Cancer and COVID-19

Gerald Paris

Clinical recommendations on lung cancer management during the COVID -19 pandemic

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Stellenbosch

Introduction

- Lung cancer highest mortality and morbidity rates in the world
- Strong risk of infection
- Badly affected by covid
- Chinese CDC analysed 72314 cases

Chinese CDC analysed 72314 cases

- 0,5% (107) cancer pts
- Crude mortality 5,6% vs 2,3% ; risk of severe events 39% vs 8% (P=,0003) esp lung, haematological, metastatic
- Reasons cited were pretty obvious

Early identification of COVID -19 and differential diagnosis in patients with lung cancer

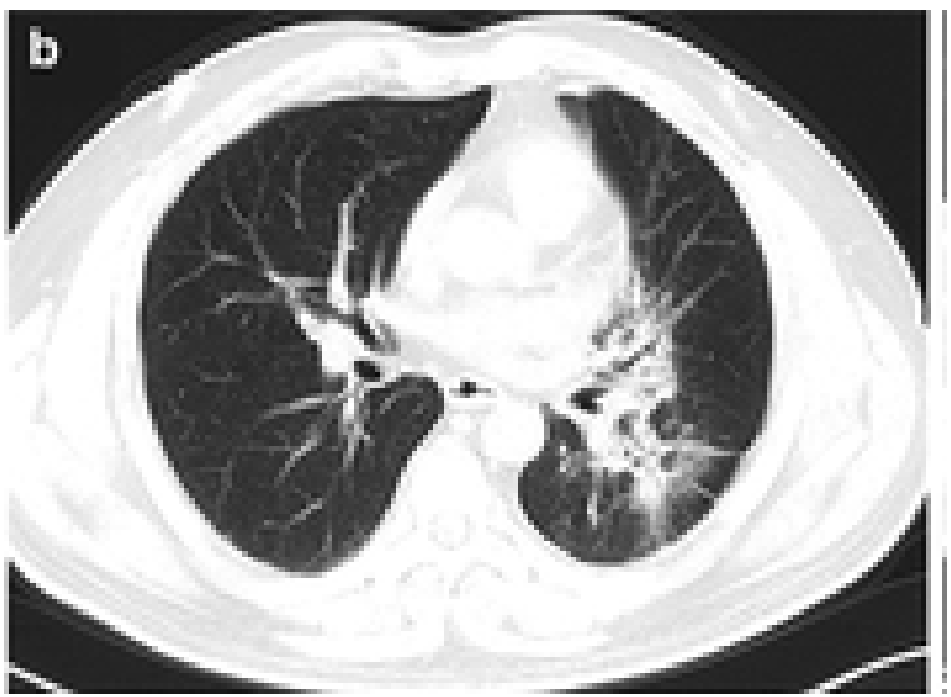
- the early identification and differential diagnosis of COVID-19 for lung cancer patients is extremely difficult, necessitating comprehensive examination for differential diagnosis and etiological identification.
- diagnosis of suspected COVID-19 requires a combination of epidemiological history and clinical manifestation:
  (i) Fever and/or respiratory symptoms;
  (ii) imaging presentation of COVID-19; and
  (iii) normal or reduced white blood cell count or lymphocytopenia during the early disease stage disease for integrated analysis.
- Patients who fulfil any of the epidemiological history criteria and any two clinical presentation criteria, or present no clear epidemiological history but fulfil three clinical presentation criteria, are diagnosed as suspected COVID-19; confirmed if one of:
  (i) Positive SARS-CoV-2 RT-PCR testing result;
  (ii) viral genetic sequence is highly homologous with the known SARS-CoV-2; and
  (iii) positive SARS-CoV-2 specific IgM antibody and IgG antibody

Differential diagnosis

- Pulmonary infections

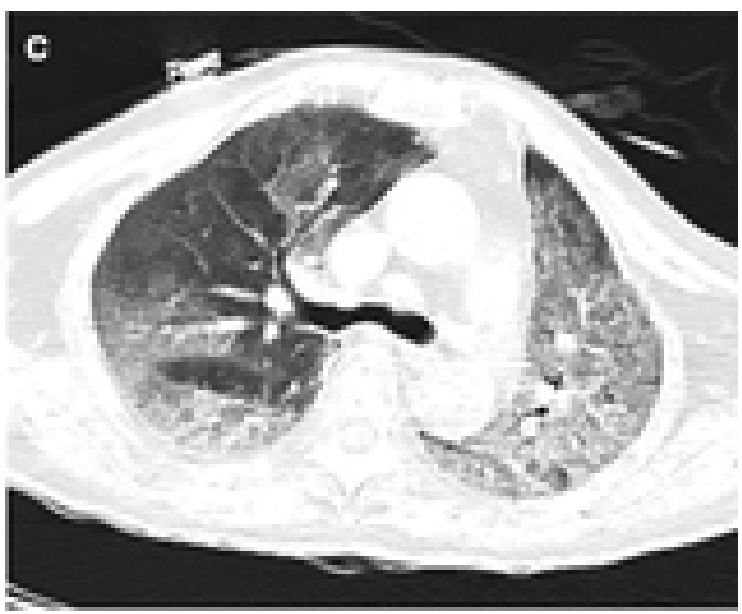
Radiation pneumonitis

- Up to 3 months after treatment; radiation does its damage through the production of free radicals
- Fever and dry cough; may have normal WCC; ct GGO and patchy shadows



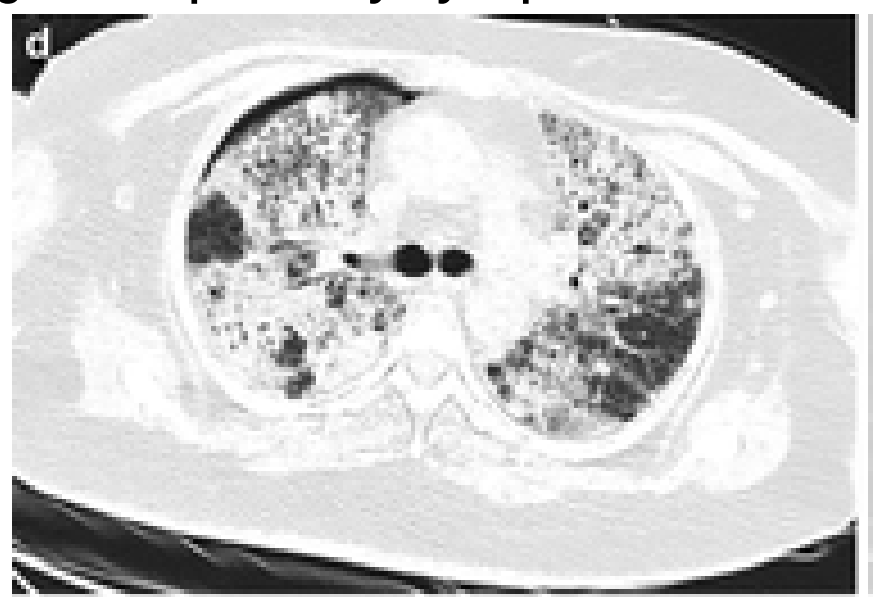
Immune checkpoint inhibitor-related pneumonitis (ICI-P)

- patients who receive immunotherapy are at risk of ICI-P The clinical presentation includes fever, worsening of cough and productive cough, worsening of dyspnea, GGOs and patchy shadows on the chest CT scan, and several patients may present with GGOs in the lungs alone.



Tumour progression/other

- lung cancer progression may result in pneumonic-type lung carcinoma , obstructive pneumonitis, lymphangitis carcinomatosa, increased pleural effusion, and pericardial effusion, which may lead to fever and/or worsening of respiratory symptoms.



Approach

- Early stage for elective surgery- postpone
- Where possible local hospital for planned surgery to avoid travel
- If scheduled with symptoms refer “fever clinic”; if contact for 14 days quarantine

Postoperative lung cancer patients

- Promote routine but local treatment

Lung cancer patients receiving radiotherapy/chemo/immunotherapy

- Extensive guidelines

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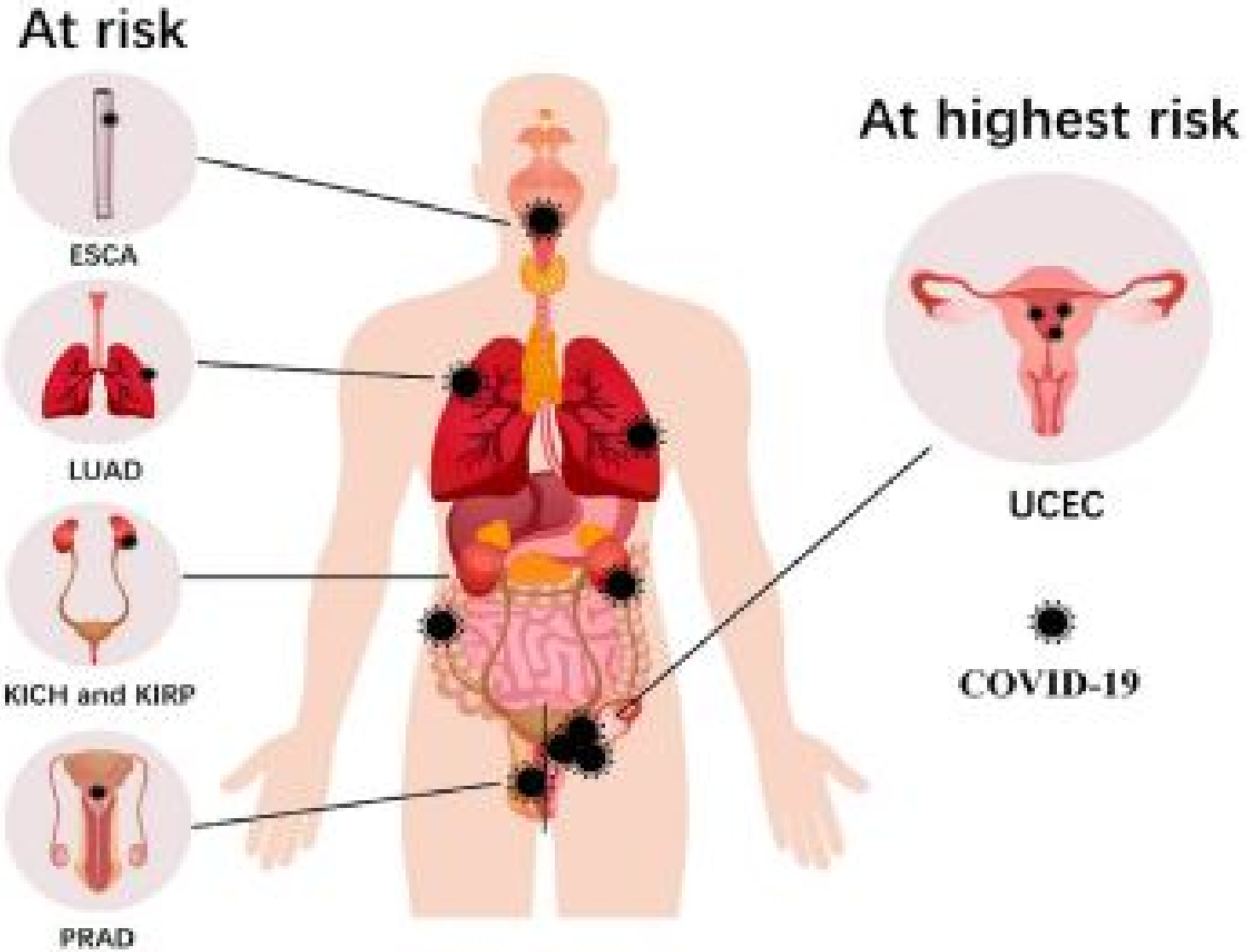
Letter to the Editor

Which cancer type has the highest risk of COVID-19 infection?

- AngiotensinConverting Enzyme 2 and Transmembrane Protease Serine 2 are the receptors for SARS-CoV-2 to invade the human body, which are mainly located in the respiratory tract, lung, and intestines. But for cancer patients, not only are these organs at risk, but many tumor cells also express ACE2 and TMPRSS2.
- Expression levels of ACE2 in Esophageal carcinoma (ESCA), Kidney renal papillary cell carcinoma (KIRP), Lung adenocarcinoma (LUAD), Uterine Corpus Endometrial Carcinoma (UCEC) are high. Similarly, TMPRSS2 levels in Kidney Chromophobe (KICH), Prostate Adenocarcinoma (PRAD), Uterine Corpus Endometrial Carcinoma (UCEC) are also increased; hence the risk of COVID-19 infection in patients
- Only UCEC is coexpressing ACE2 and TMPRSS2 receptors; therefore, patients with UCEC carry the highest risk of COVID-19 infection


At risk
ESCA
LUAD
KICH and KIRP
PRAD
At highest risk
UCEC
COVID-19

- If the SARS-CoV-2 virus infects the tumor cells, it will be difficult to clear due to the inherent immune resistance in the tumor microenvironment. Though many tissues will not be invaded by the virus, inflammatory reactions such as cytokine storms can cause tissue damage. Also, the cytokine storm caused by COVID-19, such as IL-6, may promote the progression of the tumor, such as UCEC

- There is a debate on the use of ACE inhibitors or Angiotensin Receptor Blocker. Studies have shown that Bruton Kinase (BTK) Inhibitors can reduce inflammation reaction by blocking the Toll-like receptors signalling pathways, which is a good choice for patients with lymphoma. Cytokines can promote tumour progression, indicating cytokine inhibitors, such as anti-IL-6 (Tocilizumab), may bring more benefits to cancer patients.

Zambia's National Cancer Centre response to the COVID-19 pandemic-opportunity for improved care

Zambia has a population of approximately 17 million, Its national cancer centre—Cancer Diseases Hospital (CDH) was established in 2006 Lusaka, it is the only centre in the country offering radiotherapy and serves the entire population of Zambia as well as some neighbouring countries (Malawi, Democratic Republic of Congo and Zimbabwe), Over 90% of the new cases that register for care at CDH present in a late stage and the overwhelming majority are suffering from severe symptomatology

Government response

- The country declared the outbreak on 18th March 2020. The response of the central government has been pragmatic. In formulating this approach the economic, cultural and social peculiarities of the country were taken into consideration, as well as experience with prior infectious disease outbreaks involving cholera, tuberculosis and Human Immunodeficiency Virus, to maximise the effectiveness of the public health response.
- Zambia did not go into complete lockdown but two statutory instruments were enacted by the Zambian government on the 14th of March, 2020. One designated COVID-19 as a notifiable disease and the other provided for additional regulations to facilitate its management and control. They are fairly standard

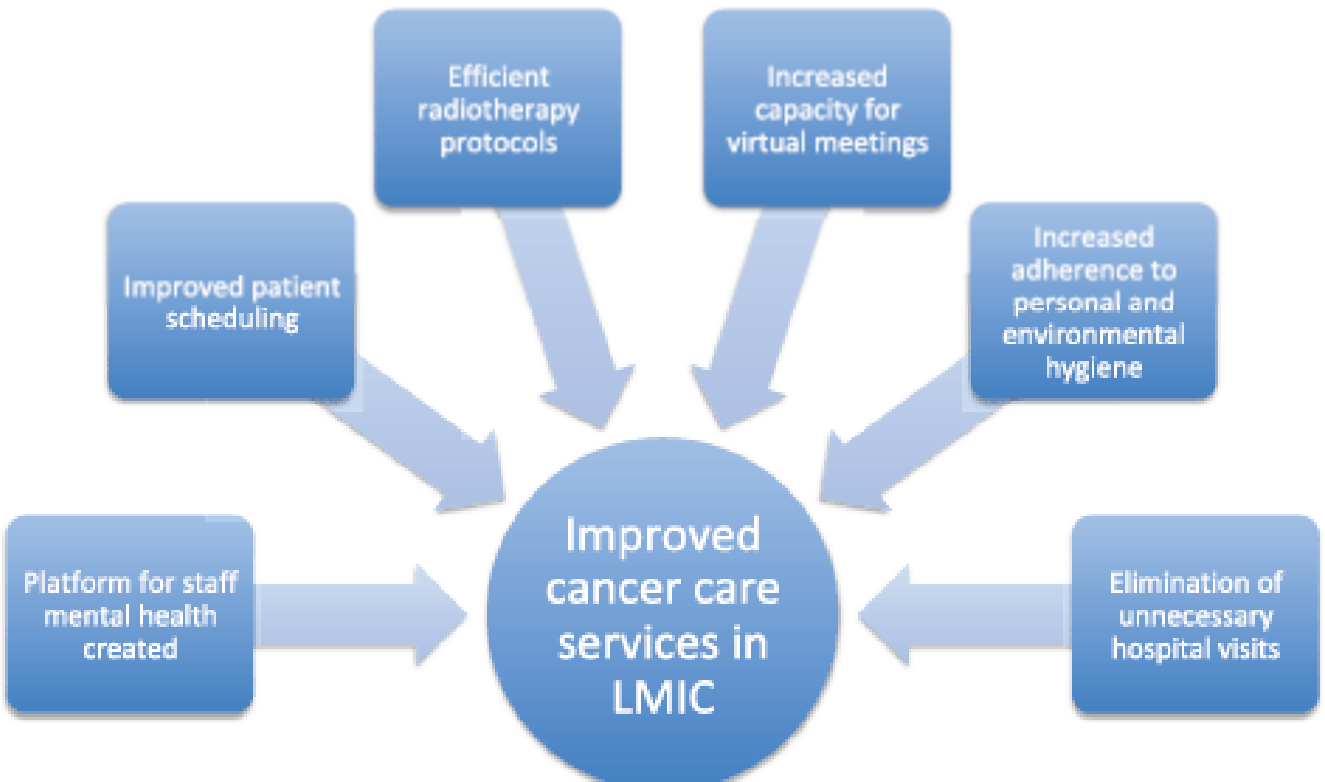
Cancer centre response

- **Cancer centre response**
- ***Establishment of a hospital level COVID-19 task force***
- Established a local response taskforce that could formulate, implement, enforce and communicate national measures to maintain the safety of patients and hospital staff. This task force included both clinical and administrative staff. Additionally, each unit was invited to nominate a senior staff member with managerial exposure in their day-to-day activities as well as a junior staff member who was on the treatment floor actively on a day-to-day basis to ensure solutions and strategies were practical

Strategies

- Numerous but generic
- All inpatients swabbed
- Most patients still presented in person
- Telephonic follow up reviews where possible
- At time of writing no on-treatment pt found positive
- Review of treatment protocols

Positive outcomes of COVID-19 response at Cancer Diseases Hospital



Other issues

- Pall care services
  - Opportunity to use strengthened communication
- Staff
  - Reduced presence where possible
  - Education in PPE and about the disease
  - Strong attention to mental health
  - All meetings virtual

COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study

Lennard Y W Lee, DPhil * • Prof Jean Baptiste Cazier, PhD * • T Starkey, MSc • C D Turnbull, DPhil • UK Coronavirus Cancer Monitoring Project Team • Rachel Kerr, FRCP † • et al. Show all authors • Show footnotes

In this prospective observational study, all patients with active cancer and presenting to our network of cancer centres were eligible for enrolment into the UK Coronavirus Cancer Monitoring Project (UKCCMP).. Eligible patients tested positive for severe acute respiratory syndrome coronavirus 2 on RT-PCR assay from a nose or throat swab. We excluded patients with a radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test. The primary endpoint was all-cause mortality, or discharge from hospital, as assessed by the reporting sites during the patient hospital admission

Patients with cancer receiving systemic anticancer treatments have been generally assumed by many to be at a higher risk from the disease than their counterparts are who are not receiving anticancer treatment. The evidence to support this claim is scarce and limited to retrospective series arising from China, the epicentre of the COVID-19 pandemic, and involving small numbers of patients.

However, despite these severe limitations, the promulgation of this hypothesis has led to widespread global changes to patterns of prescribing chemotherapy and anticancer treatment.

Patients with active cancer were defined as those with metastatic cancer, or on anticancer treatment in any setting (curative, radical, adjuvant, or neoadjuvant setting) or treated within the past 12 months with surgery cytotoxic chemotherapy, or radiotherapy

	All patients (n=800)	Patients who died (n=226)	Patients who survived (n=574)
Sex			
Male	449 (56%)	146 (65%)	303 (53%)
Female	349 (44%)	80 (35%)	269 (47%)
Other*	2 (0%)	0 (0%)	2 (0%)
Age, years	69 (59-76)	73 (66-80)	66 (57-74)
Comorbidities			
Cardiovascular disease	109 (14%)	48 (21%)	61 (11%)
Chronic obstructive pulmonary disease	61 (8%)	24 (11%)	37 (6%)
Diabetes	131 (16%)	46 (20%)	85 (15%)
Hypertension	247 (31%)	92 (41%)	155 (27%)
None	169 (21%)	27 (12%)	142 (25%)
Other†	336 (42%)	108 (48%)	228 (40%)
No information	123 (15%)	28 (12%)	95 (17%)
Cancer type			
Lip, oral cavity, and pharynx	27 (3%)	4 (2%)	23 (4%)
Digestive organs	150 (19%)	42 (19%)	108 (19%)
Respiratory and intrathoracic organs	90 (11%)	32 (14%)	58 (10%)
Melanoma (skin)	27 (3%)	4 (2%)	23 (4%)
Breast	102 (13%)	18 (8%)	84 (15%)
Female genital organs	45 (6%)	5 (2%)	40 (7%)
Male genital organs	78 (10%)	30 (13%)	48 (8%)
Urinary tract	50 (6%)	16 (7%)	34 (6%)
Central nervous system	15 (2%)	3 (1%)	12 (2%)
Lymphoma	60 (8%)	20 (9%)	40 (7%)
Other haematological	109 (14%)	40 (18%)	69 (12%)
Other or unspecified‡	47 (6%)	12 (5%)	35 (6%)
Cancer stage			
Primary tumour localised	149 (19%)	40 (18%)	109 (19%)
Primary tumour locally advanced	78 (10%)	14 (6%)	64 (11%)
Metastatic	347 (43%)	103 (46%)	244 (43%)
Remission	21 (3%)	3 (1%)	18 (3%)
No information	205 (25%)	66 (29%)	139 (24%)
(Continued from previous column)			
Cancer treatment within 4 weeks of COVID-19 diagnosis			
Chemotherapy	281 (35%)	75 (33%)	206 (36%)
Hormone therapy	64 (8%)	21 (9%)	43 (7%)
Immunotherapy	44 (6%)	10 (4%)	34 (6%)
Radiotherapy	76 (10%)	18 (8%)	58 (10%)
Surgery	29 (4%)	7 (3%)	22 (4%)
Targeted treatment	72 (9%)	16 (7%)	56 (10%)
Other§	60 (8%)	13 (6%)	47 (8%)
None	272 (34%)	92 (41%)	180 (31%)
No information	10 (1%)	1 (0%)	9 (2%)
COVID-19 severity category			
Mild	412 (52%)	22 (10%)	390 (68%)
Severe	187 (23%)	59 (26%)	128 (22%)
Critical	173 (22%)	140 (62%)	33 (6%)
No information	28 (3%)	5 (2%)	23 (4%)
COVID-19 treatment			
Intensive therapy unit	53 (7%)	23 (10%)	30 (5%)

Data are n (%), or median (IQR). UKCCMP=UK Coronavirus Cancer Monitoring Project. ICD10=International Classification of Diseases. *Includes patients who do not identify as either male or female. †Includes comorbidities that were not listed in the table. ‡Includes ICD10 cancer types including malignant neoplasia of the bone and articular tissue, endocrine glands, mesothelioma and soft tissue, and any other tumour type that was not included in the table. §Includes cancer treatments that did not fall into the cancer treatment types defined in the table.

Table 1: **Clinical features of patients in the UKCCMP registry**

Patients were assessed by the local teams and review of their medical history as to whether they had received chemotherapy (which did not include treatment with denosumab), immunotherapy, hormonal therapies, or radiotherapy within 4 weeks of contraction of COVID-19. Non-palliative chemotherapy was defined as chemotherapy that was used in a neoadjuvant, adjuvant, or radical setting. Outcomes were monitored until April 26, 2020.

Features

- Covid presentations were typical; no asymptomatic patients involved
- 226 (28%) patients died, with reports stating that the death was principally attributable to COVID-19 in most patients (211 [93%]).
- Ctx cohort was younger and “death cohort” older that their counterparts
- Patients who died were also more likely to present with symptoms of shortness of breath (57% *vs* 32%; p<0·001)

Findings

- CTX within 4 weeks of testing positive for C19- no difference in ctx cohort vs non ctx cohort
- Amongst different primaries no difference but CTX cohort was younger
- MVA age, gender, co-morbidities- still no difference
- Palliative vs radical treatment; no difference for palliative compared to no treatment

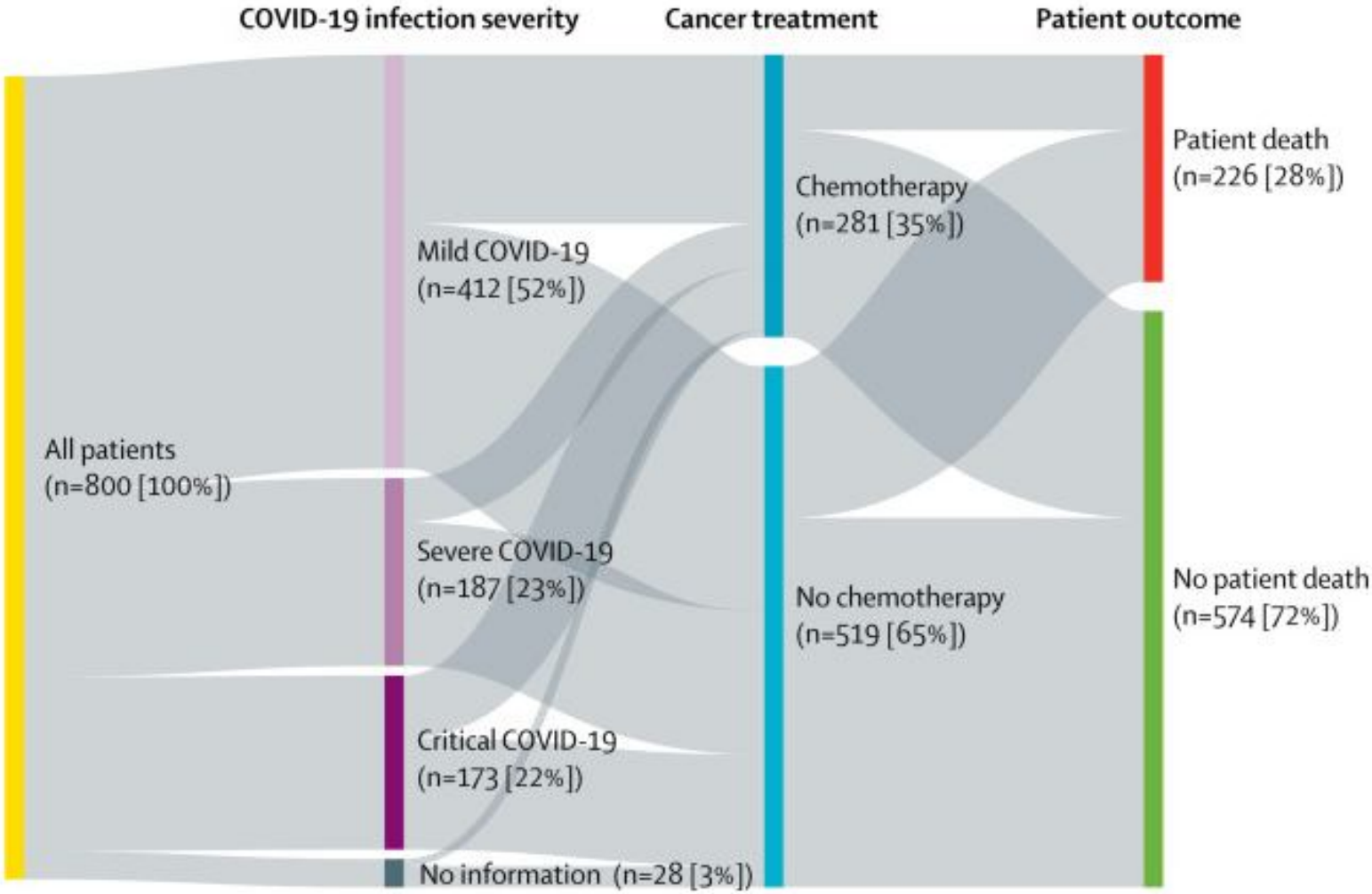


Figure 3 Relationship of chemotherapy use within 4 weeks of confirmed COVID-19 and mortality and severity of disease course

Findings with limitations

- Ca and c19 strongly driven by age and co-morbidities
- Withholding treatment carries a greater risk of ca-related M&M than covid related problems

Comments

- Risk of over and under-reporting
- Selection bias d/t cessation of CTX for other reasons
- Unknown C19 in all cancer patients
- But is prospective in nature

Developing a risk assessment score for patients with cancer during the coronavirus disease 2019 pandemic

Alice Indini • Erika Rijavec • Michele Ghidini • Monica Cattaneo • Francesco Grossi

- Owing to the peculiar pathogenesis of CoV in humans and to the mechanisms of action of novel oncologic treatments, the link between CoV and patients with cancer might not be straightforward. Unlike other common viruses, CoVs have not been shown to cause a more severe disease in immunocompromised subjects
- Along with a direct viral pathogenicity, the host's immune response plays a crucial role in COVID-19. In some individuals, CoV infection triggers an uncontrolled aberrant inflammatory response to external factors, which leads to lung tissue damage
- Since the introduction of anticancer immunotherapy (e.g. immune checkpoint inhibitors [ICIs]), most oncology patients have changed their features of immunocompromised subjects. Rather, their immune system is somehow 'boosted' by the cancer treatment they receive. This might translate into a distinct susceptibility of these subjects towards CoV infections. The cross-interference of CoV and ICIs may worsen the clinical course of COVID-19, which, in turn, may intensify ICI-related side-effects
- Altogether, this evidence suggests that in patients treated with immunotherapy, COVID-19 (e.g. ICIs) may represent a serious threat
- The present article focuses on developing a score to weight the risk of COVID-19 in patients with cancer.

Table 1
The 'Milano Policlinico ONCOVID Score' for risk evaluation in oncology during the COVID-19 pandemic.

Variables	Score	Categories of risk for patients and for treatment delays during COVID-19 diffusion
Patient characteristics		**Score <4: low risk**
Sex	F = 0 M = 1	• Maintain treatment schedule. • Consider treatment delay in the presence of additional risk factors (e.g. comorbidities[a]) or to reduce hospital access. • Consider telemedicine to monitor patients receiving an outpatient-basis treatment (e.g. oral anticancer drugs, HT).
ECOG PS	0–1 = 0 ≥2 = 1	
Age	<70 = 0 ≥70 = 1	
BMI	<30 = 0 ≥30 = 1	**Score 4–6: intermediate risk** • Consider treatment delays (e.g. modification of treatment schedules) for patients with partial response to treatment. • Consider treatment holidays for patients treated with IT or CT + IT for ≥6 months and/or with complete response to treatment. • Carefully monitor patients with history of irAEs.
Comorbidities[a]	No = 0 Yes = 1 Yes >1 = 2	
Concomitant steroid treatment[b]	No = 0 Yes = 1	
Disease characteristics		**Score ≥7: high risk** • Patients need to be frequently monitored for symptoms, also with the aid of telemedicine. • Variations in laboratory values may indicate subclinical changes. • Maintain treatment schedules only if safe administration is guaranteed; tailor treatment administration depending on the type of treatment and disease response. • Avoid unnecessary procedures (e.g. radiologic examinations) to reduce hospital access.
Thoracic tumour	No = 0 Yes = 1	
History of thoracic RT[c]	No = 0 Yes = 1	
Treatment characteristics		
Line of treatment	Adjuvant = 0 ≥1 = 1	
Type of treatment	HT/TKIs/TT/mAb = 0 CT = 1 IT/IT + CT = 2	

Table 1 (*continued*)

Variables	Score	Categories of risk for patients and for treatment delays during COVID-19 diffusion
History of irAEs[d]	No = 0 Yes = 1 Yes, pneumonitis = 2	
Laboratory values		
NLR	<5 = 0 ≥5 = 1	
LDH	<ULN = 0 ≥ULN = 1	
CRP	<ULN = 0 ≥ULN = 1	

BMI, body mass index; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, chemotherapy; ECOG, Eastern Cooperative Oncology Group; F, female; HT, hormonal therapy; irAEs, immune-related adverse events; IT, immunotherapy; LDH, lactate dehydrogenase; M, male; mAb, monoclonal antibody; NLR, neutrophil-to-lymphocyte ratio; PS; performance status; RT, radiotherapy; TKIs, tyrosine kinase inhibitors; TT, targeted therapy; ULN, upper limit of normal.

[a] Comorbidities include hypertension, cardiovascular disease, diabetes, chronic obstructive pulmonary disease and chronic systemic infections.

[b] Concomitant steroid treatment includes continuous therapy with a dose of >10 mg daily of prednisone equivalent, lasting for more than the 1-month period.

[c] Only for patients with extrathoracic tumours.

[d] Only for patients treated with IT or IT + CT.

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Tele-oncology in the COVID-19 Era: The Way Forward?

- Several organizations have endorsed the use of tele-oncology and issued guidelines for its use during COVID.]. The tiered approach of ESMO advises that low and medium priority cancer patients be referred to tele-oncology services as much as possible.
- The National Health Service in England has issued guidance to support the use of telephone or video consultation wherever possible to minimise face-to-face appointments
- Additionally, if staff have to self-isolate for any reason, they could still continue to provide care and support multidisciplinary teams (MDTs) through video consultations and virtual attendance at MDT meetings

Table 1. Summary of the Advantages and Disadvantages of Telehealth Technologies in Oncology[a]

Technology	Advantages	Disadvantages
Web conferencing	• Low cost • Wide availability	• Limited resolution of images • Participants may not see each other
Video conferencing	• Good image resolution • Participants can see each other • Readily available • Can present/interview patients	• Expensive • Requires maintenance
Tele-synergy	• A multimedia workstation integrates all components for collaborative multidisciplinary tele-oncology • Transmits images from their primary sources • Allows image manipulation • Supports comprehensive multidisciplinary case review and discussion • Supports collaborative planning of radiation and surgery	• Very expensive • Requires ~20 ISDN channels • Requires many peripheral components • Difficult to install • Requires intensive maintenance • Requires dedicated storage space
Virtual tele-microscope	• Operator can control microscope without special hardware or software	• Limited to pathology • Expensive • Performance depends on the user's computer

- Tele-oncology has an immense role to play in the care of cancer patients during this pandemic. It has started to be widely adopted by healthcare systems to reduce the risk of a potentially fatal COVID-19 infection in cancer patients. It is an excellent tool for long-term follow-up of patients, especially those in remote areas
- Tele-oncology has also helped widen collaborations across the world, in particular for challenging cancer cases. Studying the outcomes of patients that are currently receiving altered schedules for cancer care will help detect patient cohorts that may benefit from altered treatment protocols. Data collected from the delivery of care to cancer patients during COVID-19 will also help form care models and predictors for high-risk populations in future epidemics