

SARS-CoV-2 Testing in Patients With Cancer Treated at a Tertiary Care Hospital During the COVID-19 Pandemic

Anna S. Berghoff, MD, PhD¹; Margaretha Gansterer, PhD²; Arne C. Bathke, PhD³; Wolfgang Trutschnig, PhD³; Philipp Hungerländer, PhD⁴; Julia M. Berger¹; Judith Kreminger¹; Angelika M. Starzer, MD¹; Robert Strassl, MD⁵; Ralf Schmidt, MD, PhD⁵; Harald Willschke, MD⁶; Wolfgang Lamm, MD¹; Markus Raderer, MD¹; Alex D. Gottlieb, PhD⁷; Norbert J. Mauser, PhD⁷; and Matthias Preusser, MD¹

PURPOSE To analyze the prevalence of SARS-CoV-2 infection in patients with cancer in hospital care after implementation of institutional and governmental safety measurements.

METHODS Patients with cancer routinely tested for SARS-CoV-2 RNA by nasal swab and real-time polymerase chain reaction between March 21 and May 4, 2020, were included. The results of this cancer cohort were statistically compared with the SARS-CoV-2 prevalence in the Austrian population as determined by a representative nationwide random sample study (control cohort 1) and a cohort of patients without cancer presenting to our hospital (control cohort 2).

RESULTS A total of 1,688 SARS-CoV-2 tests in 1,016 consecutive patients with cancer were performed. A total of 270 of 1,016 (26.6%) of the patients were undergoing active anticancer treatment in a neoadjuvant/adjuvant and 560 of 1,016 (55.1%) in a palliative setting. A total of 53 of 1,016 (5.2%) patients self-reported symptoms potentially associated with COVID-19. In 4 of 1,016 (0.4%) patients, SARS-CoV-2 was detected. At the time of testing at our department, all four SARS-CoV-2–positive patients were asymptomatic, and two of them had recovered from symptomatic COVID-19. Viral clearance was achieved in three of the four patients 14–56 days after testing positive. The estimated odds ratio of SARS-CoV-2 prevalence between the cancer cohort and control cohort 1 was 1.013 (95% CI, 0.209 to 4.272; $P = 1$), and between control cohort 2 and the cancer cohort it was 18.333 (95% CI, 6.056 to 74.157).

CONCLUSION Our data indicate that continuation of active anticancer therapy and follow-up visits in a large tertiary care hospital are feasible and safe after implementation of strict population-wide and institutional safety measures during the current COVID-19 pandemic. Routine SARS-CoV-2 testing of patients with cancer seems advisable to detect asymptomatic virus carriers and avoid uncontrolled viral spread.

J Clin Oncol 38. © 2020 by American Society of Clinical Oncology

INTRODUCTION

In December 2019, the enveloped RNA betacoronavirus termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) associated with a respiratory illness referred to as COVID-19 was identified.^{1,2} SARS-CoV-2 is a highly contagious virus transmitted human to human via droplets because of its high concentration in fluids of the respiratory tract.³ On March 11, 2020, the WHO made the assessment that the situation can be characterized as pandemic.⁴ The estimated mortality rates vary between countries and range between < 3% in the overall population to 10% in elderly patients and 40% in critically ill patients.^{5–9} In line with international data, COVID-19 mortality is highest in elderly people in the Austrian population, as the majority of fatalities occurred in patients age \geq 60 years.¹⁰

To prevent uncontrolled viral spread, strict measures, including hygienic practices, protective gear usage,

and social distancing, have been recommended and have been implemented to varying extents by national and local public health authorities. In Austria, a series of measures (Appendix Table A1, online only) have been implemented by the government since March 16, 2020 that successfully led to a significant decrease in the daily infection rate.¹¹

Patients with an active diagnosis of cancer are prone to a variety of infections for multiple reasons, ranging from a potentially compromised immune system due to the disease itself, tumor cachexia, and malnutrition, to immunosuppression as a main adverse effect of most cancer treatments, such as chemotherapy, molecular targeted agents, and immunotherapy. In addition, patients undergoing active anticancer therapy are exposed to unavoidable social contacts with fellow citizens during transit as well as with hospital staff and other patients during regular therapy and follow-up visits at the hospital. These factors give

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on July 16, 2020 and published at ascopubs.org/journal/jco on August 14, 2020: DOI <https://doi.org/10.1200/JCO.20.01442>

CONTEXT

Key Objective

To determine the prevalence of SARS-CoV-2 in patients with cancer treated at a tertiary care hospital in relation to the general population and to patients without cancer after implementation of specific safety measures in Vienna, Austria.

Knowledge Generated

SARS-CoV-2 prevalence in patients with cancer was similar to the general population and lower than in patients without cancer. Asymptomatic viral carriers were detected in 0.4% of patients with cancer.

Relevance

Our findings show that implementation of strict safety policies including routine SARS-CoV-2 testing of patients with cancer in cancer centers is advisable to prevent uncontrolled viral spread.

reason for concern about an increased risk for SARS-CoV-2 infection and COVID-19 in patients with cancer, particularly those undergoing active antineoplastic therapy. Indeed, some data indicate an increased risk for SARS-CoV-2 infection and a severe disease course for patients with cancer.^{10,12,13} On the other hand, avoidance of health care facilities could increase cancer-related deaths, as patients with symptoms wait longer to seek medical advice.¹⁴

Here, we report the SARS-CoV-2 prevalence in a large cohort of consecutive patients treated in a large tertiary care hospital after implementation of institutional safety measures and in relation to population-based data.

METHODS

This study was approved by the ethics committee of the Medical University of Vienna (vote number 1437 of 2020).

Cancer Cohort

Clinical and treatment data of all patients routinely tested for SARS-CoV-2 between March 21 and May 4, 2020, were used. Appendix Table A2 (online only) lists the safety measures implemented at our institution.

From March 21, 2020, nasal or pharyngeal respiratory swabs were routinely taken of each patient presenting at our department, unless a negative SARS-CoV-2 test result within the past 2 weeks was available. In case of symptoms and before medical interventions, the SARS-CoV-2 test was repeated in a shorter interval.

Control Cohorts

We compiled the following two control groups to compare the SARS-CoV-2 prevalence in our patients with cancer with the general population (control cohort 1) and whether the exposure to the hospital setting increases the risk for SARS-CoV-2 infection (control cohort 2).

Control cohort 1. A random sample study launched by the Austrian Ministry of Science with the goal to determine the prevalence of SARS-CoV-2 among nonhospitalized people in the period April 1-6, 2020 (ie,

after implementation of population safety measures) was used.¹⁵ To our knowledge, this study was the first countrywide representative study in continental Europe and the first to be based on nationwide SARS-CoV-2 RNA testing. The study design and implementation were informed by the WHO's "Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection."¹⁶ From all Austrian municipalities, 249 were randomly selected, stratified in advance according to federal state and municipal size. Two methods were used to contact households for participation: (1) Households in the target municipalities were randomly selected from public telephone directories. (2) In addition, households were contacted by telephone using random-digit dialing. Self-selection into the study sample was not allowed. The person with the next birthday was asked to participate. Standard survey research strategies were applied to avoid unit nonresponse. SARS-CoV-2 testing was performed by household visits by study teams or in drive-in centers.

Control cohort 1 consisted of 1,544 nonhospitalized people, out of whom six were classified as SARS-CoV-2–positive cases, three by self-declaration of positive test and three out of 1,544 by testing. None of the persons included in control group 1 reported a diagnosis of cancer.

Control cohort 2. To evaluate the infection prevalence in our hospital setting, we analyzed all patients without cancer who consecutively presented at the entrance of the Medical University of Vienna, were tested for SARS-CoV-2 infection, and were not hospitalized at the Medical University of Vienna due to safety reasons, nonurgent medical procedures, or per treating physician recommendation between March 21 and May 4, 2020.

SARS-CoV-2 Testing

Testing for the presence of SARS-CoV-2 RNA in respiratory specimens (nasal or pharyngeal swabs) was performed at the Department of Laboratory Medicine, Medical University of Vienna, Vienna, Austria by real-time polymerase chain reaction (RT-PCR; Appendix, online only). Comparability of

the results of all test methods used were confirmed by participation in international quality control ring trials.¹⁷

Statistical Analyses

We report Agresti-Coull¹⁸ 95% CIs for the SARS-CoV-2 prevalence in the cancer cohort and both control cohorts and compare them using the estimated odds ratio and Fisher's exact test. A two-sided *P* value of .05 was defined as significance threshold. We compare proportions of age groups using the estimator of relative effects presented by Brunner et al.¹⁹

RESULTS

Specific measurements to prevent the spread of SARS-CoV-2 in Austria were implemented starting on March 16 by the Austrian government. To prevent the transmission of SARS-CoV-2 within the Medical University of Vienna, measurements were already established on March 5 by restricting work-related travel, followed by access restriction from March 10. All patients treated at the Division of Oncology were tested for SARS-CoV-2 RNA from March 21 (Appendix Fig A1, online only).

Cancer Cohort

Within the observation period between March 21 and May 4, 2020, a total of 1,688 SARS-CoV-2 tests of 1,016 patients in the cancer cohort were performed. Patient characteristics are listed in Table 1. The most common diagnoses were breast cancer (187 of 1,016; 18.4%), lung cancer (175 of 1,016; 17.2%), colorectal cancer (96 of 1,016; 9.4%), head and neck cancer (78 of 1,016; 7.7%), sarcoma (74 of 1,016; 7.3%), glioma (69 of 1,016; 6.8%), and pancreatic cancer (65 of 1,016; 6.4%; Figs 1A and 1B).

At the time of SARS-CoV-2 testing, 270 of 1,016 (26.6%) of the patients were undergoing active anticancer treatment in a neoadjuvant/adjuvant and 560 of 1,016 (55.1%) in a palliative setting. A total of 904 of 1,016 (88.0%) patients were treated in the outpatient department, and 112 of 1,016 (11.0%) received anticancer treatment during hospitalization in the ward of our department.

A total of 373 of 1,016 (36.7%) patients presented with relevant comorbidities. The median number of recorded comorbidities was zero, with a range from zero to five. The most common comorbidity was hypertension in 295 of 1,016 (29.0%) patients, followed by diabetes mellitus in 102 of 1,016 (10.0%; Fig 1C).

A total of 53 of 1,016 (5.2%) patients self-reported symptoms potentially associated with COVID-19 in a standardized questionnaire. The most frequent symptoms were malaise in 16 of 1,016 (1.6%) and diarrhea/vomiting in 16 of 1,016 (1.6%) patients, followed by dyspnea/shortness of breath in 15 of 1,016 (1.5%; Fig 1D). Two of 1,016 (0.2%) patients indicated recently visiting a COVID-19 high-risk area.

TABLE 1. Patient Characteristics for Patients With Cancer (n = 1,016)

Characteristic	Measure
Sex	
Male	448 (44.1)
Female	568 (55.9)
Age, years	63.00 (18-93)
Karnofsky performance score	
≥ 70	994 (97.8)
< 70	22 (2.2)
Active anticancer treatment	
Adjuvant	270 (36.6)
Palliative	560 (55.1)
None (follow-up)	176 (17.3)
Type of treatment	
No systemic treatment	185 (18.2)
Chemotherapy	340 (33.5)
Targeted therapy	231 (22.7)
Immunotherapy	114 (11.2)
Chemotherapy/targeted therapy	103 (10.1)
Immunotherapy/chemotherapy	35 (3.4)
Immunotherapy/targeted therapy	8 (0.8)
Time since cancer diagnosis, months	19 (0-387)

NOTE. Data presented as No. (%) or median (range).

The median time interval from diagnosis of cancer to first SARS-CoV-2 test was 19 months (range, 0-387 months; Fig 2A). The number of SARS-CoV-2 tests per patient ranged from one to five (median, one) with time intervals between the tests ranging from 1-33 (median, 14) days in individual patients (Fig 2B). A total of 469 of 1,016 (46.1%) patients had ≥ 2 tests.

SARS-CoV-2 was detected in 4 of 1,016 (0.4%) patients of the entire cancer cohort and in five of 1,688 (0.3%) performed SARS-CoV-2 tests (Figs 2C and 2D). At the time of testing at our department, all four SARS-CoV-2–positive patients were asymptomatic. Two of them had recovered from symptomatic COVID-19. Three of the four patients presented with a negative SARS-CoV-2 test 14-56 days after testing positive. One patient was followed by regular SARS-CoV-2 and has not achieved viral clearance > 28 days after initial positive test at the time of this report. All patients had planned visits to health care facilities that were prevented because of the positive SARS-CoV-2 tests (Table 2). Two of four (50.0%) of the patients who tested positive were under active anticancer treatment. One patient with metastatic stomach cancer was treated with the combination of anti-PD-1 and anti-LAG-3 monoclonal antibodies. The last restaging had been performed one month before the SARS-CoV-2 infection and showed a partial response. The 11th cycle was delayed for 35 days because of the SARS-CoV-2 infection. The other patient

was treated with poziotinib as an individualized treatment of head and neck cancer. The last restaging performed 2 months before the SARS-CoV-2 infection had shown progressive disease, and consequently, poziotinib treatment was initiated. Poziotinib treatment was paused because of SARS-CoV-2 infection, and the patient died as a result of progressive disease 56 days after COVID-19

infection. In another patient not under active treatment at the time of the positive SARS-CoV-2 test, the initiation of trabectedin for progressive metastatic sarcoma was delayed for 14 days. Table 2 lists the progression-free survival before and after COVID-19 infection as well as the overall survival since diagnosis of cancer of the four patients.

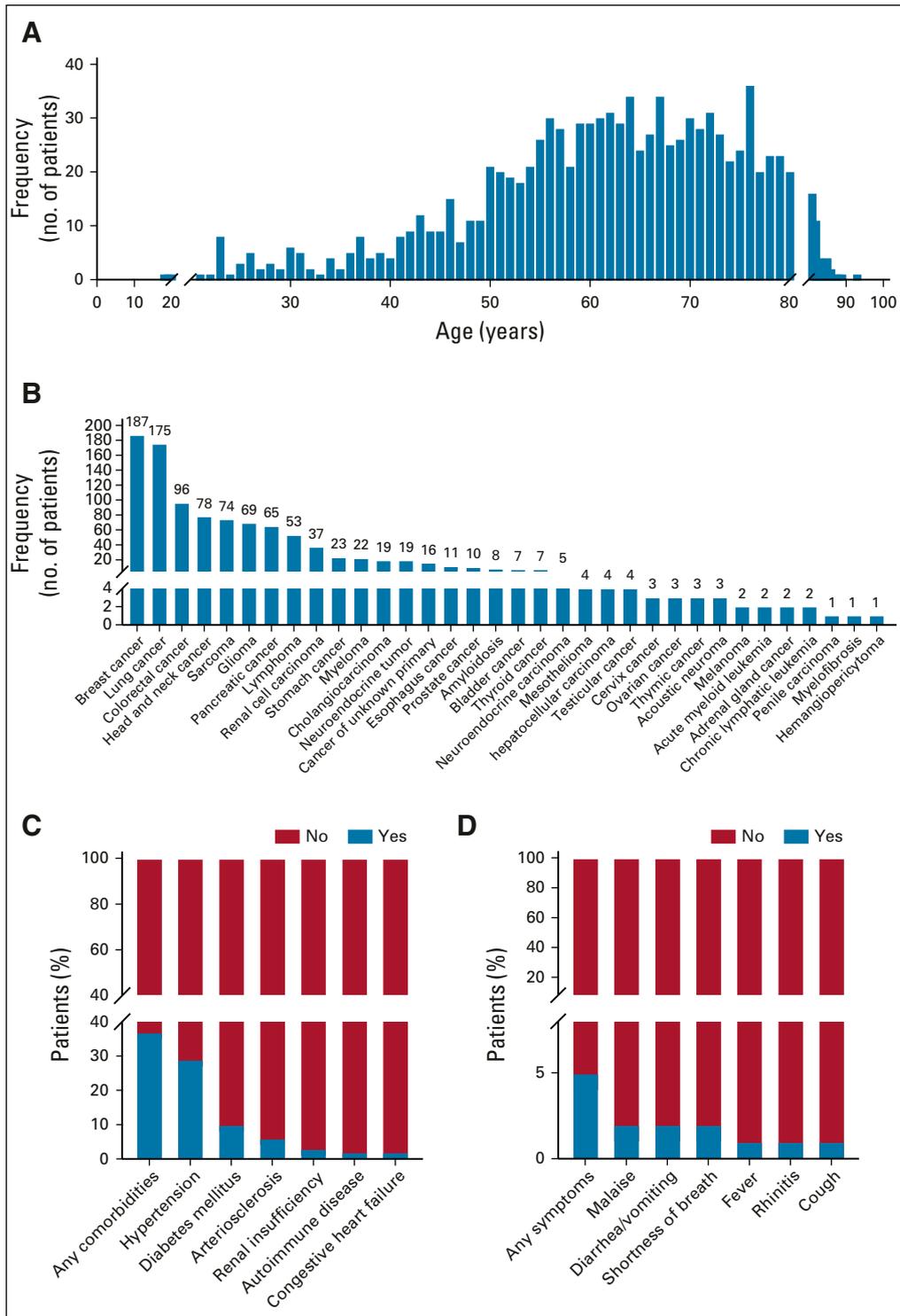


FIG 1. Characteristics of the cancer cohort. (A) Age distribution. (B) Type of primary tumor. (C) Distribution of comorbidities. (D) Prevalence of patient-reported COVID-19-suspicious symptoms.

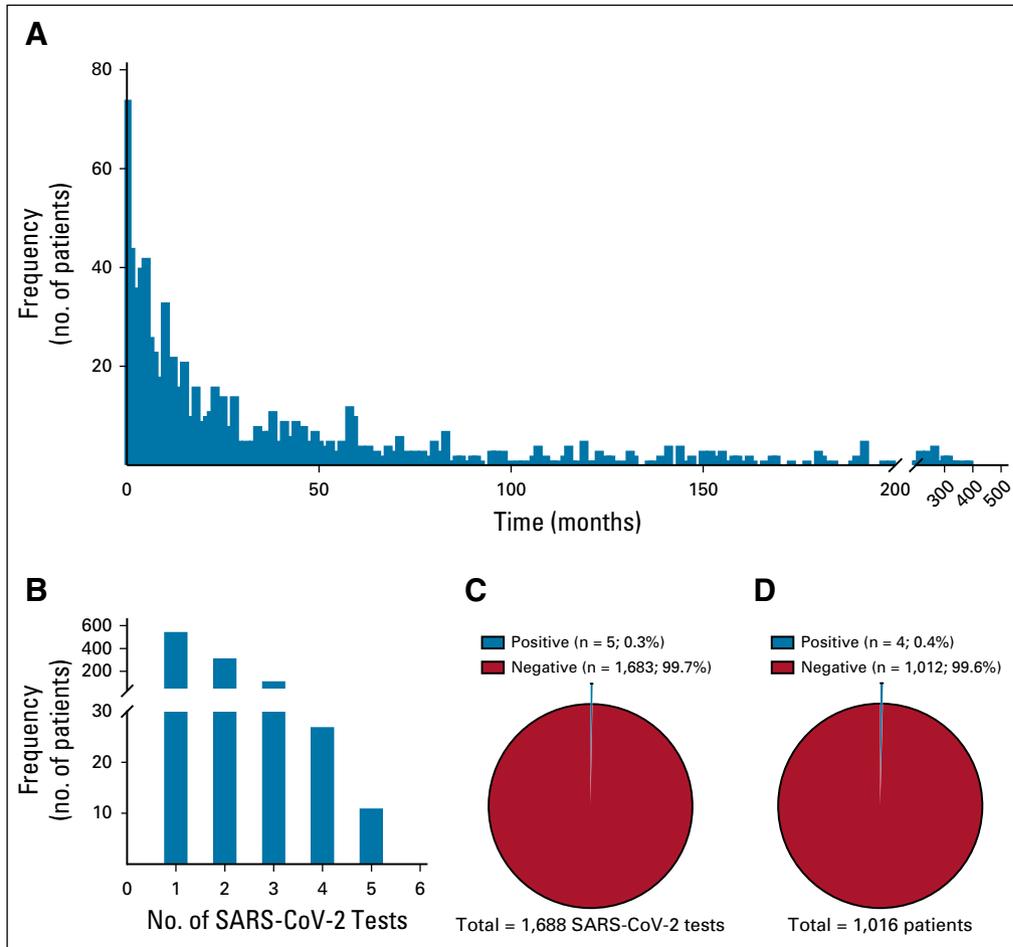


FIG 2. Characteristics of the cancer cohort. (A) Time from diagnosis of malignant disease to SARS-CoV-2 test. (B) Number of performed tests. (C) Number of SARS-CoV-2–positive test results. (D) Number of patients with SARS-CoV-2 infection.

Control Cohort 1

The control cohort is not a perfect demographic match to the cancer cohort, as patients with cancer tend to be slightly older, with an estimated nonparametric relative effect for age of 0.590 (Fig 3A). That is, with probability 0.590, a randomly selected person from the cancer cohort would

be older than a randomly selected person from the control cohort ($P < .0001$).¹⁹ In particular, the cancer cohort has a higher proportion of people in the age group 60–79 years, approximately the same proportion in the age group 40–59 years, and smaller proportions in all other 20-year age groups (median, 63 years). When only considering the

TABLE 2. Characteristics of 4 SARS-CoV-2–Positive Tested Patients With Cancer

Active Anticancer Treatment	Viral Clearance (days)	No. of Prevented Visits to Health Care Facilities	COVID-19–Related Symptoms	Cancer Entity	Age (years)	Comorbidities	Treatment Delay due to COVID-19 Infection	OS From Diagnosis of Cancer (months)	PFS Under the Current Treatment Before COVID-19 (months)	PFS After COVID-19 (months)
Yes: Anti-PD-1/LAG-3	35	2	None	Stomach cancer	63	None	35 days	12.0	8.6	2.1
No	14	1	None	Sarcoma	43	None	14 days	47.1	10.0	2.3
Yes: poziotinib	56	1	Fever, cough	Head and neck cancer	63	None	Termination of systemic treatment	40.3	3.4	1.9
No	> 28	1	Fever, cough	Head and neck cancer	61	None	None	37.9	8.3	1.0

Abbreviations: OS, overall survival; PFS, progression-free survival.

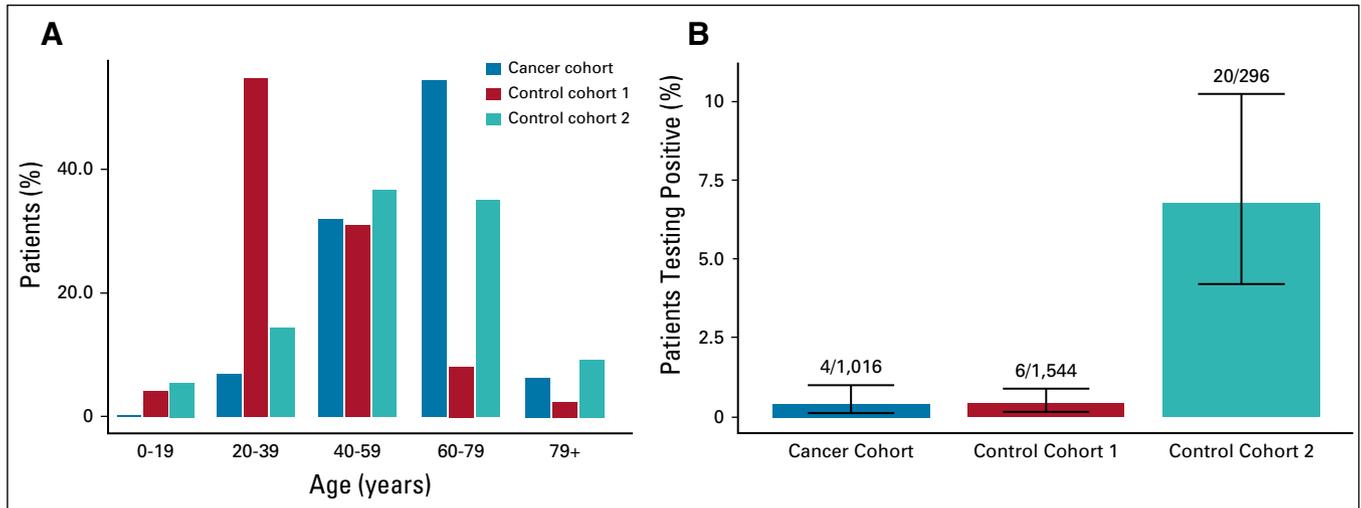


FIG 3. (A) Age distribution cancer cohort versus control cohort 1 and 2. (B) Portion tested positive and corresponding CIs, cancer cohort versus control cohort 1 and control cohort 2.

exact same time interval in which the control cohort study was investigated (April 1-6, 2020), the sample size in the cancer cohort reduces to 234 patients, and the estimated nonparametric relative effect for age is 0.574.¹⁵

The Agresti-Coull 95% CI for the control population prevalence based on six cases among 1,544 (0.4%) tested extends from 0.2% to 0.9%.¹⁸ In the cancer population, four of 1,016 (0.4%) tested positively (95% CI, 0.1% to 1.0%; Fig 3B). Comparing both proportions, the estimated odds ratio is 1.013 (95% CI, 0.209 to 4.272); Fisher's exact test yields $P = 1$. We further compared the patients from the cancer cohort screen between March 31 and April 8, 2020, with the control population to address potential changes in the incidence in the observation period. Note that the control study had most tests on the weekend, whereas the cancer cohort had very few tests on the weekend, so it is reasonable to extend the cohort to 4 working days before and 3 working days after the weekend. In these 9-day periods, one of 459 patients with cancer tested positively (ie, 0.2%; 95% CI, 0.0% to 1.4%). Comparing both proportions within these 9-day periods, the estimated odds ratio is 0.560 (95% CI, 0.012 to 4.622), and Fisher's exact test yields $P = 1$.

All of these comparisons give no indication that SARS-CoV-2 prevalence differs between patients with cancer and the remaining population. As a sensitivity analysis, a comparison was also done including only those patients with cancer who were tested during the exact same week as the control cohort, yielding qualitatively the same results.

Control Cohort 2

A total of 296 SARS-CoV-2 tests in 296 patients of control cohort 2 were performed. Twenty of 296 (6.7%) patients presented with a positive SARS-CoV-2 test. Patient characteristics are shown in Appendix Table A3 (online only).

Control cohort 2 is not a perfect demographic match to the cancer cohort, as the patients with cancer are significantly older ($P < .0001$).

The Agresti-Coull 95% CI for the control cohort 2 prevalence based on 20 cases among 296 tested extends from 4.4% to 10.3% (Fig 3B).¹⁸ Comparing control cohort 2 to the cancer cohort, the estimated odds ratio is 18.333 (95% CI, 6.215 to 54.081). That is, the odds to be infected with SARS-CoV-2 in the control cohort 2 are approximately 18 times higher than in the cancer cohort. Fisher's exact test yielded highly significant difference ($P < .0001$). Comparing control cohort 2 to control cohort 1, the estimated odds ratio is 18.575 (95% CI, 7.096 to 56.873). Fisher's exact test yielded highly significant difference ($P < .0001$). These comparisons show that prevalence in control cohort 2 is significantly higher than in both the cancer cohort and control cohort 1.

DISCUSSION

Our data show a low rate of detectable SARS-CoV-2 infections in a large cohort of consecutive patients with cancer and that this infection rate was comparable to that of the general Austrian population and lower than that of patients without cancer presenting at our hospital after implementation of institutional and population safety measures. We report that continued care and therapy for patients with cancer proved to be feasible and safe in the population of a European capital affected by the COVID-19 pandemic. At the same time, our findings highlight the need for implementation of strict policies to ensure safety of health care professionals and patients at a clinical service unit with a high patient turnover.

A previous study reported demographic, clinical, and treatment data of 1,524 patients with cancer who were

admitted to a department of radiation and medical oncology at a tertiary care hospital in Wuhan, China between December 30, 2019, and February 17, 2020.⁵ In 12 of 1,524 patients (0.79%), COVID-19 pneumonia was diagnosed. The cumulative incidence of all diagnosed COVID-19 cases reported in the city of Wuhan over the same time period was lower (0.37%), leading the authors to conclude that patients with cancer harbor a higher infection risk than the general community. The design of the study by Yu et al⁵ is limited as the study cohort was not clearly free from selection bias and balanced for non-cancer-related comorbidities.²⁰ In any case, the study by Yu et al⁵ differs significantly from our present report. Yu et al⁵ analyzed the number of patients diagnosed with manifest COVID-19 pneumonia according to specific diagnostic criteria, whereas we analyzed the number of patients with SARS-CoV-2 RNA detectability in routinely taken nasopharyngeal swabs. Furthermore, fewer than half of the infected cases in the report by Yu et al⁵ and 81.6% of our patients were undergoing active anticancer therapy. Most of our patients (88%) were managed in an outpatient setting, whereas the study by Yu et al⁵ included only hospitalized patients. Approximately one-third of our patients were treated with neoadjuvant or adjuvant intent, and most patients in palliative therapy were in early lines of treatment. To the best of our knowledge, our report provides, for the first time, systematic information on SARS-CoV-2 prevalence in patients undergoing active anticancer therapy.

In none of the four patients who were SARS-CoV-2 positive was any suspicion of SARS-CoV-2 infection raised on the day of testing by either patient-reported symptom assessment or clinical evaluation by the responsible physician. This indicates that the high variability of the clinical presentation and course of SARS-CoV-2 infections with an unknown prevalence of asymptomatic carriers renders clinical assessment of virus spreaders unreliable.²¹ Our strategy of routine SARS-CoV-2 testing of all patients presenting to our department allows us to quickly isolate contact persons of positive patients and thus to prevent uncontrolled viral spread to hospital staff and other patients.²²

Persistent viral RNA positivity in patients recovering from SARS-CoV-2/COVID-19 has repeatedly been reported.²³ Because it remains unknown whether in such cases viral transmission can still occur, we advocate home quarantine

and postponement of anticancer therapy until viral clearance has been achieved, if possible. Additional studies will need to clarify whether resolution of anticancer therapy in patients with persistent shedding of SARS-CoV-2 RNA is safe and feasible and whether delays of anticancer treatment because of SARS-CoV-2 infection is associated with insufficient tumor control.

As a limitation of our study, we cannot exclude that false-negative results of the screening method applied in our patient cohort resulted in undetected infections, although RT-PCR is the currently recommended standard test method.^{24,25} Therefore, additional safety measures, such as hygienic measures, wearing of protective masks, and separation of health care professionals in cohorts, need to be subsequently executed even in patients with negative test results. Serological antibody tests were not performed in our study and need to be done in future studies to gain a better understanding of the SARS-CoV-2 immunity status in patients with cancer. Another limitation of our study is the retrospective study design. However, the large sample size, the use of two control cohorts (one of them compiled as prospective population-based random sample) tested in the same time frame as the cancer cohort, and the confirmation of viral infection by RT-PCR in all 2,856 patients are strengths of our study that provide systematic evidence for our conclusion.

Currently, SARS-CoV-2 infection rates are decreasing in many countries in Europe and elsewhere, whereas other countries are still reporting increasing case numbers. Community-based safety measures are beginning to be lifted in some areas, leading to concerns about a potential surge (second wave) of SARS-CoV-2 infections in the coming weeks and months. COVID-19 experience (infection, death, and recovery rates and pattern) differs among countries because of various factors. However, we believe that our findings are of general relevance, as the need for continued treatment of patients with cancer, their particular vulnerability to infectious complications, and the typical high patient turnover are of concern for cancer centers worldwide in the current COVID-19 pandemic. Routine SARS-CoV-2 testing of patients with cancer as a part of safety policies seems advisable to detect asymptomatic virus carriers and avoid uncontrolled viral spread in the vulnerable population of patients with cancer and to ensure the safe continuance of oncology services.

AFFILIATIONS

¹Division of Oncology, Department of Medicine I, Medical University of Vienna, Vienna, Austria

²Faculty of Management and Economics, University of Klagenfurt, Klagenfurt, Austria

³Faculty of Natural Sciences and Intelligent Data Analytics Lab Salzburg, University of Salzburg, Salzburg, Austria

⁴Faculty of Technical Sciences, University of Klagenfurt, Klagenfurt, Austria

⁵Department of Laboratory Medicine, Medical University of Vienna, Vienna, Austria

⁶Department of Anaesthesia and General Intensive Care, Medical University Vienna, Vienna, Austria

⁷Faculty of Mathematics, Wolfgang Pauli Institute, University of Vienna, Vienna, Austria

CORRESPONDING AUTHOR

Matthias Preusser, MD, Division of Oncology, Department of Medicine I, Medical University of Vienna, Waehringerguertel 18-20, 1090 Vienna, Austria; Twitter: @MedUni_Wien; e-mail: matthias.preusser@meduniwien.ac.at.

SUPPORT

Supported by Future Operations Clearing Board (Antonella Mei-Pochtler, Stephan Rihs, Thomas Starlinger), Institute for Social Research and Consulting (SORA) (Günther Ogris, Florian Oberhuber), and The Austrian Social Science Data Archive (AUSSDA) (Lars Kaczmirek).

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI <https://doi.org/10.1200/JCO.20.01442>.

AUTHOR CONTRIBUTIONS

Conception and design: Anna S. Berghoff, Wolfgang Lamm, Markus Raderer, Matthias Preusser

Financial support: Anna S. Berghoff

Administrative support: Anna S. Berghoff, Harald Willschke

Provision of study material or patients: Anna S. Berghoff, Harald Willschke

Collection and assembly of data: Anna S. Berghoff, Margaretha Gansterer, Arne C. Bathke, Julia M. Berger, Judith Kreminger, Angelika M. Starzer, Robert Strassl, Ralf Schmidt, Harald Willschke, Matthias Preusser

Data analysis and interpretation: Anna S. Berghoff, Margaretha Gansterer, Arne C. Bathke, Wolfgang Trutschnig, Philipp Hungerländer, Ralf Schmidt, Markus Raderer, Alex D. Gottlieb, Norbert J. Mauser, Matthias Preusser

Manuscript writing: Anna S. Berghoff

Final approval of manuscript: Anna S. Berghoff

Accountable for all aspects of the work: Anna S. Berghoff

REFERENCES

- Guan WJ, Ni ZY, Hu Y, et al: Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 382:1708-1720, 2020
- Wu Z, McGoogan JM: Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 323:1239, 2020
- Xia Y, Jin R, Zhao J, et al: Risk of COVID-19 for patients with cancer. *Lancet Oncol* 21:e180, 2020
- World Health Organization: WHO announces COVID-19 outbreak a pandemic. <http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic>
- Yu J, Ouyang W, Chua MLK, et al: SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol* 6:1108-1110, 2020
- Dongarwar D, Salihi HM: COVID-19 pandemic: Marked global disparities in fatalities according to geographic location and universal health care. *Int J MCH AIDS* 9:213-216, 2020
- Petrilli CM, Jones SA, Yang J, et al: Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: Prospective cohort study. *BMJ* 369:m1966, 2020
- Nikpourghadam M, Jalali Farahani A, Alishiri G, et al: Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in Iran: A single center study. *J Clin Virol* 127:104378, 2020
- Giacomelli A, Ridolfo AL, Milazzo L, et al: 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study. *Pharmacol Res* 158:104931, 2020
- Posch M, Bauer P, Posch A, et al: Analysis of death rate during COVID-19 pandemic in Austria. https://cemsis.meduniwien.ac.at/fileadmin/cemsis/MS/data/2020_04_06_COVID_19_Analyse_Sterbezahlen.pdf
- AGES - Österreichische Agentur für Ernährungssicherheit: Austrian Agency for food safety. <https://www.ages.at/startseite/>
- Tian J, Yuan X, Xiao J, et al: Clinical characteristics and risk factors associated with COVID-19 disease severity in patients with cancer in Wuhan, China: A multicentre, retrospective, cohort study. *Lancet Oncol* 21:893-903, 2020
- Garassino MC, Whisenant JG, Huang L-C, et al: COVID-19 in patients with thoracic malignancies (TERAVOLT): First results of an international, registry-based, cohort study. *Lancet Oncol* 21:914-922, 2020
- Lai A, Pasea L, Banerjee A, et al: Estimating excess mortality in people with cancer and multimorbidity in the COVID-19 emergency. *MedRxiv* 10.1101/2020.05.27.20083287
- Australian Social Science Data Archive: Spread of COVID-19 in Austria: PCR-tests in a representative sample (SUF edition). <https://data.aussda.at/dataset.xhtml?persistentId=doi:10.11587/X2MIHW>
- World Health Organization: Population-based age-stratified seroepidemiological investigation protocol for COVID-19 virus infection. <https://apps.who.int/iris/bitstream/handle/10665/331656/WHO-2019-nCoV-Seroepidemiology-2020.1-eng.pdf?sequence=1&isAllowed=y>
- Rabenau HF, Kessler HH, Kortenbusch M, et al: Verification and validation of diagnostic laboratory tests in clinical virology. *J Clin Virol* 40:93-98, 2007
- Agresti A, Coull BA: Approximate is better than "exact" for interval estimation of binomial proportions. *Am Stat* 52:119, 1998
- Brunner E, Bathke AC, Konietschke F: Distributions and effects, in Brunner E, Bathke AC, Konietschke F: Rank and Pseudo-Rank Procedures for Independent Observations in Factorial Designs (ed 1). Springer International Publishing 2018, pp 15-74
- Cannistra SA, Haffty BG, Ballman K: Challenges faced by medical journals during the COVID-19 pandemic. *J Clin Oncol* 38:2206-2207, 2020
- Xu T, Huang R, Zhu L, et al: Epidemiological and clinical features of asymptomatic patients with SARS-CoV-2 infection. *J Med Virol* doi:10.1002/jmv.25944 [epub ahead of print on April 28, 2020]
- Madariaga A, McMullen M, Sheikh S, et al: COVID-19 testing in cancer patients: Does one size fit all? *Clin Cancer Res* [epub ahead of print on July 2, 2020]
- Xing Y, Mo P, Xiao Y, et al: Post-discharge surveillance and positive virus detection in two medical staff recovered from coronavirus disease 2019 (COVID-19), China, January to February 2020. *Euro Surveill* 10.2807/1560-7917.ES.2020.25.10.2000191
- Long C, Xu H, Shen Q, et al: Diagnosis of the coronavirus disease (COVID-19): rRT-PCR or CT? *Eur J Radiol* 126:108961, 2020
- Patel R, Babady E, Theel ES, et al: Report from the American Society for Microbiology COVID-19 International Summit, March 23, 2020: Value of diagnostic testing for SARS-CoV-2/COVID-19. *mBio* 10.1128/mBio.00722-20



AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

SARS-CoV-2 Testing in Patients With Cancer Treated at a Tertiary Care Hospital During the COVID-19 Pandemic

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians ([Open Payments](#)).

Anna S. Berghoff

Research Funding: Roche (Inst), Bristol Meyers Squibb (Inst), Daiichi Sankyo (Inst)

Travel, Accommodations, Expenses: Roche

Angelika M. Starzer

Travel, Accommodations, Expenses: PharmaMar

Ralf Schmidt

Research Funding: Roche Molecular Diagnostics (Inst)

Travel, Accommodations, Expenses: DiaSorin

Harald Willschke

Research Funding: Vasopharm (Inst)

Alex D. Gottlieb

Employment: Bristol Myers Squibb (I)

Travel, Accommodations, Expenses: Bristol Myers Squibb (I)

Matthias Preusser

Honoraria: Roche, GlaxoSmithKline, Bayer, Bristol Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMC Contrast, Mundipharma, BMJ Journals, MedMedia, Astra Zeneca, AbbVie, Eli Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dome, Tocagen

Consulting or Advisory Role: Roche, Bristol Myers Squibb, Novartis, Gerson Lehrman Group, CMC Contrast, GlaxoSmithKline, Mundipharma, AbbVie

Research Funding: Roche (Inst), GlaxoSmithKline (Inst), Boehringer Ingelheim (Inst), Merck Sharp & Dohme, Bristol Myers Squibb (Inst), Daiichi Sankyo (Inst), AbbVie (Inst)

Travel, Accommodations, Expenses: Roche, GlaxoSmithKline, Bristol Myers Squibb, MSD, Mundipharma

No other potential conflicts of interest were reported.

APPENDIX

Supplementary Methods

In the cancer cohort and in control cohort 2, one of the following test systems was used: (1) Automated nucleic acid extraction using the Altostar Purification kit 1.5 on the Altostar AM16 operator and real-time polymerase chain reaction (RT-PCR) using the RealStar SARS-CoV-2 RT-PCR Kit 1.0 (Altona Diagnostics, Hamburg, Germany); (2) Fully automated nucleic acid extraction and RT-PCR using the cobas 6800/8800 SARS-CoV-2 Test on the cobas 6800 platform (Roche Diagnostics, Basel, Switzerland); (3) Automated nucleic acid extraction using the MagNA Pure LC Total Nucleic Acid Isolation Kit on MagNA Pure LC 2.0 or Magna Pure compact instruments (Roche Diagnostics) and RT-PCR using LightMix Modular SARS and Wuhan CoV E-gene

assay (Tib-MolBiol, Berlin, Germany) on the LightCycler 480 (Roche Diagnostics); (4) Fully automated nucleic acid extraction and RT-PCR using the NeuMoDx 96 system (NeumoDx, Ann Arbor, MI) with the LightMix Modular SARS and Wuhan CoV E-gene assay (Tib-MolBiol). Finally, high urgent swab samples were run on the Qiasat-Dx instrument using the QIAstat-Dx Respiratory SARS-CoV-2 Panel (Qiagen, Hilden, Germany). In control cohort 1, the cobas 6800/8800 SARS-CoV-2 Test on the cobas 6800 platform (Roche Diagnostics) was used.¹⁵ Positive results with a Ct value > 35 were confirmed by repeated testing of the respective sample. All systems were validated according to recommendations of the German Society for Virology.¹⁷

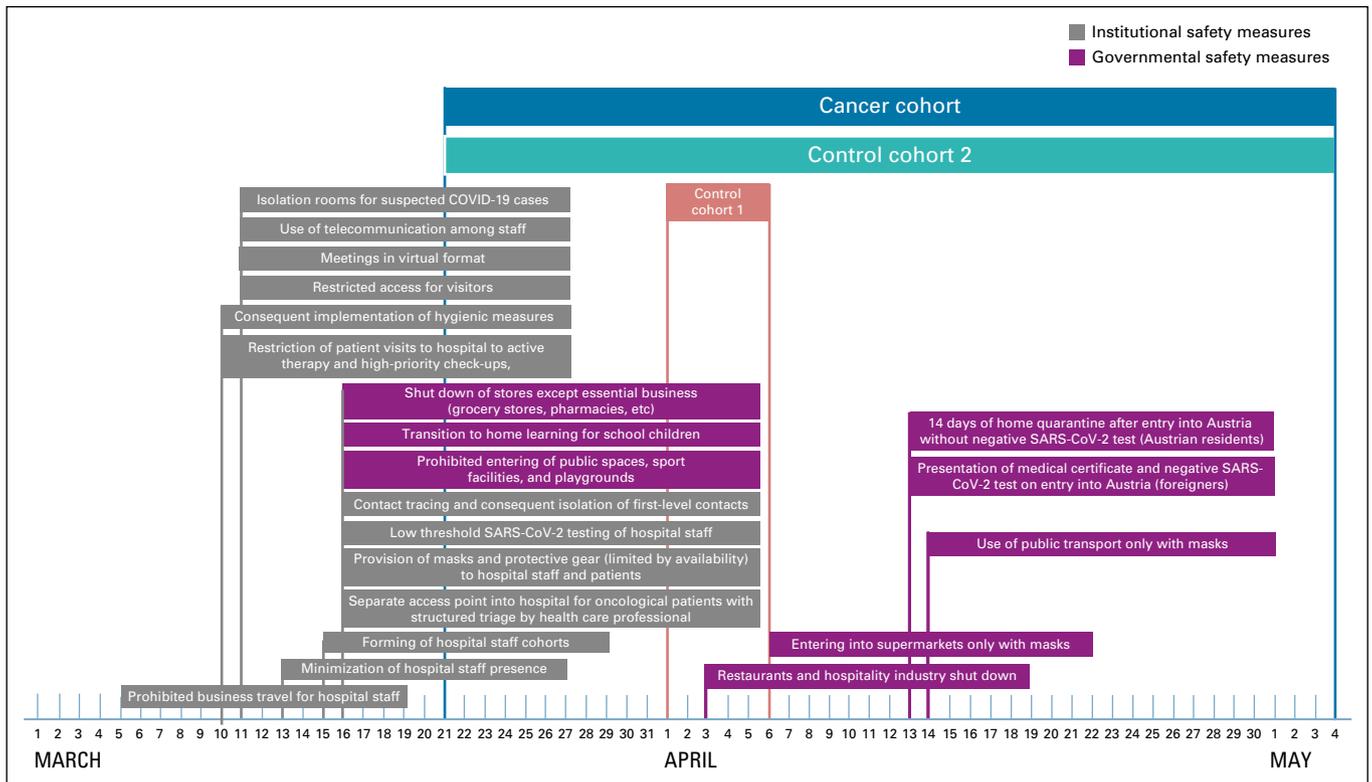


FIG A1. Timeline illustrating the safety measurements and the screening time of the cancer cohort, control cohort 1, and control cohort 2.

TABLE A1. Population-Based Safety Measures Implemented by the Austrian Government to Prevent SARS-CoV-2 Infections

Measure	Date of Implementation
Prohibited entering of public spaces	March 16, 2020
Prohibited entering of sport facilities and playgrounds	March 16, 2020
Transition to home learning for school children	March 16, 2020
Shut down of stores except essential business (grocery stores, pharmacies, etc)	March 16, 2020
Restaurants and hospitality industry shut down	April 3, 2020
Entering into supermarkets only with masks	April 6, 2020
Presentation of medical certificate and negative SARS-CoV-2 test on entry into Austria (foreigners)	April 13, 2020
Home quarantine for 14 days after entry into Austria without negative SARS-CoV-2 test (Austrian residents)	April 13, 2020
Use of public transport only with masks	April 14, 2020

TABLE A2. Institutional Safety Measures Implemented at the General Hospital of Vienna and the Division of Oncology (Medical University of Vienna, Vienna, Austria) to Prevent SARS-CoV-2 Infections

Measure	Date of Implementation
Prohibited business travel for hospital staff	March 5, 2020
Restriction of patient visits to hospital to active therapy and high-priority check-ups	March 10, 2020
Consequent implementation of hygienic measures	March 10, 2020
Restricted access for visitors	March 11, 2020
Meetings in virtual format	March 11, 2020
Use of telecommunication among staff	March 11, 2020
Isolation rooms for suspected COVID-19 cases	March 11, 2020
Minimization of hospital staff presence	March 13, 2020
Forming of hospital staff cohorts	March 15, 2020
Separate access point into hospital for oncological patients with structured triage by health care professional	March 16, 2020
Provision of masks and protective gear (limited by availability) to hospital staff and patients	March 16, 2020
Low threshold SARS-CoV-2 testing of hospital staff	March 16, 2020
Contact tracing and consequent isolation of first-level contacts	March 16, 2020

TABLE A3. Clinical Characteristic of the Cancer Cohort and Control Cohorts 1 and 2

Characteristic	Cancer Cohort (n = 1,016)		Control Cohort 1 (n = 1,544)		Control Cohort 2 (n = 296)		Cancer Cohort v Control Cohort 1	Cancer Cohort v Control Cohort 2
	No.	%	No.	%	No.	%		
Age, years, median (range)	63 (18 to 93)		40-59 age group (20 to >80)		37 (17 to 92)		< .001	< .001
Sex							.016	< .001
Male	448	44.1	757	49.0	175	59.1		
Female	568	55.9	789	51.0	121	4.9		
Comorbidities								
Hypertension	295	29.0	227	16.8	35	11.8	< .001	< .001
Diabetes mellitus	103	10.1	73	5.4	9	3.0	< .001	< .001
Arteriosclerosis	58	5.7	45	3.3	5	1.7	.005	.004
Renal insufficiency	28	2.7	n.a.	n.a.	4	1.4	n.a.	.168
Autoimmune disease	18	1.8	27	2.0	4	1.4	.691	.620
Congestive heart failure	18	1.8	33	2.4	2	.7	.267	.176
Self-reported potentially COVID-19-associated symptoms								
Malaise	16	1.6	n.a.	n.a.	143	48.3	n.a.	< .001
Diarrhea/vomiting	16	1.6	54	4.0	22	7.4	.001	< .001
Shortness of breath	15	1.5	32	2.4	68	23.0	.124	< .001
Fever	9	0.9	31	2.3	69	23.3	.009	< .001
Cough	8	0.8	146	1.8	159	53.7	< .001	< .001
Rhinitis	6	0.6	183	13.5	24	8.1	< .001	< .001

Abbreviation: n.a., not available.