Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Androgen deprivation and SARS-CoV-2 in men with prostate cancer

We read with great interest the very recent article by Montopoli et al.,[1] which reports men with prostate cancer tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Veneto, Italy, by 1 April 2020. The authors suggest that androgen deprivation therapy (ADT) could partially protect from SARS-CoV-2 infection.[1] The biological premise for this observation is the androgen receptor-mediated regulation of TMPRSS2,[2] a type II transmembrane serine protease that is important for SARS-CoV-2 entry to host cells.[3] Indeed, androgens regulate *TMPRSS2* expression also in a lung carcinoma cell line.[4]

Encouraged by the findings of Montopoli et al.,[1] we examined the health care records of patients with prostate cancer [International Classification of Diseases (ICD)-10 code C61] in the Hospital District of Helsinki and Uusimaa, Finland, using automated text mining with manual verification and structured diagnostic codes. Altogether, 352 such men were tested for SARS-CoV-2 between 7 March and 14 May 2020. A patient was classified to be on ADT if he had a history of orchiectomy, or a valid prescription for a gonadotropin-releasing hormone (GnRH) analogue, GnRH antagonist, and/or antiandrogens (flutamide, bicalutamide, enzalutamide) or the CYP17 inhibitor abiraterone before his SARS-CoV-2 test ($n = 134$) [38%, 95% confidence interval (CI): 33%–43%]. The mean age of these 134 men was 78.4 years ± 8.1 standard deviation (range 58–96 years). The frequency of being on ADT was in agreement with that observed in a survey of a large cohort of UK men with prostate cancer.[5] Conversely, a patient was classified not to be on ADT if no records of the above conditions were found or ADT had been ceased before a SARS-CoV-2 test ($n = 218$; mean age 76.5 years ± 9.4 standard deviation, range 51–96 years). The presence of SARS-CoV-2 RNA in nasopharyngeal swab samples was analyzed by RT-PCR (details available upon request). This study was based on register data, provided by the registry holder, Helsinki University Hospital, and therefore no ethical permission was required according to the Finnish Medical Research Act.

Of the 352 prostate cancer patients, 17 (4.8%, 95% CI: 2.6%–7.0%) tested positive for SARS-CoV-2, and 6 (35%, 95% CI: 13%–58%) of them were on ADT. However, the frequency of being positive for SARS-CoV-2 was not associated with ADT [6/134 on ADT versus 11/218 not on ADT; odds ratio (OR) 0.88; 95% CI 0.32–2.44, $P = 0.81$]. ADT was not associated with the severity of the disease, as assessed by occurrence of death or the need of intensive care (1/6 in the ADT-positive group versus 3/11 in the ADT-negative group; OR 0.53; 95% CI 0.04–6.66, $P = 0.63$). There were no differences in possible confounding comorbidities on coronavirus disease 2019 (COVID-19) severity between patients with and without ADT[6] (Table 1).

Table 1. The presence of potential confounding factors on COVID-19 severity in SARS-CoV-2 tested patients with prostate cancer classified on the basis of being on androgen deprivation therapy

	No ADT ($n = 218$)	On ADT ($n = 134$)	*P* value[a]
Age > 65 years	191	125	0.10
Hypertension[b]	47	30	0.89
Coronary artery disease[c]	30	21	0.64
COPD[d]	12	8	1.0
Diabetes[e]	17	16	0.26
Cardiac arrhythmia[f]	41	30	0.42
Current smoker	17	18	0.10

The distributions of diagnoses from 2015 to 2 weeks before the SARS-CoV-2 test are shown. Smoking status was extracted by using automated text mining and manual verification. The data denote the number of patients with each condition.
ADT, androgen deprivation therapy; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ICD, International Classification of Diseases; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a] Fisher's exact test.
[b] ICD-10 codes I10 and I15.
[c] ICD-10 codes I20, I21, I24 and I25.
[d] ICD-10 code J44.
[e] ICD-10 code E11.
[f] ICD-10 codes I48 and I49.

While we can only speculate on the difference between our results and those of Montopoli et al.,[1] methodological differences stand out. Montopoli et al.[1] collected data on 68 hospitals in the Veneto region, and identified 118 SARS-CoV-2-positive patients with prostate cancer of whom 4 were on ADT and 114 were not.[1] Thereafter, they compared the ratios of SARS-CoV-2-positive patients with and without ADT *per* all Venetian prostate cancer patients on (4/5273) or off ADT (114/37 161) (OR 4.05; 95% CI, 1.55–10.59).[1] However, it can be estimated that the six provinces and the Venice metropolitan city had differences in the COVID-19 infection rates on 1 April 2020 (i.e. at the time of Venetian data acquisition), the greatest difference being more than fourfold.[1,7,8] Thus, these apparent provincial differences in the infection rate represent a potential confounding factor. Accordingly, in our study we further restricted the analysis on the risk of SARS-CoV-2 infection in men with or without ADT only to the 163 patients living in Helsinki. Again, there was no significant relationship between ADT and the probability of being SARS-CoV-2-positive (data not shown).

In conclusion, our results do not support a role for ADT in the prevention of SARS-CoV-2 infection in men with prostate cancer via ADT-mediated decrease in the expression of *TMPRSS2*. These results do not encourage compassionate use of drugs that suppress pituitary gonadotropin secretion or inhibit androgen synthesis or androgen receptor in an attempt to decrease SARS-CoV-2 infection risk or to alleviate the course of COVID-19.

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DISCLOSURE

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First case of persistent pancytopenia associated with SARS-CoV-2 bone marrow infiltration in an immunocompromised patient

A 53-year-old man was referred from an intensive care unit for acute respiratory distress, pancytopenia and cytokine release syndrome. His symptoms had begun 3 weeks earlier with anosmia, ageusia, cough, fever and dyspnea. He had a medical history of mantle-cell lymphoma diagnosed in 2017, and was in complete remission following autologous bone marrow transplant in 2018 and nine-monthly maintenance infusions of anti-CD20 monoclonal antibody (last infusion 42 days before his symptoms appeared). Blood tests showed pancytopenia (hemoglobin 7.9 g/dl, leukocytes 0.8 G/l and platelets 48 G/l) and elevated inflammatory markers (C-reactive protein 235 mg/l, fibrinogen >10 g/l, ferritin 8106 ng/ml and D-dimers 1132 ng/ml). Coronavirus disease 2019 (COVID-19) tests by semiquantitative severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) reverse transcription-PCR (RT-PCR) revealed negative findings in nasopharyngeal swab samples, but positive findings in bronchoalveolar lavage fluid, blood [cycle threshold (*Ct*) value = 30] and bone marrow aspiration samples. Other microbiological examination results were negative. Bone marrow aspiration revealed neither hemophagocytosis features nor viral infection except SARS-CoV-2. Flow cytometry analysis of circulating leukocytes revealed the absence of circulating B lymphocytes, a result of the repeated anti-CD20 antibody infusions, and a low T-lymphocyte count (0.447 G/l). Serum protein electrophoresis revealed gamma globulin level of 3 g/l (versus 4.9 g/l 6 months before). Thoracic CT scan showed bilateral patchy ground-glass opacities. Upon admission, he received two successive infusions of tocilizumab (8 mg/kg) and an infusion of polyvalent immunoglobulins (400 mg/kg). He required respiratory support with noninvasive ventilation and high-flow oxygen therapy for 7 days. Clinical evolution was gradually favorable over 2 weeks, with apyrexia, reduced oxygen requirements and normalized inflammatory biomarker levels. However, at 45 days after admission, SARS-CoV-2 RT-PCR test results remained positive in blood (*Ct* value = 35) and bone marrow. Moreover, SARS-CoV-2 serological testing detected no antiviral immunoglobulin G, while pancytopenia persisted.

If respiratory complications are the most common clinical presentation of severe COVID-19, hematological involvement as described here and persistent viremia are not published in the literature.[1,2] Therefore, SARS-CoV-2 RT-PCR should be performed in blood and bone marrow aspiration in case of pancytopenia associated with typical COVID-19 symptoms, especially in case of secondary humoral immunodeficiency. Among the many therapeutic options under