

SPECIAL ISSUE

How fragile we are

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Shortly after I finished delivering a keynote lecture on minor salivary gland cancers on 23 February 2020 at the Candiolo Cancer Institute in Turin, Italy, the conference chairs Drs. Giovanni Succo and Piero Nicolai announced that the conference was urgently adjourned and the rest of the program canceled. This unexpected announcement was in compliance with the Italian government's orders to immediately end all public gatherings. Two days earlier as I set out to travel to Italy, where no cases of coronavirus infection had yet been reported, news reports were focused mostly on South Korea and Iran as hotspots of COVID-19. Out of an abundance of caution, I double-checked again before leaving for the airport and confirmed that Italy had no reported cases. Upon my arrival in Turin I was greeted by the usual warm welcome and well-known hospitality of our Italian colleagues. At the welcome reception they discussed the earlier morning report of the first five confirmed cases of COVID-19 in Lombardy region and its capital Milan. The next day, as the unplanned adjournment was announced on the first day of the 3-day conference, there were more than 120 reported cases ushering what would be the first significant outbreak in Europe. The conference chair read the Italian government emergency prohibition of public gatherings, canceling the Milan fashion week, the Venice carnival, and closing all schools and universities. But when he announced that the football (aka Soccer) game was canceled I knew that the situation was grave. As most of us know it almost takes an act of God to cancel a football game in Italy! Without delay I scrambled to get a flight back home only 24 hours after I arrived in Turin. On my way to the airport I saw on my news app that France had stopped a train of passengers from Italy and diverted it back. I was concerned about my connection in Frankfurt and

ultimately getting back to the United States. As I passed every step of screening and temperature checks I finally landed in Houston with a huge sigh of relief. Following instructions that were urgently sent that day, I immediately contacted our employee health at MD Anderson where I was carefully screened and cleared to go back to work.

1 | HOW FRAGILE WE ARE

In less than 6 weeks since my truncated trip to Italy and at the time of writing this Editorial (8 April 2020), there are more than 1.5 million reported cases and more than 85 000 deaths worldwide, and rising.¹ Earlier today as I drove home listening to the radio in my car, Sting was singing, “*How fragile we are.*” As I reflected on the lyrics, I became acutely aware that despite our collective human ingenuity, scientific discoveries, and technological advancements—such as space travel, sequencing of the human genome, massive live data acquisition and instant analysis, harnessing of these data for artificial intelligence, live-connecting people across the globe regardless of distance and time, and creating global economic growth with trade, industry, and innovation—we *remain imminently fragile and infinitely vulnerable*. A previously unknown tiny enemy, which belongs to a family of viruses that measure 120 nm,² and carries a genome size ranging from approximately 27 to 34 kb,³ suddenly challenged our globe beyond our capacity to fight or control it. More than 182 countries are in this battle, and world “superpowers” such as China, Europe, and the United States, with all their technologic might and economic power, have been brought to their knees in their fight against this tiny unseen enemy and continue to endure catastrophic loss of life. This pandemic changed and continues to radically challenge life as we know it, across the globe. All over the world, major cities

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look deserted, students stopped attending schools and universities, travel restrictions abound, restaurants and gyms closed, masked faces are everywhere we go, families can only connect virtually rather than in person, and many people are working remotely or not working at all. Sports events everywhere, including the Olympics, are canceled. Conferences and meetings across the world are rescheduled or canceled. Religious gatherings are mostly online, and business or leisure travel came to a screeching halt. The economy continues to experience a free fall as supply chains are increasingly broken and markets face unabated decline. Our modern life has been turned upside down by a nanoparticle. In contemplating our vulnerable and fragile existence, we all now have to reset our barometer of humility. Our collective humility as humans will probably be an essential weapon in this fight by enhancing our global collaboration and coordination regardless of geography, nationality, economic power, political system, social structure, or culture as we face this common threat to our lives and even our survival.

2 | IMPACT ON HEALTH CARE SYSTEMS

While almost every aspect of our lives has changed, the most dramatic impact of this pandemic is on our health care system. Priorities of care shifted rapidly to combat the virus as a top priority. Significant reduction of non-COVID-19-related health care has been universally recommended and adopted across the world. Care deemed to be “nonessential” or less “critical” is to be deferred until we win this fight. Capacity in the health care systems had to be created to accommodate the rising number of patients with COVID-19 infection, particularly those needing critical care. Hospital beds, intensive care units (ICUs), operating rooms, and emergency services had to gear up for the tsunami of the “surge.” Outpatient care for other medical conditions was drastically diminished to free up downstream resources, personnel, and protective equipment. Virtual care increasingly replaced personal care across the board. In addition to downscaling, as the “surge” hit some of the major metropolitan regions worldwide, health care systems had to quickly adapt by strategies of reallocation, repurposing, and deployment of providers, equipment and resources toward COVID-19 care. The urgent need to increase capacity also prompted the rapid construction of emergency health care facilities, repurposing of existing buildings such as convention centers for health care delivery, and recruiting additional health care support from retired health providers and the military. It is unclear right now how this shift of resources to combat COVID-19 will impact the outcomes of reduced care for other conditions. This will have to be measured after this global crisis is over.

3 | IS CANCER ELECTIVE? COVID VS CANCER

As a cancer specialist, like many others who care for patients with cancer, I was faced with the unimaginable dilemma of responding to the pressure to limit “nonessential” care. *How? Who? When? For how long?* These are the questions that immediately flooded my mind and still haunt me as I think about my previous patients, those currently being cared for by our team of expert oncologists, and new patients seeking our care. This is something we never trained for or dreamed of ever having to face. Cancer centers all over the world have to deal with this medical and largely ethical dilemma. It is a struggle for cancer centers to continue to provide much-needed cancer care while preparing and providing care for the community as they face the wrath of this pandemic coming their way. On the one hand, cancer is inherently life-threatening. How can we possibly “defer” its care? What guidelines, if any, should we follow? On the other hand, patients with cancer may have higher risk of mortality if they contract COVID-19, and cancer treatment itself may increase that risk.⁴ The most comprehensive data available to date on the cancer-specific case fatality rate is a *Report of the WHO-China Joint Mission on Coronavirus Disease* published on 28 February 2020.⁵ This report indicates that in China, as of the data cut-off (20 February 2020), the case fatality rate for patients with cancer as a comorbid condition and laboratory-confirmed infection was 7.6%. This is as compared with: overall 3.8%, no comorbid condition 1.4%, cardiovascular disease 13.2%, diabetes 9.2%, hypertension 8.4%, chronic respiratory disease 8.0%.⁶ By deferring care, are we protecting patients with cancer or are we delaying much-needed treatment for their cancer? These decisions continue to be difficult to make and are based primarily on a case-by-case risk-benefit analysis. In general, the guiding principle for these decisions depends on the nature of the cancer itself and its “aggressiveness.”⁷ Patients who are not harmed by deferring their cancer treatment, such as those with indolent slow-growing cancers, perhaps can have their treatment safely deferred for 8 to 12 weeks until their risk of contracting COVID-19 is lower and their cancer treatment less likely to adversely influence their outcome should they become infected with the virus. The decision with most cancers, however, is more agonizing.

4 | HEAD AND NECK CANCER

Head and neck oncologists have had to face similar decisions, but head and neck cancer (HNC) presents unique challenges that are different from those posed by other

cancers. With few exceptions, such as small basal cell cancers of the skin, well-differentiated thyroid cancer in young patients, low-grade salivary gland carcinomas, and low-grade sarcomas, most HNC is aggressive and life-threatening. Cancer of the upper aerodigestive tract also has the potential to threaten essential functions such as breathing, eating, swallowing, speaking, and vision if allowed to progress to more advanced stages. We also know that delay in treatment for such cancers and advancing stage negatively impact the prognosis. To add to these challenges, patients with HNC are generally elderly and have significant comorbidity, which increases their risk of COVID-19-related death if they contract the infection. In addition, treatment for HNC itself, including surgery, radiation, and systemic therapy, may reduce the patient's ability to combat a COVID-19 infection, and given the limited available data, the increased risk of COVID-19-related mortality in patients with cancer is still not completely known.⁸⁻¹²

Another major challenge in evaluating and treating patients with HNC is the added risk of potential transmission of COVID-19 virus to providers caring for such patients. The added risk stems from the high viral load that resides in the upper aerodigestive tract of infected subjects and its potential transmission from aerosol-generating procedures (AGPs) that are frequently needed in the evaluation and management of patients with HNC. Such procedures include upper aerodigestive endoscopy, intubation, tracheostomy and tracheostomy care, and surgery of the oral cavity, pharynx, larynx, and sinonasal region. Such procedures require added personal protective equipment (PPE) such as N95 masks or Powered, Air-Purifying Respirator (PAPR) for all health care providers to minimize the risk of being infected with COVID-19 while caring for patients with HNC.¹³ The Center for Disease Control (CDC)¹⁴ and the World Health Organization (WHO)¹⁵ advocated the use of added PPE such as N95 masks or PAPR while performing AGPs and recommended that, in times of shortages, these types of PPE should be prioritized for use during AGPs. Such strong recommendations were also emphasized by the American Academy of Otolaryngology, the American Head and Neck Society, the North American Skull Base Society, the American Rhinologic Society, and the American Society of Oromaxillofacial Surgery.

5 | DOES ROUTINE TESTING OF ASYMPTOMATIC PATIENTS HELP?

A recent report from Wuhan, China on 34 asymptomatic patients who had elective surgery during their incubation period of COVID-19 infection demonstrated that all of

them developed COVID-19 pneumonia shortly after surgery with abnormal findings on chest computed tomographic scans. The ICU admission and mortality rates were 44% and 20%, respectively. This makes a very good argument supporting routine preoperative testing of asymptomatic patients undergoing surgery.¹⁶

Given the challenges of making treatment decisions for patients with HNC and the significant added risk of transmission to their health care providers, routine testing for COVID-19 status in these patients, even if asymptomatic, is strongly recommended and is becoming more widely adopted in most HNC treatment centers. Treatment of patients with HNC who test positive for COVID-19 is generally deferred until they recover from their infection. The rationale for this recommendation is 2-fold; minimizing risk to the patient and to the health care providers.

As mentioned, the older age and prevalent comorbidity of patients with HNC pose added risk of mortality if they are COVID-19 positive. This is particularly true for surgical treatment. Major surgery for HNC frequently involves a lengthy procedure for resection and reconstruction, and the immediate postoperative period is complicated by frequent challenges of fluid overload, fluid shifts, reduced lung capacity, and possible postoperative lung atelectasis. These changes might challenge pulmonary function, which is critical to recovery from COVID-19 pneumonia, and may predispose these patients to the need of ventilator support and reduce their chances of recovery.

Given the high density of viral loads in the upper aerodigestive tract of patients who are COVID-19 positive and the aerosol-generating potential of surgical procedures on the mucosal surfaces of the head and neck, the risk of transmission to the surgical team and all operating room personnel, including nursing and anesthesia, is significant.¹³ Therefore, the need for maximal PPE such as PAPRs in caring for such patients is mandatory. Such level of PPE is needed for all involved personnel not just in the operating room but also over the entire course of the patient's recovery throughout the hospital, including the recovery room, ICU, step-down unit, and regular hospital floor. Even after patient discharge this level of PPE is needed in a long-term care facility or home nursing. This is particularly true if the patient undergoes tracheostomy, which is frequently performed as part of HNC resection. All nurses, respiratory therapists, occupational and physical therapists, speech language pathologists, residents, fellows, and attending physicians providing postoperative care will need this added level of PPE for at least a couple of weeks after surgery. In addition to the staggering number of PPEs needed for the care of this one patient, the risk to the hospital environment, other

patients, and mandatory isolation procedures are significant. In conclusion, it seems clear that, for the sake of minimizing risks to the patients, health care providers, and hospital systems, major surgery for HNC should be deferred in patients who test positive for COVID-19 unless it is a lifesaving measure.

Patients with HNC who test negative for COVID-19 should be considered for surgery if delaying such treatment would negatively impact their prognosis. The false-negative rate of testing is not yet known and is influenced by the testing platform, such as viral RNA-based PCR or immunoglobulin serology testing; and on the source, quality, and handling of swab specimens.¹⁷ False-negative rates of 20% to 40% have been reported for swab tests, and the testing accuracy may be significantly increased if complemented with chest imaging showing signs of infection.¹⁸ Because of these limitations, it is recommended that a negative test be interpreted with caution and appropriate PPE such as N95 masks, goggles, gowns, and gloves should be used by all health care providers involved in the surgery and postoperative care of these patients.

For patients presenting with life-threatening emergencies in whom rapid testing is not available or feasible, head and neck surgery and airway procedures should be performed assuming the patient is COVID-19 positive given the high rate of community transmission. In such cases, maximal PPE including PAPRs should be used.

Because of these challenges associated with major oncologic surgery and the need to conserve operating rooms, inpatient beds, ICU capacity, ventilators, and PPE, a recommendation for using outpatient nonsurgical therapy for patients with cancer has been advocated during the pandemic. Nonsurgical therapy may include radiation, chemotherapy, and immunotherapy. These treatments may be used either definitively or in the neoadjuvant setting in order to buy time before needing cancer surgery. Nonsurgical therapy also has inherent challenges in the face of the COVID-19 pandemic. Chemotherapy, in general, is associated with immunosuppression that may put patients with cancer at a higher risk of contracting COVID-19 or developing cancer-treatment-related complications.⁷⁻¹⁰ There are concerns that immunotherapy may increase the inflammatory response to COVID-19-associated pneumonia and promote the acute respiratory distress syndrome that is the main mode of death from this disease.⁷⁻¹⁰ Head and neck radiation may be associated with severe mucositis, poor oral intake, weight loss, dehydration, and fatigue, all of which have yet unknown impact on the risk for patients contracting COVID-19 or developing a more severe disease if they get infected. Radiation therapy also requires daily treatment for a period of 6 weeks, which is challenging for most patients in terms of logistics at a time when stay-home orders are getting more widespread, quarantine requirements

are in effect when crossing state lines, and patients' family members and caregivers are increasingly restricted from accessing the hospitals to accompany patients during their treatment visits.^{11,12}

6 | TRAINING AND EDUCATION

The COVID-19 pandemic also has significant impact on our training programs. The reduction of non-COVID-19 care across the board will have a yet-to-be measured impact on the clinical and surgical training for residents and fellows. Major head and neck oncologic surgery training is usually allocated to senior residents and fellows. In a year when major head and neck oncologic surgery is drastically reduced for 3 to 4 months and nonsurgical therapy is favored, the impact on surgical training could be significant. How will we make up for this deficit? Will surgical video demonstrations or simulations prove adequate to replace hands-on real-life surgery? Tumor boards, weekly teaching rounds, monthly grand rounds, and other trainee educational meetings that constitute the traditional media of didactic teaching have been replaced by online virtual meetings, the effectiveness of which remains to be seen. Local, regional, national, and international educational conferences, symposia, and hands-on courses that are the hallmark of continuing medical education have been postponed or canceled. Board examination, residency and fellowship application, interviews, and selection are being rescheduled or alternative ways of executing them are being explored. The effects of such changes on training and education remain unknown.

On the other hand, trainees who currently are integral members of the health care response to this global pandemic are likely to acquire skills that they would have otherwise not gained. Emergency preparedness, crisis management, and frontline lifesaving clinical expertise are some examples of such skills. In some parts of the world, including some regions in the United States, fourth-year medical students will act as interns, senior residents will assume fellows' responsibilities, and fellows may have to be appointed as independent practitioners. I have no doubt they will rise to the occasion. They always do.

7 | OUR RESPONSE: THE AMERICAN SPIRIT

The response to contain or mitigate the effects of this pandemic has been different in various parts of the world. When the first outbreak in Wuhan, China, was clearly erupting, the Chinese government imposed an enforced lockdown in the entire Hubei province. This lockdown

was augmented with stay-home orders and limitations on population movement across the entire country. These measures as severe as they may seem, succeeded in containing the effects of the epidemic to Hubei province. Resources such as medical personnel, equipment, and PPE were then mobilized to the one province where the epidemic was contained. The result is that 90% of the 82 000 cases and the 3300 deaths in China were limited to the Hubei province.¹ Major metropolitan regions and cities such as Beijing and Shanghai, which looked like ghost towns for at least 2 months, were largely spared of being the next hot spots and experienced limited mortality. Other Asian countries such as South Korea and Singapore had a different approach that applied massive broad testing, case isolation, contact tracing, and further testing and isolation of such case contacts. Both countries have had the most successful results, with South Korea having a total of 186 deaths and Singapore only 6 deaths to date.¹ As the pandemic spread to Western societies such as Europe and the United States, strategies of social distancing rather than enforced quarantines were more widely adopted with varying degrees of compliance. Testing capabilities were not as robust as in Asian countries, and case identification and contact tracing were less widely applied. In the United States, broad population testing faced challenges and delays, and uniform adoption of social distancing measures across the country was slower. Stay-home orders continue to be at the state jurisdiction level rather than a federal mandate. The global differences in response may be the result of differences in culture, government, political structure, values, and resources. Freedom, autonomy, and individual liberty are precious values in the United States and form the basis of our democracy that we all treasure. Over the years Americans fought to protect this democracy and sacrificed their lives to maintain it, a choice I would personally make if needed to preserve it. I pray that our freedom and autonomy does not cost us avoidable and catastrophic loss of life in the fight against this pandemic. At times such as these our collective sacrifice of personal freedom for the good of our country and fellow citizens is critical. During this unprecedented crisis we need to demonstrate that our democracy is our strongest attribute not our greatest vulnerability.

That brings me to my unshakable belief that in this country we will win this fight because of a unique weapon we share, the *American spirit*. This common spirit is routed in our determination to face any challenge with a matching resilience. The ingredients of this spirit are courage, faith, hope, and the commitment to prevail. As the challenge raises so does our resolve. As a young immigrant physician in the United States, I was awestruck by this spirit when I started caring for patients with cancer. In many cultures the diagnosis of cancer

was considered too tough to handle by patients and their families and, therefore, one that should be veiled from patients or their loved ones to protect them from fear and anxiety. In contrast, I observed that American patients wanted to know the gravity of their cancer, available treatments, and chances of success. They wanted to gauge their challenge to match it with a determination to win.

Our response to this pandemic is already showing the best of this American spirit. In New York alone, 40 000 retired physicians chose to leave the security and safety of their retirement and go back to the workforce facing the risks to their lives and heading in harm's way to save others. Most of them are over 65 years of age, and at least one of them is 85 years old! A sports team from the state of Massachusetts, the New England Patriots, arranged to have the team's airplane transport PPE and other supplies from China to support frontline health care workers not only in their home state of Massachusetts but also their neighboring state of New York. This involved complex collaboration between the Chinese authorities; an American sports team owner; and two US governors, one a republican and the other a democrat. Our military has engaged all its might to stand along all of us in this fight, from building hospitals in record times, deploying assets and personnel where needed, and providing large-scale logistical support. Civilians in almost every household, including mine, are producing homemade masks for others that need them. These are just a few examples of countless acts of service, courage, solidarity, goodwill, and unity, and many others abound across our nation.

The American spirit not only embodies hope, faith, and courage, it also sparks unmatched *innovation* in dealing with challenging times of crisis. For example, 3-D printing is being widely adopted in many labs and hospitals to augment our PPE and other supplies. Several hospitals and scientists are racing to develop faster, more reliable, and high-throughput tests, new effective therapeutics, and several vaccine platforms, and innovative treatment approaches augmenting convalescent sera for wide-scale therapy. The power of data technology is harnessed to bring fast and deep learning about the epidemiology of the outbreak and data modeling to combat it. Telecommunication is rapidly developing to accommodate new ways of doing business, learning, communication, and most notably innovative ways of health care delivery outside the traditional hospital or clinic setting. Such changes will undoubtedly enrich our health care system long after the pandemic is gone.

Finally, the American spirit inspires normal citizens to emerge as local selfless and courageous *leaders* in times of crisis. This is seen across the entire spectrum of our country but most notably in our health care providers. You can

witness this response in every hospital, clinic, ICU, emergency room, operating room, and nursing home. Our profession is one of sacrifice and dedication to save the lives of others, even at times when it is at our own risk.

We also need to reach out and collaborate with colleagues across the globe to fight this common enemy regardless of geography, nationality, culture, values, or political system. Our department, like many other departments across our nation, has received unsolicited donations of PPE from our colleagues and alumni from China. These acts of kindness and solidarity are uniting us with our international colleagues more than ever. Many colleagues from China, Hong Kong, Singapore, and South Korea, eager to help, have shared their clinical protocols and regional experiences treating COVID-19 and HNC during the pandemic. We thank all of them for the help, kindness, generosity, and support they extended to us during this crisis. This special issue of *Head & Neck*, "Covid-19 Versus Cancer," is dedicated to providing and disseminating information about the unique challenges of our patients, who not only suffer from the burdens of HNC but now also face the added risk of COVID-19. I would like to thank our publisher, Wiley, for making this special issue available for full content download anywhere in the world. Recommendations for managing these challenges are evolving and undoubtedly will be updated as we gain more knowledge and experience with this novel virus and its impact on patients with cancer. When we prevail over this pandemic, we will have learned so much from each other and will be ever more ready to face the next challenge. It is our duty and our honor.

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