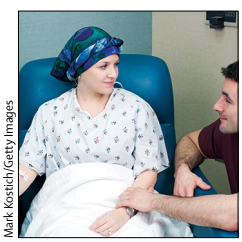
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Cancer and COVID-19: what do we really know?



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The COVID-19 outbreak challenges the medical community, including creating an unprecedented competition for health-care resources. The oncology community has suddenly needed to protect a population assumed to be vulnerable from a potentially fatal infection, without jeopardising cancer treatments. Dealing with shortages and lockdowns, the immediate reaction was ruled by the general principle of risk-to-benefit ratios.[1–4]

In *The Lancet*, Lennard Lee and colleagues[5] and Nicole Kuderer and colleagues[6] separately present early investigations of the largest multicentre studies to date collecting data from patients with COVID-19 who have cancer. The UK Coronavirus Cancer Monitoring Project (UKCCMP) prospectively collected data on 800 patients (median age 69 years, 449 [56%] men, and 349 [44%] women) with active cancer presenting between March 18 and April 26, 2020, with COVID-19. Patients were followed up from the date of hospital admission until the patient outcomes were met (death or discharge), and 226 (28%) patients died. Although risk of death was significantly associated with age, male sex, and comorbidities, no interaction between anticancer treatments within 4 weeks before testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and COVID-19 morbidity or mortality was found.[5] The US COVID-19 and Cancer Consortium (CCC19) analysed prospectively collected data between March 17 and April 16, 2020, from 928 patients (median age 66 years, 468 [50%] men, and 459 [49%] women) with current or past history of cancer who had a presumptive diagnosis of COVID-19 (888 [96%]) or positive (SARS-CoV-2) test (40 [4%]).[6] The primary endpoint was all-cause mortality within 30 days of COVID-19 diagnosis. After a median follow-up of 21 days, 121 (13%) patients died and 242 (26%) were severely ill. Increased 30-day mortality was associated with age, male sex, smoking, comorbidities, Eastern Cooperative Oncology Group performance status, active cancer, region of residence, and receipt of azithromycin plus hydroxychloroquine, but not with anticancer therapy.

The urgency with which data were obtained meant short follow-up times and high proportions of missing data. The mortality rate observed by the UKCCMP was probably due to the selection of patients who were admitted to hospital, underlying the need for data from patients without cancer from a matched population. Moreover, ending the observation after discharge does not capture the full disease trajectory. Similarly, for CCC19, by limiting observation to 30 days, and with follow-up data missing for 80 (61%) of 132 patients admitted to the intensive care unit (ICU), mortality rates are likely to increase. Subsequently, both studies are missing important data, without concise definitions of viral and cancer stage and status.

The main lesson that we might deduce from both studies is that standard oncological care should be offered if feasible, including chemotherapy administration. We strongly encourage the continuation of these and other projects that will add pieces to the complex COVID-19 puzzle and the disease's interactions with cancer and cancer treatments. Will COVID-19 negatively affect active oncological treatments or, on the contrary, might anticancer therapy be protective against the cytokine storm caused by SARS-CoV-2?[7–9] Are disease stage and status important for these interactions?

After counting the number of SARS-CoV-2 infections, hospital, and ICU admissions, and measuring mortality and acquirement of immunity, we will start measuring excess mortality, and comparing expected mortality country-wise with that during the pandemic. However, this measurement is not so simple, as data show that the lockdown influences other types of mortality. Whether the shortages of non-COVID-19-related health-care provisions will affect oncological and cardiovascular mortality is too early to predict.[10,11]

Finally, we must focus on improving future research, prospectively collecting all relevant data considering the specific local background, encouraging international collaboration, and setting a clear goal to stop, contain, control, delay, and reduce the effects of this virus at every opportunity, never forgetting that we will keep fighting together on behalf of our patients with cancer.

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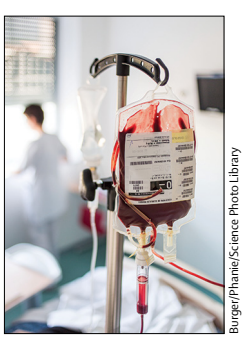
Tranexamic acid for severe gastrointestinal bleeding

Severe gastrointestinal bleeding is frequent and associated with use of blood products and endoscopic and invasive procedures, including emergency surgery, which increases the risk of mortality.[1] Interventions to stop bleeding include the use (often in an escalating manner) of proton-pump inhibitors, transfusion of blood products, therapeutic endoscopy, endovascular coiling, and open laparotomy.[1,2] Tranexamic acid is also used in some patients in an attempt to inhibit blood clot breakdown by fibrinolysis that can occur in some cases.[3] The use of tranexamic acid is supported by data from randomised trials and systematic reviews in patient groups with other conditions, including major trauma,[4] post-partum haemorrhage,[5] and surgery,[6] in whom the use of tranexamic acid reduces mortality or bleeding with few adverse events. In patients with severe gastrointestinal bleeding, the evidence for the benefit of tranexamic acid has been unclear because existing data have come from few and small randomised trials, most of which had a high risk of bias.[7]

In *The Lancet,* the HALT-IT Trial Collaborators[8] report the results of a randomised, double-blind, placebo-controlled trial investigating the effects of tranexamic acid in 12 009 adults (4266 [35·5%] female, 7743 [64·5%] male) with severe gastrointestinal bleeding, the majority of whom had signs of upper gastrointestinal bleeding. Patients were given a loading dose of 1 g tranexamic acid, which was added to 100 mL infusion bag of 0·9% sodium chloride and infused by slow intravenous injection over 10 min, followed by a maintenance dose of 3 g tranexamic acid added to 1 L of any isotonic intravenous solution and infused at 125 mg/h for 24 h. Death due to bleeding within 5 days (primary outcome) occurred in 222 (4%) of 5956 patients in the tranexamic acid group and in 226 (4%) of 5981 patients in the placebo group (risk ratio [RR] 0·99, 95% CI 0·82–1·18). The primary result was supported by sensitivity analyses, subgroup analyses, and analysis of 28-day all-cause mortality. There were no differences between the trial intervention groups in the use of other interventions for gastrointestinal bleeding and in the total number of serious adverse events. Tranexamic acid was associated with an increased risk of venous thromboembolic events (RR 1·85, 95 CI 1·15–2·98) and seizures (1·73, 1·03–2·93).[8]

The HALT-IT trial has all the strengths of a large, well conducted, pragmatic randomised trial, and the recruitment of patients in both high-income and low-and-middle-income countries increased the generalisability of the results. The primary outcome of HALT-IT, and thus the sample size, was changed during the trial, but this appeared well founded and appropriately handled. Although the primary outcome is sensible from a methodological point of view, all-cause mortality at longer follow-up is likely to be more important to patients than mortality due to bleeding within 5 days. The analysis and reporting of adverse events may also be discussed. The HALT-IT Trial Collaborators analysed each of the 14 adverse events as single outcomes, but not as a composite outcome, thereby increasing the risk of both type 1 and type 2 errors (in total, more than 40 outcomes were analysed). The estimate of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