

The impact of the coronavirus disease 2019 pandemic on the diagnosis and treatment of cancer in Northern Portugal

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Objectives The coronavirus disease 2019 (COVID-19) pandemic has affected the availability of healthcare resources, and adjustments to cancer care have been necessary considering the risk of morbidity by COVID-19 and of cancer progression. This study aims to quantify the impact of the COVID-19 pandemic on the care of patients with cancer by comparing a period of 4 months after the outbreak began (2 March 2020) with an equal period from 2019.

Methods Cancer cases of the esophagus, stomach, colon and rectum, pancreas, lung, skin-melanoma, breast, cervix, prostate, non-Hodgkin lymphoma, and leukemia from the Portuguese Oncology Institute of Porto, and diagnosed between 2 March and 1 July 2019 (before COVID-19) and 2020 (after COVID-19) were identified. Those with the first treatment outside the Portuguese Oncology Institute of Porto were excluded. Sociodemographic, clinical and treatment characteristics were obtained from the cancer registry database and clinical files.

Results The absolute number of new cancer cases decreased nearly 40% after the COVID-19 pandemic (from 1430 to 866). The largest decreases were observed for cervical (−74.3%) and prostate (−71.7%) cancers. Cases were more often diagnosed at more advanced stages in 2020 ($P = 0.001$), and the proportion of patients not starting any treatment until 1 July was just under 20%

in 2019 and nearly 40% in 2020. The median times from symptoms onset, first medical exam and first appointment to diagnosis, and from diagnosis to first appointment, multidisciplinary tumor board meeting and first treatment were shorter after COVID-19.

Conclusions There was a notable overall decrease in cancer diagnoses after COVID-19, with changes in the characteristics of incident cases. *European Journal of Cancer Prevention* 31: 204–214 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

The novel coronavirus, also known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a worldwide threat and health concern. Since its outbreak in China in late 2019, the coronavirus disease 2019 (COVID-19) has caused over 46 million confirmed cases worldwide and over 1.2 million deaths as of 1 November 2020 (World Health Organization, 2020a). The first COVID-19 case in Portugal was confirmed on 2 March 2020 in the northern region of the country (Direção-Geral da Saúde, 2020a). On 11 March 2020, the WHO announced COVID-19 was a pandemic (World Health Organization, 2020d), and on 18 March 2020, Portugal entered a State of Emergency until 2 May 2020

(Presidente da República, 2020). Unprecedented measures were adopted worldwide to mitigate the spread and morbidity of the virus through large-scale use of isolation and quarantine, closing borders, imposing social distancing limits, and enforcing nationwide lockdowns (World Health Organization, 2020c).

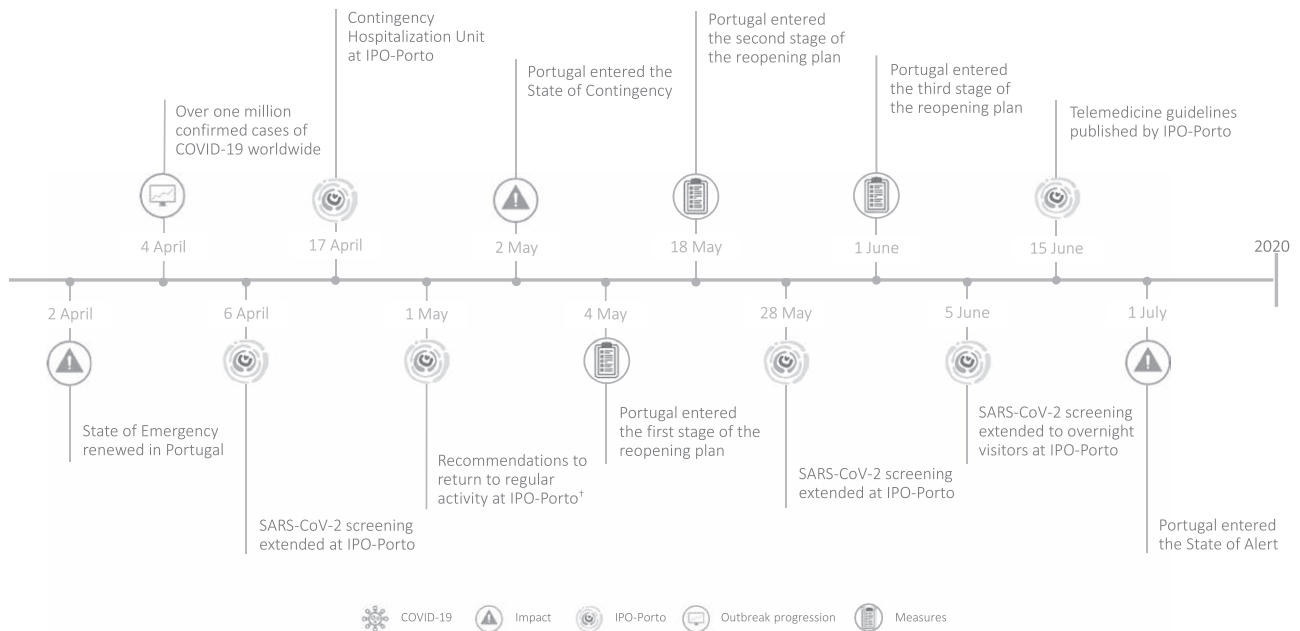
Many healthcare settings implemented minimal services, with programmed activity, including routine and specialist appointments, as well as elective procedures, being canceled, postponed or replaced by telemedicine whenever possible (Direção-Geral da Saúde, 2020b, 2020c; Mann *et al.*, 2020; Webster, 2020; World Health Organization, 2020b). Cancer screening programs were also suspended (Issaka and Somsouk, 2020; Jones *et al.*, 2020; Richards *et al.*, 2020; Roberts, 2020), with countries reporting decreases of over 80% (Green, 2020; Lusa, 2020), which led to declines in the number of cancer

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Fig. 1



Timeline of selected key events and recommendations by the Portuguese Oncology Institute of Porto during the COVID-19 pandemic.

*Recommendations by IPO-Porto on 16 March: surgical interventions; outpatient appointments; outpatient diagnostic tests and medical procedures; ambulatory care sessions; only patients who were referred by telephone were admitted to the cancer-specific emergency service.

†Recommendations to gradually and progressively return to regular activity levels at IPO-Porto in May: surgical interventions; outpatient appointments; diagnostic tests and medical procedures; regular activity for the day hospital should resume; previously suspended clinical research activities will resume. Image credit: COVID-19 - Praewpailin (Image #30784933 at VectorStock); Impact – janjf93 (Image #2126885 at Pixabay); Outbreak progression – janjf93 (Image #2126876 at Pixabay); Measures – Kaliene (Image #4747711 at Pixabay).

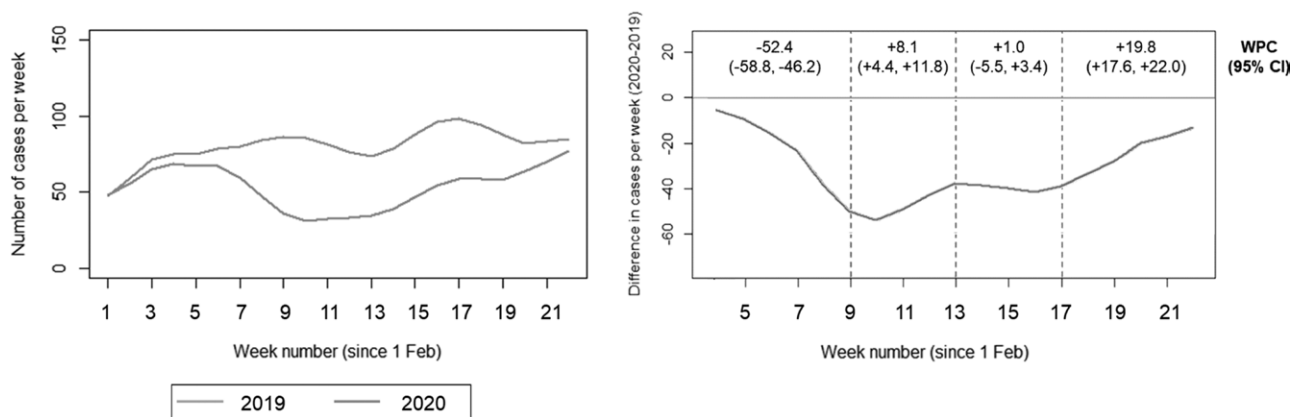
COVID-19, coronavirus disease 2019; IPO-Porto, Portuguese Oncology Institute of Porto.

cases diagnosed (Dinmohamed *et al.*, 2020; Green, 2020). Additionally, widespread restrictions were imposed on nonurgent medical admissions, while hospital-based outpatient care and transfers between hospitals were limited to urgent cases (Al-Shamsi *et al.*, 2020; Driggin *et al.*, 2020; Nepogodiev and Bhangu, 2020). These public health measures were implemented to ensure essential clinical care while reducing the risk of SARS-CoV-2 infection among patients and healthcare professionals. Concurrently, healthcare users have avoided in-person services due to fear of being infected by SARS-CoV-2 (Barómetro COVID-19, 2020; evidation, 2020). As a result, there was a decrease in the number of routine visits with healthcare professionals for follow-up of chronic diseases, such as obtaining medication refills and dose adjustments or other preventive services (evidation, 2020; Fox *et al.*, 2020; Vaduganathan *et al.*, 2020). There was also a drop in the access to immunization programs, particularly among children (McDonald *et al.*, 2020; Santoli *et al.*, 2020), bringing national and international health authorities to advise that routine immunization services should continue to function normally (Direção-Geral da Saúde, 2020d; The Regional Office for Europe of the World Health Organization, 2020).

Individuals with underlying health conditions, such as active cancer, have been found to be more vulnerable to complications from COVID-19, including increased need for ventilation or ICU admission (Liang *et al.*, 2020; Miyashita *et al.*, 2020; Zhang *et al.*, 2020), as well as higher mortality (Kuderer *et al.*, 2020; Miyashita *et al.*, 2020; Zhang *et al.*, 2020). Additionally, patients with cancer may have a higher risk of infection due to changes in their immune system, which may be related to cancer itself, certain types of treatment, poor nutrition, other health problems or medications unrelated to cancer (Rolston, 2017). Oncology centers introduced strict preventive strategies to reduce the risk of infection with SARS-CoV-2, namely robust infection and environmental control, additional hygiene measures, enforcing social distancing and reducing patients' overall time spent in a hospital setting (American Society of Clinical Oncology, 2020; European Society for Medical Oncology, 2020; Ueda *et al.*, 2020). Treatment pathways were also altered to minimize the potential exposure of patients with cancer to SARS-CoV-2 and to reduce the risk of infection (American Society of Clinical Oncology, 2020; European Society for Medical Oncology, 2020; Richards *et al.*, 2020; Ueda *et al.*, 2020).

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Fig. 2



Cancer cases diagnosed between 1 February and 1 July in 2019 and 2020 by weeks (following the exclusion of cancer cases with first treatment outside the Portuguese Oncology Institute of Porto) (left), and difference in cancer cases diagnosed per week, weekly percent change and corresponding 95% confidence intervals (right). CI, confidence interval; WPC, weekly percent change.

The COVID-19 pandemic affected every aspect of healthcare, including the delivery of care to patients with cancer. Many oncological societies around the world, namely the European Society for Medical Oncology and the American Society of Clinical Oncology, recommend that health professionals in cancer centers adjust their routines as necessary by increasing telemedicine services, reducing clinic visits, and switching to subcutaneous or oral therapies, rather than intravenous ones, when possible (American Society of Clinical Oncology, 2020; European Society for Medical Oncology, 2020). As such, healthcare professionals involved in the diagnosis, treatment and follow-up of patients with cancer had to consider how to balance the delay in cancer diagnosis or treatment against the risk of SARS-CoV-2 infection, mitigate the risks for significant care disruptions associated with the social distancing limits in place and manage the appropriate allocation of available healthcare resources (Kutikov *et al.*, 2020), all of which may impact the prognosis of patients with cancer (Al-Quteimat and Amer, 2020; Dinmohamed *et al.*, 2020; Jones *et al.*, 2020). Therefore, this study intends to quantify the impact of the COVID-19 outbreak on the care of patients treated at the Portuguese Oncology Institute of Porto (IPO-Porto) by comparing a period of four months after the beginning of the outbreak in Portugal (2 March 2020) with the same period in the previous year.

Methods

Setting

IPO-Porto is a highly differentiated organization belonging to the National Health Service, which provides specialized cancer care. IPO-Porto is the largest cancer-dedicated hospital in Portugal, admitting patients from

all over the country, though mainly from the Northern region (Instituto Português de Oncologia do Porto). IPO-Porto admits over 7500 new cancer cases per year (Registo Oncológico - Instituto Português de Oncologia do Porto, 2017), corresponding to nearly half and one-fifth of all cases diagnosed in the Northern region (Registo Oncológico Regional do Norte, 2013) and the country (Ferlay *et al.*, 2018), respectively, and provides healthcare to more than 45 000 patients covering the entire cancer continuum, from diagnosis to treatment (surgery, radiotherapy, systemic therapy and supportive care) and follow-up (Instituto Português de Oncologia do Porto, 2019). Additionally, IPO-Porto has a cancer-specific emergency service that aims to provide continuous medical care and assistance to patients with cancer. It is open 24 h a day to receive any patient with cancer registered at IPO-Porto who is in active treatment for oncological disease and whose acute situation derives from the disease itself or is induced by treatment, as well as any patient with an acute oncological pathology who has been referred (Instituto Português de Oncologia do Porto, 2020b).

The key events and recommendations by IPO-Porto during the COVID-19 pandemic are presented in Fig. 1 and described in detail in the online Supplementary Material, Supplemental digital content 1, <http://links.lww.com/EJCP/A323> (COVID-19 plan at IPO-Porto).

Study design and data collection

Cases of invasive tumors of the esophagus (code C15 of the International Statistical Classification of Diseases and Related Health Problems 10th Revision [ICD-10]) (World Health Organization, 1992), stomach (C16), colon and rectum (C18-20), pancreas (C25), lung (C34), skin-melanoma (C43), breast (C50), cervix (C53), prostate

(C61), non-Hodgkin lymphoma (C82-86, C96), and leukemia (C91-95) diagnosed between 1 February 2019 and 1 July 2019, and 1 February 2020 and 1 July 2020 at IPO-Porto were identified.

Information on cases' sociodemographic (sex, age, municipality of residence), cancer (ICD-10 code, site, laterality, histological type and stage, as applicable), presence of symptoms, referral pathway (i.e. doctor, another hospital, organized or opportunistic screening,

appointment), treatment received (surgery, radiotherapy, brachytherapy, chemotherapy, chemoradiotherapy, immunotherapy, hormone therapy, targeted therapy, as applicable) and possible complications [anastomotic dehiscence, Clavien–Dindo classification (Clavien *et al.*, 2009), oncology-specific emergency visits, hospitalizations, as applicable] were collected from the cancer registry database and clinical files, with follow-up to 1 July 2019 or 2020, as relevant. Additionally, whenever applicable, the following dates were extracted: onset of

Table 1 Sociodemographic, clinical and treatment characteristics of cancer cases diagnosed and treated before and after the onset of COVID-19 (2 March to 1 July 2019, and 2 March to 1 July 2020, respectively)

	Cancer diagnosis		P value	Proportional variation % (95% CI) ^a
	Before COVID-19 N (%)	After COVID-19 N (%)		
	1430	866		−39.4 (−44.3 to −34.1)
Sex				
Men	753 (52.7)	418 (48.3)	0.041	−44.5 (−57.4 to −37.4)
Women	677 (47.3)	448 (51.7)		−33.8 (−41.3 to −25.4)
Age (years)				
<55	349 (24.4)	220 (25.4)	0.471	−37.0 (−46.7 to −25.4)
55–64	358 (25.0)	201 (23.2)		−43.9 (−52.8 to −33.3)
65–74	434 (30.3)	251 (29.0)		−42.2 (−50.5 to −32.4)
>74	289 (20.2)	194 (22.4)		−32.9 (−44.0 to −19.8)
Place of residence ^b				
Porto Metropolitan Area	714 (49.9)	438 (50.6)	0.764	−38.7 (−45.5 to −31.0)
Outside the Porto Metropolitan Area	716 (50.1)	428 (49.4)		−40.2 (−47.0 to −62.6)
Cancer site ^c				
Esophagus	27 (1.9)	18 (2.1)	<0.001	−33.3 (−62.8 to +21.0)
Stomach	147 (10.3)	81 (9.3)		−44.9 (−58.0 to −27.7)
Colon and rectum	184 (12.9)	115 (13.3)		−37.5 (−50.5 to −21.1)
Pancreas	41 (2.9)	37 (4.3)		−9.8 (−42.1 to +40.7)
Lung ^d	209 (14.6)	164 (18.9)		−21.5 (−36.0 to −3.8)
Skin-melanoma	81 (5.7)	56 (6.5)		−30.9 (−50.8 to −2.8)
Breast ^d	370 (25.9)	227 (26.2)		−38.6 (−48.0 to −27.6)
Cervix	35 (2.4)	9 (1.0)		−74.3 (−87.6 to −46.6)
Prostate	233 (16.3)	66 (7.6)		−71.7 (−78.4 to −62.8)
Non-Hodgkin lymphoma	81 (5.7)	75 (8.7)		−7.4 (−32.4 to +26.8)
Leukemia	22 (1.5)	18 (2.1)	−18.2 (−56.1 to +52.5)	
Stage ^e				
I	455 (35.5)	216 (30.9)	0.001	−52.5 (−59.6 to −44.2)
II	282 (22.0)	151 (21.6)		−46.5 (−56.1 to −34.7)
III	246 (19.2)	113 (16.2)		−54.1 (−63.2 to −42.6)
IV	297 (23.2)	219 (31.3)		−26.3 (−38.4 to −12.2)
Missing	47	74		57.4 (+9.2 to +126.9)
Symptomatic				
No	524 (36.6)	224 (25.9)	<0.001	−57.3 (−63.4 to −50.0)
Yes	799 (55.9)	586 (67.7)		−26.7 (−34. to −18.4)
Unknown	107	56		−47.7 (−61.1 to −27.7)
Referral pathway				
Doctor	730 (51.0)	488 (56.3)	<0.001	−33.2 (−40.4 to −25.0)
Another hospital	494 (34.6)	258 (29.8)		−47.8 (−55.1 to −39.3)
Organized screening	142 (9.9)	38 (4.4)		−73.2 (−81.3 to −61.7)
Opportunistic screening	31 (2.2)	16 (1.9)		−48.4 (−71.8 to −5.6)
Appointment	30 (2.1)	54 (6.2)		80.0 (+15.2 to +181.2)
Missing	3	12		300.0 (+12.9 to +1317.4)
First treatment ^f				
Surgery	510 (35.7)	219 (25.3)	<0.001	−57.1 (−63.3 to −49.7)
Radiotherapy	209 (14.6)	50 (5.8)		−76.1 (−82.4 to −67.4)
Brachytherapy	28 (2.0)	5 (0.6)		−82.1 (−93.1 to −53.7)
Systemic treatment				
Chemotherapy	280 (19.6)	187 (21.6)	<0.001	−33.2 (−44.5 to −19.6)
Chemoradiotherapy	26 (1.8)	3 (0.3)		−88.5 (−96.5 to −61.9)
Immunotherapy	4 (0.3)	6 (0.7)		50.0 (−57.7 to +431.5)
Targeted therapy	12 (0.8)	24 (2.8)		100.0 (0.00 to +300.0)
Hormone therapy	78 (5.4)	40 (4.6)		−48.7 (−65.0 to −24.9)
Other	1 (0.1)	3 (0.3)		200.0 (−68.8 to +2784.1)
None (as of 1 July) ^g	282 (19.3)	329 (38.0)	16.7 (−0.5, to +36.8)	

(Continued)

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Table 1 (Continued)

	Cancer diagnosis		P value	Proportional variation % (95% CI) ^a
	Before COVID-19 N (%)	After COVID-19 N (%)		
Complications				
Anastomotic dehiscence (yes) ^h	10 (2.0)	2 (0.9)	0.308	−80.0 (−95.6 to −8.7)
Clavien–Dindo Classification ^h (Clavien <i>et al.</i> , 2009)				
None	449 (88.0)	200 (91.3)		−55.5 (−62.3 to −47.4)
I–II	37 (7.2)	12 (5.5)		−67.6 (−83.1 to −37.8)
III–V	24 (4.7)	7 (3.2)	0.422	−70.8 (−87.4 to −32.3)
Cancer-specific emergency visits (yes) ⁱ	173 (12.3)	131 (15.3)	0.038	−24.3 (−39.6 to −5.0)
Hospitalizations (yes) ^j	341 (24.1)	203 (23.7)	0.875	−40.2 (−50.0 to −29.2)
COVID-19 (yes) ^{kl}	1 (0.1)	4 (0.5)	–	–

CI, confidence interval; COVID-19, coronavirus disease 2019.

^aCalculated using Poisson regression.

^bPorto Metropolitan Area includes the following municipalities: Arouca, Espinho, Gondomar, Maia, Matosinhos, Oliveira de Azeméis, Paredes, Porto, Póvoa de Varzim, Santa Maria da Feira, Santo Tirso, São João da Madeira, Trofa, Vale de Cambra, Valongo, Vila Nova de Gaia, Vila do Conde.

^cInternational Statistical Classification of Diseases and Related Health Problems 10th Revision (World Health Organization, 1992): esophagus – C15; stomach – C16; colon and rectum – C18–20; pancreas – C25; lung – C34; skin-melanoma – C43; breast – C50; cervix – C53; prostate – C61; non-Hodgkin lymphoma – C82–86, C96; leukemia – C91–95.

^dLung: 95 left, 106 right, 8 unknowns/missing and 72 left, 88 right, 4 unknowns/missing; breast: 182 left, 182 right, 6 unknowns/missing and 117 left, 106 right, 4 unknowns/missing in 2 March 2019 to 1 July 2019 and 2 March 2020 to 1 July 2020, respectively.

^eSolid tumors only (P values for comparisons do not include unknowns). Esophagus: 0 I, 2 II, 7 III, 14 IV, 4 unknowns and 0 I, 1 II, 4 III, 9 IV, 4 unknowns (P value = 0.974); stomach: 42 I, 13 II, 24 III, 56 IV, 12 unknowns and 11 I, 3 II, 6 III, 37 IV, 24 unknowns (P value = 0.032); colon and rectum: 28 I, 47 II, 63 III, 37 IV, 9 unknowns and 14 I, 23 II, 39 III, 25 IV, 14 unknowns (P value = 0.776); pancreas: 4 I, 5 II, 6 III, 23 IV, 3 unknowns and 4 I, 3 II, 7 III, 19 IV, 4 unknowns (P value = 0.894); lung: 42 I, 14 II, 33 III, 115 IV, 5 unknowns and 27 I, 14 II, 18 III, 99 IV, 6 unknowns (P value = 0.380); skin-melanoma: 37 I, 18 II, 20 III, 6 IV and 28 I, 13 II, 3 III, 3 IV, 9 unknowns (P value = 0.069); breast: 263 I, 65 II, 20 III, 13 IV, 9 unknowns and 120 I, 61 II, 23 III, 14 IV, 9 unknowns (P value < 0.001); cervix: 7 I, 21 II, 4 III, 3 IV and 2 I, 6 II, 1 III, 0 IV (P value = 0.840); prostate: 32 I, 97 II, 69 III, 30 IV, 5 unknowns and 10 I, 27 II, 12 III, 13 IV, 4 unknowns (P value = 0.237) in 2019 and 2020, respectively.

^fFirst treatment received until 1 July of the respective year of diagnosis. 54 and 30 cases (2019 and 2020, respectively) received chemotherapy and targeted therapy on the same day, chemotherapy was considered as first; 1 case (2020) received hormone therapy and targeted therapy on the same day, hormone therapy was considered as first; 2 cases (2019) received chemotherapy and hormone therapy on the same day, chemotherapy was considered as first; 209 and 50 cases (2019 and 2020, respectively) received hormone therapy and radiotherapy on the same day, hormone therapy was considered as first.

^gReasons for no treatment: 168 and 259 cases awaiting treatment to begin; 22 and 19 cases with cancer too advanced for treatment; 24 and 24 cases cannot undergo treatment due to current physical condition; 36 and 8 cases currently under surveillance; 32 and 19 cases died before any treatment in 2019 and 2020, respectively.

^hFollow-up until 1 July of the respective year of diagnosis. Among those who underwent surgery as first treatment (n = 510 and n = 219 in 2019 and 2020, respectively).

ⁱFollow-up until 1 July of the respective year of diagnosis. Among 1412 patients with cancer (18 patients had two primary cancers) and 855 patients with cancer (11 patients had two primary cancers) in 2019 and 2020, respectively.

^jCOVID-19 diagnosis between 2 March and 1 July 2020.

symptoms; diagnosis; first medical exam; first scheduled appointment; multidisciplinary tumor board meeting; each treatment.

Information regarding COVID-19 diagnosis from 2 March to 1 July 2020 was also obtained for all patients with cancer included in the study.

Statistical analyses

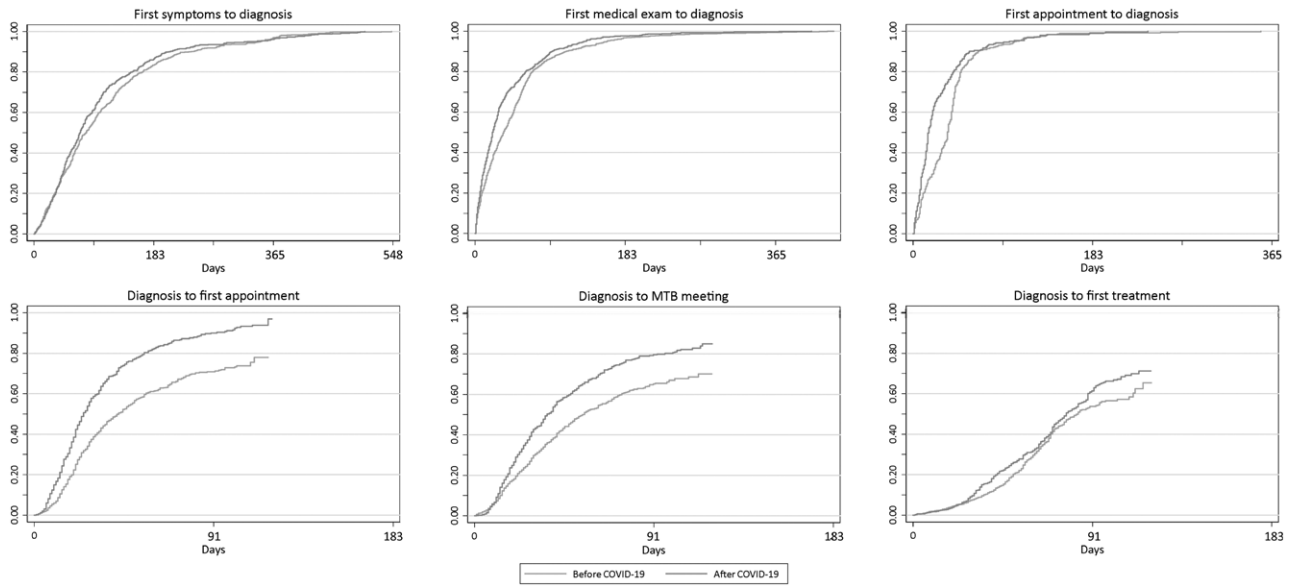
For the purposes of the current study, cancer cases who received the first cancer treatment outside IPO-Porto were excluded, except for cases with skin-melanoma. Patients' characteristics are presented as counts and proportions for all categorical variables and were compared using the chi-square test. The numbers of cancer cases per week at IPO-Porto between 1 February and 1 July 2019 and 2020 were plotted using locally estimated scatterplot smoothing (LOESS, $f = 0.3$). Additionally, Joinpoint regression (Joinpoint software, Version 4.8.0.1; (Kim *et al.*, 2000) National Cancer Institute, Bethesda, Maryland, USA) was used to evaluate changing linear trends in the difference between the numbers of cancer cases diagnosed in 2020 and 2019 across consecutive time periods (March–June) with a joinpoint occurring when the linear trend changed significantly in either direction

or magnitude. For each of the identified trends, weekly percent change (WPC) estimates and corresponding 95% confidence intervals (95% CIs) were computed by fitting a regression line to the natural logarithm of the difference in the numbers of cases using calendar week as a regression variable.

The dates of manifestation of the first symptoms or routine exams, first medical exam at IPO-Porto, first scheduled appointment at IPO-Porto, multidisciplinary tumor board meeting at IPO-Porto and first treatment received at IPO-Porto were used to calculate the time between each and the date of cancer diagnosis (i.e. the date of the first histological confirmation, usually the date when the biopsy specimen was taken).

The time in days from symptoms onset, first medical exam and first appointment to diagnosis, and from diagnosis to first scheduled appointment, multidisciplinary tumor board meeting and first treatment were plotted (1-Kaplan–Meier) and compared between the two periods [before (2 March to 1 July 2019) and after (2 March to 1 July 2020) COVID-19] using the log rank test. Additionally, the median with percentiles 25 and 75 (P25–P75) time in days were quantified.

Fig. 3



Observed cumulative proportion (calculated using the 1-Kaplan–Meier estimator) of diagnosis following first symptoms, first medical exam and first appointment, and of first appointment, multidisciplinary tumor board meeting and first treatment following diagnosis according to the period of diagnosis (2 March to 1 July 2019 vs. 2 March to 1 July 2020 with follow-up to 1 July 2019 or 2020, respectively). COVID-19, coronavirus disease 2019; MTB, multidisciplinary tumor board meeting.

Table 2 Median time in days from onset of symptoms, first medical exam and first appointment to diagnosis, and from diagnosis to first appointment, multidisciplinary tumor board meeting and first treatment before and after the onset of COVID-19 (2 March to 1 July 2019 and 2 March to 1 July 2020 with follow-up to 1 July 2019 or 2020, respectively)

	Before COVID-19			After COVID-19			P value
	Total (N)	Event [N (%)]	Median time in days (P25–P75)	Total (N)	Event [N (%)]	Median time in days (P25–P75)	
Onset of symptoms and diagnosis	567	–	84 (41–150)	448	–	71 (39–129)	0.020
First medical exam and diagnosis	1254	–	39 (14–64)	788	–	21 (8–53)	<0.001
First appointment and diagnosis	364	–	36 (15–46)	243	–	16 (8–36)	<0.001
Diagnosis and first appointment	1066	613 (57.5)	34 (20–70)	623	443 (71.1)	22 (14–38)	<0.001
Diagnosis and multidisciplinary tumor board meeting ^a	1398	692 (49.5)	46 (24–98)	846	501 (59.2)	35 (18–63)	<0.001
Diagnosis and first treatment	1430	1148 (80.3)	84 (57–...)	866	537 (62.0)	80 (51–...)	<0.001

..., not yet available.

COVID-19, coronavirus disease 2019; P25–P75, percentiles 25 and 75.

^a32 and 20 cancer cases had a multidisciplinary tumor board meeting before diagnosis in 2019 and 2020, respectively.

Stratified analyses were conducted by sex, age (<55, 55–64, 65–74, >75 years), residence (Porto vs. outside Porto), cancer site, cancer group (digestive, and lymphoid, hematopoietic and related tissue), stage (I, II, III, IV) and month of diagnosis (March, April, May, June).

All analyses were performed using STATA 15 (StataCorp, College Station, Texas, USA). Results were considered statistically significant for P values less than 0.05.

Ethics approval

The study was approved by the Ethics Committee of IPO-Porto (Ref. CES IPO: 164/020). The study was performed in accordance with the Declaration of Helsinki. The

data contained no unique personal identifiers and were extracted from the cancer registry database and clinical files. Hence, patient informed consent was not required.

Results

The numbers of cancer cases diagnosed per week at IPO-Porto between 1 February and 1 July of 2019 and 2020 are shown in Fig. 2. Overall, there was a significant decrease of 39% (95% CI: –44.3, –34.1) in the absolute number of cancer cases after the COVID-19 pandemic (from 1430 in 2019 to 866 in 2020), whereas there was no significant difference between years in February (–6.9%; 95% CI: –20.5 to 9.0; Supplementary Table S1, Supplemental digital content 1, <http://links.lww.com/EJCP/A323>). The

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difference in the numbers of cancer cases in 2020 in relation to 2019 fluctuated between March and July, with a 52.4% weekly variation in the difference until the ninth week, when the largest difference was observed (-71.4% ; 95% CI, -81.5 to -55.8 in the absolute number of cases in 2020 in relation to 2019). Following this, there was a gradual increase in the number of cases in 2020, with the number of cases reaching that of the previous year by the end of the study period in July.

Table 1 shows the sociodemographic, clinical and treatment characteristics of cancer cases diagnosed before (2 March and 1 July 2019) and after (2 March and 1 July 2020) the onset of COVID-19, and stratified analyses are presented in Supplementary Table S2, Supplemental digital content 1, <http://links.lww.com/EJCP/A323>. There was a greater decrease among males than females, which resulted in a lower proportion of cases among males after COVID-19. The largest decreases from before to after COVID-19 were observed for cervical and prostate cancers, and the lowest for non-Hodgkin lymphoma and leukemia, as well as for pancreas and lung cancers leading to a higher proportion of cases in the latter sites in 2020. After COVID-19, cases were more often diagnosed at more advanced stages and symptomatic, while less often identified through cancer screening. Just under 20% of cases diagnosed in 2019 and nearly 40% of cases from 2020 had not received any treatment until the beginning of July of the respective year of diagnosis, and there was a higher proportion of cancer-specific emergency visits among cases diagnosed in 2020. Five COVID-19 diagnoses (1 among a patient with cancer from 2019 and the remaining in patients diagnosed in 2020) were confirmed among the patients with cancer included in this study.

Figure 3 depicts the cumulative probability of diagnosis following first symptoms, first medical exam and first appointment, and of first appointment, multidisciplinary tumor board meeting and first treatment following diagnosis; the median time between each is presented in Table 2, and stratified analyses are presented in Supplementary Table S3, Supplemental digital content 1, <http://links.lww.com/EJCP/A323>. The median time between the onset of symptoms and diagnosis decreased from 84 days before COVID-19 to 71 after; likewise, the median time from first medical exam to diagnosis declined from 39 days before to 21 days after COVID-19. Regardless of when the first appointment at IPO-Porto occurred, a shorter median time was observed after COVID-19 (16 days for appointments before diagnosis and 22 days for appointments after diagnosis) than before (36 and 34 days, respectively). The median time from diagnosis to multidisciplinary tumor board meeting decreased from 46 days before COVID-19 to 35 after, and there was also a decline in the median time between diagnosis and first treatment from 84 days before COVID-19 to 80 days in 2020.

Discussion

The current study shows a notable decrease in the absolute number of cancer cases after the COVID-19 outbreak compared to the same period in the previous year. This was particularly evident during the month of March with a WPC in the difference in the number of cases of -52.4% , which was followed by a gradual increase until the end of the study period. Significant differences in the characteristics of incident cases, namely regarding sex, cancer site and stage at diagnosis, presence of symptoms, referral pathway, first treatment received, and cancer-specific emergency visits, were observed. Moreover, although fewer cancer cases received the first treatment in 2020, IPO-Porto provided timely care to patients as the median times from symptoms onset, first medical exam and first appointment to diagnosis, and from diagnosis to the first appointment, multidisciplinary tumor board meeting and first treatment were shorter after compared to before COVID-19.

The substantial impact of the COVID-19 pandemic on the number of cancer diagnoses at IPO-Porto, with a nearly 40% decrease compared to the same period in 2019, is in accordance with the observed in other countries. A study from the United States of America found that the weekly number of new cancer cases, considering breast, colon and rectum, lung, pancreas, stomach, and esophagus, decreased by over 45% during the pandemic (Kaufman *et al.*, 2020). Likewise, in the Netherlands, data from the nationwide cancer registry between 24 February and 12 April 2020 showed a decrease in the number of diagnoses compared to the period before the outbreak (Dinmohamed *et al.*, 2020).

The current study found a lower proportion of cases among males after COVID-19, which was also observed when comparing February 2019 and 2020. Although the number of cancer cases diagnosed in February was low, and the latter difference was not statistically significant, the sex proportions were similar to those before and after COVID-19. In the United States of America, Kaufman *et al.* (2020) also did not find differences in the overall sex distribution when comparing patients diagnosed from 6 January 2019 to 29 February 2020 to those from 1 March to 18 April 2020.

Among the cancer sites considered in the present study, the largest decreases were observed for cervical and prostate cancers leading to a lower proportion of cases in these sites following COVID-19. In the United States of America, the largest differences in the weekly number of new cancer cases were observed for breast cancer, followed by colorectal cancer (Kaufman *et al.*, 2020). While, in the Netherlands, the decrease in cancer cases was most pronounced for skin cancers (excluding basal cell carcinoma), followed by breast and hematological cancers (Dinmohamed *et al.*, 2020).

To relieve the demand on the healthcare system due to COVID-19, national and regional organized screening programs for breast, colorectal and cervical cancer were temporarily suspended (Green, 2020; Issaka and Somsouk, 2020; Jones *et al.*, 2020). In the United States of America, screening appointments for cervical, colon and breast cancer in March 2020 decreased by over 85% compared to mean volumes between 1 January 2017 and 19 January 2020. Also, an estimated 420 000 cancer screenings were deferred between 15 March and 16 June 2020 as a result of the COVID-19 pandemic (Mast and Rio, 2020). Likewise, data from Cancer Research UK revealed that over two million people were waiting for cancer screening, tests and treatments due to the 10-week lockdown in the country (Roberts, 2020). In Portugal, imaging centers reported to be conducting only 10% of their usual volume of mammograms, while colorectal screening by endoscopy came to a halt during the State of Emergency (Lusa, 2020). In fact, we observed a smaller number of cancer cases being referred to IPO-Porto from organized screening during the COVID-19 pandemic, and there were fewer breast, cervical and colorectal cancer cases in 2020, which are included in Portugal's organized cancer screening programs (Direção-Geral da Saúde, 2017). On the other hand, we found that cancer cases were more often diagnosed at more advanced stages, and there was a higher proportion of symptomatic cases during the COVID-19 pandemic. More importantly, the effect of cancer screening suspensions may be more pronounced in the future as early diagnoses from screening will be delayed leading to symptoms-based diagnosis at more advanced stages (Hamilton *et al.*, 2016).

The lower number of cancer diagnoses during the COVID-19 pandemic, as well as changes in the distribution of cancer sites, occurred as a result of patient, doctor and healthcare factors. Healthcare institutions, including oncology centers, implemented several measures to ensure necessary services, while reducing the risk of infection by COVID-19 among patients, as well as healthcare professionals (Direção-Geral da Saúde, 2020b; c; Mann *et al.*, 2020; Webster, 2020; World Health Organization, 2020b). At IPO-Porto specifically, a Contingency Plan was first published in mid-February, which was revised a month later with additional recommendations (Instituto Português de Oncologia do Porto, 2020a). These measures, along with the State of Emergency declared in Portugal on 18 March (República Portuguesa, 2020), likely contributed to the significant WPC decrease in the difference of the number of cancer cases diagnosed during the month of March. Additionally, beginning in May, IPO-Porto recommended that activity levels should gradually and progressively return to normal (Instituto Português de Oncologia do Porto, 2020a), and Portugal entered the State of Contingency (República Portuguesa, 2020), which probably led to the observed WPC increase in the difference of the number of cancer cases diagnosed in May and June.

Furthermore, in many healthcare settings, routine and specialist medical appointments, including opportunistic cancer screening, were canceled, postponed or replaced by telehealth (Núcleo Regional do Norte, 2020), which also likely contributed to fewer cancer diagnoses or referrals. Patients may have also delayed routine health procedures or the assessment of mild symptoms due to fear of visiting healthcare providers that were also handling suspected COVID-19 cases (Rosenbaum, 2020). Nevertheless, we may expect that patients with well-recognized symptoms, including a new mass or rectal bleeding, will present to healthcare services, while vague cancer symptoms, namely fatigue or weight loss, may be dismissed by patients (Jones *et al.*, 2020). A report from a Slovenian cancer-dedicated institute showed a significant decrease in first referrals for cancer services, first appointments, imaging studies and cancer notifications in April 2020 (Zadnik *et al.*, 2020). In the United States of America, all outpatient visits dropped by nearly 60% in April 2020, which recovered until mid-June to nearly reaching prepandemic levels by the end of July. Nevertheless, the cumulative number of missed ambulatory care visits since mid-March remained important and continued to grow (Mehrotra *et al.*, 2020). In Portugal, the National Health Service recorded a decrease of nearly half a million primary healthcare and hospital appointments, while there were 9000 fewer surgeries and emergency room visits since the COVID-19 pandemic began in March (Oliveira, 2020). Indeed, we found fewer referrals from other hospitals and from opportunistic screening, while there were more referrals from doctors and from other appointments at IPO-Porto, as well as more symptomatic cases after COVID-19.

Although IPO-Porto made several changes to their regular operations between mid-March and early May, we found that the institute was generally able to continue providing services with shorter median wait times being observed in the post-COVID-19 period. This may be due to the fact that a lower number of cancer cases was diagnosed overall during the COVID-19 pandemic and that over one-third of patients with cancer had not received the first treatment by the end of the study period in 2020 in comparison with 2019, which may have facilitated the continuum of care of the patients undergoing treatment. Treatment disruptions or modifications as a result of the pandemic were described elsewhere. The Portuguese Oncology Institute of Lisbon reported a decrease in the number of appointments during the COVID-19 period compared to the same period in the previous year, and despite delays and postponements, more chemotherapy sessions, radiotherapy and immunotherapy treatments were performed in 2020 (Simões, 2020). In Canada, thoracic oncologists at a university health center found that over half of patients receiving treatment for lung cancer between March and May 2020 underwent at least one change in their cancer treatment plan (Elkrief *et al.*, 2020). In particular, there were delays in palliative and

adjuvant chemotherapy, while some treatments stopped, and there were also changes in the dosing and scheduling of chemotherapy. Likewise, a survey conducted among patients with breast cancer in the United States of America found that nearly half encountered treatment delays, particularly younger patients (Papautsky and Hamlish, 2020). Finally, two leading cancer centers in Pakistan, which usually receive 850 new patients with cancer per month for treatment, admitted no patients in the first weeks of April 2020 (Yusuf, 2020). The authors also found that the number of patients beginning chemotherapy and radiotherapy decreased by two-thirds and by half, respectively, and less than 5% of usual elective surgical procedures were performed.

Strengths and limitations

We used two interrupted time series of 5 months for a standardized comparison of incident cancer cases diagnosed before COVID-19 and after, which allowed us to evaluate the impact of the COVID-19 pandemic at the start in March 2020 as well as the return to nearly normal levels by the end of the study period. The possibility of assessing trends since the beginning of the pandemic, and to compare them with a similar period from the previous year, as well as the comparison of data from the month of February, support the validity of our findings.

Despite a usual lag between the incidence of cancer cases and their registration, which improves data completeness and quality but prevents the timely availability of data, to overcome the potential delay in the registration of cases, particularly in 2020, we opted to exclude patients who received the first treatment outside IPO-Porto from our analyses, to ensure the comparability between the two periods. Supplementary Figure S1, Supplemental digital content 1, <http://links.lww.com/EJCP/A323>, shows the number of cancer cases diagnosed per week at IPO-Porto between 1 February and 1 July of 2019 and 2020 without excluding those with the first treatment outside IPO-Porto, and as expected, there was a higher number of patients with cancer diagnosed throughout the entire study period in 2019. This is because cancer cases diagnosed in 2019 and treated elsewhere are more likely to have potentially received additional care at IPO-Porto until 2020 than those diagnosed in 2020, and as such, were included in the cancer registry.

Detailed patient-level data were obtained, which allowed us to understand the impact of the COVID-19 pandemic on cancer diagnoses and treatment beyond quantifying differences in the distribution of cancer sites or the activity of the institution in terms of the number of surgeries, treatments or appointments. In fact, we were also able to compare median times to and from diagnosis considering symptoms, appointments and first treatment, among others, as well as describe differences in complications

among patients diagnosed with cancer before and after COVID-19.

This study includes data from a single-center located in Northern Portugal, which may impair the generalizability of our results to other settings. Nonetheless, IPO-Porto is the largest cancer-dedicated hospitals in Portugal, receiving patients from any part of the country with different sociodemographic backgrounds, and our study includes patients presenting a large spectrum of cancer sites, including all stages and histological types.

Conclusion

The results presented here describe the impact of the COVID-19 outbreak on the care of patients with cancer at IPO-Porto, while identifying needs to be considered in planning for the coming months. As the pandemic progresses, it will be important to determine how delays in diagnosis and treatment will impact clinical outcomes among these patients, which may subsequently lead to an increase in cancer morbidity and mortality. Furthermore, when normal service resumes at a population and health-service level, there will likely be a backlog of patients with potential cancer symptoms needing assessment along with the expected volume of new cancer cases under normal circumstances that may overload oncology cancer services. Therefore, healthcare services should plan accordingly to ensure high-quality cancer care for all.

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Conflicts of interest

There are no conflicts of interest.

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