

Effect of COVID-19 pandemic on vaccination and treatment pattern of prostate cancer: a comprehensive literature review, phase 2

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Abstract

During the COVID-19 pandemic, overall screening, diagnostics, and treatment have faced a downtrend, especially during the first wave and lockdown. Statistics showed improvements starting from the late era of the pandemic and the end of 2020. To improvise, the risk of delayed curative treatment was measured and treatment plans were amended accordingly in order to lower the number of hospital visits needed while the results were still contradictory. The protective role of androgen deprivation therapy on COVID-19 triggered many debates, but the majority of clinical studies found no significant association. Concerns about a reduced immune response to vaccination in patients with prostate cancer occurred, but additional research is needed. The pandemic added additional burdens to patients with prostate cancer and different aspects of the quality of life of patients were assessed. While we anticipate that we are reaching the end of the pandemic, it is essential to re-examine how the pandemic has changed the overall care of patients with prostate cancer and how to proceed even further.

Keywords: COVID-19; SARS-CoV-2; prostate cancer; urology.

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1. Introduction

During the COVID-19 pandemic, overall screening, diagnostics, and treatment have faced a downtrend, especially during the first wave and lockdown, with the statistics slowly improving by the late era of the pandemic or by the end of 2020. To improvise, the risk of delayed curative treatment was measured and treatment plans were amended to lower hospital visits while the results are still contradictory. In this review, we comprehensively reviewed additional burdens to patients with prostate cancer and different aspects of the quality of life that the COVID-19 pandemic brought.

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2. The effect of delayed treatment

Compared to the 2019, there was an average 23% reduction in surgical volume between March and December 2020 in 8 European tertiary referral centers.[1] No association was observed between surgical delay and oncologic outcomes for a large European cohort of 926 men with a median 3 months delay.[2] According to a National Cancer Database study of 128,062 men with intermediate and high-risk prostate cancer, there was no significant difference in the pathology, node-positive disease, or post-radical prostatectomy secondary treatments between those who received immediate radical prostatectomy and those who experienced any level of delay up to 12 months.[3] There was no significant association between the length of time to radical prostatectomy and risk of developing metastases.[3] However, Zattoni et al, 2021 suggested that patients who were treated during the pandemic had a higher risk of extra-prostatic disease and lymph node invasion due to a delay in the administration of curative-intent therapies in patients with localized prostate cancer.[1]

A meta-analysis of four randomized controlled trials found that overall survival and cancer-specific survival significantly worsened among intermediate-risk patients but not in the case of low- and high-risk patients whose treatment was delayed. It was suggested that a 3-month course of neoadjuvant hormone therapy could improve pathological outcomes but not oncological outcomes.[4]

Other than radical prostatectomy, to reduce the frequency of hospital visits, switching from gonadotropin-releasing hormone antagonists to luteinizing hormone-releasing hormone agonists was also a comparable option that does not diminish efficacy or worsen adverse events.[5]

Table 1. Summary of trend in diagnosis of prostate cancer since the COVID-19 pandemic

Author, year	Baseline	Result	Measure	Period of interest (1)	Result	Period of interest (2)	Result
Ip, 2021[17]	2018 to 2019	121,096,335	Physician attendances (including telehealth)	2019-2020	114,089,347 (6% reduction)	2020-2021	99,330,510 (18% reduction)
		692,021	PSA tests		657,468		706,088
		135,775	Free-to-total PSA tests	2020-2021	140,024	156,321	
		31,750	Multi-parametric MRI		35,672	35,942	
		19,923	Prostate biopsy		21,453	21,574	

Table 1. Continued

Author, Year	Baseline	Result	Measure	Period of interest (1)	Result	Period of interest (2)	Result
Ferrari, 2021[18], median (IQR)	2016 to 2019	283 (271 to 288)	Vit D	Lockdown (Mar to May, 2020)	66 (48 to 126)		
		146 (129 to 147)	Total PSA		62% (median decrease)		
	2016 to 2019	256 (228 to 280)	Vit D		Post-lockdown	295 (267 to 322)	
		135 (116 to 151)	Total PSA			181 (165 to 201)	
Fallara, 2021[19]	2017 to 2019	2,285	Total cases	2020	1,458 (36% fewer)		
Stroman 2021[20], number of centers			Prostate MRI	During the pandemic	14 (13%) centers stopped 39 (37%) centers offered with same indications 48 (46%) centers offered to selected high-risk patient group only		
	Before the pandemic	68	LATP	During the pandemic	56		
		85	GATP		32		
		83	LATRUS		34		
Surasi 2021[21], mean (SD) per week	Before the pandemic	26.0 (26.0)	Prostate MRI	Lockdown period	11.6 (8.2)		21.3 (25.3)
		7.9 (11.7)	Prostate biopsy		2.3 (3.3)		After lockdown 9.6 (8.0)
Pepe 2021[22]	2019 to 2020	2,000	Clinical office evaluation	2020 to 2021	1,015		
		351	Multi-parametric MRI		85		
		485	Prostate biopsy		201		
		187 (38.5%)	Cancer diagnosis from biopsy		96 (47.7%)		

Table 1. Continued

Author, year	Baseline	Result	Measure	Period of interest (1)	Result	Period of interest (2)	Result
Kaufman 2021[23], average monthly number	Prepandemic	465,187	PSA tests	Early Pandemic	295,786 (36.4% decrease)	Late Pandemic	483,374 (3.9% increase)
		659	PSA results \geq 50 ng/mL		506 (23.2% decrease)		674 (2.3% increase)
		1,453	Prostate biopsy results		903 (37.9% decrease)		1,190 (18.1% decrease)
		182	Gleason score \geq 8		130 (28.6% decrease)		161 (11.5% decrease)
Nossiter 2022[24]	2019	9,918/25,936 (38.2%)	Transperineal /prostate biopsy	2020	10,592/16,551 (64.0%)		
	2019	32,409	Diagnoses	2020	22,419 (30.8% reduction)		
Deukeren 2022[25]	2019	21,542	Diagnoses	2020	18,444	End of 2020	Restored to approximately 95% of expectation
		13,621 (63.2%)	N (%) of malignant pathology		12,756 (69.2%)		

Abbreviations; IQR, interquartile range; PSA, prostate-specific antigen.

3. Quality of life of patients with prostate cancer

COVID-19 did not add or induce significant anxiety in men being treated for prostate cancer,[6] but those whose operations were postponed had higher state anxiety levels than trait anxiety levels, with the younger population having been more affected by the pandemic.[7] The mean Beck Depression Inventory score was 4.3 (range, 0 to 13), signifying mild depression. This is comparable to a pre-pandemic study that identified that PSA level, patient age, and a number of comorbidities are not related to anxiety and depression in patients with prostate cancer.[8]

Additional challenges existed with patients with prostate cancer receiving ADT during the pandemic. A Portuguese prostate cancer study evaluating the Montreal Cognitive Assessment demonstrated that cognitive decline was more frequent in the ADT group, and declined even more after the onset of the COVID-19 pandemic.[9] According to a meta-analysis of three RCTs in male patients with prostate cancer on or previously treated with androgen suppression therapy, body fat is likely to be increased during COVID-19 restriction, possibly affecting metabolic health.[10]

Table 2. Summary of trend in treatment of prostate cancer since the COVID-19 pandemic

Author, year	Baseline	Result	Measure	Period of interest (1)	Result	Period of interest (2)	Result
Sciarra 2020[26]	2019		Radical prostatectomy	2020	63.6% reduction		
			Radiotherapy		84.6% reduction		
Fallara 2021[19]	2017 to 2019	1,622	Radical prostatectomy	2020	1,574 (3% reduction)		
		1,176	Radical radiotherapy		1,547 (32% increase)		
		946	ADT		709 (25% reduction)		
Ip 2021[17]	2018 to 2019	6,259	Radical prostatectomy	2019 to 2020	7,107	2020 to 2021	6,477
		2,419	Prostate fiducial markers		2,807		2,962
Pepe 2021[22]	2019 to 2020	54	Radical prostatectomy	2020 to 2021	39		
		47	External radiotherapy		52		
		pT3b: 11.2% nodal (+): 14.8 % metastatic: 5.9%	% of advanced, metastatic prostate cancer after prostatectomy		pT3b: 25.6% nodal (+): 46.1% metastatic: 9.3%		
Nossiter 2022[24]	2019	5,331	Radical prostatectomy	2020	3,896 (26.9% reduction)		
		11,309	Radical radiotherapy		9,719 (14.1% reduction)		
		785	Brachytherapy		470 (40.1% reduction)		
Deukeren 2022[25], odds ratio (95% CI)	Low-risk localized, intermediate-risk, localized, high-risk, or localized/locally advanced		Radical prostatectomy	2020 versus 2018 to 2019	1.32 (1.01 to 1.72) 1.25 (1.07 to 1.47) 1.16 (1.02 to 1.31)		

Table 2. Continued

Author, Year	Baseline	Result	Measure	Period of Interest (1)	Result	Period of Interest (2)	Result
Deukeren 2022[25], odds ratio (95% CI)	Low-risk localized, intermediate-risk, localized, high-risk, or localized/locally advanced		External beam radiotherapy and brachytherapy	2020 versus 2018 to 2019	1.09		(0.71 to 1.67)
					1.26		(1.05 to 1.51)
					0.99		(0.83 to 1.17)
					1.17		(0.80 to 1.72)
					0.63		(0.49 to 0.82)
	Brachytherapy	0.99	(0.83 to 1.17)				
	Metastatic		ADT & radiotherapy		2.27		(1.77 to 2.91)

Abbreviations; ADT, androgen deprivation therapy; CI, confidence interval.

Through a computational linguistic ethnography analysis of posts online, a more collective tone (we, affiliation, friends) was present, with increased concern about health and death in 2020.[11] Significant concerns on the impact of COVID-19 on delayed the care or the effect of prostate cancer on COVID-19, and the risks of COVID-19 itself were discussed.[11]

4. Vaccination and prostate cancer

Vaccination against COVID-19 also poses many new challenges, one of them being the presence of vaccination-associated lymphadenopathy. A non-specific increase in ipsilateral axillary lymph nodes after vaccination was commonly reported through PET/CT scans.[12] Notohamiprodjo et al., 2022 observed vaccination-associated lymphadenopathy on 18F-rhPSMA-7.3 PET with a prevalence of 45% in patients with prostate cancer, with the standardized uptake value ratio dropping significantly after 8 weeks.[13]

There were concerns about the impaired immune response to vaccination in prostate cancer: in a study of patients with hormone-refractory metastatic prostate cancer, the CD4+ T cells of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of unexposed patients had decreased CD4+ T cell immune responses to antigens from SARS-CoV-2 spike glycoprotein but not from the spiked glycoprotein of the ‘common cold’-associated human coronavirus 229E (HCoV-229E) as compared with healthy controls who responded comparably to both antigens.[14] However, a study analyzing the median titers of neutralizing antibodies against SARS-CoV-2 of twenty-five patients with prostate cancer under treatment with androgen receptor-targeted agents such as abiraterone or enzalutamide, found it to be similar to healthy volunteers.[15]

A different study suggested that a beneficial impact of COVID-19 vaccination on patients with prostate cancer as the SARS-CoV-2 spike protein reduced the survival of prostate cancer cells through inhibition of proliferation and promotion of apoptosis; downregulation of pro-proliferative molecule CDK4 and upregulation of pro-apoptotic molecule Fas ligand.[16]

5. Conclusions

During the COVID-19 pandemic, overall screening, diagnostics, and treatment have faced a downtrend, especially during the first wave and lockdown, with the statistics showing slow improving during the late era of the pandemic or by the end of 2020. To improvise, the risk of delayed curative treatment was measured, and treatment plans were amended accordingly in order to lessen hospital visits while the results are still contradictory. The protective role of androgen deprivation therapy on COVID-19 triggered many debate while the majority of clinical studies found no significant association. Concerns about a reduced immune response to vaccination in patients with prostate cancer occurred, but additional research in the future essential. The pandemic added additional burdens to patients with prostate cancer and different aspects of the quality of life of patients were assessed. While we anticipate that the end of the pandemic this coming, it is essential to re-examine how the pandemic has changed the overall care of patients with prostate cancer and how to proceed further in the future.

Capsule Summary

During the COVID-19 pandemic, overall screening, diagnostics, and treatment have faced a downtrend, especially during the first wave and lockdown, with the statistics showing slow improving during the late era of the pandemic or by the end of 2020.

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Author Contribution

All authors made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

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