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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data was processed using R version 3.6.1 (Vienna Austria). Large tables were read-in and written using R packages tidyverse (v 1.3.0), reshape2 (v 1.4.4) , and readxl (v 1.3.1) Clinical data was extracted from the Epic electronic health record (Verona, WI) using Epic Hyperspace (August 2019), Epic Clarity (February 2020) and Epic Caboodle (February 2020) databases via connecting to Oracle (18c Enterprise Edition Release 18.0.0.0.0) and SQL server (Microsoft SQL Server 2016 (SP2-CU11) (KB4527378) - 13.0.5598.27 (X64)) databases respectively.
Data analysis	SAS 9.4 (PROC GENMOD, PROC LIFETEST and PROC PHREG), GraphPad Prism 8.4.2, and R 3.6.3. (Package: ggplot2)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

The data supporting this publication is available at ImmPort (https://www.immport.org) under study accession SDY1662.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

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

Sample size	A two-sided log-rank test with an overall sample size of 674 patients (337 in each group) achieves 80% power at a 0.05 type I error to detect a hazard ratio of 2.29 when the proportion of death in the low group is 20%. In this study, we had more than 1,200 patients so that we can have enough power to detect the potential slight smaller effect sizes after adjusting for the covariates. Please refer to response to Reviewer 2 comments. We queried all available health records.
Data exclusions	The patients with the cytokines measured after the date of last follow-up and or missing status (discharge, death, or hospitalization) were excluded. 1,298 patients had cytokines measured on or before the date of last follow-up. Among them, 1,245 patients had the measurements of all four cytokines. Exclusion criteria were pre-established. Our aim was to look at patients with both an indication of SARS-CoV-2 infection and ELLA cytokine data availability.
Replication	This observational study is of a hospitalized cohort during the COVID-19 pandemic in New York City. We validated the initial findings in a second cohort. -- The ELLA platform has 3 built in replicates.
Randomization	This is not a clinical trial. Established clinical laboratory test data was used.
Blinding	This is not a clinical trial.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Please see Table 1. Patient characteristics for details of human subjects research participants.
Recruitment	Subjects were not recruited into this study, therefore, self-selection bias does not apply. Data was collected as part of normal clinical care. ELLA was ordered as a clinical test as part of standard clinical care at the MSHS during the SARS-CoV-2 epidemic. Clinical tests were ordered by the treated physician.
Ethics oversight	This research was reviewed and approved by the Human Research Protection Program at the Icahn School of Medicine at Mount Sinai (ISMMS), a comprehensive system to ensure the protection of the rights and welfare of subjects in human research. The Program for the Protection of Human Subjects (PPHS) is a key component of ISMMS' efforts to ensure human subject protections. It supports our researchers in assuring the ethical conduct of research and compliance with federal, state, and institutional regulations, and provides a professional office staff to assist both investigators, participants, and five Institutional Review Boards (IRBs).

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