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Trends in prostate cancer diagnosis during the COVID-19 crisis: A report from one high-volume Japanese center

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Abstract: Self-isolation to prevent the spread of the novel coronavirus SARS-CoV-2 began in April 2020. As a result, the number of prostate needle biopsies taken at our hospital for suspicion of prostate cancer decreased by 30.5%, from 403 in 2019 to 280 in 2020. The number of diagnoses of prostate cancer decreased by 35.4% from 189 to 122. High-risk and intermediate-risk prostate cancers were 36.5% and 49.7%, respectively, in 2019. Assuming that this situation in our hospital reflects events nationwide, approximately 32,575 (high-risk; 11,890, intermediate risk; 16,189) patients annually would be suffering delays in diagnosis. Furthermore, > 90% of the decrease are curable cases in their 60s and 70s, with prostate specific antigen levels of 30 ng/mL or less, with stage T2, and N0M0. Widely aware that more than 30,000 prostate cancers might be overlooked nationwide in 2020, we recommend establishing a health checkup system with infection control and undergoing early testing.

Keywords: coronavirus, biopsy, SARS-CoV-2, stage, prostate-specific antigen (PSA), age

A state of emergency was declared in Japan on April 7, 2020, due to the rapid nationwide spread of the novel coronavirus SARS-CoV-2. Leaving home for unnecessary or non-urgent purposes was restricted. Employees teleworked from home, and schools adopted online lessons. Accordingly, the number of outpatients at our hospital decreased by 14.4%, from 683,275 in 2019 to 585,187 in 2020; the number of outpatients in our Department also decreased by 13.4%, from 24,896 to 21,567. Except for symptomatic cases, those with extremely high prostate-specific antigen (PSA), and those with multiple metastases, patients solely with high PSA tended to avoid medical consultation due to the stay-at-home rules. Furthermore, non-urgent prostate biopsy was not prioritized, because of the restriction of hospital medical service capacity under pandemic conditions. Here, we analyze the number and breakdown of prostate needle biopsy cases in 2019 and 2020, in order to provide an estimate of the indirect influence of the novel coronavirus SARS-CoV-2 crisis nationwide on the clinical management of prostate cancer.

Patients who underwent prostate needle biopsy between January 1, 2019, and December 31, 2020 were reviewed. Biopsies for known prostate cancer cases (*i.e.*, protocol biopsy on active surveillance) were excluded from this analysis. Written informed consent was obtained for the use of patients' medical information (Ethics Committee, Faculty of Medicine, University of Tokyo; #3124). The pre-biopsy PSA value was set as the highest value within the six months prior to biopsy. T staging was performed based on magnetic resonance imaging, digital examination, and needle prostate biopsy results according to the Union for International Cancer Control TNM classification of malignant tumors 8th edition (*1*). Computed tomography and bone scintigraphy were used for detecting regional lymph node metastasis and distant metastasis. Statistical analysis was performed using JMP pro ver.15.2.1, and Fisher's exact test was used for stratified analysis.

We identified a total of 683 prostate needle biopsies taken on suspicion of prostate cancer, 403 cases in 2019 and 280 cases in 2020, representing a decrease of 123 cases (30.5%). The number of patients in their 60s and 70s decreased by 36.5%, from 312 cases to 198 cases, accounting for 92.6% of the total decrease and significantly less in 2020 compared to 2019 ($p = 0.0296$, Figure 1). The median (interquartile range) pre-biopsy PSA level (ng/mL) increased from 6.9 (5.1-11.1) in 2019 to 7.1 (5.3-11.1) in 2020. The number of cases with a pre-biopsy PSA level (ng/mL) of 30.0 or less decreased by 31.7% from 384 to 262, accounting for 99.1% of the total decrease (Figure S1, *https://www.ghmopen.com/site/supplementaldata.html?ID=24*). In contrast the number of cases with PSA higher than 30.0 ng/mL was similar, 19 in 2019 and 18 in 2020 (not significant, $p = 0.210$).

The number of diagnoses of prostate cancer

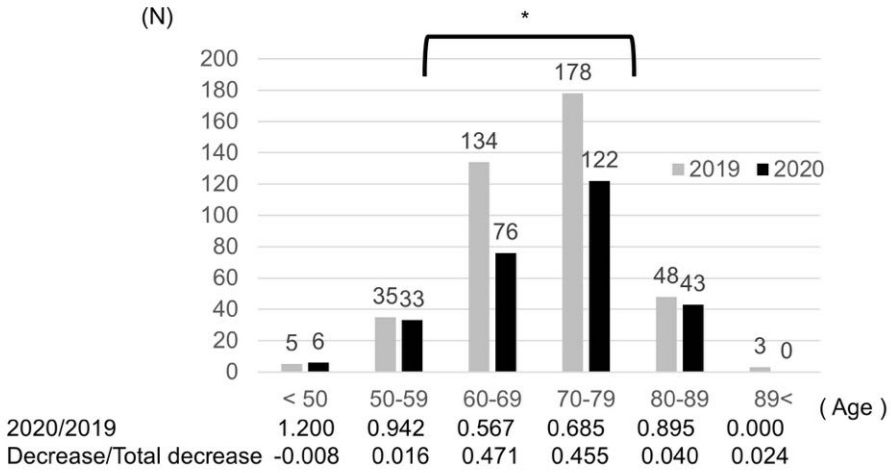

Figure 1. Numbers of prostate needle biopsies by age. The number of patients in their 60's and 70's decreased by 58 and 56, accounting for 92.6% of the total decrease. *Significantly less in 2020 compared to 2019 ($p = 0.0296$).

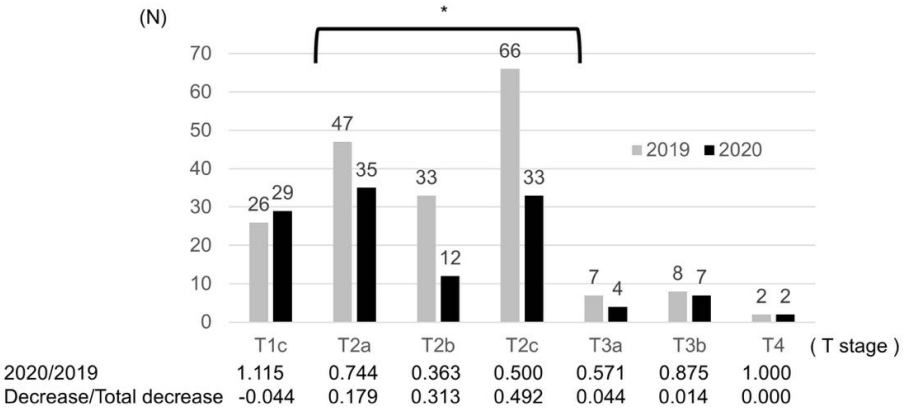

Figure 2. Numbers of prostate cancer diagnoses by T stage. Cases at T2a, T2b, and T2c decreased by 12, 21, and 33 cases, accounting for 98.5% of the total decrease. *Significantly less in 2020 compared to 2019 ($p = 0.0172$).

decreased by 35.4% from 189 to 122. Cases at T2 stage decreased by 45.2%, from 146 to 80, whereas T3 and T4 cases slightly decreased from 17 to 13 (Figure 2). The total number of patients at T2 stage decreased by 66, accounting for 98.5% of the total decrease and significantly less in 2020 than 2019 ($p = 0.0172$). Finally, the number of patients with N0 and M0 disease decreased by 36.9% from 175 to 111, accounting for 95.5% of the total decrease, but this was not significant ($p = 0.379$, Figure S2, *https://www.ghmopen.com/site/supplementaldata.html?ID=24*).

In 2020, the number of biopsies taken decreased by 30.5% compared to 2019, with > 90% of the decrease accounted for by patients in their 60's and 70's and with pre-biopsy PSA levels of 30 ng/mL or less. The number of prostate cancer diagnoses decreased by 35.4%, more than 90% of which were T2 and N0M0. In contrast, there were few changes in advanced cases including those with PSA over 30 ng/mL, with stages T3 or more, or with nodal and/or distant metastasis. These cases might be symptomatic, or might have had to have a biopsy, even during the coronavirus crisis. In our Department, the number of all outpatients in their 60's and 70's decreased by 13.0%, similar to the decrease of 13.4% across all ages, while the number of patients at this age undergoing prostate needle biopsy decreased greatly.

One Italian study on colorectal cancer screening reported that the number of tests during lockdown due to the pandemic was reduced by a quarter, but the probability of finding cancer increased from 1% to 8% (*2*). In that study, many of the cases examined during lockdown were high-risk, including those with subjective symptoms such as bloody stools and those with a family history. In contrast, the cancer detection rate in our report was similar before and after lockdown at 46.8% in 2019 and 43.5% in 2020. This might result from the lower accuracy of prostate biopsy compared with colonoscopy.

According to the National Cancer Center Institute

in Japan, the annual number of cases of prostate cancer is 92,021 in 2018 (*3*). Prostate cancer diagnoses at our hospital decreased by 35.4% from 2019 to 2020. Assuming that this rate is the same across the nation, the number of patients with a delayed diagnosis of prostate cancer will reach 32,575. The number of high-risk (Gleason Score 8 and above) and intermediate-risk cases (Gleason Score 7) was 69 (36.5%) and 94 (49.7%), respectively, of prostate cancer diagnoses at our hospital in 2019. Assuming that this rate is the same across the nation, 11,890 are likely to be in the high-risk group and 16,189 in the intermediate-risk group. Several studies have reported that the time patients can wait for treatment of prostate cancer should be 2.5-6 months in the high-risk group and 9-24 months in the intermediate-risk group (*4-11*).

Delays in diagnosis occurred worldwide. De Vincentiis *et al.* (*12*) reported that prostate cancer and bladder cancer diagnoses fell in 2020 by 75% and 66%, respectively, compared with the average number recorded in 2018 and 2019. There is also a concern that cases of more advanced prostate cancer will increase because health examinations and medical institutional consultations were postponed due to the coronavirus crisis.

One limitation of this research is that it is not necessarily applicable to Japan as a whole, and the world in general, because it involved only a single facility, a small number of cases, and was a retrospective study. No prospective study reports have been found on treatment delays, and bias is unavoidable.

In conclusion, the number of prostate diagnoses in 2020 was 35.4% lower than in 2019. More than 90% of the decrease was accounted for by patients in their 60's and 70's that would have been curable, with PSA of 30 or less, and at stage T2, N0M0. There is a concern that because of delayed diagnosis the relative proportion of more advanced prostate cancer cases will increase and some of them will no longer be curable. Widely aware that more than 30,000 prostate cancers might be overlooked nationwide in 2020, we recommend establishing a health checkup system with infection control and undergoing early testing.

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