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ORIGINAL ARTICLE

Clinical outcomes in cancer patients with COVID-19 in Sweden

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ABSTRACT

Background: The results of studies on the relationship between cancer and COVID-19 have been conflicting and therefore further studies are needed. We aimed to examine the incidence of COVID-19 among patients at one of the largest oncology departments in Sweden, and to evaluate and identify risk factors for poor outcomes, hospital care and death, associated with COVID-19 among cancer patients.

Material and methods: This retrospective study included cancer patients at a single center who tested positive for SARS-CoV-2 by PCR either in hospital, primary health care center or commercial laboratory between 1 March and 14 August 2020. Clinical and demographic data were collected from the medical records. Logistic regression analysis was used to identify variables that associated the primary outcomes of need for hospital care and death within 30 days of positive test.

Results: Of 10,774 patients from the Department of Oncology at Sahlgrenska University Hospital, 135 tested positive for SARS-CoV-2 (1.3%). Twenty-eight patients were excluded from further the data collection since they did not meet the inclusion criteria. Altogether, 107 cancer patients were included and the case fatality rate (CFR) was 12% (13) within 30 days of confirmed SARS-CoV-2 infection by PCR. Increasing years of age (OR 1.10; CI 95% 1.03–1.18), palliative treatment intent (OR 15.7; CI 95% 1.8–135.8), and transition to end-of-life care (OR 52.0; CI 95% 3.7–735.6) were associated with increased odds of death within 30 days. Male sex was associated with needing hospital care (OR 3.7; CI 95% 1.50–9.1).

Conclusion: As in the general population, male sex was found to be at greater risk of needing hospital care for COVID-19, with terminal cancer disease, and older age increasing the odds of fatality. Compared to the general population, slightly more cancer patients had COVID-19. The CFR was within the lower range of others reported in cancer patients.

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Introduction

As the world starts to recover from the pandemic, the immediate and long-term effects of COVID-19, including in cancer patients, are still being determined. Patients undergoing chemotherapy are at high risk of infections due to underlying therapy-induced granulocytopenia or opportunistic infections [1]. Early reports and subsequent studies have reported an increased risk of severe COVID-19 in patients with comorbidities, including cancer and cancer therapy [2,3]. Treatment with immune checkpoint inhibitors has also been a cause for concern, since a hyperactivated immune system could increase the cytokine storm associated with severe COVID-19 [4]. Moreover, treatments and malignancies requiring frequent hospital visits further risk exposing cancer patients to infection in the hospital environment.

In Sweden, the government and the Public Health Agency of Sweden (PHA) initially chose a more liberal approach to the pandemic compared to many other countries, mainly relying on providing recommendations to the general public and avoiding lockdowns [5–7]. The Swedish strategy has been criticized for contributing to high mortality rates in the country, especially when compared to other Nordic countries, regardless of the higher mortality rates in some other countries despite the implementation of strict lockdown strategies [6]. Based on the scientific evidence, the PHA recommended all individuals at risk of a severe outcome to strictly limit social contacts, with at-risk groups including those aged 70 or older and cancer patients, amongst others [6]. Studies have shown that at-risk groups suffered a negative impact on their quality of life and mental health, after the first initial lockdowns [8] and similar impacts in cancer patients [9]. Also, studies in Italy have shown that the SARS-CoV-2 did not only affect patients at oncology centers, but also the quality of life and an increase of psychological distress among health care professionals at these centers

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Supplemental data for this article can be accessed here.

[10,11]. One of these reports [10] showed that the majority of health care professionals were uncertain how chemotherapy and immune therapy affected the outcome of COVID-19. Both cancer and COVID-19 are heterogenous diseases, with very variable epidemiology, morbidity, and mortality in disparate populations, so understanding their complex interactions has been challenging [7]. A population-based modeling study from England estimated that the restrictions and suspension of screening programs imposed during the COVID-19 pandemic would result in ~60,000 years life lost from patients with four major cancer diagnoses in the first five years after diagnosis [12].

In order to further understand the impact of SARS-CoV-2 on the Swedish cancer population, we performed a retrospective study of the effects of six months of the COVID-19 pandemic on the clinical outcomes of cancer patients who tested positive for SARS-CoV-2 at one of the largest oncology centers in Scandinavia. The aim of the study was to provide a population-relevant data to policymakers and oncologists to allow evidence-based decision-making about the management of cancer patients in hospital and the community.

Methods

Population and data collection

Eligible patients were identified by searching in the diagnostic databases at Department of Microbiology, Sahlgrenska University Hospital and the Unilabs Laboratory, for the results of SARS-CoV-2 RNA testing of patients at the Department of Oncology and Prostate Cancer Center (PCC). These two laboratories perform the majority of testing in the western region of Sweden. A positive match was confirmed in the medical record of each patient. Two cases were identified by hospital oncologists that could not be found in the laboratory records.

Inclusion criteria were as follows: adult patients with PCR-verified SARS-CoV-2 infection between 1 March and 14 August 2020 and a diagnosis of cancer treated or being monitored at the Department of Oncology including also oncology patients at PCC of the Department of Urology, Sahlgrenska University Hospital, between 1 January and 25 September 2020. Hematological malignancies were excluded since these patients are managed by a different department. A Consolidated Standards of Reported Trials (CONSORT) diagram of inclusions and exclusions is shown in Figure 1. Each patient was encoded before data processing and the file was stored separately. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Swedish Ethical Review Authority (EPMNumber: 2020-0579).

Testing strategy

The testing capacity changed during the study period in Sweden, initially only patients with symptoms of infection requiring hospital care were offered testing with PCR [7]. Widespread testing toward patients with mild or asymptomatic disease started in primary health care in early June. However, patients in treatment at the oncological clinical were offered testing on a more liberal indication earlier on if they had cancer therapy ongoing and/or were considered as

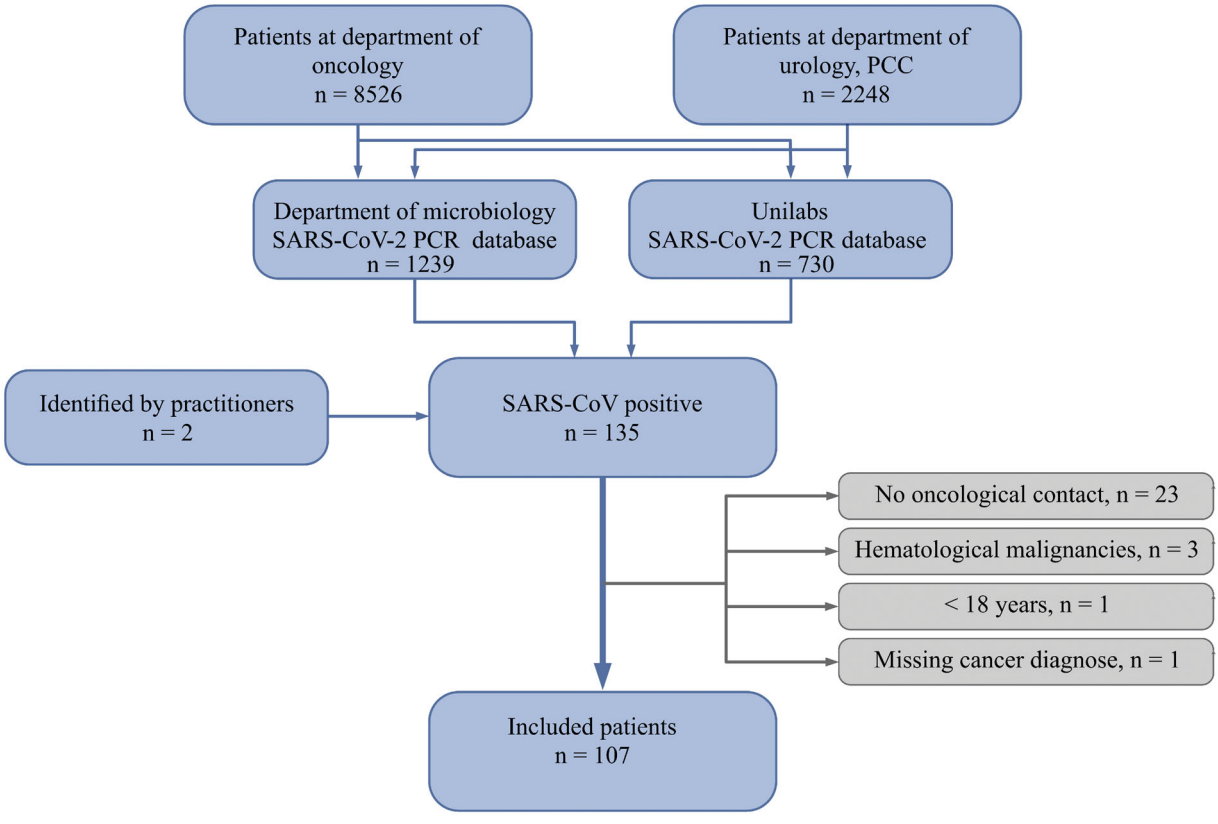

Figure 1. Consolidated standards of reported trials diagram illustrating patient identification and selection.

risk groups. Still only symptomatic patients and patients that had come in close contact with someone who has tested positive for SARS-CoV-2 within 2 weeks were tested and no other screening was implemented during the study period. During the study period, all patient SARS-CoV-2 PCR tests in the Gothenburg area were either analyzed at Department of Microbiology, Sahlgrenska University Hospital or the Unilabs Laboratory, regardless if the patients were tested at the Oncology department, other hospitals in Gothenburg area or at health care centers.

Variables

The variables were selected from known or factors that were suspected to affect the COVID-19 outcome [5,6], and from different cancer disease, stage and treatment. The following variables were included; age at positive SARS-CoV-2 PCR test, sex, date of positive test, testing site, ICD-10 code of the principal cancer diagnosis, cancer stage (defined as localized, regional, or metastatic at the time of inclusion), cancer treatment and date of recent treatment, treatment plan affected by SARS-CoV-2 (defined as paused, canceled, changed treatment type, or postponed start of treatment), palliative or curative treatment intent, transition to end of life care, days of admission, smoking habits, comorbidities [diabetes, hypertension, cardiovascular disease (defined as cardiac arrhythmias, coronary artery disease, heart failure, peripheral vascular disease, history of cardiac, or cerebrovascular event), pulmonary disease (defined as chronic pulmonary obstructive disease or asthma), and renal disease (defined as chronic renal disease or chronic renal failure)], obesity (defined as BMI $\geq$30 kg/m^2), severity of COVID-19 (defined as mild, moderate, and severe, see below), death during the inclusion period, date of death, and cause of death as registered in the hospital chart. The most recent assessed performance status (according to the ECOG scale) was collected if assessed in the last three months before the infection. The label palliative treatment intent was used for patients undergoing cancer treatment with intent to slow but not cure cancer, in contrast to curative intention. Transition to end-of-life care was chosen to specify that the responsible oncologist had made the decision that the cancer was progressing beyond treatment and that the patient now was only available for symptom relief. COVID-19 severity was defined as mild if the patient did not require admission to hospital or if admission to hospital was for observation and no treatment such as oxygen was administered; moderate was defined as requiring admission to hospital with treatment of COVID-19 symptoms; and severe was defined as requiring admission to an intensive care unit.

Outcome of interest

The primary outcomes were hospital care and 30-day mortality after a positive SARS-CoV-2 test. Hospital care was defined as when patients developed moderate or severe symptoms of COVID-19, as described above. If patients were admitted to the hospital for observation and received no treatment against COVID-19, they were not accounted as received hospital care.

Statistical methods

Statistical analyses were performed in collaboration with the statistical consulting agency 'Statistikkonsulterna Jostat & Mr Sample AB'. Baseline demographics are presented using descriptive statistics. Two-tailed Chi-square test was used to calculate the correlation between the COVID-19 outcomes and the categorical variables. Unpaired two-tailed Student's *t*-test with unequal of variance was used to calculate the *p* value of mean age differences between the severity groups. Binary logistic regression analyses were performed to explore possible associations between selected variables (Table 3 and Supplementary Table 4) and outcomes. Age was assessed as a continuous variable, while other categorical variables were redefined as binary due to the small population size. Univariable regression analyses were performed with and without adjustments for age and sex for each variable. No adjustments were made for multiple testing. All statistical analyses were carried out using SPSS version 26 (IBM Statistics, New York, NY).

Ethics

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Swedish Ethical Review Authority (EPMNumber: 2020-0579). STROBE case-control guidelines were used [13], and the checklist can be found in the Supplementary file.

Results

A total of 10,774 active oncology patients were identified from 1 January to 25 September 2020, and 1969 patients were tested for SARS-CoV-2 during the study period, of whom 135 patients (1.3%) tested positive (Supplementary Table 1). This corresponds to 1828 tested per 10,000 patients at this single oncology center. Two patients were not found in the registries but identified by practitioners, one with a laboratory result from a different region, and the other with a positive PCR result in the medical record but for unknown reasons not present in the laboratory records. After exclusions, 107 patients met the inclusion criteria and were included in the subsequent analyses (Figure 1). The number of patients that tested positive for SARS-CoV-2 differed over the study period with only 5 in March and a peak of 42 in June to then decrease to 6 in August (Supplementary Figure 1).

Demographics and clinical characteristics

Altogether, 107 patients positive for SARS-CoV-2 were included in the study (49% female). The most common cancer types were of the gastrointestinal tract, breast, and prostate. The median age at inclusion in to the study was 68 years (IQR = 57–74) with a higher median age among

Table 1. Patient demographics and clinical characteristics relative to hospital care due to COVID-19 and patients who died within 30 days after a positive test.

	SARS-CoV-2		Hospital care		Death ≤30	
	n	%[a]	*n*	%[b]	*n*	%[c]
Total	107	100%	39	36%	13	12%
Test site						
Hospital	61	57%	36	59%	11	18%
Primary health care	46	43%	3	6.5%	2	4.3%
Age, years						
<55	17	16%	1	5.9%	0	–
55–65	34	32%	9	27%	1	2.9%
66–75	34	32%	17	50%	6	18%
76–85	16	15%	9	56%	5	31%
>85	6	5.6%	3	50%	1	17%
Median (IQR)	68 (57–74)		72 (64–78)		74 (70–82)	
Sex						
Female	52	49%	11	21%	3	5.8%
Male	55	51%	28	51%	10	18%
Known comorbidities						
Hypertension	42	39%	22	52%	8	19%
CVD[f]	30	28%	15	50%	5	17%
Obesity	18	17%	8	44%	3	17%
Pulmonary disease	17	16%	9	53%	3	18%
Diabetes	16	15%	9	56%	2	13%
Renal disease	1	0.9%	1	100%	1	100%
Number of comorbidities						
0	38	36%	5	13%	0	–
1	34	32%	17	50%	7	21%
2	19	18%	7	37%	3	16%
≥3	16	15%	10	63%	3	19%
Smoking habits						
Never smoked	34	32%	9	27%	4	12%
Current/former smoker	49	46%	20	41%	7	14 %
Cancer type						
Gastrointestinal tract	18	17%	6	33%	3	17%
Breast	17	16%	3	18%	0	–
Prostate	15	14%	6	40%	1	6.7%
Lung	11	10%	6	54%	1	9.1%
Head and neck	8	7.5%	2	25%	0	–
Gynecological	7	6.5%	2	29%	1	14%
CNS	5	4.7%	2	40%	1	20%
Other	26	24%	12	46%	6	23%
Cancer stage						
Metastatic	39	36%	16	41%	7	18%
Regional spread	30	28%	12	40%	4	13%
Localized	38	36%	11	29%	2	5.3%
Current treatment						
Chemotherapy	36	34%	14	39%	5	14%
Chemotherapy < 30[e]	19	18%	9	47%	1	5,3%
Radiotherapy	26	24%	10	39%	3	12%
Radiotherapy < 30[e]	5	4,7%	3	60%	0	–
Hormone therapy	10	9.3%	3	30%	1	10%
Hormone therapy < 30[e]	8	7,5%	2	25%	0	–
Immunotherapy	5	4.7%	2	40%	0	–
Other therapy[g]	5	4.7%	1	20%	1	20%
Other therapy[g] < 30[e]	3	2,8%	1	33%	1	33%
No treatment > 2 years	5	4.7%	3	60%	1	20%
No therapy	20	19%	6	30%	2	10%
Treatment intent						
Curative	59	55%	15	25%	1	1.7%
Palliative	45	42%	23	51%	12	27%
Missing	3	2.8%	1	33%	0	–
Treatment status[h]						
Treatment > 30 days[d]	48	45%	17	35%	9	19%
Treatment < 30 days[e]	39	36%	16	41%	2	5.1%
No current treatment	20	19%	6	30%	2	10%
Transition to end-of-life care						
No	100	93%	34	34%	9	9%
Yes	7	6,5%	5	71%	4	57%
Most recent ECOG assessment						
ECOG 0	15	14%	6	40%	1	6.7%
ECOG 1–2	21	20%	10	48%	2	9.5%
ECOG >2	7	6.5%	5	71%	4	57%
Missing	64	60%	18	28 %	6	9.4%
Admission length						
Median days (IQR)	7 (4–14)		7 (4–14)		6 (4–13)	

[a]Percentage of total patients tested positive for SARS-CoV-2.
[b]Percentage of patients admitted to hospital in each demographic and clinical group.
[c]Percentage patients who died <30 days in each demographic and clinical group.
[d]Recieved therapy >30 days before tested positive for SARS-CoV-2.
[e]Recieved therapy <30 days before tested positive for SARS-CoV-2.
[f]Cardiovascular disease.
[g]Includes targeted therapy and unknown therapy (participants in randomized controlled trials).
[h]Includes chemotherapy, radiotherapy, hormone therapy, immune therapy, and other therapy.

men (70 years, IQR = 59–75) than among women (64 years, IQR = 56–73). Comorbidities were common: 42 patients (39%) had hypertension and 30 patients (28%) cardiovascular disease. Altogether, 49 patients (46%) were current or former smokers (Table 1).

There was an almost equal clinical cancer stage distribution in the SARS-CoV-2-positive population. The most common treatment was chemotherapy, with over half of patients treated with curative intent (55%), and seven (6.5%) patients transitioning to end-of-life care before the infection. A high proportion of an updated ECOG performance status data was missing, with 60% of the study population not having an assessed value in the three months prior to infection.

Outcomes from COVID-19

Thirty-nine (36%) patients were admitted to hospital care and 13 (12%) died within 30 days. Increasing age and rates of hospital care and death within ≤30 days, with the exception of the >85 years age group, showed a tendency of coinciding (Table 1). More men were admitted to hospital care and died ≤30 days after a positive test than women. Over half of patients with hypertension, cardiovascular disease, and pulmonary disease were admitted to hospital care. All patients who died had at least one comorbidity, with hypertension being the most common, and 14% of current or former smokers died within 30 days (Table 1).

Lung cancer patients were the largest proportion of patients admitted for hospital care. The highest death and admission rates were observed in patients with rarer cancer types identified as 'miscellaneous', a heterogeneous subgroup (Supplementary Table 2). The 30-day death rate was higher in patients with metastatic disease compared to patients with a loco-regional disease. Chemotherapy and radiotherapy were the most frequently observed treatments in hospitalized patients. There was a high frequency of need for hospital care and death in patients undergoing palliative treatment, 23 (51%) and 12 (27%), respectively. There was no specific relationship between recent treatment with cancer therapy and need for hospital care.

COVID-19 severity is presented in Table 2. Sixty-eight (64%) patients had mild disease, 38 (32%) moderate disease, and 5 (4.7%) severe disease. More men than women were reported with moderate and severe disease ($p = .002$). No patient with severe disease died within 30 days, with 92% of deaths occurring in the moderate category. Thirty-four patients had their cancer therapy altered due to COVID-19 infection: progression was documented in two patients in whom treatment was stopped, two patients who had the start of treatment postponed, and two patients where treatment was canceled following infection.

When identifying the cause of death in relation to the time from COVID-19 diagnosis, all five patients who had COVID-19 as a single attributable cause of death died within 30 days (Supplementary Table 3). In six patients, a single cause of death could not be established since they exhibited symptoms of both late-stage cancer and COVID-19 infection. Two patients who died ≤30 days after a positive SARS-CoV-2 test had cancer listed as a cause of death.

Logistic regression analysis

Several associations with hospitalization and 30-day mortality were observed by logistic regression (Table 3). Age was associated with an increased odds of hospitalization (OR 1.06; CI 95% 1.02–1.10) and 30-day mortality after adjusting for sex

Table 2. Severity of COVID-19 infection in relation to age, sex, alterations in oncological treatments, and documented progression of cancer.

Symptom severity	Total	Mild		Moderate			Severe		
	N	*n*	%	*n*	%	*p*	*n*	%	*p*
	107	68	64%	34	32%		5	4.7%	
Age groups, years									
<55	17	16	94%	0	–		1	5.9%	
55–65	34	25	74%	9	27%		0	–	
66–75	34	17	50%	14	41%		3	8.8%	
76–85	16	7	44%	8	50%		1	6.3%	
>85	6	3	50%	3	50%		0	–	
Mean age (SD[c])	65 (14.4)	61.7 (14.9)		72 (10.2)		**<.001**[a]	65 (17.5)		.65[a]
Sex									**.002**[b]
Female	52	41	79%	11	21%		0	–	
Male	55	27	49%	23	42%		5	9.1%	
Alterations in cancer therapy									
No change	73	49	67%	21	29%		3	4.2%	
Postponed start	7	5	71%	2	29%		0	–	
Paused	16	12	75%	3	19%		1	6.3%	
Altered treatment	3	0	–	3	100%		0		
Canceled	8	2	25%	5	63%		1	13%	
Documented outcome after treatment alterations									
No cancer progression	5	3	60%	1	20%		1	20%	
Cancer progression	6	3	50%	2	33%		1	17%	
Missing	96	62	65%	31	32%		3	3.1%	
Deaths									
Death ≤ 30 days	13	1	7.7%	12	92%		0	–	
Death > 30 days	4	3	75%	1	25%		0	–	
No information	3	2	67%	1	33%		0	–	

The bold *p* values indicate statistically significant.
[a]Calculated with Student's *t*-test with unequal variance of mean age difference between mild versus moderate, and mild versus severe.
[b]Chi-square test.
[c]Standard deviation.

Table 3. Logistic regression analysis of odds of hospital care and death within 30 days.

Variable	Univariable				Adjusted for sex and age			
	Hospital care OR[a]	*p*	Death ≤ 30 days OR[a]	*p*	Hospital care OR[a]	*p*	Death ≤ 30 days OR[a]	*p*
Age	**1.06 (1.02–1.10)**	**.002**	**1.10 (1.03–1.17)**	**.04**	**1.06 (1.02–1.10)**[b]	**.003**	**1.10 (1.03–1.18)**[b]	**.006**
Male vs female	**3.9 (1.7–9.0)**	**.002**	3.7 (0.96–14.41)	.057	**3.7 (1.5–9.1)**[c]	**.004**	3.6 (0.85–15.29)[c]	.083
Comorbidities > 2 vs ≤ 2	**2.9 (1.1–8.1)**	**.037**	1.52 (0.37–6.19)	.559	1.69 (0.55–5.16)	.358	0.70 (0.16–3.15)	.642
Former or current smoker vs nonsmoker	1.92 (0.74–4.96)	.180	1.30 (0.35–4.90)	.686	1.36 (0.46–4.06)	.577	1.06 (0.24–4.61)	.940
Metastatic disease vs non-metastatic disease	1.36 (0.60–3.07)	.457	2.3 (0.70–7.30)	.174	1.25 (0.51–3.10)	.624	2.0 (0.56–7.28)	.281
Chemotherapy ≤ 30 days vs no treatment[d]	1.60 (0.47–5.40)	.406	0.4 (0.04–4.07)	.881	3.0 (0.7–13.3)	.588	0.5 (0.04–6.36)	.195
Treatment < 30 days vs treatment ≥ 30 days[e]	1.50 (0.63–3.56)	.361	0.3 (0.1–1.3)	.105	1.91 (0.72–5.06)	.196	0.3 (0.1–1.7)	.182
Palliative vs curative treatment intent	**3.1 (1.3–7.0)**	**.008**	**23.2 (2.9–187.0)**	**.003**	2.3 (0.88–5.81)	.091	**15.7 (1.8–135.8)**	**.012**
ECOG > 2 vs ECOG ≤ 2	3.1 (0.53–18.28)	.206	**21.3 (2.7–168.9)**	**.004**	4.2 (0.47–37.11)	.201	–	–
Transition to end-of-life care vs no transition to end-of-life care	4.9 (0.89–26.33)	.067	**19.8 (3.2–123.4)**	**.001**	4.8 (0.69–33.47)	.114	**52.0 (3.7–735.6)**	**.003**

The bold values indicate significant results.
[a]95% confidence interval.
[b]Adjusted for sex.
[c]Adjusted for age.
[d]Includes no treatment > 2 years.
[e]Includes chemotherapy, radiotherapy, hormone therapy, immune therapy, and other therapy.

(OR 1.10; CI 95% 1.03–1.18). Being male was associated with a greater odds of hospital care, an association that remained after adjusting for age (OR 3.7; CI 1.5–9.1). There were associations between having more than two comorbidities and hospital care (OR 2.9; CI 95% 1.1–8.1) and palliative treatment intent and hospital care (OR 3.1; CI 95% 1.3–7.0), which were not apparent after adjusting for age and sex. However, palliative treatment intent was associated with an increased odds of 30-day mortality regardless of age and sex (OR 15.7; CI 95% 1.8–135.8). Transition to end-of-life care was also associated with an increase in odds of death within 30 days after adjusting for age and sex (OR 52.0; CI 95% 3.7–735.6). An ECOG value above 2 was associated with 30-day mortality in univariable analysis without adjustments (OR 21.0; CI 95% 2.7–169.0); the analysis with adjustments for age and sex could not be performed due to few observations for females in this category. Also, a logistic regression analysis where 30-day mortality caused by COVID-19 were used as outcome was performed (Supplementary Table 4). In COVID-19 related death the association with increased odds of death remained with increasing age and palliative treatment intent. Transition to end-of-life care was not associated with death in the same degree in this analysis (OR 6.7; CI 95% 0.9–51.8). No cancer diagnose were associated with higher odds for hospitalization or death within 30 days (data not shown).

Discussion

In this single center study, we analyzed data on cancer patients with mild to severe COVID-19 regardless of whether they had contact with the hospital or were tested in the community in order to identify factors that might predict severe disease or death from COVID-19.

During the study period, 135 patients (1.3%) tested positive for SARS-CoV-2. This is slightly higher than the fraction of the Swedish general population (0.8%) during the same time period [14]. This greater proportion is likely due to more frequent testing, and therefore a higher discovery rate. Indeed, among the patients at this single oncology center 6.9% of the PCR tests were positive, as compared with 8.7% of all PCR tests in Sweden, and testing was more frequent, 1828 tests per 10,000 among the patients at the Oncology Department compared to 936 tests per 10,000 overall in Sweden [15]. Taken together, the PCR positivity mirrored the general population. Reports of SARS-CoV-2 antibodies seroprevalence in cancer patients before the introduction of vaccine at single centers in Italy also correlate well with the viral spread at different regions, ranging from 0.7% at low transmission region up to 31% at high transmission region [16,17].

There have been concerns that cancer patients are more susceptible to infection with SARS-CoV-19 compared to the general population [18]. Our results suggest that SARS-CoV-19 transmission was not more widespread among cancer patients compared to the general population in Sweden, in agreement with the observation of a cancer center in the United States [19].

Age and male sex were associated with an increased risk of severe COVID-19, with a 6% increased odds of needing hospital care and 10% increased odds of death in $\leq$30 days with each increasing year of age. With an OR of 3.70, male sex was associated with a greater risk of needing hospital care compared to women. After adjustment for sex, OR (1.10) remained the same for death in $\leq$30 days with age, which imply that increased age increases the odds for death regardless of sex. These data are consistent with established risk factors for COVID-19 in the general population and cancer populations [20,21]. Increased odds for 30-day mortality were also observed for patients with palliative treatment (OR 15.7) and transition to end-of-life care (OR 52.0). These observations should be interpreted with caution since the 95% confidence interval (CI) for OR of palliative treatment and transition to end-of-life care were wide. Regression analysis of COVID-19 related death suggested that a palliative treatment intent increases the odds (OR 10.0), although also suffering from a wide 95% CI. These findings are interesting in light of other studies showing that metastatic disease, palliative treatment intent, and high ECOG values are associated with an increased odds of death, indicating that patients with late-stage disease might be a particularly vulnerable group [18,21–23].

It has recently been questioned whether cancer patients have the same access to ICUs as other populations who might benefit from ICU care. In the cohort studied, none of the patients who died were admitted to the ICU. This may indicate that cancer patients that need ICU care are not admitted or that the intensivist correctly identified the patients that have the highest chance of benefiting from ICU care. While our sample size is small and therefore does not fully answers the question, 4.7% of patients in our cohort were admitted to ICU compared to 3.0% in the general population in Sweden during the same period [24].

No solid cancer type has been definitively associated with an increased risk of severe COVID-19. Reports from China and one European cross-sectional study suggest that lung cancer patients might be at greater risk of severe COVID-19 [18,25]. However, lung cancer is the most common cancer type in China and, when adjusting for cancer prevalence, lung cancer is not over reported [26,27]. Our analysis suggests that a large proportion of patients admitted to hospital care for COVID-19 had lung cancer but that mortality was not increased. There was no significantly increased risk of the primary outcomes according to cancer type in our study (data not shown). Interestingly, no breast cancer patient died within 30 days of infection, something that may be attributed to their sex, younger age and that many receive only adjuvant treatment.

There are reports of an association between recent cancer treatments prior to COVID-19 and an increased risk of poorer outcomes in terms of death or ICU admission [28]. There have also been contradicting reports of whether immune checkpoint inhibitor therapy is associated with an increased risk of hospitalization and severe disease [29,30]. Importantly, a recent report by Bange and coworkers has suggested that CD8 positive T-cells may compensate for impaired humoral

immunity and influence clinical outcome of COVID-19 [31]. We did not detect any significant association between cancer treatments and hospital care or death ≤30 days of COVID-19 diagnosis, although we acknowledge that the subgroups in our study were small.

Cancer patients are reported to be at increased risk of death and severe COVID-19, although case fatality rates (CFR) vary across the world. The earliest studies from Wuhan reported a high CFR of 29% in cancer patients [30,32], as did a study from the UK (28%) [21], but subsequent studies based on larger populations from Spain, the USA, and Canada reported a lower CFR of 13% [22]. The British study reported that 12% of cancer patients testing positive for SARS-CoV-2 were not admitted to hospital compared to the 64% of patients that were not admitted to hospital in our study. This discrepancy reflects the patients in the UK study, who presented with more severe symptoms demanding hospital care, thereby contributing to the high CFR [21]. Our population, with a higher proportion of mild disease cases, is likely to more accurately reflect the cancer population. Overall, differences in reported CFRs between countries reflect the differing demographics of the study population, the local spread of disease, and test capacity and infection control at the time of study. This highlights the importance of conducting research in different populations to better estimate the impact of cancer on COVID-19 outcomes.

The CFR in the general population in Sweden was 6.8% compared to 12% in our cancer population [15]. In our cohort, two out of the 13 patients who died within 30 days died from cancer according to the medical records, and six patients had cancer as a contributing cause of death. In the regression analysis, which only COVID-19 associated death within 30 days was used, the association between end-of-life care and death was no longer that apparent. These findings, together with our patients having a relatively high median age compared to the general population, may explain the higher CFR. Since infection control strategies have been different in Sweden compared to other countries, the impact on cancer patients in this setting is particularly interesting and indicates that the Swedish COVID-19 strategy has not had a major impact on CFR in cancer patients. It was recently reported that patients with cancer had a higher incidence of positive SARS-CoV-2 tests in Sweden during the first three months of the pandemic [33]. The same study also reported that patients with cancer had significantly higher odds of COVID-19-related death and patients who received chemotherapy had a greater odds of ICU admission. These conflicting findings might be because cancer patients were compared to the general population in Larfors et al. [33] rather than different subgroups of cancer patients. Patients with cancer tend to have a more limited life expectancy and a higher median age than the general population. Also, Larfors et al. [33] examined a period during which there was a shortage of SARS-CoV-2 tests in Sweden and when testing was limited to hospitals, which cancer patients had easier access to.

To our knowledge, this is the first single center clinical outcome assessment of the first wave of COVID-19 pandemic in cancer patients in Sweden. In contrast to other international studies, the inclusion of patients from a single center tested both in hospital and the community might provide a better estimate of symptom severity and case fatality among cancer patients. Owing to limited testing resources in Sweden, testing in primary health care was restricted until early June, and patients who presented with severe symptoms might have been prioritized at the beginning of the pandemic and patients with asymptomatic and mild symptoms might have been undiagnosed.

In conclusion, a total of 10,774 active patients were identified between 1 January and 25 September 2020, at the Oncology department at Sahlgrenska University hospital and 1969 of these patients were tested for SARS-CoV-2 of whom 135 patients (1.3%) tested positive. This higher incidence compared to the general population (0.8%) in Sweden during the first wave of the pandemic is probably due to higher discovery rate. Cancer patients seems to suffer the same odds of a poor outcome as the wider population, with age and male sex particularly notable risk factors. Furthermore, cancer patients undergoing palliative treatment seem to be at higher odds of death from COVID-19. The second wave of the pandemic seems to have affected younger age groups more than in the first wave, advocating for a continued follow-up and analysis of COVID-19 in the cancer population with changing demographics and interactions between viral spread and the consequent risks for cancer patients.

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