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Clinical Paper

Real world outcomes in cancer patients with COVID-19 infection: Northern Ireland experience.

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ABSTRACT

Background

Cancer has been assumed to be associated with a high-risk of morbidity and mortality from COVID-19. Protective measures have incorporated modifications in cancer treatments. There are conflicting data about the impact of COVID-19 infection and outcomes in cancer patients. We aim to describe the impact of demographic and clinical characteristics on COVID-19 outcomes in patients with cancer in Northern Ireland reported within the UK Coronavirus Cancer Monitoring Project (UKCCMP).

Method

Prospective data collection including demographics, cancer stage and type, treatment and outcomes occurred for all Northern Irish patients enrolled in the UKCCMP. The primary endpoint was all-cause mortality. Descriptive statistics and logistic regression analysis were performed using SPSSv25.

Results

Between March 2020 and March 2021, 110 cases were registered. Median age was 63 years (range 27 to 87). Seventy patients (63.6%) were >60 years and 59 (53.8%) were females. Co-morbidities were reported in 83 patients (72.7%). Most patients had metastatic disease (64, 58.2%). Sixty-seven patients (60.9%) received anticancer treatment in the 4 weeks prior to COVID-19 infection. Of those patients, 35 (52.2%) received chemotherapy. Thirty-nine patients (58.2%) continued treatment as planned; 24 (36.9%) stopped treatment due to SARS-CoV-2 infection. The majority of patients were asymptomatic or experienced mild symptoms (67, 60.9%). Fifty-one (46.3%%) were admitted to hospital for COVID-19. Risk of severe/critical COVID-19 disease was significantly associated with age (OR 1.07 [95% CI 1.03-1.11); p=0.004), pre-existing hypertension (OR 3.29 [95% CI 1.42-7.62]; p=0.02) and thoracic primary malignancy (OR 4.41 [95% CI 1.52-12.74]; p=0.042). Twenty-nine patients (26.3%) died of whom 15 (57.7%) died of COVID-19 and 13 (44.8%) died due to cancer. Risk of death was significantly associated with age (OR 1.05 [95% CI 1.01-1.09]; p=0.014), male sex (OR 3.76 [95% CI 1.51-9.34]; p=0.008) and thoracic primary malignancy (OR 5.35 [95% CI 1.88-15.25]; p=0.014). When corrected for age, gender and co-morbidities, chemotherapy within the past 4 weeks was not significantly associated with mortality (OR 0.65 [95% CI 0.20-2.11]; p=0.476).

Conclusion

Age and thoracic cancer diagnosis correlated with survival. Comparison of performance during the pandemic with national benchmarks can inform how regional services should be adapted in preparation for future healthcare crises.

Keywords: COVID-19 infection, cancer patients, Northern Ireland, UKCCMP

Background

The COVID-19 pandemic has had a profound global impact and has presented challenges for healthcare systems and governments around the world. As of 16 November 2022, there have been over 632 million confirmed cases of COVID-19 globally and nearly 6.6 million deaths.[1] Considerable difficulties in cancer care have included decisions around cancer treatments, access to diagnostic services and surgical procedures, and determining optimal methods of protecting patients with cancer from infection.

Early in the pandemic shielding advice for the clinically vulnerable in many countries included the cancer population, who were assumed to be at high risk of infection and mortality due to disease and treatment related immunosuppression. A nationwide Chinese analysis published in March 2020 found that patients with cancer had a higher risk of severe COVID-19 or death than patients without cancer, and particularly those receiving chemotherapy or surgery within the previous month.[2] Furthermore, this study, and a single centre Chinese study[3] published one month earlier, found that patients with

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cancer had a higher risk of infection with COVID-19 than the general population. However, the number of patients with cancer included in these studies were small (n=18 and n=12 respectively). A larger study (n=334) in New York City published in April 2020 found that patients under 50 years old with cancer had a higher rate of mortality from COVID-19 than patients without cancer.[4] Early studies such as these were followed by guidelines from the National Institute for Health and Care Excellence (NICE) and the European Society for Medical Oncologists, containing consensus statements on the management of Oncology patients during the pandemic.[5,6] These recommendations included measures such as treatment interruptions, switching from intravenous to oral regimens, use of hypofractionated radiotherapy (RT) and assignment of prioritisation to systemic anticancer treatment (SACT) clinical scenarios. Given the lack of strong evidence to substantiate such changes in the initial stages of the pandemic and considering the perceived shift in the risk-benefit margin for cancer treatments amongst clinicians, the recommendations were readily and rapidly adopted.

Cancer patients as a whole comprise a heterogeneous group, with considerable differences in treatment modalities and outcomes due to patient factors, such as fitness and co-morbidities, as well as tumour characteristics, such as primary site, stage and histology. The vulnerability of each patient to COVID-19 is likely to be similarly individual, and so globally there are ongoing efforts to rationalise the blanket approach initially taken as more data emerges. In accurately estimating the risk of COVID-19 infection to patients with cancer, Oncologists will be better equipped to strike the optimal balance between cancer treatment and ongoing risk of COVID-19.[7] Given the international variability in cancer epidemiology and healthcare systems, as well as the COVID-19 burden in specific countries, there is a need for real world data on COVID-19 outcomes. Furthermore, as regional variation is observed between cancer populations within the United Kingdom (UK), an analysis of regional data is warranted.[8,9] Additionally, regional variations in the scope and timing of COVID-19 restrictions could also impact on outcomes and analysis of regional data is therefore justified. As observed through work carried out by the UK Cancer Registry, regular collection of prevalence data which corresponds with epidemiological evidence is vital for analyses like this and should remain a priority for the UK Government and devolved Administrations.[9]

In this prospective cohort study, we generated a database of patients with cancer in Northern Ireland (NI) who were diagnosed with COVID-19 with the aim of describing their disease characteristics and outcomes. A secondary aim of this study was to evaluate the impact of the COVID-19 pandemic on cancer treatment delivery in NI. This study was part of a national effort by oncology clinicians known as the UK Coronavirus Cancer Monitoring Project (UKCCMP), which aimed to track cancer patients who tested positive for COVID-19 across the UK.

Methods

Study design and participants

This database was designed as a public health surveillance registry for the COVID-19 pandemic in conjunction with a group working nationally to deliver the UK Coronavirus Cancer Monitoring Project (UKCCMP) seeking to support rapid clinical decision making. The national database was initiated in accordance with the UK Policy Framework for Health and Social Care Research, the UK National Research Ethics Service, and the UK Governance Arrangement for Research Ethics Committees. The Health Research Authority deemed ethical approval not to be required, and local approval and information governance processes were followed.

Written, informed consent was not required for inclusion in this study. Eligibility criteria for enrolment on the NI registry were as follows: adult patients (aged ≥18 years); active cancer; presenting to the oncology speciality service between 18th March 2020 and the 30th March 2021; and a positive SARS-CoV-2 RT-PCR test from a nose or throat swab. Patients with active cancer were defined as those with metastatic cancer or those undergoing anticancer treatment in any setting (palliative, curative, radical, adjuvant, or neoadjuvant) or those treated within the past 12 months with surgery, SACT, or RT. Stages of tumour were divided into primary tumour localised, which were localised to organ and therefore potentially resectable; primary tumour locally advanced, which had spread locally from the primary organ and was not resectable; metastatic, when tumour had spread to distant part(s) of the body; and patients in remission. Management of cancer patients with COVID-19 was directed by the patient's clinical team without input from the local research team or the UKCCMP and was based on local policies and standard clinical practice. Decisions about intensive care unit admission and ventilation were guided by the UK National Health Service National Institute of Health and Care Excellence COVID-19 rapid guidelines. This study was performed in accordance with the STROBE statement.[10]

Data collection and analysis

Case reporting was led by a COVID-19 emergency response reporting individual (LF) supported by a local emergency response reporting group (AH, AL, KT, CO, GW) who are all trainee Oncologists. Cases were screened for inclusion when identified by the treating clinical teams. Patient demographics, treatment details, COVID-19 disease course, and cancer features were obtained by the direct assessment of the electronic hospital medical records. Eligible patients were registered in the database when a positive SARS-CoV-2 test was noted and data fields were subsequently updated when treatment and outcomes became available. The COVID-19 severity category was determined according to World Health Organisation (WHO) guidelines.[11] Tumour types were classified according to International Classification of Diseases, 10th Revision (ICD-10) codes. All data was de-identified at source to ensure data anonymity and was entered with the research electronic data capture (REDCap)

Table 1: Summary of patient demographics.

		All patients (n=110)	Patients who survived (n=78) [a]	Patients who died (n=29) [a]	P value
Sex					
	Male	51	29 (37%)	20 (69%)	0.004†
	Female	59	49 (63%)	9 (31%)	
Age (years)	Median (IQR)	63 (55-74)	70 (63-77)	61 (53-74)	
COVID-19 severity					
	Asymptomatic	18	15 (19%)	3 (10%)	<0.0001*
	Mild	49	44 (56%)	4 (14%)	
	Severe	34	15 (19%)	17 (59%)	
	Critical	9	4 (5%)	5 (17%)	
Comorbidities[c]					
	Hypertension	34	21 (27%)	13 (45%)	
	Cardiovascular disease	17	12 (15%)	5 (17%)	
	Diabetes	15	10 (13%)	4 (14%)	
	Chronic obstructive pulmonary disease	12	7 (9%)	5 (17%)	
	None	27	24 (31%)	2 (7%)	
	Other	39	28 (36%)	10 (34%)	
Cancer type[b] [c]					
	Breast	28	22 (28%)	5 (17%)	
	Digestive organs	22	16 (21%)	5 (17%)	
	Respiratory and intrathoracic organs	19	8 (10%)	11 (38%)	
	Melanoma (skin)	15	14 (18%)	1 (3%)	
	Male genital organs	8	4 (5%)	4 (14%)	
	Female genital organs	7	6 (8%)	1 (3%)	
	Urinary tract	6	5 (6%)	1 (3%)	
	Bone and articular cartilage	2	2 (3%)	0 (0%)	
	Mesothelial and soft tissue	1	0 (0%)	0 (0%)	
	Lip, oral cavity, and pharynx	1	0 (0%)	1 (3%)	
	Thyroid / other endocrine	1	1 (1%)	0 (0%)	
Cancer stage					0.115*
	Primary tumour localised	27	23 (29%)	3 (10%)	
	Primary tumour locally advanced	13	9 (12%)	3 (10%)	
	Metastatic	64	42 (54%)	21 (72%)	
	Remission	1	0 (0%)	1 (3%)	
	Unknown	5	4 (5%)	1 (3%)	
Cancer treatment within 4 weeks of COVID-19 diagnosis [c]					
	Chemotherapy	35	29 (37%)	5 (17%)	
	Radiotherapy	10	9 (12%)	1 (3%)	
	Targeted treatment	14	12 (15%)	1 (3%)	
	Hormone therapy	8	4 (5%)	4 (14%)	
	Immunotherapy	7	6 (8%)	1 (3%)	
	Surgery	1	1 (1%)	0 (0%)	
	Other	4	4 (5%)	0 (0%)	
	None	43	24 (31%)	18 (62%)	
COVID-19 management					
	Not admitted	54	49 (63%)	5 (17%)	
	Admission	51	26 (33%)	22 (76%)	
	Unknown	5	3 (4%)	2 (7%)	
	Intensive therapy unit	2	1 (1%)	1 (3%)	
	Non-invasive ventilation	7	4 (5%)	3 (10%)	

[a] No survival data available for three patients. [b] Classified according to ICD10 classification.
[c] Some patients fall into more than one category. † Mann Whitney U test *Kruskal Wallis test

application, an electronic data capture software system that is browser based and metadata driven. This secure electronic data capture platform is hosted by the Institute of Translational Medicine at the University of Birmingham, Birmingham, UK.

Outcomes

The primary endpoint was all-cause mortality. This definition included deaths described as related to COVID-19 whether during admission or out of hospital, as well as deaths reported as a consequence of any other cause, such as due to cancer progression or treatment toxicity. Secondary outcomes included COVID-19 severity, disruption to anti-cancer therapies and hospital admissions.

Data processing and analysis

Anonymised case identifier data was collected and stored within secure health trust storage. Data was then entered into the REDCap system and was transferred securely through to the Compute and Storage for Life Science (CaStLeS) infrastructure as part of the Birmingham environment for academic research local cloud at the Centre for Computational Biology, University of Birmingham.

Descriptive analysis was performed to display the demographic, diagnostic, staging and outcome data. Analysis of association between the specified clinical outcomes and patient characteristics was undertaken with univariate logistic regression statistical analysis and described as odds ratios. A p-value threshold of 0·05 was used to indicate a significant difference. We used SPSS for data processing and visualisation.

Results

Patient Demographics

Between March 2020 and March 2021, 110 cases were registered for Northern Ireland. Patient demographics are shown in Table 1. The median age was 63 years (range 27 to 87), and gender was approximately balanced (54% female). The most common tumour sites included breast (28, 25%), digestive organs (22, 20%), respiratory and intrathoracic organs (19, 17%) and melanoma (15, 14%). Approximately a third of the patients had localised disease (40, 36%), and over a half had metastatic disease (64, 54%). Co-morbidities were reported in 83 (75%) patients, the most common being hypertension (34, 31%), cardiovascular disease (17, 15%) and diabetes (15, 14%).

Sixty-seven patients (61%) had received anti-cancer treatment in the 4 weeks prior to COVID-19 infection. Of those 67 patients, 35 (52%) received chemotherapy, 14 (21%) received targeted therapy and 7 (10%) received immunotherapy. Thirty-nine patients (58%) continued treatment as planned, whilst 24 (36%) stopped treatment due to COVID-19 infection. The majority of patients were asymptomatic or experienced mild symptoms (67, 61%). Fifty-one patients (46%) required hospital admission due to COVID-19 infection. Of these, 7 required non-invasive ventilation and 2 patients required admission to the intensive therapy unit.

Survival outcomes

Outcome data was available for 107 out of 110 patients, summarised in Table 1. During the study period, 29 patients (27%) died (all causes). Of these 29 patients, the cause of death was attributed to COVID-19 infection in 15 (52%) and 13 deaths (44%) were reported as cancer related. A higher proportion were male (20, 69%) and only 2 (7%) had no co-morbidities recorded. A higher percentage of patients who died had metastatic disease but the difference was not significant (72% versus 54%).

Table 2 summarises the univariable analysis of all-cause mortality. Risk of death was significantly associated with age (OR 1.05 [95% CI 1.01-1.09]; p=0.014), male sex (OR 3.76 [95% CI 1.51-9.34]; p=0.008) and thoracic primary malignancy (OR 5.35 [95% CI 1.88-15.25]; p=0.014). When corrected for age, gender and co-morbidities, chemotherapy within the past 4 weeks was not significantly associated with mortality (OR 0.65 [95% CI 0.20-2.11]; p=0.476) (Table 3).

COVID-19 severity

Following univariable analysis, risk of severe or critical COVID-19 disease was significantly associated with age (OR 1.07 [95% CI 1.03-1.11]; p=0.004), pre-existing hypertension (OR 3.29 [95% CI 1.42-7.62]; p=0.020) and thoracic primary malignancy (OR 4.41 [95% CI 1.52-12.74]; p=0.042) (Table 4).

Table 2: Univariable analysis of mortality (all causes)[a].

		Odds ratio (95% CI)	p value	Adjusted p value
Sex (male vs. female)		3.76 (1.51-9.34)	0.004	0.008
Age		1.05 (1.01-1.09)	0.007	0.014
COVID-19 severity				
	Asymptomatic or Mild	0.080 (0.02-0.28)	<0.001	0.001
	Severe or Critical	12.47 (3.62-42.94)	<0.001	0.001
Comorbidities				
	Hypertension	2.21 (0.90-5.35)	0.080	0.320
	Cardiovascular disease	1.15 (0.37-3.59)	0.815	1
	Diabetes	1.09 (0.31-3.79)	0.895	1
	Chronic obstructive pulmonary disease	2.11 (0.61-7.28)	0.236	0.944
Cancer type				
	Breast	0.53 (0.18-1.57)	0.251	1
	Digestive organs	0.81 (0.27-2.25)	0.705	1
	Respiratory and intrathoracic organs	5.35 (1.88-15.25)	0.002	0.014
	Melanoma (skin)	0.16 (0.02-1.30)	0.087	0.609
	Male genital organs	2.96 (0.69-12.72)	0.145	1
	Female genital organs	0.43 (0.05-3.72)	0.442	1
	Urinary tract	0.52 (0.06-4.66)	0.560	1
Cancer stage				
	Primary tumour localised	0.27 (0.74-0.99)	0.048	0.144
	Primary tumour locally advanced	0.88 (0.22-3.52)	0.856	1
	Metastatic	2.36 (0.89-6.21)	0.083	0.249
Cancer treatment within 4 weeks of COVID-19 diagnosis				
	Chemotherapy	0.35 (0.12-1.02)	0.055	0.275
	Radiotherapy	0.27 (0.03-2.26)	0.229	1
	Targeted treatment	0.13 (0.02 - 1.58)	0.126	0.630
	Hormone therapy	2.96 (0.69-12.72)	0.145	0.725
	Immunotherapy	0.43 (0.05-3.72)	0.442	1
COVID-19 management				
	Intensive therapy unit or NIV	5.21 (1.15-23.42)	0.031	0.031

[a] No survival data available for three patients. Univariable analysis performed by comparing each factor to the absence of each category as a reference, with the exception of sex and age. Male sex compared with female sex. Bonferroni *p* value adjustment performed. NIV, non-invasive ventilation.

Table 3: Multivariate regression analysis and odds of death

Multivariate model	Odds ratio (95% CI)	p value
Gender (Male v female)	3.42 (1.29 - 9.08)	0.014
Age	1.03 (0.98 - 1.07)	0.233
Co-morbidities (Present v absent)	4.19 (0.81 - 21.8)	0.088
Chemotherapy	0.65 (0.20 - 2.11)	0.476

Table 4: Univariable analysis of COVID-19 severity.

		Odds ratio (95% CI)	p value	Adjusted p value
Sex (male vs. female)		1.60 (0.74-3.46)	0.231	0.462
Age		1.07 (1.03-1.11)	0.002	0.004
Comorbidities				
	Hypertension	3.29 (1.42-7.62)	0.005	0.020
	Cardiovascular disease	1.11 (0.38-3.17)	0.848	1
	Diabetes	1.43 (0.48-4.29)	0.513	1
	Chronic obstructive pulmonary disease	5.65 (1.43-22.25)	0.013	0.052
Cancer type				
	Breast	0.54 (0.21-1.36)	0.190	1
	Digestive organs	0.52 (0.19-1.45)	0.209	1
	Respiratory and intrathoracic organs	4.41 (1.52-12.74)	0.006	0.042
	Melanoma (skin)	0.75 (0.24-2.37)	0.624	1
	Male genital organs	2.81 (0.64-12.41)	0.174	1
	Female genital organs	1.81 (0.25-5.56)	0.833	1
	Urinary tract	0.77 (0.14-4.39)	0.767	1
Cancer stage				
	Primary tumour localised	0.56 (0.22-1.42)	0.222	0.666
	Primary tumour locally advanced	0.95 (0.29-3.12)	0.927	1
	Metastatic	1.56 (0.69-3.50)	0.285	0.855
Cancer treatment within 4 weeks of COVID-19 diagnosis				
	Chemotherapy	0.62 (0.26-1.44)	0.262	1
	Radiotherapy	1.04 (0.28-3.93)	0.951	1
	Targeted treatment	0.59 (0.17-2.00)	0.392	1
	Hormone therapy	1.62 (0.338-6.83)	0.515	1
	Immunotherapy	4.28 (0.79-23.13)	0.092	0.460

Univariate analysis performed by comparing each factor to the absence of each category as a reference, with the exception of sex and age. Male sex compared with female sex. Bonferroni p value adjustment performed.

Impact on delivery of anti-cancer treatments

As a secondary outcome this study sought to demonstrate how the health system in Northern Ireland was impacted through excess inpatient care and ITU care due to COVID-19. The number of cycles of SACT administered regionally was reduced during the time period March to August 2020, compared with the remainder of the study period **(Fig. 1A)**. However, the number of new SACT courses commenced was decreased during April and May 2020 only **(Fig. 1B)**. The number of new RT courses commenced at the regions' two RT departments was grossly unaltered during the first waves of the pandemic **(Fig. 2A)**. Although not captured in this data set, a number of patients switched from primary surgery to radical (chemo-)RT during this period which may have influenced these numbers. There was a trend towards hypofractionation (i.e. higher doses of radiation per visit, with a reduced number of total visits), which has been sustained, as reflected in the reduced number of fractions per new course (data for Belfast City Hospital only) **(Fig. 2B)**. This is reflected as a diminished number of fractions administered over the study period **(Fig. 2C)**, despite a preserved rate of new RT courses. These data should be interpreted with caution as they lack granularity with respect to several of the pandemic-specific protocols i.e. increased usage of single-fraction palliative RT treatments and oral therapies in place of more intensive parenteral regimes.

Discussion

The COVID-19 pandemic has introduced additional complexity for patients with cancer, particularly those embarking on active treatment. Early Chinese data indicated that patients with cancer are more likely to develop COVID-19, and more likely to develop severe disease.[2,3] In response, Oncology departments rapidly instigated new processes capable of ameliorating the risk of infection in this population, including tightened selection criteria for systemic therapy, and hypofractionated RT courses.[12,13]

As the pandemic has progressed and more data has become available, there have been conflicting reports regarding

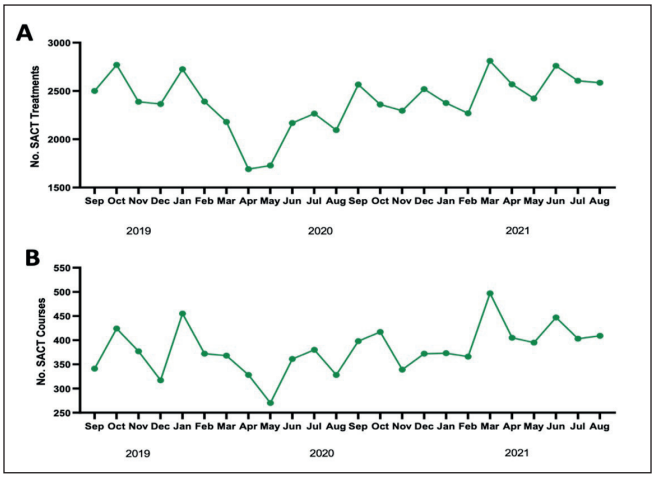

Figure 1: Trends in systemic anti-cancer therapy (SACT) delivery plotted as total number of systemic anti-cancer treatments given (A), and number of new courses commenced (B) per month between September 2019 and August 2021

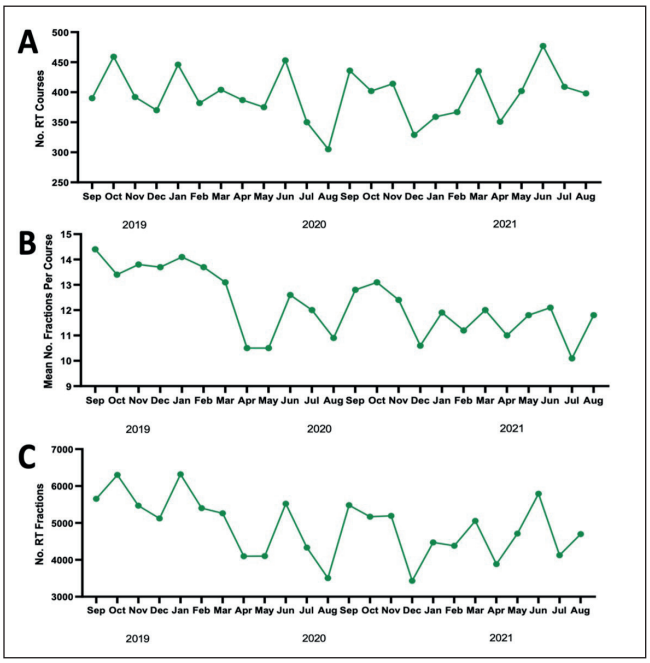

Figure 2: Trends in radiotherapy (RT) delivery plotted as number of courses commenced (A), mean number of fractions per course (B), and total number of fractions delivered (C) per month between September 2019 and August 2021

the risk of COVID-19 infection and death in patients with cancer. More mature data from the first wave of the pandemic subsequently demonstrated that increased mortality was not associated with specific cancer treatments.[14-16] Whilst reassuring, this data contradicted earlier studies, and also the assumption of Oncologists about the cancer population, a cohort generally classified as one with diminished immune systems and physical reserve.[17,18]

The UKCCMP is a UK-wide database for patients with COVID-19 who have cancer. Initial results from this cohort published in May 2020 found that receipt of chemotherapy, immunotherapy, targeted treatments, hormone therapy or RT within the 4 weeks prior to infection had no significant effect on mortality from COVID-19.[14] More recently, international data from various countries, including the United States of America, have also reported that patients with cancer are not at increased risk of severe COVID-19.[19] In contrast, another American study found that in patients with cancer and COVID-19, recent treatment with immune checkpoint inhibitors, chemotherapy or targeted therapies were all significantly associated with greater odds of all-cause mortality.[20]

A systematic review of sixteen studies found inconsistent results, but concluded no excess risk of severe COVID-19 following chemotherapy, immunotherapy, targeted treatments, RT or surgery; however, it did find an increased risk of death with chemotherapy administration within 30 days preceding COVID-19 diagnosis[21] These large, multicentre studies enabled clinicians to cautiously relax some of the stringent measures that had been established to maximise patient safety at the beginning of the pandemic.[22] This project sought to assess the interaction of COVID-19 and patients with cancer in NI specifically during the first year of the pandemic, with the ultimate aims of better risk-stratification of Oncology patients during the remainder of the pandemic, and informing planning for future pandemics. Although not the remit of the current study, more recent studies have reported that mortality from COVID-19 infection in patients with cancer has improved in Europe over time and this has been attributed to earlier diagnosis, improved management and dynamic changes in community transmission over time.[23]

COVID-19 infection was uncommon in the NI cancer population identified in this study. In addition, a minority of patients had treatment stopped due to the pandemic. A large proportion of patients included had metastatic disease, and less than half of patients were undergoing chemotherapy at the time of their COVID-19 diagnosis. Almost half of the affected patients required inpatient care, but intensive therapy was rarely required. Age and pre-existing hypertension were associated with severity of disease, and patients with thoracic cancer were more likely to be affected. Age and pre-existing hypertension were also factors associated with death in the cohort presented, as was a diagnosis of thoracic cancer.

Although the inclusion criteria differed, many of the data from NI are comparable to the UK-wide study; for example, the low recent chemotherapy, treatment interruption, and ITU admission rates.[14] This cohort of over 800 patients from 55 hospitals found no association of COVID-19 with cancer treatments but rather that patient factors such as age and male gender did correspond with risk of mortality, which was mirrored in the current cohort.

In a regional analysis of the Oncology service, the number of patients embarking on new courses of SACT and RT delivery were reduced transiently only, during April-May 2020 and August 2020 respectively. Reduced activity may in part reflect diminished diagnostic capacity delayed presentation of patients during lockdown and suspension of cancer

screening programmes in the early stages of the pandemic.[24] Trends resulting from pandemic-specific clinical protocols complicate the interpretation of these data, such as increased usage of single-fraction palliative RT treatments, and oral SACT regimes in place of more intravenous treatment. Also not captured specifically in this dataset, a sizeable proportion of patients would have had their primary treatment modality switched from surgery to radical chemo-RT in order to accommodate resource issues. Of note, due to the rapidly unfolding healthcare crisis, SACT guidance issued nationally was initially instigated on basic principles, in the absence of a robust evidence base. Similarly, the Royal College of Radiologists published UK-specific recommendations in relation to the use of hypofractionated RT, which some UK centres would have had a limited degree of familiarity with only.[25]

More recently, time-dependent improvements in outcomes have been reported comparing the earlier and later phases of the pandemic supporting universal vaccination of patients with cancer as a protective measure against morbidity and mortality.[26] However, this could not be explored in the cohort included in this study as only patients diagnosed during the early phase were included. Furthermore, vaccination programs in NI commenced in December 2020 and was not routinely collected for the majority of participants in this study during the time of data collection.

The medium and long-term impact of COVID-19 in patients with cancer is unknown. However, evidence suggests that sequelae post-COVID-19 affects a proportion of cancer patients and has an adverse effect on survival and oncological outcomes after recovery.[27] The data collection period included in this study does not allow us to address these issues. Ongoing follow up of sequalae and oncological outcomes is required to further understand the impact of COVID-19 infection in patients with cancer.

This study has a number of limitations. Firstly, it is impossible to exclude selection bias from the enrolled cohort given that the investigators relied on colleagues referring cases for consideration of study inclusion. The intensive nature of delivering most anticancer therapy meant that patients on active treatment were more likely to be referred. Secondly, the impact of changes to service delivery in the initial months of the pandemic could not be determined from this dataset; for example, mortality may have been increased through the reduced use of palliative cytotoxic therapy. Thirdly, the investigators did not have access to testing data at a population level and so denominators could not be calculated. Lastly, testing policies in the UK varied during the study window, meaning some potential cases of COVID-19 infection many have been missed. In addition, sample sizes were small particularly in subgroup analyses, and this is reflected by wide confidence intervals. Nonetheless, the small population size, coupled with electronic healthcare and a unified healthcare system makes Northern Ireland well placed to conduct population-based research, including in groups of the population such as cancer patients, especially in a pandemic situation where there is a need for rapid evaluation of the severity of COVID-19 in a vulnerable patient cohort.

Conclusion

In summary, we present a region-wide prospective cohort study of patients with cancer diagnosed with COVID-19. Although the co-occurrence of these conditions was uncommon in this study cohort, and the mortality rate was low in this population, specific groups were identified as having increased susceptibility. While these data and those of other prospective studies are informative, it is likely that dedicated studies for specific cancer treatments (i.e. cytotoxic chemotherapy, hypofractionated RT) and specific risk groups (i.e. thoracic cancer, young adults) will be required in order to draw robust conclusions about COVID-19 and cancer. This study will go some way in describing the impact of COVID-19 on mortality and treatment delivery in cancer patients in NI and may help to inform our response in future pandemics.

AUTHORS' CONTRIBUTIONS

L.F., A.H., A.L., G.W. and K.T. were involved in the study design; L.F., A.H., A.L., G.W., K.T. and C.O. were involved in the data collection, acquisition and management; L.F., A.H., A.L. and G.W. were involved in data analysis and interpretation; writing—review and editing, all authors; supervision, R.T.; All authors have read and agreed to the published version of the manuscript.

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ETHICS APPROVAL

The UKCCMP database was designed as a public health surveillance registry in accordance with the UK Governance Arrangement for Research Ethics Committees.

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DECLARATION OF INTERESTS

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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