

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. of the randomized trials he points out, as well as the 1995 meta-analysis of the 10-year survival in 7 randomized trials, which also showed equivalent outcomes between breast-conserving therapy (BCT) and mastectomy for patients with early-stage breast cancer (ESBC).²

First, while we absolutely acknowledge limitations inherent in retrospective studies, we need to recognize that much has changed, both in our understanding and management of breast cancer, since these trial patients were enrolled over 30 years ago. Our knowledge of breast cancer subtypes, radio-sensitivities and resistances, local recurrence, and metastatic potential has enhanced our understanding of breast cancer biology significantly since that time. Additional advances were also made in nonoperational management, which include preoperative imaging and diagnostics, pathologic evaluation of margins and nodal status, and systemic adjuvant and neoadjuvant therapies—just to name a few.

Second, we do not believe that the results of a single retrospective study in isolation should lead to a complete change in practice; and in this particular case, we are not encouraging an abandonment of mastectomy for ESBC. However, our results are not in isolation. They complement those of several other very large, modern retrospective studies in which BCT demonstrated improved survival over mastectomy. We outlined several potential mechanisms for this in our discussion, as others have done as well. Third, quite contrary to our results, there has been an observed increase in the use of mastectomy for ESBC in the US—an alarming trend that appears to have no basis in improving outcomes.³

Therefore, in light of these factors, we do think that our results (and those like it) should give the breast cancer community a moment of pause and an opportunity to reconsider and re-evaluate the paradigms that have driven our field for the past 30 years, especially when so much has changed in the interim.

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Elective Operation Scheduling during the COVID-19 Pandemic



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We were greatly interested to read the article by Prachand and colleagues¹ on the scoring system that empowers surgery departments to prioritize medically necessary operations that should not be delayed because of risk associated with COVID-19. COVID-19 is reducing the ability to perform surgical procedures worldwide, giving rise to a multitude of ethical and medical dilemmas. A critical issue is balancing the benefit of surgery against the unknown risk of developing COVID-19 and its associated complications. All elective/nonurgent procedures have been cancelled or postponed to a later date all over the globe. In such a scenario, this scoring system seems to be a promising tool for assessing and scheduling elective operations.

There are a few concerns regarding the Medically Necessary, Time Sensitive (MeNTS) instrument, which has been proposed to stratify cases for operation. Surgical team size under the "Procedure" factor starts with a scoring of 1 for 1 member. Most operations would require at least a team of 2 surgeons to operate. Also, the experience of the surgeons has not been taken into consideration. In a recently published paper by Shrikhande and colleagues,² 494 elective cancer operations were performed, and postoperatively, 6 patients tested positive for COVID-19. These procedures were performed by surgical teams with an average age of 40 years led by senior consultants with an average age of 48 years. All had higher grade operations, but none required escalated or intensive care treatment related to COVID infection. Risk of COVID transmission increases with prolonged operation and we feel, to mitigate this, surgical teams should have experienced surgeons guided by senior consultants.

The Royal College of Surgeons published guidelines on good practice for surgical teams during COVID-19 on March 31.³ However, advice is lacking on operation selection when more than 1 procedure is available. One must also ask, how does this affect longterm outcomes? Does the short-term benefit outweigh the long-term risk? Does medical/conservative management have better long-term outcomes in comparison to operation?

The scoring system does not take into consideration the diagnostic burden and the number of contacts the patient

has to encounter when getting prepped for elective operation. Gastrointestinal malignancies, for example, would require CT scans, colonoscopies, X-rays, etc, and this would result in multiple consultations with other departments, which can result in further spread of COVID-19 because of asymptomatic patients.

The audit, which was done for a period of 6 days, totalling 41 patients, was very miniscule. The subset factors under the "Patient" heading include variables such as loss of blood and operating time, which are subjective and highly variable, depending on the operating surgeon. Also, we believe the impact on 2-week and 6week delays on disease progression and surgical difficulty has a huge spectrum of variation for benign and malignant diseases.

Densely populated developing countries have a huge disease burden. There are about 1 million new cancer cases in India, of which around 0.2 million will require operation. In the absence of surgery, most patients will experience disease progression with resultant mortality. Given that death due to COVID-19 in India is 99 per million of population, with case fatality rate of about 3%,⁴ the cancer mortality in absence of definitive surgery will far exceed the mortality due to infection with COVID-19.

Shrikhande and associates² at the TATA Memorial Cancer Institute in Mumbai have done 494 elective cancer operations during the COVID pandemic, of which 423 (85.6%) were higher grade complex procedures (IV–VI). Six patients tested positive for COVID-19 postoperatively. However, all patients recovered, and there were no deaths. The results were achieved based on individual case selection, adopting best surgical practices and having the best operating teams.

Though the MeNTS instrument looks promising, it needs further validation and should comply with the AGREE guidelines reporting checklist.⁵ Also, clinical judgment, ethical decision-making, and individual case selection can supersede patient selection.

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Normal Response to Fibrinolytic Challenge in COVID-19 Patients: Viscoelastic Evaluation Using Urokinase-Modified Thromboelastography

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Patients hospitalized with COVID-19 frequently show coagulation derangements, such as prothrombin time and D-dimer elevation, resulting in a tendency toward thrombosis.1 Administration of increased doses of antithrombotic prophylaxis has been proposed for critically ill patients.² We have recently shown that thromboelastography (TEG) parameters are consistent with hypercoagulability in patients with COVID-19, as shown by short reaction times, K values, and increased maximum amplitude of the TEG tracings.³ Another feature of COVID-19 coagulopathy might reside in fibrinolysis alteration, even though high D-dimer might indicate hyperactive fibrinolysis. In the recent article by Wright and colleagues,⁴ increased persistence of clot firmness at TEG was observed in the majority of patients with severe COVID-19, and this pattern predicted venous thromboembolic episodes, as well as need for hemodialysis. Lastly, Nougier and colleagues⁵ reported hypofibrinolysis associated with raised plasminogen activator inhibitor 1 in patients with COVID-19, and high thrombin generation capacity was maintained. This combination leads to simultaneous hypercoagulability and hypofibrinolysis, eventually increasing risk for thrombosis.

We reported previously that a modified TEG assay named urokinase-modified TEG (UK-TEG) is a feasible bedside tool to detect sepsis-induced defective fibrinolysis in real time.⁶ Briefly, 4 µL urokinase (Urochinasi Crinos,