Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Prevalence and impact of COVID-19 sequelae on treatment and survival of patients with cancer who recovered from SARS-CoV-2 infection: evidence from the OnCovid retrospective, multicentre registry study

*David J Pinato, Josep Tabernero, Mark Bower, Lorenza Scotti, Meera Patel, Emeline Colomba, Saoirse Dolly, Angela Loizidou, John Chester, Uma Mukherjee, Alberto Zambelli, Alessia Dalla Pria, Juan Aguilar-Company, Diego Ottaviani, Amani Chowdhury, Eve Merry, Ramon Salazar, Alexia Bertuzzi, Joan Brunet, Matteo Lambertini, Marco Tagliamento, Anna Pous, Ailsa Sita-Lumsden, Krishnie Srikandarajah, Johann Colomba, Fanny Pommeret, Elia Seguí, Daniele Generali, Salvatore Grisanti, Paolo Pedrazzoli, Gianpiero Rizzo, Michela Libertini, Charlotte Moss, Joanne S Evans, Beth Russell, Nadia Harbeck, Bruno Vincenzi, Federica Biello, Rossella Bertulli, Raquel Liñan, Sabrina Rossi, Maria Carmen Carmona-García, Carlo Tondini, Laura Fox, Alice Baggi, Vittoria Fotia, Alessandro Parisi, Giampero Porzio, Maristella Saponara, Claudia Andrea Cruz, David García-Illescas, Eudald Felip, Ariadna Roqué Lloveras, Rachel Sharkey, Elisa Roldán, Roxana Reyes, Irina Earnshaw, Daniela Ferrante, Javier Marco-Hernández, Isabel Ruiz-Camps, Gianluca Gaidano, Andrea Patriarca, Riccardo Bruna, Anna Sureda, Clara Martinez-Vila, Ana Sanchez de Torre, Luca Cantini, Marco Filetti, Lorenza Rimassa, Lorenzo Chiudinelli, Michela Franchi, Marco Krengli, Armando Santoro, Aleix Prat, Mieke Van Hemelrijck, Nikolaos Diamantis, Thomas Newsom-Davis, Alessandra Gennari, Alessio Cortellini, on behalf of the OnCovid study group**

Summary

Background The medium-term and long-term impact of COVID-19 in patients with cancer is not yet known. In this study, we aimed to describe the prevalence of COVID-19 sequelae and their impact on the survival of patients with cancer. We also aimed to describe patterns of resumption and modifications of systemic anti-cancer therapy following recovery from SARS-CoV-2 infection.

Methods OnCovid is an active European registry study enrolling consecutive patients aged 18 years or older with a history of solid or haematological malignancy and who had a diagnosis of RT-PCR confirmed SARS-CoV-2 infection. For this retrospective study, patients were enrolled from 35 institutions across Belgium, France, Germany, Italy, Spain, and the UK. Patients who were diagnosed with SARS-CoV-2 infection between Feb 27, 2020, and Feb 14, 2021, and entered into the registry at the point of data lock (March 1, 2021), were eligible for analysis. The present analysis was focused on COVID-19 survivors who underwent clinical reassessment at each participating institution. We documented prevalence of COVID-19 sequelae and described factors associated with their development and their association with post-COVID-19 survival, which was defined as the interval from post-COVID-19 reassessment to the patients' death or last follow-up. We also evaluated resumption of systemic anti-cancer therapy in patients treated within 4 weeks of COVID-19 diagnosis. The OnCovid study is registered in ClinicalTrials.gov, NCT04393974.

Findings 2795 patients diagnosed with SARS-CoV-2 infection between Feb 27, 2020, and Feb 14, 2021, were entered into the study by the time of the data lock on March 1, 2021. After the exclusion of ineligible patients, the final study population consisted of 2634 patients. 1557 COVID-19 survivors underwent a formal clinical reassessment after a median of 22·1 months (IQR 8·4–57·8) from cancer diagnosis and 44 days (28–329) from COVID-19 diagnosis. 234 (15·0%) patients reported COVID-19 sequelae, including respiratory symptoms (116 [49·6%]) and residual fatigue (96 [41·0%]). Sequelae were more common in men (*vs* women; p=0·041), patients aged 65 years or older (*vs* other age groups; p=0·048), patients with two or more comorbidities (*vs* one or none; p=0·0006), and patients with a history of smoking (*vs* no smoking history; p=0·0004). Sequelae were associated with hospitalisation for COVID-19 (p<0·0001), complicated COVID-19 (p<0·0001), and COVID-19 therapy (p=0·0002). With a median post-COVID-19 follow-up of 128 days (95% CI 113–148), COVID-19 sequelae were associated with an increased risk of death (hazard ratio [HR] 1·80 [95% CI 1·18–2·75]) after adjusting for time to post-COVID-19 reassessment, sex, age, comorbidity burden, tumour characteristics, anticancer therapy, and COVID-19 severity. Among 466 patients on systemic anti-cancer therapy, 70 (15·0%) permanently discontinued therapy, and 178 (38·2%) resumed treatment with a dose or regimen adjustment. Permanent treatment discontinuations were independently associated with an increased risk of death (HR 3·53 [95% CI 1·45–8·59]), but dose or regimen adjustments were not (0·84 [0·35–2·02]).

Interpretation Sequelae post-COVID-19 affect up to 15% of patients with cancer and adversely affect survival and oncological outcomes after recovery. Adjustments to systemic anti-cancer therapy can be safely pursued in treatment-eligible patients.

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*Members are listed in the appendix (pp 14–17)

Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital, London, UK (D J Pinato PhD, M Patel BSc, J S Evans MPhil, A Cortellini MD); **Division of Oncology** (D J Pinato, F Biello MD, A Gennari PhD), **Division of Radiotherapy** (M Krengli MD), **Division of Haematology** (G Gaidano MD, A Patriarca MD, R Bruna MD), **Unit of Medical Statistics** (L Scotti PhD, D Ferrante PhD), **Department of Translational Medicine, University of Piemonte Orientale, Novara, Italy; Azienda Ospedaliera Maggiore Della Caritá, Novara, Italy** (F Biello, A Gennari, M Krengli, G Gaidano, A Patriarca, R Bruna); **Medical Oncology** (Prof J Tabernero PhD, J Aguilar-Company MD, D García-Illescas MD, E Roldán MD), **Haematology** (L Fox MD), **and Infectious Diseases** (I Ruiz-Camps PhD), **Vall d'Hebron University Hospital and Institute of Oncology, Barcelona, Spain; Department of Oncology** (Prof M Bower PhD, A Dalla Pria MD, R Sharkey RN, T Newsom-Davis PhD) **and National Centre for HIV**

Malignancy (Prof M Bower, A Dalla Pria, R Sharkey, T Newsom-Davis)**, Chelsea and Westminster Hospital, London, UK; Department of Cancer Medicine, Institut Gustave Roussy, University of Paris Saclay, Villejuif, France** (E Colomba MD, J Colomba MD, F Pommeret MD)**; Medical Oncology, Guy's and St Thomas' NHS Foundation Trust, London, UK** (S Dolly PhD, A Sita-Lumsden PhD, K Srikandarajah MBBS)**; Department of Infectious Diseases, Internal Medicine, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium** (A Loizidou MD)**; Medical Oncology, School of Medicine, Cardiff University, Cardiff, UK** (Prof J Chester PhD)**; Medical Oncology, Velindre Cancer Centre, Cardiff, UK** (Prof J Chester)**; Medical Oncology, Barts Health NHS Trust, London, UK** (U Mukherjee PhD, N Diamantis PhD)**; Oncology Unit, Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy** (A Zambelli MD, C Tondini MD, V Fotia MD, L Chiudinelli MD, M Franchi MD)**; Cancer Division, University College London Hospitals, London, UK** (D Ottaviani PhD, A Chowdhury MD, E Merry MD, I Earnshaw MBCHB)**; Department of Medical Oncology** (R Salazar PhD) **and Haematology Department** (A Sureda PhD)**, ICO L'Hospitalet, Oncobell Program, Hospitalet de Llobregat, Barcelona, Spain; Medical Oncology and Hematology Unit, Humanitas Cancer Center, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy** (A Bertuzzi MD, S Rossi MD, L Rimassa MD, Prof A Santoro MD)**; Department of Medical Oncology, Catalan Institute of Oncology, University Hospital Josep Trueta, Girona, Spain** (J Brunet PhD, R Liñan MD, M C Carmona-García MD, A Pous MD, E Felip MD, A Roqué Lloveras MD)**; Medical Oncology Department, IRCCS Ospedale Policlinico San Martino, Genova, Italy** (M Lambertini PhD, M Tagliamento MD)**; Department of Internal Medicine and Medical**

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Introduction

Despite the higher clinical vulnerability of patients with cancer to SARS-CoV-2,[1–6] 60% to 80% of patients with cancer infected with SARS-CoV-2 survive a severe infection, leaving uncertainties regarding the medium-term and long-term impact of SARS-CoV-2 infection on cancer prognosis and cancer care following COVID-19.[1–9]

It has now been recognised that a substantial proportion of COVID-19 survivors can have protracted symptomatic and physiological changes after acute infection with SARS-CoV-2.[10] A wide range of multi-system sequelae of various severity levels have been described, from mild neurocognitive disturbances, including insomnia, depression, and anxiety, to more severe respiratory sequelae, including persisting lung diffusion impairment and abnormal chest imaging 6 months after the infection.[10]

Long-lasting sequelae affect up to 60% of the general population[10–13] and 30% of patients with chronic myeloproliferative disorders.[14] However, little is known about the prevalence and clinical significance of COVID-19 sequelae in the general cancer population, in which higher clinical vulnerability to SARS-CoV-2 infection and concomitant symptomatic burden from underlying malignancy might impose a greater toll on COVID-19 recovery.

In this study, we sought to describe the prevalence of COVID-19 sequelae and their impact on the survival of patients with cancer. In addition, because deferral and modification of systemic anti-cancer therapy has been commonplace during the early phases of the pandemic,[15] we also aimed to describe patterns of resumption and modifications of systemic anti-cancer therapy following recovery from SARS-CoV-2 infection.

Methods

Study design and participants

OnCovid is an active European registry study enrolling consecutive patients who are aged 18 years or older, have a diagnosis of RT-PCR confirmed SARS-CoV-2 infection,[16] and have a history of solid or haematological malignancy (either active or in remission at the time of COVID-19 diagnosis). The study population was accrued from 35 institutions across six countries (Belgium, France, Germany, Italy, Spain, and the UK; appendix p 10). Patients diagnosed with SARS-CoV-2 infection between Feb 27, 2020, and Feb 14, 2021, were included at the time of data lock (March 1, 2021), and COVID-19 survivors reassessed at participating institutions after COVID-19 recovery were eligible for analysis in this study.

OnCovid was granted central approval by the UK Health Research Authority (UK HRA; 20/HRA/1608) and by the corresponding research ethics committees at each participating institution. Full waiver of consent was granted by the UK HRA because of the the anonymised nature of patient data and retrospective nature of the study. Core study data were collated from electronic medical records into a case report form designed using

Research in context

Evidence before this study

We searched PubMed from database inception to July 24, 2021, for articles published in English on the impact of COVID-19 on patients with cancer using the search terms ("COVID-19" OR "SARS-CoV-2") AND ("oncology" OR "cancer" OR "malignancy"). Although registry studies have provided evidence of high case fatality rates (ranging from 20–40%), there is no evidence to document the medium-term and long-term outcomes of these patients. In particular, the prevalence and clinical impact of COVID-19 sequelae is poorly understood in patients with cancer. Most published studies derived information on the impact of COVID-19 in patients with cancer by evaluating all-cause mortality during short observation times without considering the longer-term impact of COVID-19 and discontinuation of anticancer therapy in COVID-19 survivors.

Added value of this study

To our knowledge, this is the first study to document that 15% of patients with cancer who survive COVID-19 have a wide range of sequelae, most commonly fatigue and respiratory symptoms. We found that patients with sequelae from COVID-19 have significantly inferior survival and are more likely to permanently discontinue systemic anti-cancer therapy. Only permanent treatment discontinuations, not treatment modifications, led to inferior survival outcomes; a finding that supports efforts aimed at continuing to actively manage a patient population viewed as being highly clinically vulnerable to SARS-CoV-2.

Implications of all the available evidence

Our study describes the clinical characteristics of patients who survive COVID-19. Clinical evidence of post-COVID-19 syndrome is documented in 15% of patients with cancer, in whom COVID-19 sequelae represent a significant barrier towards the continuation of systemic therapy. Prospective studies are urgently needed to identify effective management strategies of COVID-19 related sequelae.

the Research Electronic Data Capture software (REDCap, Vanderbilt University, Nashville, TN, USA). Multisite access and data curation was coordinated by the Medical Statistics Unit in Novara (Italy).

Procedures

Methods have been previously published.[4,6,17] The clinical definition of COVID-19 followed WHO criteria.[18] In this analysis, we focused on patients who survived COVID-19 and underwent a formal clinical reassessment in the oncology clinic at each participating institution after recovery from COVID-19. The timing of follow-up was not standardised but dictated as per standard of care at each institution.

We documented prevalence and type of COVID-19 sequelae at the time of first oncological assessment after COVID-19 recovery. These data were assessed by treating physicians during clinical consultation on the basis of symptom review, physical examination, and imaging or laboratory findings. Patients were evaluated at each participating institution by investigators as per local practice, when clinically indicated.

No predefined timepoints for follow-up were dictated to treating physicians and patients were entered into the database at any time of their COVID-19 history. Clinical definitions of COVID-19 sequelae followed Centers for Disease Control and Prevention criteria.[19] Sequelae were categorised according to the system or organ involved into respiratory symptoms (including dyspnoea and chronic chough), residual fatigue, weight loss, neurocognitive sequelae (including cognitive impairment, visual impairment, anosmia, dysosmia, aysgeusia, dysgeusia, headache, confusion, and lethargy), non-respiratory residual organ dysfunction (including heart failure and kidney failure), and others (eg, residual fever, muscle cramps, arthralgia, and skin conditions).

To describe clinical attitudes towards resumption of systemic anti-cancer therapy, investigators were asked to provide, when available, the specific reason underlying permanent cessations of systemic anti-cancer therapy (among performance status deterioration, disease progression during COVID-19, and residual organ dysfunction) and dose or regimen adjustments (including avoiding potential immune suppression or other adverse events, reducing hospital attendance, avoiding intravenous administration, and others; appendix p 6).

To evaluate the post-COVID-19 anti-SARS-CoV-2-S (spike) IgG seroprevalence, investigators were asked to report pre-vaccination anti-SARS-CoV-2-S IgG antibody information, as per local national guidelines. A detailed description of our study methods is provided in the appendix (pp 8–9).

Statistical analysis

The main objectives of this analysis were to describe prevalence and impact of COVID-19 sequelae and post-COVID-19 systemic anti-cancer therapy resumption in the OnCovid population. Univariable and multivariable Cox proportional hazards models were used to assess the impact on the risk of death of COVID-19 sequelae and permanent cessation or regimen adjustments of systemic anti-cancer therapy in the relevant analyses.

For statistical analyses, COVID-19 sequelae were clustered as respiratory (either alone or combined with other complications) and non-respiratory sequelae, and according to the presence of more than one concomitant sequelae. In addition, to provide an estimate of COVID-19 severity and sequelae distribution across different age groups, we reported sequalae proportions with the corresponding rates of COVID-19 complications and hospital admission due to COVID-19 within six predefined age categories: <40 years, 40–49 years, 50–59 years, 60–69 years, 70–79 years, and ≥80 years.

We evaluated the impact of sequelae on post-COVID-19 survival (ie, after recovery from COVID-19, measured in days) with univariable and multivariable analysis, defined as the interval from the date of the first post-COVID-19 clinical reassessment and the date of patients' death or last follow-up. Accounting for the unbalanced distribution of patient and disease-related features across the subgroups, we adopted a fixed multivariable regression model, adjusting all survival estimates for clinical characteristics already known to affect clinical outcomes in patients with COVID-19 and cancer.[1–6] The included covariates were incorporated following clinical prioritisation. All of the included covariates have been shown to be associated with both the short-term (30-day mortality) and medium-term (6-month mortality) outcomes at the latest update of the registry, which included 1392 patients.[17]

The following variables of interest were used as covariates within the survival analysis: (1) sex (male *vs* female), (2) age (≥65 years *vs* <65 years), (3) number of comorbidities (0–1 *vs* ≥2; appendix p 8), (4) primary tumour (clustered as breast, gastrointestinal, gynaecological or genitourinary, haematological, thoracic, or other), (5) tumour stage (defined as advanced *vs* non-advanced by radiological assessment for solid tumours or disease-specific criteria [eg, Rai and Binet criteria for haematological malignancies]), (6) tumour status (presence of active *vs* non-active disease by disease-specific criteria), (7) receipt of any anticancer therapy within 4 weeks of SARS-CoV-2 infection, including non-systemic therapy (yes *vs* no), (8) having at least one COVID-19 complication, including acute respiratory failure, acute respiratory distress syndrome, kidney injury, secondary infection, sepsis, septic shock, acute cardiac injury, acute liver injury, or other (yes *vs* no), (9) receipt of any COVID-19-specific therapy, including antivirals, antimalarials, antibiotics, corticosteroids, or other (yes *vs* no), and (10) hospitalisation (pre-existing for any cause, including cancer *vs* due to COVID-19 *vs* not required).

Because COVID-19 survivors were assessed at multiple timepoints throughout the study, we also evaluated the

Specialties, School of Medicine, University of Genova, Genova, Italy (M Lambertini, M Tagliamento)**; Department of Medical Oncology** (E Seguí MD, C A Cruz MD, R Reyes MD, Prof A Prat PhD) **and Department of Internal Medicine** (J Marco-Hernández MD)**, Hospital Clinic, Barcelona, Spain; Multidisciplinary Breast Pathology and Translational Research Unit, Azienda Socio Sanitaria Territoriale Cremona, Cremona, Italy** (Prof D Generali PhD)**; Department of Medical, Surgical and Health Sciences, University of Trieste, Trieste, Italy** (Prof D Generali)**; Medical Oncology Unit, Spedali Civili, Brescia, Italy** (S Grisanti PhD, A Baggi MD)**; Medical Oncology Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy** (S Grisanti, A Baggi, G Rizzo MD)**; Department of Internal Medicine and Medical Therapy, University of Pavia, Pavia, Italy** (Prof P Pedrazzoli MD)**; Medical Oncology Unit, Fondazione Poliambulanza Istituto Ospedaliero, Brescia, Italy** (M Libertini MD)**; Translational Oncology and Urology Research, School of Cancer and Pharmaceutical Sciences, King's College London, London, UK** (C Moss MRes, B Russell PhD, Prof M Van Hemelrijck PhD)**; Department of Gynecology and Obstetrics, Breast Center and Gynecological Cancer Center and Comprehensive Cancer Center Munich, University Hospital Munich, Munich, Germany** (Prof N Harbeck PhD)**; Policlinico Universitario Campus Bio-Medico, Rome, Italy** (B Vincenzi PhD)**; Medical Oncology 2, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy** (R Bertulli MD)**; Department of Life, Health & Environmental Sciences** (A Parisi MD) **and Department of Biotechnology and Applied Clinical Sciences** (G Porzio MD, A Cortellini) **University of L'Aquila, L'Aquila, Italy; Melanoma and Sarcoma Medical Treatment Unit, Istituto Europeo di Oncologia, Milan, Italy** (M Saponara MD)**; Fundació Althaia Manresa, Manresa, Spain** (C Martinez-Vila MD)**; Hospital Universitario XII de Octubre, Madrid, Spain**

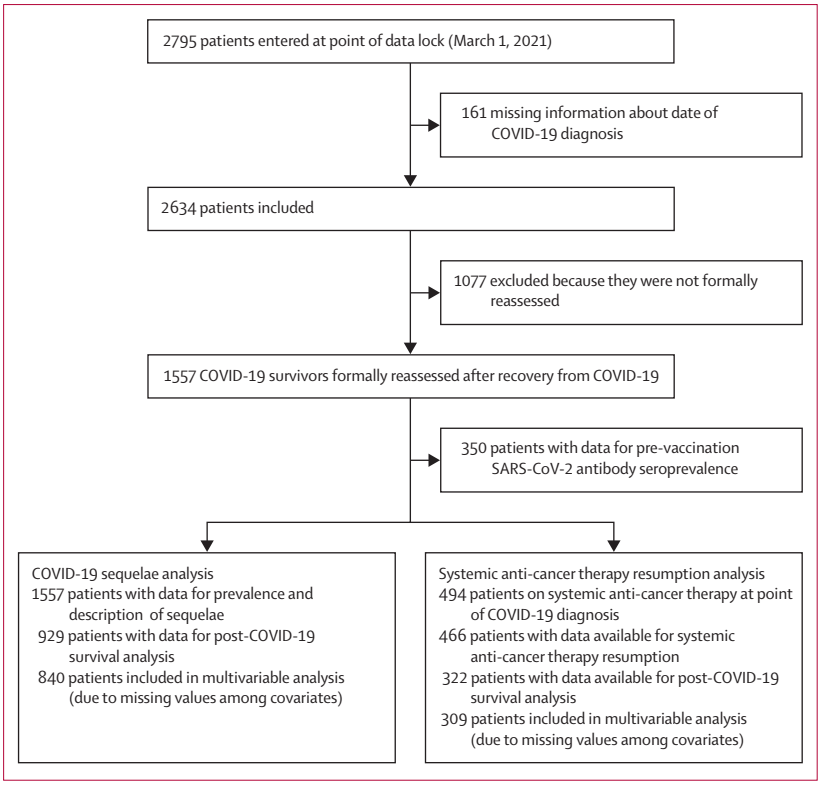

Figure 1: **Study flow diagram**

(A Sanchez de Torre MD); **Medical Oncology, Azienda Ospedaliero Universitaria, Ospedali Riuniti, Polytechnic University of the Marche Region, Ancona, Italy** (L Cantini MD); **Medical Oncology, Sant'Andrea Hospital, Rome, Italy** (M Filetti MD); **Department of Biomedical Sciences, Humanitas University, Milan, Italy** (L Rimassa, Prof A Santoro); **Translational Genomics and Targeted Therapies in Solid Tumors, IDIBAPS, Barcelona, Spain, Barcelona, Spain** (Prof A Prat)

Correspondence to: Dr David J Pinato, Department of Surgery and Cancer, Imperial College London, Hammersmith hospital, London W12 0HS, UK **david.pinato@imperial.ac.uk**

See Online for appendix

prognostic impact of time from cancer diagnosis to post-COVID-19 reassessment (patients with missing date of cancer diagnosis were excluded) and time from COVID-19 diagnosis to post-COVID-19 reassessment. Additionally, we provided separate analysis reporting of the impact of sequelae on post-COVID-19 survival in patients with remission or non-measurable disease versus active malignancy. We then evaluated patterns of resumption of systemic anti-cancer therapy in patients who were on active treatment within 4 weeks of their COVID-19 diagnosis. Additionally, we evaluated the associations between systemic anti-cancer therapy dose adjustments, permanent discontinuation of systemic anti-cancer therapy, and patients' characteristics, and described the corresponding proportion of COVID-19 sequelae according to systemic anti-cancer resumption pathways (ie, unchanged, resumption following dose or regimen adjustments, and cessation). We also evaluated the impact of different patterns of systemic anti-cancer therapy resumption on post-COVID-19 survival with univariable and multivariable analysis, following the same criteria.

Lastly, we evaluated the post-COVID-19 anti-SARS-CoV-2-S IgG seroprevalence in a subgroup of patients. To define patient or disease characteristics possibly related to seroconversion, their distribution according to antibody status were analysed with univariable analysis. Serum SARS-CoV-2 antibodies were tested in clinical practice at participating institutions and seroconversion was defined as the presence of a positive anti-SARS-CoV-2-S IgG antibody test after COVID-19 resolution. Given the pragmatic nature of this registry, for all analyses, we decided to exclude all patients with incomplete information, missing information, or who did not have follow-up data after COVID-19 diagnosis to preserve the integrity of our results and avoid incurring bias, as per standard of care clinical practice.

Baseline characteristics were summarised as categorical variables and reported using descriptive statistics. Associations between categorical variables were tested using Pearson's χ^2 test. Linear trends were tested with the Cochran-Armitage test. All time-to-event intervals without censored data, including time from cancer diagnosis or COVID-19 diagnosis to post-COVID-19 reassessment, were reported as median values with relative IQR. Survival intervals were computed from post-COVID-19 reassessment at each participating institution to death or last follow-up. All estimates and analyses of post-COVID-19 survival were done with the Kaplan-Meier method, with comparisons computed with the log-rank test. A p value of less than 0·05 was considered significant. The median post-COVID-19 follow-up was estimated with the reverse Kaplan-Meier method.

Results of Cox regression analysis were presented as hazard ratios (HR) and 95% CIs. All the described patient and disease characteristics have been included in the multivariable regression model, in view of their role in determining mortality within the study population[4,6,17] and because of their differential distribution across the cohorts of interest. Analyses were done using the MedCalc Statistical Software version 20 and R (survival and survminer packages) version 3.6.3. The OnCOVID study is registered in ClinicalTrials.gov, NCT04393974.

Role of the funding source

OnCovid was sponsored by Imperial College London and received direct project funding and infrastructural support by the National Institute for Health Research (NIHR) Imperial Biomedical Research Centre. Neither the sponsor nor the funder of the study had any role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Of 2795 patients eligible for inclusion in this analysis, 161 (5·8%) were excluded because they did not have a confirmed date of COVID-19 diagnosis, leaving a study population of 2634 patients (figure 1). At the point of database lock on March 1, 2021, 1557 (59·1%) of 2634 COVID-19 survivors underwent clinical reassessment after a median time from cancer diagnosis of 22·1 months (IQR 8·4–57·8; computed for 1284 patients) and a median time from COVID-19 diagnosis of 44 days (28–329 [all 1557 patients included). Out of 1557 patients included in the baseline descriptive analysis, 929 (59·7%)

	Without COVID-19 sequelae (n=1323)	With COVID-19 sequelae (n=234)	p value
Sex			0·041
Male	624 (47·2%)	127 (54·5%)	
Female	697 (52·8%)	106 (45·5%)	
Missing	2	1	
Age, years			0·048
<65	683 (51·9%)	105 (44·9%)	
≥65	634 (48·1%)	129 (55·1%)	
Missing	6	0	
Comorbidities			0·0006
0–1	841 (63·6%)	121 (51·7%)	
≥2	482 (36·4%)	113 (48·3%)	
Smoking history			0·0004
Never smoker	646 (57·7%)	86 (44·1%)	
Former or current smoker	474 (42·3%)	109 (55·9%)	
Missing	203	39	
Primary tumour			0·048
Breast	314 (24·0%)	46 (19·7%)	
Gastrointestinal	212 (16·2%)	43 (18·4%)	
Gynaecological or genitourinary	246 (18·8%)	51 (21·8%)	
Haematological	187 (14·3%)	31 (13·2%)	
Thoracic	149 (11·4%)	39 (16·7%)	
Other	199 (15·2%)	24 (10·3%)	
Missing	16	0	
Tumour stage			0·90
Local or loco-regional	625 (50·6%)	116 (51·1%)	
Advanced	609 (49·4%)	111 (48·9%)	
Missing	89	7	
(Table 1 continues in next column)			
(Continued from previous column)			
Tumour status at COVID-19 diagnosis			0·43
Remission or non-measurable disease	448 (34·3%)	72 (31·6%)	
Active malignancy	859 (65·7%)	156 (68·4%)	
Missing	16	6	
Anticancer therapy at COVID-19 diagnosis*			0·52
No	692 (54·1%)	127 (56·4%)	
Yes	587 (45·9%)	98 (43·64%)	
Missing	44	9	
COVID-19 therapy			0·0002
No	627 (47·4%)	80 (34·2%)	
Yes	696 (52·6%)	154 (65·9%)	
COVID-19 complications			<0·0001
No	1047 (79·1%)	107 (45·8%)	
Yes	276 (20·9%)	127 (54·3%)	
Hospitalisation			<0·0001
Not required	492 (37·4%)	27 (11·52%)	
Required	542 (41·2%)	169 (72·2%)	
Pre-existing	280 (21·3%)	38 (16·2%)	
Missing	9	0	

Missing data are not included in the denominators. *Within 4 weeks of COVID-19 diagnosis.

Table 1: **Distribution of baseline patient, tumour, and COVID-19 characteristics in formally reassessed patients (n=1557)**

were eligible for analysis of post-COVID-19 survival, whereas the remaining 628 patients did not have survival follow-up information after post-COVID-19 reassessment. Baseline characteristics of 1557 patients who were formally reassessed after recovery from COVID-19 are shown in table 1. Most patients had uncomplicated COVID-19 (1154 [74·1%]). Clinical characteristics of all 2634 patients included in the study are shown in the appendix (p 11).

Among 1557 patients included in the COVID-19 sequelae analysis, 234 (15·0%) had at least one sequela from COVID-19 at first oncological reassessment (median time from COVID-19 diagnosis to post COVID reassessment: 44 days; IQR 28–329). These sequelae included respiratory symptoms (116 [49·6%] of 234 patients), residual fatigue (96 [41·0%]), weight loss (13 [5·5%]), neurocognitive symptoms (17 [7·3%]), non-respiratory organ dysfunction (four [1·7%]), and other complications (43 [18·4%]). A breakdown of specific COVID-19 sequelae is reported in the appendix (p 3).

Compared with patients without sequelae, patients with COVID-19 sequelae were more likely to be men than women (p=0·041), aged 65 years or older compared with other age groups (p=0·048), have two or more comorbidities compared with one or none (p=0·0006), have a history of smoking compared with no history (p=0·0004), have higher rates of COVID-19 complications (p<0·0001), require therapy for COVID-19 (p=0·0002), and require hospitalisation (p<0·0001; table 1). The distribution of primary tumours was also significantly different between the two groups (p=0·048).

The corresponding proportions of patients with COVID-19 sequelae who required hospitalisation due to COVID-19 and who had complications associated with COVID-19 according to six predefined age categories are shown in figure 2. Although a linear trend with increasing age was reported for COVID-19 sequelae (χ^2 for trend 7·1; p=0·0077), hospital admission (χ^2 for trend 37·6; p<0·0001), and COVID-19 complication rates (χ^2 for trend 66·6; p<0·0001), the highest prevalence of sequelae was in the 60–69 year age group (82 [22·2%] of 370 patients), followed by an unaligned decreasing proportion for the 70–79 year age group (63 [15·9%] of 396 patients) and the 80 year and older age group (24 [13·3%] of 180 patients).

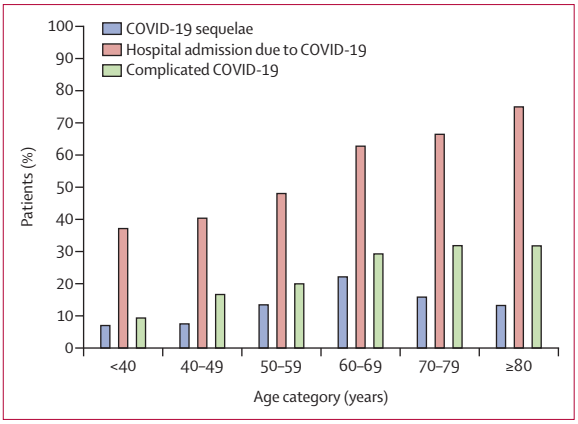

Figure 2: **Prevalence of COVID-19 sequelae, hospital admissions due to COVID-19, and complicated COVID-19 across the six defined age categories**
Linear trends were tested with the Cochran–Armitage test. Numbers of patients are different across categories and age groups (appendix p 17).

After a median post-COVID-19 follow-up of 128 days (95% CI 113–148), median post-COVID-19 survival in 929 patients with data was not reached (95% CI [not reached–not reached]; 143 deaths; appendix p 2). Patients who had one or more COVID-19 sequelae reported a significantly shorter post-COVID-19 survival compared with patients with complete COVID-19 resolution (median not reached [not reached–not reached], 104 deaths *vs* median not reached [not reached–not reached], 39 deaths]; HR 2·43 [95% CI 1·54–3·82]; p=0·0001; figure 3A). When considering respiratory and non-respiratory sequelae separately, both had a significant impact on post-COVID-19 survival, with similar post-COVID-19 survival between the two categories of sequelae (figure 3B). Compared with patients without sequelae, patients having one or two or more sequelae had an increased risk of death (figure 3C).

Time from cancer diagnosis to post-COVID-19 reassessment did not affect post-COVID-19 survival as either a continuous covariate (HR 0·99 [95% CI 0·99–1·01; p=0·9988]) or when dichotomised by median value (1·03 [0·72–1·47]; p=0·86, appendix p 4). Time from COVID-19 diagnosis to post-COVID-19 reassessment significantly affected post-COVID-19 survival when considered as a continuous covariate (HR 0·99 [95% CI 0·98–0·99]; p=0·0307), but not when dichotomised by median value (1·13 [0·81–1·22]; p=0·44, appendix p 4), justifying its use as adjusting factor in all multivariable analyses.

After adjusting for time from COVID-19 diagnosis to post-COVID-19 reassessment, sex, age, comorbidity burden, primary tumour site, tumour stage, tumour status, receipt of anticancer and COVID-19 therapy, COVID-19 complications, and hospitalisation, the presence of COVID-19 sequelae remained independently associated with an increased risk of death in fixed multivariable models (HR 1·80 [95% CI 1·18–2·75], table 2).

Post-COVID-19 survival in patients in remission or with non-measurable disease was immature (median survival time was not reached [not reached–not reached]; ten deaths). In this subgroup, COVID-19 sequelae did not have a significant impact on survival (compared with patients with no sequelae: HR 1·65 [95% CI 0·36–7·49]; p=0·51). Although post-COVID-19 median survival time in patients with active malignancy was also not reached (not reached–not reached; 130 deaths), in this subgroup, COVID-19 sequelae were associated with inferior survival (compared with patients with no sequelae: 3·32 [2·01–5·48]; p<0·0001, appendix p 5).

Among the 1557 COVID-19 survivors reassessed in the clinic, 494 (31·7%) had been on systemic anti-cancer therapy within 4 weeks of COVID-19 diagnosis, 466 (94·3%) of whom had information regarding their oncological pathway of care post-COVID-19 (figure 1). 70 (15·0%) of 466 patients permanently discontinued systemic anti-cancer therapy. The underlying reason for permanent discontinuation, documented in 31 patients, were as follows: performance status deterioration (19 [61·3%] of 31 patients), disease progression (nine [29·0%]), and residual organ dysfunction (three [9·7%]). 178 (38·2%) of 466 patients resumed systemic anti-cancer therapy after a dose or regimen adjustment to avoid potential immune suppression (which occurred in 89 [50·0%] of 178 patients), reduce hospital attendance (46 [25·8%]), avoid intravenous administration (14 [7·9%]), avoid adverse events (34 [19·1%]), and for other reasons (36 [20·2%]; appendix p 6). Permanent systemic anti-cancer therapy discontinuation rates were not different in patients with advanced (51 [26·0%] of 196 patients) versus non-advanced malignancies (19 [21·1%] of 90 patients, p=0·37).

Compared with patients who resumed systemic anti-cancer therapy without any changes to dose or regimen, those who permanently discontinued or received a dose or regimen adjustment were more likely to be former or current smokers (p=0·042), be survivors of COVID-19 complications (p<0·0001), have been hospitalised during COVID-19 diagnosis (p=0·032), or have had COVID-19 sequelae (p=0·021; table 3). The prevalence of COVID-19 sequelae was associated with higher rates of systemic anti-cancer therapy discontinuation post-COVID-19 (p=0·016; appendix p 6). Changes in oncological management post-COVID-19 were also significantly different depending on primary tumour site (p=0·0002). Oncological continuity of care was more frequently disrupted in haematological malignancies compared with other malignancies (46 [67·6%] of 68 patients; appendix p 7).

In patients who were on systemic anti-cancer therapy at COVID-19 diagnosis, patients who continued or resumed systemic anti-cancer therapy with dose or regimen adjustments had a similar outcome compared with those who continued or resumed systemic anti-cancer therapy without changes to dosage or regimen

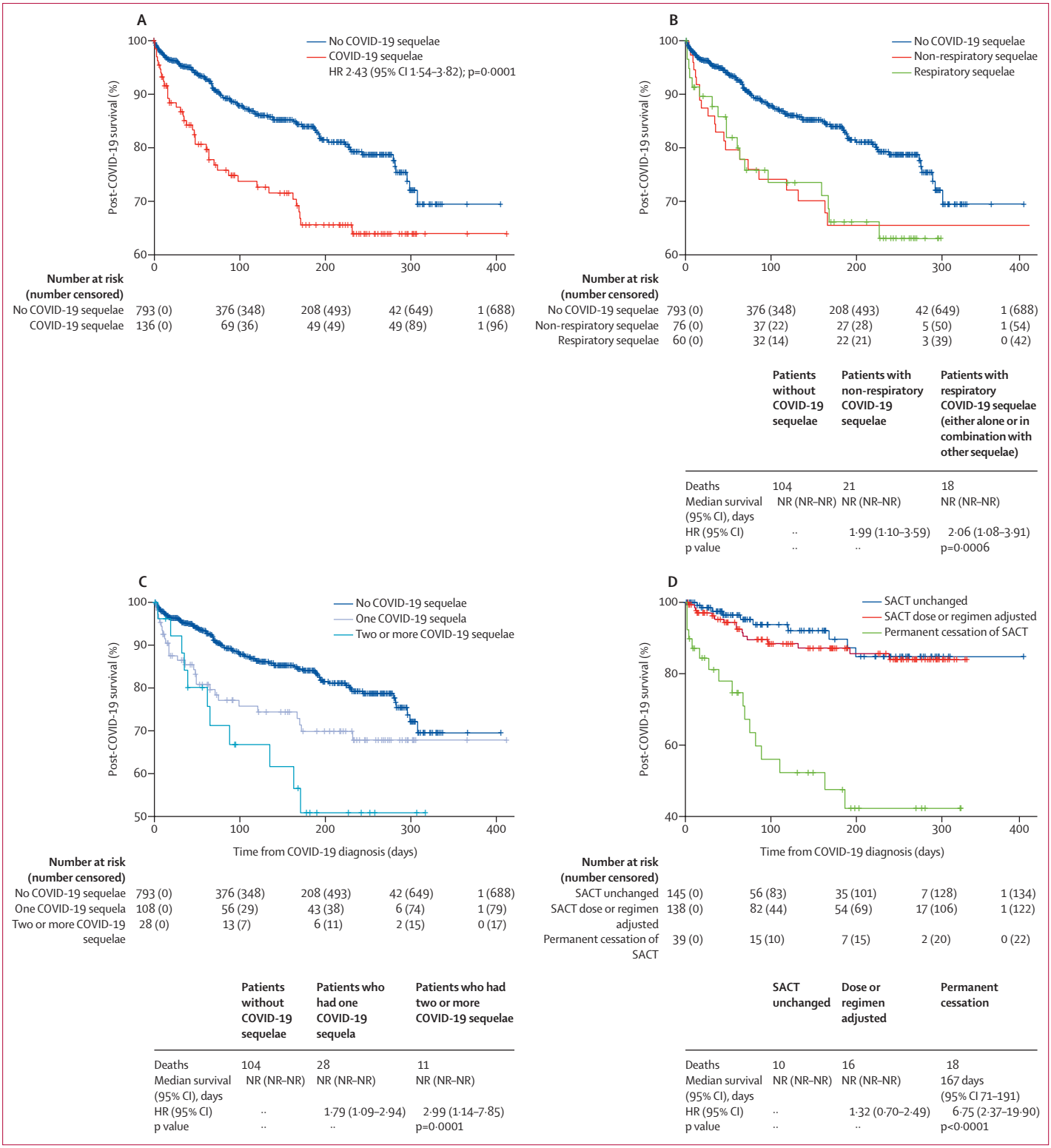

***Figure 3*: Kaplan-Meier survival estimate of post-COVID-19 survival (days from post-COVID-19 reassessment to date of death or last follow-up)**
(A) Post-COVID-19 survival by presence of COVID-19 sequelae. (B) Post-COVID-19 survival by presence of COVID-19 respiratory or non-respiratory sequelae. (C) Post-COVID-19 survival by presence of one or two or more COVID-19 sequelae. (D) Post-COVID-19 survival by oncology therapeutic pathway. HR=hazard ratio. NR=not reached. SACT=systemic anticancer therapy.

	Hazard ratio (95% CI)
COVID-19 sequelae	
No	1 (ref)
Yes	1·80 (1·18–2·75)
Time from COVID-19 diagnosis to post-COVID-19 reassessment	
Continuous	0·99 (0·98–1·00)
Sex	
Female	1 (ref)
Male	1·15 (0·78–1·70)
Age, years	
<65	1 (ref)
≥65	0·96 (0·66–1·40)
Comorbidities	
0–1	1 (ref)
≥2	2·28 (1·55–3·35)
Primary tumour	
Haematological	1 (ref)
Breast	0·74 (0·33–1·64)
Gastrointestinal	1·33 (0·76–2·33)
Gynaecological or genitourinary	0·97 (0·55–1·70)
Thoracic	0·68 (0·33–1·39)
Other	1·34 (0·74–2·44)
Tumour stage	
Local or loco-regional	1 (ref)
Advanced	2·07 (1·35–3·18)
Tumour status	
Remission or non-measurable disease	1 (ref)
Active malignancy	6·05 (2·66–13·75)
Anticancer therapy at COVID-19 diagnosis*	
No	1 (ref)
Yes	1·43 (0·98–2·09)
COVID-19 complications	
0	1 (ref)
≥1	1·44 (0·97–2·09)
COVID-19 therapy	
No	1 (ref)
Yes	0·78 (0·54–1·13)
Hospitalisation	
Not required	1 (ref)
Required due to COVID-19	2·22 (1·21–4·06)
Pre-existing	4·57 (2·49–8·38)

*Within 4 weeks of COVID-19 diagnosis.

Table 2: **Fixed multivariable regression model for post COVID-19 survival (n=840)**

(figure 3D). However, systemic anti-cancer therapy discontinuation was associated with shortened post-COVID-19 survival compared with that for patients with unchanged therapy (figure 3D). After adjusting for sex, age, comorbidity burden, primary tumour, tumour stage and status, receipt of COVID-19 therapy, presence of complicated COVID-19, hospitalisation, and sequelae, permanent systemic anti-cancer therapy cessation was confirmed to be independently associated with an increased risk of death (HR 3·53 [95% CI 1·45–8·59]; p=0·0017) but dose or regimen adjustments were not (0·84 [0·35–2·02], p=0·2744; appendix p 12).

350 patients were tested for pre-vaccination anti-SARS-CoV-2-S IgG antibodies by the time of their first oncological reassessment, of whom 318 (90·9%) tested positive. The distribution of patient, tumour, and COVID-19 characteristics according to anti-SARS-CoV-2 antibody status are reported in the appendix (p 13). With the exception of a higher proportion of patients who had received COVID-19-specific therapy of those who were seropositive (199 [62·6%] of 318 patients *vs* 13 [40·6%] of 32 patients; p=0·015), no other feature was found to be associated to SARS-CoV-2 antibody status. 49 (92·5%) of 53 patients who received systemic chemotherapy within 4 weeks of COVID-19 diagnosis, ten (100%) of ten patients who received immune checkpoint inhibitors within 4 weeks of COVID-19 diagnosis, and three (75%) of four patients who received CD20 inhibitors within 4 weeks of COVID-19 diagnosis developed SARS-CoV-2 antibodies.

Discussion

To our knowledge, this study provides for the first time a detailed account of clinical characteristics and outcomes from the largest European registry of patients with cancer and COVID-19, focusing specifically on SARS-CoV-2 infection survivors. Despite evidence of protective anti-SARS-CoV-2 IgG titres in over 90% of evaluable patients, we identified that 15% of COVID-19 survivors with cancer present to their first oncological follow-up with sequelae from SARS-CoV-2 infection, most commonly fatigue and respiratory symptoms. We provide novel and clinically important evidence showing that the presence of COVID-19-related sequelae identifies a subgroup of patients with significantly worse survival independent of background oncological characteristics and risk factors for worse outcome from COVID-19.

Evolving evidence suggests that morbidity from COVID-19 extends beyond the natural course of SARS-CoV-2 replication within the host. Alongside complications that occur during the acute phase of the disease, the persistence of symptoms beyond 21 days after infection has been described in 36% of patients who survive COVID-19.[20] Up to 25% of patients report symptoms for more than 6 months after COVID-19 resolution,[12] with evidence of psychophysical compromise requiring medical treatment in 14% of COVID-19 survivors.[11]

Protracted asthenia is a dominant symptomatic consequence from SARS-CoV-2 infection in over 60% of hospitalised COVID-19 survivors up to 6 months after discharge.[10] Similarly, dyspnoea and other respiratory symptoms are highly prevalent in the post-acute phase, especially after severe COVID-19.[12] In line with published evidence, we show that sequelae are more likely in

	SACT unchanged (n=218)	SACT adjustments or discontinuations (n=248)	p value
Sex			0·078
Male	83 (38%)	114 (46%)	
Female	135 (62%)	133 (54%)	
Missing	0	1	
Age, years			0·37
<65	126 (58%)	134 (54%)	
≥65	90 (42%)	113 (46%)	
Missing	2	1	
Comorbidities			0·26
0–1	159 (73%)	169 (68%)	
≥2	59 (27%)	79 (32%)	
Smoking history			0·042
Never smoker	125 (65%)	121 (55%)	
Former or current smoker	67 (35%)	98 (45%)	
Missing	26	29	
Primary tumour			0·0002
Breast	70 (32%)	52 (21%)	
Gastrointestinal	31 (14%)	52 (21%)	
Gynaecological or genitourinary	50 (23%)	31 (13%)	
Haematological	22 (10%)	46 (19%)	
Thoracic	25 (12%)	37 (15%)	
Other	18 (8%)	29 (12%)	
Missing	2	0	
Tumour stage			0·55
Local or loco-regional	71 (33%)	72 (30%)	
Advanced	145 (67%)	166 (70%)	
Missing	2	10	
Tumour status at COVID-19 diagnosis			0·97
Remission or non-measurable disease	42 (19%)	48 (20%)	
Active malignancy	175 (81%)	198 (81%)	
Missing	1	2	
COVID-19 therapy			0·32
No	96 (44%)	98 (40%)	
Yes	122 (56%)	150 (61%)	
Complicated COVID-19			<0·0001
No	179 (82%)	160 (65%)	
Yes	39 (18%)	88 (36%)	
COVID-19 sequelae			0·021
No	197 (90%)	206 (83%)	
Yes	21 (10%)	42 (17%)	
Hospitalisation			0·032
Not required	92 (42%)	77 (31%)	
Required	99 (45%)	126 (51%)	
Pre-existing	27 (12%)	44 (18%)	
Missing	0	1	

(Table 3 continues in next column)

(Continued from previous column)

Missing data are not included in the denominators.

Table 3: **Distribution of baseline patient, tumour, and COVID-19 characteristics in patients taking systemic anticancer therapy (SACT) at COVID-19 diagnosis according to the post COVID-19 oncological therapeutic pathway**

patients with cancer who had been hospitalised or treated medically for severe COVID-19 and in patients who, before COVID-19, displayed significant risk factors for life-threatening illness, including older age, male sex, higher comorbidity burden, and a history of smoking.[10,13]

Given the positive association between age and rates of complicated COVID-19, we evaluated the age-related distribution of COVID-19-related sequelae in the OnCovid population. Surprisingly, we reported a peak in the prevalence of COVID-19 sequelae in patients in the seventh decade of life, highlighting a non-progressive association between age, COVID-19 severity, and proportion of hospitalisation. Although it is recognised that post-COVID-19 syndrome can affect young patients and those who were never hospitalised for SARS-CoV-2 infection,[12] the reduction in the prevalence of COVID-19 sequelae in patients aged 80 years and older is an unexpected finding, suggesting a potential role for immune senescence as a mechanistic contributor that leads to higher mortality but lower risk of developing sequelae.[21,22]

Oncological characteristics, including tumour stage, presence of active cancer, and, most importantly, exposure to anti-cancer therapy before COVID-19 were not associated with the emergence of SARS-CoV-2 sequelae; a finding of paramount importance in understanding the natural course of recovery from SARS-CoV-2 infection in patients with cancer as it provides further data in support of the safe delivery of anti-cancer therapy in the context of an ongoing pandemic threat.

Although this study is, to our knowledge, the first to show the association between COVID-19 sequelae and worse survival outcomes in patients with cancer, consolidating evidence suggests that radiological, biochemical, and symptomatic impairment of at least one physiological function is documented in up to 70% of COVID-19 survivors[23] and that ensuing multiorgan dysfunction contributes to a substantial excess in mortality after initial hospitalisation for COVID-19.[24]

Unlike populations without cancer, outcomes of patients with cancer who survive COVID-19 are strongly affected by features of underlying malignancy and capacity to continue or promptly resume effective anti-cancer treatment. This observation is particularly true for our dataset, in which 50% of patients had a diagnosis of

advanced malignancy and 66% had active disease at the time of SARS-CoV-2 infection.

In our study, resumption of systemic anti-cancer therapy occurred in most patients who survived COVID-19. Patients with haematological malignancies reported the highest rates of treatment cessations or modifications. This finding is perhaps unsurprising considering the higher clinical vulnerability to COVID-19 of this patient group[3] and the higher intensity of treatment regimens, characterised by an increased risk of myelosuppression compared with those delivered in solid tumours.

Albeit limited by a short follow-up period, the initial evidence that dose and regimen adjustments that were required in 40% of patients did not lead to worse survival seems to be reassuring, underscoring the importance of maintaining individualised oncological management to preserve oncological outcomes. However, approximately 15% of patients permanently discontinued systemic anti-cancer therapy after COVID-19 in the context of worsening performance status or interval disease progression. The emergence of COVID-19 sequelae was a leading contributor to the decision to permanently withdraw systemic anti-cancer therapy.

It should be emphasised that the evaluation of post-COVID clinical status is difficult to assess in patients with cancer given that constitutional symptoms (eg, fatigue and anorexia) are overlapping features of progressive malignancy and post-COVID-19 syndrome. Fatigue and dyspnoea are also frequently reported by cancer survivors as a late effect of active anti-cancer therapy.[25] Although it is likely that the decision to interrupt treatment might have been dictated by a combination of factors, the non-negligible proportion of permanent discontinuations in our study is concerning and calls for prospective efforts aimed at facilitating a prompter recognition and treatment of reversible factors to facilitate safe reintroduction of systemic anti-cancer therapy. Sadly, clinical experience from SARS survivors suggests that fatigue, a key symptomatic determinant of post-COVID-19 syndrome and a likely contributor of worsening performance status in patients with cancer, can last for more than 40 months in up to 40% of patients.[26]

In a disease area lacking level 1 evidence for interventions, interest is growing in the development of multidisciplinary programmes aimed at combining physical therapy, rehabilitation, and psychological support to COVID-19 survivors.[27] Our data argue for improved awareness, recognition, and early treatment of COVID-19 sequelae in patients with cancer as an important step towards the promotion of optimal oncological outcomes in COVID-19 survivors.

An important aspect of our study is that it included only survivors of COVID-19, and thus several features associated with survival of COVID-19 were more represented compared with other registry data that included patients who died from COVID-19,[2,5,6,17] including higher representation of female sex, patients age 65 years or younger, low burden of comorbidities, no history of smoking, hospitalisation not required for COVID-19, and not requiring oxygen.

A limitation of our study stems from the fact that COVID-19 sequelae were primarily defined symptomatically during clinical consultation, rather than on the basis of periodic and pre-planned diagnostic tests (eg, pulmonary function or cross-sectional imaging), leading to a potential underreporting of asymptomatic or minimally symptomatic sequelae. Moreover, the higher symptomatic burden of patients with active cancer might have affected a correct causal attribution of symptoms to either COVID-19 or underlying malignancy. The absence of predefined timepoints for the assessment of sequelae and patients' data entry into the registry exposes our analysis to unavoidable selection bias. However, there is evidence to suggest that patient and clinician reported prevalence of symptoms post-COVID-19, reported at 13·7% by the UK Office of National Statistics,[28] scales well with the proportion of patients with a confirmed clinical diagnosis of post-COVID syndrome, reported as 14% in population-based studies in the UK.[11]

In addition, the median follow-up period of 4 months in our study partially limited our capacity to evaluate longer-term outcomes of COVID-19, which require follow-up times of at least 6 months, as shown in the general population.[12] Nonetheless, the prognosis of patients with cancer is poorer than COVID-19 survivors without cancer, and a slightly shorter observation time enabled us to describe characteristics of COVID-19 survivors with cancer, a fragile patient population requiring tailored management strategies.

Lastly, we must consider that by the database lock on March 1, 2021, only 178 (7%) of 2634 patients received at least one dose of anti-SARS-CoV-2 vaccination, all of them after COVID-19 recovery. Therefore, we were not able to account for the possible role that the vaccines will have in preventing or reducing the impact of COVID-19 sequelae.

Despite the acknowledged limitations, our study brings novel evidence to the growing field of research on COVID-19 that suggests that, in patients with cancer, organ damage, of which symptomatic sequelae are a proxy, could contribute to a significant worsening of patients' survival, irrespective of oncological prognosis. Taken together, our data underscore the clinical significance of post-COVID syndrome in patients with cancer, a newly emerging prognostic domain that should be promptly identified in the clinic. Further research should prioritise the discovery of viral and host factors that are linked to the development of sequelae to allow for an improved diagnosis and for the implementation of better tailored treatment strategies to improve survival and quality of life of COVID-19 survivors with cancer.

Contributors

DJP, ACo, LS, and DF were involved in the study concept and design. DJP, JT, MB, LS, MP, EC, SD, AL, JCh, UM, AZ, ADP, JA-C, DO, ACh,

EM, RSa, ABe, JB, MLa, MT, APo, AS-L, KS, JCo, FP, ES, DG, SG, PP, GR, MLi, CM, JSE, BR, NH, BV, FB, RBe, RL, SR, MCC-G, CT, LF, ABa, VF, APar, GP, MS, CAC, DG-I, EF, ARL, RSh, ER, RR, IE, DF, JM-H, IR-C, GG, APat, RBr, ASu, CM-V, ASdT, LCa, MFi, LR, LCh, MFr, MK, ASa, APr, MVH, ND, TN-D, AG, and ACo were involved in the acquisition of data. DJP and ACo were involved in data verification. DJP, ACo, LS, and DF were involved in the analysis and interpretation of data. DJP and ACo were involved in drafting the manuscript. DJP, JT, MB, LS, MP, EC, SD, AL, JCh, UM, AZ, ADP, JA-C, DO, ACh, EM, RSa, ABe, JB, MLa, MT, APo, AS-L, KS, JCo, FP, ES, DG, SG, PP, GR, MLi, CM, JSE, BR, NH, BV, FB, RBe, RL, SR, MCC-G, CT, LF, ABa, VF, APar, GP, MS, CAC, DG-I, EF, ARL, RSh, ER, RR, IE, DF, JM-H, IR-C, GG, APat, RBr, ASu, CM-V, ASdT, LCa, MFi, LR, LCh, MFr, MK, ASa, APr, MVH, ND, TN-D, AG, and ACo were involved in manuscript revision, input, and approval. LS, ACo, and DF were involved in statistical analysis. DJP was responsible for obtaining funding and for study supervision. DJP and ACo had full access to all data in the study and take responsibility for data integrity, verification, and analysis. All authors had access to all the data reported in the study. All authors read and approved the submitted version of the manuscript (and any substantially modified version that involves the author's contribution to the study). Each author has agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature. The corresponding author (DJP) had full access to all of the data and the final responsibility to submit for publication.

Declaration of interests

DJP reports lecture fees from ViiV Healthcare, Bayer Healthcare, Bristol Myers Squibb, Roche, Eisai, and Falk Foundation; travel expenses from Bristol Myers Squibb and Bayer Healthcare; consulting fees from Mina Therapeutics, Eisai, Roche, DaVolterra, and Astra Zeneca; and research funding (to institution) from Merck Sharp and Dohme and Bristol Myers Squibb, outside of the submitted work. MLa acted as consultant for Roche, Novartis, Lilly, and AstraZeneca, outside of the submitted work, and received speaker honoraria from Roche, Novartis, Lilly, Pfizer, Takeda, and Sandoz, outside of the submitted work. EF reports research funding to institution from Pfizer, outside of the submitted work, and travel expenses from Lilly, Novartis, Pfizer, and Esai, outside of the submitted work. 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Data sharing

Individual, de-identified participant data and data dictionary can be made available at the request of investigators who propose to use the data in a way that has been approved by the OnCovid consortium steering committee following review of a methodologically sound research proposal. Data will be made available 6 months after article publication, with no end date. Requests for de-identified data should be made to the study Chief Investigator (DJP).

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References

1 Lee LY, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020; **395:** 1919–26.

2 Garassino MC, Whisenant JG, Huang LC, et al. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. *Lancet Oncol* 2020; **21:** 914–22.

3 Lee LYW, Cazier JB, Starkey T, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol* 2020; **21:** 1309–16.

4 Pinato DJ, Lee AJX, Biello F, et al. Presenting features and early mortality from SARS-CoV-2 infection in cancer patients during the initial stage of the COVID-19 pandemic in Europe. *Cancers (Basel)* 2020; **12:** e1841.

5 Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020; **395:** 1907–18.

6 Pinato DJ, Zambelli A, Aguilar-Company J, et al. Clinical portrait of the SARS-CoV-2 epidemic in European cancer patients. *Cancer Discov* 2020; **10:** CD-20-0773.

7 Tartarone A, Lerose R. COVID-19 and cancer care: what do international guidelines say? *Med Oncol* 2020; **37:** 80.

8 Jazieh AR, Chan SL, Curigliano G, et al. Delivering cancer care during the COVID-19 pandemic: recommendations and lessons learned from ASCO Global webinars. *JCO Glob Oncol* 2020; **6:** 1461–71.

9 Curigliano G, Banerjee S, Cervantes A, et al. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. *Ann Oncol* 2020; **31:** 1320–35.

10 Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; **397:** 220–32.

11 Daugherty SE, Guo Y, Heath K, et al. Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: retrospective cohort study. *BMJ* 2021; **373:** n1098.

12 Logue JK, Franko NM, McCulloch DJ, et al. Sequelae in adults at 6 months after COVID-19 infection. *JAMA Netw Open* 2021; **4:** e210830.

13 Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nat Med* 2021; **27:** 626–31.

14 Barbui T, Iurlo A, Masciulli A, et al. Long-term follow-up of recovered MPN patients with COVID-19. *Blood Cancer J* 2021; **11:** 115.

15 Clark JJ, Dwyer D, Pinwill N, Clark P, Johnson P, Hackshaw A. The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: a retrospective analysis. *Lancet Oncol* 2021; **22:** 66–73.

16 Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020; **25:** pii=2000045.

17 Pinato DJ, Scotti L, Gennari A, et al. Determinants of enhanced vulnerability to coronavirus disease 2019 in UK patients with cancer: a European study. *Eur J Cancer* 2021; **150:** 190–202.

18 WHO. Expanding our understanding of post COVID-19 condition: report of a WHO webinar. 2021. https://www.who.int/news-room/events/detail/2021/06/15/default-calendar/expanding-our-understanding-of-post-covid-19-condition-webinar-2 (accessed July 24, 2021).

19 Centers for Disease Control and Prevention. Post-COVID conditions 2021. https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects.html accessed July 24, 2021).

20 Tenforde MWRE, Billig Rose E, Lindsell CJ, et al. Characteristics of adult outpatients and inpatients with COVID-19—11 academic medical centers, United States, March–May 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 841–46.

21 Vellas C, Delobel P, de Souto Barreto P, Izopet J. COVID-19, virology and geroscience: a perspective. *J Nutr Health Aging* 2020; **24:** 685–91.

22 Cunha LL, Perazzio SF, Azzi J, Cravedi P, Riella LV. Remodeling of the immune response with aging: immunosenescence and its potential impact on COVID-19 immune response. *Front Immunol* 2020; **11:** 1748.

23 Dennis A, Wamil M, Alberts J, et al. Multiorgan impairment in low-risk individuals with post-COVID-19 syndrome: a prospective, community-based study. *BMJ Open* 2021; **11:** e048391.

24 Ayoubkhani D, Khunti K, Nafilyan V, et al. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. *BMJ* 2021; **372:** n693.

25 Gegechkori N, Haines L, Lin JJ. Long-term and latent side effects of specific cancer types. *Med Clin North Am* 2017; **101:** 1053–73.

26 Lam MH, Wing YK, Yu MW, et al. Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up. *Arch Intern Med* 2009; **169:** 2142–47.

27 Singh SJ, Barradell AC, Greening NJ, et al. British thoracic society survey of rehabilitation to support recovery of the post-COVID-19 population. *BMJ Open* 2020; **10:** e040213.

28 Office for National Statistics. Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK: 1 April 2021. 2021. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/prevalenceofongoingsymptomsfollowingcoronaviruscovid19infectionintheuk/1april2021 (accessed July 24, 2021).