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BRIEF COMMUNICATION

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Outcomes of COVID-19 and risk factors in patients with cancer

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Patients with cancer are at higher risk for adverse coronavirus disease 2019 (COVID-19) outcomes. Here, we studied 1,253 patients with cancer, who were diagnosed with severe acute respiratory syndrome coronavirus 2 at a tertiary referral cancer center in India. Most patients had mild disease; in our settings, recent cancer therapies did not impact COVID-19 outcomes. Advancing age, smoking history, concurrent comorbidities and palliative intent of treatment were independently associated with severe COVID-19 or death. Thus, our study provides useful insights into cancer management during the COVID-19 pandemic.

The COVID-19 pandemic has infected over 446 million people globally, causing over 6 million deaths (https://covid19.who.int/; accessed 9 March 2022). Global data suggest that increasing age, concurrent illnesses and immunosuppression are risk factors for poor outcomes after COVID-19[1,2]. Patients with cancer are often immunosuppressed by the disease and its treatment; in addition, important predisposing factors for cancer, such as smoking and obesity, also independently contribute to adverse outcomes after COVID-19. Patients with cancer have higher rates of severe disease and fatality after COVID-19 than the general population[3]. Concurrent comorbidities, poor performance status, specific cancer types and recent systemic anticancer therapy (SACT) have been variably identified as adverse prognostic factors in patients with cancer and COVID-19[3–5]. However, the actual risk associated with these factors is unclear.

Forty-three million individuals have been infected with COVID-19 in India, resulting in 515,000 deaths (https://covid19.who.int/, accessed 9 March 2022). Case fatality rates in general have been lower in India compared to other countries, especially Western Europe and the United States. While this has been attributed to underreporting of cases (and deaths), the difference cannot be explained on this basis alone (https://cgdev.org/publication/three-new-estimates-indias-all-cause-excess-mortality-during-covid-19-pandemic, accessed 30 November 2021). Possible factors including acquired immunity due to the population being infected by non-SARSCoV-2 coronaviruses in the past and other less known factors may have contributed to the low fatality rate[6]. There are scarce data from India on the outcomes of COVID-19 in patients with cancer[7,8]. Given that cancer treatment is a priority, reliable data are necessary to guide management during future surges of the pandemic. We analyzed the short-term outcomes of COVID-19 in patients with cancer at a tertiary referral cancer center in India and identified risk factors for adverse outcomes.

We collected data from 1,253 patients (479 retrospective, from 11 April to 30 June 2020; 774 prospective, from 1 July 2020 to 28 February 2021) with a confirmed diagnosis of cancer and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The patient baseline characteristics are described in Table 1. At a median follow-up of 76 d, 160 patients (12.8%) met the composite end point of severe COVID-19 or death within 30 d of COVID-19 diagnosis. The 30-d all-cause mortality was 10.9% (138 deaths).

The severity of COVID-19 was mild (grade 1–3 on the World Health Organization (WHO) ordinal scale) in 1,014 (81%) patients, moderate (WHO grade 4 or 5) in 167 (13%) patients and severe (WHO grade 6 or 7) in 72 (6%) patients. In patients with limited life expectancy due to advanced cancer who were considered unsuitable for therapy escalation, the severity of COVID-19 was graded according to the treatment provided; therefore, actual severity may have been underestimated. All-cause 30-d mortality was 2.4% (24 out of 1,014), 38.3% (64 out of 167) and 69.4% (50 out of 72), respectively in patients with mild, moderate, and severe COVID-19.

In a multivariable logistic regression analysis for the composite outcome, advancing age, smoking, ≥2 comorbidities, and palliative intent of treatment were independent predictors for worse outcomes (Table 2). A separate multivariable analysis with 30-d mortality as the outcome identified advancing age (odds ratio (OR) = 1.02; 95% confidence interval (CI) = 1.01–1.03; $P = 0.003$) and palliative intent of treatment (OR = 4.05; 95% CI = 2.73–5.99; $P < 0.001$) as independent risk factors. Among patients treated with palliative intent, 25% (36 out of 145) of those who received SACT <30 d before COVID-19 had an event, compared to 26% (52 out of 199) in those who did not. In patients older than 65 years who received SACT <30 d before COVID-19 (10 out of 34), 29% experienced the composite end point compared to 20% (25 out of 125) in those who had not received SACT.

In our cohort of patients with cancer who developed COVID-19, advancing age, smoking history, palliative intent of treatment and presence of ≥2 comorbidities were independent risk factors for

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Table 1 | Patient baseline characteristics

Characteristic	
Age, years	
<18	161 (12.8)
18–64	933 (74.5)
≥65	159 (12.7)
Sex	
Male	730 (58.3)
Female	523 (41.7)
Smoking (*n* = 1,227)	
Yes	186 (15.2)
No	1,041 (84.8)
Hypertension (*n* = 1,240)	
Yes	209 (16.9)
No	1,031 (83.1)
Diabetes (*n* = 1,241)	
Yes	185 (14.9)
No	1,056 (85.1)
Comorbidities (*n* = 1,241)	
None	847 (68.3%)
One	249 (20.1%)
Two or more	145 (11.7%)
Polypharmacy (5 or more medications) (*n* = 1,243)	
Yes	73 (5.9)
No	1,170 (94.1)
Cancer diagnosis	
Hematolymphoid	293 (23.4)
Solid	960 (76.6)
Cancer type	
Oral/oropharyngeal	135 (10.8)
Breast	114 (9.1)
Acute lymphoblastic leukemia	107 (8.5)
Non-Hodgkin lymphoma	92 (7.3)
Colorectal	92 (7.3)
Other hematolymphoid	89 (7.1)
Bone	57 (4.5)
Cervix	53 (4.2)
Lung	51 (4.1)
Stomach	43 (3.4)
Gallbladder and bile duct	41 (3.3)
Ovary	40 (3.2)
Esophagus	36 (2.9)
Pancreas	36 (2.9)
Central nervous system	31 (2.5)
Liver	29 (2.3)
Bladder	29 (2.3)
Prostate	23 (1.8)
Thyroid	20 (1.6)
Other cancers[a]	135 (10.8)
Intent of management	
Under evaluation	9 (0.7)
Curative intent	900 (71.8)
Palliative intent	344 (27.4)
Current treatment	
Awaiting treatment	302 (24.1)
On active treatment	863 (68.9)
Chemotherapy	398
Targeted therapy	60
Immunotherapy	3
Multimodality	216
Radiation	31
Surgery	78
Combination (chemotherapy + targeted therapy)	51
Other treatment (hormonal therapy, steroids, interventional procedures, transarterial chemotherapy)	26
Follow-up	88 (7.0)
Whether on systemic anticancer treatment within 30 d before COVID-19	
Yes	439 (35.0)
Chemotherapy	337
Targeted therapy	54
Immunotherapy	2
Combination	46
No	814 (65.0)

Data represent actual numbers with percentages in parentheses. [a]Other cancers included skin, soft tissue, kidney, larynx, uterus, hypopharynx, nasopharynx, testis, penis, vulva, mediastinum, melanoma, appendix and adrenal.

severe COVID-19 or death within 30 d. Advancing age and palliative intent of treatment remained independently associated with 30-d mortality. Recent SACT, sex and cancer type were not significantly associated with adverse outcomes.

Since the onset of the COVID-19 pandemic, there have been concerns about the outcomes of COVID-19 in patients with cancer. A meta-analysis (26 studies, 23,736 patients) found a pooled all-cause in-hospital mortality rate of 19%, with nearly threefold higher odds of dying than those without cancer[3]. Early studies from China suggested that patients with cancer and COVID-19 had considerably poorer survival than the general population, with mortality estimates between 20 and 29%[9,10]). Subsequent studies from other countries reported short-term mortality rates between 10 and 29%, with the UK and other European countries reporting higher fatality rates[4,5,11–13].

The dissimilarity in results between studies needs to be interpreted keeping in mind that they were done in different settings and with different population characteristics, at various times, corresponding to different phases of the pandemic. Studies early in the pandemic typically reported higher case fatality rates because little was known about the disease and its management. Also, differences in testing strategies between countries imply that in some studies, patients with cancer who were symptomatic with mild disease and potentially favorable outcomes may not have been identified, compared to those with moderate and severe disease, resulting in higher estimated fatality rates. In addition, the outcomes of patients with cancer and COVID-19 need to be compared to outcomes in the general population for that same country. Countries such as Italy and the UK have reported population case fatality rates of 3–5%

Table 2 | Risk factors for the composite outcome

		Composite outcome	Unadjusted analysis		Adjusted analysis	
			OR with 95% CI	*P*	OR with 95% CI	*P*
Age, years		–	1.03 (1.02–1.04)	<0.001	1.02 (1.01–1.03)	0.006
Sex	Female	69 out of 523 (13%)	ref.		ref.	
	Male	91 out of 730 (13%)	0.94 (0.67–1.31)	0.704	0.79 (0.53–1.12)	0.25
Smoking	No	120 out of 1,041 (12%)	ref.		ref.	
	Yes	36 out of 186 (19%)	1.84 (1.22–2.78)	0.004	1.78 (1.09–2.88)	0.021
Comorbidities	None	86 out of 847 (10%)	ref.		ref.	
	One	40 out of 249 (16%)	1.69 (1.13–2.54)	0.011	1.35 (0.86–2.11)	0.189
	Two or more	31 out of 145 (21%)	2.41 (1.53–3.79)	<0.001	1.89 (1.13–3.15)	0.016
Cancer type	Solid	122 out of 960 (13%)	ref.		ref.	
	Hematolymphoid	38 out of 293 (13%)	1.02 (0.69–1.51)	0.907	1.60 (0.99–2.57)	0.052
Treatment intent	Curative	70 out of 900 (8%)	ref.		ref.	
	Palliative	88 out of 344 (26%)	4.08 (2.89–5.75)	<0.001	3.50 (2.42–5.05)	<0.001
On active SACT within 30 d before COVID-19 diagnosis	No	99 out of 812 (12%)	ref.		ref.	
	Yes	61 out of 439 (14%)	1.16 (0.83–1.64)	0.390	1.11 (0.74–1.67)	0.628

compared to 1.1% in India. These differences could be partly related to population characteristics, with developed countries having a high proportion of older individuals with comorbidities[14]. The age pyramid in low- and middle-income countries like India is skewed toward a higher proportion of younger individuals; similarly, a relatively larger proportion of cancers occur at a younger age than in high-income countries. This is reflected in the median age of patients in our study (44 years), which is much lower than reported in other studies (>65 years)[5]. Similarly, many African countries where the population is predominantly young have reported low COVID-19 fatality rates[15]. Other associated factors include time trends in the spread of the pandemic, capacity and strategy for testing and the accuracy of reporting deaths[14]. The low COVID-19 fatality rate in India could also be because of the decreased severity of infection, possibly due to cross-immunity from exposure to other coronaviruses that are endemic in the population[6].

Research on COVID-19 in patients with cancer has focused on identifying prognostic factors to aid risk stratification and early recognition of patients likely to have adverse outcomes. In keeping with the published literature, we found that advancing age was an independent risk factor for poor outcomes after COVID-19; within this group, older patients who had received recent SACT had worse outcomes than those who did not[5,10,11]. Like other studies, we found that concurrent comorbidities and smoking adversely affected COVID-19 severity and outcomes[5,13]. Our study also showed no impact of sex, cancer type or recent SACT on COVID-19 outcomes. These findings should be interpreted with the understanding that our cohort was different from other studies in some aspects, such as younger median age, spectrum of cancers and less frequent use of monoclonal antibodies and immunotherapy. Broadly, our findings strongly support the continuation of cancer care in most patients during future surges of the pandemic.

Our results showed that treatment with palliative intent was a significant adverse prognostic factor for COVID-19 outcomes, regardless of whether active anticancer treatment had been recently administered. This can be attributed to the debilitation caused by the cancer itself, compounded by the effects of COVID-19. Our study suggests that treatment of patients with advanced metastatic cancers should be guided by the magnitude of benefit based on the nature of the cancer, expected benefits and toxicities with treatment and potential risks of COVID-19-related complications. This is particularly true when healthcare systems are overwhelmed by COVID-19 and resources diverted to palliative chemotherapy would be at the expense of care delivery to those with other diseases, including patients with cancer who are on treatment with curative intent.

A systematic review found that chemotherapy within 30 d before diagnosis of COVID-19 increased the risk of death but not of severe COVID-19 while other therapies (including radiation and immunotherapy) had no such effect[16]. While this may be explained on the basis of the intense immunosuppression caused by chemotherapy, it needs to be interpreted cautiously. First, many studies have not been able to capture reliable data on the nature and timing of systemic therapy in relation to COVID-19. Second, studies grouped all anticancer therapy, which would dilute the effect of individual treatments. Third, changes in practice during the pandemic may have resulted in only fitter patients receiving intensive chemotherapy, thus confounding the results.

Our study has several strengths and some limitations. To the best of our knowledge, it is one of the largest single-center studies examining the outcomes of COVID-19 in patients with cancer and provides possibly the most robust prospective data available from this part of the world. Second, this was a pragmatic study that included all patients regardless of age, cancer type or COVID-19 severity. Finally, being a referral center for patients with cancer who developed COVID-19, it is likely to be fairly representative of the real world. One possible limitation is that a small proportion of patients who were relatively less symptomatic but did not have facilities for home isolation were admitted to hospital for social rather than medical reasons, potentially skewing the severity scoring of the illness; however, these numbers were low.

The results of our study have important policy-level implications. We have demonstrated that in our setting, most patients with cancer who developed COVID-19 had mild disease and favorable outcomes. Considering that India has a huge burden of COVID-19 and has had multiple pandemic surges, our findings are important to assuage fear in patients and treatment providers. With growing realization of the adverse outcomes of deferring active cancer treatment, our results support continuation of cancer care even during pandemics. Cancer treatment during the pandemic has been severely hampered due to multiple reasons: inability of patients to access care due to fear of contracting COVID-19 or travel restrictions; reduction in existing cancer care facilities because of

conversion to COVID-19 centers or staffing issues (illness, quarantine or travel restrictions); and recommendations to downscale or delay cancer therapies. A study across 41 cancer centers in India found substantial reductions in care delivery during the pandemic[17]. Even in the pre-pandemic period, several low- and middle-income countries faced challenges with cancer care related to lack of access, delayed stage presentation and poor outcomes[18]. In such settings, further reductions in cancer care are likely to have disastrous consequences. Many countries are now seeing new waves of COVID-19 infections and the findings of this study reinforce that cancer care should be prioritized even during a pandemic.

Methods

We performed an ambi-directional cohort study of patients with cancer diagnosed on PCR with reverse transcription (RT–PCR) with SARS-CoV-2 infection at the Tata Memorial Hospital, Mumbai. The study was approved by the institutional ethics committee, registered with the Clinical Trials Registry of India (CTRI/2020/07/026339) and carried out in accordance with the principles of good clinical research practice.

We included all patients (adult and pediatric) with a proven cancer diagnosis at any stage of management (under evaluation, on active treatment (curative or palliative intent) or on follow-up), with SARS-CoV-2 infection confirmed by a positive RT–PCR test during the study period; these patients were identified from a central database of all patients undergoing RT–PCR testing for suspected SARS-CoV-2 infection.

We collected data from electronic medical records for the following variables: age; sex; comorbidities; smoking status (ever versus never-smoker); date of cancer diagnosis; type of cancer; intent of management (curative versus palliative); status of management (evaluation, active treatment, follow-up); type of management (chemotherapy, radiation therapy, surgery, palliative care, combination or other); date of completion of last systemic anticancer treatment (defined as chemotherapy, immunotherapy, targeted therapy or a combination); date of COVID-19 diagnosis; maximum severity of COVID-19 (classified using the WHO ordinal scale); and COVID-19 outcome (dead or alive). The WHO ordinal scale uses the intervention used to treat COVID-19 as a measure of severity, and not the symptoms; hence, it would underestimate the severity in situations where care was not escalated due to the terminal nature of a comorbid disease such as cancer. Therefore, we used a composite outcome of severe COVID-19 (WHO grade ≥6) or death within 30 d from COVID-19 diagnosis as our primary outcome. We used a multivariable logistic regression model for the association between independent predictors—age, sex, smoking status, presence of comorbidities, cancer type, intent of management, duration from last SACT to COVID-19 diagnosis and primary outcome. We also conducted a multivariable analysis to identify risk factors for 30-d mortality. Data were collected and analyzed with SPSS v.25.0; statistical tests were interpreted at a two-tailed 5% significance level.

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request. Source data are provided with this paper.

Code availability

The manuscript has no computer code or algorithms.

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Author contributions

M.S., G.C., P.R. and C.S.P. conceptualized and designed the study, analyzed the data and co-wrote the paper. M.S. and G.C. contributed equally to all aspects of the paper and should be considered joint first authors. A.A., S.B., P.C., C.D., J.D., K.D'S., H.J., S.L., N.R.M., N.M., S.N., L.N., P.N. and S.P. contributed to data collection, analyses and interpretation, revised the paper and approved the final draft. P.P., A.R., O.S., A.S., E.S., J.T. and R.B. contributed to data collection, review of manuscript and approval of final draft.

Competing interests

The authors declare no competing interests.

Additional information

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Sample size	This was an ambi-directional cohort study and we included all patients with a confirmed diagnosis of cancer and SARS-CoV2 between 11th April 2020 to 28th February 2021. No formal sample size calculations were done, but our study is one of the largest single-centre studies ever done on the impact of COVID-19 on patients with cancer
Data exclusions	No patients' data were excluded from the analyses. In some patients in whom complete data were not available, available data were used for analyses. In tables 1 and 2, the number of evaluable patients has been listed for all variables which had missing data
Replication	This is an observational study and therefore, single observations were made on patients, which could not be replicated
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Randomization	*If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.*

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	*Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.*
Research sample	*Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National*

Research sample	*Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.*
Sampling strategy	*Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.*
Data collection	*Describe the data collection procedure, including who recorded the data and how.*
Timing and spatial scale	*Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Reproducibility	*Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.*
Randomization	*Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.*
Blinding	*Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.*

Did the study involve field work? ☐ Yes ☐ No

Field work, collection and transport

Field conditions	*Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).*
Location	*State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).*
Access & import/export	*Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).*
Disturbance	*Describe any disturbance caused by the study and how it was minimized.*

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☑	☐ Antibodies
☑	☐ Eukaryotic cell lines
☑	☐ Palaeontology and archaeology
☑	☐ Animals and other organisms
☐	☑ Human research participants
☐	☑ Clinical data
☑	☐ Dual use research of concern

Methods

n/a	Involved in the study
☑	☐ ChIP-seq
☑	☐ Flow cytometry
☑	☐ MRI-based neuroimaging

Antibodies

Antibodies used	*Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Validation	*Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.*

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	*State the source of each cell line used.*

Authentication	*Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.*
Mycoplasma contamination	*Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.*
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Palaeontology and Archaeology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information). Permits should encompass collection and, where applicable, export.*
Specimen deposition	*Indicate where the specimens have been deposited to permit free access by other researchers.*
Dating methods	*If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	*For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals.*
Wild animals	*Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.*
Field-collected samples	*For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.*
Ethics oversight	*Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.*

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Human research participants

Policy information about studies involving human research participants

Population characteristics	We included all patients (adult and paediatric) with a proven cancer diagnosis at any stage of management [under evaluation, on active treatment (curative or palliative intent) or on follow-up], with SARS-CoV2 infection confirmed by a positive RT-PCR test during the study period.
Recruitment	Patients were identified from a central database of all patients undergoing RT-PCR testing for suspected SARS-CoV2 infection.
Ethics oversight	The study was approved by the Institutional Ethics Committee of the Tata Memorial Hospital and carried out in accordance with the principles of good clinical research practice. Informed consent was taken from patients for the prospective part of the cohort; consent waiver was granted by the IEC for the retrospective part of the cohort

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Clinical Trials Registry of India (CTRI/2020/07/026339)
Study protocol	Clinical Trials Registry of India (CTRI/2020/07/026339)
Data collection	We collected data for patients diagnosed with SARS CoV2 infection between 11th April 2020 and 28th February 2021 from electronic medical records for the following variables: age, sex, co-morbidities, smoking status (ever vs never-smoker), date of cancer diagnosis, type of cancer, intent of management (curative versus palliative), status of management (evaluation, active treatment, follow-up), type of management (chemotherapy, radiation therapy, surgery, palliative care, combination or other), date of completion of last systemic anti-cancer treatment (defined as chemotherapy, immunotherapy, targeted therapy or a combination), date of COVID-19 diagnosis, maximum severity of COVID-19 (classified using the WHO ordinal scale) and COVID-19 outcome (dead or alive).
Outcomes	We used a composite outcome of severe COVID-19 (WHO grade ≥6) or death within 30 days from COVID-19 diagnosis as our primary outcome. We used a multivariable logistic regression model for association between independent predictors – age, sex, smoking status, presence of comorbidities, type of cancer, intent of management, duration from last SACT to COVID-19 diagnosis and the primary outcome. We also conducted a multivariable analysis to identify risk factors for 30-day mortality.

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
X	☐	Public health
X	☐	National security
X	☐	Crops and/or livestock
X	☐	Ecosystems
X	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
X	☐	Demonstrate how to render a vaccine ineffective
X	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
X	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
X	☐	Increase transmissibility of a pathogen
X	☐	Alter the host range of a pathogen
X	☐	Enable evasion of diagnostic/detection modalities
X	☐	Enable the weaponization of a biological agent or toxin
X	☐	Any other potentially harmful combination of experiments and agents

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links *May remain private before publication.*	*For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.*
Files in database submission	*Provide a list of all files available in the database submission.*
Genome browser session (e.g. UCSC)	*Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.*

Methodology

Replicates	*Describe the experimental replicates, specifying number, type and replicate agreement.*
Sequencing depth	*Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.*
Antibodies	*Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.*
Peak calling parameters	*Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.*
Data quality	*Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.*
Software	*Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.*

Flow Cytometry

Plots

Confirm that:

☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☐ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	*Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.*
Instrument	*Identify the instrument used for data collection, specifying make and model number.*
Software	*Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.*
Cell population abundance	*Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.*
Gating strategy	*Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.*

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type	*Indicate task or resting state; event-related or block design.*
Design specifications	*Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.*
Behavioral performance measures	*State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).*

Acquisition

Imaging type(s)	*Specify: functional, structural, diffusion, perfusion.*
Field strength	*Specify in Tesla*
Sequence & imaging parameters	*Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.*
Area of acquisition	*State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.*

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software	*Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).*
Normalization	*If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.*
Normalization template	*Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.*
Noise and artifact removal	*Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and physiological signals (heart rate, respiration).*

Volume censoring

Define your software and/or method and criteria for volume censoring, and state the extent of such censoring.

Statistical modeling & inference

Model type and settings

Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).

Effect(s) tested

Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference
(See Eklund et al. 2016)

Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.