

Delaying Radical Prostatectomy, Cancer Screening, and Care Due to COVID-19

Two Retrospective Analyses Show No Associated Adverse Outcomes With Delayed RP

Kevin Wright

The results of 2 studies showed no association between delayed radical prostatectomy (RP) and adverse oncological outcomes, supporting current recommendations of urologic societies for surgical treatment of patients with intermediate- and high-risk prostate cancer during the coronavirus disease 2019 (COVID-19) pandemic.

A retrospective analysis published in the *Journal of Urology* indicated that a delay of up to 12 months did not result in worse outcomes when compared with immediate surgery within 3 months of diagnosis.¹

When compared with patients receiving RP within 3 months of diagnosis, patients undergoing surgery 4 to 12 months after diagnosis did not have increased odds of adverse pathology, upgrading on RP, or node-positive disease.

The investigators accrued data from the National Cancer Database for men with intermediate- and high-risk prostate cancer who received RP between 2010 and 2016. Surgery ≤ 3 months from diagnosis was defined as immediate RP, with delayed RP being evaluated in 3-month intervals up to 12 months (4-6 months, 7-9 months, 10-12 months).

Overall, the analysis included 128,062 patients with a median age of 63 years (interquartile range [IQR], 58-67) and a median PSA at diagnosis of 6.3 ng/mL. Just over

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MEET OUR EXPERT



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Are COVID-19 Delays a Basis for Concern? Can We Use This for Future Good?

Judd W. Moul, MD

In my 30-plus years in medicine and as a urologic oncologist, I have never had to triage civilian patients for elective surgery, but that is exactly what we were asked to do from March 2020 onward as the coronavirus disease 2019 (COVID-19) pandemic engulfed our communities. We had the opportunity to report our early experience with triage for localized prostate cancer in the May 2020 issue of *ONCOLOGY*.¹ From mid-March to mid-May 2020, I postponed about 20 patients with low- to high-risk localized prostate cancer scheduled for radical prostatectomy (RP). However, as I write now in mid-August, I can report that we cared for these men with a surgical delay averaging less than 3 months. We were fortunate that our health system had sufficient personal protective equipment and that the impact of COVID-19 in our area was less severe than in many other parts of the United States, which allowed our teams to ramp back up to full capacity by early June 2020. Recent articles by Diamand et al in the *World Journal of Urology* and Ginsberg et al in the *Journal of Urology* found that modest delay in RP did not impact outcomes.^{2,3} I am not surprised. For all but the most severe cases of localized prostate cancer, modest delay of 2 to 6 months is unlikely to affect long-term survival.

However, this does not mean that COVID-19 will not affect the survival and outcomes of

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Retrospective Analyses

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half (50.1%) of the patients had Grade Group (GG) 2 disease. The median interval between diagnosis and treatment was 3 months (IQR, 2-4). Overall, 73.2% (n = 93,764) of patients underwent RP within 0 to 3 months of diagnosis, 23.7% (n = 30,337) within 4 to 6 months, 2.5% (n = 3213) within 7 to 9 months, and 0.6% (n = 748) within 10 to 12 months.

Compared with the immediate RP group, the odds of adverse pathology were not higher with the delays of 4 to 6 months (odds ratio [OR], 0.98; 95% CI, 0.94-1.02; $P = .310$), 7 to 9 months (OR, 1.02; 95% CI, 0.91-1.13; $P = .773$), and 10 to 12 months (OR, 1.00; 95% CI, 0.80-1.26; $P = .98$). Separate subgroup analyses of men with GG 2/3 and 4/5 disease also did not show a significant difference in adverse pathology among any of the 3 delay intervals compared with immediate RP.

There was also no link between delayed RP and pathologic upgrading.

The odds of pathologic upgrading at RP were similar among the delayed RP cohorts compared with the immediate RP cohort: 4 to 6 months (OR, 1.0; 95% CI, 0.95-1.05; $P = .922$), 7 to 9 months (OR, 1.09; 95% CI, 0.95-1.24; $P = .228$), and 10 to 12 months (OR, 1.06; 95% CI, 0.82-1.37; $P = .649$).

European Study Results Align With Recommendations

A second study, published in *World Journal of Urology*, analyzed the outcomes of 926 men undergoing RP for intermediate- and high-risk prostate cancer across Europe. Median follow-up and surgical delay were 26 months (IQR, 10-40) and 3 months (IQR, 2-5) respectively. No significant association between surgical delay and oncologic outcomes were found.²

The findings lend support to the current National Comprehensive Cancer Network guideline for prostate cancer management during the COVID-19 pandemic.³

Data were retrospectively gathered from 1139 patients receiving surgery between March 2012 and September 2019 across European centers in Belgium,

France, Switzerland, and Italy. Patients in the study were categorized according to the European Association of Urology (EAU) risk categories, with time from diagnosis counted as a continuous variable.

The multivariable analysis demonstrated no significant association between surgical delay and upgrading on final specimen (OR, 0.98; 95% CI, 0.94-1.02; $P = .3$), pathologically locally advanced disease (OR, 1.00; 95% CI, 0.97-1.03; $P = .8$), need for adjuvant therapy (OR, 0.96; 95% CI, 0.84-1.11; $P = .6$), or lymph node invasion (OR, 0.88; 95% CI, 0.77-1.01; $P = .07$). The lack of impact was observed across all EAU risk categories.

While the investigators noted that most men in the study were operated on within a postdiagnosis period of close to 3 months, and they warned of extrapolating the results for much longer treatment delays, similar studies demonstrated that proposals of delays of up to 6 months for high-risk disease were reasonable, while low- and intermediate-risk groups could be delayed further. ■

For references visit cancernetwork.com/delayedRP

Basis for Concern & Future

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countless other cancer patients in this country and throughout the world.⁴⁻¹⁰ Many other malignancies are much faster-growing than prostate cancer, and COVID-19 delays could have serious consequences. In the urologic cancer area, testicular cancer and bladder cancer immediately come to mind as more concerning, since delay in diagnosis has been a perennial problem even in good times.¹¹ A PubMed search of “cancer+COVID-19+delay” on August 22, 2020, found more than 125 publications, and this is just the beginning. Only time and

further research will ultimately determine the long-term impact.

While I am less worried about modest delay in RP due to COVID-19, I do worry about delays in screening for prostate cancer by primary care providers that are exacerbated by COVID-19. Prostate cancer screening with the prostate-specific antigen (PSA) blood test has been controversial and hotly debated since 2011, when the US Preventive Services Task Force (USPSTF) gave PSA screening a “D” rating (more harm than good).¹² Many advocates for patients with prostate cancer feel this rating was misguided by poor or immature data from 2 randomized controlled trials. Nevertheless, this was the “law

of the land” for 8 years. In 2018, the USPSTF revised the guideline to a “C” rating for men aged between 55 and 69 years, citing some evidence of benefit and recognizing less overtreatment of low-risk prostate cancer, as active surveillance was more widely accepted. From 2018 to early 2020, urologists began to see more referrals from primary care providers for elevated PSA, as many began to recognize the new PSA guideline. Then COVID-19 hit. Sadly, not only did COVID strike communities of color to a greater degree, but prostate cancer is much more common in African American men.¹³ I worry about an “adding insult to injury” effect for Black men in this country regarding delay in

diagnosis of prostate cancer (and many other health conditions as well). It was difficult enough to get the message out about the importance of early diagnosis of prostate cancer in the African American community, and now it's potentially much more difficult when you combine that with COVID-19.

In our practice, we began partnering with our Duke primary care network in 2018 (corresponding to the USPSTF change) to reengage prostate cancer awareness and PSA screening, focusing on our large minority high-risk population. While we lost about 3 or 4 months (March to June 2020) due to COVID-19, we are now very mindful of getting back

in full swing for timely screening, urology referral, and further work-up. For men who prefer a telehealth consult to urology for elevated PSA, we now offer a novel exosome-based urine test (ExosomeDx; Bio-Techne) by mail to replace the in-person visit digital rectal examination (DRE).^{14,15} This new COVID-19–motivated process could tip the scales in favor of more rapid, efficient risk stratification for prostate biopsy or prostate MRI for high-risk men. Considering that the dread of a DRE prevents some men, and particularly some men of color, from going to the doctor, this new process might be a good option made possible by quick innovation indirectly

caused by the COVID-19 pandemic.

In summary, cancer care is impacted by COVID-19—no question about that. Delay in diagnosis is an obvious adverse effect, deserving of further study, of which we all must be mindful, and which we must try our best to mitigate. However, out of tragedy and great adversity comes rapid advances. In addition to vaccines and effective therapies for COVID-19, we in the oncology field must strive to use this pandemic to improve our care of cancer over the long term, and to think outside the box. ■

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