Letter to the Editor

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Love (Pancreatic Surgery) in the Time of Cholera (COVID-19)

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Dear Editor,

As of April 4, the Italian Health Ministry reports more than 120,000 total cases and 15,000 deaths from coronavirus disease 2019 (COVID-19) nationwide [1]. Because of the striking and often unforeseeable rapidity of respiratory deterioration, about 10–25% of hospitalized patients require invasive ventilation [2]. This has led to an unprecedented challenge for healthcare providers, especially in northern Italy, the nation's center of severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) outbreak. Although Italy's national health system has 3.2 hospital beds per 1,000 people (as compared with 2.8 in the USA), the ability to test, contain people with suspected infection, and meet the needs of critically ill patients simultaneously has been outpaced.

After a time-lag of few weeks, in other countries – including the USA – hospitals are now overflowing with COVID-19 patients. With the aim of reducing unnecessary patient traffic in the hospitals, protecting the safety of healthcare professionals, and allocating potentially scarce resources for the care of COVID-19 patients, the American College of Surgeons has recommended that hospital leaderships review and curtail all elective procedures until the predicted inflection point of the SARS-CoV-2 exposure graph is reached [3]. However, most surgical cases in tertiary care hospitals are scheduled for malignancies, which will continue to progress at variable, disease-specific rates.

Among solid tumors, pancreatic ductal adenocarcinoma portends a postoperative survival rate of only 30–35 months when a multimodal treatment strategy, including chemotherapy or chemoradiation is applied [4, 5]. Furthermore, the risk of PDAC progression with care delay is very high [6]. We herein describe the dynamics associated with SARS-CoV-2 outbreak at the Verona Pancreas Institute, a national referral center located in northern Italy and performing about 500 pancreatic resections annually. Furthermore, we discuss practical hints for patient triaging in pancreatic cancer surgery.

The number of COVID-19 cases skyrocketed in Veneto region and Verona area in mid-March. Our hospital had been shortly after designated as a regional COVID hub. Because of a very rapid shortage of ventilators, non-emergent surgical procedures were initially halved and then canceled as of March 16, when the operating theaters were reshaped into makeshift ICU. After 2 weeks, thanks to the opening of additional ICU spots, pancreatic procedures were resumed at 25% of the usual volume.

The shortage of operative slots calls for a framework to guide the patient selection process. More than 70% of patients operated at our institution are from outside Veneto and live a considerable distance away. Although traveling is against the principle of limiting people circulation, a selection process based primarily on geographical criteria would contrast the patient's right of choosing his/her care

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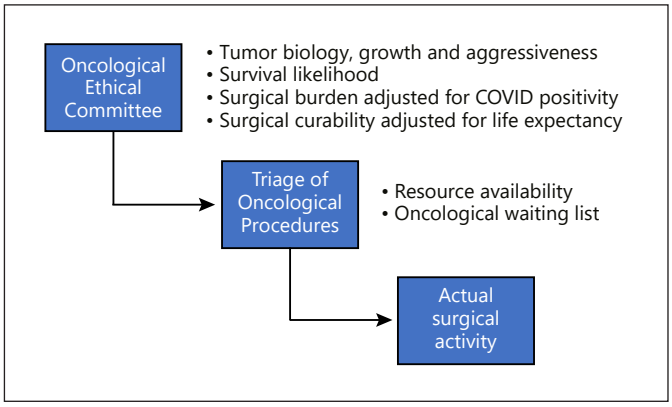

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Fig. 1. Flowchart of elective oncologic surgery during a pandemic.

providers, an important aspect in pancreatic surgery, whereby the volume-outcome correlation is well established. Nonetheless, the sharp reduction of domestic flights and high-speed train frequencies has led some patients from southern Italy to withdraw from our waiting list and seek immediate care at their local institutions.

The 2nd and most important question is which type of pancreatic malignancies prioritizes for surgery. During the highest peak of SARS-CoV-2 outbreak, in a "damage-control perspective," there may be no room for pancreatic surgery because of the associated postoperative complications (with a 20% rate of ICU admission), the elevated costs, and the relatively poor oncologic outcomes as compared to other cancers. Yet, the plateau phase Italy has entered – the duration of which could be in the range of several weeks to months – will likely prolong the operative slots constraints and the surgical waiting list. Therefore, in accordance with the Italian Society of Surgery and the American College of Surgeons, an Oncological Review/Ethics Committee, composed of surgeons, oncologists, radiation oncologists, anesthesiologists, radiologists, and psycho-oncologists has been established to provide clear and equitable judgment (Fig. 1). The plans for case triage are also shared with hospital administrators to account for local circumstances and site-specific COVID-19 prevalence. Recommendations based on our approach to pancreatic surgery in a COVID hub with reduced resources for elective cancer cases are as follows:

Upfront pancreatectomy for PDAC should be discouraged. The Oncological Review Committees should always consider neoadjuvant therapy, which acts as a biology equalizer at every stage of localized PDAC. Nonetheless, the authors are aware that in certain circumstances, concern may arise as to whether chemotherapy-induced immunosuppression could increase the risk of becoming seriously ill from COVID-19.

Patients eligible for surgical exploration following neoadjuvant/induction chemotherapy or chemoradiation should be prioritized. It has been indeed shown that the rate of post-pancreatectomy morbidity following neoadjuvant therapy is reduced, despite the clinical burden of complications could be remarkable [7]. However, there is a wide spectrum of surgical candidates following primary chemotherapy, ranging from resectable patients to patients exhibiting major solid tumor contacts with peripancreatic vasculature, in whom vascular resection is anticipated. For these latter cases with a high likelihood of prolonged operative time, blood loss, and postoperative ICU utilization, the risk of surgical delay to the individual patient must be carefully balanced against the imminent availability of these resources for patients with COVID-19.

Although PDAC is by far the most common malignancy, attention should be paid to other cancer types, including ampullary and duodenal adenocarcinoma, which are associated with a better prognosis relative to PDAC. Remarkably, no neoadjuvant strategies have been established for these cancer types.

All patients scheduled for pancreatectomy should be tested for SARS-CoV-2 prior to hospital admission. Positive testing imposes surgical delay and re-testing following a 14-day quarantine period.

COVID-19 is a competing risk for patients requiring surgical care. Age and comorbidities should be carefully weighed against the expected oncological outcomes and the risk of severe symptoms and mortality in the circumstances of COVID-19 during the postoperative period or recovery phase.

Pancreatectomies for low-grade or benign neoplasms should be delayed.

These hints can be coupled with general principles provided from surgical associations around the world as we triage pancreatic cancer patients during the pandemic:

- Prioritize the protection of all healthcare providers (#SavetheHospital).
- Convert to virtual practices (electronic messaging, telephone, and vide ocalls) for patient visits and multidisciplinary boards.
- Allocate psychological-support resources to help patients, families, and providers dealing with disruption of normal services.
- Stay in touch with patients whose surgery has been delayed, in order to monitor their clinical conditions and improve the quality of life during this difficult period.

This may prevent any feelings of abandonment that patients may experience.

– Interrupt research programs on technical innovation in surgery (e.g., minimally invasive surgery and robotic surgery programs) if funded by public institutions, given the possible upcoming severe economic recession.

The authors are aware that these recommendations are not evidence based. However, we are abruptly asked to make decisions for which many of us will not be prepared. Shared recommendations by Oncological Review Committees can help optimizing the resource allocation process and mitigate the enormous emotional burden to which we are individually exposed in an unprecedented crisis. Because of its aggressive biology, PDAC would virtually require immediate care. Many pancreatic cancer patients in Italy will receive suboptimal care or even no treatment as referral hospitals are carrying the catastrophic brunt of thousands of COVID-19 cases. These "indirect" deaths that will inevitably occur, although hard to track, should be added to the overall lethality of SARS-CoV-2 as the outbreak has finally faded away. In these difficult times, our love (pancreatic surgery) in the time of cholera (COVID-19) is tremendously struggling.

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Authors Contributions

All authors contributed equally.

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