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Prostate Cancer Diagnosis and Management During One Year of the COVID-19 Pandemic

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Abstract. *Background/Aim: To evaluate the diagnosis and treatment of prostate cancer (PCa) during 1 year of the COVID-19 pandemic. Patients and Methods: The management of men with PCa during COVID-19 pandemic (March 2020-2021) was compared with the clinical activity of the 12 months before the COVID-19 pandemic (March 2019-2020). Results: The number of clinical visits, prostate biopsy, and men enrolled in active surveillance was significantly lower during the COVID-19 pandemic ($p<0.05$); on the contrary, the number of cases with advanced (pT3b: 11.2 vs. 25.6%; nodal positive: 14.8 vs. 46.1%) and metastatic (5.9 vs. 9.3%) PCa increased. The number of open radical prostatectomies increased compared with the ones using a laparoscopic approach; moreover, more men were treated with external radiotherapy (25.1 vs. 54.2%). Conclusion: The guideline recommendations in the management of PCa should constantly adapt to the epidemiological evolution, but the overall cost of delayed diagnosis will increase in the near future.*

The coronavirus disease COVID-19 has dramatically modified our way of looking at medical information and its clinical application; currently, the international urological guidelines are of utmost importance and a great deal of effort is continuously made to offer the highest level of patient care. In the case of urological tumor, board and faculty discussions may provide a rational and adoptable treatment option; in this respect, recently, the National Comprehensive Cancer Network, the European Association of Urology (EAU) and the British Association of Urological Surgeons (1-3) have focused on diagnosis and management of prostate cancer (PCa).

In this study, the diagnosis and management of PCa during 1 year of the COVID-19 pandemic has been compared with previous results (4).

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Key Words: Prostate cancer, COVID-19 pandemic, prostate cancer management.

Patients and Methods

The diagnosis and treatment of men with PCa during 1 year of the COVID-19 pandemic (March 2020-2021) was retrospectively evaluated and compared with the clinical activity of the 12 months before the pandemic (March 2019-2020). Our emergency hospital has continued to guarantee urological assistance throughout this pandemic. The clinical workload was evaluated and compared for: Clinical office evaluation, number of multiparametric magnetic imaging (mpMRI) procedures performed, number of systematic and fusion biopsies (5, 6), and PCa diagnosis. In addition, the number of men who underwent active surveillance for low risk PCa, watchful waiting, radical prostatectomy, and external radiotherapy was recorded. Finally, definitive specimens of men submitted to surgery plus adjuvant oncological treatment were reported.

Statistics. For our statistical analysis, Student's *t*-test was used with a value of $p<0.05$ as statistically significant.

Results

In the Table I the urological workload (*i.e.*, clinical visits, prostate biopsy, mpMRI) are summarized; Table II shows the comparison of the clinical parameters of PCa diagnosed in 1 year pre-COVID *vs*. during the COVID-19 pandemic. Finally, in Table III, the definitive histology of men submitted to radical prostatectomy plus adjuvant treatment is detailed.

The number of clinical visits, prostate biopsies and mpMRI procedures were significantly lower during the past year of the COVID-19 pandemic ($p<0.05$); on the contrary, the number of cases with advanced (pT3a/pT3b), nodal positive and metastatic PCa were higher by approximately two-fold or more because of the higher rate of referral for prostate biopsy of men at risk of high-grade cancer. During the past year, the vast majority of men underwent open radical prostatectomy rather than a laparoscopic approach compared with approximately half in the year preceding the pandemic. In addition, the proportion of men treated by external radiotherapy combined with medical therapy doubled. Finally, clinical re-evaluation of patients enrolled in active surveillance was postponed and, conversely, a very low percentage of men were enrolled in the active surveillance protocol.

Table I. *Prostate cancer diagnosis and treatment pre-COVID 19 (March 2019-2020) compared with during the COVID-19 pandemic (March 2020-2021).*

Diagnosis and management	Pre COVID-19	COVID-19	*p*-Value
Clinical office evaluation, n	2,000 (cases)	1,015 (cases)	<0.05
Median age (range), years	61 (42-84)	66 (41-80)	
Prostate biopsies, n (%)	485 (24.5%)	201 (19.8%)	>0.05
mpMRI, n (%)	351 (72.4%)	85 (42.3%)	<0.05
Extended prostate biopsy, n (%)	485 (100%)	201 (100%)	>0.05
Prostate fusion biopsy, n (%)	180 (37.1%)	70 (34.8%)	>0.05
Cancer diagnosis from biopsy, n (%)	187 (38.5%)	96 (47.7%)	<0.05
AS enrollment, n (%)	25 (13.4%)	1 (1%)	<0.05
Watchful waiting, n (%)	2 (1%)	-	-
Radical prostatectomy, n (%)	54 (28.9%)	39 (40.6%)	<0.05
External radiotherapy, n (%)	47 (25.1%)	52 (54.2%)	<0.05
Oncological therapy, n (%)	10 (5.3%)	8 (8.3%)	<0.05

mpMRI: Multiparametric resonance imaging; AS: active surveillance.

Discussion

As a consequence of COVID-19 pandemic, several measures have been taken in order to reduce the fast spread of the virus, protect health professionals from infection during their work, guarantee the health of in-patients, and to ensure the availability of health resources to address the vast number of patients suffering from the coronavirus disease. Subsequently, clinical and surgical strategies in urology have been forced to adapt to the changes brought about by COVID-19 but the EAU guideline recommendations for the management of PCa in the COVID-19 era are based on only level 2-3 evidence (6), therefore, not on robust evidence but mostly on expert consensus (7-10).

Regarding elective visits, the recommendation suggests postponing the procedure or transitioning to telehealth visits to further reduce the exposure risk; for men who must be seen in the clinic, social distancing should be promoted to ensure minimal contact with staff and other patients. It has been reported that SARS-CoV-2 is present in the stool of patients with COVID-19 and fecal-oral transmission is possible; while it has not been demonstrated that the transrectal prostate biopsy procedure itself would be a means of COVID-19 transmission, we advise avoidance or deferral of almost all prostate biopsies. In this respect, the transperineal prostate biopsy approach might reduce this risk of infection. The indication to perform a prostate biopsy should be reserved for cases in which factors for high-risk PCa are present: Prostate specific antigen >20 ng/ml, doubling time <6 months, suspicious digital rectal examination, or clinical T3 disease, with/without local or systemic symptoms. On the other hand, in the absence of high-risk factors, biopsy may be postponed by 3 to 6 months, or even 12 months according to National Comprehensive Cancer Network recommendations (1). Since PCa prognosis is generally favorable, most biopsies could safely be delayed, while active surveillance must almost be mandatory in those patients with low-risk PCa. In regard to mpMRI, the EAU recommends upfront pre-biopsy mpMRI if resources allow. However, if the patient is suspected to be liable to risk of progression and metastasis, biopsy can be performed without prior MRI (1-3).

Definitive PCa treatments such as radical prostatectomy as well as external radiotherapy are actually being postponed. It has been shown that in patients with localized low- and intermediate-risk PCa, 6 to 9 months of delay from biopsy to radical prostatectomy is associated with an increased risk of biochemical recurrence, or clinical recurrence at 5 years of lower than 18% and 0.6%, respectively; on the contrary, for high-risk patients, the risk of biochemical recurrence is higher (close to 24% after 9-12 months from biopsy) (11). In this respect, several studies have proven the transmission of different viruses during surgery (12, 13); according to a recent publication, this risk might be higher during laparoscopic/robotic procedures compared to open ones (14). This is due to the concentrated aerosol formed in the abdominal cavity during the operation being released suddenly when trocars are removed, small incisions are made or instruments are exchanged (15). In addition, airborne transmission is possible through intubation and extubation. Moreover, urologists can consider using lower pressure on insufflation system with integrated active smoke evacuation mode. Ultimately, presence in the operating room should be restricted to essential staff and the operating surgeon; this fact has led the EAU Robotic Urology Section to propose some recommendations to safeguard the health of surgical staff (16).

Nevertheless, each PCa case must be considered individually and the proposed recommendations should constantly adapt to the epidemiological evolution of the situation.

In our series, in accordance with the international guideline recommendations, the number of clinical visits, prostate biopsies and mpMRIs was significantly lower during the past

Table II. *Clinical parameters of prostate cancer diagnosed in 1 year pre COVID-19 (March 2019-2020) compared with during the COVID-19 pandemic (March 2020-2021).*

Clinical stage		Pre COVID-19	COVID-19	*p*-Value
PSA, ng/ml	Median (range)	5.9 (2.9-379)	9.8 (4.8-762)	>0.05
DRE, n (%)	Abnormal	45 (9.3%)	53 (26.4%)	<0.05
ISUP Grade group, n (%)	1	42 (22.5%)	10 (10.4%)	<0.05
	2	52 (27.8%)	22 (23%)	>0.05
	3	40 (21.4%)	34 (35.4%)	<0.05
	4	35 (18.7%)	18 (18.7%)	>0.05
	5	18 (9.6%)	12 (12.5%)	>0.05
GPC, n (%)	≤50%	118 (63.1%)	45 (46.8%)	<0.05
	>50%	69 (46.9%)	54 (53.2%)	>0.05
Stage, n (%)	cT1c	115 (61.5%)	41 (42.7%)	<0.05
	cT2	42 (22.5%)	35 (36.5%)	<0.05
	cT3	29 (15.5%)	19 (19.8%)	>0.05
	cT4	1 (0.5%)	1 (1%)	>0.05
Metastatic disease, n (%)	Yes	11 (5.9%)	9 (9.3%)	<0.05

PSA: Prostate-specific antigen; ISUP: International Society of Urological Pathology; DRE: digital rectal examination; GPC: greatest percentage of cancer.

Table III. *Definitive histological findings pre COVID-19 (March 2019-2020) compared with during the COVID-19 pandemic (March 2020-2021) in patients who underwent prostatectomy.*

Finding		Pre COVID-19 (n=54), n (%)	COVID-19 (n=39), n (%)	*p*-Value
Stage	pT2	29 (53.7%)	3 (7.7%)	<0.05
	pT3a	19 (35.1%)	26 (66.7%)	<0.05
	pT3b	6 (11.2%)	10 (25.6%)	<0.05
PSM		10 (18.5%)	20 (51.2%)	<0.05
Nodes	Positive	8 (14.8%)	18 (46.1%)	<0.05
Adjuvant therapy	Radiotherapy	9 (16.6%)	23 (59%)	<0.05
	LHRH	5 (9.2%)	14 (35.9%)	<0.05
ISUP Grade group	2	15 (27.8%)	4 (10.2%)	<0.05
	3	25 (46.3%)	15 (38.4%)	>0.05
	4	10 (18.5%)	16 (41%)	<0.05
	5	4 (7.4%)	4 (10.2%)	>0.05
Prostatectomy	Open	30 (55.5%)	35 (89.7%)	<0.05
	Laparoscopic	24 (44.5%)	4 (10.3%)	<0.05

ISUP: International Society of Urological Pathology; LHRH: luteinizing hormone-releasing hormone; PSM: positive surgical margins.

year of the COVID-19 pandemic; on the contrary, the proportion of cases of locally advanced and metastatic PCa increased because of the higher selection for prostate biopsy of men at high risk for cancer. Therefore, the number of men submitted to open radical prostatectomy instead of a laparoscopic approach also increased as suggested by guidelines to optimize the use of the operating theatre (less operative time), especially in men with high-risk PCa.

Regarding our data, some considerations should be made. Our data refer to a low number of patients, therefore, a large series of Urological Centers should be evaluated. The lack of early diagnosis/screening for PCa has worsened the detection rate for cancer, reducing the opportunity to perform minimally invasive treatment with the intent to improve the quality of life of patients. Finally, the overall cost of delayed diagnosis and treatment will increase in the near future (17).

In conclusion, each PCa case must be considered individually and the proposed recommendations should constantly adapt to the epidemiological evolution of the situation; the cost of delayed PCa diagnosis and treatment will be evaluated in the near future.

Conflicts of Interest

The Authors declare no conflicts of interest exist in regard to this study.

Authors' Contributions

All Authors contributed equally to this article. Pepe Pietro carried out design, analysis and interpretation of the study. Pepe Ludovica, Pennisi Michele, and Fraggetta Filippo made substantial contributions to acquisition of data, or analysis and interpretation of data. All Authors read and approved the final article.

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