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Original Research Article

A retrospective evaluation of the value of COVID-19 screening and testing in patients with cancer: Aiming at a moving target

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ABSTRACT

Background: Diagnosis of COVID-19 infection in cancer patients is critical to co-manage their underlying disease and infection appropriately. Our study aimed at evaluating the sensitivity and specificity of screening patients with cancer for COVID-19 infection.
Methods: All oncology patients receiving care at Department of Oncology at King Abdulaziz Medical City in Riyadh were screened using the acute respiratory infection (ARI) survey. Nasopharyngeal and throat swap for polymerase chain reaction (PCR) testing for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was performed on patients who have high ARI score (i.e. $\geq$ 4), or any patient requiring elective/emergency hospitalization, undergoing a procedure as well as screening asymptomatic patients receiving chemotherapy between April 1st and July 30, 2020. Institutional Review Board approval was obtained. Descriptive and inferential analyses were done and sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated considering the COVID-19 PCR as the gold standard.
Results: During the study period, a total of 473 patients were included with a median age was 56 years (14–104), 51% were female, 73% had solid tumors, and 66% received treatment within the last 3 months. These patients underwent 688 PCR tests along with ARI survey screening. Testing was done in the outpatient, inpatient, and emergency department setting in 41%, 40% and 19% of the patients, respectively. Majority of tests were screening of asymptomatic patients and only 23% were tested for suspected infections with ARI $\geq$ 4. A total of 54 patients (8%) had positive PCR for COVID-19 infection. The prevalence of infection varied from month to month ranging from 1.09% in April up to 19.70% in June and correlated with the average daily and active case load at a national level. The diagnostic yield of the ARI score also correlated with infection burden nationally. The PPV and NPV of the ARI as a screening tool was 18.24% (0–31.8) and 95.6% (86.36–98.86%) with the PPN fluctuating considerably in parallel with the prevalence of COVID-19 result. Similarly, the sensitivity and specificity of the ARI were 55.77% (0–70.59) and 79.4 (69.19–92), respectively.
Conclusion: The yield of screening asymptomatic patients with cancer varies based on the community burden of COVID-19 infection. As universal screening can cause delays to patient care, it should be tailored based on the individual patient risks and infection burden in the region.

Background

The 2019 novel coronavirus (COVID-19) pandemic significantly affected cancer patients due to the interruption of their care and their risk of infections [1–5]. Providing optimal care to patients with cancer requires timely delivery of cancer therapy while protecting

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them from the risk of infection. This approach requires implementations of many interventions to prevent disease transmission such as social distancing, hand hygiene, global masking, and others. One of the most critical measure is early recognition of suspected cases through preemptive screening programs and quarantining them to prevent dissemination of the virus to other patients or staff [6,7]. Suspected cases by clinical screening can undergo laboratory testing by nasal swab and real time-PCR (RT-PCR) test for the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Identifying positive patients will help protecting others form transmission of disease, help in providing close monitoring for any deterioration, and guide in the timing of cancer treatment or procedures by either postponing them or if urgent, performing them under special precautions. The acute respiratory infection (ARI) screening tool is frequently used to identify suspected cases by asking specific questions about symptoms related to COVID-19 or exposure to confirmed cases. Patients with high score of ARI will undergo RT-PCR testing. However, many physicians are screening patients with cancer by RT-PCR routinely irrespective of their symptoms or ARI score especially prior to chemotherapy, radiotherapy, or procedures.

In order to decrease spread of COVID-19 among this vulnerable population, screening, early recognition, and quarantining may be necessary interventions. There are different recommendations on how and when to screen oncology patients for COVID-19 infection including clinical screening and laboratory testing. Multiple groups and organizations including the American Society of Clinical Oncology (ASCO) released guidelines on managing cancer patients during the COVID-19 pandemic [1,8–10]. Among their recommendations, they included screening patients prior to their hospital visit and apply triage protocols if patients have suspicious symptoms and testing asymptomatic patients 48–72 h prior to administration of chemotherapy, stem cell transplantation and other immunesuppressive treatments depending on testing capability. The aim of this study was threefold. First, to assess the yield of COVID-19 RT-PCR testing among oncology patients in different settings. Second, to validate the utility of the locally developed ARI screening tool in predicting the PCR results. Third, to correlate the local incidence and prevalence of infection to the national result.

Methods

Study design

Following due institutional review board approval, this was a retrospective study performed at the oncology department at King Abdulaziz Medical City in Riyadh, Saudi Arabia. The department serves patients with all solid and hematological malignancies and provide all modalities of treatments including surgery, radiation therapy, stem cell transplant and all systemic therapies.

During the period of March to July 2020, consecutive patients seen at the department whom underwent a COVID-19 RT-PCR test were eligible for inclusion. Nasopharyngeal and throat swabs for COVID-19 real time PCTR were obtained from all patients using appropriate personal protective equipment including N95 respirators within a negative pressure room. All patient and disease related variables were retrospectively collected from the electronic medical records.

Acute respiratory infection (ARI) screening

All patients were contacted via phone call prior to their appointment in the outpatient infusion suite by a health care professional to ensure they were symptom free. In case COVID-19 related symptoms were present, patients were advised not to attend to their scheduled visit and the most responsible physician (MRP) of the patient was contacted to arrange for an alternative and appropriate medical plan. Patients planned for outpatient chemotherapy administration, procedure or an elective admission underwent COVID-19 RT-PCR screening prior. Patients admitted from the emergency department also underwent PCR screening regardless of the reason for admission.

Table 1
Acute respiratory infection screening tool to identify patients with suspected signs and symptoms of COVID-19 infection and those with exposure risk.

Question	Point(s)
A. Clinical symptoms/signs	
Fever (≥38 °C)	4
Cough (new or worsening)	4
Shortness of breath (new or worsening)	2
Sore throat and/or runny nose	2
Nausea/vomiting AND diarrhea	2
B. Risk of exposure to COVID-19	
Unprotected exposure to confirmed COVID-19 case in last two weeks	4
Any health care facilities staff (healthcare worker or supporting services)	2

A score ≥4 → place patient in an isolation room and inform MD for assessment.

Furthermore, all patients underwent ARI form screening at the time of initial contact with the health care professional (Table 1). This is a locally developed screening tool aiming to identify patients with risk factors of COVID-19 infection, such as symptoms of infection and suspected or confirmed exposure to a positive case. In the outpatient setting, patients scoring ≥ 4 points were placed in an isolation room and COVID-19 RT-PCR swab was done, the MRP was contacted for patients scoring >0 but <4 for appropriate disposition whereas patients with score of 0 proceeded to receive their scheduled treatment.

Statistical analysis

This was a retrospective study including oncology patients whom were served at our center between March and July 2020. Data were collected retrospectively which included age, gender, diagnosis, systemic therapy used over the last three months, ARI score, indication for RT-PCR testing, location of testing and result. Baseline characteristics were reported using descriptive statistics (numbers, medians and percentage). For inferential statistics, the relationship between the categorical and continuous variables with the study variables will be analyzed using the Pearson's Chi-square and and Wilcoxon/Kruskal–Wallis as appropriate. Calculation of sensitivity, specificity, positive and negative predictive values were performed considering the COVID-19 RT-PCR as the gold standard.

Results

Baseline patient characteristics & indications for COVID-19 PCR swabs

During the study period, a total of 473 patients were included with a median age of 56 years (14–104), 51% of whom were female. Underlying diagnosis was solid malignancy in 73%, 92 (19%) had a hematological malignancy while 8 (2%) underwent a hematopoietic stem cell transplantation. About two thirds of patients received treatment within the last three months. Most common types of treatment was chemotherapy in 230 (73%) patients followed by targeted therapy (oral or intravenous) in 45 (14%) of patients followed by immunotherapy in 17 (5%) of patients.

A total of 688 COVID-19 PCR tests were done in 473 patients. The indication for testing was for screening purposes in the majority of

Table 2
Baseline characteristics of the patient cohort that underwent COVID-19 swab along with its indication.

Characteristic	N (%)
Female gender, n (%)	243 (51)
Age, median (range)	56 (14–106)
Area, n (%)	
Outpatient	282 (41)
Inpatient	271 (40)
Emergency	130 (19)
Reason for testing, n (%)	
Screening (chemo or procedure)	219 (32)
Screening (pre-admission)	235 (34)
Suspected	159 (23)
Unknown	70 (10)
Diagnosis, n (%)	
Medical oncology	344 (73)
Malignant hematology	92 (19)
Other hematology disorder	26 (6)
Stem cell transplant	8 (2)
Other	3 (<1)
Oncology treatment within three months, n (%)	
Yes	311 (66)
No	162 (34)
Oncology treatment type, n (%)	
Chemotherapy	230 (73)
Targeted oral/intravenous	45 (14)
Hormonal	12 (4)
Immunotherapy	17 (5)
Radiotherapy	9 (3)

patients (prior to chemotherapy, a medical procedure or admission to hospital) in 454 (66%) of swabs. Another 159 (23%) swabs were performed in patients suspected to have infection due to symptoms, unprotected exposure to a positive case or a high ARI screen. Finally, 70 (10%) swabs had an unknown indication due to lack of documentation in the medical records. The swabs were taken in the outpatient, inpatient and emergency department in 41%, 40% and 19% of the time, respectively. These results are shown further in Table 2.

Utility of acute respiratory infection screening

The median ARI score was 2 (0–10) with 314 (46%) swabs having a score of 0 while 159 (23%) swabs having an ARI score ≥4. Overall, a total of 54 (8%) of swabs were positive for a total of 43 patients. There were a total of 215 repeated swabs, 11 of whom were repeat positive. These results are shown further in Table 3.

Table 3
Result of all COVID-19 polymerase chain reaction swabs and acute respiratory infection score.

Characteristic	N (%)
ARI score, median (range)	2 (0–10)
ARI score, n (%)	
0	314 (46)
1–<4	210 (31)
≥4	159 (23)
Unknown	5 (<1)
Result of testing, n (%)	
Positive	54 (8)
Negative	634 (92)

Stratified by ARI score (high vs. low), patient gender, underlying diagnosis and treatment received were similar between the two cohorts. High ARI score was significantly associated with swabs taken in the emergency department (39% vs. 13%, $p < 0.0001$), having a suspected case (53% vs. 14%, $p < 0.0001$) and having a positive COVID-19 PCR result (18% vs. 4%, $p < 0.0001$). These results are shown further in Table 4.

Over the study period, the performance of the ARI as a screening tool was examined on a monthly basis. Overall, the prevalence of COVID-19 infection was 7.61% ranging from 1% in April to 19.7% in at its peak in June (Fig. 1). Considering COVID-19 PCR as the gold standard for diagnosis, the PPN and NPV of the ARI as a screening tool was 18.24% (0–31.8) and 95.6% (86.36–98.86% with the PPN fluctuating considerably in parallel with the prevalence of COVID-19 result. Similarly, the sensitivity and specificity of the ARI were 55.77% (0–70.59) and 79.4 (69.19–92), respectively. Furthermore, the prevalence of COVID-19 infection locally correlated with the infection burden on a national level measured as average daily new infections and daily active infections as shown in Table 5.

Discussion

The COVID-19 pandemic presented considerable challenges in delivering optimal cancer care to patients. A number of societies

Table 4
Relationship between characteristics of cancer patients and their results of PCR test for COVID-19 according to acute respiratory infection score value.

Characteristic	ARI < 4	ARI ≥ 4	p Value
Female gender, n = 473 (%)	195 (52)	180 (48)	0.66
Age n = 473, median (range)	55 (14–103)	61 (14–106)	0.0003
Area, n = 688 (%)			<0.0001
Outpatient	244 (47)	38 (24)	
Inpatient	212 (40)	59 (37)	
Emergency	68 (13)	62 (39)	
Reason for testing, n = 688 (%)			<0.0001
Screening (chemo or procedure)	193 (37)	26 (16)	
Screening (pre-admission)	209 (40)	26 (16)	
Suspected	75 (14)	84 (53)	
Unknown	47 (9)	23 (14)	
Diagnosis, n = 473 (%)			0.49
Medical oncology	270 (72)	74 (76)	
Malignant hematology	72 (19)	19 (20)	
Other hematology disorder	23 (6)	3 (3)	
Stem cell transplant	7 (2)	1 (1)	
Other	3 (1)	0	
Treatment within three months, n = 688 (%)			0.25
Yes	375 (72)	121 (76)	
No	121 (28)	38 (24)	
Result of testing, n = 688 (%)			<0.0001
Positive	23 (4)	29 (18)	
Negative	501 (96)	130 (82)	

[a]5 pts with unknown ARI were excluded.

Table 5
Performance and utility of the ARI score locally compared with the infection burden on a national level.

	April	May	June	July	Cumulative
Average daily COVID-19 cases at national level, n	711	2016	3519	2745	2250
Average daily active COVID-19 cases at national level, n	390	7970	26,396	53,570	26,333
Total number of PCR tests done, n	196	147	134	204	681[a]
PCR positive tests, n (%)	2 (1)	7 (5)	26 (20)	17 (8)	52 (8)
Percentage of positive PCR tests in ARI ≥ 4, n (%)	0	3 (43)	14 (54)	12 (71)	29 (56)
Sensitivity	0.00%	42.86%	53.85%	70.59%	55.77%
Specificity	92.02%	82.86%	71.70%	69.19%	79.40%
Positive predictive value	0	11.11%	31.82%	17.39%	18.24%
Negative predictive value	98.86%	96.67%	86.36%	96.24%	95.61%
Prevalence	1.05%	4.76%	19.70%	8.42%	7.61%

[a] An additional 7 PCR swabs were done in March 2020 but not included herein.

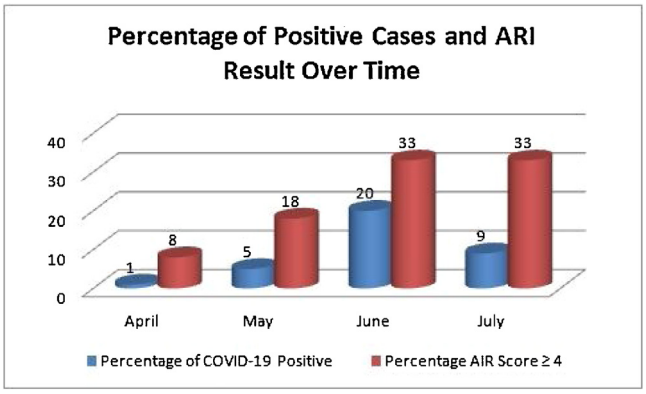

Fig. 1. Percentage of COVID-19 positive cases and acute respiratory infection score on a monthly basis.

including the European Society of Medical Oncology (ESMO) as well as ASCO recommended to screen patients prior to cancer treatment but additional factors such as laboratory capacity with PCR turnaround time must be considered at each institution as it can further cause delays to care delivery. The ESMO reported the utility of a pre-screening tool for COVID-19 infection using a patient-reported platform [11]. Using this tool, COVID-19 related symptoms are monitored and uploaded in the patient's electronic records, with an alarm triggered in such cases to advise the patient to report for PCR testing.

The issue of screening asymptomatic cancer patients is subject to debate. Lee et al., reported on 1989 tests in 1226 patients at the UK Birmingham chemotherapy cancer center and observed an infection prevalence of 0.6% among asymptomatic patients [12]. On the other hand, Al-Shamsi et al., 109 asymptomatic cancer patients underwent serial screening swabs totaling 384 specimens and noted that 25 out of 32 patients (78.1%) were diagnosed while asymptomatic [13]. From these reports and our own observations, such numerical quantitation is variable based on the community status of the pandemic at a given time point. Therefore, giving a percentage of prevalence among this population is inaccurate as it is time-bound and correlates with external variables. Herein, we noted that the overall prevalence of infection during the study period was 7.61%, however, it varied considerably with time correlating with the proportion of active cases at a national level. The predictive value of the ARI screening tool varied with the prevalence of the infection over time. Specifically, the PPV performance of the ARI was poor ranging from 0 to 31% indicating that this screening tool is not ideal for ruling in infection. On the other hand, the NPV ranged from 86 to 98% indicating that it would be a helpful tool in ruling out infection. Furthermore, even the value of ARI screening correlated with the disease burden in the community and when the case load was low, there was an overestimation of the suspected cases among cancer patients leading to performing of more tests. Collectively, the ARI would be most helpful to rule out infection in a time of low infection burden nationally.

This analysis carries a number of limitations that should be highlighted. First, the attributes of the ARI screening tool were compared to the PCR test which is considered to be the gold standard. However, false negative PCR samples are possible particular due to the nasopharyngeal swab acquisition technique and other limitations of the techniques itself may lead to underestimation of the ARI value [14–18]. Second, approximately 10% of the cohort did not have ARI results and it was unclear whether it was due to lack of administration or documentation in the medical records. Lastly, it is possible but less likely that patients may not report their infection symptoms due to fears of delaying their planned oncology treatments.

In conclusion, these findings challenge the application of universal recommendations of screening all Oncology patients prior to treatment without consideration of the status of the pandemic in the community. Furthermore, there are variations in the type of treatments, procedures, type of underlying malignancies, patients' general condition and underlining comorbidities [19]. Screening at the surge of the pandemic for patients with certain malignancies (hematologic malignancies, lung cancer or metastatic cancers), or procedure (particularly aerosol generating procedures) is probably justifiable. However, universal screening when the prevalence in the community is low may not be cost effective or practical as it may cause unnecessary delays to treatments and inconvenience to the patients. Adapting the recommendations for local setting and situations is required similar to what was suggested for testing asymptomatic healthcare workers [20].

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Competing interests

None declared.

Ethical approval

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