

Management of surgical lung cancer patients during the COVID-19 pandemic in the financially and resource strained Greek health care system

To the Editor,

In 430 bc, the city-state of Athens suffered a plague that caused it to lose the Second Peloponnesian War as well as one of its greatest statesmen, Pericles, son of Xanthippus. Today, more than 2500 years later, our country is amidst a new global pandemic afflicting both the available medical resources and our society's cohesive structure.

Infectious disease outbreaks are indeed a period of great uncertainty for societies. In many countries, such crises can rapidly overwhelm the capacities of health care systems, forcing physicians to make difficult decisions about the allocation of available resources and even more, about human lives. Therefore, critical decisions for public health protection have to be made promptly before the limited capacities of the medical system become further stretched leading to a system collapse. During such distressing times, ethical questions concerning the allocation of medical interventions and medications or the utilization of health care resources often arise.

Health care delivery was markedly affected by the financial crisis in Greece, which has been experiencing severe economic hardship and political turmoil since 2008. The implemented fiscal control-centered policies and public health expenditure reductions of up to 43% between 2009 and 2014 have decreased the extent and the service quality provided by the hospitals in the Greek National Health Care System (NHS).¹ During this time, it has been particularly challenging to continue providing quality lung cancer care to our patients. The financial crisis has hindered our ability as health service providers to ensure the best possible results in accordance with the current scientific knowledge, using the most effective and modern surgical techniques and protocols with minor-associated iatrogenic risk.^{1,2} Naturally, the current coronavirus disease (COVID-19) pandemic introduces significant new and urgent constraints in an already overstretched system. The Greek government, as most other governments worldwide, focused on the immediate threat downgrading all other nonurgent medical care. The lack of resources, especially intensive care (ICU) beds (the median number of ICU beds in Greece are far below the median number/habitant in the European Union), isolation wards, and chronic staff shortages, forced the government to cease all nonurgent/nonpriority surgery and reduce the number of daily operations performed, including thoracic surgery, repurpose cardiothoracic ICUs, and combine non-COVID-19 wards so as to create dedicated COVID-19 ones to care for infected patients. This was done *carte blanche* in all public hospital-based

surgical units across the country regardless of their designation as a COVID-19 care facility or not. In addition, regular outpatient clinics were also canceled.

As a result, diagnosis and management of malignancy, including lung cancer, has been significantly hindered, although theoretically it still remains a priority for the Greek NHS. Lung cancer is the most common cause of cancer death with 1 761 007 deaths worldwide in 2018.³ However, lung cancer surgical treatment in our country has now become even more challenging as it has to adapt to the new resource diversions and pandemic practice restrictions and risks.

We wish to present the ethical dilemmas and worries that we as Greek lung cancer specialists are facing during the COVID-19 outbreak and present the necessary management adjustments we have to undertake for patients with operable lung cancer so as to continue providing them with quality medical care in a chronically resource-starved health system during this pandemic.

It has been suggested that patients with cancer are more susceptible to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. A recent study from China, reporting on the effect of the outbreak of severe acute respiratory syndrome SARS-CoV-2, indicated that patients with a history of cancer, mainly lung, had a higher risk of severe events (admission to the ICU, acute respiratory distress syndrome), and need for invasive ventilation) as well as poorer outcomes (death).⁴ Such susceptibility of lung cancer patients to SARS-CoV-2 infection could be explained by the respiratory insufficiency directly related to malignancy, the immunosuppressive status as a result of systemic treatment, and their associated comorbidities, most commonly chronic obstructive pulmonary disease linked to their habitual smoking history.⁴ Moreover, patients with less than 1 month history of surgery or chemotherapy had a higher risk of clinically severe events compared to other patients.⁴

Therefore, the strategy adapted by most surgical teams worldwide was to try reducing the potential exposure risk of cancer patients by postponing surgeries and invasive diagnostic procedures with high infective potential such as bronchoscopy and endobronchial ultrasound-guided biopsy. Management is relying more on noninvasive imaging modalities such as positron emission tomography (PET) and in rescheduling regular follow-up appointments or conducting them via telemedicine.

However, postponing lung cancer-related surgery is not always feasible as many of these patients need prompt treatment. In case of

other forms of cancer, such as colorectal, the 10-year survival is known to be lower if the treatment is started more than 90 days from diagnosis, while the ideal time for its resection has been estimated to be between 3 and 6 weeks from diagnosis.⁵ Similar studies that have investigated the association of the time from lung cancer diagnosis to surgery and survival have shown conflicting results mainly due to molecular heterogeneity and the associated growth rates, as estimated by volume doubling times, which are highly variable depending on histological subtype.^{6,7} For example, a median doubling rate at 191 days (6 months) for lung cancer has been reported in the literature; however, patients with stage IA squamous cell carcinoma, who had surgery 38 days or more after diagnosis, had significantly worse 5-year survival than patients who had surgery earlier.^{6,7}

In our everyday clinical practice, we as surgeons, respiratory physicians, and oncologists have to deal with considerable ethical dilemma concerning decisions of delaying or cancelling cancer-related surgery. We have to consider the potential harms of such decisions and the appropriate management of these patients while postponing surgical intervention.⁸ However previously, the cases that required such decisions, in contrast to the current situation, were few and there was more flexibility in developing our management plan as resources were more readily available. No clear formal guidance existed and we relied more on individual assessment and a multidisciplinary approach in making those decisions.

Consequently, the global pandemic caught most national and international surgical societies and organizations unprepared for such an unprecedented event, with many scrambling to produce surgical management and handling guidelines.⁹⁻¹³ This has caused quite variability on recommendations, partly due to regional differences in resources and practices.¹¹ However, there is one common theme that most recommendations agree upon: "cancer patients should receive appropriate and prompt surgical care depending on the availability of resources taking into consideration the options of nonsurgical management whenever possible."^{10,12,13}

Therefore, the main ethical dilemma most surgeons are facing currently is not only how to provide oncologic surgery to patients safely, by minimizing the risk of SARS-CoV-2 infection, but also of other potential complications realizing that the resources available to manage them are reduced. In addition, they have to consider the need of providing continuous surgical management of cancer patients to avoid "losing the window to treat" and consequently, face a later increase in their mortality due to

suboptimal treatment.^{8,12} If surgery is not possible, they need to consider the alternative of the previous neoadjuvant chemotherapy provided that it is an available safe option given its immunosuppression and associated risks.⁸ Consequently, balancing risk of therapy vs the availability of resources, such as blood products and ICU beds, in such dynamic circumstances demands exceptional virtuosity, and obviously established priorities and indicators of quality standards need to be reset and adapted.^{5,8}

Considering the above and wishing to preserve the principles of respect for individual person, nonmaleficence (avoiding harm) and justice, our medical team formulated a management plan utilizing recommendations from national and international bodies adapted to the Greek health care system constraints and idiosyncrasies.

Most recommendations advice maintaining a multiple professional perspective while making individualized patient management decisions.^{10,11,13} In this regard, we also continued our multidisciplinary oncological council assessment of new and postoperative cases, however reducing the number of participants to key specialties (surgery, respiratory medicine and oncology) and transforming them into virtual instead of in-person meetings. Cases to be discussed are distributed well in advance so that all participants can review the medical file and radiology reports.

Following published advice and our own team's consensus, we formulated a management plan in which surgery in previously diagnosed patients with stage Ia to IIa disease was postponed for 8 weeks (Table 1). This is slightly longer than the length utilized by other teams; but as all recommended postponement periods are actually arbitrary, this length was decided after balancing lung cancer growth rates with the Greek system's known waiting times.⁹⁻¹² A more intensive surveillance schedule was decided for these patients with new imaging obtained every 6 weeks.

Surgery is still performed in selected patients with a disease stage with a high (>50%) curative rate and a low risk profile in which resection can be performed as minimally invasive as possible, and providing a short hospital stay is probable (Table 1). All such patients are initially screened for symptoms (fever, cough, myalgia, fatigue, and diarrhea), and surgery is performed only after laboratory testing for SARS-COV-2 virus with nucleic acid amplification analysis.¹⁴ Procedures are performed with the minimal amount of surgical staff (surgeon and assistant), usually of middle to senior grade. Unfortunately, due to the need for expedience and to minimize staff exposure risk, surgical training has been significantly curtailed.

TABLE 1 Management recommendations for surgical lung cancer patients utilized in our unit

Lung cancer stage		
Ia-IIa	IIb-IIIa	IIIb
Postpone surgery for 8 wk following multidisciplinary team review	Induction chemotherapy for 2 cycles	Chemotherapy for downstaging according to established strategies
Surgery performed in certain low-risk patients with high potential for curative resection		Chemotherapy continued for 1 additional cycle or surgery performed in low-risk patients
6-wk follow-up with new imaging		Follow-up as per protocol

The patients with IIb and IIIa disease were the subject of significant discussion amongst us because no clear recommendations exist. On the basis of suggestions and considering the risk vs the need to provide some form of treatment to these patients, we decided that these patients should be referred for induction chemotherapy for at least two cycles (Table 1). Our chemotherapy unit is staffed with dedicated staff and since the beginning of the pandemic has taken steps to isolate patients receiving chemotherapy and minimize their exposure to infection by implementing stronger personal protection provisions, limiting the number of people accompanying patients to a single companion and providing dedicated entrance and exit routes.

Patients with stage IIIb lung cancer, which is potentially resectable following downstaging strategies, continue to be referred for induction chemotherapy, but again measures are taken by our oncology colleagues to minimize infection exposure risk and possible complications. Patients which have responded to induction chemotherapy either continue treatment for an additional cycle or are referred for surgery depending on their associated risk profile as provided above (Table 1).

Although, as per guidance, we have been trying to reduce the number of invasive diagnostic and staging procedures relying more on imaging (computed tomography [CT] and PET CT) to make diagnosis, some minor procedures continue to be performed in an outpatient and as small day cases with significant exposure precautions for staff and patients.¹³ Because bronchoscopic procedures are aerosol generating, special attention has to be paid in reducing the potential for the transmission of COVID-19 infection. However, in patients with a low risk of COVID-19 infection with urgent conditions or for whom a potential diagnostic delay would be detrimental to their prognosis, bronchoscopy is performed after laboratory testing for SARS-COV-2 virus with nucleic acid amplification tests.¹⁴ CT-guided fine needle core biopsies of peripheral lesions and ultrasound-guided or surgical supraclavicular lymph node biopsies under local anesthetic are still being performed, when necessary, in our hospital as day cases.

As previously mentioned, scheduled outpatient clinics were canceled forcing us to adopt new ways to interact with patients. Most new as well as postoperative follow-up appointments are now conducted via telephone or video calling. The recently implemented electronic distant prescribing system in Greece has been particularly helpful in reducing patient doctor visits. Because a significant percentage of our patients were referrals from outside the metropolitan area of Athens, a scheme was already in place to conduct long-term follow-up evaluations via distance methods. In addition, we have been utilizing comprehensible home wound care discharge instructions so as to eliminate or minimize follow-up doctor visits.

The current pandemic of SARS-COV-2 is indeed an extraordinary challenge for all our health systems. Consequently, there is a need to prepare specific and comprehensive international guidelines and recommendations to address the current situation and also future catastrophic pandemics.

Given the unprecedented nature of the situation we are facing and the chronic deficiencies of our NHS, we as Greek physicians can only hope that the management decisions we are currently making will be of benefit or at least of no harm to our surgical lung cancer patients in the future. The ethical responsibility of these choices weigh heavily on all of us and only time will tell if they were correct. Maybe when making these decisions, we should follow the advice of the Athenian statesman Pericles who perished in that ancient plague long ago "What you leave behind is not what is engraved in stone monuments, but what is woven into the lives of others."¹⁵


CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.


AUTHOR CONTRIBUTIONS

Emmanouil I. Kapetanakis and Ioannis P. Tomos came up with the original concept idea and outline, reviewed the pertinent literature, and wrote the manuscript together. Anna Karakatsani, Anna Koumariou, and Periklis I. Tomos refined the original concept idea, provided guidance, and advice as needed and extensively edited the manuscript. The authors are members of the multidisciplinary team providing lung cancer care at our hospital and face the ethical dilemmas discussed above jointly.

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