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COMMENTARY

How Long Is It Safe to Delay Gynecologic Cancer Surgery?

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Editor's note: Find the latest COVID-19 guidance in Medscape's COVID-19 Clinical Guidelines Resource Center.

As I write this column, there are more than 25,000 current cases of COVID-19 in the United States with an expected exponential rise in these numbers. Hospitals are issuing directives to cancel or postpone "elective" surgery to preserve the finite essential personal protective equipment (PPE), encourage social distancing, prevent exposure of at-risk patients within the hospital, and ensure bed and ventilator capacity for the impending surge in COVID-19 patients.

This directive leaves gynecologic oncologists asking themselves, "How elective is my patient's cancer surgery?" Many health systems have defined which surgeries they consider permissible, typically by using time parameters such as would not cause patient harm if not performed within 4 weeks, or 7 days, or 24 hours. This leaves surgeons in the unfamiliar position of rationing health care, a role with which, over the coming months, we may have to become increasingly comfortable.

This is an enormous responsibility, the shift of resources between one population in need and another, and decisions should be based on data, not bias or hunch. We know that untreated cancer is life threatening, but there is a difference between untreated and delayed. What is a safe time to wait for gynecologic cancer surgery after diagnosis without negatively affecting survival from that cancer?

As I looked through my own upcoming surgical schedule, I sought guidance from the American College of Surgeons' website, updated on March 17, 2020. In this site they tabulate an "Elective Surgery Acuity Scale" in which "most cancers" fit into tier 3a, which corresponds to high acuity surgery — "do not postpone." This definition is fairly generalized and blunt; it does not account for the differences in cancers and occasional voluntary needs to postpone a patient's cancer surgery for health optimization.

There are limited data that measure the impact of surgical wait times on survival from gynecologic cancer. Most of this research is observational, and therefore, is influenced by confounders causing delay in surgery (e.g., comorbid conditions or socioeconomic factors that limit access to care). However, the current enforced delays are involuntary; driven by the system, not the patient; and access is universally restricted.

Endometrial Cancer

Most data regarding outcomes and gynecologic cancer delay come from endometrial cancer. In 2016, Shalowitz et al. evaluated 182,000 endometrial cancer cases documented within the National Cancer Database (NCDB), which captures approximately 70% of cancer surgeries in the United States.[1] They separated these patients into groups of low-grade (grade 1 and 2 endometrioid) and high-grade (grade 3 endometrioid and nonendometrioid) cancers, and evaluated the groups for their overall survival, stratified by the time period between diagnosis and surgery. Interestingly, those whose surgery was performed under 2 weeks from diagnosis had worse perioperative mortality and long-term survival.

This seems to be a function of lack of medical optimization; low-volume, nonspecialized centers having less wait time; and the presentation of more advanced and symptomatic disease demanding a more urgent surgery. After those initial 2 weeks of worse outcomes, there was a period of stable outcomes and safety in waiting that extended up to 8 weeks for patients with low-grade cancers and up to 18 weeks for patients with high-grade cancers.

It may be counterintuitive to think that surgical delay affects patients with high-grade endometrial cancers less. These are more aggressive cancers, and there is patient and provider concern for metastatic spread with time elapsed. But an expedited surgery does not appear to be necessary for this group. The Shalowitz study demonstrated no risk for upstaging with surgical delay, meaning that advanced stage was not more likely to be identified in patients whose surgery was delayed, compared with those performed earlier.

This observation suggests that the survival from high-grade endometrial cancers is largely determined by factors that cannot be controlled by the surgeon such as the stage at diagnosis, occult spread, and decreased responsiveness of the tumor to adjuvant therapy. In other words, fast-tracking these patients to surgery has limited influence on the outcomes for high-grade endometrial cancers.

For low-grade cancers, adverse outcomes were seen with a surgical delay of more than 8 weeks. But this may not have been caused by progression of disease (low-grade cancers also were not upstaged with delays), but rather may reflect that, in normal times, elective delays of more than 8 weeks are a function of necessary complex medical optimization of

comorbidities (such as obesity-related disease). The survival that is measured by NCDB is not disease specific, and patients with comorbidities will be more likely to have impaired overall survival.

A systematic review of all papers that looked at endometrial cancer outcomes associated with surgical delay determined that it is reasonable to delay surgery for up to 8 weeks.[2]

Ovarian Cancer

The data for ovarian cancer surgery is more limited. Most literature discusses the impact of delay in the time between surgery and the receipt of adjuvant chemotherapy, but there are limited data exploring how a delay in primary debulking negatively affects patients. This is perhaps because advanced ovarian cancer surgery rarely is delayed because of symptoms and apparent advanced stage at diagnosis. When a patient's surgery does need to be voluntarily delayed, for example for medical optimization, there is the option of neoadjuvant chemotherapy (NACT) in which surgery is performed after three or more cycles of chemotherapy. NACT has been shown in multiple studies to have noninferior cancer outcomes, compared with primary debulking surgery.[3,4]

Perhaps in this current environment in which access to operating rooms and supplies is rationed, we should consider offering more, or all, patients NACT? Hospital stays after primary cytoreductive surgeries are typically 3-7 days in length, and these patients are at a higher risk, compared with other gynecologic cancer surgeries, of ICU admission and blood transfusions, both limited resources in this current environment.

The disadvantage of this approach is that, while chemotherapy can keep patients out of the hospital so that they can practice social distancing, this particular therapy adds to the immunocompromised population. However, even patients who undergo primary surgical cytoreductive surgery will need to rapidly transition to immunosuppressive cytotoxic therapy; therefore it is unlikely that this can be avoided entirely during this time.

Lower Genital Tract Cancers

Surgery for patients with lower genital tract cancers — such as cervical and vulvar cancer — also can probably be safely delayed for a 4-week period, and possibly longer. A Canadian retrospective study looked collectively at cervical, vaginal, and vulvar cancers evaluating for disease progression associated with delay to surgery, using 28 days as a benchmark for delayed surgery.[5] They found no significant increased progression associated with surgical delay greater than 28 days. This study evaluated progression of cancer and did not measure cancer survival, although it is unlikely we would see impaired survival without a significant increase in disease progression.

We also can look to outcomes from delayed radical hysterectomy for stage I cervical cancer in pregnancy to provided us with some data. A retrospective cohort study observed no difference in survival when 28 women with early-stage cervical cancer who were diagnosed in pregnancy (average wait time 20 weeks from diagnosis to treatment) were compared with the outcomes of 52 matched nonpregnant control patients (average wait time 8 weeks). Their survival was 89% versus 94% respectively (P = .08).[6]

Summary

Synthesizing this data, it appears that, in an environment of competing needs and resources, it is reasonable and safe to delay surgery for patients with gynecologic cancers for 4-6 weeks and potentially longer. This includes patients with high-grade endometrial cancers. Clearly, these decisions should be individualized to patients and different health systems. For example, a patient who presents with a cancer-associated life-threatening bowel obstruction or hemorrhage may need an immediate intervention, and communities minimally affected by the coronavirus pandemic may have more allowances for surgery.

With respect to patient anxiety, most patients with cancer are keen to have surgery promptly, and breaking the news to them that their surgery may be delayed because of institutional and public health needs will be difficult. However, the data support that this is likely safe.

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