancer patients was retained. Studies with inappropriate designs for the purposes of each pooled analysis were also excluded, i.e. studies deliberately selecting cancer patients or selecting on the basis of another co-morbidity/admission reason, for the pooled cancer prevalence analysis; studies with a short follow-up or not reporting death/discharge outcomes for the pooled mortality risk analysis; and case-control studies selecting patients on the basis of specific adverse outcomes such as death or intensive therapy unit admission for both analyses. Case series or reports, and studies including hospital staff or out-patients in their cohort were also excluded from both analyses. The pooled analyses were conducted using a random-effects model after the Freeman–Tukey Double Arcsine Transformation of variances in the Metaprop package in Stata 14 [13]. Here, exact or Clopper Pearson 95% confidence intervals were calculated for individual studies [14]. To address heterogeneity between studies, we used random-effects models that incorporate the assumption that studies are estimating different, however related, effects. Specifically, the I^2 statistic was used to assess statistical heterogeneity.

Results

Study Selection

We retrieved 4635 titles through a systematic search and identified 10 further studies through manual searches of the reference lists. After removing duplicate records, 805 titles were retained for title and abstract screening, of which 311 articles were selected for full-text screening. In total, 110 records were subsequently included in the qualitative synthesis (see Appendix B). Of these, 37 studies were used to calculate the pooled prevalence of cancer in hospitalised patients with COVID-19, 30 studies were used to characterise the presenting features of COVID-19 and 17 studies were used to calculate the pooled mortality risk (see Appendix C).

Study Characteristics

Eighty cohort studies, six cross-sectional studies, two case-control studies, one interventional trial, 10 case series and 11 case reports were included (Figure 1). Sixty-seven (60.9%) of the included studies were preprint copies. Given the geographical emergence and spread of COVID-19, most studies were from China ($n = 82$), Italy ($n = 10$) and the US ($n = 8$). Two pairs of studies considered exactly the same cohorts [10,12,15,16], 31 studies had overlapping patient cohorts (study site and recruitment window) with possible duplication of included patients, two studies [10,17] described themselves as case series but were categorised as cohort studies, and one study described itself as a cross-sectional survey but was categorised as a case series [18]. Due to the inherent selection and reporting biases of this study design, all case series and reports ($n = 21$) were classified as high risk of bias. Eighty-one other papers were identified as having a high risk of bias, three a moderate risk of bias and only five a low risk of bias.

The characteristics of the study populations are outlined in Table 1. Most studies ($n = 93$) described a general cohort of COVID-19 patients with coincidental inclusion of co-morbid cancer. Socio-demographically, 23 studies reported age, 25 reported gender, six reported socioeconomic status, four reported smoking status and two reported occupational status. Thirty studies distinguished cancer types, nine identified tumour size and/or metastases and three provided cancer stage. Twenty-three studies reported recent cancer treatment (chemotherapy, radiotherapy, immunotherapy or surgery), six described the aim of treatment (palliative, radical, maintenance), 12 referenced the time since treatment (current or <12 months) and only one paper reported on immune competence.

Prevalence of Cancer in Hospitalised COVID-19 Patients

The pooled prevalence of active cancer in hospitalised patients with COVID-19 across 37 cohort studies was 2.6% (95% confidence interval 1.8%, 3.5%) (Figures 2, 3) [10,12,19–51]. The prevalence in China and Western countries was 1.7% (95% confidence interval 1.3%, 2.3%) [10,12,19–45] and 5.6% (95% confidence interval 4.5%, 6.7%), respectively [46–51]. There was significant heterogeneity in the estimates for each group ($P < 0.001$), with $I^2 = 92.0\%$ across all 10 countries, and specifically, 57.6% for China and 82.3% for Western countries.

Presenting Features of COVID-19 in Cancer Patients

The clinical presentation of COVID-19 in hospitalised cancer patients across 30 studies is detailed in Table 2. Here, 16 (53.3%) were observational cohort studies, five were case series and nine were case reports. Patients most commonly presented with non-specific symptoms of fever, cough,

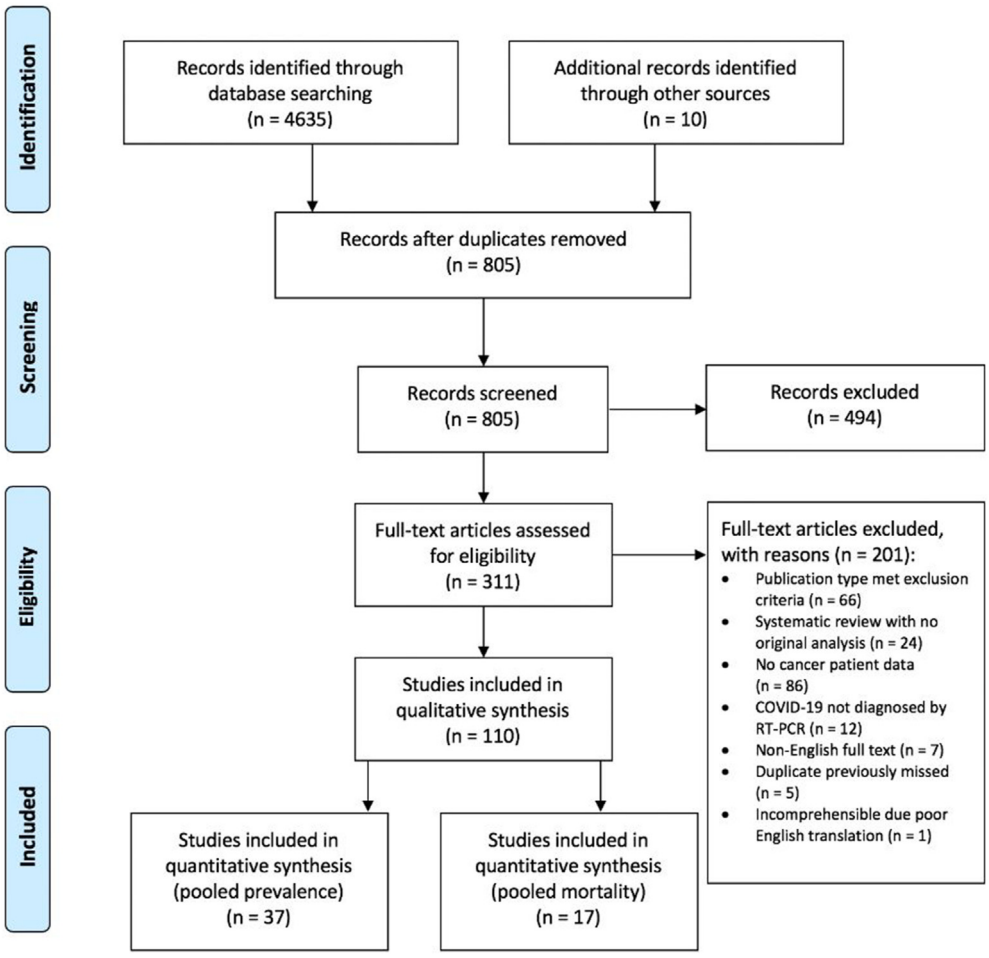

Fig 1. Flowchart of included and excluded studies. Eighty cohort studies, six cross-sectional studies, two case-control studies, one interventional trial, 10 case series and 11 case reports were included.

dyspnoea, fatigue, myalgia, chest tightness and headache. Where computed tomography was carried out, abnormal changes (including ground glass opacities) were seen up to 6 days in advance of the clinical presentation. Laboratory findings included non-specific changes in inflammatory markers and decreased arterial oxygen saturations.

In-hospital Mortality Risk for Cancer Patients with COVID-19

Across 17 retrospective cohort studies, clinical outcomes were identified in 904 hospitalised patients with cancer and COVID-19 [11,16,22,28,30,39,43,44,47,52–58]. The pooled in-hospital mortality risk was 14.1% (95% confidence interval 9.1%, 19.8%; Figure 3). There was significant heterogeneity in the estimate ($P = 0.01$) with $I^2 = 55.9\%$. Only six of 17 studies reported the outcome for all cancer patients at the end of the study observation window [11,22,43,44,56,59]. The median length of in-hospital observation was 7–31 days [39,43,44,53–56,59] and 0–75% of the cancer patients remained hospitalised at the end of the study [11,22,43,44,56,59]. Furthermore, only eight studies specified the cancer type and severity and/or treatment during admission or within the past 12 months [9,11,22,30,43,55,56,58–60]. Of these, only two studies reported both cancer type and treatment for all included patients [11,43]. Together, cancer types were reported for 276 patients and genitourinary, gastrointestinal and respiratory system cancers accounted for 91.6% of all reported cancers [1,9,11,22,26,30,43,55,56,58,59,61]. Oncological treatments were reported for 68 patients, and more than a third were treated with chemotherapy [11,30,43,55,56,59].

Across 14 case reports and series, 24 cancer patients with COVID-19 were identified [18,60–72]. Nine died, three remained in hospital and 12 were discharged by the end of the study period. Of these, 23 had active cancer [18,60–68,70–72] and one was in remission [69]. The average in-patient stay was 18 days. Cancer types included 20 solid organ cancers (lung, ovarian, cervical, endometrial, breast) [60,61,63–66,68–70,72] and four haematological cancers [18,62,67,71] with different stages of severity. Although cancer treatments were non-homogenous, all patients received oxygen therapy, antibiotics, intensive care

Table 1
Study characteristics

Study characteristics	No. of studies *n* (%)
Publication status	
Peer-reviewed	43 (39.1)
Non-peer-reviewed (preprint)	67 (60.9)
Country	
China	82 (74.5)
Italy	10 (9.1)
USA	8 (7.3)
UK	2 (1.8)
South Korea	1 (0.9)
France	1 (0.9)
Spain	1 (0.9)
Netherlands	1 (0.9)
Denmark	1 (0.9)
Brazil	1 (0.9)
Multiple	2 (1.8)
Study design	
Interventional trial	1 (0.9)
Prospective cohort	6 (5.5)
Retrospective cohort	74 (67.3)
Case-control	2 (1.8)
Cross-sectional	6 (5.5)
Case series (≥2 cases)	10 (9.1)
Case report (1 case)	11 (10.0)
Study setting	
Community (out-patient)	5 (4.5)
Hospital (in-patient)	95 (86.4)
Community and hospital	10 (9.1)
Population	
Patients with COVID-19, including some with cancer	93 (84.5)
Patients with cancer, including some with COVID-19	4 (3.6)
Patients with cancer and COVID-19 only	13 (11.8)
Reporting of cancer cohort features	
Age (median)	23 (20.9)
Gender (male:female)	25 (22.7)
Other co-morbidities than cancer	13 (11.8)
Lifestyle factors	3 (2.7)
Cancer type	32 (29.1)
Cancer stage	15 (13.6)
Time since last treatment	21 (19.1)
Treatment type	21 (19.1)
Treatment objective (palliative, radical, maintenance)	8 (7.3)
Study duration (days)	
<7	5 (4.5)
7–13	9 (8.1)
14–29	19 (17.3)
≥30 days	8 (7.3)
Not reported	69 (62.7)
Reported outcomes for patients with cancer and COVID-19	
Disease severity	63 (57.3)
Mortality	52 (47.3)
Not reported	40 (36.4)
Risk of bias	
Low (good quality)	5 (4.5)
Moderate (fair quality)	3 (2.7)
High (poor quality)	102 (92.7)

admission and mechanical ventilation for treatment of COVID-19 [18,60–72].

Discussion

We narratively synthesised results from 110 studies across 10 countries. Included studies were predominantly from China ($n = 82$), Italy ($n = 10$) and the USA ($n = 8$), in line with the evolution of the pandemic.

Prevalence of Co-morbid Cancer

From 37 studies, the overall prevalence of active cancer as a co-morbidity among hospitalised patients with COVID-19 was estimated to be 2–4%, with a higher prevalence seen in studies from Western settings (5–7%) compared with studies conducted in China (1–2%). These findings are unsurprising considering a recent study that reported a lower incidence of total cancer in China compared with Western countries such as the USA and UK [73].

Clinical Presentation

Cancer patients with COVID-19 seem to most commonly present with non-specific symptoms of fever, dyspnoea and chest tightness, in addition to decreased arterial oxygen saturation, ground glass opacities on computed tomography and non-specific changes in inflammatory markers. One study [55] reported that cancer patients more commonly presented with confusion. Consistent with the presentation of COVID-19 in non-cancer patients [74], laboratory findings in cancer patients showed non-specific changes in inflammatory markers, decreased arterial oxygen saturations and abnormal computed tomography scans. Where patients presented with lymphopenia, non-localising symptoms and disseminated infection, underlying immunosuppression must be considered.

Mortality

The estimated in-hospital mortality risk for patients with COVID-19 and cancer is between 9 and 20% across all settings. The pooled mortality risk estimate of 14.1% among hospitalised patients with COVID-19 and cancer is at least five times higher than the reported mortality risk of COVID-19 in non-elderly patients without underlying predisposing conditions across Europe and America [75]. These results corroborate a recently published systematic review and meta-analysis [76] that reported that malignancy, among age and other co-morbidities, is associated with a greater risk of death from COVID-19 infection.

The findings in this review are in line with findings from four of the included studies that independently reported increased mortality risks in their respective cohorts. Specifically, two studies reported a higher risk of mortality in cancer patients with COVID-19 when adjusting for age and sex

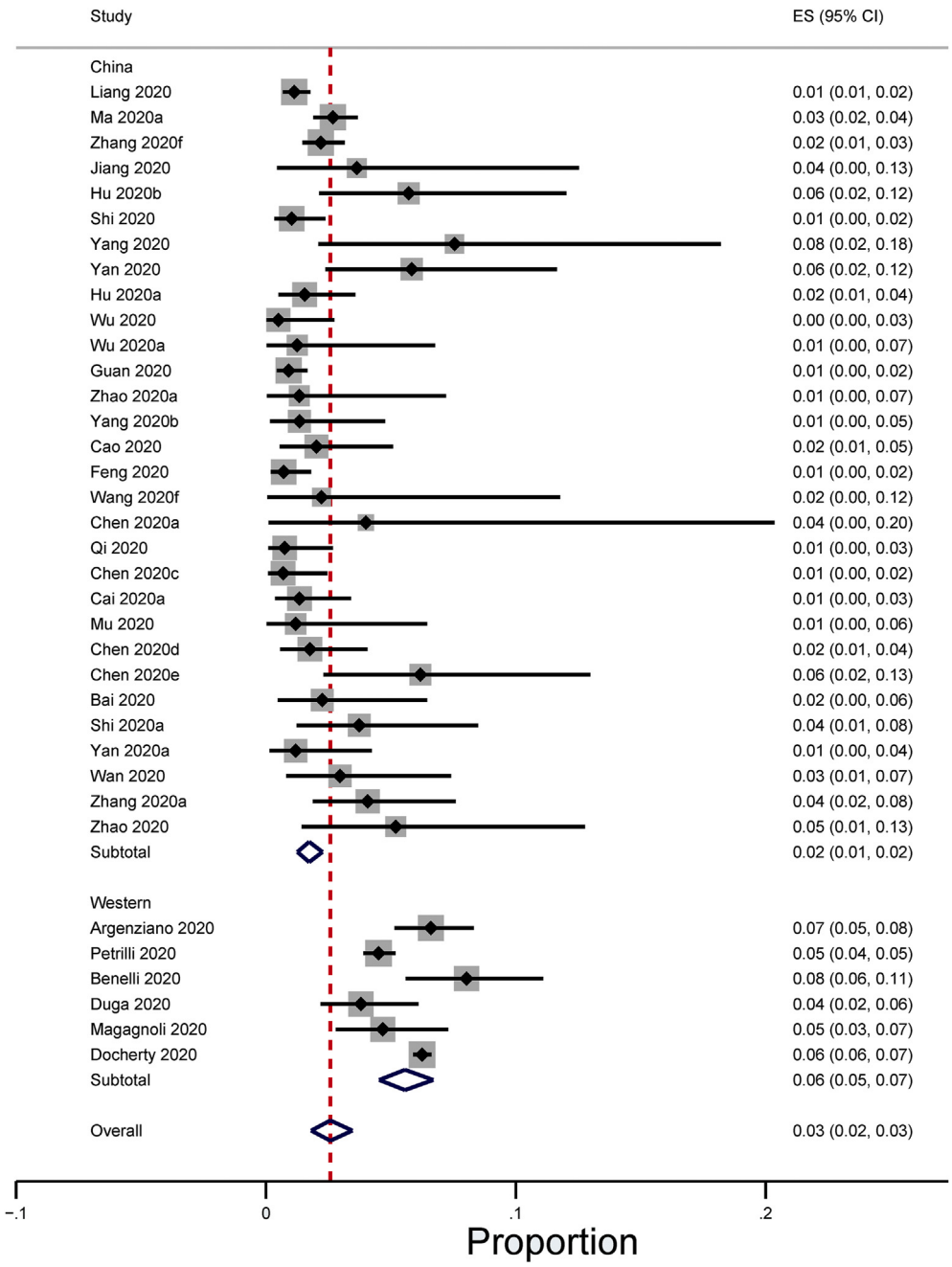

Fig 2. Proportion of hospitalised COVID-19 patients with cancer. The pooled prevalence of active cancer in hospitalised patients with COVID-19 across 37 cohort studies was 2.6% (95% confidence interval 1.8%, 3.5%). In China and Western countries, the prevalence figures were 1.7% (95% confidence interval 1.3%, 2.3%) and 5.6% (95% confidence interval 4.5%, 6.7%), respectively.

(hazard ratio 1.4; 95% confidence interval 1.0–2.0) [43,77] and another reported a significantly higher relative risk of mortality in cancer patients under the age of 50 years compared with non-cancer patients in the same age group (relative risk 5.01; 95% confidence interval 1.55–16.2) [58]. Finally, cancer patients were found to have a higher composite risk of admission to an intensive care unit, invasive ventilation or death when adjusting for both age and smoking status (hazard ratio 3.501; 95% confidence interval 1.604–7.643) [16].

Methodological Considerations

There are several important limitations inherent in the available evidence that restrict the inferences that can be drawn from these findings. Here, we first review the limitations of the available data and then address specific measures that should be undertaken to ensure that studies examining prevalence, risk and mortality differences are epidemiologically robust from the outset.

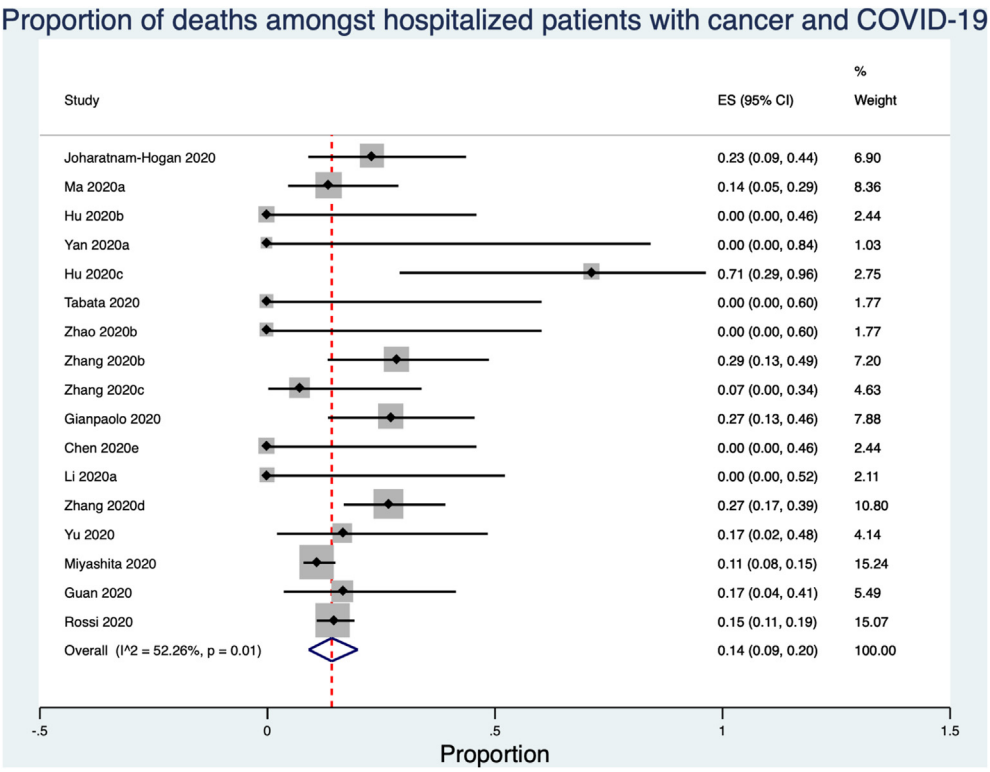

Fig 3. Proportion of deaths among hospitalised patients with cancer and COVID-19. The pooled in-hospital mortality risk among patients with COVID-19 and cancer was 14.1% (95% confidence interval 9.1%, 19.8%).

Table 2
Clinical presentation of COVID-19 in cancer patients

Features	4 observational and cohort studies				14 case reports and case series
	Ma *et al.*, 2020 ($n = 37$)	Hrusak *et al.*, 2020 ($n = 9$)	Zhang *et al.*, 2020 ($n = 67$)	Yang *et al.*, 2020 ($n = 3$)	$n = 23$
Fever	75.7%	77.8%	79.1%	100%	$n = 14$
Cough	56.8%	ND	74.6%	33.3%	$n = 8$
Dyspnoea	32.4%	ND	65.7%	ND	$n = 12$
Hypoxia/reduced SpO_2	ND	ND	ND	33.3%	$n = 1$
WBC	↑ neutrophil	↓ neutrophil and lymphocyte	ND	↑ in 33.3%	↑ lymphocyte: $n = 2$ ↑ neutrophil: $n = 1$
CRP	ND	ND	↑	↑	9
Other inflammatory markers	↑ IL-6 and LDH	ND	↑ LDH	66.6% ↑ D-dimer	↑ LDH: $n = 2$ ↑ D-dimer: $n = 7$
Imaging modality	ND	CT	CT	ND	CT: $n = 18$ X-ray: $n = 2$
Other symptoms	Headache, myalgia, fatigue, diarrhoea	Diarrhoea	Fatigue, diarrhoea, nausea, myalgia, and vomiting	ND	Myalgia: $n = 3$ Diarrhoea: $n = 3$ Nausea and vomiting: $n = 2$ Fatigue: $n = 2$ Asymptomatic cases: $n = 3$

CRP, C-reactive protein; CT, computed tomography; IL-6, interleukin-6; LDH, lactate dehydrogenase; ND, no data available; WBC, white blood cells.

All included studies accurately reported the prevalence of cancer in hospitalised patients with a confirmed diagnosis of COVID-19. Although this provides insight into the proportion of co-morbid cancer, it is not a measure of the risk of COVID-19 acquisition among people with cancer. Notably, the need for hospitalisation may be inflated due to extensive clinical monitoring, a group coached to present early with infection or may have been an incidental finding [58]. Together, behavioural and healthcare factors such as self-surveillance, health literacy, access to healthcare and

Recommendations for future studies

1. To assess susceptibility amongst cancer patients, SARS-CoV-2 transmission should be explored within both healthcare and household settings. For inpatients, the primary admission reason should be reported to distinguish nosocomial from community acquired infections.

2. To assess the relative risk of infection, the incidence of SARS-CoV-2 infection should be longitudinally measured in large cohorts of individuals with and without cancer, recruited using probabilistic sampling methods.

3. To assess mortality risk, both in-hospital and community deaths must be taken into account; for this, cause of death information can be linked with COVID-19 surveillance data.

4. To distinguish mortality risk related to COVID-19 from mortality related to cancer, implementation of ceilings of care should be considered and palliative versus curative therapeutic objectives should be reported.

5. To assess the impact of confounding variables, key demographic, social, and clinical characteristics should be reported for all patients:
   a. Demographic: age, sex, ethnicity.
   b. Social: occupation, socio-economic status, smoking status.
   c. Clinical: BMI, performance status, co-morbidities, cancer type, cancer stage, treatment type, treatment history and therapeutic strategy.

Fig 4. Recommendations for future studies of COVID-19 in cancer patients.

thresholds for testing or admission may lead to earlier presentation and over-representation of cancer patients within the COVID-19 cohort. Cancer patients with COVID-19 were largely identified coincidentally in cohort studies, where the primary objective was not to investigate the prevalence, clinical presentation or course of disease. Consequently, relevant confounders, including demographic, social and clinical characteristics, were not considered or reported. Most studies did not report the specific cancer type or treatment history for included cancer patients, nor did they outline the primary reason for hospital admission. This means that for certain patients with cancers requiring closer monitoring or more frequent contact with healthcare services, there may be a bias with regards to the detection of COVID-19 symptoms and consequent diagnosis. There may also be a bias towards detection of COVID-19 in patients whose disease or therapy causes symptoms similar to COVID-19, prompting higher rates of testing and, consequently, detection. For this review, only studies examining data from hospital in-patients were considered. However, none of the included studies specified the original reason for admission. Therefore, it remains uncertain whether included patients were originally admitted for reasons specific to their cancer diagnosis,

such as elective admission for cancer treatment or emergency admission for cancer-related complications, or whether they were admitted due to illness caused primarily by COVID-19, which poses a significant challenge when interpreting the available data with regards to risk of infection. Furthermore, differences in study design, study population and risk of bias inevitably lead to heterogeneity between studies, and this is particularly present in combined pooled estimates of prevalence in the West and China. To address these heterogeneities, we used a random-effects model that incorporates an assumption that studies are estimating different, yet related, effects. We also examined these regions separately and heterogeneity was lower when we did this, particularly for China, which shows that some of the heterogeneity is explained by between-country differences. Heterogeneity is often high in meta-analyses of proportions [78–81] and care must be taken if the results from the analysis are used for clinical decision making.

Outcomes for 75% [82] of patients in cohort studies remain unknown due to insufficient follow-up periods and the specific causes of mortality are not specified. Without cause of death information, it is not possible to distinguish between mortality caused by cancer or its associated treatment complications and mortality as a direct result of COVID-19; in cases where COVID-19 causes decompensation of underlying disease, even cause of death data may be unreliable. Excess all-cause mortality in cancer patients diagnosed with COVID-19 would provide the only robust metric of the risk posed by COVID-19 and requires routine setting-specific data and large sample sizes to ascertain.

Development of Future Studies

Included studies were largely (92.7%) assessed as having a high potential of bias, and we uncovered significant limitations in the existing literature base, which must be addressed (Figure 4). It is recommended that future studies include data on cancer type and treatment regimens of all cancer patients, as well as primary admission reason for all patients, with details on the causes of death if mortality data are presented. To estimate the relative risk of SARS-CoV-2 infection in cancer patients, the incidence of COVID-19 should be measured through longitudinal follow-up of cohorts of individuals with and without cancer. Additionally, sub-cohorts of specific cancer types and stages should be considered; ideally, without prior or current SARS-CoV-2 infection at baseline. Cohorts must be selected through probabilistic sampling methods to ensure they are balanced and representative, particularly with respect to other demographic and clinical variables. Follow-up duration should adequately allow for declining incidence, and inconsistency in follow-up duration should be addressed using person–time metrics. Studies must define, collect and present data on all potential confounding and interacting variables, such as those discussed under 'Methodological considerations', and adjust for these at the point of design or analysis. We further encourage future studies to report comprehensive social, demographic and clinic characteristics of cancer patients. Clinical characteristics of interests pertain specifically to performance status, co-morbidities, cancer type, cancer stage, treatment type, history and plan.

Future studies will need to reflect the changing epidemiology of COVID-19 with regards to their design and outcomes of interest. In light of the current resurgence, or 'second wave', with high community transmission nationally, community-based follow-up of known cancer patients should also be undertaken; specifically considering household and occupational exposures, as well as healthcare exposures, and linking this with hospital admission and clinical outcomes data. Aggregated findings from outbreak analyses based on household or institutional clusters may reveal insights regarding transmission risk for cancer patients compared with non-cancer contacts of COVID-19 cases. In order to examine mortality risks, it is essential to capture both in-hospital and out-of-hospital deaths. Routine mortality data, such as cause of death certification, should be utilised, which can be linked with both national COVID-19 surveillance data and healthcare datasets. When community transmission is effectively controlled, researchers should continue to monitor large cohorts of cancer patients over the course of treatment, with a focus on nosocomial transmission.

Going forward, ceilings of care for those receiving palliative versus curative therapy should be considered, and the effects of immunosuppressive chemotherapy versus targeted immunotherapy, radiotherapy, surgery or other types of treatment should be reported.

Conclusions

The results from this review show that cancer constitutes a co-morbidity in 1–2% of hospitalised COVID-19 patients in China and 5–7% in Western countries. They present similarly clinically to non-cancer patients, and the preliminary evidence suggests there is an increased in-hospital mortality risk in patients with cancer and COVID-19. However, a comprehensive assessment of the qualities of the included studies show the need for longitudinal follow-up studies, where cohorts are selected through probabilistic sampling methods, and follow-up duration is extended to encompass clinical progression and outcome. In order to improve generalisability, granularity and understanding of heterogeneity, we further encourage future studies to report detailed social, demographic and clinic characteristics of cancer patients, including but not limited to, performance status, other co-morbidities, cancer type and stage, and treatment type, history and plan. We recommend that future studies include primary admission reason for all patients, with details on the causes of death if mortality data are presented. Finally, in light of the current 'second wave' of COVID-19 with high community transmission, it is essential to report both in-hospital and out-of-hospital deaths, and community-based follow-up should be implemented.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Acknowledgements

The authors would like to thank Akhila Kadgathur Jayaram and Polygeia, the youth-led global think tank based in the UK, USA and Hong Kong.

Appendices. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clon.2020.11.006.

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