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ACS Guidelines for Triage and Management of Elective Cancer Surgery Cases During the Acute and Recovery Phases of Coronavirus Disease 2019 (COVID-19) Pandemic

Developed by the leaders within the ACS Cancer Programs (American Joint Committee on Cancer [AJCC], Clinical Research Program [CRP], Commission on Cancer [COC], National Accreditation Program for Breast Cancer [NAPBC], National Accreditation for Rectal Cancer [NAPRC], and the Quality Integration Committee [QIC]). Collaboration with and input from specialty societies acknowledged where appropriate in the disease sections.

Objective

The objective of this document is to continue to provide a framework for how providers can consider the many challenging aspects of cancer patients' needs during the pandemic, including during the acute phase, a time defined by governmental bans on elective surgery, and during the recovery phase when, no doubt, bans will be lifted and backlogs of patients will need urgent attention. While most among us would not consider cancer surgery as elective, some cancer operations are more urgent than others, and this document helps to provide some guidance on prioritization strategies that may be helpful. As before, we fully appreciate that nothing takes the place of sound medical judgment and that local conditions and resources will dictate how and when patients receive their care.

Introduction

When we drafted the first document for prioritizing cancer surgery in late March, the world had recorded 250,000 cases and 24,000 deaths from COVID-19, and elective surgery had just been banned, and so we shared our thoughts on how to triage cases during the acute phase of the pandemic. As we write this draft, three weeks later, the world has recorded 2 million cases and more than 100,000 deaths from COVID-19, with a few U.S. sites reporting a plateau of new cases, and so we now share our thoughts on how to manage the recovery phase of the pandemic. While we are grateful to be considering the recovery side of this crisis, we have learned from our international colleagues some of the difficult realities about how cancer and surgery patients have fared poorly during the pandemic.

The data reported from other countries strongly suggest that cancer surgery patients face a double jeopardy. On the one hand, cancer patients are both at increased risk of contracting COVID-19 infections because they have frequent interactions with medical facilities, and they are vulnerable, so they are at higher risk for suffering serious adverse effects of COIVD-19 infections, including a perioperative mortality rate of 20 percent. On the other hand, delaying surgery for some cancers is known to be associated with poor cancer outcomes. This new evidence suggests that hospitals need to leverage restricted health care resources and achieve some balance between the immediate needs of COVID-19

patients and the ongoing needs of non-COVID-19 patients who need lifesaving medical care and limited exposure to nosocomial infections. This requires tight control of inventory and secure knowledge of the ongoing impact of local COVID-19 case volumes, and it requires prioritization criteria for the non-COVID-19 patients, including cancer surgery patients. It also requires that hospitals implement multiple measures to reduce the risk of nosocomial COVID-19 infections so that vulnerable patient populations do not inadvertently fall victim to COVID-19 complications while seeking vital care.

Background—Emerging Data

During the COVID-19 pandemic, clinicians are facing increasingly difficult decisions about how to best offer the safest care to help ensure optimal patient outcomes. Although the entire population appears to be at risk for COVID-19 infection, certain subgroups of patients are at increased risk of experiencing significant morbidity and mortality if they become infected. Two of these high-risk groups include patients with cancer and patients older than 60 years of age; unfortunately, many cancer patients also fall into the latter group. One study showed that cancer patients with active or past treatment were more likely to have worse outcomes with COVID-19 infection than patients without cancer. Thirty-nine percent of cancer patients required an intensive care unit (ICU) stay with ventilation or died of COVID-19 compared with 8 percent of patients without cancer (*Lancet Oncology.* 2020;21:335. PMID 32066541). Recent data from China and Europe also have shown that postoperative mortality in COVID-19-positive patients exceeds 20 percent. Moreover, approximately two-thirds of these patients were asymptomatic and not suspected of having COVID-19. Unfortunately, routine universal preoperative COVID-19 testing is not available and none of the currently employed tests is 100 percent sensitive and specific. Thus, even presumption of being COVID-19-free prior to surgical treatment is not a guarantee of an optimal outcome. Cancer and surgery can cause immune suppression, which is one of the postulated mechanisms of more severe COVID-19 infection; the synergy of cancer, surgery, and COVID-19 may all contribute to this high mortality rate. We must recognize that these data continue to evolve but will inform future recommendations for cancer patients as we move through the different stages of the COVID-19 pandemic.

Guiding Principles for Cancer Surgery Triage and Management

Pandemic Phases

Recognizing that COVID-19 conditions are highly variable across different regions of the country, and that conditions are very fluid, we have organized triage and management guidance into three acute phases and two recovery phases and anticipate that hospitals will progress through these phases over the next several weeks to months. Furthermore, given the impact of the incidence and prevalence of COVID-19 on all aspects of care—from protection of patients from COVID-19, to the availability of resources—we discuss the pandemic phases first and suggest it is highly critical to key strategies of cancer surgery care.

Acute Phases of the Pandemic

The acute phase of the pandemic describes semi-urgent to emergent conditions of the COVID-19 pandemic, a time defined, in part, by governmental bans on elective surgery. For the most part, this is the time when hospitals are either preparing for a surge of COVID-19 patients or experiencing high volumes of COVID-19 patients. Local hospital resources and the trajectory of the pandemic determine

the urgency of the acute phase. We are fortunate that modern databases now provide for accurate modeling of regional growth curves of COVID-19 cases and provide reasonable estimates of when states will experience their peak of COVID-19 cases. Local teams should be familiar with regional data, as it will help them understand where they are in the pandemic.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID 19 patients, hospital resources not exhausted, institution still has ICU ventilator capacity, and COVID-19 trajectory not in rapid escalation phase. *Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within next three months.*

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, operating room (OR) supplies limited or COVID-19 trajectory within hospital in rapidly escalating phase. *Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within next few days.*

ACUTE PHASE III: Hospital resources are all routed to COVID 19 patients, no ventilator or ICU capacity, OR supplies exhausted. *Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few hours.*

Recovery Phases of the Pandemic

While there is general agreement that a region can be said to have reached its plateau when there is a stable number of or sustained decline in new case volumes for at least two weeks, unfortunately, there is less agreement on what the actual recovery phase will look like. Little is known about what to expect for the duration and volume of the pandemic tail and/or how recovery will be influenced by the shape of the curve; that is, whether the curve was flattened. There is also considerable uncertainty as to whether there is likely to be a resurgence following the initial recovery, which means we should not expect to return to a "normal," pre-pandemic health care environment anytime soon.

EARLY-PHASE RECOVERY: Past the peak of COVID-19, with fewer new cases recorded each day. Resources are starting to become available, including hospital and ICU beds, ventilators, blood, healthy staff, personal protective equipment (PPE), and critical testing. Social distancing is still required for general containment, but some sort of COVID-19-free environment has been secured with adequate testing and PPE.

LATE-PHASE RECOVERY: Well past the peak of new COVID-19 cases by at least 14 days. Resources are more readily available to near normal levels, including hospital and ICU beds, ventilators, blood, healthy staff, PPE, and readily available testing to track cases and monitor, as needed, individuals entering the hospital environment. A substantial and high-functioning COVID-19- free environment has been established.

<u>Resource Considerations</u>

What has become clear and evident is that we have not had, nor do we have yet, resources requisite to manage COVID-19 while still conducting medical care according to our standards. To overcome the resource constraints has meant that hospitals have had to be proactive in judging their resource needs and gaps. To properly prepare, hospital leaders have had to understand the availability of local resources and the prevalence of COVID-19 in their community, and to have used predictive models to

ensure they are ready for peak case volumes. Continuous inventory and management of key resources, including diagnostic kits, PPE, ICU beds, ventilators, blood components, and healthy staff, has been crucial for successful outcomes for COVID-19 and non-COVID-19 patients.

An important goal for the management of the pandemic has been to keep the transmission of disease within the hospital to the lowest possible levels to protect the staff and vulnerable patients. Measures that can help reduce transmission include reducing traffic in the facility to only essential employees and only personnel who are healthy based on some kind of monitoring of symptoms, signs (e.g., temperature), or diagnostic testing (as available and appropriate). Visitors should not be allowed for the most part, if at all, and as many patient care interactions as possible should occur virtually. The staff and the environment also can be protected by severely minimizing exposure to high-risk interventions where COVID-19 particles can be aerosolized, such as bronchoscopic, endoscopic, and laparoscopic procedures. Patient testing plays an important role in taking every precaution possible to separate COVID-19-infected patients from individuals who are negative, vulnerable, and need the facility for lifesaving care. Based on current evidence, and resources allowing, patients going to surgery should undergo some kind of evaluation and/or testing to ensure they are not in the incubation phase of COVID-19 to reduce the risk of perioperative COVID-19-related complications and mortality.

In the acute phase of the disease, several government agencies banned elective surgery to ensure the availability of resources for the COVID-19 surge. As an aside, this may have had the unintended consequence of reducing the unnecessary COVID-19 complications and mortality from operating on patients with asymptomatic COVID-19. In response to the bans and recognizing that delaying elective surgery comes with differing disease outcomes, the triage criteria that follow were developed as guideposts for managing or mitigating the risk of cancer surgery delays. Disease-specific prioritization criteria and safe alternatives were developed based on expert opinion and best available knowledge of the potential for adverse cancer outcomes, according to the extent of the delay.

In the recovery phase of the pandemic, as COVID-19 cases are on the decline, resources are more readily available, and bans on elective surgery are being lifted, there will be significant backlogs of patients needing access to the hospitals for lifesaving care. Although it is more difficult to predict the duration and COVID-19 impact of the recovery phase, the goals and priorities are similar to those considered during the acute phase; specifically, resources need to be tightly monitored and strategically deployed and nosocomial infections need to be minimized as much as possible. In fact, the goal of minimizing nosocomial infections probably takes on greater importance in the recovery phase as we now know that patients who are in the incubation phase of COVID-19 are at risk for major postoperative complications and mortality. Depending on the degree to which the pandemic affected census in the hospital and on the degree to which hospitals were able to minimize nosocomial infections, efforts to contain viral transmission may need to accelerate before elective surgery ramps up. Assuming more PPE and diagnostic testing becomes available during the recovery phase, this may help to identify COVID-19-positive patients and staff and facilitate more accurate tracking. Criteria for prioritizing during the recovery phase are intended to balance the risk of COVID-19-related complications versus the risk of further cancer surgery delays.

Cancer Care Coordination and Approaching Patients

Cancer care coordination is more important than ever during the “acute” and “recovery” phases of this pandemic. With cancer and surgery patients at higher risk for COVID-19 infection and complications and

with resources constrained, following “standard of care” cancer practices may put patients in harm’s way, and so adjustments to typical plans may need to be made according to emerging evidence. Virtual teams, with multidisciplinary representation, should be aware of resource constraints they may be facing for all types of cancer treatments and should work to adjust cancer plans considering all that is known about access, risks, and benefits. For institutions with multidisciplinary tumor boards and relatively small cancer volumes, it may be possible to discuss the management of individual cases using a consensus approach to derive optimal care plans. Care plans based on multidisciplinary team input should help in reassuring patients that all issues pertinent to their situation were considered. For institutions with higher case volumes, there may be more utility in discussing the triage and management approaches that can be applied and that make sense for the local conditions and for the acute or recovery phases of the pandemic they are in at the time. Cancer patients should be prospectively assigned prioritization for surgery according to specialty-specific recommendations to determine which patients can go to the OR during both the acute and recovery phases of the pandemic.

Shared decision making should be encouraged. As much as is feasible, the holistic needs of patients, such as the management of anxiety, should be considered when decisions around delays in treatment are under discussion. As possible, patients should be informed that decisions regarding elective cancer surgery are consensus-based, based on emerging data, and are founded on both wanting to give them the best chances of good outcomes from their cancer and wanting to minimize their risk of harm from COVID-19. Multidisciplinary teams may wish to develop some manner of reassuring language for informed consent during the pandemic, such as: “You are being offered surgery now because at this time we feel that your risk of being exposed to and/or harmed by the COVID-19 within the hospital is low, and that delaying surgery could reduce your chances of being cured of cancer. It is impossible to know either the risk of delaying surgery or the chance of getting an infection with perfect accuracy, but a group of colleagues from multiple specialties looked at your case, and it is our group’s opinion that surgery is reasonable at this time.”

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CANCER CARE TRIAGE AND MANAGEMENT: BREAST CANCER PATIENTS

Developed by the COVID-19 Pandemic Breast Cancer Consortium (this consortium comprises representatives from the NAPBC, COC, American Society of Breast Surgeons, National Comprehensive Cancer Network, and American College of Radiology).

A priority classification system was developed for breast cancer patients based on the Ontario Health Pandemic Planning Clinical Guideline for Patients with Cancer. Priority categories were defined based on the severity of an individual patient's condition and potential efficacy of treatment. Within each phase of the COVID-19 pandemic, priority levels can be assigned to each patient to guide triage and management of breast cancer patients.

Priority A patients have a life-threatening condition, are clinically unstable, and for whom even a short delay would significantly alter the prognosis or quality of life. Assuming efficacious treatment, these patients are given top priority even if resources become scarce.

Priority B patients do not have immediately life-threatening conditions, but for whom treatment or services should not be indefinitely delayed until the end of the pandemic. A short delay (for example, six to 12 weeks) would not affect overall outcome for these patients. Longer delays could affect outcomes in some priority B patients, and triage may become necessary to justify which patients should undergo treatment versus further delay.

Priority C patients are patients for whom certain treatment or services can be deferred indefinitely until the pandemic is over without adversely affecting outcomes.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19-positive patients, hospital resources not exhausted, institution still has ICU and ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if an operation is not performed within next three months.

<u>Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few weeks):</u>

- Priority A:
  - Breast abscess in a septic patient
  - Expanding hematoma in a hemodynamically unstable patient
- Priority B1:
  - Ischemic autologous tissue flap
  - Revision of a full-thickness ischemic mastectomy flap with exposed prosthesis
  - Patients who have completed neoadjuvant chemotherapy for inflammatory breast cancer
  - TNBC or HER2 positive patients*†
- Priority B2:
  - Patients finishing neoadjuvant therapy where there is a window of time that surgery should be performed†
  - Patients progressing on neoadjuvant therapy
- Priority B3:

- Clinical stage T2 or N1 ER+HER2- tumors[†‡]
- Discordant biopsies likely to be malignant, i.e., ER- ductal carcinoma in situ (DCIS) that presents as a palpable mass
- Malignant or suspected local recurrence

*In some cases, institutions may decide to proceed with surgery rather than subject a patient to an immunocompromised state with neoadjuvant chemotherapy; these decisions will depend on institutional resources.

[†]Encourage use of breast-conserving surgery whenever possible, defer definitive mastectomy and/or reconstruction until after the COVID-19 pandemic resolves provided radiation oncology services are available. Autologous reconstruction should be deferred for those patients undergoing mastectomy.

[‡]Consider neoadjuvant hormonal treatment or chemotherapy (depending on molecular characteristics) and delaying surgery.

<u>Cases that should be deferred:</u>

- Priority C1:
  - ER- DCIS (Unless presenting as a palpable mass)
  - Positive margin for invasive cancer (for minimal margin involvement consider adjuvant hormone or chemotherapy as appropriate and radiation, with margin re-resection delayed)
  - Clinical stage T1N0 ER+ HER2- cancers (use of neoadjuvant hormone therapy for three to six months)
  - BC patients requiring additional axillary surgery (consider adjuvant chemotherapy and radiation, with delayed completion axillary dissection)
- Priority C2:
  - ER+ DCIS (follow without treatment or treat with preoperative hormone therapy)
  - High-risk lesions
  - Reconstruction for previously completed mastectomy
- Priority C3:
  - Excision of benign lesions
  - Discordant biopsies likely to be benign
  - Prophylactic surgery for cancer or noncancer

<u>Alternative treatment approaches to be considered (assuming resources permit):</u>

- Clinical Stage T1N0 estrogen receptor positive/progesterone receptor positive/HER2- tumors can receive neoadjuvant hormonal therapy*
- Some Clinical Stage T2 or N1 ER+//HER2- tumors can receive neoadjuvant hormonal therapy or neoadjuvant chemotherapy depending on molecular characteristics*
- Triple negative and HER2+ tumors can undergo neoadjuvant therapy prior to surgery depending on institutional resources
- Inflammatory and locally advanced breast cancers should receive neoadjuvant therapy prior to any surgery

*Many women with early stage, ER+, HER2- breast cancers, particularly those with low–intermediate grade tumors, lobular breast cancers, low risk genomic assays, or "luminal A" signatures can be safely and effectively treated with three to 12 months of primary endocrine therapy deferring surgery until that time. Patients with ER+, HER2- tumors with molecular profiles that suggest need for neoadjuvant or adjuvant chemotherapy can be safely treated with three to six months of neoadjuvant chemotherapy.

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited, or COVID-19 trajectory within hospital in rapidly escalating phase

Surgery restricted to patients likely to have survivorship compromised if the operation is not performed within next few days.

<u>Cases that need to be done as soon as feasible (recognizing status of hospital likely to progress over next few days):</u>

- Priority A:
    - Breast abscess in a septic patient
    - Expanding hematoma in a hemodynamically unstable patient

<u>Cases that should be deferred:</u>

- All breast procedures excluding those mentioned in Priority A above

<u>Alternative treatment approaches RECOMMENDED (assuming resources permit):</u>

- Clinical Stage T1N0 estrogen receptor positive/progesterone receptor (PR)+/HER2- tumors can receive hormonal therapy*
- Some ER+ cases can receive hormonal therapy
- Triple negative and HER2 positive tumors can undergo neoadjuvant therapy prior to surgery depending on institutional resources
- Some Clinical Stage T2 or N1 ERp+/PR+/HER2- tumors can receive hormonal therapy*
- Inflammatory and locally advanced breast cancers should receive neoadjuvant therapy prior to any surgery

*Many women with early-stage, ER+, HER2- breast cancers, particularly those with low–intermediate grade tumors, lobular breast cancers, low risk genomic assays, or "luminal A" signatures can be safely and effectively treated with three to 12 months of primary endocrine therapy deferring surgery until that time. Patients with ER+, HER2- tumors with molecular profiles that suggest need for neoadjuvant or adjuvant chemotherapy can be safely treated with three to six months of neoadjuvant chemotherapy.

ACUTE PHASE III: Hospital resources are all routed to COVID 19 patients, no ventilator or ICU capacity, OR supplies exhausted.

Surgery restricted to patients likely to have survivorship compromised if an operation is not performed within next few hours.

<u>Cases that need to be done as soon as feasible (status of hospital likely to progress in hours):</u>

- None

All other cases deferred

Alternate treatment recommended:

- Same as above
- Percutaneous aspiration of a breast abscess or hematoma could be considered temporizing measures for hours or at least one day

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some sort of COVID-19-free environment has been secured with adequate testing and PPE.

Cases that need to be done as soon as feasible:

- Priority A:
    - Breast abscess in a septic patient
    - Expanding hematoma in a hemodynamically unstable patient
- Priority B1:
    - Ischemic autologous tissue flap
    - Revision of a full thickness ischemic mastectomy flap with exposed prosthesis
    - Patients who have completed neoadjuvant chemotherapy for inflammatory breast cancer
    - TNBC or HER2+ patients who are not undergoing upfront neoadjuvant therapy
- Priority B2:
    - Patients finishing neoadjuvant therapy where there is a window of time that surgery should be performed
    - Patients progressing on neoadjuvant therapy
- Priority B3:
    - Clinical stage T2 or N1 ER+HER2- tumors
    - Discordant biopsies likely to be malignant, i.e., ER- DCIS that presents as a palpable mass
    - Malignant or suspected local recurrence

Cases that could be deferred or that may be higher risk for exposure to COVID-19 during early recovery

- Cases that can be deferred:
    - Priority C1:
        - ER- DCIS (Unless presenting as a palpable mass)
        - Positive margin for invasive cancer
        - Clinical stage T1N0 ER+ HER2- cancers
        - BC patients requiring additional axillary surgery
    - Priority C2:
        - ER+ DCIS
        - High risk lesions
        - Reconstruction for previously completed mastectomy
    - Priority C3:
        - Excision of benign lesions
        - Discordant biopsies likely to be benign
        - Prophylactic surgery for cancer or noncancer

- Cases that are considered higher risk for exposure to COVID-19 during early recovery period:
    - Patients with invasive breast cancer (versus noninvasive disease)
    - Patients who have finished recent cytotoxic chemotherapy or immunotherapy
    - Patients older than age 65
    - Patients with comorbidities known to increase risk of COVID-19 severity, such as diabetes, lung disease, cardiovascular disease, obstructive sleep apnea, immunocompromised
    - Exposure to a known COVID-19 positive person in past 14 days

<u>Role of outpatient surgery—reduced COVID-19 exposure and less intense consumption of resources:</u>

- Consider IV sedation when possible for breast conserving surgery cases (some hospitals may consider intubation of all OR cases safer for COVID-19 exposure then IV sedation)
- Consider IV sedation when possible for sentinel node biopsy cases (some hospitals may consider intubation of all OR cases safer for COVID-19 exposure then IV sedation)
- Recommend use of regional blocks to enable same-day discharge for patients undergoing mastectomy with and without reconstruction

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high-functioning, COVID-19-free environment has been established.

<u>Cases that need to be done as soon as feasible:</u>

These would presumably be patients that were either deferred from above (and have not had surgery) or cases in higher priority levels that did not have surgery during the early phase recovery period for whatever reason:

- Priority B2
    - TNBC or HER2+ cases finishing neoadjvuant therapy for whom there is a window of when surgery should be performed
    - Patients progressing on neoadjuvant therapy
- Priority C1:
    - ER- DCIS (unless presenting as a mass in which case they would move to B3)
    - Positive margin for invasive cancer
    - Clinical stage T1N0 ER+ HER2- cancers
    - BC patients requiring additional axillary surgery
- Priority C2:
    - ER+ DCIS
    - High-risk lesions
    - Reconstruction for previously completed mastectomy
- Priority C3:
    - Excision of benign lesions
    - Discordant biopsies likely to be benign
    - Prophylactic surgery for cancer or noncancer

CANCER CARE TRIAGE AND MANAGEMENT: COLORECTAL CANCER PATIENTS

Developed by NAPRC in collaboration with ASCRS.

Care of the patient with colon and rectal cancer is complex because of the multimodality and multidisciplinary nature of treatment planning for these patients, whether or not during the COVID-19 pandemic. The combination of chemotherapy, radiation therapy, surgery using local excision or radical resection, ostomy for diversion or palliation, endoscopic procedures, and the incorporation of time to determine treatment effect on the cancer is the basis for optimal treatment of these patients. In the acute phase of the COVID-19 pandemic, where truly emergency care is the focus, a plan should be made to get patients with colorectal malignancy to the optimal window of time to treat and potentially cure the patient. The timing of chemotherapy, radiation, and surgery can be flexible, or it can be constrained by failure to use the benefits of the different treatments in the appropriate order with appropriate rest periods or follow-up procedures to take advantage of each modality to the fullest. While no cancer patient can be thought of as being in a purely elective group of patients, options exist for converting the treatment plan to a deferred time point or for changing the order of multimodality care to ultimately provide the best outcome possible for our patients.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

<u>Cases that need to be done as soon as feasible:</u>

- Nearly obstructing rectal cancer
- Cancers requiring frequent transfusions
- Asymptomatic colon cancers
- Rectal cancers after neoadjuvant chemoradiation with no response to therapy
- Cancers with concern about local perforation and sepsis
- Early stage rectal cancers where adjuvant therapy not appropriate

<u>Diagnoses that could potentially be deferred:</u>

- Malignant polyps, either with or without prior endoscopic resection
- Prophylactic indications for hereditary conditions
- Large, benign appearing asymptomatic polyps
- Small, asymptomatic colon carcinoids
- Small, asymptomatic rectal carcinoids

<u>Alternative treatment approaches to delay surgery that can be considered:</u>

- Locally advanced, resectable colon cancer
    - Neoadjuvant chemotherapy for two to three months followed by surgery
- Rectal cancer cases with clear and early evidence of downstaging from neoadjuvant chemoradiation
    - Where additional wait time is safe
    - Where additional chemotherapy can be administered

- Locally advanced rectal cancers or recurrent rectal cancers requiring exenterative surgery
    - Where additional chemotherapy can be administered
- Oligometastatic disease where effective systemic therapy is available

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few days):

- Nearly obstructing colon cancer where stenting is not an option
- Nearly obstructing rectal cancer (should be diverted)
- Cancers with high (inpatient) transfusion requirements
- Cancers with pending evidence of local perforation and sepsis

Cases that could be considered for deferral:

- All colorectal procedures typically scheduled as routine

Alternative treatment approaches:

- Transfer patients to hospital with capacity
- Consider neoadjuvant therapy for colon and rectal cancer
- Consider more local endoluminal therapies for early colon and rectal cancers when safe

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients for whom death is likely within hours if surgery is deferred.

Cases that need to be performed as soon as feasible:

- Perforated, obstructed, or actively bleeding (inpatient transfusion dependent) cancers
- Cases with sepsis

All other cases deferred

Alternate treatment recommended:

- Transfer patients to hospital with capacity
- Diverting stomas
- Chemotherapy
- Radiation

RECOVERY PHASE

As mentioned earlier, the criteria for restarting delayed cases in the OR to surgically treat colorectal cancer will need some structure and should not jeopardize the long-term outcome of any patient affected by this pandemic either by postponement or disease contraction. The proposed prioritization plan is based on the knowledge that there are some windows of optimal opportunity for patients to receive definitive surgical care for colorectal cancer and achieve the best chance for cure or palliation.

The Priority stratification for scheduling cases is based on time limits for waiting to provide definitive operative care:

- Priority 1: EARLY PHASE RECOVERY
- Priority 2: EARLY PHASE RECOVERY
- Priority 3: LATE PHASE RECOVERY
- Priority 4-: LATE PHASE RECOVERY

Rectal cancer low anterior resection or abdominoperineal resection:

Priority 1: Patient completed neoadjuvant therapy > 24 weeks

Priority 2: Patient completed total neoadjuvant therapy > 1 month

Priority 2: Patient completed chemoradiotherapy (ChemoRT) > 8 weeks ago but < 12 weeks with poor response

Priority 2: Patient completed ChemoRT > 12 weeks ago with incomplete response

Recurrent cancer after local excision of rectal cancer or during Watch and Wait protocol needing radical excision:

Priority 1: No other treatment possible or no response/growth during adjuvant chemotherapy and failure to operate would result in distant or local spread and increase the requirements for cure

Priority 3: Further chemotherapy possible

Priority 3: Further ChemoRT possible

Rectal cancer with metastasis treated with systemic therapy needing resection of the primary:

Priority 2: Metastasis treated and patient is disease free

Priority 3: Further ChemoRT to the primary tumor is possible

Ileostomy closure is Priority 4

Colostomy closure is Priority 4

Excision of a large rectal polyp:

Priority 2: Bx positive for cancer or high-grade dysplasia and possible to cure with local excision

Priority 3: Bx negative for cancer and tumor greater than 4 cm

Priority 4: Polyp smaller than 4 cm and no dysplasia

Colectomy for large colon polyp:

Priority 2: Biopsy positive for cancer/high-grade dysplasia and not resectable endoscopically

Priority 3 or 4: Biopsy negative for cancer, greater than 4 cm but not resectable endoscopically

Colon cancer (bleeding slowly and non-obstructing) possibly diverted and/or completed neoadjuvant chemotherapy for advanced local disease:

Priority 1 or 2: Based on patient comorbidities and frailty

Total colectomy for multiple polyps or polyposis syndrome:

Priority 1: At least one biopsy positive for cancer

Priority 3: Biopsy negative for cancer

Multiple synchronous colon cancers:

Priority 1 or 2: No metastasis

Priority 2: Patient is > 1 month after metastases treated with ablation and systemic chemotherapy

CANCER CARE TRIAGE AND MANAGEMENT: KIDNEY CANCER PATIENTS

General Management Recommendations

This guidance is based on the American Urological Association guideline document and best available evidence.[1-3]

Prior to the COVID-19 pandemic, the incidence of kidney cancer had increased due to the liberal use of cross-sectional imaging. The current situation may decrease the incidental detection of renal masses, but this remains to be seen. The hallmark of treatment for localized kidney cancer is surgical therapy. Fortunately, risk-stratification schemes exist to help triage these cases during these difficult times.

The small renal mass represents a unique subset of largely indolent kidney cancers; up to 30 percent of these masses may be benign. Patients with these tumors may choose between the following management options: Active surveillance, biopsy, thermal ablation, and surgery. Data from von-Hippel-Lindau patients and various sporadic cohorts reveal that the metastatic potential of these tumors is negligible when the tumor is less than 3 cm in size, with some rare exceptions including certain familial syndromes like hereditary leiomyomatosis and renal cell carcinoma (HLRCC) or succinate dehydrogenase B (SDHB)-associated kidney cancer, which can be aggressive when small. Great care must be exercised in patients with sickle cell trait or when the tumor has an atypical appearance. These rare situations could be the manifestation of more aggressive cancers.

Larger clinically localized masses may behave more aggressively. Retrospective data exist supporting the safety of delaying surgery up to three months. These datasets suffer from a selection bias but, nonetheless, provide some reassuring information regarding delays. While biopsy can provide a diagnosis in the majority of cases and be helpful for risk stratification, it suffers from accuracy issues when it comes to assigning a grade. The presence of necrosis, sarcomatoid / rhabdoid elements, or high-grade components are all aggressive features that should prompt more immediate surgery. The use of thermal ablation in select smaller tumors is an alternative to surgical excision. Thermal ablation data for tumors greater than 3 cm in size is in general inferior to surgical resection. Percutaneous ablation is particularly attractive as it is generally an outpatient procedure performed using local anesthesia.

Some tumors are amenable to partial nephrectomy. For such tumors, the decision to proceed with partial versus radical nephrectomy will depend on patient factors (baseline renal function) and surgeon experience balanced by existing resources. Partial nephrectomy has a small but measurable likelihood of postoperative bleeding and urine leak requiring adjunct procedures. Radical nephrectomy in some situations may be a quicker and less complicated option. The decision to proceed with partial nephrectomy and whether surgery is performed via a robotic, laparoscopic, or open approach should take into account potential intra and postoperative complications. In terms of hospital stay, the majority of partial and radical nephrectomy procedures are associated with short hospital stays (1 to 3 days). Select cases can be more involved however and require intensive care use and longer lengths of stay.

Patients with localized / locally advanced kidney cancer generally do not receive systemic therapy. A few studies have investigated the role of tyrosine kinase inhibitors on shrinking tumors to aid in nephron sparing or to downstage tumors with venous invasion. These agents have some activity in this setting

and thus could theoretically be used in highly select patients during the pandemic if the situation locally is dire. Studies investigating such a strategy did not evaluate long-term oncological outcomes.

Nephrectomy with vena cava thrombectomy can be quite complex and involve multidisciplinary teams and significant resource use postoperatively. There is also the potential for tumor embolization intraoperatively leading to right heart failure and, even, death. These cases are oncologically urgent but are also resource-intensive and should be performed at high-volume centers whenever possible.

Historically cytoreductive (CN) nephrectomy was preferred in patients diagnosed with metastatic kidney cancer with the primary tumor in place; however, recent data from the Clinical Trial to Assess the Importance of Nephrectomy (CARMENA) trial has highlighted the importance of patient selection. The overall survival in this trial for CN was not significantly different than sunitinib alone in the intention to treat population. Patients who do well with systemic therapy may receive delayed nephrectomy and have a favorable outcome. CN may still be beneficial, however, in patients with one International Metastatic RCC Database Consortium (IMDC) risk factor especially if they only have one site of metastatic disease.

ACUTE PHASE I. Semi-urgent setting (Preparation phase)*:* Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next 3 months.

- Surveillance for tumors <3 cm in size
- Surgery for patients with tumors 4 to 7 cm in size diagnosed >3 months ago otherwise surveillance
- Surgery for patients with clinical stage ≥T2 (including tumor thrombus cases)
- Surgery for patients with known high-grade or rhabdoid/sarcomatoid histology regardless of clinical stage
- Surgery for well-selected patients with metastatic kidney cancer (clear cell, good performance status, one IMDC risk factor, and one site of metastatic disease)
- Metastatectomy in select recurred patients (long disease-free interval, favorable site, single location)

<u>Alternative Options</u>:

- Thermal ablation: Best outcomes for tumors <3 cm that are exophytic and not adjacent to critical structures (vessels, bowel, ureter)
- Biopsy: may help risk stratify
- Interval imaging especially in tumors 4 to 7 cm in size as a significant proportion may be indolent and show no growth
- Systemic therapy/clinical trial for metastatic disease

ACUTE PHASE II. Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next few days.

- Nephrectomy for patients with kidney cancer with tumor thrombus
- Nephrectomy for symptomatic kidney cancer (bleeding)
- Surveillance for all other clinically localized kidney cancer
- Systemic therapy for metastatic kidney cancer

Alternative Options

Endovascular embolization for bleeding is effective and may use fewer resources than surgery
systemic therapy for tumor thrombus cases or growing localized tumors (weak evidence).

- Interval imaging
- Clinical trial if available

ACUTE PHASE III. Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients *for* whom death is likely within hours if surgery *is* deferred.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next few hours.

- Nephrectomy for symptomatic kidney cancer (bleeding)
- Nephrectomy for select patients with extensive inferior vena cava thrombus; however, these patients rarely need surgery within hours

Alternative Options

Endovascular embolization for bleeding is effective and may use fewer resources than surgery
systemic therapy for tumor thrombus cases or growing localized tumors (weak evidence)
Interval imaging.

EARLY-PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

- Same as Acute Phase I.

LATE-PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high functioning COVID-19-free environment has been established.
Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

Cases that need to be prioritized in this phase:

- Surgery for patients with tumors 4 to 7 cm in size diagnosed >3 months ago otherwise surveillance
- Surgery for patients with clinical stage ≥T2 (including tumor thrombus cases)
- Surgery for patients with known high-grade or rhabdoid/sarcomatoid histology regardless of clinical stage
- Surgery for very select patients with metastatic kidney cancer (clear cell, good performance status, one IMDC risk factor, and one site of metastatic disease)
- Metastatectomy in select recurred patients (long disease-free interval, favorable site, single location)

Other indicated procedures may be performed during this phase depending on the local situation.

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CANCER CARE TRIAGE AND MANAGEMENT: MELANOMA PATIENTS

Incorporates guidelines published by SSO and NCCN.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

Cases that need to be done as soon as feasible (recognizing status of each hospital likely to evolve over next few weeks):

- For patients with clinical stage IB melanoma with involved biopsy margins or clinical stage II melanoma, wide excision with resection margins based on tumor thickness, as well as intraoperative lymphatic mapping and sentinel node biopsy of regional node basins at risk are offered as local resources permit, with priority afforded to patients with higher-risk primary tumors
- Patients with anorectal melanoma are generally considered to be high-risk regardless of clinical presentation and also are prioritized
- Palliative resection for symptomatic metastatic lesions (i.e., bleeding, bowel obstruction) if deemed appropriate following multidisciplinary and goals-of-care discussion
- Efforts should be made to perform procedures in an outpatient setting to limit use of inpatient OR resources

Diagnoses that could be deferred three months:

- Melanoma in situ and clinical stage IA melanoma
- Clinical stage IB melanoma with negative biopsy margins
- If significant delay of definitive primary tumor excision is anticipated, the precise location of the biopsy site should be accurately documented (i.e., via photography, with marking of site by patient or caregiver, ideally with anatomic reference points also in field of view) and saved to the patient's electronic medical record to facilitate accurate identification at a later time). If site unclear per patient, consider collaboration with referring provider, if possible.

Alternative treatment approaches to delay surgery that can be considered:

- For patients with resectable stage III or IV melanoma (at diagnosis or recurrent), multidisciplinary case review should be performed to determine modality, sequence, and timing of treatment with consideration of neoadjuvant systemic therapy when clinically feasible
- Consider palliative radiation for bulky/symptomatic disease
- Given intensive hospital resource requirements required, use of talimogene laherparepvec (TVEC) for cutaneous/nodal/in-transit metastasis should be cautiously considered and, if possible, deferred until after the COVID-19 crisis abates

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few days):

- Palliative surgery for symptomatic metastatic lesions (i.e., bleeding, bowel obstruction) if deemed appropriate following multidisciplinary discussion and goals-of-care discussion

- Patients with anorectal melanoma are generally considered to be high-risk regardless of clinical presentation and can be assessed in a multidisciplinary setting (virtual if necessary)

Cases that should be deferred:

- Melanoma in situ, clinical stages I and II melanoma regardless of biopsy margins
- If significant delay of definitive primary tumor excision is anticipated, the precise location of the biopsy site should be accurately documented (that is., via photography, with marking of site by patient or caregiver, ideally with anatomic reference points also in field of view) and saved to the patient's electronic medical record to facilitate accurate identification at a later time). If site unclear per patient, consider collaboration with referring provider, if possible.

Alternative treatment approaches:

- Refer/transfer patients to hospital with capacity
- For patients with resectable stage III or IV melanoma (at diagnosis or recurrent), multidisciplinary case review is performed to determine modality, sequence, and timing of treatment with consideration of neoadjuvant systemic therapy when clinically feasible
- Consider palliative radiation for bulky/symptomatic disease (i.e., bleeding) if deemed appropriate following multidisciplinary and goals-of-care discussion

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery is deferred.

Cases that need to be performed as soon as feasible (status of hospital likely to progress in hours):

- All but emergent, lifesaving operations should be deferred
- Consider nonsurgical methods to temporize (i.e., endoscopic or percutaneous procedures for management of gastrointestinal tract issues, management of bleeding with interventional radiology procedures and/or radiation therapy

All other cases deferred

Alternate treatment recommended:

- Refer/transfer patients to hospital with capacity
- For patients with resectable stage III or IV melanoma (at diagnosis or recurrent), multidisciplinary case review should be performed to determine modality, sequence, and timing of treatment with consideration of neoadjuvant systemic therapy when clinically feasible

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

- Available institutional resources and those of nearby transfer centers
- Likelihood of cure with surgery, and progression with surgical delay
- Presence or absence of concurrent symptoms
- Availability of alternate therapies such as neoadjuvant therapy
- Physiologic status of the patient

Cases that need to be done as soon as feasible:

- Previously treated, potentially curable patients who have completed all appropriate neoadjuvant therapy
- Previously untreated, potentially curable patients anticipated to have a short and uncomplicated hospital course
- Potentially curable patients who are at risk for imminent and significant physiological decline
- Consider using outpatient surgery and IV sedation when feasible

Cases that could be deferred or that may be higher risk for exposure to COVID-19 during early recovery:

- Potentially curable patients eligible for initial treatment with neoadjuvant therapy

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high functioning COVID-19-free environment has been established.

Cases that need to be done as soon as feasible:

- Cases that were either deferred from above (and have not had surgery) or cases in higher priority levels that did not have surgery during the early phase recovery period for whatever reason
- New patients meeting priority criteria outlined above

CANCER CARE TRIAGE AND MANAGEMENT: PANCREAS AND PERIAMPULLARY CANCER PATIENTS

Operations performed to remove pancreatic, ampullary, and duodenal neoplasms have historically been notable for significant rates of adverse events, prolonged hospitalization, and readmission following surgery. These adverse events may be the result of one or more of the following: technical complexity of these operations, tumor-related factors such as cachexia and malnutrition, and patient-related factors such as age and comorbidities. These cases thus have the potential to consume a significant amount of hospital resources in the postoperative period. Further, they may be associated with particularly high rates of perioperative morbidity and mortality when performed in asymptomatic COVID-19-positive patients, a fact that must be considered in settings in which testing is not universally available.

It should also be noted that although surgery is necessary for cure of localized pancreatic cancer, most patients who undergo pancreatectomy for this disease are not cured. Factors such as serum CA 19-9 level and tumor anatomy should be critically evaluated for each patient to determine the role of surgery. And, every case should be discussed in a multidisciplinary forum to establish the most appropriate care plan.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

In this phase, patients selected for “elective” surgery should have a limited comorbidity profile and a physiologic status, which is optimized so that the associated length of stay and the extent of resource utilization are both predictable and minimized.

<u>Cases that need to be performed as soon as feasible (recognizing status of each hospital likely to evolve over next few weeks):</u>

- Previously treated, potentially curable pancreatic cancer in patients who have completed all appropriate neoadjuvant therapy
- Previously untreated, potentially curable pancreatic cancer in patients anticipated to have a short and uncomplicated hospital course
- Potentially curable pancreatic cancer associated with biliary and/or gastric obstruction in patients who are at risk for imminent and significant physiologic decline
- Pancreatic cystic lesions or duodenal neoplasms with clinical evidence of high-grade dysplasia

<u>Diagnoses that could be deferred for three months:</u>

- Potentially curable pancreatic cancer eligible for initial treatment with systemic chemotherapy and/or (chemo)radiation
- Pancreatic cystic lesions without a solid component or other clinical evidence for high-grade dysplasia or cancer
- Low-grade pancreatic neuroendocrine tumors, particularly those that are small
- Duodenal polyps without clinical evidence of high-grade dysplasia or cancer

Alternative treatment approaches to delay surgery that can be considered:

- Neoadjuvant systemic chemotherapy +/- (chemo) radiation for localized pancreatic cancer
- Neoadjuvant systemic chemotherapy for duodenal or ampullary cancer
- Duodenal stenting for gastric outlet obstruction
- Biliary stenting or percutaneous drainage of biliary obstruction
- Physiologic resuscitation with nutrition and exercise should be encouraged for all patients in whom surgery is to be considered

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few days):

- All but emergent, lifesaving operations should be deferred in this phase. Note that essentially all emergencies associated with these cancers are effectively palliated using nonsurgical methods (for example, endoscopic or percutaneous drainage for biliary sepsis, endoscopic management of gastric outlet obstruction, radiologic management of bleeding).

Cases that should be deferred:

- All elective pancreatic or duodenal procedures

Alternative treatment approaches:

- Transfer patients to hospital with capacity
- Neoadjuvant systemic chemotherapy +/- (chemo)radiation for localized pancreatic cancer
- Neoadjuvant systemic chemotherapy for duodenal or ampullary cancer
- Duodenal stenting for gastric outlet obstruction
- Biliary stenting or percutaneous drainage of biliary obstruction
- Physiologic resuscitation with nutrition and exercise should be encouraged for all patients in whom surgery is to be considered

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery deferred.

Cases that need to be performed as soon as feasible (status of hospital likely to progress in hours):

- All but emergent, lifesaving operations should be deferred in this phase. Note that essentially all emergencies associated with these cancers are effectively palliated using non-surgical methods (e.g., endoscopic or percutaneous drainage for biliary sepsis, endoscopic management of gastric outlet obstruction, management of bleeding with interventional techniques or radiation).

All other cases deferred

Alternate treatment recommended:

- Transfer patients to hospital with capacity

- Neoadjuvant systemic chemotherapy +/- (chemo)radiation for localized pancreatic cancer
- Neoadjuvant systemic chemotherapy for duodenal or ampullary cancer
- Duodenal stenting for gastric outlet obstruction
- Biliary stenting or percutaneous drainage of biliary obstruction
- Interventional techniques or radiation for gastrointestinal bleeding
- Physiologic resuscitation with nutrition and exercise should be encouraged for all patients in whom surgery is to be considered

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19- free environment has been secured with adequate testing and PPE.

<u>Cases that need to be done as soon as feasible:</u>

- Previously treated, potentially curable pancreatic cancer in patients who have completed all appropriate neoadjuvant therapy
- Previously untreated, potentially curable pancreatic cancer in patients anticipated to have a short and uncomplicated hospital course
- Potentially curable pancreatic cancer associated with biliary and/or gastric obstruction in patients who are at risk for imminent and significant physiologic decline
- Pancreatic cystic lesions or duodenal neoplasms with clinical evidence of high-grade dysplasia

<u>Cases that could be deferred or that may be higher risk for exposure to COVID-19 during early recovery:</u>

- Potentially curable pancreatic cancer eligible for initial treatment with systemic chemotherapy and/or (chemo)radiation
- Pancreatic cystic lesions without a solid component or other clinical evidence for high-grade dysplasia or cancer
- Low-grade pancreatic neuroendocrine tumors, particularly those which are small
- Duodenal polyps without clinical evidence of high-grade dysplasia or cancer

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high-functioning COVID-19-free environment has been established.

Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

- Available institutional resources and those of nearby transfer centers
- Likelihood of cure with surgery and progression with surgical delay
- Presence or absence of concurrent symptoms, such as pain, biliary obstruction, or gastric outlet obstruction, which may benefit from surgical palliation
- Availability of alternate therapies such as preoperative chemotherapy or (chemo)radiation
- Physiologic status of the patient

CANCER CARE TRIAGE AND MANAGEMENT: PROSTATE CANCER PATIENTS

Procedures related to prostate cancer will be addressed with regards to three patient categories:

1. Patients with abnormal digital rectal examination, elevated prostate-specific antigen (PSA), and/or abnormal magnetic resonance imaging (MRI). These patients are at an increased risk of harboring prostate cancer and would typically have a prostate biopsy.
2. Patients with clinically localized prostate cancer seeking potentially curative radical prostatectomy
3. Patients with an established diagnosis of low-risk prostate cancer who are on active surveillance and for whom an interval biopsy (surveillance or confirmatory) is planned

Prostate biopsies are short outpatient procedures usually performed in the ambulatory setting without the need for intubation. This procedure can be performed using a transrectal or a transperineal approach with a complication rate requiring hospitalization of approximately 3-4 percent. COVID-19 virus has been shown to shed in the stool and a transperineal approach minimizes manipulation of the rectal compartment. The aim of the procedure is to establish a diagnosis of prostate cancer or rule out the disease. The specific patient situation may drive the urgency of such procedures as a proportion of these men will have high risk or metastatic disease. Men seeking a prostate biopsy solely due to a small increase in PSA are good candidates for serial PSA testing during the pandemic as this number may normalize. Additionally, risk adjustment adjuncts are available to assist in stratification of these patients such as MRI imaging and blood/urine-based biomarkers (e.g., prostate health index (PHI), 4Kscore, PCA3, SelectMDx, etc).

Radical prostatectomy (RP) is a safe and common procedure performed under general endotracheal anesthesia that typically only requires an extended recovery (23-hour stay) in a hospital. Major perioperative complications (Clavien III and IV) are rare following radical prostatectomy (approximately 1 percent). There is a paucity of prospective studies with survival as an endpoint on the effect of delaying radical prostatectomy but the retrospective literature supports a safe delay of up to six months for most of these men. Longer delays may be associated with higher biochemical recurrence rates. Functional outcomes (urinary continence and erectile dysfunction) and the ability to spare critical neurovascular structures is dependent on disease stage and it is known that these outcomes are best in earlier stage patients regardless of ultimate oncological outcome. Most men also desire to avoid adjuvant and salvage therapies that have an adverse impact on their quality of life. Radiation therapy is an alternative curative therapy for most men with clinically localized prostate cancer.

For patients with PSA levels >20, clinical stage ≥T3, or ominous MRI findings (suspicion of extraprostatic extension, seminal vesical invasion, and/or lymph node involvement) additional staging evaluation with bone scintigraphy may uncover a likely diagnosis of metastatic disease without tissue diagnosis. It is currently unknown however whether the risk of a biopsy from a pandemic perspective is higher than that of obtaining further imaging and evaluation.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next three months.

- RP for unfavorable intermediate AND high-risk prostate cancer diagnosed >3 months prior
- Prostate biopsy for patients with PSA >10, Clinical stage >=T2b, and/or adverse MRI findings
- "Confirmatory" prostate biopsy in active surveillance candidates with adverse features (e.g., PSA >10, PSA density >0.2, etc.)
- Defer all surveillance biopsies on active surveillance patients

Alternative treatments:

- Brachytherapy in patients who are candidates for this treatment:
    - One-time outpatient procedure with limited complication profile
- Definitive radiation therapy for men seeking RP:
    - Presents similar pandemic specific issues
    - Requires multiple visits (daily for multiple weeks) to health care facility
- Androgen deprivation therapy (ADT) for men seeking RP anxious about delay:
    - Not curative
    - May make definitive surgery harder
    - No evidence it helps in this setting but does lower the PSA level to manage anxiety
- Bone scintigraphy to uncover likely metastatic disease in men seeking a prostate biopsy with PSA >20 and/or clinical stage >=T3 in lieu of a tissue diagnosis
- In patients with suspected metastatic disease, prostate-specific membrane antigen positive emission tomography (PSMA PET) may be beneficial when available
- MRI imaging for active surveillance patients who are seeking a surveillance biopsy

There are few indications for radical prostatectomy in this phase for men recently diagnosed with localized disease. It is feasible, however, that men diagnosed a few months prior to the acute phase I period were scheduled, or were planning to schedule, surgery during now what is the acute phase I in some regions. These patients may be facing a cumulative greater than six-month delay in treatment from date of diagnosis if asked to further delay surgery by three months. In such select cases, particularly in younger men with high-risk prostate cancer, treatment may be considered but is not mandated. Delay of greater than six months may be very reasonable in men with lower risk disease.

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few days.

Although it is not possible to envision every possible scenario related to prostate cancer that may occur, there should be very few to no indications to perform radical prostatectomy or prostate biopsy during this phase of the COVID-19 crisis.

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery deferred.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few hours.

Similar to Acute Phase II, while it is not possible to envision every possible scenario related to prostate cancer that may occur, there should be very few to no indications to perform radical prostatectomy or prostate biopsy during this phase of the COVID-19 crisis.

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

Same as Acute Phase I

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high-functioning COVID-19-free environment has been established.
Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

Cases that need to be prioritized in this phase:

- RP for men with intermediate and high-risk prostate cancer particularly those who are > 6 months from diagnosis
- RP for men seeking a biopsy stratified by risk group based on PSA > 10, clinical stage >=T2b, or adverse MRI findings

- Prostate biopsy for men under consideration for active surveillance but have a high likelihood of harboring high-risk disease (high PSA, high clinical stage, adverse MRI)
- Prostate biopsy for men with prostate cancer who are overdue for a prostate biopsy by >6–12 months should be prioritized or if they had a change in parameters suspicious for progression

Other patient groups can be managed during this phase depending on the local situation.

CANCER CARE TRIAGE AND MANAGEMENT: SOFT TISSUE SARCOMA PATIENTS

Soft tissue sarcomas occur in children and adults in many different anatomic locations and are comprised of over 50 histologic types. The decision making regarding appropriate treatment options requires comprehensive review of pathology and imaging studies followed by multidisciplinary discussion with experts in all facets of diagnosis and treatment. Depending on the age of the patient, the anatomic site, clinical stage, and histology, treatment plans can vary from surgery alone, to surgery before or after radiation therapy, to surgery with systemic therapy and radiation therapy—to include multiple sequencing options. Surgery may require several surgical teams for extirpation and reconstruction depending on the anatomic site and extent of surrounding organ involvement. The complexity of the surgical procedure, likelihood of achieving a margin negative resection, physiologic status of the patient, and availability of alternate therapeutic options must be considered in each individual patient. As discussed in other disease sites, increasing complexity of the surgical procedure (especially in the setting of neoadjuvant radiation therapy and/or chemotherapy) can lead to higher rates of adverse events, need for ICU care, prolonged hospitalizations, and readmission following surgery. This leads to the potential to consume significant hospital resources in the postoperative period. However, this must be considered with the knowledge that many types of soft tissue sarcomas do not have effective systemic therapies and radiation therapy may not be feasible with very large retroperitoneal tumors or those where large amounts of small bowel or other critical structures (spinal cord, etc.) would be in the treatment field. In addition, the risk of death to patients with myelosuppressive chemotherapy (with many regimens utilized in soft tissue sarcomas) may be higher than with surgery, so delaying surgery and prolonging chemotherapy may well increase the risk of death in this population.

While surgery is necessary for the cure of localized soft tissue sarcomas, many patients who undergo surgery for this disease are not cured and will develop locally recurrent or metastatic disease. Factors such as tumor histology, anatomy, and expected functional outcomes should be critically evaluated for each patient to determine the role of surgery. Full assessment should be performed including underlying comorbidities (e.g., cardiovascular disease, chronic respiratory disease, diabetes and renal insufficiency) in addition to performance status, physiologic age, and fitness status. Every case should be discussed in a multidisciplinary forum with all disciplines to establish the most appropriate care plan.

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

In this phase, patients selected for “elective” surgery should have a limited comorbidity profile and a physiologic status that is optimized so that the associated length of stay and the extent of resource utilization are both predictable and minimized.

<u>Cases that need to be performed as soon as feasible (recognizing status of each hospital likely to evolve over next few weeks):</u>

- Previously treated, potentially curable soft tissue sarcoma in patients who have completed all appropriate neoadjuvant therapy
- Previously untreated, potentially curable soft tissue sarcoma in patients anticipated to have a short and uncomplicated hospital course

- Potentially curable soft tissue sarcomas associated with obstruction or compromise of the aerodigestive tract, urinary tract, vascular system, or central nervous system in patients who are at risk for imminent and significant physiologic decline
- Soft tissue neoplasms that cannot be fully classified with respect to histologic subtype based on core needle biopsy

Discussion about deferral of surgery should include:

- Patients who have received preoperative therapy:
    - Radiation: How long can the window between radiation and surgery be extended—consideration of delaying additional two-four weeks as deemed appropriate
    - Systemic therapy: Is it possible to safely continue systemic therapy in patients with favorable response or stable disease
- Likelihood for significant transfusion requirements with surgical resection (i.e., leiomyosarcoma originating from major vascular structures such as the inferior vena cava or extremity sarcoma requiring significant vascular resection/reconstruction)
- Patient has any significant likelihood for ICU stay postoperatively
- Patient is likely to require free flap reconstruction because of exposure of critical vascular or neurologic structures
- Cases in which outcome unlikely to be adversely affected by eight- to 12-week delay:
    - Recurrent disease, progressive disease with findings suggestive of metastasis on advance imaging, palliative indications for surgery
    - Low-grade soft tissue sarcomas unlikely to have any change in growth within three to six months and unlikely to impact the extent of surgical resection (example: dermatofibrosarcoma protuberans (DFSP), small gastrointestinal stromal tumors (GIST) of the stomach)
    - Cases with a reasonable systemic therapy option (example: GIST that is stable in size or responding to imatinib; desmoid tumor that can be treated with systemic therapy, radiation therapy or cryoablation)

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few days):

- All but emergent, lifesaving operations should be deferred in this phase. Note that essentially all emergencies associated with these tumors may be effectively palliated using nonsurgical methods (e.g., endoscopic management of gastric or airway obstruction, interventional radiology procedures for management of bleeding).

Cases that should be deferred:

- All elective soft tissue sarcoma procedures that have alternative treatment options

Alternative treatment approaches:

- Transfer patients to hospital with capacity

- Neoadjuvant systemic chemotherapy +/- (chemo)radiation for localized tumors
- Neoadjuvant radiation therapy for appropriate extremity or retroperitoneal tumors

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery is deferred.

Cases that need to be done as soon as feasible (status of hospital likely to progress in hours):

- All but emergent, lifesaving operations should be deferred in this phase. Consider nonsurgical methods to temporize (e.g., endoscopic or percutaneous procedures for management of gastrointestinal tract, urinary tract or airway obstruction, management of bleeding with interventional radiology procedures or radiation).

All other cases deferred

Alternate treatment recommended:

- Transfer patients to hospital with capacity

Neoadjuvant systemic therapy +/- radiation for localized tumors as appropriate based on clinical stage and histologic type

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

Cases that need to be performed as soon as feasible:

- Potentially curable soft tissue sarcoma patients who have completed all appropriate neoadjuvant systemic therapy and/or radiation therapy
- Previously untreated, potentially curable soft tissue sarcoma patients anticipated to have a short and uncomplicated hospital course
- Potentially curable soft tissue sarcoma patients with obstruction of the digestive tract or urinary tract in patients who are at risk for imminent and significant physiologic decline or organ dysfunction
- Retroperitoneal or pelvic soft tissue sarcomas with clinical evidence of vascular involvement that could lead to thromboembolic disease or limb ischemia

Cases that could be deferred or that may be higher risk for exposure to COVID-19 during early recovery:

- Potentially curable soft tissue sarcoma patients eligible for initial treatment with systemic chemotherapy and/or radiation therapy
- Retroperitoneal tumors which require multi-organ resection and complex reconstruction
- Pelvic soft tissue sarcomas which require an exenterative procedure
- Low-grade soft tissue tumors without neurovascular involvement, particularly those which are small in size

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high-functioning COVID-19-free environment has been established.

Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

- Available institutional resources for complex, multi-team cases that require long operative times and extended hospital stay
- Likelihood of cure with surgery, and progression with surgical delay
- Need for extensive rehabilitation following truncal or extremity resection and reconstruction
- Pulmonary function assessment of thoracic and chest wall sarcomas in patients that may require mechanical ventilation
- Presence or absence of concurrent symptoms, such as pain, bleeding, or obstruction of the aerodigestive tract, which may benefit from surgical palliation
- Availability of alternate therapies such as preoperative chemotherapy, targeted therapies or radiation therapy
- Performance status of the patient

CANCER CARE TRIAGE AND MANAGEMENT: TESTICULAR CANCER PATIENTS

General Management Recommendations

The management of testicular cancer—germ cell tumors of the testicle—and masses suspicious for TC is nuanced, and individual circumstances may not ascribe to general recommendations for the management of the disease. Given the relative rarity of testicular cancer it is highly recommended that providers seek the opinion of regional or national experts in the triage and management of unclear circumstances. When creating a management plan, physicians should consider reducing the physical interaction between the patient and the medical outfit as well as decreasing periods of immunocompromise. The management of testicular cancer is often multidisciplinary with the coordination of medical oncology, urology, and radiation oncology. This document will focus on the effect of COVID-19 on the surgical management of this disease.

Procedures related to the surgical management of testicular cancer will be addressed with regard to four patient categories:

1. Men with abnormal testicular findings (physical examination and/or ultrasound) that are suspect for a testicular germ cell tumor.
2. Men with stage I testicular cancer considering primary retroperitoneal lymph node dissection (RPLND).
3. Men with early-stage testicular cancer (Stage IIA-IIB) considering primary RPLND.
4. Men with advanced testicular cancer (Stage IIC-III) requiring post-chemotherapy RPLND.

Surgical Treatments for Testicular Cancer

Radical inguinal orchiectomy (RIO) is the gold standard for the initial diagnosis and management of testicular cancer of any stage. RIO is typically performed in an outpatient setting with rare complications (2-4 percent) and risk of readmission. RIO may be performed with endotracheal intubation although it can be performed with a laryngeal mask or regional anesthesia. RIO is required in most settings to establish the diagnosis of testicular cancer and define histologic subtype (and subsequent management paradigm), and it may be curative in men with Stage I testicular cancer.

RPLND can be performed in the primary setting (prior to chemotherapy) or post-chemotherapy for men with advanced disease. In general, RPLND is a major operation requiring endotracheal intubation and hospitalization for 1 to 5 days. Primary RPLND is associated with lower complication rates and readmission; however, post-chemotherapy RPLND is associated with complication and readmission rates of up to 25 percent and 17 percent respectively. Primary RPLND can effectively stage and treat men with low-volume nodal metastases and men with teratoma, which is chemotherapy- and radiation-resistant. Post-chemotherapy RPLND is essential for disease control in men with nonseminomatous germ cell tumors with residual disease after chemotherapy. Post-chemotherapy RPLND is, in general, performed 4 to 12 weeks following completion of the last cycle of chemotherapy to allow for recovery, to minimize risk of complications related to chemotherapy, and without detriment to oncologic outcome.

There is a paucity of data regarding the effect of delay of RIO and RPLND on ultimate testicular cancer outcomes. While there is some suggestion that a delay to definitive disease management may effect stage and treatment response (including likelihood of a complete response and survival), it is unclear what extent of delay imparts meaningful influence given the high cancer-specific survival for the disease. Timely diagnosis, especially for symptomatic patients, is associated with earlier stage diagnosis, less total therapy, and subsequent long-term toxicity. The impact of delay in management may be more significant for nonseminomatous germ cell tumors (NSGCT) given the longer period of localized disease and better response to chemotherapy in seminoma. Prior evaluation of delay from symptom onset to treatment found that delay of more than three months was associated with worse survival in NSGCT. Prior consensus statements recommend RIO within 7 to 10 days of diagnosis and recent recommendations from the European Association of Urology recommended a postponement of no longer than 2 to 3 days for RIO. (https://uroweb.org/guideline/covid-19-recommendations/)

Additional testicular cancer procedures—including biopsy of the contralateral testicle, placement of a testicular prosthesis, sperm banking, and testicular sperm extraction—can be performed at the time of RIO, are considered low priority during an active COVID-19 pandemic, and can be safely deferred if being considered as an independent procedure. Sperm banking may proceed based on patient and family preferences and the safety of the fertility lab and cryopreservation facility.

Considerations of Diagnostic Workup, Staging Evaluation, and Radical Inguinal Orchiectomy

Physicians are encouraged to exercise telehealth to review pertinent signs, symptoms, laboratory evaluations, and imaging studies to potentially limit physical exposure of patients and health care personnel to individuals that have tested positive for COVID-19.

All noninvasive diagnostics related to the workup of a testicular mass suspicious for testicular cancer should proceed as delay in diagnosis may adversely affect outcome. These diagnostics include but are not restricted to the following:

- Physical examination of the genitals and sites of possible metastatic disease
- Scrotal ultrasound with doppler
- Serum tumor markers
- Staging Imaging (computed tomography, magnetic resonance imaging, X ray of the abdomen, pelvis, and chest; head imaging as indicated)

RIO should proceed in most circumstances as this is a low-risk procedure and clinical harm may occur if delayed greater than six weeks.

- RIO should not be delayed extensively (beyond two weeks) in patients with elevated serum tumor markers or symptoms.
- Asymptomatic patients with normal serum tumors and small testicular masses (less than 2 cm) may consider staging diagnostics, surveillance of the testicle, or delayed RIO in lieu of immediate surgery given the high probability (up to 80 percent) of benign masses in men meeting these criteria.
- If access to operating rooms (ORs) is limited, consider staging diagnostics with safe surveillance of patients with presumptive stage I testicular cancer and prioritization of RIO for patients with

advanced disease in whom RIO may impact treatment. Men with significant metastatic disease can initiate chemotherapy with deferred orchiectomy.

ACUTE PHASE I. Semi-urgent setting (Preparation phase) - Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next 3 months.

Radical inguinal orchiectomy should proceed without restriction (as above).

Early-stage TC (Stage I-IIB) considering Primary RPLND

- **Stage I Seminoma and NSGCT**: *Surveillance should be prioritized for all patients with stage I TC including seminoma, low- and high-risk NSGCT*. Surveillance is a guideline-directed safe alternative with CSS rates >98% for all stage 1 patients regardless of histology. Adjuvant chemotherapy or primary RPLND, while associated with reduced risk of recurrence require increase healthcare exposure for the patient and healthcare providers, as well as consume PPE without significant improvement on cancer-specific survival. Individual patients may be unwilling to accept surveillance and may consider adjuvant chemotherapy or primary RPLND. The interaction between chemotherapy, immunosuppression, and COVID infection is not well understood; minimizing exposure to chemotherapy may reduce risk of COVID-related events.
- **Stage IIA-B Seminoma and NSGCT**: *Management choices should be based on the probability of cure from a single therapy (multiple therapies increase risk of exposure, consume more PPE, add toxicity) and be based on guideline-directed care.* Patients with Stage II TC will require additional therapy in the form of multi-agent, platinum-based chemotherapy, radiotherapy (for seminoma only), and/or RPLND. Induction chemotherapy and radiotherapy require routine exposure to healthcare facilities; placing both patient and healthcare providers at increased risk of exposure. All three approaches require consumption of PPE. Special consideration may be given to select patients with small volume, IIA disease in which a period of surveillance over 6-8 weeks may provide for safer administration of curative therapy.

Advanced stage TC following chemotherapy

- **Seminoma with residual mass and normal markers**: Prioritize observation as surveillance is an acceptable option and a three-month delay is unlikely to impact outcome with ability to salvage with additional chemotherapy and/or surgery.
- **Nonseminoma, stage II-III, negative markers, no residual mass or <1 cm**: Prioritize observation or strategic delay in surgery given the low probability of viable germ cell tumor in these patients and unlikely effect on long-term outcome.
- **Nonseminoma, stage II-III, negative markers, residual mass >1 cm:**
    - Proceed according to institutional policy and timing for surgery post-chemotherapy
        - Consider surveillance and delayed RPLND for good-risk International Germ Cell Cancer Collaborative Group men with low-volume disease
        - Consider prioritization of RPLND for patients with teratoma or concern and particularly somatic transformation

- Consider regional/geographic COVID burden and potentially refer to centers of excellence in low COVID-exposed areas
- Consider referral to high-volume surgeon and/or center to minimize the risk of complications, length of stay, and readmission.
- Imaging and tumor markers should be up to date prior to RPLND (per guideline recommendations)

ACUTE PHASE II. Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few days.

Radical inguinal orchiectomy should proceed without restriction (as above).

Early-stage TC (Stage I-IIB) considering Primary RPLND should proceed as recommended in Acute Phase I with a prioritization of chemotherapy for men with IIB disease.

Advanced stage TC requiring post-chemotherapy RPLND

- **Seminoma with residual mass and normal markers; or**
- **Non-seminoma, stage II-III, negative markers, no residual mass or <1cm:**
  - Prioritize observation or strategic delay in surgery until early phase recovery achieved.
- **Non-seminoma, stage II-III, negative markers, residual mass >1cm:**
  - Proceed as recommended in Acute Phase I.

ACUTE PHASE III. Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery deferred.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few hours.

While it is not possible to envision every possible scenario related to testicular cancer that may occur, there should be very few indications for RPLND during this phase.

Consider post-chemotherapy RPLND only in **symptomatic patients** (i.e. abdominal mass/pain, gastrointestinal symptoms, pulmonary compromise, neurologic deficits) in which **additional chemotherapy is not indicated** (i.e. large teratoma). Given the rarity of this clinical situation, consultation with expert centers is highly recommended before management decisions are finalized. Surveillance should be prioritized for all early stage TC considering primary RPLND.

EARLY-PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

- Same as Acute Phase I.

LATE-PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high functioning COVID-19-free environment has been established.

Cases should be prioritized within the context of a complete multidisciplinary evaluation. RIO should proceed without restriction (as above). Post-chemotherapy RPLND with delays beyond 12 weeks (three months) should be prioritized above primary RPLND.

CANCER CARE TRIAGE AND MANAGEMENT: THORACIC MALIGNANCY PATIENTS

ACUTE PHASE I: Semi-urgent setting (preparation phase): Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity, and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next three months.

Cases that need to be performed as soon as feasible (recognizing status of hospital likely to progress over next few weeks):

- Solid or predominantly solid (>50 percent) lung cancer or presumed lung cancer ≥2 cm, clinically node-negative
- Node-positive lung cancer
- Post-induction therapy completed
- Esophageal cancer T1b or greater
- Chest wall tumors of high malignant potential not manageable by alternative therapy
- Stenting for obstructing esophageal tumor
- Staging to start treatment (mediastinoscopy, diagnostic VATS for pleural dissemination)
- Symptomatic mediastinal tumors—diagnosis not amenable to needle biopsy
- Patients enrolled in therapeutic clinical trials

Cases that should be deferred:

- Predominantly ground glass (<50 percent solid) nodules or cancers
- Solid nodule or lung cancer < 2 cm
- Indolent histology (for example, carcinoid, slowly enlarging nodule)
- Thymoma (non-bulky, asymptomatic)
- Pulmonary oligometastases—unless clinically necessary for pressing therapeutic or diagnostic indications (i.e., surgery will affect treatment)
- Patients unlikely to separate from mechanical ventilation or likely to have prolonged ICU needs (i.e., particularly high-risk patients)
- Tracheal resection (unless aggressive histology)
- Bronchoscopy
- Upper endoscopy
- Tracheostomy

Alternative treatment approaches to be considered (assuming resources permit):

- Early stage esophageal cancer (stage T1a/b superficial) managed endoscopically
- If eligible for adjuvant therapy, then give neoadjuvant therapy (for example chemotherapy for 5 cm lung cancer)
- Stereotactic ablative radiotherapy (SABR)[f]

- Ablation (e.g., cryotherapy, radiofrequency ablation)
- Stent for obstructing cancers then treat with chemoradiation
- Debulking (endobronchial tumor) only in circumstance where alternative therapy is not an option due to increased risk of aerosolization (e.g., stridor post-obstructive pneumonia not responsive to antibiotics)
- Nonsurgical staging (endobronchial ultrasound, imaging, interventional radiology biopsy)
- Follow patients after their neoadjuvant for "local only failure" (that is, salvage surgery)
- Extending chemotherapy (additional cycles) for patients completing a planned neoadjuvant course

ACUTE PHASE II: Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited, or COVID-19 trajectory within hospital in rapidly escalating phase.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few days.

<u>Cases that need to be done as soon as feasible (recognizing status of hospital likely to progress over next few days):</u>

- Perforated cancer of esophagus—not septic
- Tumor associated infection—compromising, but not septic (e.g., debulking for post-obstructive pneumonia)
- Management of surgical complications (hemothorax, empyema, infected mesh)—in a hemodynamically stable patient

<u>Cases that should be deferred:</u>

- All thoracic procedures typically scheduled as routine/elective (i.e., not add-ons)

<u>Alternative treatment approaches RECOMMENDED (assuming resources permit):</u>

- Transfer patient to hospital that is in Phase I
- If eligible for adjuvant therapy then give neoadjuvant therapy
- SABR
- Ablation (such as cryotherapy, radiofrequency ablation)
- Reconsider neoadjuvant as definitive chemoradiation, and follow patients for "local only failure" (that is, salvage surgery)

ACUTE PHASE III: Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted.

Surgery restricted to patients likely to have survivorship compromised if surgery not performed within next few hours.

<u>Cases that need to be done as soon as feasible (status of hospital likely to progress in hours):</u>

- Perforated cancer of esophagus—septic patient
- Threatened airway
- Tumor-associated sepsis

- Management of surgical complications—unstable patient (active bleeding not amenable to nonsurgical management, dehiscence of airway, anastomotic leak with sepsis)

All other cases deferred

Alternate treatment recommended:

Same as previous General Recommendations

Case status (i.e., risk of death time frame) determination made by division, ideally in a multi-clinician setting (case review conference)

Recovery Phase - Thoracic

The prioritization of patients must take into consideration the estimated risk of further delay, in terms of compromising survival or permanent function, and the likely time interval the hospital will require to work through the backlog of operations (e.g., one month, three months). Prioritization will be a function of the stage and histopathology of the tumor, the duration of delay that has already taken place, and the observed tumor trajectory during the period of delay (i.e., did the tumor grow or was the tumor responding to preoperative treatment).

The following priority categorization is proposed:

	Description	Target Case Completion
Priority 1	Survival currently impacted by delay Active risk for permanent deficit	As soon as safety can be established
Priority 2	Survival impacted if delay > 3 months Risk of permanent deficit if delay > 3 months	Within 3 months of evaluation
Priority 3	Survival impacted if delay > 6 months Risk of permanent deficit if delay > 6 months	Within 6 months of evaluation
Priority 4	Surgery does not impact survival No risk of permanent deficit	As soon as access for higher priority cases no longer impacted

Expanded Detail

Priority 1

- Few cases
- Would have qualified for surgery under “urgent” designation, but risk felt to be prohibitive (patient risk factors, hospital environment, magnitude of surgery)
- These patients could go into COVID-minimal pathway as resources and COVID-census permit
- Examples:
    - Esophagectomy after neoadjuvant therapy, lobectomy for lung cancer in an elderly patient felt to be higher risk

Priority 2

- More cases
- Time-sensitive, but not urgent. Initial delay was reasonable, but an additional three months (i.e. waiting to get through backlog) would be unsafe

- These would be the majority of the “first wave” cases as access improves
- IMPORTANT NOTE during delay, patients may convert from priority 2→1
    - Depending on duration of their delay
    - Additional imaging, evaluations
- Examples:
    - Solid lung cancer > 1 cm, enlarging on imaging

Priority 3

- Many cases
- Impact survival or function, but six-month delay should be tolerated without significant consequence
- Survival and long-term function should be similar if surgery performed within six months of when backlog management starts
- Impact on patient’s quality of life is important consideration
- Example
    - Slow growing, predominantly ground glass cancer < 2 cm

Priority 4

- Many cases for hospital, but less common in cancer population
- Elective, but important to patients
- Impact on patient’s quality of life is important consideration
- Example:
    - Esophageal leiomyoma causing moderate dysphagia, but stable in size.

EARLY PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

Cases that need to be done as soon as feasible:

- Priority 1 and 2 cases

LATE PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high-functioning COVID-19-free environment has been established.

Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

- Priority 3 and 4 cases

CANCER CARE TRIAGE AND MANAGEMENT: UROTHELIAL BLADDER AND UPPER-TRACT CANCER PATIENTS

General Management Recommendations

This section will cover urothelial cancer (UC) that occurs both in the upper urinary tracts (kidneys, ureter) and lower urinary tracts (bladder, urethra). The prognosis and disease course of UC varies greatly based on grade, stage, and location of the disease. The natural disease course can range from relatively indolent disease, in which a three-month or longer delay is of limited consequence, to aggressive cancers in which surgical delays of eight weeks or greater have demonstrably poorer cancer-specific survival. There is a limited role for surgery if metastatic disease is either confirmed or suspected and systemic therapy should be used first-line in those cases. For locally confined disease, surgical management is often first-line and highly effective. Procedures related to UC will be addressed with regard to the following patient categories:

- Patients indicated for diagnostic workup due to symptoms or abnormal labs such as microscopic hematuria, gross hematuria, abnormal imaging findings, or irritative voiding symptoms. These patients are at an increased risk of harboring urothelial cancer and would typically require a cystoscopy and upper tract imaging.
- Patients with non-muscle invasive urothelial bladder cancer and low-grade upper tract urothelial cancer (UTUC) undergoing surveillance and possible endoscopic or instillation treatments.
- Patients with muscle-invasive bladder cancer or high-grade UTUC with planned treatment usually with extirpative surgery.

When considering the risks and benefits of treating UC patients during the COVID-19 pandemic, patient risk factors combined with local conditions, hospital resources such as staff and PPE, disease trajectory, and guidance from hospital and local leadership must all be considered and will supersede generalized guidelines presented here. The UC population is generally a high-risk category of patients who could potentially fare poorly if they contract the COVID-19 virus. The mean age of diagnosis of UC is 65 years and enriched for smokers who may have impaired pulmonary status. The competing risks of harm from exposure to COVID-19 versus the risks from progression of UC in each patient must be considered on a case-by-case basis.

Diagnosis of bladder cancer is typically made by cystoscopy, which is performed for gross hematuria, microscopic hematuria, irritative voiding symptoms in the absence of infection, or incidental identification of mass or bladder abnormality on imaging as the most common indications. Upper tract imaging is typically performed as part of gross or microscopic hematuria evaluation as well, which can identify UTUC of the renal pelvis or ureter. Cystoscopy is a safe, outpatient procedure which does not require general anesthesia and is often performed in the clinic or surgery center setting with limited PPE requirements. The rate of diagnosis of bladder cancer in asymptomatic microscopic hematuria without risk factors is on the order of 1 to2 percent. Incidence of bladder cancer in the setting of gross hematuria is closer to 20 percent and can represent more advanced disease.

Treatments for UC of the bladder and UTUC range from endoscopic management to extirpative surgery of the affected kidney or bladder. Endoscopic treatments such as transurethral resection of bladder tumor (TURBT) or ureteroscopy with fulguration or ablation of tumor in the upper urinary tract are

typically short procedures under general anesthesia that do not require an overnight hospital stay. These procedures are generally safe with an overall complication rate of 5 to 10 percent with the vast majority of those as Clavien-Dindo grade I or II. Ureteroscopy with laser or cautery ablation of UTUC is similarly a safe, typically outpatient procedure.

Instillation treatments of agents such as bacillus Calmette–Guerin (BCG)or chemotherapies such as mitomycin, gemcitabine, and others are used commonly in bladder cancer, although they can also be used in some cases of UTUC. These treatments are generally performed in the outpatient clinic and do not require general anesthesia, but do require multiple visits for serial instillation of treatments which may be a risk factor for COVID-19 exposure.

Aggressive UTUC and bladder cancer may require extirpative surgery under general anesthesia, greater numbers of ancillary staff in the OR, and potentially longer hospital stays, all of which increase exposure and use resources such as PPE. UTUC may require a nephroureterectomy, which can be performed open or minimally invasively. Recovery is typically a few days in the hospital and complication rates are approximately 15 percent, which may require further visits, hospital resources, and treatment. Radical cystectomy with urinary diversion is a major operation with complication rates ranging from 50 to 70 percent. Historically, this operation carries a 1 to 2 percent perioperative mortality rate, in part attributed to the advanced age and cardiopulmonary comorbidities suffered by this patient population largely from a significant smoking history. Hospital recovery is typically 4 to10 days and readmission to the hospital within 30 days occurs in nearly 30 percent of patients, mostly commonly from dehydration, urinary tract infection, or gastrointestinal related complications.

Neoadjuvant chemotherapy (NAC) is considered standard of care for most patients with invasive bladder cancer and some evidence exists for its benefit in UTUC patient populations, as well. There are risks and benefits to NAC that are of particular relevance during the COVID-19 pandemic. NAC allows the patient to avoid the immediate risk of extirpative surgery, with the attendant risks of hospitalization with exposure to the health care system, but still allows patients to immediately start treatment for invasive bladder cancer. However, providers and patients must also consider the unique risks of NAC, which will require numerous visits to the clinic or hospital for infusions of treatments, as well as serial laboratory testing to monitor for side effects. There are risks of complications with chemotherapy, such as anemia, neutropenia, and sepsis that could require hospitalization, although this is relatively uncommon. Neoadjuvant immunotherapy in patients who are ineligible for standard cisplatin-based NAC is also a consideration and carries the benefit of fewer infusions.

Lastly, in select patients with bladder cancer, trimodal therapy (TMT) with maximal transurethral resection of the bladder tumor (TURBT) and combination chemoradiation as curative intent treatment is an option. While TMT avoids the perioperative morbidity and mortality risks of extirpative surgery and does not require a prolonged hospitalization, it does carry its own risks. Patients who undergo TMT are susceptible to adverse effects of chemotherapy, such as anemia, neutropenia, and sepsis, which may require hospitalization. The radiation component varies but generally requires radiation doses five days per week for several weeks. Patients must also undergo surveillance office cystoscopy with their urologist and frequently requires an OR procedure for repeat TURBT.

The effects of delay of treatment for UC have been studied in limited, retrospective studies. While these studies may provide some guidance, they are prone to multiple biases and should be interpreted within that context. Regardless, numerous studies have demonstrated that delays greater than 12 weeks from diagnosis of muscle invasive bladder cancer to cystectomy in patients not opting for NAC can result in

disease progression and poorer bladder cancer specific mortality. In patients who are eligible for NAC, a delay of greater than eight weeks was associated with adverse pathologic outcomes in a national registry-based study. For UTUC, fewer studies are available to characterize the impact of delay on outcomes. In patients potentially candidates for endoscopic management of the UTUC, delays of definitive nephroureterectomy due to attempted, but failed, endoscopic management did not result in disease progression. However, in another study considering all patients undergoing radical nephroureterectomy, a delay of greater than three months was associated with more advanced disease and higher cancer-specific mortality.

ACUTE PHASE I. Semi-urgent setting (Preparation phase)-Few COVID-19 patients, hospital resources not exhausted, institution still has ICU and ventilator capacity and COVID-19 trajectory not in rapid escalation phase.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next three months.

Diagnosis: Patients with gross hematuria or incidental mass on imaging can be considered for complete diagnostic cystoscopy and imaging. TURBT or UTUC sampling will be necessary as indicated in particular to properly grade and stage the bladder cancer for future triage of management. Asymptomatic microscopic hematuria, particularly in the absence of other risk factors, can likely be deferred if necessary due to local COVID-19 related conditions. Presence of other risk factors may raise suspicion of bladder cancer and may prompt workup at this phase per discretion of the treating physician and local conditions. Imaging as an initial triage may assist optimized management of the patient as identification of an obvious mass and may allow skipping of cystoscopy directly into OR procedure.

Non-invasive UC:

Bladder: Small papillary low-grade (LG) recurrences may be deferred. Larger (>1 cm) or multifocal tumors as well as HG tumors and gross hematuria associated with bladder tumor warrant TURBT at this time. Repeat TURBT for HGTa or HGT1 should also be performed as there is a significant risk of undiagnosed T2 disease. BCG Induction should be completed at least to instillation five of six if feasible and safe, and the first maintenance should be completed to two of the three treatments if feasible. For patients who have undergone at least one year of maintenance BCG, additional instillations may be forgone. Further delay of subsequent courses of BCG are subject to appearance of bladder urothelium and proclivity for recurrence of the tumor based on interim cystoscopy. Surveillance cystoscopy should be considered for history of high-generation tumor within recent history for the patient or for new onset of symptoms such as gross hematuria. Surveillance cystoscopy deferral may be considered in stable patients with no symptoms and no recent recurrence at least one year out.

UTUC: Kidney-sparing instillation treatment or endoscopic ablation should be attempted in patients who are candidates for this treatment. In select cases of patients with known, recurrent disease that requires repeated treatments and tumors with observed slow growth rate, surveillance and/or delayed treatment may be reasonable per surgeon judgement.

Aggressive UC:

Bladder: Patients indicated for radical cystectomy for urothelial cancer with stage T2 or higher disease should be considered for treatment during this period. The risks and benefits of NAC as described in this document should be considered. Radical cystectomy in patients with BCG unresponsive or T1 bladder cancer may be considered, however alternatives such as intravesical instillation therapies may be an option to consider at this time as well. Chemoradiation may be considered although limitations during the COVID-19 crisis as detailed above should be taken into account.

UTUC: Patients that are not candidates for or who failed kidney-sparing approaches and require nephroureterectomy can be considered for this surgical treatment during this phase.

ACUTE PHASE II. Urgent setting: Many COVID-19 patients, ICU and ventilator capacity limited, OR supplies limited.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next few days.

A cystoscopy may be indicated during acute phase II in patients where identification of bladder cancer will impact treatment decisions in the near future. Using the recently published VI-RADS (Vesical Imaging-Reporting and Data System) protocol with a pelvic MRI, or urinary markers specifically designed to rule out malignancy may be alternative ways to triage patients in extenuating circumstances for urgent procedural indications.

Most initiation of instillation treatments can likely be delayed on the order of 1 to 2 weeks. Avoiding interruption of ongoing therapy is desired if feasible, particularly in induction or early maintenance cycles.

TURBT for the setting of severe hematuria causing hospitalization may be indicated. Cystectomy and nephroureterectomy in cases of severe bleeding or infection may be indicated. Less invasive means if available such as TURBT to control bleeding or embolization may be considered as well depending on local conditions and expertise availability. Symptomatic large and/or clinically invasive upper tract tumors can consider nephroureterectomy with or without neoadjuvant chemotherapy.

ACUTE PHASE III. Hospital resources are all routed to COVID-19 patients, no ventilator or ICU capacity, OR supplies exhausted. Patients in whom death is likely within hours if surgery *is* deferred.

Surgery restricted to patients likely to have survivorship compromised if surgery is not performed within the next few hours.

Cases of hematuria causing hemodynamic instability or causing severe challenges in maintaining urinary drainage may necessitate TURBT and fulguration in this phase.

Indications for urgent nephroureterectomy or cystectomy are uncommon at this phase; however, emergencies such as bladder perforation from tumor may necessitate urgent surgery in this time frame.

EARLY-PHASE RECOVERY: Past the peak of COVID-19, resources are more available, and some kind of COVID-19-free environment has been secured with adequate testing and PPE.

- Same as Acute Phase I.

LATE-PHASE RECOVERY: Well past the peak of new COVID-19 cases, resources are nearly back to normal levels, and a substantial and high functioning COVID-19-free environment has been established. Cases should be prioritized within the context of a complete multidisciplinary evaluation. The following should be specifically considered:

Cases that need to be prioritized in this phase:

- Patients with active urothelial cancer who deferred treatment (local instillation, endoscopic, systemic, or extirpative surgery) should undergo these treatments at this point
- Patients indicated for surveillance endoscopic or imaging procedures of known history of UC should also be followed up at this point
- Patients indicated for workup such as cystoscopy for hematuria

Other patient groups can be managed during this phase depending on the local situation.

Updated May 7, 2020