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On Cancer, COVID-19 and CT scan: a monocentric retrospective study.

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ABSTRACT

Background

The acknowledgment of computed tomography (CT) defined diagnosis in high prevalence northern Italy may identify more patients with Coronavirus Disease-2019 (COVID 19) infection, than RT-PCR alone.

Methods

We retrospectively reviewed 148 chest CT scans of oncological patients who were referred to the Radiological Unit of Policlinico S. Marco from 1st of February 2020 to 30th of April 2020, during the Covid-19 outbreak in Bergamo area. Therefore, we analyzed RT-PCR tests of these 148 patients.

Results

Among 32 patients with diagnosis of COVID-19 infection: 17 patients were asymptomatic or had mild symptoms (53.1%), while 15 developed severe disease (46.8%). The incidence of COVID-19 infection is 22.9%, the mortality rate is 18.8%. Severe COVID-19 disease is associated with higher median age. We did not find any correlation between disease severity and sex, smoke or cardiovascular comorbidities. Remarkably, patients who were on treatment developed milder disease than cancer patients who were not on treatment.

Conclusions

The acceptance of CT-defined diagnosis in high prevalence area like Bergamo highlighted a larger number of COVID-19 oncological population than RT-PCR alone, in particular asymptomatic and mild symptomatic patients.

We observed that actively treated patients had milder disease, according to previous studies that suggested a protective role of immunosuppression.

KEY WORDS

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COVID-19 infection, CT-scan, oncological patients

BACKGROUND

According to three recently published Chinese studies, patients with cancer have a higher risk of COVID-19. (1; 2; 3) Consequently, physicians have been encouraged to withhold or postpone cancer treatment during the pandemic. Liang's study was criticized because he concluded that patients with cancer had a higher risk of COVID-19, observing a higher percentage of patients with cancer in the COVID-19 cohort than in the overall population. However, the incidence of COVID-19 in patients with cancer would be more enlightening in determining whether or not patients with cancer have an increased risk of COVID-19 (4). Moreover, it is difficult to determine if the worse outcome of COVID-19 infection in patients with cancer is related to other confounding factors such as history of smoking, older age, comorbidities than the cancer history itself. (5; 6)

Finally, the reports of benign course of immunocompromised patients suggests that immunosuppression can be a "double-edged sword": adaptive immune response can contribute to recovery or disease. (7; 8)

Diagnosis of COVID-19 infection can be challenging: some sources consider chest CT findings more sensitive than RT-PCR (nasopharyngeal swabbing) in detecting COVID-19. (9; 10; 11; 12)

The acknowledgment of CT defined diagnosis in high prevalence northern Italy may identify more patients with COVID 19 infection, than RT-PCR alone. (13) However, in Italy chest CT has usually been used to monitor the progression and complications of the infection, instead of being used to diagnose COVID-19 infection.

METHODS

We retrospectively reviewed chest CT scan of actively treated oncological patients and of cancer

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patients in follow-up after treatment or in a watch and wait follow-up, who were referred to the Radiological Unit of Policlinico S. Marco from 1st of February 2020 to 30th of April 2020, during the Covid-19 outbreak in Bergamo area.

148 CT scans were acquired with and/or without contrast medium injection. Reconstructed images were then displayed on a ICIS view workstation and interpreted by experienced radiologists.

Chest CT typically shows ground-glass opacities (GGOs) or bilateral pulmonary consolidations. Infiltrates that can be associated with cancer metastases or radiation pneumonitis were ruled out.

We retrospectively reviewed RT-PCR test of the patients who underwent CT scan in the same period of time.

The *incidence* of Covid-19 infection was calculated as the ratio between number of cancer patients with diagnosis of COVID-19 infection (CT scan suspicious of viral infection and/or positive RT-PCR test) and total number of cancer patients who underwent CT scan in the period from 1st of February to 30th of April.

The *mortality* rate of Covid-19 infection was calculated as the ratio between number of patients whose death was related to viral pulmonary infection, and total number of cancer patients with diagnosis of COVID-19 infection (CT scan suspicious of viral infection and/or positive RT-PCR test) from 1st of February to 30th of April.

Chi-square and Fisher's exact tests were used to compare categorical variable. $P<0.05$was considered to be statistically significant. Yates's correction was applied when needed.

Continuous variables were shown as median and percentages were presented for categorical variables.

RESULTS

Among 148 scans of 140 patients (8 patients underwent more than one CT scan in the observed period), we identified 32 cases whose imaging findings are suggestive for COVID-19 infection.

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Table 1 and 2

The incidence of COVID-19 infection in our group of patients is 22.9%.

The mortality rate is 18.8% (6 patients died among 32 cases of COVID-19 infection).

Eleven patients were asymptomatic. Nevertheless, they had CT scan features that were strongly suggestive of COVID-19 infection. Five of them underwent nasopharyngeal swabbing during the clinical visit at the hospital after a median of 7-10 days from the CT scan execution: only one was positive. RT-PCR test were not performed at the same time of CT scan, because COVID-19 infection was a casual finding in asymptomatic patients.

Six patients had mild symptoms. One of them did not refer to the clinician for nasopharyngeal swabbing. The other five patients underwent RT-PCR test: 4 of them were positive, while one was negative. Two patients with RT-PCR positivity and mild symptoms had negative CT scan. However, in these two cases CT scan was performed after symptoms remission for cancer follow-up.

Fifteen patients developed severe disease: all of them underwent CT scan and RT-PCR at the same time: 12 patients had positive CT scan and RT-PCR, while 3 had negative RT-PCR.

Considering the high prevalence of the infection in Bergamo area, all the patients had an exposure history.

Among 32 patients with COVID-19 infection: 11 patients were asymptomatic (34.3%), 6 had mild symptoms (18.7%), while 15 developed severe disease (46.8%):14 patients needed hospital recovery and 3 of them needed ICU admission (9.3%).

Median age of patients with severe COVID-19 disease is higher (73.9 years) than that of patients with mild COVID-19 infection (63.1 years) and that of not infected patients (66.6 years).

In our group more women than men were infected ($p= 0.04$), but there is no statistically significant difference between men and women considering disease severity ($p= 1$) and mortality ($p= 0.6$).

There is no significant difference of COVID-19 infection's incidence, mortality and disease severity between smoker (current and former) and no smoker cancer patients ($p= 0.1$; $p= 0.07$; $p= 0.1$ respectively).

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There is no significant difference of COVID-19 infection's incidence, mortality and disease severity between patients with cardiovascular (CV) comorbidity and patients without CV comorbidity (p= 0.6; p= 0.1 and p=0.07 respectively).

There is no significant difference of COVID-19 infection's incidence between cancer patient actively treated and patients who were not on treatment at the time of CT scan (p= 0.9). However, actively treated patients had milder clinical picture and a lower mortality rate than patients who were not on treatment (odds ratio (OR) 0.1 p= 0.01 and OR =0.08 p= 0.02 respectively).

DISCUSSION

The incidence of COVID-19 infection in our group of patient is 22.9%. The mortality rate is 18.8% (6 patients died among 32 cases of COVID-19 infection).

It is difficult to make comparison between incidence and mortality rate in cancer patients and non-oncological patients, considering that CT scan as a screening tool could not be applied to general population. Consequently, we are not able to know at the moment how many asymptomatic or mild symptomatic non oncological people had the infection. A recent published single- center's retrospective study reported an infection rate of 2.7% among 1380 cancer patients and the severe/critical proportion was 54.1%. However, in this study, COVID-19 diagnosis was made by RT-PCR or antibody test for SARS-CoV-2. (14)

We hypothesized that CT scan is more sensitive than RT-PCR, especially in asymptomatic or mild symptomatic patients whose viral load could be lower than that of severe symptomatic patients. We assume that in area with high prevalence, COVID-19 infection can be diagnosed despite RT-PCR negativity.

Median age of patients with severe COVID-19 disease is higher (73.9 years) than that of patients with mild COVID-19 infection (63.1 years) and that of not infected patients (66.6 years).

We did not find any correlation between disease severity and sex, smoke or cardiovascular

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comorbidities.

In our study, patients who were on treatment developed milder disease than cancer patients who were not on treatment. However, this result should be cautiously assumed, as we underline the higher risk of treated hematological patients with suppressed lymphocytes related immunity.

Six patients died: only one was on treatment, the other five were being followed up. Remarkably, six cycles of immunochemotherapy (R-CHOP/R-DHAP) with antiCD20 monoclonal antibody (Mab) and high dose glucocorticoids, had been administered to the patient who died on treatment; consequently, lymphocytes count and immunoglobulin levels were much lower than other patients on treatment. Anti-CD20 Mab has been known to reactivate certain viral infection. In the context of COVID-19 infection, delaying non urgent immunochemotherapy should be considered. However, more multicentric retrospective studies are needed to better understand COVID-19 infection in cancer patients and to help clinicians to decide continuing vs stopping cancer treatment in the context of COVID-19 risk. An American and Canadian cohort study is still ongoing and preliminary results had already been published. (15)

CONCLUSIONS

The acceptance of CT-defined diagnosis in high prevalence area like Bergamo highlighted a larger number of COVID-19 oncological population than RT-PCR alone, in particular asymptomatic and mild symptomatic patients. In our study severe COVID-19 disease is associated with higher median age, but we did not find any correlation between disease severity and sex, smoke or cardiovascular comorbidities. Remarkably, we observed that actively treated patients had milder disease, according to previous studies that suggested a protective role of immunosuppression.

LIST OF ABBREVIATION

CT computed tomography

RT-PCR real time polymerase chain reaction

COVID-19 coronavirus disease 19

GGO ground-glass opacities

CV cardiovascular

OR odds ratio

R-CHOP/R-DHAP: Rituximab-Cyclophosphamide-Hydroxydaunorubicin-Oncovin-Prednisone/ Rituximab-Dexamethasone-Ara-C-Cisplatin.

Mab monoclonal antibody

DECLARATIONS

Ethical Approval and Consent to Partecipate: the authors have no ethical conflicts to disclose. Informed written consent was obtained from individual participant included in the study. The study was approved by Ethics Committee of Bergamo- Papa Giovanni XXIII Hospital.

The study was performed in accordance with the Declaration of Helsinki.

Consent for publication: Informed consent was obtained from individual participant included in the study.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request..

Conflict of interest statement: the authors declare that they have no conflict of interest.

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Authors‘ contributions: FM analyzed and interpreted the patients’ data and drafted the manuscript; AD was a major contributor in writing the manuscript; all authors critically read and approved the final manuscript.

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Table 1Characteristics of cancer patients with COVID-19 infection

Patient	Sex	Age	CT features	Cancer type	Chemotherapy or follow up	Radiotherapy	Setting	Comorbidities	Smoking	SIAARTI stage	Hospital admission	Nasofaringeal swabbing	oucome
B.G.	F	74.8	GGO	Pancreas	Gemcitabine-Abraxane		T2 N+M0	Diabetes mellitus; Hypertension	former	asymptomatic	no	Negative	alive
B.V	M	56.8	GGO	Colon	FOLFIRI-Bevacizumab		Advanced	No	No	II (fever)	No	Negative	alive
B.M.	F	53.5	GGO (resolving)	Breast	Follow-up		T2N3Mo	No	Former	Asymtomatic	No	No	alive
B.G	M	73.0	GGO	Abdominal mesothelioma	Carboplatin-pemetrexed		Advanced, progression of disease	Dyslipidemia, previous colon cancer	No	III (fatigue, anorexia, abdominal pain)	No	Negative	alive
C.M.	F	61.01	GGO	Colon+breast	FOLFOX ; Everolimus+exemestane ongoing		T3 N1b M0 (colon); IV stadio (breast)	no	Former	Asymptomatic	No	No	alive
F.G.	F	72.1	GGO	Breast	Follow-up		T1bN0	Diabetes mellitus; Hypertension; ischemic cardiomiopathy	Former	Asymtpomatic	No	No	alive
F.G.	F	79.52	GGO	Colon and Breast		Yes	Advanced (colon); T2N0 (breast)	Pulmonary Embolism; Hypertension; Congestive heart failure; Chronic kidney disease	no	Asymptomatic	No	No	alive
G.M.	F	74.5	GGO and left pulmonary consolidation	Breast	Carboplatin		Advanced	Pulmonary embolism; dyslipidemia	No	II (cought)	No	No (symtoms referrred after remission)	alive
M.M.	F	58.02	GGO	Oesophageal	FLOT		Locally advanced (neoadjuvant)		si	Asymptomatic	No	No	alive
M.T.	F	70.3	GGO	Breast	Paclitaxel-Bevacizumab	20Gy (bone metastasis)	T2 N0 M1	Pulmonary embolism	former	III (fever dyspnea)	Yes	Positive	alive
S.G.	M	82.15	GGO and pulmonary consolidation	Urothelial and colon	FOLFOX		T3N2b (colon) adjuvant	Hypertension,COPD	Former	II (fever)	No	Positive	alive
S.G.	M	68.6	GGO	Bone metastasis of gastric cancer		20 Gy (bone metastasis)	advanced	Pulmonary embolism		Asymptomatic	yes for pulmonary embolism	Negative (10 days after CT scan)	alive
S.O.	F	41.95	GGO and pulmonary consolidation	Breast	Adriamycine-cyclophosphamide-taxol		T4 N2bM0 (neoadjuvant)	No	No	Asymptomatic	No	No	alive
T.E.	M	56.8	GGO	Pancreas	FOLFIRINOX		T4N1	Hypertension	No	II (fever, cought)	No	Positive	alive
T.A.	F	70.8	GGO	Breast	Adriamycine-cyclophosphamide		T1c N0 M0 (adjuvant)	HBV related HCC; hypotiroidism,previous gastric cancer; coeliac disease; COPD.	former	Asymptomatic	No	No	alive

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V.G.	M	76.3	GGO and pulmonary consolidation	LNH DLBCL	Follow-up		I A Ann Arbor	Hypertension, rheumatoid arthritis	No	Asymptomatic	No	No	alive
V.M.	M	51.6	GGO	Head and neck	Cisplatin	Yes	T 3 N0/1 M0	HCV	Yes	Asymptomatic	No	No	alive
Z.L.	F	56.7	GGO	LNH MCL	R-CHOP/R-DHAP		IV Ann Arbor	Previous choroidal melanoma	No	III->VI (fever and cought at the onset)	Yes ICU	Positive	dead
S.G.	M	74.3	GGO	Prostatic	Follow-up		Not followed in our hospital	Hypovitaminosis D	No	III (fever, cought)	Yes	Positive	alive
R.R.	F	65.47	Pulmonary consolidation	Head and neck	Carboplatin	yes	T 1N3b adjuvant. Not followed in our hospital	Hypertension, COPD, peripheral artherial disease, pulmonary embolism	Former	III (dyspnea, cought) concomitant pulmonary embolism	Yes	**Negative**	Alive
M.L.	F	78.15	GGO	Breast	Follow-up		Not followed in our hospital	Hypertension, radiation indiced pulmonary fibrosis	No	III->VI (fever, dyspnea, cought at the onset)	Yes ICU	Positive	Dead
B.A.	F	72.27	GGO	Breast	Follow-up		T 1cN0	Hypertension, Diabetes mellitus, Dyslipidemia	No	III (fever, dyspnea)	Yes	Positive	alive
C.M	F	77.4	GGO, pulmonary consolidation	Breast	Follow-up		Advanced	Hypertension	No	III->VI (nausea, fever,anorexia)	Yes ICU	Positive	Dead
R.M.	M	78.3	GGO	Urothelial	Follow-up		Not followed in our hospital	Hypertension, COPD, congestive heart failure, atrial fibrilation, ictus	No	III->VI (nausea, fever,anorexia)	Yes	Positive	Dead
N.G.	F	86.7	Pulmonary consolidation	CLL	Watch and wait follow up (never treated)			Hypertension, diabetes mellitus	No	III->VI (fever, cought, dyspnea, asthenia)	Yes	Positive	Dead
M.L.	F	62.29	GGO	MH	ABVD 6 cycles		IV b Ann Arbor. Not followed in our hospital	Previous gynecological cancer	No	III (fever)	Yes	Positive	Alive
S.M.	F	75.13	GGO	Breast	Follow-up		Not followed in our hospital	Hypertension, atrial fibrillation, diabetes mellitus	No	III->VI (fever, asthenia, cought)	Yes	Positive	Dead
G.C.	F	92.54	GGO	Gastric	Follow-up		T 3N0	Previous breast cancer, hypertension, chronic gastric reflux	No	III (dyspnea) concomitant atrial fibrillation and congestive heart failure	Yes	**Negative**	Alive
C.E.	M	56.5	GGO and pulmonary consolidations	CLL	Follow-up		Not followed in our hospital	No	No	III (fever, cought, dyspnea)	Yes	Positive	alive

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M.L.	M	85.79	GGO	Lung	Follow-up		Advanced, Progression disease. Not followed in our hospital	Dyslipidemia, hypertension, COPD, chronic renal disease	Former	III (dyspnea, fever)	Yes	Positive	Alive
F.N.	F	54	**Negative**	Breast	Adriamycine-cyclophosphamide		Locally advanced (neoadjuvant)	No	No	II (fever)	No	Positive	Alive
S.A.	F	40	**Negative** (CT scan after symptoms' remission)	Breast	Trastuzumab		T2N1M1	Hypothyroidism, multiple sclerosis	No	II (fever, cought)	No	Positive	alive

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		COVID-19 Positive		COVID-19 Negative	Total number
	Characteristics	Severe	Mild-Asymptomatic		
		15 (11%)	17 (12%)	108 (77%)	140
	Median Age (years)	73,7 (56,6÷92,5)	63,1 (58÷82,2)	66,6 (29,4÷96,1)	
Sex	Female	10	11	47	(49%)
	Male	5	6	61	(51%)
Cancer Type	GI	1	4	33	(27,1%)
	Breast	5	7	21	(23,6%)
	Lung	1	0	15	(11,4%)
	Blood Cancer	4	1	11	(11,4%)
	Utothelial	1	0	7	(5,7%)
	Pancreatic	0	2	5	(5,0%)
	Head and neck	1	1	2	(2,9%)
	Gynecological	0	0	4	(2,9%)
	Others**	0	0	4	(2,9%)
	Prostatic	1	0	2	(2,1%)
	Mesothelioma	1	0	1	(1,4%)
	Testicular	0	0	2	(1,4%)
	2 concomitant cancers	0	2*	1	(0,7%)
Comorbidity	Yes	12	8	65	(60,7%)
	No	3	9	43	(39,3%)
Smoker	Yes / Former	3	9	56	(48,6%)
	No	12	14	52	(55,7%)
On treatment	Yes	5	3	61	(49,3%)
	No	10	14	47	(50,7%)

*colon+breast; colon+urothelial; prostatic+lung

** kidney, melanoma, NET

Table 2 Clinical characteristics of cancer patients with severe, mild-asymptomatic COVID-19 infection and without infection.