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The Untold Toll — The Pandemic's Effects on Patients without Covid-19

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In late March, Zoran Lasic, an interventional cardiologist at Jamaica Hospital Medical Center and Lenox Hill Hospital in New York, was finishing afternoon clinic when he was approached by a nurse colleague seeking his advice. Her husband — a 56-year-old whose father died of sudden cardiac arrest at 55 — had been feeling chest pressure. The pressure radiated down his arms and occasionally to his neck and, the previous day, had been accompanied by dyspnea and diaphoresis, making him worried enough to call an ambulance. The emergency medical technicians did an electrocardiogram, said it looked OK, and told him to call his primary care doctor. He did, and he was advised that given New York's Covid-19 outbreak, it was not a good time to go to the hospital. Now, a day later, his colleague asked Lasic, what should they do?

Nearly apoplectic, Lasic advised urgent coronary angiography, which he performed a few hours later. The man had a thrombus extending from his proximal-to-midleft anterior descending artery and became hemodynamically unstable during the procedure. Nevertheless, revascularization was successful, and he was discharged the following day with preserved left ventricular function. Lasic, describing a precipitous decline across the New York region in patients presenting with acute coronary syndromes, worries that others won't be so lucky. "I think the toll on non-Covid patients will be much greater than Covid deaths," he said.

As the coronavirus pandemic focuses medical attention on treating affected patients and protecting others from infection, how do we best care for people with non–Covid-related disease? For some, new risks may warrant reconsideration of usual standards of care. For others, the need to protect caregivers and preserve critical care capacity may factor into decisions. And for everyone, radical transformation of the health care system will affect our ability to maintain high-quality care. As Michael Grossbard, chief of hematology at New York University's Langone Hospital, told me, "Our practice of medicine has changed more in 1 week than in my previous 28 years combined."

Cancer care, which often involves immunosuppressive therapy, tumor resection, and inpatient treatment, has been disproportionately affected by Covid-19. Like other oncologists I spoke with, Grossbard, who primarily treats lymphoma, has been tasked with revising chemotherapy protocols to minimize both the frequency of chemotherapy visits and the degree of immunosuppression. For example, though patients with low-grade lymphoma typically receive maintenance therapy, it will not be recommended for now because it requires an office visit, worsens immunosuppression, and improves progression-free but not overall survival. Other protocol modifications have arisen because of cancellations of elective surgeries. For instance, some patients with solid tumors, such as breast and rectal cancers, are being offered systemic therapy before, rather than after, surgery.

Many modifications may not affect long-term outcomes. Eric Winer, a breast oncologist at Dana-Farber Cancer Institute, believes, for instance, that giving antihormonal therapy to women with hormone-receptor–positive breast tumors and delaying surgery probably won't alter overall survival, though this approach hasn't been formally tested in Stage I disease. But even when there's greater uncertainty about treatment modifications, Winer has been impressed by many patients' graceful acceptance.

I spoke to Ms. C., a 40-year-old patient of

Winer who was recently diagnosed with inflammatory breast cancer. Treatment typically involves 4 to 6 months of chemotherapy followed by surgical excision, though as Ms. C. said, "When you have cancer, your first reaction is 'Just get it out of my body now.'" But as she and Winer watched Covid-19 decimate Italy, they began discussing what the evolving situation would mean for her. She'd started receiving an anthracycline, which heightened her risk of infection, and was supposed to have surgery in May. When we spoke, it wasn't clear whether or when her surgery would proceed, but she and Winer had agreed that if it was postponed, she would resume targeted systemic therapy. She seemed to take this uncertainty in stride, partly because the hallmark rash of inflammatory breast cancer disappeared after she began receiving Herceptin (trastuzumab) a few months ago. "I literally saw my cancer shrink," she told me, "and I'm so thankful we are where we are now, as opposed to 25 years ago."

Suspending other aspects of cancer care will have graver consequences. David Ryan, chief of oncology at Massachusetts General Hospital (MGH), told me that three patient groups worry him most. The first are the subgroup of patients with lymphoma for whom CAR-T therapy is potentially curative. More than half these patients receive therapy in clinical trials, many of which have been paused amid society-wide shutdowns; even if enrollment could continue, there's concern about the need for ICU care in a resource-constrained system. A related concern is for patients requiring bone marrow transplants, given their high risk of infection and potential need for ICU care.

Finally, and most wrenching to Ryan, are patients with refractory tumors who are nearing the end of life, but for whom an experimental targeted therapy may hold promise; Ryan would otherwise offer these patients enrollment in an early-phase trial. One recent analysis suggests that such enrollment is associated with clinical benefit in nearly 20% of patients,[1] and participation allows patients to have some hope in their dying days and to feel like they're "giving back" to the scientific community.

The individual toll, as clinical trials slow to a crawl, is mirrored by a societal one. As Ryan, who sent me an email message while serving a volunteer shift in the hospital's Covid unit, lamented, "There's no question that clinical research in cancer will be set back by at least a year as we all drop what we're doing to take care of the surge of patients."

PROTECTING OUR PATIENTS, PRESERVING OURSELVES

Another distressing trade-off is that between patients' needs for procedures and the need to protect caregivers from infection and preserve hospital capacity. A cardiologist friend, for example, told me about a woman in her 70s with some cardiac risk factors who developed chest pressure and shortness of breath. She was reluctant to go to the hospital, and when she presented (at a highly regarded institution), she needed urgent intubation. When chest radiography revealed bilateral interstitial edema, she became a "Covid rule-out" and was transferred to the ICU. As her team awaited the Covid test results, her troponin level climbed, causing increasing concern about an acute coronary syndrome. Though this suspicion would usually prompt more urgent coronary angiography, the uncertainty about Covid status delayed the procedure. When the Covid result came back negative, she underwent urgent coronary angiography, which revealed an acute coronary occlusion. By then, however, she had developed progressive cardiogenic shock, and she ultimately died.

Though physicians must often make judgments amid uncertainty, we typically focus on the patient's risk, not our own. In an infectious disease epidemic, our calculus must incorporate our own exposure risk — and how exposure would limit our ability to care for future patients. The agony and complexity of these decisions is currently compounded by shortages of personal protective equipment (PPE). Ajay Kirtane, an interventional cardiologist at Columbia who has coauthored recommendations for cardiac catheterization laboratories during the pandemic,[2] told me that "People are being told to do procedures with inadequate protection." Though these recommendations aim to minimize both staff exposure and resource utilization, Kirtane recognizes the potential consequences of caution. "One of the yet-to-be-told stories of the Covid-19 pandemic is the recognition that the (necessary) proscriptions on the performance of less urgent cases has led to collateral damage to

so many patients with medical conditions that truly couldn't wait."

Although canceling procedures such as elective hernia repairs and knee replacements is relatively straightforward, for many interventions the line between urgent and nonurgent can be drawn only in retrospect. As Brian Kolski, director of the structural heart disease program at St. Joseph Hospital in Orange County, California, told me, "A lot of procedures deemed 'elective' are not necessarily elective." Two patients in his practice whose transthoracic aortic valvular replacements were postponed, for example, died while waiting. "These patients can't wait 2 months," Kolski said. "Some of them can't wait 2 weeks." Rather than a broad moratorium on elective procedures, Kolski believes we need a more granular approach. "What has been the actual toll on some of these patients?" he asked.

Mr. R., a 75-year-old man with advanced heart failure, is another of Kolski's patients for whom the toll has been great. Because he had progressive volume overload and delirium, Kolski referred him to a hospital for an LVAD workup in early March. Then, as his wife, Ms. R., told me, "the world went wonky, and everything went down the toilet." Having begun admitting patients with coronavirus, the hospital told the couple it was kicking everyone else out. "They are telling me my husband has 6 to 12 months to live without this procedure," Ms. R. said, "and now they are canceling it on us." They were then quarantined at home — 2 hours away from the hospital — with no plan in place. Mr. R.'s health quickly deteriorated again, but his wife had been advised to keep him out of the hospital. When they finally had a video visit on April 9, he'd become so ill that the heart failure physician didn't recognize him. Mr. R. was promptly admitted, and the LVAD was placed. Though Ms. R. is relieved, ongoing challenges include her husband's persistent delirium, a visitor policy that allows her to be at the bedside only intermittently, and the need for nearby lodging that they can't afford.

As painful as these stories are, the degree of uncertainty renders calculated risk–benefit analyses impossible. Should hospitals schedule LVAD placements when ICU and ventilator capacity may soon be exceeded? Is a patient with severe aortic stenosis more likely to die from his underlying valvular disease or from a valve-replacement hospitalization that leaves him with coronavirus infection? How many times can you expose a cath-lab team to patients with Covid-19–associated myocarditis, which can mimic an acute coronary syndrome, before so many staff members are infected that no one remains to treat patients with real myocardial infarction? No one knows the answers to these questions because modern medicine has never faced them before.

Indeed, as Robert Yeh, an interventional cardiologist and health services researcher at Boston's Beth Israel Deaconess Medical Center, emphasized, "there perhaps has never been a greater gap between what we need to know urgently and what is actually knowable." From policy questions, such as how long to postpone elective procedures, to treatment decisions, such as whether to treat Covid-19 with investigational therapies, the stakes of "failing to understand the universe we don't pursue" have increased. Referring to the global reduction in patients presenting with acute coronary syndromes, Yeh worries that our emphasis on social mitigation measures makes people who truly need care afraid to seek it. Equally worrisome is how we treat people with myocardial infarction who do reach the hospital. Concern about proceduralists' exposure has led some physicians to advocate using thrombolytics rather than the standard revascularization strategy, but Yeh asks, "Are we protecting ourselves at the cost of worse patient outcomes?"

Yeh and his colleagues plan to attempt to answer some of these questions empirically, but as we await epidemiologic data, he cautioned against dismissing anecdotes emerging from around the world in the name of scientific purity. Right now, he emphasized, "the sum total of what we hear from our colleagues at other institutions is the best data we have."

TRADE-OFFS WE DON'T HAVE TO MAKE

Ms. D. is a 51-year-old ICU nurse who was recently diagnosed with breast cancer and underwent lumpectomy in late February; unfortunately, the margins were not clear. When she then learned in early March that she carried the *BRCA2* mutation, she discussed with her surgeon either further excision and intense monitoring or bilateral mastectomy. Ms. D chose the latter but wanted some time to process the decision. With "Covid barreling in," however, she was urged not to delay. Pathology studies then revealed cancer in

the contralateral breast. Though Ms. D. was relieved to have the procedure over with, the rush was hard. "I wished I had time to say goodbye to my breasts," she recalled.

Harder still was follow-up. Ms. D. was discharged with bilateral axillary drains, which she removed herself, as was "strongly recommended." But the most difficult moment was the postsurgical multidisciplinary meeting, which would typically be a discussion of treatment options with the team who'd be caring for her, followed by an opportunity to learn about social and emotional support resources. For Ms. D., this meeting instead happened more quickly over the phone, without the visual cues we rely on to signal that we may be overwhelmed or confused. She knows she received lifesaving care. Indeed, sidelined by her illness while watching her nurse colleagues risk their lives on the front lines, she jokes that cancer saved her life. But the lack of face-to-face interaction, compounded by the unavailability of typical support systems, has made it difficult to cope. "Cancer is so emotionally loaded," she told me, "You need some love. The human part is falling by the wayside."

Humanity absent sound medical judgment is meaningless. But though the pandemic may force difficult choices, my sense from both doctors and patients is that making these decisions thoughtfully and transparently helps patients feel cared for. Under some circumstances, simply hewing to medicine's foundational principles will suffice. For example, when I asked Brian Bergmark, a colleague and interventional cardiologist at Brigham and Women's Hospital, about whether our cath lab would use thrombolytics in lieu of the usual revascularization strategy for acute coronary syndromes, he said his group would maintain the standard of care as long as possible: "We still have the capacity to provide the right therapy for the right disease for the right patient."

But what should we do when capacity limitations necessitate delays? Hugh Auchincloss, a thoracic surgeon at MGH, who, like many surgeons, has had to delay some cases, notes that patients may "think that a bunch of administrators and bureaucrats are issuing blanket proclamations about their care." Auchincloss emphasizes how important it is for patients to know that he has personally reviewed their cases and postponed only those he has deemed nonurgent. Having spoken to all his patients facing delays, he said that despite the difficulty of these conversations, patients are reassured knowing that their doctor has made a personal judgment.

These caring gestures probably assume greater importance in pandemic circumstances. The common fear of "bothering the doctor" is magnified amid images of doctors risking their lives on the front lines. Even Ms. C., the woman with inflammatory breast cancer, felt guilty asking Winer, her oncologist, how Covid might affect her care. "I felt very selfish bringing it up," she told me. "The whole world is going through this crisis, and here I am thinking about my own situation. But I am also facing life and death." Yet despite not knowing whether her mastectomy will proceed, Ms. C. feels as cared for as ever. She trusts Winer. He articulated a clear rationale for alternative therapies, and he and his nurse practitioner leave her feeling as if, for her, they have all the time in the world.

Perhaps the greatest challenge, then, is an invisible one: How do we help people who are afraid to seek care to begin with? To date, much public health messaging regarding Covid has focused on social distancing, hand hygiene, PPE for health care workers, and the need for increased testing. Yet as we begin to observe fewer admissions for common emergencies such as heart attack and stroke,[3,4] the need for vigilance about viral transmission need not detract from an equally important message: Covid or no Covid, we are still here to care for you.

Disclosure forms provided by the author are available at NEJM.org.

Dr. Rosenbaum is a national correspondent for the *Journal*.

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