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Nosocomial COVID-19 at a comprehensive cancer center during the first year of the pandemic: Lessons learned

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A B S T R A C T

Background: The spread of coronavirus disease 2019 (COVID-19) in health care settings endangers patients with cancer. As knowledge of the transmission of COVID-19 emerged, strategies for preventing nosocomial COVID-19 were updated. We describe our early experience with nosocomial respiratory viral infections (RVIs) at a cancer center in the first year of the pandemic (March 2020–March 2021).

Methods: Nosocomial RVIs were identified through our infection control prospective surveillance program, which conducted epidemiologic investigations of all microbiologically documented RVIs. Data was presented as frequencies and percentages or medians and ranges.

Results: A total of 35 of 3944 (0.9%) documented RVIs were determined to have been nosocomial acquired. Majority of RVIs were due to SARS CoV-2 (13/35; 37%) or by rhinovirus/enterovirus (12/35; 34%). A cluster investigation of the first 3 patients with nosocomial COVID-19 determined that transmission most likely occurred from employees to patients. Five patients (38%) required mechanical ventilation and 4 (31%) died during the same hospital encounter.

Conclusions: Our investigation of the cluster led to enhancement of our infection control measures. The implications of COVID-19 vaccination on infection control policies is still unclear and further studies are needed to delineate its impact on the transmission of COVID-19 in a hospital setting.

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In December 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, and quickly spread across the world. Because transmission dynamics were poorly understood in the early stages of the pandemic, there was sparse guidance on the best strategies to prevent spread of SARS-CoV-2 both in the community and in health care settings; 44% of new COVID-19 cases were suspected to have been transmitted nosocomially from initial reports.^{1,2} Expanding knowledge of SARS-CoV-2 transmission, escalation of public health and infection control measures for prevention of the spread of SARS-CoV-2, and better definition of nosocomial COVID-19 have reduced rates of hospital transmission between 6.8% and 12.5% based on later reports during the first year of the pandemic.^{3,4} Enhanced

infection control measures and visitor restriction protocols for immunocompromised patients such as those with cancer have been supported by multiple medical societies.^{5,6}

Patients with cancer are at a higher risk for complications associated with COVID-19 when compared to the general population.^{7–10} Case fatality rates from COVID-19 in cancer patients were reported to be as high as 25% and 37% in patients with solid tumors and hematologic malignancies, respectively.¹⁰ In addition, in patients with cancer, health care–associated COVID-19 was independently associated with shorter median overall survival than was community-acquired COVID-19, with a reported hazard ratio of 2.3 (95% confidence interval: 1.2–4.4).⁹

SARS-CoV-2 is primarily transmitted through respiratory secretions as droplets or aerosols,^{11–13} and potentially via fomites.¹⁴ Based on the known modes of transmission, infection control measures have centered on universal masking, hand washing, social distancing, and a low threshold for testing patients with signs and symptoms of respiratory infections. In addition, many cancer centers, including ours, have implemented routine testing of hospitalized cancer patients without COVID-19 during extended hospital stays. These enhanced infection control protocols may have reduced hospital transmission of COVID-19 and other health care–associated infections.

Nosocomial transmission of other respiratory viruses such as influenza virus, respiratory syncytial virus (RSV), parainfluenza virus (PIV), and human metapneumovirus (HMPV)¹⁵ can have detrimental effects on hospitalized cancer patients by causing nosocomial outbreaks in the absence of community spread.^{15–21} Many of the public health measures adopted during the pandemic; mandatory use of masks, were instituted to prevent the spread of SARS-CoV-2, but an additional benefit has been the notably lower rate of other community-acquired respiratory viruses,²² with a similar reduction in nosocomial spread of these viruses (such as RSV).²³

The aim of our study was to describe our early experience with nosocomial COVID-19 at a comprehensive cancer center and the steps implemented to limit the spread of this virus in our health care settings. We also aimed to investigate the impact of the pandemic and the associated stricter infection control measures on the incidence of other nosocomial respiratory viral infections (RVIs) in our center.

METHODS

Setting

This retrospective study was conducted at a National Cancer Institute-designated comprehensive cancer center with approximately 680 hospital beds and 22,000 employees; All hospitalized patients reside in private rooms. Patients with confirmed COVID-19 are housed on specifically designated floors away from other patients. Patients presenting with respiratory symptoms are tested for respiratory viruses regardless of the time of year via nasopharyngeal or bronchoalveolar lavage sampling; all patients diagnosed with any respiratory viral infection is reported to infection control. Cases of microbiologically documented RVIs, including COVID-19, in admitted patients are investigated by the Infection Control team for possible hospital-associated transmission and for potential clusters. Once hospital-associated transmission is suspected in a patient with COVID-19, an investigation focusing on testing staff and other patients on the affected units is conducted. Visitors and staff who were in contact with the index patient were contacted by local nursing leadership for assessment of respiratory symptoms and to highly recommend SARS CoV-2 testing. A follow up phone call was conducted and pertinent data such as results of SARS CoV-2 testing was provided to infection

control, when done. In addition, qualitative analysis, including interviews and observations, are carried out to identify any opportunities for improvement and for additional interventions if needed.

Infection control protocols and testing for COVID-19

Since March 13, 2020, all patients and staff are screened for COVID-19–related symptoms and fever at all hospital entrances. Since March 24, 2020, hospitalized patients with COVID-19 and persons under investigation (PUI) for suspected COVID-19 are housed on designated floors or units. Universal masking with medical-grade (ASTM 3) face masks for all employees and patients in clinical and nonclinical areas was instituted on April 1, 2020. Patients with symptoms concerning for RVIs are tested for COVID-19, and routine testing for asymptomatic patients is undertaken prior to planned hospital admissions and procedures, or at the time of hospital admission via the emergency room. In addition, asymptomatic testing started in July 2020 for all admitted patients with hematologic malignancies and recipients of hematopoietic cell transplantation (HCT) and cellular therapy every 7 days while hospitalized. [Table 1](#) lists a full timeline of the interventions undertaken to prevent or limit the spread of SARS-CoV-2 in our center.

SARS-CoV-2 testing is performed using one of 2 real-time polymerase chain reaction assays, the Cobas SARS-CoV-2 test performed on the Cobas 6800 (Roche Diagnostics) or the Abbott SARS-CoV-2 assay performed on the m2000. Patients with respiratory symptoms were also tested for common respiratory viruses using the Biofire Respiratory Panel performed on the BioFire Torch platform (bioMérieux). The RP detects Adenovirus, Human Coronaviruses, HMPV, Human Rhinovirus/Enterovirus, Influenza A and B, PIV, and RSV. Prior to the COVID-19 pandemic, patients with respiratory symptoms were tested for most community respiratory viruses using the Biofire respiratory panel on nasopharyngeal swabs at the providers' discretion all year long. Contact and droplet precautions are instituted on the inpatient setting and until discharge for all patients with documented respiratory viral infection. In addition, during the study period (March 1st, 2020 to March 31st, 2021), the alpha strain was the predominant circulating variant in the Houston Metropolitan area.²⁴

Case definitions

Following guidelines from the Centers for Disease Control and Prevention (CDC), transmission of SARS-CoV-2 was determined to be nosocomial if the onset of COVID-19 symptoms occurred more than 14 days after admission for conditions other than COVID-19 or if 2 or more SARS-CoV-2 infections were identified among epidemiologically linked health care workers and/or patients (ie, those working or residing on the same units).²⁵ For other respiratory viruses, determination of nosocomial infections relies on shorter incubation periods (ie, 4 days or more after admission for RSV and PIV). A cluster was determined to be present if there were 2 or more cases of COVID-19 among health care workers who worked in the same unit and/or among 2 or more patients housed in the same units at overlapping times and within 2 weeks of each other.

Data collection and statistical analysis

We collected demographic, medical history, oncologic history, COVID-19 treatments, laboratory, and clinical outcome data at the time of diagnosis from the records of patients diagnosed with nosocomial COVID-19. Data are presented as frequencies and percentages or medians and ranges.

Table 1
Timeline of infection control interventions

Date	Intervention	Description
03/05/2020	Limit two visitors per patient	Initial restrictions on the number of visitors
03/13/2020	Alternative work arrangements	Nonessential staff encouraged to work from home
03/13/2020	Patient entry screening	Screening at all entries included use of thermal sensors to detect fever and a survey to detect symptoms
03/15/2020	COVID-19 testing available	COVID-19 testing made available for both patients and employees
03/16/2020	Employee entry screening	All on-site employees required to attest to absence of any potential COVID-19 symptoms or exposure; use of thermal sensors to detect fever
03/19/2020	Limit one visitor per patient	Number of visitors further restricted
03/24/2020	Cohorting hospitalized persons under investigation and confirmed COVID-19 patients in specific units	Specific units housed patients in private negative pressure rooms with dedicated HCWs (eg, nursing staff) for cohort care. Appropriate PPE such as N95 masks and gowns was required and provided
03/24/2020	No visitors permitted, except in specific circumstances or with exemptions	No visitors permitted unless special circumstances, for example, pediatric patients, patients admitted for planned HCT or other cellular therapies. Caregivers (boarders) required to stay in patients' rooms.
03/27/2020	Mandatory face masks for patients and visitors	All visitors and patients required to use supplied face masks on entry to the institution
04/01/2020	Mandatory face masks for all on campus	All employees, visitors, and patients required to use supplied face masks anywhere on premises
05/14/2020	Pre-admission COVID-19 testing for all patients	Patients with planned admission or admission via the ED tested via NP swab for PCR SARS-CoV-2 testing
07/05/2020	Mandatory changing of face masks between patient encounters	All providers required to change face masks between patient encounters on hematologic malignancy floors, intensive care units, and ED
07/15/2020	Weekly screening of all patients on hematologic malignancy floors	All patients on hematologic malignancy floors, irrespective of symptoms, screened weekly with NP swabs for PCR SARS-CoV-2 testing
07/29/2020	Face shields required for every patient encounter in outpatient and inpatient settings	All providers required to use face shields in addition to face masks for all patient encounters

ED, emergency department; HCT, hematopoietic cell transplant; HCW, health care worker; NP, nasopharyngeal; PCR, polymerase chain reaction; PPE, personal protective equipment.

Ethical considerations

This study was approved by our Institutional Research Board under protocol number PA15-0002, and a waiver of the requirement for informed consent was granted due to the retrospective nature of this study.

RESULTS

Active surveillance of RVIs

Between March 1, 2020 and March 31, 2021, 3944 RVIs were documented in our infection control database. Most were SARS-CoV-2 infections (3,247/3,944; 82.3%); the remaining infections were mostly caused by rhinovirus/enterovirus (182/3,944; 4.6%) (Fig 1). During the same time period, we had 2 significant surges of COVID-19 in our community; first between June and August 2020 and a second between December 2020 and February 2021 (Fig 2). Of the 3944 microbiologically documented RVIs, 35 (0.9%) were determined to have been nosocomially acquired according to our institutional definitions aligned with the CDC definitions as shown in Figure 3. Of the 35 nosocomial respiratory virus infections during the study period, most were caused by SARS-CoV-2 (n = 13, 37.1%), followed by rhinovirus/enterovirus (n = 8, 22.9%) during the study period. However, the overall incidence of nosocomial COVID-19 was 0.7 cases per 10,000 patient days compared to 1.3 cases per 10,000 patient days for other nosocomial RVIs.

In comparison, we documented 128 nosocomial RVIs between March 2019 and February 2020 (the year before the start of the pandemic), most of which were caused by rhinovirus/enterovirus (45/128; 35.2%) and PIV (40/128; 31.3%) (Fig 3). The amount of testing for respiratory viruses excluding SARS CoV-2 using the Biofire assay increased from 8,418 to 9793 tests between March 2019-February 2020 and March 2020-March 2021, respectively. The annual incidence of nosocomial RVIs prior to the COVID-19 pandemic remained stable ranging from 6.9 cases per 10,000 patient days in 2017-2018 and 6.9 cases per 10,000 patient days in 2018-2019, and 5.8 cases per 10,000 patient days in 2019-2020. Thus, when compared to the year before the start of the COVID-19 pandemic, the rate of nosocomial RVIs was 73% lower in the first year of the pandemic. Specifically, nosocomial infections with influenza virus fell by 58% (from 12 to 5 cases), with PIV by 95% (from 40 to 2 cases), with RSV by 90% (from 10 cases to 1 case), with HMPV by 83% (from 6 cases to 1 case), with rhinovirus/enterovirus by 82% (from 45 to 8 cases), and with other respiratory viruses such as human coronaviruses and bocavirus by 67% (from 15 to 5 cases).

Nosocomial COVID-19 and cluster investigation

Among the 13 patients with nosocomial COVID-19, epidemiological investigation determined that 3 (P1, P2, and P3) were part of a

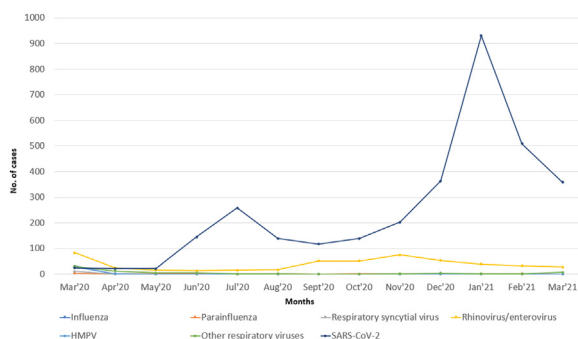


Fig 1. Number of community-acquired respiratory viral infections detected, March 2020-March 2021. Abbreviations: HMPV, human metapneumovirus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

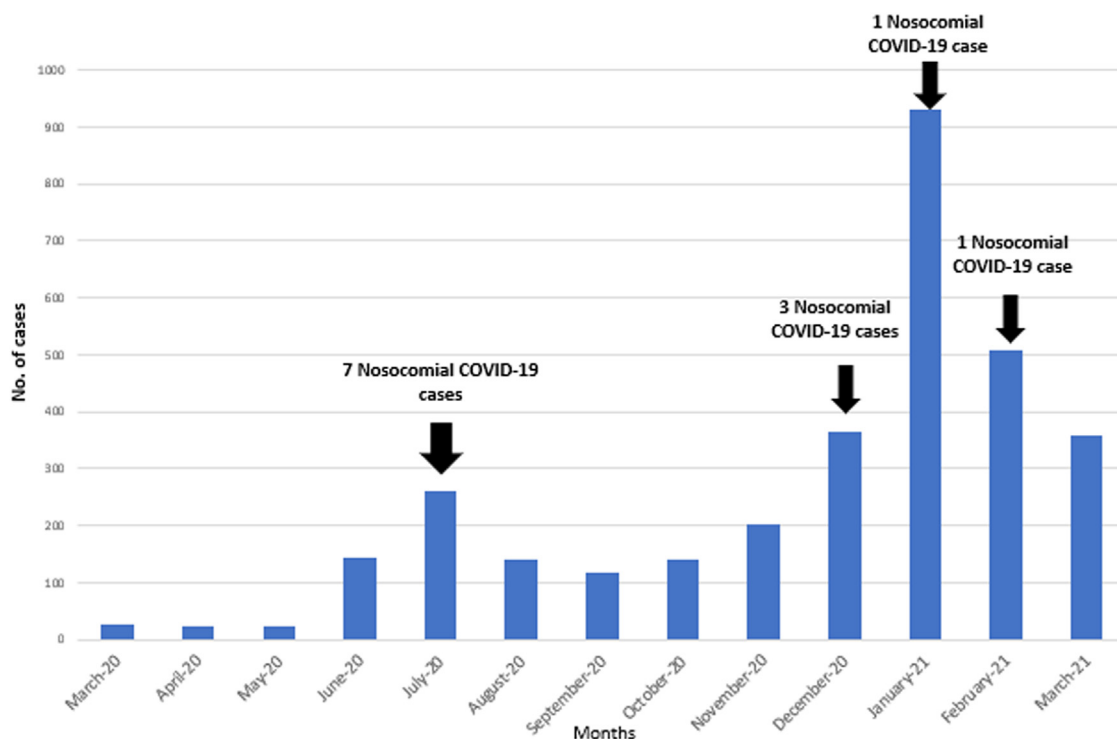


Fig 2. Distribution of COVID-19 cases by month, March 2020–March 2021.

cluster. After the index patient, P1, was identified, 8 of the 73 (11%) employees who were tested due to proximity to P1 had positive SARS-CoV-2 tests. P1 had a caregiver who boarded during the patient’s hospital stay and who also tested positive for SARS-CoV-2. An additional 29 patients housed in the same location as P1 were screened for SARS-CoV-2, and an additional 2 tested positive (P2 and P3). Based on the results of this investigation, we determined that transmission had occurred from one or more infected employees to the 3 patients and from employee to employee in the same location, and no direct patient-to-patient transmission had occurred. Figure 4 illustrates the results of our investigation and the likely SARS-CoV-2 transmission patterns. Briefly, over a 1-month period from mid-June to mid-July 2020, 19 employees who worked on the same floor on which P1 was housed had positive SARS-CoV-2 tests. No other

patient clusters were identified, and only sporadic patients with nosocomial COVID-19 were detected for the remainder of the study period.

Of the 13 patients with nosocomial COVID-19 during the first year of the pandemic, 4 (31%) were cared for by health care workers who later tested positive for SARS-CoV-2, 5 (38%) were exposed to both infected caregivers and health care workers, and 4 (31%) had no clear source of exposure.

Characteristics and clinical outcomes of patients with nosocomial COVID-19

Demographic and clinical characteristics of the 13 patients with nosocomial COVID-19 are shown in Table 2. Their median age was

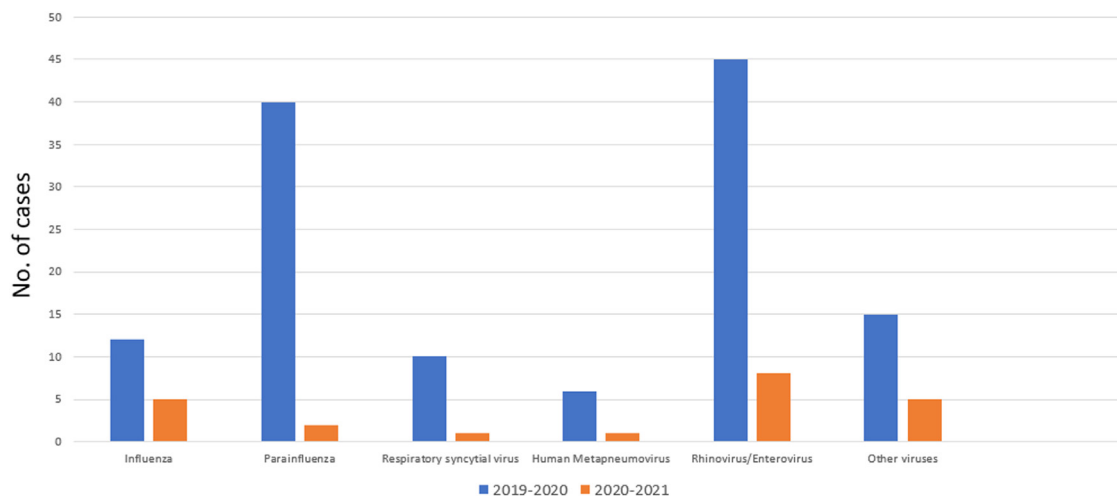


Fig 3. Comparison of nosocomial respiratory viral infections during the year before the COVID-19 pandemic (March 2019–February 2020) and during the first year of the pandemic (March 2020–March 2021).

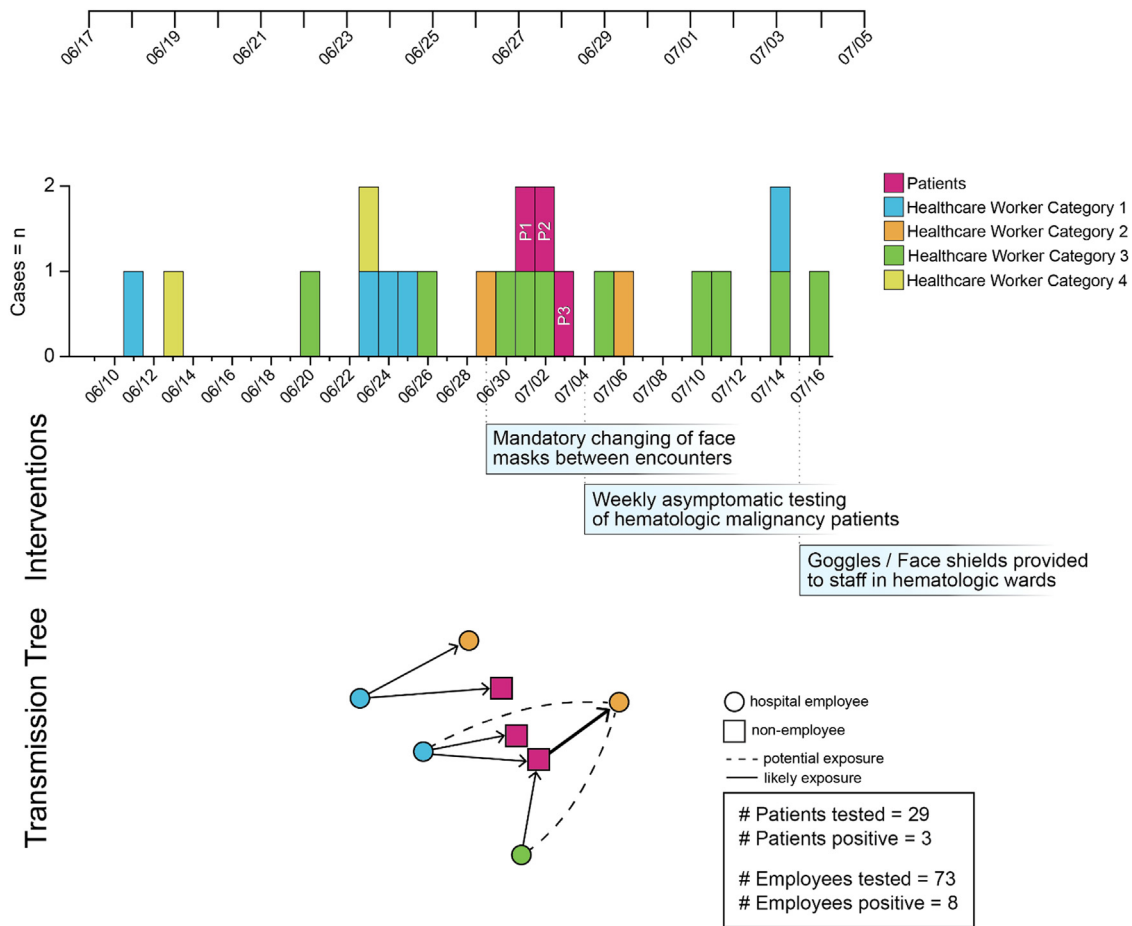


Fig 4. Potential nosocomial COVID-19 transmission dynamics between patients and health care workers, June-July 2020. Top: Timeline of positive COVID-19 patients and employees in the same unit from 6/10/2020 to 7/16/2020 Bottom: Transmission tree linking possible exposures to infected patients from 6/17/2020 to 7/5/2020. Examples of health care workers involved included nurses, patient care technicians and patient care navigators.

68 years (range: 21-80), 54% (n = 7) were White, 54% (n = 7) were female, 77% (n = 10) had a hematologic malignancy, 69% (n = 9) were recipients of cellular therapy, and 69% (n = 9) were on active chemotherapy at least 30 days before their COVID-19 diagnosis. The median time from cellular therapy to COVID-19 was 15 days with a range of 4-128 days. Routine asymptomatic screening identified 5 of these 13 patients, and all 5 developed signs and symptoms of COVID-19 later. The remaining 8 patients were tested after displaying signs and symptoms suggestive of COVID-19.

In 11 patients, computed tomography (CT) imaging of the chest was suggestive of pneumonia at the time of COVID-19 diagnosis. The CT findings were described as ground-glass opacities (8/11; 72%), nodular opacities (2/11; 18%), or diffuse consolidations (1/11; 9%). Interestingly, 2 patients were diagnosed with COVID-19 based on a positive SARS-CoV-2 assay using a bronchoalveolar lavage specimen after multiple tests using nasopharyngeal swabs were negative. Median laboratory values at the time of COVID-19 diagnosis were white blood cell count of 2.7 K/ μ L (range: 0-13.90), absolute neutrophil count of 2.38 K/ μ L (range: 0-12.41), absolute lymphocyte count of 0.11 K/ μ L (range: 0.00-1.00), procalcitonin level of 0.18 ng/mL (range: 0.09-1.95), ferritin level of 1429 ng/mL (range: 233-6339), and IL-6 level of 31 pg/mL (range: 4-249) (Table 2).

Almost all patients (11/13; 85%) were treated for COVID-19 at the time of diagnosis; 10 patients received remdesivir, 7 received steroids, and 8 received convalescent plasma. Many patients required use of mechanical ventilation (5/13, 38%), a high-flow nasal cannula (2/13, 15%), or a nasal cannula (2/13, 15%). Three of the 13 (23%)

patients developed sepsis requiring vasopressor support. Four patients died during their hospital stay, all with respiratory failure due to COVID-19, for an inpatient mortality rate of 31%. Of the 9 survivors, 4 required readmissions to the hospital within 30 days.

Protocols introduced after the cluster investigation

Given that many patients with hematologic malignancies have long hospital stays, we implemented routine weekly screening for SARS-CoV-2 in these high-risk patients for the duration of their hospital stay and regardless of their symptoms (weekly retesting was performed on the same day of the week as the patient's admission day). We also required that clinical staff caring for patients with hematologic malignancies change face masks between patient encounters to reduce the risk of cross-contamination in addition to the use of face shields during patient encounters. After implementation of these measures, only sporadic patients were found to have nosocomial COVID-19, and no additional clusters were identified. Figure 4 illustrates the timing of these interventions in relation to the identified cluster of nosocomial infections.

DISCUSSION

Our report describes our experience with nosocomial transmission of SARS CoV-2 in a comprehensive cancer center during the first year of the COVID-19 pandemic and highlights the lessons learned and the effects of the interventions implemented. We identified a

Table 2
Clinical characteristics and outcomes of patients with nosocomial COVID-19

Case Number	Age (y)	Race or ethnicity Sex	Underlying cancer	Noncancer comorbidities	On chemo before COVID-19	Prior cellular therapy	High-dose steroids before COVID-19	Dx date (symptom onset)	Source of sample	O ₂ use at dx	Chest CT results	ALC at dx (K/ μ L)	ANC at dx (K/ μ L)	Procalcitonin at dx (ng/mL)	Ferritin at dx (ng/mL)	IL-6 at dx (pg/mL)	COVID-directed therapy	Peak O ₂ use	In-hospital mortality
1	69	White Male	MM	HPT, HTN	Yes	Autologous HCT	No	7/1/2020	NP	Room air	Bilateral peripheral GGOs	0.16	2.38	0.09	987	6	None	Room air	No
2	60	Black Male	MM	HTN, CKD	Yes	Autologous HCT	N/A	7/2/2020	NP	Room air	No findings	0.04	1.34	0.19	974	4	Steroids, Toci	Room air	No
3	69	White Male	CLL	Gout	Yes	MRD HCT	No	7/3/2020	NP	Nasal cannula	Bilateral peripheral GGOs	0	0	0.31	1617	73	Steroids, CCP, Remdesivir, Toci, Anakinra	Mechanical	No
4	71	White Female	ventilation HL	Yes CAD	No	Autologous HCT	No	7/5/2020	NP	Room air	Bilateral diffuse GGOs	0.51	8.79	0.18	1260	51	Steroids, CCP, Remdesivir, Toci	High flow nasal cannula	No
5	70	White Female	Breast cancer	None	No	None	Yes	7/15/2020	NP	Nasal cannula	Bilateral extensive GGOs	0.11	6.03	0.4	1429	78	Steroids, Remdesivir, Toci	Mechanical	No
6	26	Black Female	ventilation CML	Yes None	Yes	None	No	7/16/2020	NP	Room air	Right lung subpleural nodule	0	0	0.89	3834	<LLQ	None	Room air	No
7	58	Hispanic Female	DLBCL	HTN	Yes	CAR-T	Yes	7/23/2020	NP	Nasal cannula	Bilateral GGOs	0.1	0.83	0.15	4345	20	Steroids, Remdesivir, CCP, Anakinra	Mechanical	No
8	70	Other Female	ventilation MM	Yes HPT, Dyslipidemia	Yes	Autologous HCT	No	11/24/2020	NP	Room air	Right lung GGOs	0	0	0.14	233	54	Remdesivir, CCP	Room air	No
9	68	White Male	MM	ESRD	Yes	Autologous HCT	No	12/7/2020	NP	Room air	Bilateral peripheral GGOs	0.08	7.14	1.95	4002	13	Remdesivir, CCP	Nasal cannula	No
10	52	Black Male	Germ cell tumor	CKD	Yes	Autologous HCT	Yes	12/20/2020	BAL (NP neg)	High flow nasal cannula	Bilateral peripheral GGOs	0.24	12.41	0.45	6339	10	Steroids, Remdesivir	Mechanical	No
11	80	White Male	ventilation Paget disease	Yes HTB, DM type 2, COPD, CAD	No	None	No	12/24/2020	NP	Nasal cannula	N/A	1	5.59	0.15	242	249	Steroids, Remdesivir, CCP	High flow nasal cannula	No
12	58	White Female	AML	COPD, CAD	Yes	None	No	1/14/2021	NP	Nasal cannula	Bilateral nodular opacities	0.3	0.2	0.09	1266	6	Remdesivir, CCP	Nasal cannula	No
13	21	Hispanic Female	ALL	HPT, HG	No	MUD HCT and CAR-T	Yes	2/1/2021	BAL (NP neg)	Mechanical	ventilation diffuse	Bilateral							No

consolidations 0.327.290.16433042 Remdesivir, CCP Mechanical ventilation No

AML, acute myeloid leukemia; ALL, acute lymphocytic leukemia; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; BAL, bronchoalveolar lavage; CAD, coronary artery disease; CAR-T, chimeric antigen receptor T-cell therapy; CCP, COVID-19 convalescent plasma; CKD, chronic kidney disease; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; COPD, chronic obstructive pulmonary disease; CT, computed tomography; DM, diabetes mellitus; DLBCL, diffuse large B-cell lymphoma; Dx, diagnosis; ESRD, end-stage renal disease; HCT, hematopoietic cell transplantation; HG, hypogammaglobulinemia; HL, Hodgkin lymphoma; HPT, hypothyroidism; HTN, hypertension; GGO, ground-glass opacity; LLQ, lower limit of quantitation; MM, multiple myeloma; MRD, match related donor; MUD, match unrelated donor; N/A, not available; NP, nasopharyngeal; Neg, negative; Toci, tocilizumab.

single COVID-19 cluster involving 3 patients and multiple health care workers and described the subsequent steps taken to prevent future clusters. We showed a reduction in both community-acquired and hospital-acquired infections with other respiratory viruses during the study period. Finally, we described the clinical characteristics, and the subsequent poor outcomes of nosocomial COVID-19 in cancer patients.

We found a rate of nosocomial COVID-19 among SARS-CoV-2–infected cancer patients of 0.4% during the first year of the pandemic. In a May 2020 meta-analysis, the rate of nosocomial COVID-19 was as high as 44%; however, the included studies were of low quality and conducted early in the pandemic, when strict infection control measures had not yet been implemented to prevent the spread of SARS-CoV-2.¹ Importantly, the definitions of nosocomial transmission varied in these studies and could reflect only identified clusters, not sporadic cases. Thus, use of relatively strict definitions may lead to an underestimate of the actual incidence of nosocomial COVID-19, for example in one study that reported a rate of 0.2% for definite nosocomial transmission.²⁶ Other institutions have defined in hospital transmission for patients with positive COVID-19 tests at any time during a hospitalization if they tested negative at time of admission.^{26,27} This definition does not account for the long incubation period for SARS-CoV-2 and the possible false negative initial testing at admission. Nonetheless, it is clear that infection control interventions are effective at reducing nosocomial transmission of COVID-19, although other factors, such as the spatial blueprints of health care settings (eg, the use of shared/semiprivate vs. private rooms) may also influence transmission patterns.^{27,28}

Our cluster investigation underscored the substantial role that health care workers and caregivers play in the transmission of SARS-CoV-2 to immunocompromised cancer patients, who often have long hospital stays after surgery, during induction chemotherapy, or after receiving cellular therapies such as HCT or chimeric antigen receptor T (CAR-T) cell therapy. Investigations of clusters of nosocomial COVID-19 in the Veterans Administration system²⁹ had similar findings, with several infected health care personnel in each cluster; in 2 instances, those investigations confirmed personnel-to-patient transmission by whole genome sequencing.²⁹ Moreover, because patients with cancer have worse outcomes from nosocomial infections, including COVID-19, than do other hospitalized patients,^{30–32} strict infection control strategies should be in place to prevent nosocomial transmission of pathogens and to detect infections promptly. Based on our observation of clinical staff touching and adjusting their face masks when caring for their patients and with available supply on hand, we recommended exchange of face masks between patients' encounters to prevent cross contamination, however, this strategy was not supported by strong evidence.³³ We also implemented routine weekly testing for all high-risk inpatients such as HCT recipients and patients with hematologic malignancies. However, the role and optimal timing of serial testing are still debated, and not enough is known to recommend this as a routine practice.^{26,34}

We found an in-hospital mortality rate of 31% in patients with nosocomial COVID-19, higher than that typically reported for cancer patients with COVID-19,^{35,36} and compared to approximately 12% for all admitted patients with COVID-19 at our institution during the first year of the pandemic (personal communication). In one study, COVID-19–related mortality was higher in cancer patients than in other hospitalized patients (20% vs 11%) despite the use of aggressive therapies.³⁷ In a retrospective study of HCT recipients with COVID-19, the COVID-19–associated mortality rate was around 21%.³⁵ In addition, age of 50 years or greater, male sex, and development of COVID-19 within 12 months of HCT were independently associated with higher mortality. However, that study did not consider nosocomial infections separately. Thus, a robust surveillance program for early detection of nosocomial COVID-19 and initiation of therapy

may mitigate the impact on vulnerable cancer patients, such as HCT or CAR-T cell therapy recipients or patients on active chemotherapy.

Along with the widespread circulation of SARS-CoV-2, we and others observed a stark reduction in the detection of other RVIs amongst our patients from the year before the pandemic through its first year of the pandemic.^{22,38} According to the CDC, the number of reported only 0.2% of respiratory samples tested were positive for influenza.²² This substantial reduction in other circulating respiratory viruses could be explained in part by the infection control and public health measures put in place to stop the spread of SARS-CoV-2, which may have affected both the transmission of other respiratory viruses. As public health measures were relaxed in many communities, other respiratory viruses have resurged, even exhibiting off-season peaks and, potentially, more serious manifestations.³⁹

Our study has some limitations. First, whole genome sequencing was not performed for confirmation of the transmission of SARS-CoV-2 among health care workers, caregivers, and patients. Instead, our investigations relied on clinical and epidemiologic data. Second, this study reflects a single cancer center's experience and our findings and recommendations may not all apply to other institutions. Lastly, we cannot clearly link reduction in nosocomial COVID-19 to infection control measures only as decline in community transmission may have also played a role.

In conclusion, nosocomial transmission of SARS-CoV-2 is an unfortunate consequence of the COVID-19 pandemic and has led to adoption of rigorous infection control practices in health care settings. To protect our most vulnerable patients, every effort should be made to prevent the potentially fatal consequences of nosocomial COVID-19. The implications of widespread COVID-19 vaccination on infection control policies in health care settings are still unclear, and further studies are needed to better elucidate the level of protection provided by vaccines against the transmission of COVID-19 in a hospital setting.

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