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Letter to the Editor

Impact of covid-19 on patients in radiotherapy oncology departments in Spain



On December 31, 2019 a cluster of cases of pneumonia were first described in Wuhan, caused by a novel type of coronavirus called SARS-CoV-2. This virus causes various clinical manifestations encompassed under the term COVID-19 [1]. On March 11, 2020 the World Health Organization declared COVID-19 a global pandemic [2]. In Spain, the most critical period was between February 15 and May 15, 2020. During this time, various different case definitions were provided [3,4]. Initial data showed that patients with cancer are at highest risk of developing severe COVID-19 disease [5].

In this pandemic context, risks and benefits of receiving cancer treatment should be carefully weighted. Treatment RT delays and interruptions can negatively impact outcome and long-term survival. Another fact to consider is that in a ROD protective measures among staff and changes in its regular workflow must be implemented when treating COVID-19 patients [6].

The objectives of this study are to analyze the incidence of COVID-19 in patients referred to RODs in Spain, subsequent treatment modifications and to determine death-related risk factors due to COVID-19.

Material and methods

A retrospective, observational multicenter study was carried out by 66 ROD in Spain throughout a nationwide survey between February 15 and May 15, 2020. All patients scheduled for or in treatment were registered as well as those with a confirmed/suspected case of COVID-19 according to case definitions at the time [3].

Demographic data and information regarding COVID-19 infection, tumor and RT treatment was collected. SPSS statistical software package (v.22.0; IBM-SPSS; Chicago, IL; USA) was used. The study was approved by the Clinical Research Ethics Committee and is in compliance with Regulation (EU) 2016/679 on the protection of data.

Results

Between February 15 and May 15 2020, 39.848 patients were registered in all 66 RODs 329 cases of COVID-19 were declared, which represents an incidence of 0.8%. The highest incidences were recorded in Madrid (2.2%) and the Basque Country (2%). Geographical distribution can be seen in the [supplementary material](#).

Complete data for 235 COVID-19 patients was provided and analyzed. Patient characteristics are shown in [Table 1](#). Patients mean age was 65 ± 14 years. The most common symptoms were fever (63,4%), cough (42,6%) and dyspnea (31,6%). Chest radio-

graphs were performed on 82% of patients, demonstrating pneumonia in 52%, bilateral in 37%. Reverse-transcription polymerase chain reaction assay was performed in 214 patients, with positive results in 146 patients (62%). Cases were classified as: confirmed (66,4%), discarded (15,7%), probable (8,1%) and suspicious (9,8%).

The original treatment scheme was modified in 166 patients (70,6%). These treatment changes were: hypofractionation (6%), reduction of dose and/or total fractions (3%), suspension of systemic treatment (2%), RT suspension (15,3%), RT interruption (20,4%) and initiation delay (23,8%). 118 patients (50,2%) completed treatment with no incidents, 33 (14%) completed RT with a higher overall treatment time, 42 (17,8%) patients completed RT treatment before expected (due to infection, toxicity or death). 10 patients (4,2%) successfully cured from COVID-19 but died due to tumor progression.

151 patients (64,3%) required hospital admission due to COVID-19 related complications, only 4 of which (2,6%) were admitted to the Intensive Care Units. 52 patients (mortality 22,1%) died due to COVID-19 or secondary complications.

The incidence of COVID-19 in our study was 0,8%, 64,3% required hospital admission and COVID-19 mortality were 22,1%. In our study, death-related risk factors were advanced age, liver comorbidities, upper GI tract primary tumors, presence of brain metastases, palliative radiotherapy, dyspnea, pneumonia and elevated LDH levels. COVID-19 infection modified cancer treatment in 70,6%. In the univariant analysis ([supplementary material](#)), various prognostic factors for death were identified. The multivariate analysis is shown in [Table 2](#).

Discussion

COVID-19 incidence in cancer patients compared to the general population has been reported in various studies in China 1% vs 0,29% [7], in a Wuhan hospital 0,79% vs 0,37% [8] and in Madrid 4,2% vs 0,63% [9]. The prevalence of COVID-19 among cancer patients has been reported as 2,0% [10].

Patients with recent cancer diagnosis were at significantly increased risk for COVID-19 infection (OR, 7.14) and had significantly worse outcomes with higher rates of hospitalization 47,46% and death 14,93% [11].

The probability of death from COVID-19 in patients with cancer published in different studies is 25,6% [12], 28% [13,14], 30,6% [15]. In the study by Mehta et al. [13] the risk factors for death were older age, higher composite comorbidity score, ICU admission, and elevated inflammatory markers (D-dimer, lactate, and LDH). In a prospective study [14] death-related risk factors were male, advanced age, hypertension and cardiovascular disease. Leukemia

Table 1
Characteristics of COVID-19 cancer patients.

		n	%			n	%	
Sex	Male	149	63,4	Previous treatments	Surgery	89	38	
	Female	86	36,6		Chemotherapy	73	31	
comorbidities	Cardiovascular	88	37,4	RT treatment intent	Adjuvant	60	25,5	
	HTA	90	38,4		Palliative	68	28,9	
	Diabetes	47	20		Radical	107	45,5	
	Pulmonary	63	26,8	RT type	EBRT	230	97,9	
	Hepatic	15	6,4		BT	2	0,9	
	Renal	21	8,9		EBRT + BT	3	1,3	
	Primary tumour	Obesity	35	14,9	Systemic treatment	Total	130	61,3
		Upper Gastrointestinal	17	7,2		Chemotherapy	98	41,7
		Lower Gastrointestinal	13	5,5		Hormone therapy	36	15,3
		Gynecological	14	6	Timing of RT-systemic treatment	Immunotherapy	11	4,7
Haematological		16	6,8	Targeted treatments		2	0,9	
Breast		24	10,2	Concomitant		77	32,8	
Tumor Stage		Head and Neck	36	15,3	Palliative treatments	Sequential	31	13,2
		Prostate	34	14,5		Both	41	17,4
		Lung	52	22,1		Bone metastases	42	17,9
		Central Nervous System	13	5,5	Spinal compression	12	5,1	
	Urological (non-prostate)	8	3,4	Moment of COVID-19 Diagnosis	Brain metastases	22	9,4	
	Others	8	3,4		Before RT	94	40	
	I	29	12,3		During RT	118	50,2	
	II	34	14,5	After RT	23	9,8		
	III	68	28,9					
	IV	100	42,6					

Table 2
Multivariate analysis of prognostic factors for COVID-19-related death.

Variant	Cure	Death	p	OR	IC 95%
Age	63,8 ± 14 years	69,77 ± 13 years	0,000	1,069	1,031–1,106
hepatic comorbidity	Yes	8 (53,3%)	0,042	0,263	0,072–0,954
	No	175 (79,5%)			
Upper GI tumor	Yes	5 (38,5%)	0,004	7,300	1,903–28,000
	No	178 (80,2%)			
brain metastases	Yes	11 (50%)	0,006	0,222	0,075–0,653
	No	172 (80,8%)			
RT treatment	Adjuvant/radical	142 (85%)	0,041	0,320	0,107–0,955
	Palliative	41 (60,3%)			
Dyspnea	Yes	47 (60,3%)	0,000	0,251	0,115–0,545
	no	136 (86,6%)			
Pneumonia	si	80 (65,6%)	0,008	0,221	0,073–0,669
	no	68 (93,2%)			
LDH	317,9 ± 184,19	558,8 ± 553,8	1,003	1,000–1,006	

(OR 2.25) was also identified a death related risk factor in another study [15]. In our study there are very few hematological tumors (only 16 patients) and in the multivariate analysis, upper digestive tumors are those with the highest risk of death (OR 7.3).

The ESTRO Radiation Therapist Committee [16] published a series of recommendations to adapt routine clinical practice in an RT department in a pandemic situation.

Given the severity of COVID-19 infection in these patients, it is important to avoid unnecessary visits to the hospital and promote remote visits when possible, a careful selection of patients that will benefit from radiotherapy as well as those in which treatment may be delayed or even omitted, and shortening of radiation therapy [17,18]. Multiple studies have proposed different hypofractionation schemes [19]. In our study, only 6% of treatments were modified to a hypofractionation scheme, probably due to the fact that most guidelines and hypofractionation recommendations appeared after our inclusion period had concluded [20,21,22].

Conclusions

Cancer patients are at higher risk of developing more severe cases of COVID-19 with increased mortality. Therefore, it is important optimize patient and treatment selection. In patients that will

benefit from RT treatment and present mild symptoms, treatment shall be continued using hypofractionated schemes and proper protective measures.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.radonc.2021.06.001>.

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