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Changes in postoperative outcomes of emergency general and digestive surgery during the COVID-19 pandemic in Spain: a propensity-score-matched comparison of COVID-19-infected, non-infected and pre-pandemic patients (COVID-CIR study).

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Complete List of Authors:	<p>Osorio, Javier; Hospital Universitari de Bellvitge, Digestive Surgery MADRAZO, ZOILO; Hospital Universitari de Bellvitge, GENERAL SURGERY Videla, Sebastian ; IDIBELL, Clinical Research Support Unit Sainz, Beatriz ; Complejo Hospitalario de Navarra, Department of Surgery Rodríguez-González, Araceli; Hospital de Donostia, Department of Surgery Campos, Andrea; Fundacio Parc Tauli, Department of Surgery Santamaria, Maite; Hospital Universitari Arnau de Vilanova, Department of Surgery Pelegrina, Amalia; Consorci Parc de Salut MAR de Barcelona, Department of Surgery González-Serrano, Carmen; Hospital Universitario Basurto, Department of Surgery Aldeano, Aurora; Granollers Hospital Asylum Foundation, Department of Surgery Sarriugarte Lasarte, Aingeru ; Hospital de Basurto, Department of Surgery Gómez-Díaz, Carlos; Hospital Universitario Cruces, Department of Surgery Ruiz-Luna, David; Terrassa Health Consortium, Department of Surgery García-Ruiz-de-Gordejuela, Amador; Vall d'Hebron University Hospital, Department of General Surgery Gómez-Gavara, Concepción; Vall d'Hebron University Hospital, Hepatobiliopancreatic Surgery and Transplantation Department Gil-Barrionuevo, Marta; Hospital of Viladecans, Department of Surgery Vila, Marina; Hospital de Mataró, Department of Surgery Clavell, Arantxa; University Hospital Germans Trias i Pujol, Department of Surgery Campillo, Beatriz; Fundació Hospital Sant Joan de Déu de Martorell, Department of Surgery Millan, Laura; Hospital Doctor Jose Molina Orosa, Department of Surgery Olona, Carles; Joan XXIII University Hospital in Tarragona, Department of Surgery</p>

	Sanchez-Cordero, Sergio; Igualada Hospital, Department of Surgery Medrano, Rodrigo; Hospital de la Santa Creu i Sant Pau, Department of Surgery López-Arévalo, Camilo; Hospital de Sant Joan Despi Moises Broggi, Department of Surgery Pérez-Romero, Noelia; Fundacio Assistencial de Mutua de Terrassa FPC, Department of Surgery Artigau, Eva; Hospital Universitari de Girona Doctor Josep Trueta, Department of Surgery Calle, Miguel; Hospital Alto Deba, Department of Surgery Echenagusia, Victor; Hospital Universitario Araba sede Txagorritxu, Department of Surgery Otero, Aurema; Bellvitge Institute for Biomedical Research, Department of Clinical Pharmacology Tebe, Cristian; IDIBELL, Statistics advisory service Pallares, Natalia; Institut d'Investigacio Biomedica de Bellvitge Biondo, Sebastiano; Bellvitge University Hospital, Department of Surgery
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Authors: Osorio J^{1*}, Madrazo Z^{1*}, Videla S^{2*}, Sainz B³, Rodríguez-González A⁴, Campos A⁵, Santamaría M⁶, Pelegrina A⁷, González-Serrano C⁸, Aldeano A⁹, Sarriugarte A¹⁰, Gómez-Díaz CJ¹¹, Ruiz-Luna D¹², García-Ruiz-de-Gordejuela A¹³, Gómez-Gavara C¹⁴, Gil-Barrionuevo M¹⁵, Vila M¹⁶, Clavell A¹⁷, Campillo B¹⁸, Millán L¹⁹, Olona C²⁰, Sánchez-Cordero S²¹, Medrano M²², López-Arévalo A²³, Pérez-Romero N²⁴, Artigau E²⁵, Calle M²⁶, Echenagusia V²⁷, Otero A², Tebe C²⁸, Pallares N²⁸, Biondo S¹, and the COVID-CIR Collaborative Group.

- 1 Department of Surgery, Hospital Universitari de Bellvitge, L'Hospitalet del Llobregat, Barcelona, Spain.
- 2 Clinical Research Support Unit, Clinical Pharmacology Department, Bellvitge University Hospital/Bellvitge Biomedical Research Institute (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain.
- 3 Department of Surgery, Complejo Hospitalario de Navarra, Pamplona, Spain.
- 4 Department of Surgery, Donostia University Hospital, San Sebastian, Spain.
- 5 Department of Surgery, Parc Taulí Health Corporation, Sabadell Hospital, Sabadell, Spain.
- 6 Department of Surgery, Arnau de Vilanova University Hospital, Lleida, Spain.
- 7 Department of Surgery, Hospital del Mar University Hospital, Barcelona, Spain.
- 8 Department of Surgery. Basurto University Hospital, Bilbao, Spain.
- 9 Department of Surgery, Granollers General Hospital, Granollers, Spain.
- 10 Department of Surgery, Cruces University Hospital, Bilbao, Spain.
- 11 Department of Surgery, Althaia Foundation, Manresa, Spain.
- 12 Department of Surgery, Terrassa Health Consortium, Terrassa Hospital, Terrassa, Spain.

- 1
2
3 13 General Surgery Department, Vall d'Hebrón University Hospital, Barcelona, Spain.
4
5 14 Hepatobiliopancreatic Surgery and Transplantation Department, Vall d'Hebrón
6 University Hospital, Barcelona, Spain.
7
8 15 Department of Surgery, Viladecans Hospital, Viladecans, Spain.
9
10 16 Department of Surgery, Mataró Hospital, Maresme Health Consortium, Mataró, Spain.
11
12 17 Department of Surgery, Germans Trias i Pujol University Hospital, Badalona, Spain.
13
14 18 Department of Surgery, Sant Joan de Deu Hospital Foundation, Martorell, Spain.
15
16 19 Department of Surgery, Dr. José Molina Orosa Hospital, Lanzarote, Spain.
17
18 20 Department of Surgery, Joan XXIII University Hospital, Tarragona, Spain.
19
20 21 Department of Surgery, Igualada University Hospital, Anoia Health Consortium,
21 Igualada, Spain.
22
22 22 Department of Surgery, Sant Pau University Hospital, Barcelona, Spain.
23
23 23 Department of Surgery. Moisès Broggi Hospital, Sant Joan Despí, Spain.
24
24 24 Department of Surgery, Mútua de Terrassa University Hospital, Terrassa, Spain.
25
25 25 Department of Surgery, Girona Dr. Josep Trueta University Hospital, Girona, Spain.
26
26 26 Department of Surgery, Alto Deba Hospital, Mondragon, San Sebastián, Spain.
27
27 27 Department of Surgery, Araba University Hospital, Txagorritxu Hospital, Vitoria,
28 Spain.
29
30 28 Statistical unit of the Bellvitge Biomedical Research Institute (IDIBELL), L'Hospitalet
31 de Llobregat, Barcelona, Spain.
32
33
34
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36

37 * Osorio J, Madrazo Z, and Videla S have contributed equally and share first authorship.
38
39

40 **Corresponding author:** Javier Osorio, MD, PhD.

41
42 Department of Surgery. Hospital Universitari de Bellvitge. Avinguda de la Feixa
43 Llarga S/N. 08907 L'Hospitalet del Llobregat, Barcelona, Spain.
44

45
46 Electronic address: josorio@bellvitgehospital.cat.
47

48
49 Telephone: +34 637286009
50

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Collaborators - The COVID-CIR Collaborative Group:

- María José Sara. Department of Surgery, Complejo Hospitalario de Navarra, Pamplona, Spain. Electronic address: mj.sara.ongay@navarra.es
- Aitor Ariceta. Department of Surgery, Complejo Hospitalario de Navarra, Pamplona, Spain. Electronic address: aitor.ariceta.lopez@navarra.es
- Rocío Ruiz-Marzo. Department of Surgery, Complejo Hospitalario de Navarra, Pamplona, Spain. Electronic address: rocio.ruiz.marzo@navarra.es
- Ainhoa Andrés. Department of Surgery, Donostia University Hospital, San Sebastian, Spain. Electronic address: ainhoa.andresimaz@osakidetza.eus
- Lorena Arrabal. Department of Surgery, Donostia University Hospital, San Sebastian, Spain. Electronic address: lorena.arrabalagueera@osakidetza.eus
- Alba Garcia-Trancho. Department of Surgery, Donostia University Hospital, San Sebastian, Spain. Electronic address: alba.garciatrancho@osakidetza.eus
- Anna Muñoz-Campaña. Department of Surgery, Parc Taulí Health Corporation, Sabadell Hospital, Sabadell, Spain. Electronic address: amunozc@tauli.cat
- Ariadna Cidoncha. Department of Surgery, Parc Taulí Health Corporation, Sabadell Hospital, Sabadell, Spain. Electronic address: acidoncha@tauli.cat
- Victoria Lucas. Department of Surgery, Parc Taulí Health Corporation, Sabadell Hospital, Sabadell, Spain. Electronic address: vlucas@tauli.cat
- Núria Mestres. Department of Surgery, Arnau de Vilanova University Hospital, Lleida, Spain. Electronic address: nmestres.lleida.ics@gencat.cat
- Jaume Ortega. Department of Surgery, Arnau de Vilanova University Hospital, Lleida, Spain. Electronic address: jaortega.lleida.ics@gencat.cat
- Silvia Pérez-Farré. Department of Surgery, Arnau de Vilanova University Hospital, Lleida, Spain. Electronic address: sperezf.lleida.ics@gencat.cat
- Estela Membrilla. Department of Surgery, Hospital del Mar University Hospital, Barcelona, Spain. Electronic address: 94934@parcdesalutmar.cat

- 1
2
3 – Alex Morera. Department of Surgery, Hospital del Mar University Hospital, Barcelona,
4 Spain. Electronic address: 64267@parcdesalutmar.cat
5
6
7 – Elisabet Baena. Department of Surgery, Hospital Universitari de Bellvitge,
8 L'Hospitalet del Llobregat, Barcelona, Spain. Electronic address:
9
10 ebaena@bellvitgehospital.cat
11
12
13 – Natàlia Cornellà. Department of Surgery, Hospital Universitari de Bellvitge,
14 L'Hospitalet del Llobregat, Barcelona, Spain. Electronic address:
15
16 ncornella@bellvitgehospital.cat
17
18
19 – Jon Ignacio Uriarte. Department of Surgery. Basurto University Hospital, Bilbao, Spain.
20 Electronic address: jonignacio.uriarteteran@osakidetza.eus
21
22
23 – Eneko Gonzalez-Aguirregomezcorta. Department of Surgery. Basurto University
24 Hospital, Bilbao, Spain. Electronic address:
25
26 eneko.gonzalezaguirregomezcorta@osakidetza.eus
27
28
29 – Martin Amarelo. Department of Surgery. Basurto University Hospital, Bilbao, Spain.
30 Electronic address: martin.amarelogarcia@osakidetza.eus
31
32
33 – Nares Arroyo. Department of Surgery, Granollers General Hospital, Granollers, Spain.
34 Electronic address: narroyo@fphag.org
35
36
37 – Maria Batlle. Department of Surgery, Granollers General Hospital, Granollers, Spain.
38 Electronic address: mbatlle@fphag.org
39
40
41 – Miriam Flores. Department of Surgery, Granollers General Hospital, Granollers, Spain.
42 Electronic address: mfloresy@fphag.org
43
44
45 – Eva Alonso. Department of Surgery, Cruces University Hospital, Bilbao, Spain.
46 Electronic address: eva.alonsocalderon@osakidetza.eus
47
48
49 – Marina Esgueva. Department of Surgery, Cruces University Hospital, Bilbao, Spain.
50 Electronic address: marina.esguevaangulo@osakidetza.eus
51
52
53 – Ibabe Villalabeitia. Department of Surgery, Cruces University Hospital, Bilbao, Spain.
54 Electronic address: ibabe.villalabeitiaateca@osakidetza.eus
55
56
57
58
59
60

- 1
2
3 – Claudio Antonio Guariglia. Department of Surgery, Althaia Foundation, University
4 Healthcare Network, Manresa, Spain. Electronic address: caguariglia@althaia.cat
5
6
7 – Alexander Leonel Osorio. Department of Surgery, Althaia Foundation, University
8 Healthcare Network, Manresa, Spain. Electronic address: alosorio@althaia.cat
9
10
11 – Lorena Sanchón. Department of Surgery, Althaia Foundation, University Healthcare
12 Network, Manresa, Spain. Electronic address: lsanchon@althaia.cat
13
14
15 – Carlos Gustavo Petrola. General Surgery Department, Vall d’Hebrón University
16 Hospital, Barcelona, Spain. Electronic address: cpetrola@vhebron.net
17
18
19 – Rocio Martín-Sánchez. Hepatobiliopancreatic Surgery and Transplantation
20 Department, Vall d’Hebrón University Hospital, Barcelona, Spain. Electronic
21 address: rocio.martin@vhebron.net
22
23
24 – Miriam Moratal. Hepatobiliopancreatic Surgery and Transplantation Department,
25 Vall d’Hebrón University Hospital, Barcelona, Spain. Electronic address:
26 mmoratal@vhebron.net
27
28
29 – Pere Clos. Department of Surgery, Mataró Hospital, Maresme Health
30 Consortium, Mataró, Spain. Electronic address: pclos@csdm.cat
31
32
33 – Elisenda Garsot. Department of Surgery, Germans Trias i Pujol University Hospital,
34 Badalona, Spain. Electronic address: egarsot.germanstrias@gencat.cat
35
36
37 – Albert Caballero. Department of Surgery, Germans Trias i Pujol University Hospital,
38 Badalona, Spain. Electronic address: acaballero.germanstrias@gencat.cat
39
40
41 – Javier Corral. Department of Surgery, Germans Trias i Pujol University Hospital,
42 Badalona, Spain. Electronic address: jcorral.germanstrias@gencat.cat
43
44
45 – Araceli Rocío Romero. Department of Surgery, Dr. José Molina Orosa Hospital,
46 Lanzarote, Spain. Electronic address: aromdor@gobiernodecanarias.org
47
48
49 – Andrea Rossetti. Department of Surgery, Dr. José Molina Orosa Hospital, Lanzarote,
50 Spain. Electronic address: arosset@gobiernodecanarias.org
51
52
53
54
55
56
57
58
59
60

- 1
2
3 – Elvira Vaillo. Department of Surgery, Dr. José Molina Orosa Hospital,
4 Lanzarote, Spain. Electronic address: evaimar@gobiernodecanarias.org
5
6
7 – Aleidis Caro. Department of Surgery, Joan XXIII University Hospital, Tarragona,
8 Spain. Electronic address: acarо.hj23.ics@gencat.cat
9
10
11 – Robert Memba. Department of Surgery, Joan XXIII University Hospital,
12 Tarragona, Spain. Electronic address: rmembai.hj23.ics@gencat.cat
13
14
15 – Rosa Jorba. Department of Surgery, Joan XXIII University Hospital, Tarragona,
16 Spain. Electronic address: rjorba.hj23.ics@gencat.cat
17
18
19 – David Salazar. Department of Surgery, Igualada University Hospital, Anoia
20 Health Consortium, Igualada, Spain. Electronic address: dsalazar@csa.cat
21
22
23 – Carla Galmés. Department of Surgery, Igualada University Hospital, Anoia
24 Health Consortium, Igualada, Spain. Electronic address: cgalmes@csa.cat
25
26
27 – Mariano Artigot. Department of Surgery, Igualada University Hospital, Anoia
28 Health Consortium, Igualada, Spain. Electronic address: martigot@csa.cat
29
30
31 – Silvia Rofín. Department of Surgery, Sant Pau University Hospital, Barcelona,
32 Spain. Electronic address: srofin@santpau.cat
33
34
35 – Lilian María Escobar. Department of Surgery, Sant Pau University Hospital,
36 Barcelona, Spain. Electronic address: LEscobar@santpau.cat
37
38
39 – Melisa Arias. Department of Surgery, Mútua de Terrassa University Hospital, Terrassa,
40 Spain. Electronic address: marias@mutuaterrassa.cat
41
42
43
44 – Cinta Benaiges. Department of Surgery, Mútua de Terrassa University Hospital,
45 Terrassa, Spain. Electronic address: cbenaiges@mutuaterrassa.cat
46
47
48 – Eloy Maldonado. Department of Surgery, Girona Dr. Josep Trueta University Hospital,
49 Girona, Spain. Electronic address: emaldonadom.girona.ics@gencat.cat
50
51
52
53
54
55
56
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ABSTRACT

Word count: 249

Background: Concern has risen on whether COVID-19 infection increases complications and mortality of surgical patients. Besides, overwhelmed hospitals could have decreased ability to rescue patients from postoperative complications. This cohort's study aims to determine whether postoperative outcomes of emergency digestive surgery worsened during the COVID-19 pandemic both for COVID-19-infected and uninfected patients.

Methods: Patients undergoing emergency general and digestive surgery from March to June, 2020, and from March to June, 2019 in 25 Spanish hospitals were included. Main outcome: 30-day mortality. Secondary outcomes: postoperative complications, severe complications (Clavien-Dindo score \geq IIIA) and failure-to-rescue (death rate among complicated patients). Propensity-score matching was done between intra-pandemic COVID-19-positive and -negative patients (1:3); and between COVID-19-negative intra- and pre-pandemic patients (1:1). A logistic regression model was done in matched cohorts.

Results: 5 307 patients were included (183 COVID-19-positive, 2 132 intra-pandemic COVID-19-negative, 2 992 pre-pandemic). COVID-19-positive patients presented higher analytical markers of inflammatory response and tissular damage and had more complications (1.8-fold risk), severe complications (1.7-fold), and mortality (2.1-fold) than intra-pandemic COVID-19-negative patients. Intra-pandemic COVID-19-negative patients, in comparison to pre-pandemic controls, had similar analytical markers, complication and severe complication rates, but higher failure-to-rescue (1.6-fold risk).

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3 **Conclusions:** COVID-19-infected patients submitted to emergency surgeries are at
4 increased risk of postoperative complications and mortality; therefore, non-surgical
5 management should be prioritized in these patients. Moreover, COVID-19-negative
6 patients operated on during the pandemic presented higher-than-expected failure-to-
7 rescue; an effort to invest on and better organize public health system should be made to
8 minimize avoidable deaths in future sanitary crisis.
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INTRODUCTION

Since the beginning of 2020, the rapid spread of the COronaVirus-19 Disease (COVID-19) has stressed many health-care systems worldwide, forcing cancellation of most programmed surgeries¹⁻⁵. However, non-delayable surgeries continued to be performed, sometimes in patients infected by COVID-19^{6,7}. Patients undergoing emergency surgery are at higher risk of postoperative complications and mortality than those submitted to elective interventions^{8,9}. In addition, COVID-19-positive patients could be susceptible of poor postoperative outcomes due to the immunological dysregulation and hyperinflammatory response to surgery, and need of mechanical ventilation¹⁰⁻¹⁵. Therefore, COVID-19-positive patients with potentially urgent surgical diseases put clinicians in the dilemma of forcing an uncertain conservative management^{12-14,16,17}. Most guidelines and recommendations are based on expert opinion¹⁸⁻²¹. Studies describing the risk of performing surgery in COVID-19-infected patients are needed to help evidence-based decision making.

Cohort studies of COVID-19-infected patients submitted to surgery show poor postoperative outcomes¹¹⁻¹⁴. However, these findings should be benchmarked with caution, as during the pandemic, all patients were at risk of worse-than-expected outcomes: fear or difficulty of visiting hospitals could make surgical pathologies reach a more advanced stage at consultation²¹⁻²³; and hospitals' work overload may difficult rescue from postoperative complications^{9,23}. Spanish public health system could be especially vulnerable to the pandemic resilience test, as austerity following the 2008 financial crisis left it understaffed, under-resourced and under strain²⁴. Reliable data on the consequences of hospital collapse are needed in order to draw lessons for the future^{25,26}.

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3 Our hypothesis was that, from March to June 2020, 30-day mortality following
4 emergency general and digestive surgery increased for COVID-19-infected patients,
5 compared to contemporary COVID-19-uninfected ones; and also, for COVID-19-
6 uninfected patients, compared with patients operated on before the pandemic.
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METHODS

Study design

This is a multicentre retrospective cohorts' study in patients undergoing emergency general and digestive surgery at 25 Spanish hospitals. The study protocol (COVID-CIR) was approved by the Institutional Review Board at the leading and participating hospitals and has been previously published²⁷. Informed patients' consent was waived given the retrospective nature of the study. It was conducted in accordance with STROBE guidelines and the principles of the Declaration of Helsinki²⁸. A high degree of confidentiality, in compliance with the provisions of personal data protection as required by Spanish Law (LOPD 3/2018), was ensured. Protocol registration identifier: ClinicalTrials.gov NCT04479150, July 21st, 2020.

Three cohorts of patients submitted to emergency general or gastrointestinal surgery were defined:

Cohort 1: COVID-19-infected operated on between March 1st and June 30th, 2020;

Cohort 2: COVID-19-non-infected operated on between March 1st and June 30th, 2020;

and

Cohort 3: patients operated on between March 1st and June 30th, 2019.

Participants

Participant hospitals and investigators are detailed in the *Supplementary material (Table S1)*. All patients aged 18 or more undergoing emergency digestive or general surgery during the pandemic and pre-pandemic periods were included. Programmed procedures were excluded, but urgent reinterventions to treat complications of elective surgeries were included. If patients had multiple emergency operations, the first one was

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3 considered as the index procedure. Patients were considered as COVID-19-positive if
4 confirmed by quantitative RT-PCR (reverse transcription-polymerase chain reaction)
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6 detection of viral RNA in nasopharyngeal sample within 15 days before or 30 days after
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8 surgery or in case of clinical suspicion sustained by chest CT-scan findings. Otherwise,
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10 patients were COVID-19-negative.
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14 15 **Variables**

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18 Anonymized data were gathered in an eCRF based on REDCap® (Research Electronic
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20 Data Capture) software.
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24 Demographic data included: age, sex, Body Mass Index (BMI), American Society of
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26 Anaesthesiologists (ASA) surgical risk score, functional status, and previous
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28 comorbidities: smoking habit, respiratory function, Chronic Obstructive Pulmonary
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30 Disease (COPD), cardiac function, ischemic heart disease, cerebrovascular accident,
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32 peripheral arterial disease, arterial hypertension, and diabetes.
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36 Index surgery day data included: physiological variables (temperature, blood pressure,
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38 heart rate, and Glasgow coma score); electrocardiogram findings; analytical parameters
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40 (sodium, potassium, urea, alanine aminotransferase [ALT], haemoglobin, leucocytes,
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42 neutrophils, lymphocytes, platelets, C-reactive protein, D-dimer, ferritin, procalcitonin,
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44 troponin, and prothrombin time); neutrophil / lymphocyte ratio (NLR), platelet /
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46 lymphocyte ratio (PLR) and Systemic Immune-inflammation Index (SII, neutrophil x
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48 platelet / lymphocyte counts). Operative variables included: clinical priority (urgent or
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50 emergency surgery), surgical access, malignancy, type and extension of peritoneal
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52 exudates, estimate blood loss, surgical procedure(s), and complexity of primary
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54 intervention, as defined by the Physiological and Operative Severity Score for the
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56 enUmeration of Mortality and Morbidity (POSSUM) scale²⁹. Prognostic surgical scales
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3 POSSUM (mortality and morbidity), Portsmouth-POSSUM (P-POSSUM, mortality),
4 and aLicante sUrgical Community Emergencies New Tool for the enUmeration of
5 Morbidities (LUCENTUM, morbidity) were calculated (*Table S2*)²⁹⁻³⁰.
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10 Besides, in COVID-19-positive patients, we detailed pre- or postoperative diagnosis and
11 PCR confirmation.
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15 16 **Outcomes**

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18 Main outcome was 30-day mortality for any cause, being day 0 the index surgery.
19 Secondary outcomes were: 90-day mortality; 30-day overall postoperative
20 complications; pulmonary complications (pneumonia, respiratory infection, respiratory
21 failure, pleural effusion, or pulmonary atelectasis); thromboembolic complications
22 (deep venous thrombosis, pulmonary embolism, acute myocardial infarction, stroke,
23 acute limb ischemia, or acute mesenteric ischemia); severe complications (graded \geq
24 IIIA Clavien-Dindo classification); Failure-To-Rescue (FTR), defined as percentage of
25 patients dying as a consequence of any postoperative complication^{31,32}; ICU stay ≥ 24
26 hours after surgery; ≤ 30 -day hospital readmission; ≤ 30 -day surgical reintervention; and
27 length of stay, defined as number of days from admission to hospital discharge or death.
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42 **Statistical analysis**

43 *Data quality*

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45 Before analysis, the principal investigators (JO, ZM and SV) confirmed completeness
46 and accuracy of data with senior surgeons from each centre. Hospitals failing to include
47 at least 90% of eligible patients were excluded to avoid selection bias. Patients with
48 relevant missing information (age, sex, functional status, previous comorbidities,
49 malignancy, COVID-19 infection status, date of surgery, urgency, type and complexity
50 of surgery, and 30-day postoperative follow-up) were excluded.
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Sample size

Due to the design of the study and the nature of our aim, no formal calculation of sample size was performed, being defined as the number of patients fulfilling inclusion criteria.

Statistical Procedures

Patients' baseline characteristics were summarized by cohort using standard descriptive statistics. A raw and adjusted cumulative incidence (and its 95% confident interval) comparison was performed between cohort 1 and cohort 2, and between cohort 2 and cohort 3. A mixed effects logistic regression model was used to estimate odds ratio to quantify the effect on each outcome. Mixed effects were used to account for centre-effects. The adjustment factors used in the model were sex, age (linear and quadratic term), functional status, COPD, hypertension, malignancy, clinical priority, and surgical complexity.

A propensity matching score analysis was done using a logistic regression model, in which COVID-19 status or year was regressed on observed baseline characteristics. Variables taken into account were: age, sex, functional status, smoking status, hypertension, COPD, diabetes, cardiovascular diseases, malignancy, clinical priority, surgical complexity, and centre. Participants with similar value of propensity score were matched 3:1 when comparing cohort 1 and cohort 2, and 1:1 when comparing cohort 2 and cohort 3. In matched cohorts, to identify imbalance between groups, standardized mean difference on observed baseline characteristics was estimated and plotted. A mixed effects logistic regression model was used to estimate odds ratio to quantify the effect on each outcome. Mixed effects were used to account for centre-effects. Variables remaining imbalanced between groups after matching were added to the logistic model with an adjusting purpose. With a sensitivity purpose, a stratified analysis by centre was

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3 predefined in the statistical analysis plan. Analysis was performed using R version 3.5.3
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5 [R Core Team (2020). R: A language and environment for statistical computing. R
6
7 Foundation for Statistical Computing, Vienna, Austria. URL [https://www.R-](https://www.R-project.org/)
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9 [project.org/](https://www.R-project.org/)].
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FOR REVIEW ONLY

RESULTS

Twenty-five surgical teams participated in the study (*Supplementary material, Table S1*), registering 5 599 patients, of whom 5 307 (183 COVID-19-positive, 2 132 intra-pandemic COVID-19-negative and 2 992 pre-pandemic patients) fulfilled inclusion and data quality criteria (*Fig. 1*). COVID-19 infection diagnosis was confirmed before surgery in 112 patients (61.2%) and after in 71 (38.8%), by RT-PCR in 164 patients (89.6%), and by clinical and radiological findings in 19 (10.4%).

Patients' characteristics

Table 1 shows patients' basal characteristics. Surgical procedures are detailed in the *Supplementary material (Table S3)*.

Intra-pandemic patients: COVID-19-positive versus negative. COVID-19-positive patients were older (+7.0 years difference), more overweight (+7.1%), had higher ASA scores (+15.4% ≥ 3), worse functional status (+5.8% dependence), more respiratory pathology (+3.3%), COPD (+2.0%), heart failure (+4.0%), arterial hypertension (+9.9%), diabetes (+9.3%) and cardiovascular disease (+5.4%). They were more often hospitalized in ICU before surgery (+11.5%), with lower preoperative Glasgow coma score, submitted to emergency surgery (+5.6%), of higher surgical complexity (+12.7% with major or major+ surgeries), affected of malignant pathology (+5.7%) and with diffuse peritonitis (+5.3%). Besides, COVID-19-positive patients presented lower lymphocyte count ($-0.4 \times 10^9/L$), higher C-reactive protein values (+42 mg/L), higher urea and ALT values (+1.9 mmol/L and +9.3 U/L), and higher inflammatory indexes: +1.8 difference NLR; +44 PLR; and $+329 \times 10^9/L$ SII. They also had higher surgical prognostic scores: +10.3% POSSUM morbidity; +6.4% POSSUM mortality; +4.8 P-

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3 POSSUM (mortality); +5.4% LUCENTUM-logistic regression (morbidity); and +4.5
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5 LUCENTUM-CHAID (morbidity).
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8 ***COVID-19-negative patients: intra- versus pre-pandemic.*** COVID-19-negative
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10 patients from both periods had similar age, BMI, ASA score, functional status, and
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12 basal comorbidities. There were no relevant differences either in ICU before surgery,
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14 priority and complexity of surgeries, malignancy, peritonitis extent, analytical variables
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16 nor surgical prognostic scores.
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19 20 21 **Outcomes**

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23 *Table 2* shows raw postoperative outcomes of study population. Complications are
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25 detailed in *Supplementary material (Table S4)*.
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29 ***Intra-pandemic patients: COVID-19-positive versus negative.*** COVID-19-positive
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31 patients presented higher mortality (+8.0% at 30 days and +11.2 at 90 days); more
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33 complications (+17.6%), of pulmonary, thromboembolic, other medical and surgical
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35 types; more severe complications (+11.6%); more postoperative ICU hospitalization
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37 (+18.8%); longer hospital stay (+3 days); and higher re-hospitalization and re-
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39 intervention taxes (+3.5% and +1.5%). FTR was also higher in raw comparison
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41 (+11.0%). Propensity-score selection matched 179 COVID-19-positive with 503
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43 COVID-19-negative patients (*Fig. 1*). Distribution of matched cohorts is presented in
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45 the *Supplementary material (Fig. S1 and Fig. S2)*. In propensity-score analysis,
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47 COVID-19-positive patients maintained higher mortality at 30 and 90 days (odds ratio
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49 [OR], 2.05 [95% CI, 1.17-3.60]; $P = 0.012$); more complications (OR, 1.83 [95% CI,
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51 1.27-2.62]; $P < 0.001$); more severe complications (OR, 1.70 [95% CI, 1.12-2.58]; $P =$
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53 0.012); higher need of postoperative intensive care assistance ($P = 0.001$); and longer
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55 hospital stay ($P < 0.001$) (*Fig. 2 and Table S5*). Postoperative complications affecting
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3 more frequently COVID-19-infected patients were of pulmonary type ($P = 0.001$), with
4 thromboembolic and surgical complications nearly reaching significant difference ($P =$
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FTR taxes between matched intra-pandemic cohorts.

COVID-19-negative patients: intra- versus pre-pandemic. Raw outcomes of COVID-19-negative patients are shown in *Table 2*. Intra-pandemic patients had higher mortality (+1.4% at 30 days and +1.5% at 90 days) and FTR (+6.4%), with no significant differences in complication, length of stay, re-hospitalization and re-intervention taxes. For propensity-score analysis, 2 033 COVID-19-negative intra-pandemic and 2 033 pre-pandemic control patients were matched (*Fig. 1 and Fig. S3 and Fig. S4*). COVID-19-negative intra-pandemic patients had significantly higher 30 day-mortality (OR, 1.41 [95% CI, 1.02-1.95]; $P = 0.04$) and FTR (OR, 1.59 [95% CI, 1.12-2.24]; $P = 0.009$) (*Fig. 3 and Table S6*). Complication rate, type and severity, postoperative ICU admission, hospital stay, re-hospitalization and re-intervention taxes were similar.

DISCUSSION

This large multicentre propensity-score matched study (COVID-CIR) demonstrates that COVID-19 infection worsened postoperative complication and mortality rates in patients submitted to emergency general and digestive surgery. Moreover, COVID-19-negative patients operated on during the first wave of the pandemic in Spain had similar complication rates than pre-pandemic ones, but worse mortality deriving from them. To our knowledge, this is the first study providing adjusted comparison of postoperative outcomes of surgical intra-pandemic COVID-19-positive and -negative patients, together with pre-pandemic controls. This benchmarking allows control of the principal factors potentially explaining worse postoperative outcomes observed during the COVID-19 pandemic: first, the influence of COVID-19 infection; second, the possible advanced stage of pathologies at consultation, due to patients' fear or difficulty of visiting the hospital ("lockdown effect"); and third, the collapse of hospital services needed to rescue patients from complications in the pandemic context.

The effect of COVID-19-infection on postoperative outcomes

Great concern has arisen on to which degree COVID-19 infection can worsen postoperative outcomes of surgical patients, in order to recommend delaying or avoiding surgery^{11,20,33}. In this study, 90-day mortality rate in the matched COVID-19-positive cohort was 17.8%, higher than the 8.9% of matched COVID-19-negative patients and also higher than the 10.6% overall mortality of non-surgical patients of the same age range hospitalized for COVID-19 infection in Spain³⁴. This finding reinforces the hypothesis of a synergistic effect of COVID-19 infection and surgery: mechanical ventilation, anaesthesia and tissue damage associated to surgical interventions provoke a proinflammatory cytokine and immunosuppressive response, potentially worsening the

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3 evolution of COVID-19 infection^{10,11,14}. It has been probed that upregulation of the
4 systemic inflammatory response is a primary contributor to postoperative death in
5 emergency surgical patients⁸. Interestingly, COVID-19-positive patients in this study
6 presented higher preoperative values of analytical markers of inflammatory and
7 immunological response (CRP, neutrophil count, NLR, PLR, and SII), higher
8 parameters of tissular damage (ALT and urea) and lower values in lymphocyte count
9 than COVID-19-negative patients; all these findings have been probed as bad
10 prognostic factors both for COVID-19 infection and for emergency surgery^{10,35-38}.

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13 In this study, COVID-19-positive patients had high pulmonary and thromboembolic
14 complication rates (17.5% and 6.0% respectively), in accordance with previous reports
15 but with lower raw incidences^{11,12,14}. In addition to this, 30-day mortality rate of non-
16 matched COVID-19-infected surgical patients was 12.6%, close to the lower range
17 described to date (4.3%-42.8%).^{7,11-13,21,32,39,40}. This heterogeneity may be partially
18 attributed to differences in national health systems, but also to a potential selection bias
19 of studies including patients from many surgical specialties, especially in large hospitals
20 under significant stress. As far as we are aware, this study is based in the largest cohort
21 of COVID-19-infected patients submitted to emergency surgery of a single surgical
22 speciality published to date.

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25 Raw postoperative outcomes associated to COVID-19 infection should be evaluated
26 with caution, as COVID-19-positive patients had higher risk baseline characteristics:
27 more advanced age, more overweight, higher ASA scores, lower functional status, and
28 more basal comorbidities. Accordingly, previous studies reported that surgical COVID-
29 positive patients were mostly aged 70 years or older (50%-66%), staged as ASA score 3
30 to 5 (60%-91%), and having two comorbidities or more (61%-67%)^{11,12,14}. This
31 underlines the need of meticulous benchmarking. Three previous studies comparing
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3 outcomes of surgical COVID-positive with contemporary COVID-negative patients
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5 reached contradictory conclusions: in two of them, COVID-19 infection was associated
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7 to poorer postoperative outcomes^{13,14}, while in another one it was not⁴¹. The findings of
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9 the present study, based on a large homogeneous cohort with propensity-score matched
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11 analysis, confirm the higher risk of emergency surgery in COVID-19-infected patients.
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13 This fact should be taken in consideration when balancing individual risks and benefits
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15 of submitting a COVID-19-positive patient to an emergency surgical intervention. An
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17 effort should be made to promote conservative non-surgical treatments in these patients
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19 whenever possible.
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25 ***The lockdown effect***

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28 Some studies described significant delay of patients with potentially surgical
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30 pathologies to attend at Emergency Departments during the COVID-19 pandemic, due
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32 to fear of contagion and home confinement, resulting in more evolved acute diseases
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34 (for example, more extended peritonitis) and worse postoperative prognosis^{7,23,41}. In
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36 contrast, in the present study, COVID-19-negative patients showed similar
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38 inflammatory parameters and indices, peritonitis extent, intraoperative blood loss and
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40 surgical prognostic score values to those of patients operated on during the same period
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42 of the previous year. Moreover, their complication and severe complication rates did
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44 not increase. Therefore, the higher mortality of COVID-19-negative patients operated
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46 on from March to June 2020 in Spain cannot be attributed to the effect of lockdown.
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52 ***The effect of hospital collapse***

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56 In this study, COVID-19-negative patients submitted to emergency digestive surgery
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58 during the pandemic had a significantly higher risk of death as a consequence of
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3 postoperative complications (FTR) than pre-pandemic patients. High quality literature
4 has directly related FTR of surgical patients with delay in detection of morbidity and
5 therapeutical scalation³¹. Several hospital-related risk indicators, such as outdated
6 communication technology, nurse understaffing, hierarchy barriers, and communication
7 errors have been identified as root causes of incapability of surgical services in stopping
8 transition from an initial complication to a progressive cascade of adverse occurrences
9 leading to death³¹. All these factors are likely to have been altered in Spanish hospitals
10 during the pandemic. Spanish health system was systematically under-resourced and
11 understaffed in the last decade, and was therefore overwhelmed by the resilience test of
12 the COVID-19 pandemic²⁴. Excess deaths attributed to causes other than COVID-19
13 during the pandemic could reflect disruptions produced by hospital collapse, such as the
14 one found in this study^{5,42}. Diminishing avoidable deaths during present and future
15 sanitary crisis will require increasing resources for overwhelmed health care workers
16 and hospitals and a better coordination among Health Care leaders^{25,43}. We also suggest
17 it could be recommendable to coordinate deriving non-delayable surgeries to non-
18 collapsed hospitals in the same area.

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41 This study has some limitations. It only involves one country, Spain, a fact that could
42 limit generalizability of the results. However, it also grants the homogeneity of the
43 cohorts and limits selection bias. The retrospective design is a further limitation, which
44 was intended to be minimized by the thorough data quality control and the exclusion of
45 patients with relevant missing variables. In 10% of COVID-19-positive patients,
46 diagnosis was not based in nasopharyngeal RT-PCR, but in clinical and radiological
47 findings, especially at the initial phase of the pandemic, when COVID-19 diagnostic
48 protocols were not yet standardized. Other studies have similar proportion of COVID-
49 19 diagnosis based on clinical and radiological findings, having them comparable
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3 outcomes to the laboratory-confirmed COVID-19-positive patients¹¹. Finally, it must be
4 reminded that the propensity score adjustment cannot balance for unknown or known
5 unmeasured confounding variables; but it is plausible that matching would
6 appropriately correct the impact of baseline variables into the model.
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13 In conclusion, this large multicentre propensity-score matched study probed that
14 COVID-19-infected patients submitted to emergency general and digestive surgeries are
15 at increased risk of postoperative complications and mortality; therefore, non-surgical
16 management should be prioritized in these patients. Moreover, COVID-19-negative
17 patients operated on during the pandemic presented higher-than-expected failure-to-
18 rescue; an effort to invest on and better organize public health system should be made to
19 minimize avoidable deaths in future sanitary resilience tests.
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47 This study, including its analysis plan, was registered in ClinicalTrials.gov with
48 Identifier NCT04479150 before data collection and analysis were performed. The
49 preregistration adheres to the disclosure requirements of the institutional registry.
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55 The datasets generated and analysed during the current study are not publicly available
56 but are available from the corresponding author on reasonable request.
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REFERENCES

- 1 World Health Organization. WHO announces COVID-19 outbreak a pandemic. March 12, 2020. <https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic>. Accessed February 11, 2021.
- 2 World Health Organization (WHO). Coronavirus disease (COVID-19) Weekly Epidemiological Update and Weekly Operational Update. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>. Accessed February 11, 2021.
- 3 Ministry of Health, Consumption and Social Welfare, Spain. Health Alert and Emergency Co-ordination Centre (CCAES). COVID-19 in Spain (2020). <https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCoV/situacionActual.htm>. Accessed February 11, 2021.
- 4 Horton R. Offline: COVID-19 and the NHS-"a national scandal". *Lancet* 2020; **395**: 1022.
- 5 Bilinski A, Emanuel EJ. COVID-19 and Excess All-Cause Mortality in the US and 18 Comparison Countries. *JAMA* 2020; **324**: 2100-2102.
- 6 Cano-Valderrama O, Morales X, Ferrigni CJ, Martín-Antona E, Turrado V, García A *et al*. Reduction in emergency surgery activity during COVID-19 pandemic in three Spanish hospitals. *Br J Surg* 2020; **107**: e239.

- 1
2
3 7 Cano-Valderrama O, Morales X, Ferrigni CJ, Martín-Antona E, Turrado V,
4
5 García A *et al.* Acute Care Surgery during the COVID-19 pandemic in Spain:
6
7 Changes in volume, causes and complications. A multicentre retrospective
8
9 cohort study. *Int J Surg* 2020; **80**: 157-161.
10
11
12
13 8 Becher RD, Hoth JJ, Miller PR, Meredith JW, Chang MC. Systemic
14
15 inflammation worsens outcomes in emergency surgical patients. *J Trauma Acute*
16
17 *Care Surg* 2012; **72**: 1140-1149.
18
19
20 9 Mullen MG, Michaels AD, Mehaffey JH, Guidry CA, Turrentine FE, Hedrick
21
22 TL *et al.* Risk Associated With Complications and Mortality After Urgent
23
24 Surgery vs Elective and Emergency Surgery: Implications for Defining
25
26 "Quality" and Reporting Outcomes for Urgent Surgery. *JAMA Surg* 2017; **152**:
27
28 768-774.
29
30
31
32 10 Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC.
33
34 Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus
35
36 Disease 2019 (COVID-19): A Review. *JAMA* 2020; **324**: 782-793.
37
38
39
40 11 COVIDSurg Collaborative. Mortality and pulmonary complications in patients
41
42 undergoing surgery with perioperative SARS-CoV-2 infection: an international
43
44 cohort study. *Lancet* 2020; **396**: 27-38.
45
46
47
48 12 Doglietto F, Vezzoli M, Gheza F, Lussardi GL, Domenicucci M, Vecchiarelli L
49
50 F *et al.* Factors Associated With Surgical Mortality and Complications Among
51
52 Patients With and Without Coronavirus Disease 2019 (COVID-19) in Italy.
53
54 *JAMA Surg* 2020; **155**: 1-14.
55
56
57
58
59
60

- 1
2
3 13 Knisely A, Zhou ZN, Wu J, Huang Y, Holcomb K, Melamed A *et al.*
4 Perioperative Morbidity and Mortality of Patients With COVID-19 Who
5 Undergo Urgent and Emergent Surgical Procedures. *Ann Surg* 2021; **273**:34-40.
6
7
8
9
10
11 14 Jonker PKC, van der Plas WY, Steinkamp PJ, Poelstra R, Emous M, van der
12 Meij W *et al.* Perioperative SARS-CoV-2 infections increase mortality,
13 pulmonary complications, and thromboembolic events: A Dutch, multicenter,
14 matched-cohort clinical study. *Surgery* 2020; **169**: 264-274.
15
16
17
18
19
20
21 15 Kibbe MR. Surgery and COVID-19. *JAMA* 2020; **324**: 1151-1152.
22
23
24 16 Hogan A. COVID-19 and emergency surgery. *Br J Surg* 2020; **107**: e180.
25
26
27 17 COVIDSurg Collaborative. Delaying surgery for patients with a previous
28 SARS-CoV-2 infection. *Br J Surg* 2020; **107**: e601-e602.
29
30
31
32 18 COVIDSurg Collaborative. Global guidance for surgical care during the
33 COVID-19 pandemic. *Br J Surg* 2020; **107**: 1097-1103.
34
35
36
37 19 Moletta L, Pierobon ES, Capovilla G, Costantini M, Salvador R, Merigliano S *et*
38 *al.* International guidelines and recommendations for surgery during Covid-19
39 pandemic: A Systematic Review. *Int J Surg* 2020; **79**: 180-188.
40
41
42
43
44 20 Balibrea JM, Badia JM, Rubio Pérez I, Martín Antona E, Álvarez Peña E,
45 García Botella S *et al.* Surgical Management of Patients With COVID-19
46 Infection. Recommendations of the Spanish Association of Surgeons. *Cirugía*
47 *Española (English Edition)* 2020; **98**: 251-259.
48
49
50
51
52
53
54 21 Guadalajara H, Muñoz de Nova JL, Fernandez Gonzalez S, Yiasemidou M,
55 Recarte Rico M, Juez LD *et al.* Patterns of acute surgical inflammatory
56
57
58
59
60

- 1
2
3 processes presentation of in the COVID-19 outbreak (PIACO Study): Surgery
4 may be the best treatment option. *Br J Surg* 2020; **107**: e494-e495.
5
6
7
- 8 22 Aminian A, Safari S, Razeghian-Jahromi A, Ghorbani M, Delaney CP. COVID-
9 19 Outbreak and Surgical Practice: Unexpected Fatality in Perioperative
10 19 Outbreak and Surgical Practice: Unexpected Fatality in Perioperative
11 Period. *Ann Surg* 2020; **272**: e27-e29.
12
13
14
- 15 23 McLean RC, Young J, Musbahi A, Lee JX, Hidayat H, Abdalla N *et al.* A
16 single-centre observational cohort study to evaluate volume and severity of
17 emergency general surgery admissions during the COVID-19 pandemic: Is there
18 a "lockdown" effect?. *Int J Surg* 2020; **83**: 259-266.
19
20
21
22
23
24
- 25 24 The Lancet Public Health. COVID-19 in Spain: a predictable storm?. *Lancet*
26 *Public Health* 2020; **5**: e568.
27
28
29
- 30 25 Legido-Quigley H, Mateos-García JT, Campos VR, Gea-Sánchez M, Muntaner
31 C, McKee M. The resilience of the Spanish health system against the COVID-19
32 pandemic. *Lancet Public Health* 2020; **5**: e251-e252.
33
34
35
36
37
- 38 26 Madrazo Z, Osorio J, Biondo S, Otero A, Videla S, on behalf of the COVID-
39 CIR Collaborative Group. Comments to: Patterns of acute surgical inflammatory
40 processes presentation of in the COVID-19 outbreak (PIACO Study): Surgery
41 may be the best treatment option. *Br J Surg* 2021; **108**: e40-e41.
42
43
44
45
46
47
- 48 27 Madrazo Z, Osorio J, Otero A, Biondo S, Videla S, on behalf of the COVID-
49 CIR Collaborative Group. Postoperative complications and mortality following
50 emergency digestive surgery during the COVID-19 pandemic: a multicentre
51 collaborative retrospective cohort study protocol (COVID-CIR). *Medicine*
52 2021; **100**: 5 (e24409).
53
54
55
56
57
58
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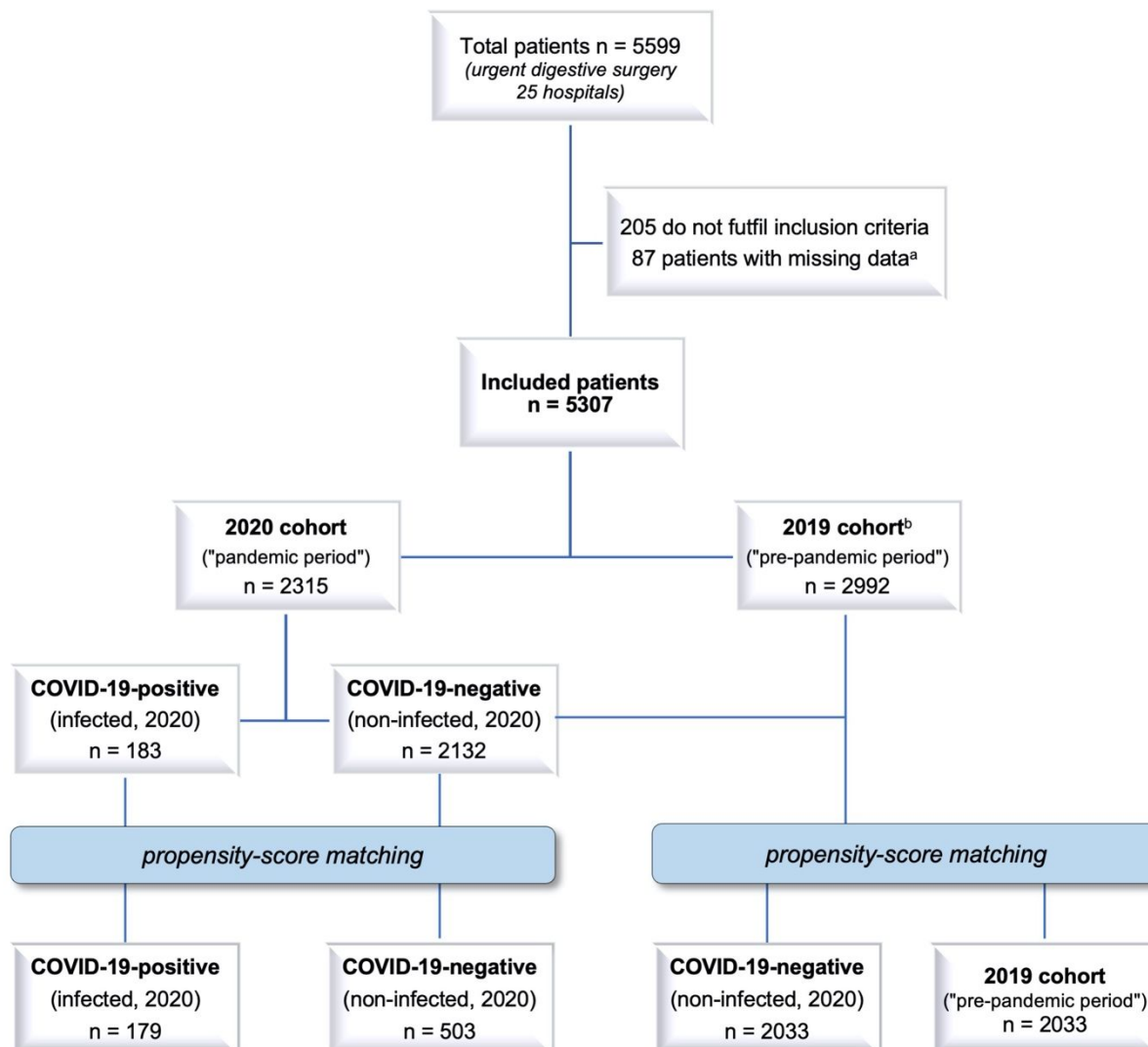
- 1
2
3 28 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP;
4
5 STROBE Initiative. The Strengthening the Reporting of Observational Studies
6
7 in Epidemiology (STROBE) statement: guidelines for reporting observational
8
9 studies. *Ann Intern Med* 2007; **147**: 573-577.
10
11
12
13 29 Whiteley MS, Prytherch DR, Higgins B, Weaver PC, Prout WG. An evaluation
14
15 of the POSSUM surgical scoring system. *Br J Surg* 1996;**83**:812-815.
16
17
18 30 Villodre C, Rebasá P, Estrada JL, Zaragoza C, Zapater P, Mena L *et al.* aLicante
19
20 sUrgical Community Emergencies New Tool for the enUmeration of
21
22 Morbidities: a simplified auditing tool for community-acquired gastrointestinal
23
24 surgical emergencies. *Am J Surg* 2016; **212**: 917-926.
25
26
27
28 31 Johnston M, Arora S, Anderson O, King D, Behar N, Darzi A. Escalation of care
29
30 in surgery: a systematic risk assessment to prevent avoidable harm in
31
32 hospitalized patients. *Ann Surg* 2015; **261**: 831-838.
33
34
35
36 32 Seeliger B, Philouze G, Cherkaoui Z, Felli E, Mutter D, Pessaux P. Acute
37
38 abdomen in patients with SARS-CoV-2 infection or co-infection. *Langenbecks*
39
40 *Arch Surg* 2020; **405**: 861-866.
41
42
43 33 Fu D, Zhang P, Wang L, Liu W, Tan H, Di M *et al.* Emergency abdominal
44
45 surgery in COVID-19 patients: a note of caution from Wuhan. *Br J Surg* 2020;
46
47 **107**: e262.
48
49
50
51 34 Casas-Rojo JM, Antón-Santos JM, Millán-Núñez-Cortés J, Lumbreras-Bermejo
52
53 C, Ramos-Rincón JM, Roy-Vallejo E *et al.* Clinical characteristics of patients
54
55 hospitalized with COVID-19 in Spain: results from the SEMI-COVID-19
56
57 Registry. *Rev Clin Esp (Barc)* 2020; **220**: 480-494.
58
59
60

- 1
2
3 35 Seyit M, Avci E, Nar R, Senol H, Yilmaz A, Ozen Meyit M *et al.* Neutrophil to
4 lymphocyte ratio, lymphocyte to monocyte ratio and platelet to lymphocyte ratio
5 to predict the severity of COVID-19. *Am J Emerg Med* 2020;
6 <https://doi:10.1016/j.ajem.2020.11.058> [Epub ahead of print].
7
8
9
10
11
12
13 36 Fois AG, Paliogiannis P, Scano V, Cau S, Babudieri S, Perra R *et al.* The
14 Systemic Inflammation Index on Admission Predicts In-Hospital Mortality in
15 COVID-19 Patients. *Molecules* 2020; **25**: 5725.
16
17
18
19
20
21 37 Tjendra Y, Al Mana AF, Espejo AP, Akgun Y, Millan NC, Gomez-Fernandez C
22 *et al.* Predicting Disease Severity and Outcome in COVID-19 Patients: A
23 Review of Multiple Biomarkers. *Arch Pathol Lab Med* 2020; **144**: 1465-1474.
24
25
26
27
28
29 38 Vaughan-Shaw PG, Rees JR, King AT. Neutrophil lymphocyte ratio in outcome
30 prediction after emergency abdominal surgery in the elderly. *Int J Surg* 2012;
31 **10**: 157-162.
32
33
34
35
36
37 39 Seretis C, Archer L, Lalou L, Yahia S, Katz C, Parwaiz I, *et al.* Minimal impact
38 of COVID-19 outbreak on the postoperative morbidity and mortality following
39 emergency general surgery procedures: results from a 3-month observational
40 period. *Med Glas (Zenica)* 2020; **17**: 275-278.
41
42
43
44
45
46 40 González-Calatayud DM, Vargas-Ábrego DB, Gutiérrez-Uvalle DGE, López-
47 Romero DSC, González-Pérez DLG, Carranco-Martínez DJA *et al.*
48 Observational study of the suspected or confirmed cases of sars COV-2 infection
49 needing emergency surgical intervention during the first months of the pandemic
50 in a third level hospital: Case series. *Ann Med Surg (Lond)* 2020; **60**:149-154.
51
52
53
54
55
56
57
58
59
60

- 1
2
3 41 Zhao N, Wu L, Cheng Y, Zheng H, Hu P, Hu C *et al.* The effect of emergency
4 surgery on acute abdomen patients with COVID-19 pneumonia: a retrospective
5 observational study. *Aging (Albany NY)* 2020; **12**: 15771-15783.
6
7
8
9
10
11 42 Woolf SH, Chapman DA, Sabo RT, Weinberger DM, Hill L. Excess Deaths
12 From COVID-19 and Other Causes, March-April 2020. *JAMA* 2020; **324**: 510-
13 513.
14
15
16
17
18 43 Koh HK, Geller AC, VanderWeele TJ. Deaths From COVID-19. *JAMA* 2021;
19 **325**: 133-134.
20
21
22
23
24
25
26
27
28
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33
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FIGURES AND TABLES

Figure 1. Flow diagram of included patients



^a Excluded patients: those lacking any of the following data: date of surgery, age, gender, functional status, previous pathologies, malignancy, urgency, complexity of surgery, 30-day and 90-day outcomes.

^b Three hospitals did not provide all consecutive patients from control cohort (2019).

Table 1. Demographics, comorbidities, clinical, analytical and surgical variables in the study population

Variable	No. (%)			
	COVID-19- positive (n = 183)	COVID-19- negative (n = 2 132)	Total 2020 cohort (n = 2 315)	2019 cohort (n = 2 992)
Men	113 (61.7)	1 272 (59.7)	1 385 (59.8)	1 754 (58.6)
Women	70 (38.3)	860 (40.3)	930 (40.2)	1 238 (41.4)
Age, median (IQR), years	63 (48-73)	56 (40-72)	56 (41-72)	57 (40-72)
Body Mass Index, mean (SD), kg/m ²	27.9 (5.6)	27.2 (5.6)	27.3 (5.6)	27.3 (5.9)
Body Mass Index classification				
Underweight	1 (0.7)	35 (2.7)	36 (2.5)	48 (2.7)
Normal weight	43 (30.7)	465 (36.1)	508 (35.6)	604 (33.9)
Overweight	58 (41.4)	442 (34.3)	500 (35.0)	684 (38.4)
Obesity	38 (27.1)	346 (26.9)	384 (26.9)	447 (25.1)
ASA score				
ASA 1	34 (18.7)	612 (28.9)	646 (28.1)	875 (29.4)
ASA 2	66 (36.3)	876 (41.4)	942 (41.0)	1 149 (38.7)
ASA 3	59 (32.4)	523 (24.7)	582 (25.3)	784 (26.4)
ASA 4	22 (12.1)	104 (4.9)	126 (5.5)	155 (5.2)
ASA 5	1 (0.6)	3 (0.1)	4 (1.2)	9 (0.3)
Functional status				
Independent	155 (84.7)	1 930 (90.5)	2 085 (90.1)	2 727 (91.1)
Partially dependent	26 (14.2)	187 (8.8)	213 (9.2)	236 (7.9)
Fully dependent	2 (1.1)	15 (0.7)	17 (0.7)	29 (0.9)
Respiratory system ^a				
Normal	158 (86.3)	1 910 (89.6)	2 068 (89.4)	2 737 (91.5)
Dyspnea with exercise	14 (7.7)	161 (7.6)	175 (7.6)	182 (6.1)
Limiting dyspnea	7 (3.8)	53 (2.5)	60 (2.6)	61 (2.0)
Dyspnea at rest	4 (2.2)	7 (0.3)	11 (0.5)	10 (0.3)
Cardiac system				
Normal (no failure)	137 (74.9)	1 681 (79.0)	1 818 (78.6)	2 254 (75.3)
Diuretics, digoxin, antianginal or antihypertensive drugs	38 (20.8)	391 (18.4)	429 (18.6)	630 (21.1)
Peripheral edemas, warfarin, incipient cardiomegaly	5 (2.7)	53 (2.5)	58 (2.5)	97 (3.2)
Elevated jugular venous pressure, cardiomegaly	3 (1.6)	4 (0.2)	7 (0.3)	11 (0.4)
Comorbidities				
Arterial hypertension ^b	79 (43.2)	709 (33.3)	788 (34.0)	1 030 (34.4)
Diabetes ^b	40 (21.9)	268 (12.6)	308 (13.3)	416 (13.9)
Active smoker	27 (14.8)	377 (17.7)	404 (17.5)	523 (17.5)
COPD	19 (10.4)	180 (8.4)	199 (8.6)	196 (6.6)
Cardiovascular disease ^c	31 (16.9)	245 (11.5)	276 (11.9)	397 (13.3)
Preoperative Glasgow coma score ≤8	16 (8.7)	16 (0.8)	32 (1.4)	21 (0.7)
Preoperative analytical data, mean (SD)				
Urea, mmol/L	8.8 (8.4)	6.9 (5.4)	7.1 (5.7)	7.3 (13.5)
ALT, U/L	53.2 (161)	43.9 (142)	44.8 (143)	36.7 (79.4)
Hemoglobin, g/dL	11.7 (3.8)	11.5 (4.7)	11.5 (4.7)	11.7 (4.6)
Leukocytes, x10 ⁹ /L	13.4 (6.8)	13.0 (5.9)	13.0 (6.0)	12.6 (5.7)
Neutrophils, x10 ⁹ /L	12.6 (12.6)	11.7 (11.3)	11.8 (11.4)	13.0 (15.1)
Lymphocytes, x10 ⁹ /L	1.5 (1.3)	1.9 (2.5)	1.9 (2.4)	2.2 (3.6)
Platelets, x10 ⁹ /L	254 (112)	252 (96.9)	252 (98.1)	255 (101)
NLR	11.9 (10.5)	10.1 (12.5)	10.3 (12.3)	9.7 (10.1)
PLR	272 (207)	228 (212)	231 (212)	230 (249)
SII, x10 ⁹ /L	2 948 (2937)	2 619 (3720)	2 644 (3666)	2 496 (3361)
CRP, mg/L	143 (268)	101 (147)	105 (161)	105 (183)
PT, %	78.6 (23.9)	79.5 (25.4)	79.4 (25.3)	75.5 (29.6)
PT, Quick value	1.2 (0.2)	1.2 (0.3)	1.2 (0.3)	1.3 (1.1)
PT, seconds	13.1 (1.4)	13.9 (4.7)	13.8 (4.4)	13.8 (7.8)
ICU admission before urgent surgery	27 (14.8)	70 (3.3)	97 (4.2)	132 (4.4)
Surgery type ^d				
Urgent	164 (89.6)	2 030 (95.2)	2 194 (94.8)	2 810 (93.9)
Emergency	19 (10.4)	102 (4.8)	121 (5.2)	182 (6.1)
Surgical approach				
Open	108 (60.0)	1 111 (52.4)	1 219 (53.0)	1 655 (55.5)
Laparoscopy	72 (40.0)	1 008 (47.6)	1 080 (47.0)	1 327 (44.5)
Malignancy				
No	160 (87.4)	1 983 (93.0)	2 143 (92.6)	2 789 (93.2)
Localized tumor	15 (8.2)	86 (4.0)	101 (4.4)	126 (4.2)

Table 1. Demographics, comorbidities, clinical, analytical and surgical variables in the study population (continued)

Variable	No. (%)			
	COVID-19- positive (n = 183)	COVID-19- negative (n = 2 132)	Total 2020 cohort (n = 2 315)	2019 cohort (n = 2 992)
Peritoneal exudate (intraoperative)				
None	67 (36.8)	979 (45.9)	1 046 (45.2)	1 513 (50.6)
Serous	47 (25.8)	492 (23.1)	539 (23.3)	615 (20.6)
Localized purulent	39 (21.4)	435 (20.4)	474 (20.5)	551 (18.4)
Diffuse purulent	29 (15.9)	225 (10.6)	254 (11.0)	313 (10.5)
Blood loss (intraoperative)				
<100 mL	135 (73.8)	1 859 (87.2)	1 994 (86.2)	2 542 (85.0)
101-500 mL	37 (20.2)	226 (10.6)	263 (11.4)	336 (11.2)
501-1000 mL	8 (4.4)	27 (1.3)	35 (1.5)	47 (1.6)
>1000 mL	3 (1.6)	19 (0.9)	22 (0.9)	65 (2.2)
Surgical complexity^e				
Minor	35 (19.1)	477 (22.4)	512 (22.1)	773 (25.8)
Moderate	74 (40.4)	1 063 (49.9)	1 137 (49.1)	1 393 (46.6)
Major / Major +	74 (40.4)	592 (27.8)	666 (28.8)	826 (27.6)
Surgical prognostic scores, mean (SD), %				
POSSUM mortality	16.3 (21.6)	9.9 (13.8)	10.4 (14.7)	10.1 (14.3)
P-POSSUM mortality	9.0 (18.5)	4.2 (10.2)	4.6 (11.2)	4.3 (9.9)
POSSUM morbidity	45.3 (28.7)	35.0 (24.7)	35.9 (25.2)	34.9 (25.4)
LUCENTUM-logistic regression morbidity	28.1 (19.5)	22.7 (17.7)	23.1 (17.9)	22.4 (17.8)
LUCENTUM-CHAID morbidity	22.0 (17.3)	17.5 (15.3)	17.8 (15.5)	17.3 (15.7)

Abbreviations: IQR, interquartile range; SD, standard deviation; ASA, American Society of Anesthesiologists; COPD, Obstructive Chronic Pulmonary Disease; ALT, alanine-aminotransferase; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index (neutrophil x platelet/lymphocyte counts); CRP, C-reactive protein; PT, prothrombin time (expressed as %, Quick value or seconds); ICU, Intensive Care Unit; POSSUM, Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity; P-POSSUM, Portsmouth POSSUM score; LUCENTUM, aLicante sUrgical Community Emergencies New Tool for the enUmeration of Morbidities.

^a Respiratory system: normal: no dyspnea and chest X-ray with no signs of COPD; dyspnea with exercise: dyspnea with exercise and/or chest X-ray with minimal signs of COPD; limiting dyspnea: limiting dyspnea (1 landing) and/or chest X-ray with moderate signs of COPD; dyspnea at rest: dyspnea at rest (≥ 30 breaths/minute) and/or chest X-ray with fibrosis or consolidation.

^b Arterial hypertension and diabetes, defined as patient needing specific pharmacological treatment.

^c Cardiovascular disease: antecedent of ischemic heart disease, cerebrovascular accident (transient ischemic attack, stroke) or peripheral artery disease.

^d Surgery type: emergency surgery: less than 2 hours since indication; urgent surgery: between 2 and 24 hours since indication.

^e Surgical complexity: minor: hernia/ventration repair, perineal surgery, pilonidal sinus; moderate: cholecystectomy, appendectomy; major: gastrointestinal perforation suture, intestinal resection, colectomy, main bile duct surgery, gastrectomy, lysis of adhesions, internal hernia repair, enterolithotomy, splenectomy or minor liver trauma, exploratory laparotomy/laparoscopy, surgical control of intra-abdominal bleeding; major+: pancreatectomy or pancreatic necrosectomy, damage control surgery (due to trauma, bleeding, ischemia or peritonitis). Performed surgical procedures are detailed in complementary material.

Table 2. Table 2. Study outcomes of the study population

Variable	No. (%)			
	COVID-19- positive (n = 183)	COVID-19- negative (n = 2 132)	Total 2020 cohort (n = 2 315)	2019 cohort (n = 2 992)
30-day mortality	23 (12.6)	98 (4.6)	121 (5.2)	97 (3.2)
90-day mortality ^a	29 (17.4)	119 (6.2)	148 (7.1)	139 (4.7)
Patients with 30-day postoperative complications	76 (41.5)	509 (23.9)	585 (25.3)	754 (25.2)
Failure-to-rescue, % ^b	30.3	19.3	20.7	12.9
Type of complication (at least, one of the following)				
Pulmonary ^c	32 (17.5)	119 (5.6)	151 (6.5)	165 (5.5)
Thromboembolic ^d	11 (6.0)	38 (1.8)	49 (2.1)	38 (1.3)
Other medical	33 (18.0)	210 (9.9)	243 (10.5)	304 (10.2)
Surgical	46 (25.1)	328 (15.4)	374 (16.2)	521 (17.4)
Clavien-Dindo system				
I	5 (2.7)	51 (2.4)	56 (2.4)	126 (4.2)
II	27 (14.8)	206 (9.7)	233 (10.1)	263 (8.8)
IIIA	3 (1.6)	40 (1.9)	43 (1.9)	69 (2.3)
IIIB	5 (2.7)	64 (3.0)	69 (2.9)	101 (3.4)
IVA	5 (2.7)	26 (1.2)	31 (1.3)	42 (1.4)
IVB	8 (4.4)	24 (1.1)	32 (1.4)	57 (1.9)
V	23 (12.6)	98 (4.6)	121 (5.2)	97 (3.2)
Patients with severe complications ^e	44 (24.0)	252 (11.8)	296 (12.8)	365 (12.2)
Need of postoperative ICU for ≥24 hours	55 (30.1)	241 (11.3)	296 (12.8)	389 (13.0)
Length of stay, median (IQR), days	7 (3-18)	4 (2-8)	4 (2-8)	4 (2-9)
30-day rehospitalization	16 (10.2)	135 (6.7)	151 (6.9)	190 (6.6)
30-day surgical reintervention	11 (6.9)	110 (5.4)	121 (5.5)	153 (5.3)

Abbreviations: ICU, Intensive Care Unit; IQR, interquartile range.

^a Only considered for patients with registered 90-day follow-up (91.3%, 90.3%, 90.4% and 98.5% in each group, respectively).

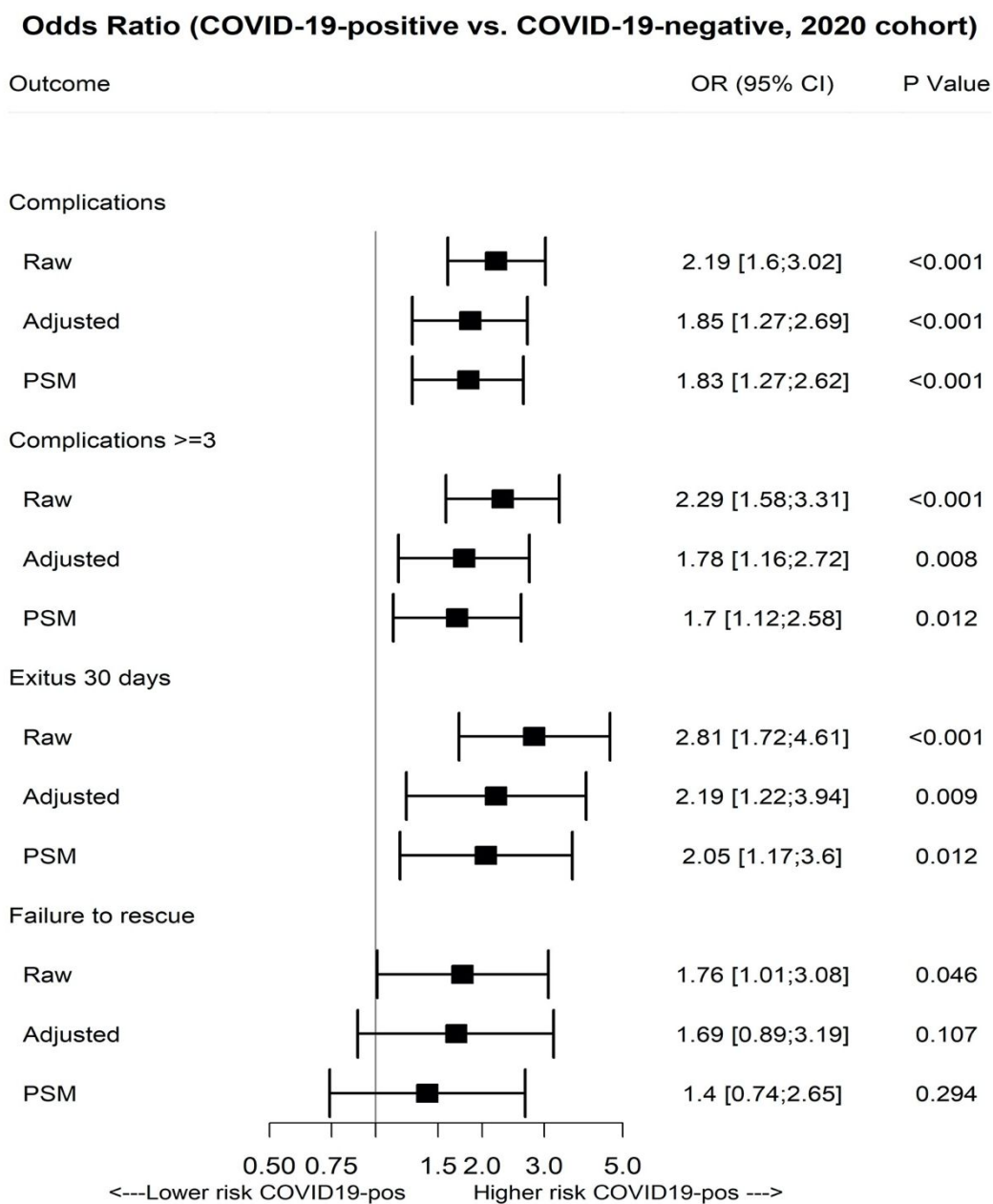
^b Failure-to-rescue (%): 30-day deaths divided by 30-day complicated patients.

^c Pulmonary complications: respiratory infection or pneumonia, defined as purulent expectoration with positive bacteriological/virological culture, with or without changes in chest X-ray, or fever associated to pulmonary consolidation in chest X-ray; respiratory failure, defined as dyspnea requiring ventilator urgent support and/or PaO₂<60mmHg and PaCO₂>45mmHg without oxygen assistance; and pleural effusion/pulmonary atelectasis.

^d Thromboembolic complication: deep venous thrombosis and/or pulmonary embolism; acute myocardial infarction, stroke, acute limb ischemia, acute mesenteric ischemia.

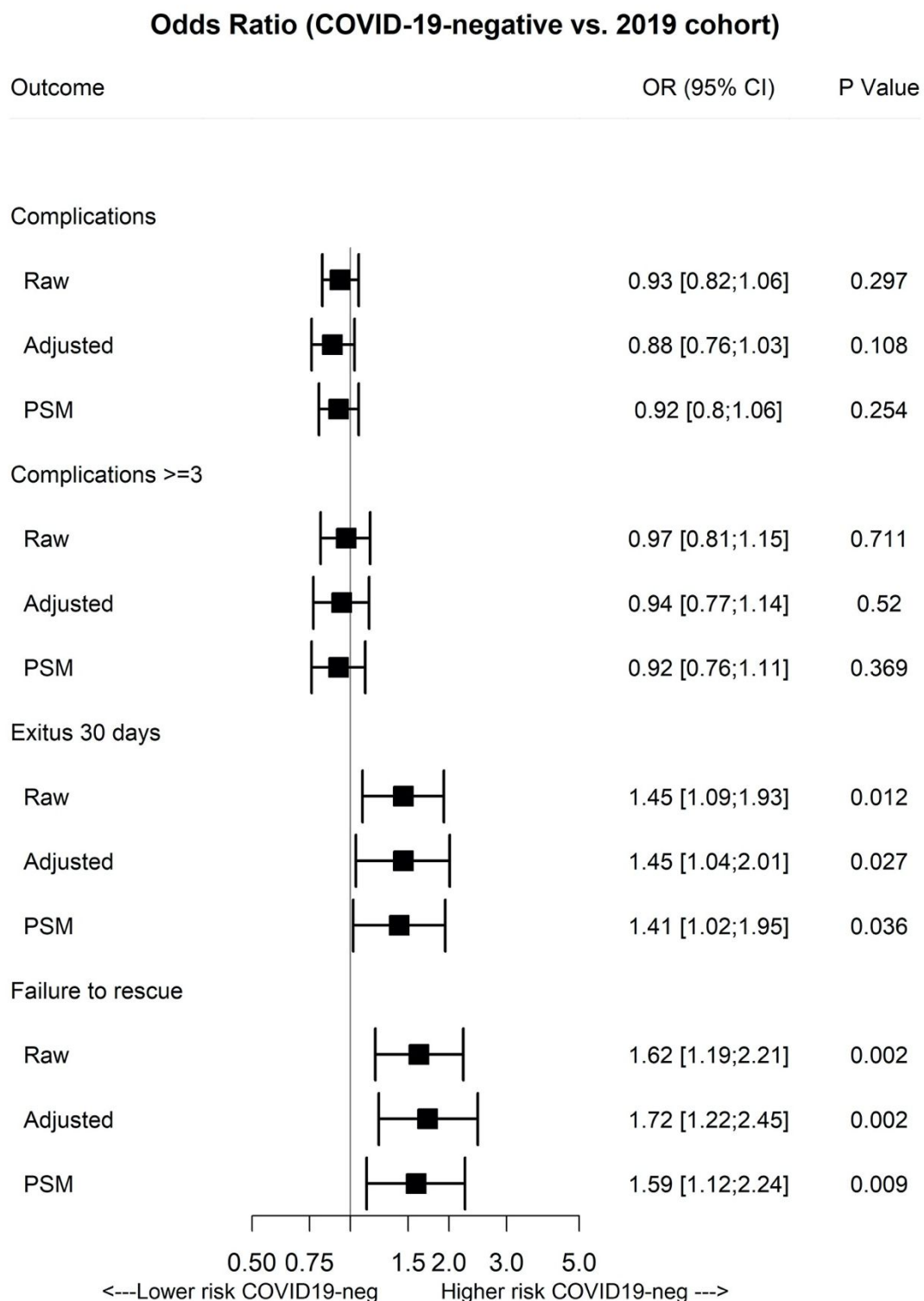
^e Clavien-Dindo grade ≥IIIA

Figure 2. Forest plot of raw, adjusted and propensity-score-matched (PSM) outcomes of 2020 COVID-19-positive versus 2020 COVID-19-negative patients^a



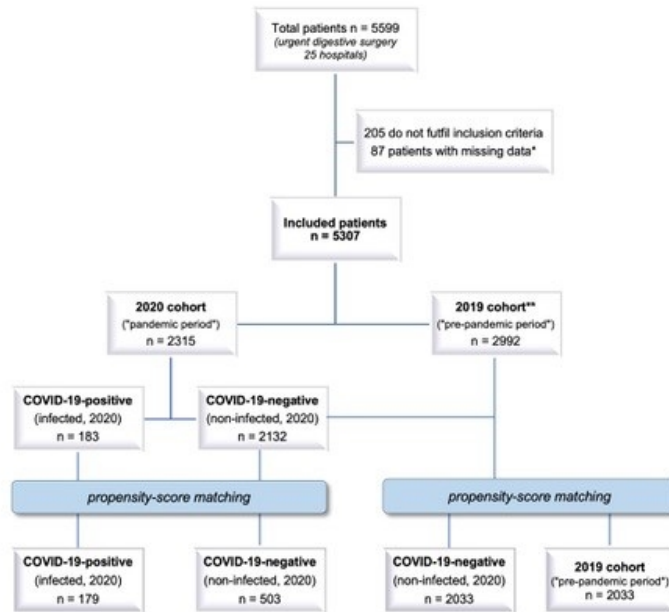
^a Model adjusted by sex, age (linear and quadratic term), functional status, COPD, cardiovascular pathology, arterial hypertension, diabetes, smoking, surgery type (urgency/emergency), malignancy, and surgical complexity

Figure 3. Forest plot of raw, adjusted and propensity-score-matched (PSM) outcomes of 2019 cohort versus 2020 COVID-19-negative patients^a



^a Model adjusted by sex, age (linear and quadratic term), functional status, COPD, cardiovascular pathology, arterial hypertension, diabetes, smoking, surgery type (urgency/emergency), malignancy, and surgical complexity

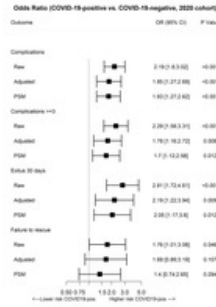
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Flow diagram of included patients

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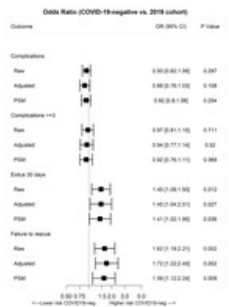
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Forest plot of raw, adjusted and propensity-score-matched (PSM) outcomes of 2020 COVID-19-positive vs 2020 COVID-19-negative patients

225x70mm (72 x 72 DPI)

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Forest plot of raw, adjusted and propensity-score-matched (PSM) outcomes of 2019 cohort vs 2020 COVID-19-negative patients

225x70mm (72 x 72 DPI)

Supplementary material

Table S1. List of surgical teams participating in the study (COVID-CIR Collaborative Group)

Table S2. Surgical prognostic scores

Table S3. Performed emergency surgical procedures in the study population (n = 5 658 procedures in 5 307 patients)

Table S4. Type of postoperative complications in the study population

Figure S1. Density plot to view the distribution of distance among matched cohorts of COVID-19-positive and intra-pandemic COVID-19-negative patients (nearest neighbor matching)

Figure S2. Comparison of means and prevalences of baseline characteristics among matched cohorts of COVID-19-positive and intra-pandemic COVID-19-negative patients

Table S5. Outcomes of the 2020 COVID-19-positive and COVID-19-negative matched cohorts (n = 682)

Figure S3. Density plot to view the distribution of distance among matched cohorts of COVID-19-negative intra- and pre-pandemic patients (nearest neighbor matching)

Figure S4. Comparison of means and prevalences of baseline characteristics among matched cohorts of COVID-19-negative intra- and pre-pandemic patients

Table S6. Outcomes of the COVID-19-negative (2020) and 2019 matched cohorts (n = 4 066)

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hospital code CNH^a	surgical team, hospital	principal investigator (PI) and co-investigators (Co-PI)
080752	Bellvitge University Hospital, Barcelona (coordinating center)	Javier Osorio Aguilar (PI) e-mail: josorio@bellvitgehospital.cat Zoiló Madrazo González (PI) e-mail: zmadrazo@bellvitgehospital.cat Elisabet Baena Sanfeliu (Co-PI) e-mail: ebaena@bellvitgehospital.cat Natàlia Cornellà Garceso (Co-PI) e-mail: ncornella@bellvitgehospital.cat Cristian Tebé Cordero (Co-PI) e-mail: ctebe@idibell.cat Natàlia Pallarès Fontanet (Co-PI) e-mail: npallares@idibell.cat
200261	Donostia University Hospital, San Sebastian	Araceli Rodríguez González (PI) e-mail: araceli.rodriguezgonzalez@osakidetza.eus Ainhoa Andrés Imaz (Co-PI) e-mail: ainhoa.andresimaz@osakidetza.eus Lorena Arrabal Agüera (Co-PI) e-mail: lorena.arrabalagueera@osakidetza.eus Alba Garcia Trancho (Co-PI) e-mail: alba.garciastrancho@osakidetza.eus
080057	Hospital del Mar University Hospital, Barcelona	Amalia Pelegrina Manzano (PI) e-mail: 64144@parcdesalutmar.cat Estela Membrilla Fernández (Co-PI) e-mail: 94934@parcdesalutmar.cat Alex Morera Grau (Co-PI) e-mail: 64267@parcdesalutmar.cat
080958	Parc Taulí Health Corporation, Sabadell Hospital, Sabadell	Andrea Campos-Serra (PI) e-mail: acampos@tauli.cat Anna Muñoz-Campaña (Co-PI) e-mail: amunozc@tauli.cat Ariadna Cidoncha-Secilla (Co-PI) e-mail: acidoncha@tauli.cat Victoria Lucas-Guerrero (Co-PI) e-mail: vlucas@tauli.cat
480176	Cruces University Hospital, Bilbao	Aingeru Sarriugarte Lasarte (PI) e-mail: aingeru.sarriugartelasarte@osakidetza.eus Eva Alonso Calderón (Co-PI) e-mail: eva.alonsocalderon@osakidetza.eus Marina Esgueva Angulo (Co-PI) e-mail: marina.esguevaangulo@osakidetza.eus Ibabe Villalabeitia Ateca (Co-PI) e-mail: ibabe.villalabeitiaateca@osakidetza.eus
080898	Sant Joan de Deu Hospital Foundation, Martorell Hospital, Martorell	Beatriz Campillo Alonso (PI) e-mail: bcampillo@hmartorell.es
081326	Mataró Hospital, Maresme Health Consortium, Mataró	Marina Vila Tura (PI) e-mail: Mvilatu@csdm.cat Pere Clos Ferrero (Co-PI) e-mail: pclos@csdm.cat
081075	Terrassa Health Consortium, Terrassa Hospital, Terrassa	David Ruiz Luna (PI) e-mail: druiz@cst.cat
081141	Viladecans Hospital, Viladecans	Marta Gil Barrionuevo (PI) e-mail: mgil.hv@gencat.cat

Table S1. List of surgical teams participating in the study (COVID-CIR Collaborative Group) (continued)

hospital code CNH ^a	surgical team, hospital	principal investigator (PI) and co-investigators (Co-PI)
250019	Arnaú de Vilanova University Hospital, Lleida	Maite Santamaría Gómez (PI) e-mail: mtsantamaria.lleida.ics@gencat.cat Núria Mestres Petit (Co-PI) e-mail: nmestres.lleida.ics@gencat.cat Jaume Ortega Alcaide (Co-PI) e-mail: jaortega.lleida.ics@gencat.cat Silvia Pérez Farré (Co-PI) e-mail: sperezf.lleida.ics@gencat.cat
080863	Althaia Foundation, University Healthcare Network, Manresa	Carlos Javier Gómez Díaz (PI) e-mail: cjgomez@althaia.cat Claudio Antonio Guariglia (Co-PI) e-mail: caguariglia@althaia.cat Alexander Leonel Osorio Ramos (Co-PI) e-mail: alosorio@althaia.cat Lorena Sanchón Fructoso (Co-PI) e-mail: lsanchon@althaia.cat Cristina Soto Montesinos (Co-PI) e-mail: csoto@althaia.cat Rafael Gerardo Díaz del Gobbo (Co-PI) e-mail: rgdiaz@althaia.cat Roser Flores Clotet (Co-PI) e-mail: rfloresc@althaia.cat Raquel Sánchez Jiménez (Co-PI) e-mail: rsanchezj@althaia.cat Roser Farré Font (Co-PI) e-mail: rfarre@althaia.cat Pablo Collera Ormazabal (Co-PI) e-mail: pcollera@althaia.cat
430017	Joan XXIII University Hospital, Tarragona	Carles Olona Casas (PI) e-mail: colona.hj23.ics@gencat.cat Aleidis Caro Tarragó (Co-PI) e-mail: acarohj23.ics@gencat.cat Robert Memba Ikuga (Co-PI) e-mail: rmembai.hj23.ics@gencat.cat Rosa Jorba Martín (Co-PI) e-mail: rjorba.hj23.ics@gencat.cat
081094	Mútua de Terrassa University Hospital, Terrassa	Noelia Pérez Romero (PI) e-mail: nperez@mutuaterrassa.es Melisa Arias Aviles (Co-PI) e-mail: marias@mutuaterrassa.cat Cinta Benaiges Calvet (Co-PI) e-mail: cbenaiges@mutuaterrassa.cat
170010	Girona Dr. Josep Trueta University Hospital, Girona	Eva Artigau Nieto (PI) e-mail: eartigau.girona.ics@gencat.cat Eloy Maldonado Marcos (Co-PI) e-mail: emaldonadom.girona.ics@gencat.cat
310150	Hospital Complex of Navarra, Pamplona	Beatriz Sainz Villacampa (PI) e-mail: mb.sainz.villacampa@navarra.es María José Sara Ongay (Co-PI) e-mail: mj.sara.ongay@navarra.es Aitor Ariceta Lopez (Co-PI) e-mail: aitor.ariceta.lopez@navarra.es Rocío Ruiz Marzo (Co-PI) e-mail: rocio.ruiz.marzo@navarra.es

Table S1. List of surgical teams participating in the study (COVID-CIR Collaborative Group) (continued)

hospital code CNH ^a	surgical team, hospital	principal investigator (PI) and co-investigators (Co-PI)
010090	Araba University Hospital, Txagorritxu Hospital, Vitoria	Victor Echenagusia Serrats (PI) e-mail: victor.echenagusiaserrats@osakidetza.eus
480078	Basurto University Hospital, Bilbao	Carmen González Serrano (PI) e-mail: mariacarmen.gonzalezserrano@osakidetza.eus Jon Ignacio Uriarte Teran (Co-PI) e-mail: jonignacio.uriartetaran@osakidetza.eus Eneko Gonzalez Aguirregomezorta (Co-PI) e-mail: eneko.gonzalezaguirregomezorta@osakidetza.eus Martin Amarelo Garcia (Co-PI) e-mail: martin.amarelogarcia@osakidetza.eus María Pintado Izquierdo (Co-PI) e-mail: maria.pintadoizquierdo@osakidetza.eus Ane Murua Ruiz (Co-PI) e-mail: ane.muruaruiz@osakidetza.eus
080734	Granollers General Hospital, Granollers	Aurora Aldeano Martín (PI) e-mail: aaldeanom@fphag.org Nares Arroyo García (Co-PI) e-mail: narroyo@fphag.org Maria Batlle Figueras (Co-PI) e-mail: mbattle@fphag.org Miriam Flores Yélamos (Co-PI) e-mail: mfloresy@fphag.org Nicolás Garriga Rodríguez (Co-PI) e-mail: nngarriga@fphag.org Montserrat Juvany Gómez (Co-PI) e-mail: mjuvany@fphag.org Esther Nve Obiang (Co-PI) e-mail: enve@fphag.org Arantxa Rada Palomino (Co-PI) e-mail: arada@fphag.org Patricia Ruiz de León Muñoz (Co-PI) e-mail: pruiздеleon@fphag.org
081347	Vall d'Hebrón University Hospital, General Surgery Department, Barcelona	Amador García Ruiz de Gordejuela (PI) e-mail: amador.garcia@vhebron.net Carlos Gustavo Petrola Chacon (Co-PI) e-mail: cpetrola@vhebron.net
081347	Vall d'Hebrón University Hospital, Hepatobiliopancreatic Surgery and Transplantation Department, Barcelona	Concepción Gómez-Gavara (PI) e-mail: concepcion.gomez@vhebron.net Rocio Martín Sánchez (Co-PI) e-mail: rocio.martin@vhebron.net Miriam Moratal Cloquell (Co-PI) e-mail: mmoratal@vhebron.net
080667	Germans Trias i Pujol University Hospital, Badalona	Arantxa Clavell Font (PI) e-mail: aclavell.germanstrias@gencat.cat Elisenda Garsot Savall (Co-PI) e-mail: egarsot.germanstrias@gencat.cat Albert Caballero Boza (Co-PI) e-mail: acaballero.germanstrias@gencat.cat Javier Corral Rubio (Co-PI) e-mail: jcorral.germanstrias@gencat.cat

Table S1. List of surgical teams participating in the study (COVID-CIR Collaborative Group) (continued)

hospital code CNH ^a	surgical team, hospital	principal investigator (PI) and co-investigators (Co-PI)
080291	Sant Pau University Hospital, Barcelona	Rodrigo Medrano Caviedes (PI) e-mail: rmedrano@santpau.cat Silvia Rofín Serra (Co-PI) e-mail: srofin@santpau.cat Lilian María Escobar Lezcano (Co-PI) e-mail: LEscobar@santpau.cat
082066	Sant Joan Despí Moisès Broggi Hospital, Sant Joan Despí	Camilo Andrés López Arévalo (PI) e-mail: CamiloAndres.LopezArevalo@sanitatintegral.org
081885	Igalada University Hospital, Anoia Health Consortium, Igualada	Sergi Sánchez Cordero (PI) e-mail: ssanchezco@csa.cat David Salazar Terceros (Co-PI) e-mail: dsalazar@csa.cat Carla Galmés Huerta (Co-PI) e-mail: cgalmes@csa.cat Mariano Artigot Pellicena (Co-PI) e-mail: martigot@csa.cat Xavier Guedes de la Puente (Co-PI) e-mail: xguedes@csa.cat Marta Domingo González (Co-PI) e-mail: mdomingo@csa.cat
200185	Alto Deba Hospital, Mondragon, San Sebastián	Miguel Calle Baraja (PI) e-mail: miguel.callebaraja@osakidetza.eus
350228	Dr. José Molina Orosa Hospital, Lanzarote	Laura Millán Paredes (PI) e-mail: lmilpar@gobiernodecanarias.org Araceli Rocío Romero Dorado (Co-PI) e-mail: aromdor@gobiernodecanarias.org Andrea Rossetti (Co-PI) e-mail: arosset@gobiernodecanarias.org Elvira Vaillo Martin (Co-PI) e-mail: evaimar@gobiernodecanarias.org

^a National Catalog of Hospitals (CNH) 2019, Ministry of Health, Consumption and Social Welfare, Spain.

Table S2. Surgical prognostic scores

surgical score	equation	prediction
POSSUM ^a (mortality)	$\text{Ln [R/(1-R)]} = -7.04 + (0.13 \times \text{physiological score}) + (0.16 \times \text{operative severity score})$	postoperative mortality
POSSUM ^a (morbidity)	$\text{Ln [R/(1-R)]} = -5.91 + (0.16 \times \text{physiological score}) + (0.19 \times \text{operative severity score})$	postoperative morbidity
P-POSSUM ^a	$\text{Ln [R/(1-R)]} = -9.065 + (0.1692 \times \text{physiological score}) + (0.155 \times \text{operative severity score})$	postoperative mortality
LUCENTUM ^b - logistic regression	$\text{Ln [R/(1-R)]} = -4.461 + (0.257 \times \text{age}) + (0.261 \times \text{sodium}) + (0.167 \times \text{Hb}) + (0.364 \times \text{white cell count}) + (0.397 \times \text{operative severity})$	postoperative morbidity
LUCENTUM ^b - CHAID	$\text{Ln [R/(1-R)]} = -5.835 + (0.757 \times \text{cardiac function}) + (0.563 \times \text{sodium}) + (0.411 \times \text{peritoneal soiling}) + (0.778 \times \text{operative severity})$	postoperative morbidity

Abbreviations: R, predicted risk of postoperative mortality/morbidity (≤ 30 days); Hb, hemoglobin (g/dL).

^a Units for POSSUM and P-POSSUM scores: total physiological and operative severity score²⁹.

^b Units for LUCENTUM scores: age (years); sodium (mmol/L); hemoglobin (g/dL); white cell count ($\times 10^9/L$); operative severity (*minor, moderate, major, major+*); cardiac function (no failure, any abnormality); peritoneal soiling (none/serous, local pus/diffuse peritonitis/hemoperitoneum/free bowel content)³⁰.

Table S3. Performed emergency surgical procedures in the study population (n=5658 procedures in 5307 patients)

Variable	No. (%)			
	2020 cohort			
	COVID-19- positive (n = 183)	COVID-19- negative (n = 2 132)	Total cohort (n = 2 315)	2020 2019 cohort (n = 2 992)
Minor surgical complexity				
perianal surgery	22 (11)	309 (13.7)	331 (13.5)	488 (15.3)
hernia/eventration repair	12 (6)	205 (9.1)	217 (8.8)	335 (10.5)
Moderate surgical complexity				
appendectomy	45 (22.5)	735 (32.6)	780 (31.7)	860 (26.9)
cholecystectomy	32 (16)	337 (14.9)	369 (15.0)	523 (16.3)
Major surgical complexity				
colectomy	25 (12.5)	144 (6.4)	169 (6.9)	188 (5.9)
intestinal resection	10 (5)	132 (5.9)	142 (5.8)	188 (5.9)
lysis of adhesions or internal hernia repair or enterolithotomy	12 (6)	107 (4.7)	119 (4.8)	140 (4.4)
gastrointestinal perforation suture	8 (4)	70 (3.1)	78 (3.2)	143 (4.5)
other surgical procedures ^a	16 (8)	82 (3.6)	98 (3.9)	120 (3.8)
surgical control of intra-abdominal bleeding	5 (2.5)	20 (0.9)	25 (1.0)	48 (1.5)
exploratory laparotomy ^b	3 (1.5)	36 (1.6)	39 (1.6)	31 (0.9)
splenectomy or minor liver trauma	1 (0.5)	11 (0.5)	12 (0.5)	25 (0.8)
gastrectomy	1 (0.5)	16 (0.7)	17 (0.7)	14 (0.4)

main bile duct surgery	2 (1)	5 (0.2)	7 (0.3)	11 (0.3)
Major + surgical complexity				
damage control surgery	5 (2.5)	44 (1.9)	49 (1.9)	74 (2.3)
pancreatectomy or pancreatic necrosectomy	1 (0.5)	5 (0.2)	6 (0.2)	12 (0.4)
Total procedures	200	2 258	2 458	3 200

The same patient may have required several surgical procedures during an intervention.

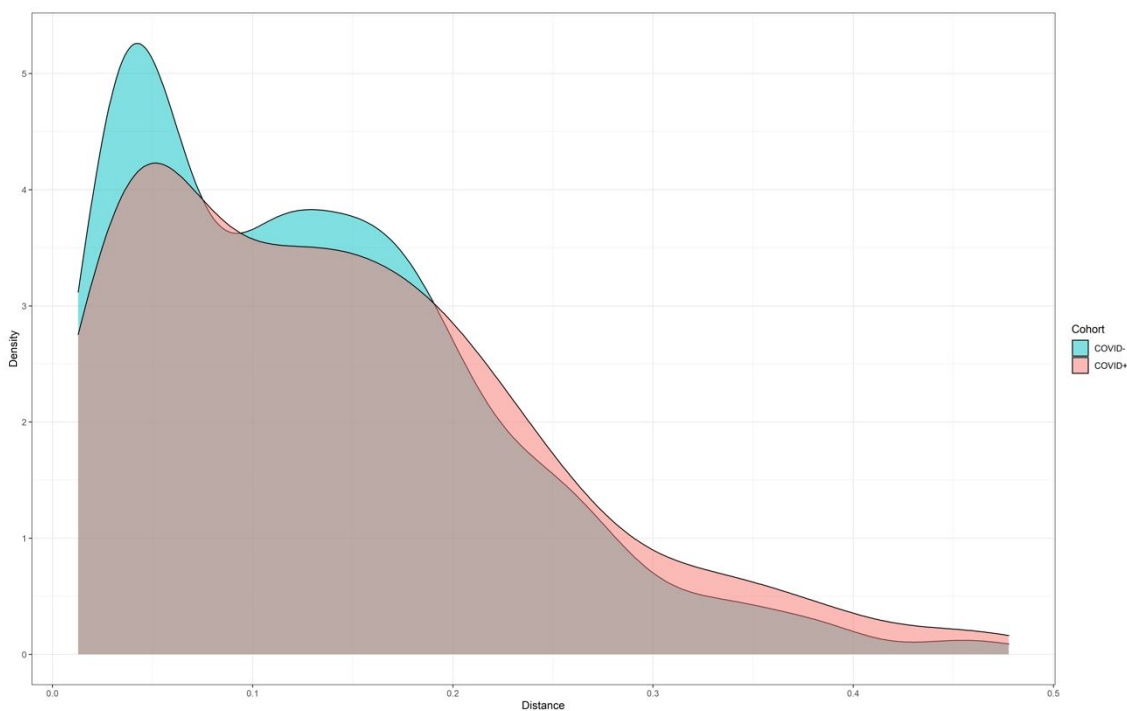
^a The "*other surgical procedures*" category includes: debridement of skin and soft tissue infection, surgical site infection, or necrotizing fasciitis (60 cases); other surgical procedures (43 cases); derivative ostomy or intestinal bypass (39 cases); abdominal washout and drainage (33 cases); postoperative evisceration (12 cases); hemostasis of surgical incision or abdominal wall (11 cases); surgical airway (8 cases); choleperitoneum (7 cases); reconnection of an ostomy or anastomosis (5 cases).

^b The "*exploratory laparotomy*" category includes: suspected intestinal perforation, dehiscence or peritonitis (22 cases); peritoneal carcinomatosis (14 cases); massive intestinal ischemia (12 cases); suspected intestinal obstruction (9 cases); other surgical procedures (7 cases); suspected intestinal ischemia (6 cases).

Table S4. Type of postoperative complications in the study population

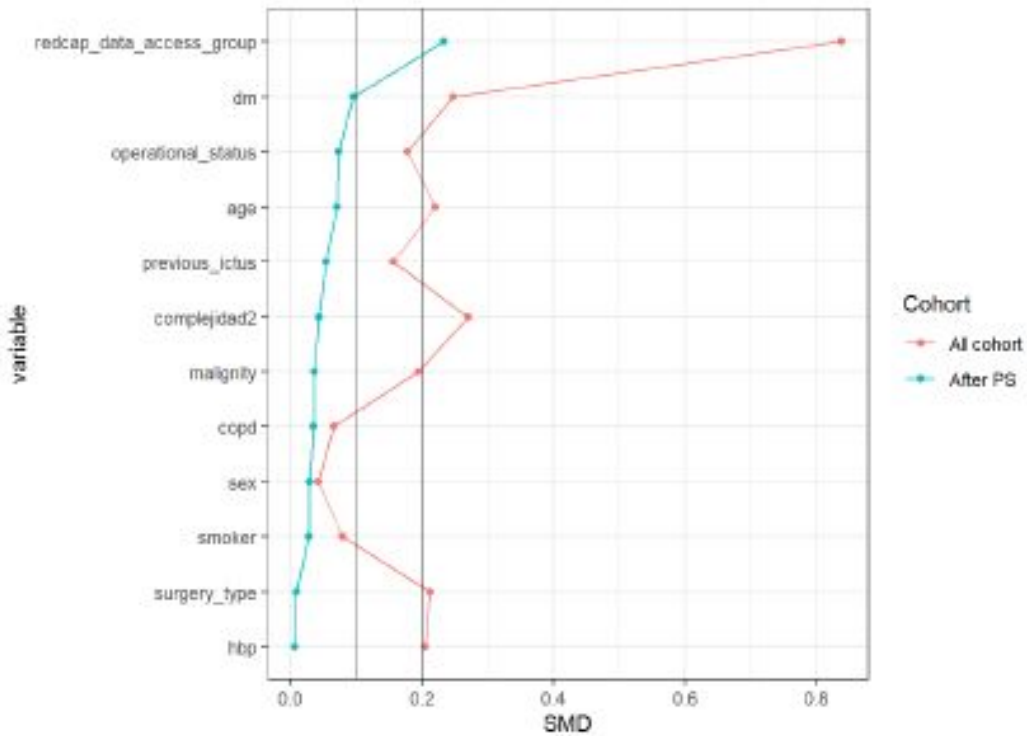
Variable	No. (%)			
	2020 cohort			2019 cohort (n = 2 992)
	COVID-19- positive (n = 183)	COVID-19- negative (n = 2 132)	Total 2020 cohort (n = 2 315)	
Pulmonary				
Pneumonia/respiratory infection	24 (13.1)	61 (2.9)	85 (3.7)	56 (1.9)
Respiratory failure	16 (8.7)	70 (3.3)	86 (3.7)	110 (3.7)
Pleural effusion/pulmonary atelectasis	2 (1.1)	20 (0.9)	22 (0.9)	40 (1.3)
Thromboembolic				
Deep venous thrombosis and/or pulmonary embolism	7 (3.8)	17 (0.8)	24 (1.0)	24 (0.8)
Acute myocardial infarction, stroke, acute limb ischemia	1 (0.6)	9 (0.4)	10 (0.4)	4 (0.1)
Acute mesenteric ischemia	3 (1.6)	12 (0.6)	15 (0.7)	10 (0.3)
Other medical complications				
Heart failure or acute pulmonary edema	5 (2.7)	28 (1.3)	33 (1.4)	50 (1.7)
Fever of unknown origin	5 (2.7)	23 (1.1)	28 (1.2)	23 (0.8)
Hypotension	11 (6.0)	75 (3.5)	86 (3.7)	119 (3.9)
Urinary infection	2 (1.1)	22 (1.0)	24 (1.0)	30 (1.0)
Renal failure	15 (8.2)	84 (3.9)	99 (4.3)	133 (4.5)
Bacteremia/sepsis	7 (3.8)	60 (2.8)	67 (2.9)	81 (2.7)
Blood glucose disturbances >24 hours	0 (0.0)	7 (0.3)	7 (0.3)	10 (0.3)
Atrial fibrillation	5 (2.7)	18 (0.8)	23 (0.9)	42 (1.4)
Hypertensive crisis	0 (0.0)	7 (0.3)	7 (0.3)	6 (0.2)
Acute confusional syndrome	3 (1.6)	14 (0.7)	17 (0.7)	34 (1.1)
Cardiomyopathy or pericarditis	0 (0.0)	3 (0.1)	3 (0.1)	2 (0.1)
Surgical				
Anastomotic leak/intestinal fistula	5 (2.7)	48 (2.3)	53 (2.3)	81 (2.7)
Superficial wound dehiscence	4 (2.2)	20 (0.9)	24 (1.0)	36 (1.2)
Mild bleeding	6 (3.3)	30 (1.4)	36 (1.6)	42 (1.4)
Severe bleeding	4 (2.2)	28 (1.3)	32 (1.4)	52 (1.7)
Superficial wound infection	13 (7.1)	76 (3.6)	89 (3.8)	146 (4.9)
Deep wound infection	13 (7.1)	96 (4.5)	109 (4.7)	157 (5.3)
Postoperative ileus	20 (10.9)	105 (4.9)	125 (5.4)	149 (4.9)
Intestinal perforation	0 (0.0)	10 (0.5)	10 (0.4)	21 (0.7)
Wound seroma or hematoma	2 (1.1)	23 (1.1)	25 (1.1)	43 (1.4)
Intestinal obstruction	2 (1.1)	10 (0.5)	12 (0.5)	14 (0.5)
Ostomy complication	1 (0.6)	3 (0.1)	4 (0.2)	14 (0.5)
Gastrointestinal bleeding	1 (0.6)	3 (0.1)	4 (0.2)	16 (0.5)
Evisceration	0 (0.0)	7 (0.3)	7 (0.3)	15 (0.5)

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3 **Figure S1. Density plot to view the distribution of distance among matched**
4 **cohorts of COVID-19-positive and intra-pandemic COVID-19-negative patients**
5 **(nearest neighbor matching)**
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PREVIEW ONLY

Figure S2. Comparison of means and prevalences of baseline characteristics among matched cohorts of COVID-19-positive and intra-pandemic COVID-19-negative patients



Red dots are standardized differences in the cohort, and green dots are standardized differences in the matched cohort. Vertical lines in 0.1 and 0.2 are standard cut-off to identify negligible differences.

PREVIEW ONLY

Table S5. Outcomes of the 2020 COVID-19-positive and COVID-19-negative matched cohorts (n=682)

Variable	No. (%)		P value
	COVID-19-positive (n = 179)	COVID-19-negative (n = 503)	
30-day mortality	23 (12.9)	34 (6.8)	0.02
90-day mortality ^a	29 (17.8)	41 (8.9)	0.003
Patients with 30-day postoperative complications	76 (42.5)	147 (29.2)	0.002
Failure-to-rescue, % ^b	30.3	23.1	0.31
Type of complication			
Pulmonary ^c	32 (17.9)	44 (8.8)	0.001
Thromboembolic ^d	11 (6.2)	14 (2.8)	0.07
Other medical	33 (18.4)	79 (15.7)	0.46
Surgical	46 (25.7)	95 (18.9)	0.07
Patients with severe complications ^e	44 (24.6)	81 (16.1)	0.005
Need of postoperative ICU for ≥24 hours	52 (29.4)	89 (17.7)	0.001
Length of stay, median (IQR), days	7 (3-18)	5 (2-9)	<0.001
30-day rehospitalization	16 (10.5)	34 (7.3)	0.28
30-day surgical reintervention	11 (7.1)	26 (6.2)	0.83

Abbreviations: ICU, Intensive Care Unit; IQR, interquartile range.

^a Only considered for patients with registered 90-day follow-up (91.1% in both groups).

^b Failure-to-rescue (%): 30-day deaths divided by 30-day complicated patients.

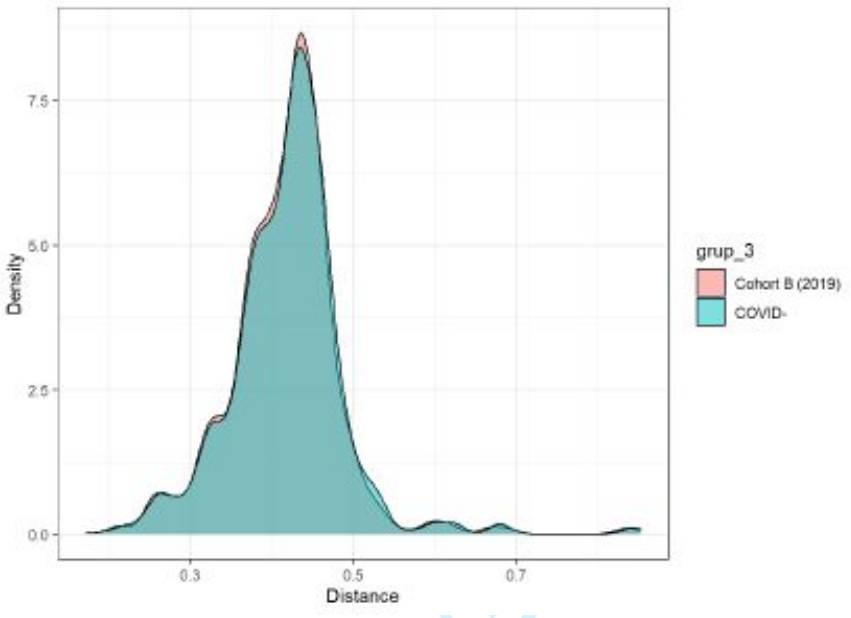
^c Pulmonary complications: respiratory infection or pneumonia, defined as purulent expectoration with positive bacteriological/virological culture, with or without changes in chest X-ray, or fever associated to pulmonary consolidation in chest X-ray; respiratory failure, defined as dyspnea requiring ventilator urgent support and/or PaO₂<60mmHg and PaCO₂>45 mmHg without oxygen assistance; and pleural effusion/pulmonary atelectasis.

^d Thromboembolic complication: deep venous thrombosis and/or pulmonary embolism; acute myocardial infarction, stroke, acute limb ischemia, acute mesenteric ischemia.

^e Clavien-Dindo grade ≥IIIA

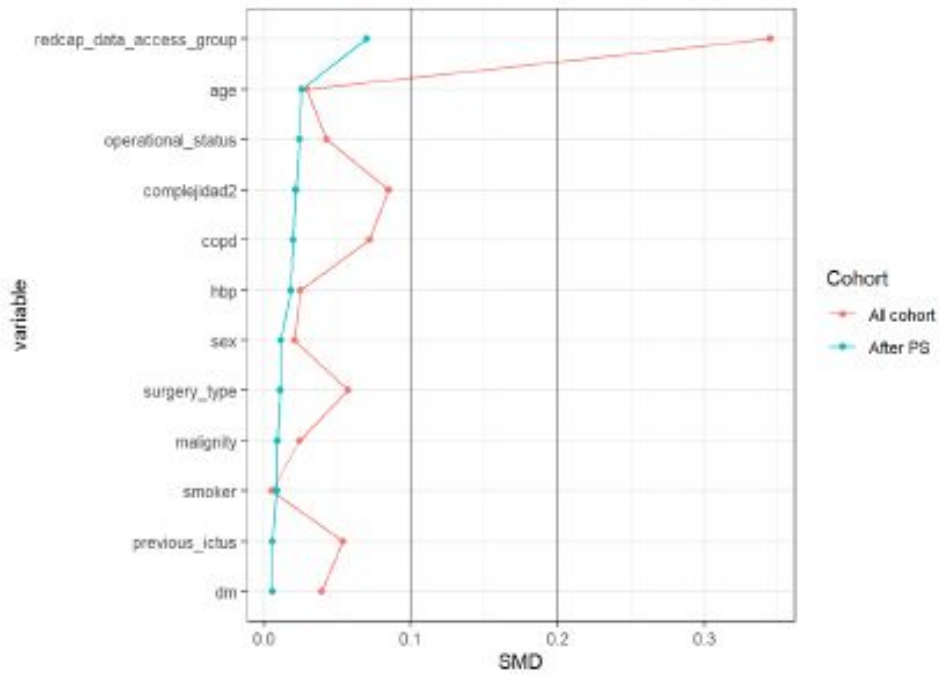
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Figure S3. Density plot to view the distribution of distance among matched cohorts of COVID-19-negative intra- and pre-pandemic patients (nearest neighbor matching)



VIEW ONLY

Figure S4. Comparison of means and prevalences of baseline characteristics among matched cohorts of COVID-19-negative intra- and pre-pandemic patients



Red dots are standardized differences in the cohort, and green dots are standardized differences in the matched cohort. Vertical lines in 0.1 and 0.2 are standard cut-off to identify negligible differences.

Table S6. Outcomes of the COVID-19-negative (2020) and 2019 matched cohorts (n= 4 066)

Variable	No. (%)		P value
	COVID-19-negative 2020 (n = 2 033)	2019 cohort (n = 2 033)	
30-day mortality	92 (4.5)	66 (3.3)	0.04
90-day mortality ^a	111 (5.9)	93 (4.6)	0.07
Patients with 30-day postoperative complications	485 (23.9)	515 (25.3)	0.29
Failure-to-rescue, % ^b	19.0	12.8	0.01
Type of complication			
Pulmonary ^c	117 (5.8)	109 (5.4)	0.63
Thromboembolic ^d	36 (1.8)	25 (1.2)	0.19
Other medical	196 (9.6)	200 (9.8)	0.87
Surgical	313 (15.4)	359 (17.7)	0.06
Patients with severe complications ^e	240 (11.8)	258 (12.7)	0.54
Need of postoperative ICU for ≥ 24 hours	224 (11.0)	254 (12.5)	0.16
Length of stay, median (IQR), days	4 (2-8)	4 (2-9)	0.60
30-day rehospitalization	128 (6.6)	133 (6.8)	0.84
30-day surgical reintervention	108 (5.6)	108 (5.5)	>0.99

Abbreviations: ICU, Intensive Care Unit; IQR, interquartile range.

^a Only considered for patients with registered 90-day follow-up (91.2% and 98.6% in each group, respectively).

^b Failure-to-rescue (%): 30-day deaths divided by 30-day complicated patients.

^c Pulmonary complications: respiratory infection or pneumonia, defined as purulent expectoration with positive bacteriological/virological culture, with or without changes in chest X-ray, or fever associated to pulmonary consolidation in chest X-ray; respiratory failure, defined as dyspnea requiring ventilator urgent support and/or PaO₂<60mmHg and PaCO₂>45 mmHg without oxygen assistance; and pleural effusion/pulmonary atelectasis.

^d Thromboembolic complication: deep venous thrombosis and/or pulmonary embolism; acute myocardial infarction, stroke, acute limb ischemia, acute mesenteric ischemia.

^e Clavien-Dindo grade \geq IIIA