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3 Delaying cancer cases in Urology during COVID-19: review of the literature.

4 Authors: Isamu Tachibana¹, Ethan L. Ferguson¹, Ashorne Mahenthiran², Jay P. Natarajan³,
5 Timothy A. Masterson¹, Clinton D. Bahler¹, Chandru P. Sundaram^{1*}6 ¹Indiana University School of Medicine, Indianapolis, IN7 ²Feinberg School of Medicine, Northwestern University, Chicago, IL8 ³College of Medicine, Northeast Ohio Medical University, Rootstown, OH

9 *Corresponding Author:

10 Chandru P. Sundaram

11 535 Barnhill Drive RT 150

12 Department of Urology

13 Indiana University School of Medicine

14 Indianapolis, IN 46202

15 sundaram@iupui.edu

16 P: 317-944-7451

17 F: 317-948-2619

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24 Isamu Tachibana: isatachi@iupui.edu25 Ethan L. Ferguson: elfergus@iupui.edu26 Ashorne Mahenthiran: ashorne.mahenthiran@northwestern.edu27 Jay P. Natarajan: jnatarajan@neomed.edu

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28 Timothy A. Masterson: tamaster@iupui.edu

29 Clinton D. Bahler: cdbahler@iupui.edu

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33 Abstract

34 Purpose: Coronavirus Disease 2019 (COVID-19) is a global pandemic affecting hospital systems
35 and the availability of resources for surgical procedures. Our aim is to provide guidance for
36 urologists to help prioritize urologic cancer surgeries.

37 Material and Methods: We reviewed published literature on bladder cancer, upper tract urothelial
38 carcinoma (UTUC), penile cancer, testis cancer, prostate cancer, renal cancer, and adrenal
39 cancer.

40 Results: For muscle invasive bladder cancer (MIBC), delays should be less than roughly 10
41 weeks and neoadjuvant chemotherapy should be considered. For non-MIBC, patients should be
42 counseled appropriately based on risk and intravesical therapies can continue. UTUC should also
43 be treated with minimal delays for high risk patients, especially with ureteral tumors. Surgery for
44 T1 renal cancers when indicated can be delayed until adequate resources are available. Patients
45 with T2 renal cancer should be considered for early surgery if there are unfavorable pre-
46 operative characteristics. Higher stage renal tumors should be considered for early surgery. Early
47 multi-disciplinary approach is recommended for metastatic renal cancers. High risk prostate
48 cancer may need preferential treatment and consideration of neoadjuvant hormonal therapy.
49 Penile cancer can have worse sexual or oncologic outcome with prolonged surgical delay.
50 Likewise, adrenal cancer is aggressive and needs early surgical treatment. Testicular cancer
51 should be treated in a timely manner with surgery or chemotherapy, as indicated.

52 Conclusions: This review should further assist urologists in recognizing patients with potentially
53 aggressive tumor biology that warrant early treatment.

54 Introduction

55 Severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2) can induce a severe
56 respiratory compromise with rapid human-to-human transmission stressing entire hospital
57 systems. In order to conserve resources and prevent further spread of COVID-19, the CDC and
58 hospital systems have requested physicians to reconsider non-urgent procedures. Here, we aim to
59 discuss the effect of COVID-19 on urologic cancers, specifically regarding anticipated delays in
60 surgical treatment.

61 Background

62 COVID-19 is highly transmissible and can cause respiratory issues requiring ventilation,
63 ICU care, and death. Epidemiologic factors and high rates of hospitalization for patients with
64 COVID-19 have resulted in widespread cancellation of elective surgical procedures in favor of
65 prioritizing urgent procedures.

66 In response to COVID-19, recommendations for prioritizing cases have been published¹.
67 With reopening of operating rooms, region-specific factors should guide treatment as resources
68 and COVID-19 surges vary across the world. Throughout this process, urologists should assist in
69 appropriate timing of treating urologic cancers. Thus, our aim is to provide further guidance by
70 demonstrating the potential biases in the literature and add to published recommendations.
71 Tumor biology may dictate treatment that deviates from these recommendations and should be
72 discussed with patients.

73 Bladder Cancer

74 Several publications have discussed potential consequences in delaying extirpative
75 surgery for muscle invasive bladder cancer (MIBC). Boeri et al. studied their cohort of MIBC
76 patients (cT2-T4) and found that a delay greater than 10 weeks after the last neoadjuvant
77 chemotherapy (NAC) cycle led to worse outcomes for cancer-specific and overall mortality.
78 Delays in surgery increased mortality even when accounting for age, gender, and extent of
79 disease². Similarly, in patients that only underwent radical cystectomy without NAC, Sanchez-
80 Ortiz et al. found that even after adjusting for pathologic aggressiveness, patients who were
81 delayed longer than 12 weeks had worse survival – 3-year estimated survival for the delayed
82 group was 34.9%±13.5% compared to 62.1%±4.5% for patients receiving surgery before 12
83 weeks³. Other groups had similar findings that a delay in surgery led to worse outcomes when
84 greater than 90 days passed from diagnosis or NAC to surgery⁴.

85 Despite these studies suggesting the importance of performing cystectomy in a timely
86 manner, Alva et al. demonstrated that there was no survival benefit to earlier cystectomy (<10
87 weeks after last dose of NAC)⁵. The study also found no difference between groups of patients
88 that were delayed 12 weeks, but 10 weeks was used as a cut off to add confidence to their
89 conclusions. This group found that pathologic stage was a factor in overall survival but could not
90 find that actual timing of radical cystectomy played a role in survival outcomes. Park et al. also
91 published a retrospective review that found no significantly detrimental impact to delaying
92 surgery until 28 weeks after the TURBT diagnosis⁶. Furthermore, a 6-week delay in NAC
93 initiation or a 22-week delay from NAC initiation to RC did not affect survival (about 10-12
94 weeks from NAC completion to RC). This group found that inferior outcomes were related to the

95 presence of extravesical disease. In patients that did not undergo NAC, Nielsen et al. also found
96 that interval from diagnosis to radical cystectomy of 3 months was not necessarily associated
97 with progression and worse survival outcomes⁷.

98 Patients with variant histology on final surgical pathology after cystectomy, and patients
99 experiencing an 8 week delay had worse overall survival⁸. Within the same study, however,
100 patients with clinical variants (diagnosed at TURBT) had 12 weeks as the cutoff for survival
101 differences. This study did not specify any differences between variant histology.

102 NAC should be carefully discussed with patients by their medical oncologist as there may
103 be associated risks with exposure and decreased immunity to COVID-19. Audenet et al. found
104 that delays from time of TURBT to NAC by more than 8 weeks, without delay from NAC to
105 radical cystectomy, can affect the disease course⁹. After a median follow up time of 45.7 months,
106 no significant changes in overall survival were noted, but patients that had a delay to NAC were
107 more likely to be upstaged on final surgical pathology. RFS or CSS were not calculated in this
108 study.

109 For diagnosing bladder cancer, Wallace et al. found that delays occur between onset of
110 symptoms and diagnosis. This study divided delay times between onset of symptoms to general
111 practitioner (GP), GP to specialist, and then time to the OR. The delay from onset of symptoms
112 to GP greater than 14 days played a significant role in survival outcomes because these patients
113 consequently had higher stage tumors and worse survival outcomes of 5% at 5 years compared to
114 those that did not have any delay¹⁰. During this pandemic, patients likely will experience a delay
115 in seeing a GP due to widely issued stay-at-home orders. This stresses the importance of

116 continuing to perform screening cystoscopy, during the pandemic, for patients suspected to have
117 bladder cancer in order to accurately identify the aggressiveness of disease.

118 For NMIBC, the literature is limited for the effects of delaying intravesical therapy.
119 However, studies have compared early versus late cystectomy for high risk NMIBC patients and
120 have found that prolonged delays can affect survival. Jager et al. studied effects on delayed
121 cystectomy for high risk NMIBC and found that patients that were delayed for ≥ 13 months may
122 start to see an effect on CSS¹¹. The survival outcomes for aggressive NMIBC is likely dependent
123 on the tumor biology rather than specific timing delays. Hautmann et al. studied specifically T1
124 G3, high risk disease and found that CSS was 83.9% vs 74.8% at 5 years and at 10 years 78.9%
125 versus 64.5% in favor of immediate cystectomy (within 90 days) compared to deferred
126 cystectomy (second TURBT, BCG administration and repeat TURBT), which is likely result of
127 the lack of response to therapy¹². And for patients with initial response to intravesical therapy by
128 looking at patients that had recurrent NMIBC disease, patients that received one additional
129 salvage intravesical treatment were able to retain their bladder for 1.7 years longer without any
130 survival detriment¹³. Results with deferred cystectomy is highly variable due to the differences in
131 tumor biology and responsiveness to intravesical therapy and it is hard to generalize for the
132 purposes of this review. For high-risk NMIBC that are considering cystectomy, delays
133 experienced due to the COVID-19 pandemic should pose minimal risk to survival outcomes, but
134 urologists should still carefully assess the aggressiveness of each patient's individual cancer to
135 determine appropriate timing of cystectomy.

136 For NMIBC, patients requiring intravesical therapy, especially induction dose, for
137 intermediate or high-risk NMIBC should still be considered with the clear benefits of intravesical
138 therapy.

139 *Discussion:* A systematic review and meta-analysis discussing potential delays in treating
140 MIBC ultimately found that an acceptable length of delay could not be determined, but
141 recognized that delays do cause a detrimental effect on overall survival⁴. Based on these past
142 studies, patients with MIBC should consider NAC and should undergo radical cystectomy within
143 10-12 weeks either after TURBT without NAC or after NAC completion. However, as many of
144 these studies demonstrated issues with delaying surgery in terms of disease progression, MIBC
145 especially those that are extravesical may be prioritized. For new patients, surveillance
146 cystoscopy to assess risk and burden of disease is still important and should continue during this
147 pandemic (Table 1). Finally, the literature on delaying intravesical therapy is lacking, but they
148 should continue with proper counseling.

149 Upper Tract Urothelial Cancer (UTUC)

150 Literature review of UTUC demonstrated that delay in surgical time likely does affect
151 overall survival outcomes in higher risk cases. Lee et al. found that surgical delay of greater than
152 1 month was not an independent prognostic factor when all 138 patients with upper tract
153 urothelial carcinoma were included in their survival curves¹⁴. However, once the analysis was
154 further sub-categorized by location to renal pelvic tumor and ureteral tumors, tumors in the
155 ureter had worse prognosis for patients that delayed surgery by one month -CSS (87.9% vs
156 54.5%) and RFS (85.6% vs 60.7%). Of note, both low-grade and high-grade urothelial carcinoma
157 were included in their analysis. A study done by Waldert et al. found that a 3 month delay to

158 radical nephroureterectomy (RNU) may not necessarily have worse survival outcomes at 3 and 5
159 years¹⁵. This study treated delay time as a continuous variable as well and found that longer time
160 to surgery was correlated with advancing pathologic stage, higher tumor grade, concomitant CIS,
161 tumor necrosis, infiltration, worse CSS, and increased likelihood of recurrence. This study
162 performed a subgroup analysis with muscle invasive disease (\geq pT2), which demonstrated that
163 there was no significant difference in survival outcomes (RFS and CSS) using 3 months as a
164 cutoff point. However, once again they noted that these muscle invasive patients experiencing a
165 delay in surgery had worsening surgical pathology (advanced stage, higher grade, infiltrative
166 tumor architecture, and lymphovascular invasion). Nison et al. also found similar findings with
167 no significant difference with survival outcomes CSS, RFS, and metastasis free survival (MFS)
168 in a muscle invasive subgroup. Their group compared patients that had median time of 62 days
169 compared to 47 days until RNU¹⁶. Sundi et al. studied the consequences of a 3-month delay prior
170 to RNU and did not find any negative effect with respect to RFS, DSS, and OS. Patients in this
171 cohort had approximately 79% high risk patients. Even after excluding patients from the delayed
172 group that had undergone NAC, there was no decrement in 5- year DSS (71.6% vs 81.5%) and
173 OS (61.3% vs 77%) among those waiting longer than 3 months. In this secondary analysis, of the
174 delayed group (54 patients) – 27 had NAC and 9 more patients were delayed from being on
175 surveillance and endoscopic management, meaning that a portion of patients that were delayed
176 likely had lower risk disease¹⁷.

177 *Discussion:* It has been well established that low grade UTUC is less aggressive and safe
178 to keep on surveillance and undergo endoscopic management. Until burden and risk of disease is
179 determined, similarly to bladder cancer, patients should undergo thorough evaluation with
180 endoscopy. In evaluating these studies, patients with high-risk disease may be preferentially

181 treated as many studies were retrospective and preferentially treated aggressive patients sooner
182 (<3 months). Patient with tumor location in the ureter may also require limited delay (Table 1).
183 While some studies have shown efficacy with NAC and could delay surgery, those patients in
184 whom immunosuppression is of concern, adjuvant therapy after early surgery may be offered
185 with success¹⁸.

186 Renal Cancer

187 For small renal masses (≤ 4 cm), active surveillance has become an acceptable standard
188 of care. These patients are typically followed to monitor growth kinetics to determine
189 intervention, and typical follow-up during active surveillance was in 6-month to 12-month
190 intervals. Uzosike et al. noted in their evaluation of patients in the Delayed Intervention and
191 Surveillance for Small Renal Masses (DISSRM) trial that no patients on active surveillance died
192 from kidney cancer or developed metastatic disease¹⁹. Other studies looking at the SEER
193 database have found a small rate (<4%) of metastasis for masses <5cm²⁰.

194 For larger renal masses (≥ 4 cm), Mano et al. evaluated data from 1,278 patients in a
195 retrospective analysis of which 267 (21%) patients had surgical wait times (SWT) greater than 3
196 months. Median mass size was 6.2 cm (6.5 cm for $SWT \leq 3$ mo. and 5.7 cm for $SWT > 3$ mo.)²¹.
197 On analysis, SWT were not associated with disease upstaging, recurrence, or cancer specific
198 survival. Stec et al. also retrospectively analyzed a cohort of patients with a mean renal mass size
199 of 6.4 ± 4.4 cm. and found no differences in overall survival (OS), cancer-specific survival
200 (CSS), or recurrence-free survival (RFS) when delaying surgery for patients and accounting for
201 differences in tumor grade and pathology²². Their group found that 5-year OS, CSS, or RFS was
202 determined based on the staging of disease, histology, tumor grade, and extent of spread at

203 presentation. RFS was found to be worse in patients who underwent surgery within a month
204 likely because larger, more aggressive-appearing masses were preferentially treated. In a study
205 by Kim et al., similar findings were shown in a retrospective review of 1,732 patients who
206 underwent surgery for RCC for masses with a mean size of 8.9 ± 2.6 cm that were at least stage
207 T2a²³. Their group found that SWT of 1-3 months compared to SWT of <1 month was not an
208 independent predictor of pathological upstaging, RFS, or CSS. This study also discussed the
209 impact of SWT on symptomatic patients as they had higher clinical and pathologic stages, but
210 there was no association between SWT and pathologic upstaging, CSS, or RFS. Considering the
211 literature, these studies were retrospective in nature and clinicians appeared to selectively and
212 more urgently operate on patients with more aggressive-appearing renal tumors. Also with
213 symptomatic patients, Lee et al. found that patients with flank pain, hematuria, varicocele,
214 constitutional symptoms correlated to aggressive histology and worse survival outcomes²⁴. DSS
215 was 91% at 5 years for non-symptomatic patients versus 68% at 5 year for symptomatic patients.
216 Thus, RCC (\geq T2) can be further risk-stratified to determine urgency of treatment. To assist in
217 predicting which renal masses are more aggressive, nomograms can help predict high-risk, high-
218 grade pathology that requires more urgent attention²⁵. Renal mass biopsy may provide some
219 benefit, clear cell RCC, papillary RCC, and chromophobe typically correctly identify the
220 pathology, however Fuhrman grade is less concordant. Abel et al. also studied concordance for
221 high risk pathological features and found that 31.7% of patients had the same Fuhrman grade as
222 final path and 67.9% had same concordance if stratified by low and high risk²⁶.

223 Metastatic renal cell carcinoma that is under consideration for cytoreductive nephrectomy
224 (CN) should consider neoadjuvant therapy based on early results. Deferring immediate CN may
225 not cause any harm in survival outcomes based on the SURTIME and CARMENA trials^{27, 28}.

226 The SURTIME trial accrued fewer patients than the CARMENA trial, but demonstrated that
227 there was no significant difference in survival for patients that deferred CN compared to patients
228 that underwent upfront CN²⁷. Of the 48 patients that deferred CN, 14 patients went against
229 protocol and 6 underwent surgery. When these off-protocol patients were studied, the deferred
230 CN patients seemed to have improved overall survival. There still appears to be some role in CN,
231 especially in those patients that have some response to neoadjuvant immunotherapy which can
232 also help to delay surgery. For more localized renal cell carcinomas, Rini et al. also demonstrated
233 that Pazopanib can be administered for 8-16 weeks prior to surgery to decrease tumor size in a
234 Phase II trial (92% of patients)²⁹.

235 *Discussion:* Patients with renal masses ($\geq T2$) should undergo careful evaluation, as these
236 patients still carry a risk for metastasis. These studies looking at delaying surgery are
237 retrospective and patients with high-risk features typically had operations without significant
238 delay, which may account for the similar survival outcomes. Priority should be given to those
239 with aggressive features— imaging findings, possible renal mass biopsy results, symptoms etc.
240 (Table 1). For those with metastatic kidney cancer, neoadjuvant options should be discussed with
241 medical oncologists for immune risks with COVID-19.

242 Prostate Cancer

243 Delaying radical prostatectomy (RP) for prostate cancer depends heavily on the clinical
244 staging. Meunier et al. published a retrospective analysis of 513 patients by selecting
245 biochemical recurrence (BCR) as the primary endpoint³⁰. The study found that for surgical delay,
246 there was no threshold for patients with Gleason 6 (3+3), a 90-day threshold for Gleason 7, and a
247 60-day threshold for Gleason ≥ 8 cancers. Other studies using biochemical recurrence as the

248 endpoint, found 3 months to 6 months as a cut-off point^{31,32}. Similar findings were found for
249 patients considering radiation therapy, where patients had a higher likelihood of PSA failure for
250 patients with high risk disease after a 2.5 month period, which is similar to the outcomes for
251 surgical delay³³.

252 Other studies have suggested that it is possible to delay surgery for longer periods of
253 time. Recently, Ginsburg et al. performed a retrospective review of the National Cancer Database
254 and found that delays up to 12 months did not have worse oncological outcomes (adverse
255 pathology, upstaging on RP, or secondary treatment) for intermediate and high-risk prostate
256 cancer³⁴. Gupta et al. did not find any significant differences in adverse pathologic outcomes or
257 BCR or MFS comparing those treated within 3 month to those waiting 3-6 months³⁵. Gleason
258 Group 5 patients primarily underwent RP at <3 mo. (87%). Patel et al also found 6 months to be
259 an acceptable delay, but acknowledges that to evaluate the data, Grade Group 3,4,and 5 were
260 included together as high-risk patients³⁶. Fossati et al. studied 2,653 patients that had undergone
261 RP and found that 283 patients experienced BCR and 84 patients developed clinical recurrence
262 (CR)³⁷. Furthermore, patients with highest risk started to experience higher rates of BCR and CR
263 after 12 months of surgical treatment delay. Similarly, most high-risk patients were treated
264 within 12 months (386 patients) and 208 patients were treated within 3 months. Only a total of
265 17 patients were treated after 12 months delay.

266 The role of neoadjuvant therapies may play a role in higher risk prostate cancer. A
267 randomized study for neoadjuvant hormonal therapy (NHT) demonstrated that patients
268 undergoing 12 weeks of cyproterone acetate tended to have prostatectomy specimens with lesser
269 weights, smaller tumor volumes, and greater Gleason scores. There were significantly fewer

270 positive margin rates in patients undergoing NHT (27.7% vs. 64.8%, $p < 0.01$). Interestingly,
271 treated patients had higher rates of seminal vesicle involvement (27.7% vs 14.3%, $P < 0.05$)³⁸.
272 Patients followed for 36 months showed no difference between the two groups in terms of
273 biochemical progression, and at long-term follow up (median time 6 years), there was a
274 biochemical recurrence-free survival benefit in patients with initial PSA greater than 20ng/ml
275 that had received NHT³⁸. Another long-term study followed 354 patients who received Goserelin
276 and Flutamide for 3 months³⁹. In the initial studies, patients undergoing NHT demonstrated
277 improved pathological outcomes after RP. These patients were then followed over 4 years, and
278 patients with cT2 tumors showed lower local recurrence rates in patients undergoing NHT.
279 However, this finding was not present in the cT3 group. Although there were fewer positive
280 margin rates in the initial study, the NHT cohort did not necessarily translate to better PSA
281 progression rates after 4 years of follow up³⁹. Of note, Meyer et al. did find that patients
282 receiving more than 3 months of NHT prior to RP had a lower risk of PSA failure compared to
283 patients receiving only surgery without NHT at the 5-year mark⁴⁰.

284 Lastly, recent studies have compared patients neoadjuvant chemohormonal therapy
285 (NCHT) with RP to high risk (>cT3a, Gleason 8-10, PSA > 50ng/ml, or pelvic metastatic
286 involvement) patients only undergoing RP or RP with NCHT. Patients receiving NCHT
287 (docetaxel-based) combined with RP were more likely to achieve undetectable postoperative
288 PSA as well as more favorable surgical pathology with organ confined disease and less pT3 or
289 pT4 disease⁴¹. Biochemical recurrence also occurred earlier in the untreated group (9 months vs
290 13 months biochemical PFS). In the latest CALGB 90203 Phase III randomized study of patients
291 undergoing NCHT and RP to patients having RP alone, the NCHT group had lower pathologic
292 T-stage, lower likelihood of seminal vesicle invasion, positive lymph nodes, or positive surgical

293 margins⁴². The survival outcome remains to be studied. It remains important to note that
294 treatment with NCHT is associated with adverse side effects such as immunosuppression.

295 *Discussion:* For prostate cancer, the literature provides significant variability in safe
296 delay times. Some found delays of 60 days can affect recurrence free survival, whereas other
297 studies found no survival outcome differences up to 12 months. Studies finding that longer
298 delays were feasible may be the fact that most high-risk patients were treated within 3 months.
299 Studies have also demonstrated that a 3-month course of NHT does not negatively impact long-
300 term survival and would allow patients to safely delay surgery. We recommend consideration of
301 neoadjuvant therapy in high-risk patients that may have prolonged delay (Table 1). In terms of
302 diagnosing prostate cancer, patients with higher risk of prostate cancer based on PSA, age,
303 physical exam and other adjunctive screens should preferentially be biopsied.

304 Adrenal Cancer

305 Adrenocortical Carcinoma (ACC) is an aggressive malignancy, the median disease
306 specific survival (DSS) of ACC is 34 months and 5-year DSS is 39% from a study of patients
307 with localized primary disease⁴³. Meyer et al. followed 20 patients that underwent operative
308 treatment for adrenal cortical carcinoma⁴⁴. From this cohort, Stage I and II had mean survival for
309 65 months compared to Stage III which was 38 months and Stage IV which was 19 months. The
310 5-year survival rate was 23%. Neoadjuvant therapy for adrenocortical carcinoma demonstrating
311 significant differences in clinical outcomes is lacking. Adrenocortical carcinoma is an aggressive
312 disease that needs complete surgical resection, if feasible, to achieve improved survival rates.
313 Studies found patients that underwent resection of localized disease had median survival of 101
314 months for Stage 1 and Stage 2 tumors⁴⁵.

315 *Discussion:* Patients should be prioritized in surgical treatment of adrenal cancer (Table
316 1).

317 Testicular Cancer

318 Testicular cancer primarily affects younger men and any issues with management can
319 have lasting effects. Any significant delay (4-6 months) in diagnosis of testicular cancer
320 increased the probability of metastatic disease - 20% of patients with a delay <30 days had
321 metastasis compared to 55% of patients with a delay >4-months⁴⁶.

322 After diagnosis, patients with clinical stage I or clinical stage II would need to consider
323 management options, including primary retroperitoneal lymph node dissection (P-RPLND). For
324 Stage I tumors, surveillance is a feasible choice during the pandemic, even for patients with high
325 risk features⁴⁷. Similarly, patients with Stage II tumors that may be amenable to RPLND will
326 need to be counseled, and their final decision on surgery may depend on person preferences and
327 hospital resources. Furthermore, chemotherapy may cause immediate side effects such as nausea,
328 vomiting, nephrotoxicity but also lasting issues such as hypogonadism, infertility, pulmonary
329 toxicity, cardiovascular disease, secondary malignancies, and neuropathy⁴⁸. In reviewing the
330 literature, the topic of delaying post-chemotherapy retroperitoneal lymph node dissection is
331 lacking.

332 *Discussion:* Based on this data, patients with testicular cancer would likely benefit with
333 minimized delays and diagnosis with orchiectomy should try to be prioritized. Whether patients
334 choose chemotherapy, surgery, or surveillance for Stage II disease should be a multidisciplinary
335 approach (Table 1).

336 Penile Cancer

337 Even outside of a pandemic, current literature describes that patients with penile cancer
338 may experience delays in receiving medical care. In one study by Gao et al. of 254 patients, the
339 average delay from initial symptoms to initial consultation was 116 days (SD=17.2)⁴⁹. Patients
340 that had delays in care demonstrated issues with sexual function at the 3-month mark, and
341 patients with delays of greater than 6 months had significantly worse survival outcomes. In terms
342 of the pathological effects, patients with a 3-month delay were found to have worse surgical
343 pathology. Chipollini et al. retrospectively reviewed patients that had delays in care from time of
344 primary surgery to inguinal lymph node dissection (ILND)⁵⁰. In terms of RFS, ILND within 3
345 months had rates of 77% at 5-year RFS compared to 37.8% for > 3-month delay. For 5-year
346 DSS, early resection < 3 months was 64.1% compared to 39.5% for > 3 months. This was further
347 subdivided based on aggressiveness of disease. In patients with cN0 disease, 5-year DSS was
348 78.6% for patients that had undergone resection in < 3 months and 45.8% for patients
349 undergoing ILND > 3 months. Patients with more aggressive disease (cN+) 5-year DSS was
350 31.8% (< 3 months) compared to 35.3% (> 3 months).

351 *Discussion:* Since many penile cancer patients already experience delay for initial
352 consultation, early surgical care is important for these patients to optimize both sexual function
353 and survival outcomes with resectable disease (Table 1).

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357 Conclusion

358 COVID-19 has significantly altered the management of urologic cancers. With the
359 possibility of another surge with COVID-19, critical analysis of the literature on surgical delay
360 can guide timing of treatment to minimize risk to the patient and hospital resources.

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Table 1. Recommendations on urologic cancer from review of literature during the COVID-19 pandemic

Urologic Cancer	Recommendation
Bladder Cancer	<p>MIBC: Minimize delay to surgery especially high risk and variant histology. Neoadjuvant therapy should be considered.</p> <p>NMBIC: Appropriately counsel patients on intravesical therapy based on risk of disease.</p> <p>Delay in TURBT can lead to worse prognosis, especially in higher risk cases. Early imaging and screening cystoscopy are important to identify burden of disease.</p>
Renal Cancer	<p>T1a: patients can be followed with active surveillance</p> <p>T1b: delaying surgical intervention is appropriate</p> <p>≥T2: consider urgent surgery if patients have unfavorable pre-operative characteristics on imaging or biopsy.</p> <p>Locally Advanced/Metastatic RCC: Systemic therapy may benefit and allow safe surgical delay. This may also help identify patients that would benefit most from cytoreductive nephrectomy. Prefer oral therapy rather than IV/immune checkpoint inhibitors.</p>
Prostate Cancer	<p>Low risk prostate cancer – no significant effect with prolonged delays</p> <p>Higher risk prostate cancer: Likely can delay</p>

	for several months. Can recommend neoadjuvant hormonal therapy. Risks associated with neoadjuvant chemohormonal therapy.
Penile Cancer	<p>ILND: should undergo without significant delay from time of penectomy.</p> <p>Penectomy: delays can affect sexual function, can be done as outpatient.</p>
Testis Cancer	<p>Orchiectomy: should be done as outpatient and avoid significant delay in diagnosis</p> <p>Primary RPLND: other choices available depending on clinical stage. Multidisciplinary approach with urologist and oncologist.</p> <p>Post-chemo RPLND: should not undergo any delay.</p>
UTUC	<p>High risk: should undergo surgery, without delay, especially in ureter</p> <p>Low risk: delay should not have significant effect on surgical outcomes</p> <p>Thorough evaluation should be performed to assess disease burden prior to consideration of delaying secondary procedures.</p>
Adrenal Cancer	Should undergo surgical resection, relatively poor prognosis