Effects of pre-operative isolation on postoperative pulmonary complications after elective surgery: an international prospective cohort study

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Effects of pre-operative isolation on postoperative pulmonary complications after elective surgery: an international prospective cohort study

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Summary

We aimed to determine the impact of pre-operative isolation on postoperative pulmonary complications after elective surgery during the global SARS-CoV-2 pandemic. We performed an international prospective cohort study including patients undergoing elective surgery in October 2020. Isolation was defined as the period before surgery during which patients did not leave their house or receive visitors from outside their household. Primary outcome was postoperative pulmonary complications, adjusted in multivariable models for measured confounders. Pre-defined subgroup analyses were performed for the primary outcome. A total of 96,454 patients from 114 countries were included and, overall, 26,948 (27.9%) patients isolated before surgery. Postoperative pulmonary complications were recorded in 1947 (2.0%) patients of which 227 (11.7%) were associated with SARS-CoV-2 infection. Patients who isolated pre-operatively were older, had more respiratory comorbidities and were more commonly from areas of high SARS-CoV-2 incidence and high-income countries. Although the overall rates of postoperative pulmonary complications were similar in those that isolated and those that did not (2.1% vs. 2.0%, respectively), isolation was associated with higher rates of postoperative pulmonary complications after adjustment (adjusted OR 1.20, 95%CI 1.05–1.36, p = 0.005). Sensitivity analyses revealed no further differences when patients were categorised by: pre-operative testing; use of COVID-19-free pathways; or community SARS-CoV-2 prevalence. The rate of postoperative pulmonary complications increased with periods of isolation longer than 3 days, with an OR (95%CI) at 4–7 days or ≥ 8 days of 1.25 (1.04–1.48), p = 0.015 and 1.31 (1.11–1.55), p = 0.001, respectively. Isolation before elective surgery might be associated with a small but clinically important increased risk of postoperative pulmonary complications. Longer periods of isolation showed no reduction in the risk of postoperative pulmonary complications. These findings have significant implications for global provision of elective surgical care.

Introduction

Several strategies have been explored to mitigate against the risk of peri-operative SARS-CoV-2 infection, given the high associated postoperative pulmonary complication rates and mortality [1]. It has become clear that a range of measures are needed to ensure safe surgery, including: COVID-19-free surgical pathways; patient testing for SARS-CoV-2; and delaying surgery in patients with SARS-CoV-2 infection [2, 3]. These measures will still be needed despite the roll-out of vaccination programmes, which may take years to achieve globally, be less effective against SARS-CoV-2 variants and not achieve universal implementation [4, 5].

Isolation before elective surgery has been recommended by several national surgical associations [6-8]. This attempts to reduce the risk of asymptomatic carriers undergoing surgery, thereby protecting individual patients and reducing in-hospital transmission to other patients and staff. It presents potential problems for patients, including: logistical considerations; reducing patient mobility before major surgery; and social isolation. It also means that last minute additions to operating theatre lists are less likely, thereby representing an additional potential burden to surgical recovery plans.

These limitations would be acceptable if there was clear evidence of benefit in regard to reduction of postoperative complications, both related to SARS-CoV-2 and otherwise. Demonstrating benefit and optimum duration will support wider rollout of global best practice in elective surgery. Demonstrating no benefit will allow units to tailor clinical guidance and consider reducing the burden of isolation. We aimed to determine the impact of pre-operative isolation on postoperative pulmonary complications after elective surgery.

Methods

This was a planned sub-study of an international prospective cohort study of patients undergoing surgery in hospitals, regardless of local SARS-CoV-2 infection prevalence or isolation policies during at least one seven-day study period in October 2020. Full methodology has been previously reported [9]. Hospitals providing surgical care for patients under any surgical specialty were eligible to participate. Local and national approvals were obtained according to local regulations. In the UK, this study was registered as clinical audit or service evaluation at each participating site. Patient consent was obtained when demanded by local governance requirements, which was not required in the UK. The study was registered prospectively and we adhered to the strengthening of the reporting of observational studies in epidemiology (STROBE) statement for observational studies [10].

All consecutive patients undergoing elective surgery for any indication were included. Elective surgery was defined as any procedure routinely performed in an operating theatre by a surgeon during a planned admission. A list of excluded procedures (such as central line insertion) was provided to all collaborators (see online Supporting Information Table S1). Patients undergoing emergency surgery or who had a pre-operative SARS-CoV-2 diagnosis were excluded.

Pre-operative isolation was defined as limitation of social contacts before surgery during which time patients stayed at home, avoided public spaces and transport and did not receive visitors from outside of their household. Patients who were not required to follow any social distancing or isolation measures before surgery were considered to have not been exposed to pre-operative isolation. The number of days that each patient was required to follow the isolation measures was recorded as the duration of isolation. Patients were categorised according to the duration of pre-operative isolation into three groups: up to 3 days; 4 to 7 days; or ≥ 8 days before their planned surgery.

Multiple variables were collected for each patient: age; sex; ASA physical status; revised cardiac risk index (RCRI); presence of respiratory comorbidities; indication for surgery; and grade of surgery. Consistent with previous analyses, age was categorised as < 70 or ≥ 70 y. Country-level income was defined according to the World Bank index classification (updated in 2019) based on gross national income per capita, which determines three income groups: high income; upper-middle income; lower middle-income (including patients from both low and lower-middle income countries).

Pre-operative testing was defined as a reverse transcription-polymerase chain reaction (RT-PCR) or antigen swab test performed within 3 days before surgery. A patient was considered to have undergone surgery in a COVID-19-free surgical pathway if a completely segregated pathway was provided (including ward, operating theatre and critical care areas) or the hospital was not admitting patients with SARS-CoV-2 infection. If otherwise, the surgical pathway was recorded as non-segregated.

Community SARS-CoV-2 prevalence was determined for each patient based on the 14-day case notification rate at the time of surgery in each participating country. These rates were extracted from the World Health Organization, European Centre for Disease Control, US Centre for Disease Control and specific national registries via the Our World in Data platform [11]. Hospitals were classified as being in communities with either a low (< 100 cases per 100,000 population) or high (≥ 100 cases per 100,000 population) SARS-CoV-2 prevalence.

The primary outcome of this study was postoperative pulmonary complications, defined as pneumonia, acute respiratory distress syndrome or unexpected mechanical ventilation within 30 days after surgery. The main secondary outcome was 30-day mortality. Other secondary outcomes were postoperative SARS-CoV-2 infection and SARS-CoV-2 postoperative pulmonary complications within 30 days for surgery. Postoperative SARS-CoV-2 diagnosis was based on any one of the following criteria: positive RT-PCR nasopharyngeal swab; positive rapid antigen test; chest computed tomography (CT) scan showing changes consistent with pneumonitis secondary to SARS-CoV-2 infection; positive immunoglobulin-G or immunoglobulin-M antibody test showing active infection; or clinical diagnosis (in the absence of negative RT-PCR swab results). A SARS-CoV-2 postoperative pulmonary complication was defined as a pulmonary complication within 30 days of surgery in a patient with a postoperative SARS-CoV-2 infection (see online Supporting Information Appendix S2).

Descriptive results are reported with absolute and proportional frequencies. Chi-square tests were used to assess unadjusted differences between groups. Multivariate logistic regression models were performed to test for an independent effect of pre-operative isolation on postoperative pulmonary complications and mortality, adjusting for patient, surgical and local setting factors. The results of the adjusted models were summarised using univariate and multivariate OR (95%CI). The statistical significance threshold used was $p < 0.05$. Missing data were reported in all tables and figures. Statistical analyses were performed using R studio V 3.6.1 (RStudio, Boston, USA) and the packages dplyr, tidyverse, gmodels, finalfit, ggplot2 and forestplot.

The adjusted model for the primary outcome was repeated in key subgroups to determine the effect of pre-operative isolation in patients: with high vs. low ASA physical status; in settings where pre-operative testing was or was not available; where COVID-19-free surgical pathways were or were not established; and where the community SARS-CoV-2 prevalence was high or low. A sensitivity analysis was performed to explore the impact of duration of isolation on postoperative pulmonary complications, comparing patients who were isolated for: up to 3 days; 4 to 7 days; and ≥ 8 days before surgery. An interaction term was used in adjusted models to account for the fact that isolation was likely to be less common in low- and middle-income countries where there is a proven higher rate of postoperative complications and mortality [12].

Results

A total of 96,454 patients were included from 1634 hospitals in 114 countries. There were 62,839 (65.1%) patients who underwent surgery in areas with high SARS-CoV-2 prevalence and 33,615 (34.9%) patients in areas of low prevalence. The study included 65,228 (67.6%) patients from high income countries and 31,226 (32.4%) patients from low- and middle-income countries. There were 74,347 (77.1%) patients who underwent surgery for a benign condition and 57,079 (59.2%) who underwent major surgery (see online Supporting Information Table S2). Overall, 26,948 (27.9%) of the patients isolated before surgery, 80,200 (83.1%) underwent surgery in a COVID-19-free pathway and 67,612 (70.1%) had a pre-operative SARS-CoV-2 test.

Patients who isolated before surgery were older, had more respiratory comorbidities and higher ASA physical statuses. Pre-operative isolation was more common in areas of high SARS-CoV-2 prevalence and in high-income countries (Table 1). Patients who isolated pre-operatively were also more frequently tested for SARS-CoV-2 before surgery and were operated in a COVID-19-free surgical pathway more often (see online Supporting Information Figure S1).

The overall rate of postoperative pulmonary complications was reported in 1947 (2.0%) and postoperative mortality was reported in 648 (0.7%). Of all the postoperative pulmonary complications, 227 (11.7%) occurred in patients with a concomitant postoperative SARS-CoV-2 infection. Compared with patients who had isolated before surgery, those who did not isolate had similar postoperative pulmonary complication rates (2.1% vs. 2.0%), lower mortality (0.4% vs. 0.8%) and similar SARS-CoV-2 infection rates (0.8% vs. 0.8%) (Fig. 1). After adjustment for measured confounders, isolation was associated with higher postoperative pulmonary complication rates (adjusted OR 1.20, 95%CI 1.05–1.36, $p = 0.005$) (Fig. 2) but with no significant difference in postoperative mortality (adjusted OR 0.80, 95%CI 0.62–1.02, $p = 0.081$) (see online Supporting Information Table S3).

Multiple factors were independently associated with increased postoperative pulmonary complication rates, including: age > 70 y; male sex; high ASA physical status; previous respiratory comorbidities; cancer surgery; and major surgical procedures (Fig. 2). Pre-operative testing was associated with reduced postoperative pulmonary complication rates (OR 0.81 ,95%CI 0.73–0.89, $p < 0.001$) (online Supporting Information Table S4).

Isolation was not associated with reduced postoperative pulmonary complications across any of the pre-defined subgroups (Fig. 3). Pre-operative isolation was associated with higher postoperative pulmonary complication rates in: patients with ASA physical status 1–2; those undergoing surgery in a high SARS-CoV-2 prevalence area; a COVID-19-free pathway; or those who did not undergo pre-operative testing (see online Supporting Information Tables S5-S12).

Of patients who isolated before surgery, 6971 (26.0%) isolated for up to 3 days, 10,691 (39.9%) for 4 to 7 days, and 9164 (34.2%) for ≥ 8 days (see online Supporting Information Table S13). Patients isolating for longer durations were progressively older and had a greater comorbid burden, including respiratory comorbidities.

A duration of isolation of up to 3 days before surgery did not show a difference in postoperative pulmonary complication rates compared with no isolation (OR 0.90, 95%CI 0.70–1.13, $p = 0.377$).

Patients isolating for longer durations had higher rates of postoperative pulmonary complications when isolating for 4 to 7 days (OR 1.25 ,95%CI 1.04–1.48, p = 0.015) and for ≥ 8 days (OR 1.31, 95%CI 1.11–1.55, p = 0.001) (Table 2).

Discussion

Pre-operative isolation was associated with a small but clinically important increase in postoperative pulmonary complications. A sensitivity analysis looking at the duration of pre-operative isolation found that patients who isolated for longer periods had higher rates of postoperative pulmonary complications. Although there was a difference in mortality rates, the numbers were small and the difference was not statistically significant following adjustment. There were no clinically relevant differences in SARS-CoV-2 positivity or SARS-CoV-2-related postoperative pulmonary complication rates. We also showed no benefit with pre-operative isolation: in areas of different SARS-CoV-2 community prevalence; when pre-operative testing was implemented; or when COVID-19-free surgical pathways were in place.

Although this study did not directly identify causes for an association between isolation and increased postoperative pulmonary complication rates, it provides an opportunity to generate hypotheses. Isolation is associated with decreased physical activity, worse nutritional habits and higher levels of anxiety and depression [13-16]. These effects in already vulnerable patients may have contributed to an increased risk of pulmonary complications. Further, there is increasing evidence demonstrating that prehabilitation before surgery improves patient recovery and outcomes [17-19]. It is possible that isolation may have, therefore, conversely led to patient deconditioning and functional decline [20], adversely influencing patient outcomes. Although patients who isolated were slightly more comorbid than those who did not, these findings remained present after adjustment. Our evidence suggests that removing pre-operative isolation strategies is unlikely to lead to worse postoperative outcomes for patients, but institutions should monitor their postoperative pulmonary complication rates as strategies evolve.

Whereas unadjusted mortality rates appeared lower for patients who isolated, this did not remain significant after adjustment. Combined with small numbers, a clear benefit of isolation on 30-day mortality cannot be drawn from our data. There is a known interaction between mortality, failure to rescue patients from surgical complications and lower income surgical settings [12, 21]. Although such an interaction is likely to have contributed to this finding, it was beyond the scope of this predefined analysis to explore further, especially in the context of small event numbers and the likelihood of further unmeasured confounders.

However, benefits of pre-operative isolation are not only for the individual patient but also to other patients and staff in hospitals who are at risk from asymptomatic carriers of SARS-CoV-2. Although this study included all patients operated upon during the same week in each specialty and hospital, it was not designed to capture cross infection in surgical wards as only individual level outcomes were collected. Social isolation can have a system-wide benefit in preventing the admission of patients incubating SARS-CoV-2 that was not captured by our study. Further, a systems risk of undiagnosed SARS-CoV-2 infection in institutions that operate COVID-19-free surgical pathways is the risk of individual patients affecting these pathways and other patients within them. For example, a COVID-19-free ward could become a COVID-19-positive ward if one patient tests positive, thereby undermining the entire pathway. Finally, symptomatic screening and pre-operative testing are likely to remain key components of elective surgery admissions processes to prevent nosocomial infection by SARS-CoV-2 [22].

Our study has limitations. Firstly, postoperative SARS-CoV-2 rates were similar in both groups, suggesting that pre-operative isolation is not effective in reducing nosocomial SARS-CoV-2 infection. However, we did not include patients who isolated and then tested positive who may have had their surgery delayed or cancelled. This might have underestimated the SARS-CoV-2 incidence and postoperative pulmonary complication rates in patients who did not isolate. Secondly, although a definition of pre-operative isolation was stated in the study protocol, slightly different strategies could have been reported as pre-operative isolation. Patient compliance to the isolation recommendations was not measured, which could have contributed to underestimation of the benefits of isolation. However, the large numbers and heterogeneous sites contribute to a pragmatic study design and generalisability of our conclusions. Thirdly, although adjustment was done for all the available variables, there might be residual confounding that affected results. We addressed this through multiple sensitivity analyses, in which the findings were consistent. Finally, community SARS-CoV-2 prevalence was collected from the most reliable sources available, but we acknowledge that they might be inaccurate in some settings, influencing the adjusted analysis [23, 24]. These were assessed at a national level, possibly lacking the granularity of regional variation within countries.

Healthcare providers may wish to take these findings into consideration when reviewing local and national guidance. Relaxation of pre-operative isolation policies appears to be safe for individual patients, especially in the presence of pre-operative testing, which this and previous studies showed to be beneficial [2]. Selected isolation practices may remain in place in certain conditions (such as high-risk patients and periods of high community prevalence). Further research is needed to explore the most effective method of maintaining patient fitness and conditioning for patients that are isolating, which may include home or remote prehabilitation [25, 26]. Postoperative pulmonary complications related to SARS-CoV-2 accounted for only a small proportion of observed postoperative pulmonary complications. Going forward, research to target other causes of postoperative pneumonias is needed, since endemic pathogens may be the more common organisms.

This study demonstrates that patient isolation before elective surgery might be associated with a small increased risk in postoperative pulmonary complications. Longer periods of isolation showed no reduction in the risk in postoperative pulmonary complications. These findings have implications for global provision of elective surgery.

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Table 1 Baseline characteristics of patients who isolated and those that did not isolate before surgery. Values are number (proportion). Proportions are expressed as per column total.

		No isolation n = 69,436	**Isolation n = 26,948**	**p value**
Age	< 70 y	56,593 (81.5%)	20,129 (74.7%)	< 0.001
	≥ 70 y	12842 (18.5%)	6819 (25.3%)	
	Missing	1	0	
Sex	Female	36,609 (52.7%)	14,370 (53.3%)	0.096
	Male	32,824 (47.3%)	12,578 (46.7%)	
	Missing	3	0	
ASA physical status	1–2	53,452 (77.0%)	20,275 (75.3%)	< 0.001
	3–5	15,973 (23.0%)	6654 (24.7%)	
	Missing	11	19	
Revised cardiac risk index	0	32,045 (46.2%)	12,401 (46.0%)	< 0.001
	1–2	35,484 (51.1%)	13,950 (51.8%)	
	≥ 3	1881 (2.7%)	583 (2.2%)	
	Missing	26	14	
Respiratory comorbidities	No	63,651 (91.7%)	23,676 (87.9%)	< 0.001
	Yes	5740 (8.3%)	3250 (12.1%)	
	Missing	45	22	
Surgical indication	Benign	54,148 (78.0%)	20,143 (74.8%)	< 0.001
	Cancer	15,287 (22.0%)	6803 (25.2%)	
	Missing	1	2	
Surgery grade	Minor/intermediate	27,716 (39.9%)	11,611 (43.1%)	< 0.001
	Major	41,703 (60.1%)	15,336 (56.9%)	
	Missing	17	1	
Surgery area	Abdominopelvic	34,202 (50.2%)	12,717 (48.2%)	< 0.001
	Thoracic	3188 (4.7%)	1317 (5.0%)	
	Head and neck	7276 (10.7%)	2727 (10.3%)	
	Limb	9498 (13.9%)	4533 (17.2%)	
	Other	13,930 (20.5%)	5111 (19.4%)	
	Missing	18	1	
Anaesthesia	Local	6525 (9.4%)	2789 (10.4%)	< 0.001

	Regional	11,172 (16.1%)	3492 (13.0%)	
	General	51,712 (74.5%)	20,655 (76.7%)	
	Missing	27	12	
SARS-CoV-2 community prevalence	Low	30,282 (43.6%)	3326 (12.3%)	< 0.001
	High	39,154 (56.4%)	23,622 (87.7%)	
Country income	High	42,025 (60.5%)	23,166 (86.0%)	< 0.001
	Upper middle	13,192 (19.0%)	2979 (11.1%)	
	Low/low-middle	14,219 (20.5%)	803 (3.0%)	

Table 2 Multivariable logistic regression model exploring the association between pre-operative isolation length and postoperative pulmonary complications, adjusting for patient, surgery and surgical setting factors. Community incidence of SARS-CoV-2 was defined as the median 14-day cumulative country case notification rate per 100,000 population during October 2020. Values are number (proportion).

		No PPC	**PPC**	**Univariable OR 95%CI**	**p value**	**Multivariable OR 95%CI**	**p value**
Duration of isolation	No Isolation	67,993 (98.0%)	1386 (2.0%)	Reference	–	Reference	–
	≤ 3 days	6877 (98.7%)	91 (1.3%)	0.69 (0.54–0.87)	0.002	0.90 (0.70–1.13)	0.377
	4–7 days	10,483 (98.1%)	206 (1.9%)	0.99 (0.83–1.17)	0.887	1.25 (1.04–1.48)	0.015
	≥ 8 days	8910 (97.2%)	252 (2.8%)	1.51 (1.29–1.77)	< 0.001	1.31 (1.11–1.55)	0.001
Age	< 70 y	75,397 (98.3%)	1328 (1.7%)	Reference	–	Reference	–
	≥70 y	19,045 (96.9%)	619 (3.1%)	1.85 (1.67–2.03)	< 0.001	1.22 (1.09–1.36)	< 0.001
Sex	Female	50,218 (98.5%)	783 (1.5%)	Reference	–	Reference	–
	Male	44,222 (97.4%)	1164 (2.6%)	1.69 (1.54–1.85)	< 0.001	1.53 (1.39–1.68)	< 0.001
ASA physical status	1–2	72,837 (98.8%)	884 (1.2%)	Reference	–	Reference	–
	3–5	21,566 (95.3%)	1063 (4.7%)	4.06 (3.71–4.45)	< 0.001	2.33 (2.09–2.60)	< 0.001
Revised cardiac risk index	0	44,029 (99.0%)	425 (1.0%)	Reference	–	Reference	–
	1–2	48,109 (97.3%)	1314 (2.7%)	2.83 (2.54–3.16)	< 0.001	1.52 (1.30–1.77)	< 0.001
	≥ 3	2258 (91.7%)	205 (8.3%)	9.41 (7.91–11.15)	< 0.001	2.44 (1.95–3.03)	< 0.001
Respiratory comorbidities	No	85,760 (98.2%)	1560 (1.8%)	Reference	–	Reference	–
	Yes	8609 (95.7%)	384 (4.3%)	2.45 (2.19–2.74)	< 0.001	1.67 (1.48–1.89)	< 0.001
Surgical indication	Benign	73,141 (98.5%)	1151 (1.5%)	Reference	–	Reference	–
	Cancer	21,299 (96.4%)	796 (3.6%)	2.37 (2.17–2.60)	< 0.001	1.70 (1.54–1.88)	< 0.001
Surgery grade	Minor/intermediate	39,019 (99.2%)	306 (0.8%)	Reference	–	Reference	–
	Major	55,409 (97.1%)	1638 (2.9%)	3.77 (3.34–4.27)	< 0.001	2.15 (1.88–2.46)	< 0.001
Anaesthesia	Local	9261 (99.5%)	48 (0.5%)	Reference	–	Reference	–
	Regional	14,524 (99.0%)	154 (1.0%)	2.05 (1.49–2.86)	< 0.001	1.68 (1.20–2.40)	0.003
	General	70,620 (97.6%)	1745 (2.4%)	4.77 (3.62–6.44)	< 0.001	2.49 (1.86–3.43)	< 0.001
Surgical area	Abdominopelvic	47,310 (98.1%)	921 (1.9%)	Reference	–	Reference	–
	Thoracic	10,196 (98.4%)	168 (1.6%)	0.85 (0.71–1.00)	0.049	1.20 (0.98–1.45)	0.069
	Head and neck	13,883 (98.8%)	167 (1.2%)	0.62 (0.52–0.73)	< 0.001	1.08 (0.89–1.30)	0.448
	Limb	18,909 (98.8%)	226 (1.2%)	0.61 (0.53–0.71)	< 0.001	1.04 (0.87–1.24)	0.671
	Other	4129 (89.9%)	462 (10.1%)	5.75 (5.11–6.45)	< 0.001	2.73 (2.40–3.10)	< 0.001
Pre-operative	No test	39,375 (97.8%)	871 (2.2%)	Reference	–	Reference	–

SARS–CoV–2 testing							
	Test	54,957 (98.1%)	1066 (1.9%)	0.88 (0.80–0.96)	0.004	0.82 (0.74–0.91)	< 0.001
Surgical pathway	Non-segregated	15,830 (97.8%)	354 (2.2%)	Reference	–	Reference	–
	COVID-19-free	78,559 (98.0%)	1587 (2.0%)	0.90 (0.81–1.02)	0.087	0.99 (0.87–1.12)	0.828
SARS-CoV-2 community prevalence	Low	32,876 (97.9%)	698 (2.1%)	Reference	–	Reference	–
	High	61,567 (98.0%)	1249 (2.0%)	0.96 (0.87–1.05)	0.341	1.08 (0.95–1.22)	0.235
Country income*	High	64,024 (98.2%)	1190 (1.8%)	Reference	–	Reference	–
	Upper middle	15,740 (97.3%)	438 (2.7%)	1.47 (1.29–1.67)	< 0.001	1.99 (1.72–2.29)	< 0.001
	Lower middle/low	14,679 (97.9%)	319 (2.1%)	1.19 (1.04–1.37)	0.010	2.03 (1.71–2.40)	< 0.001
Interaction term	Isolated ≤ 3 days, LMIC	–	–	1.71 (0.59–3.91)	0.256	1.54 (0.53–3.57)	0.366
	Isolated ≤ 3 days, UMIC	–	–	0.93 (0.41–1.84)	0.847	0.77 (0.34–1.56)	0.505
	Isolated 4–7 days, LMIC	–	–	0.62 (0.28–1.20)	0.197	0.52 (0.23–1.03)	0.087
	Isolated 4–7 days, UMIC	–	–	0.89 (0.63–1.26)	0.531	0.80 (0.55–1.13)	0.212
	Isolated ≥ 8 days, LMIC	–	–	1.23 (0.43–2.76)	0.660	0.82 (0.28–1.89)	0.682
	Isolated ≥ 8 days, UMIC	–	–	1.28 (0.86–1.86)	0.213	0.82 (0.55–1.21)	0.340

*Country income groups defined as per the World Bank classification. LMIC, low-to-middle income country; UMIC, upper-to-middle income country.

Figure 1 Flowchart of patient inclusion, with postoperative outcomes by isolation group. SARS-CoV-2 associated postoperative pulmonary complications were defined as the presence of postoperative pulmonary complications (PPC) in patients with a postoperative diagnosis of SARS-CoV-2 infection. Missing data for the presented variables: pre-operative isolation n = 70; postoperative pulmonary complications n = 64; postoperative mortality n = 55.

Figure 2 Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, adjusting for patient, surgery and surgical setting factors.

Number in dataframe = 96,454; number in model = 96,067; missing = 387; AIC = 16,680.6; C-statistic = 0.784. Full model presented in online Supporting Information Table S4, including an interaction term of isolation and country income. Community prevalence of SARS-CoV-2 was defined as the median 14-day cumulative country case notification rate per 100,000 population during October 2020. Country income groups defined as per the World Bank classification.

Figure 3 Forest plot of the adjusted odds ratio (95%CI) for the effect of isolation in postoperative pulmonary complications across patient subgroups for ASA physical status, pre-operative testing, COVID-19-free pathways, and community prevalence. Odds ratios are adjusted for the same variables used in the main model, including an interaction term of isolation and country income.

Supporting Information

Figure S1. Rates of pre-operative testing, COVID-free surgical pathways and community incidence by isolation group.

Table S1. List of excluded procedures.

Table S2. Detailed list of included procedures.

Table S3. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative mortality, adjusting for patient, surgery and surgical setting factors.

Table S4. Full multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, in all patients included in the study.

Table S5. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients with mild comorbidities (ASA physical status 1-2).

Table S6. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients with major comorbidities (ASA physical status 3-5).

Table S7. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who were tested pre-operatively.

Table S8. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who were not tested pre-operatively.

Table S9. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who underwent surgery in a COVID-19-free pathway.

Table S10. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who underwent surgery in a non-segregated pathway.

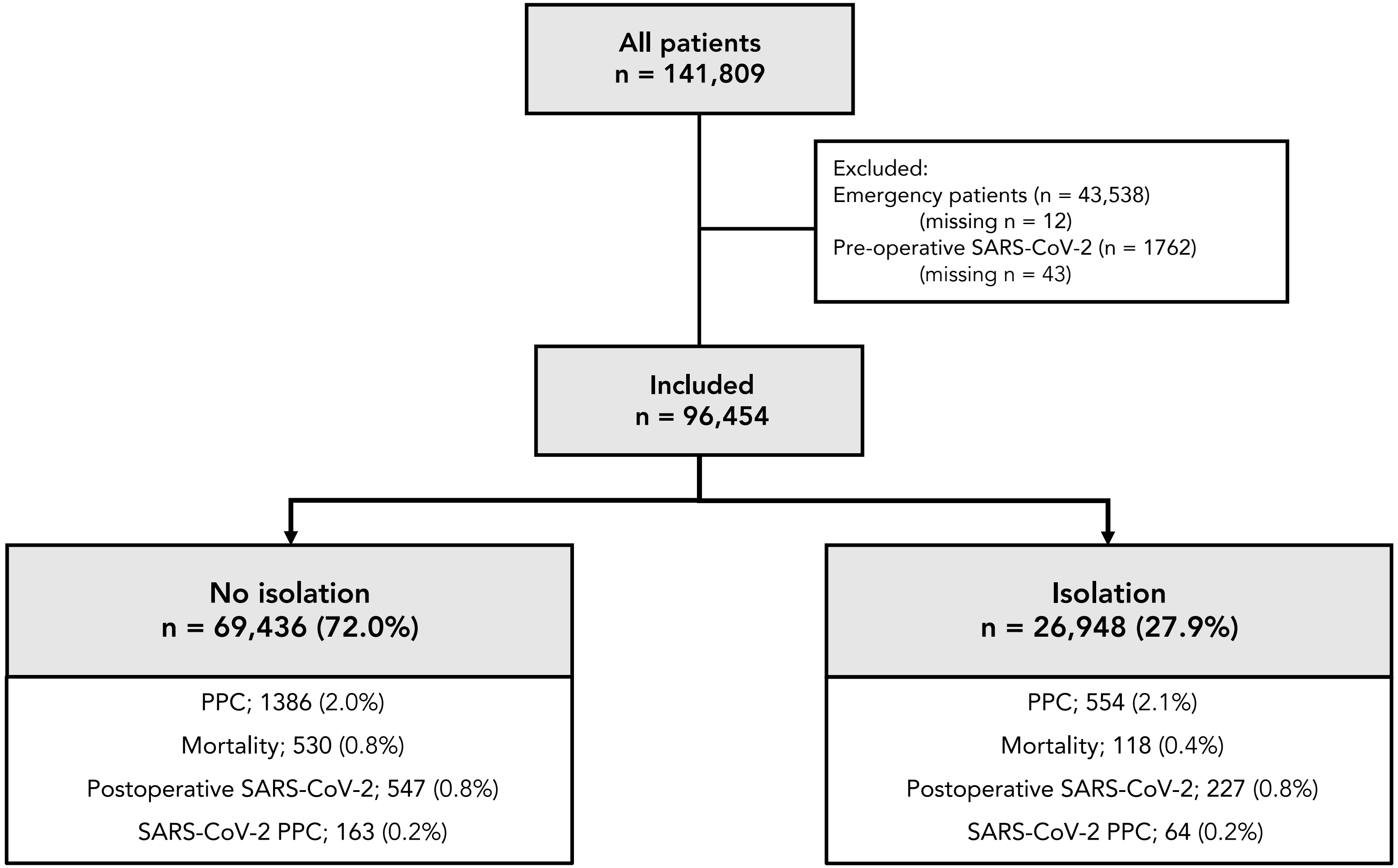
Table S11. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who underwent surgery in a community with high SARS-CoV-2 prevalence.

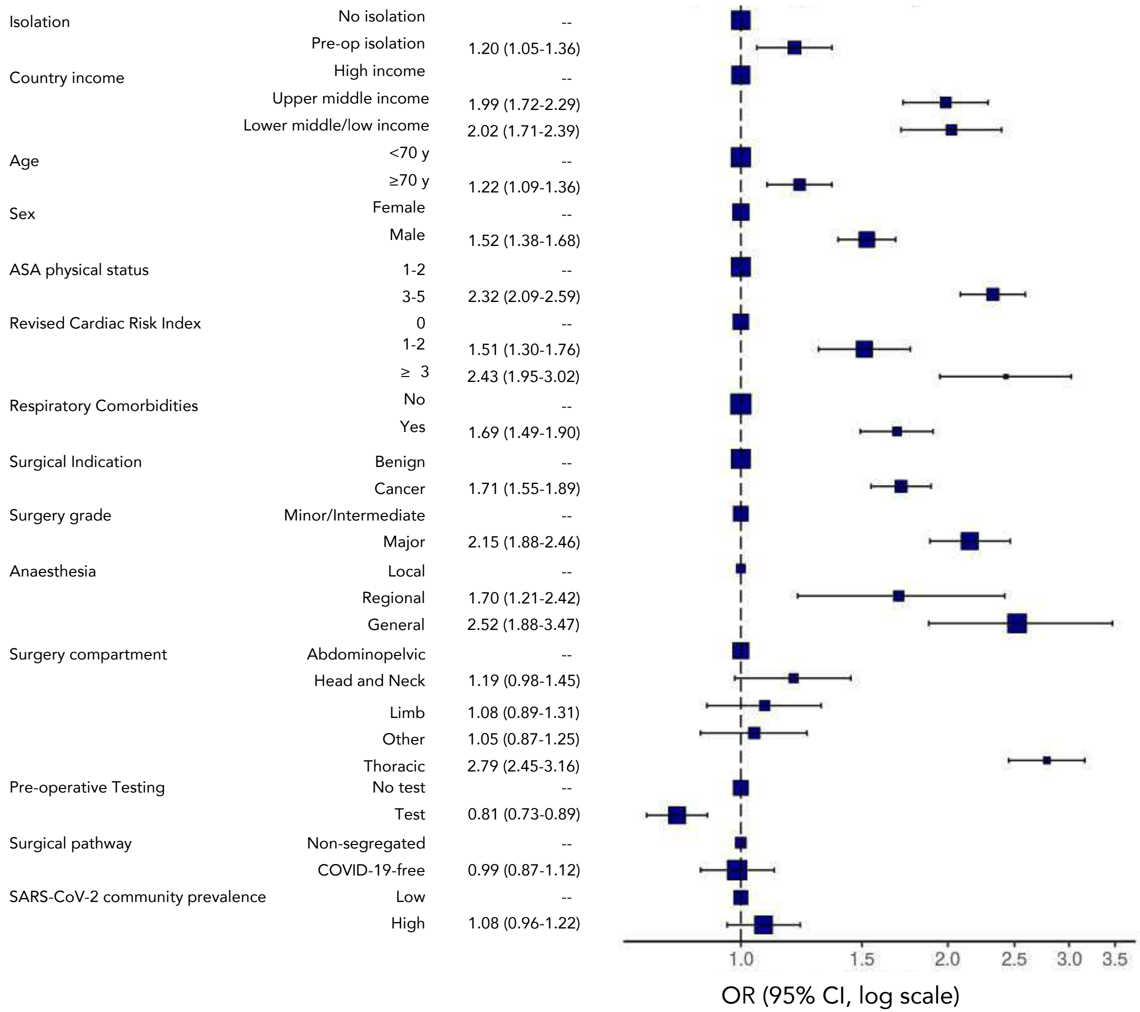
Table S12. Multivariable logistic regression model exploring the association between pre-operative isolation and postoperative pulmonary complications, only for patients who underwent surgery in a community with low SARS-CoV-2 prevalence.

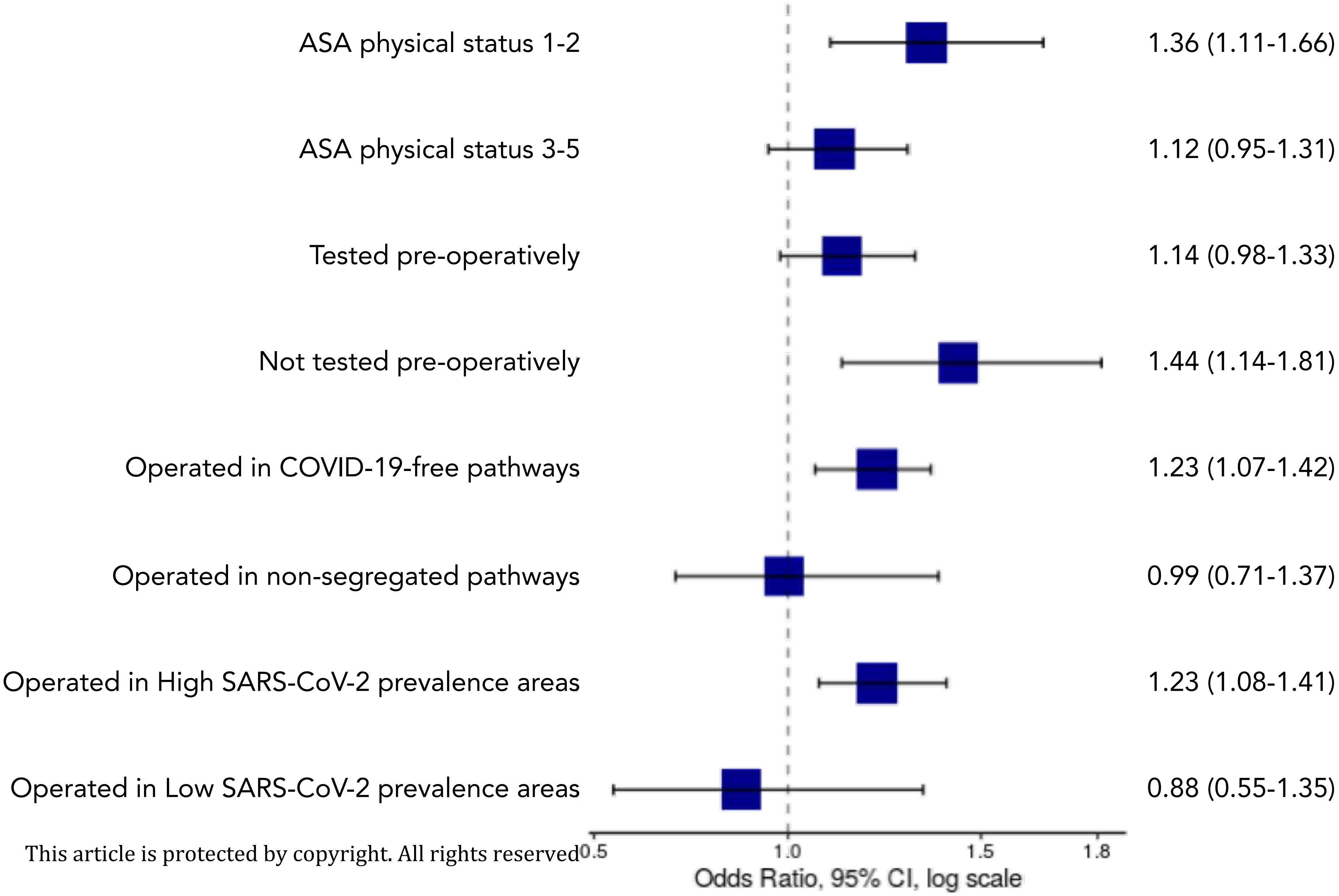
Table S13. Demographic features of patients by status and length of pre-operative isolation.

Appendix S1 COVIDSurg Collaborative and GlobalSurg Collaborative authors.

Appendix S2 Study definitions.


All patients
n = 141,809
Excluded:
Emergency patients (n = 43,538)
(missing n = 12)
Pre-operative SARS-CoV-2 (n = 1762)
(missing n = 43)
Included
n = 96,454
No isolation
n = 69,436 (72.0%)
PPC; 1386 (2.0%)
Mortality; 530 (0.8%)
Postoperative SARS-CoV-2; 547 (0.8%)
SARS-CoV-2 PPC; 163 (0.2%)
Isolation
n = 26,948 (27.9%)
PPC; 554 (2.1%)
Mortality; 118 (0.4%)
Postoperative SARS-CoV-2; 227 (0.8%)
SARS-CoV-2 PPC; 64 (0.2%)


Isolation
No isolation --
Pre-op isolation 1.20 (1.05-1.36)
Country income
High income --
Upper middle income 1.99 (1.72-2.29)
Lower middle/low income 2.02 (1.71-2.39)
Age
<70 y --
≥70 y 1.22 (1.09-1.36)
Sex
Female --
Male 1.52 (1.38-1.68)
ASA physical status
1-2 --
3-5 2.32 (2.09-2.59)
Revised Cardiac Risk Index
0 --
1-2 1.51 (1.30-1.76)
≥ 3 2.43 (1.95-3.02)
Respiratory Comorbidities
No --
Yes 1.69 (1.49-1.90)
Surgical Indication
Benign --
Cancer 1.71 (1.55-1.89)
Surgery grade
Minor/Intermediate --
Major 2.15 (1.88-2.46)
Anaesthesia
Local --
Regional 1.70 (1.21-2.42)
General 2.52 (1.88-3.47)
Surgery compartment
Abdominopelvic --
Head and Neck 1.19 (0.98-1.45)
Limb 1.08 (0.89-1.31)
Other 1.05 (0.87-1.25)
Thoracic 2.79 (2.45-3.16)
Pre-operative Testing
No test --
Test 0.81 (0.73-0.89)
Surgical pathway
Non-segregated --
COVID-19-free 0.99 (0.87-1.12)
SARS-CoV-2 community prevalence
Low --
High 1.08 (0.96-1.22)
1.0
1.5
2.0
2.5
3.0
3.5
OR (95% CI, log scale)


ASA physical status 1-2
1.36 (1.11-1.66)
ASA physical status 3-5
1.12 (0.95-1.31)
Tested pre-operatively
1.14 (0.98-1.33)
Not tested pre-operatively
1.44 (1.14-1.81)
Operated in COVID-19-free pathways
1.23 (1.07-1.42)
Operated in non-segregated pathways
0.99 (0.71-1.37)
Operated in High SARS-CoV-2 prevalence areas
1.23 (1.08-1.41)
Operated in Low SARS-CoV-2 prevalence areas
0.88 (0.55-1.35)
0.5
1.0
1.5
1.8
Odds Ratio, 95% CI, log scale

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S;Fotopoulou, C;Fowler, A;Futaba, K;Ganly, I;James, HG;Griffiths, E;Gronchi, A;Hutchinson, P;Hyman, GY;Incorvia, J;Jain, R;Jenkinson, M;Khan, T;Knight, SR;Kolias, A;Kudsk-Iversen, S;Kwan, TY;Leung, E;Mayol, J;McKay, S;Meara, JG;Mills, E;Moug, S;Patel, A;Perinotti, R;Rice, HE;Roberts, K;Schache, A;Shaw, R;Smart, N;Stephens, M;Stewart, GD;Teasdale, E;Vaughan-Shaw, P;Vidya, R;Wright, N;Wuraola, F;Zimmelman, N;Agastra, E;Thereska, D;Martin Lucchini, S;Laudani, V;Boccalatte, L;Chwat, C;Pedraza Salazar, II;Pantoja Pachajoa, DA;Duro, A;Calderon Arancibia, JA;Cox, D;D'Aulerio, G;Dudi-Venkata, N;Egoroff, N;Farik, S;Lott, N;Moss, J-L;Pockney, P;Rennie, S;Tan, L;Varghese, C;Vo, UG;Watson, D;Watters, D;Wright, D;Bright, T;Hollington, P;Zhou, X;Kroon, HM;Farfus, A;Barker, J;Watson, E;Stevens, S;Latif, H;Dawson, AC;Chuan, A;Muralidharan, V;Wong, E;Ackermann, T;Pacilli, M;Hodgson, R;Heriot, A;Choong, P;Brown, W;Lidder, S;Yeung, J;Traeger, L;Regalo, G;Gourlay, R;Pockney, P;Badiani, S;Koh, C;Putnis, S;Dawson, AC;Haider, F;Mitul, AR;Komen, N;Dhondt, B;Cappeliez, S;Pigeolet, M;van Ramshorst, G;Schoneveld, M;Stijns, J;Oosterlinck, W;Flamey, N;Kpangon, C;Agbadebo, M;Tobome, SR;Cerovac, A;Barros, AV;Aguiar Junior, S;Baiocchi, G;do Amaral Campos, HG;Gross, J;Fernandez Coimbra, FJ;Kowalski, LP;Makdissi, F;Nakagawa, S;Duprat Neto, JP;Vartanian, JG;Yazbek, G;Zequi, SC;Flumignan, R;Slavchev, M;Jaworska, N;Dell, A;Shanthanna, H;Martin, J;Behzadi, A;Nessim, C;Mozel, M;St-germain, P;Russell, C;Groot, G;Safieddine, N;Wijeysundera, D;Eskander, A;Chadi, S;MacKenzie, S;Flexman, A;Heredia, F;Marta Modolo, M;Villanueva, J;Waissbluth, S;Macchiavello, R;Escudero, MI;Fuentes, T;Mimica, X;Olivos, M;Bolivar Saenz, D;Caicedo, L;Pablo Alzate, J;Luna, J;Pedraza Alonso, NF;Ortiz Silva, C;Rodriguez, J;Silva-Igua, L;Torres, ML;Maria Trujillo, L;Nieto Calvache, AJ;Balanta-Melo, J;Figueroa-Casanova, R;Garcia-Montoya, O-J;Marulanda Toro, CA;Velez Botero, M;Mendoza Arango, MC;Diaz Martinez, E;Gutierrez Perdomo, V;Montenegro, E;Mihanovic, J;Aviles Jimenez, PM;Gouvas, N;Novysedlak, R;Rodriguez-Abreu, J;Mejia, D;Lincango-Naranjo, E;Abouelnagah, G;Shehata, S;Rida, AHEF;Hassan, RA;Saad, MM;Loaloa, MR;Mostafa, B;Qassem, M;Fahmy, M;Abozied, H;Azzam, AY;Ghozy, S;Sallam, A;Shehta, A;Emile, S;Abdelkhalek, M;Samaka, R;Morsy, A;Sherif, AE;Negussie, A;Fisseha, T;Shumbash, K;Abebe, M;Hailu, S;Yasin, SM;Akililu, YB;Megersa, A;Tefera, T;Assefa, M;Atnafu, B;Tsegaye, B;Bezabih, YS;Sisay, S;Bekele, K;Jira, M;Mengesha, MG;Derilo, H;Degefa, E;Tadesse, A;Nidaw, M;Sarjanoja, E;Kauppila, JH;Testelin, S;Boucher, S;Jouffret, L;Lakkis, Z;Le Bian, AZ;Harper, L;des Deserts, MD;Andre, B;Slim, K;Verhaeghe, R;Police, A;Girard, E;Chebaro, A;Nkembi, AS;Arnalsteen, L;Ballouhey, Q;Mege, D;Jeandel, C;Duchalais, E;Bouche, P-A;Manceau, G;Cretolle, C;Hervieux, E;Girard, N;Seguin-Givelet, A;Gaujoux, S;De Simone, B;Boisson, M;Bergeat, D;Arnaud, AP;Fredon, F;Nappi, F;Kassir, R;Scalabre, A;Migliorelli, F;Verhaeghe, R;Ezanno, A-C;Seeliger, B;Vaysse, C;Charbonneau, H;Misrai, V;Abbo, O;Angeles, MA;Brunaud, L;Demetrashvili, Z;Modabber, A;Wolf, S;Kamphues, C;Hoehn, P;Glowka, TR;Rokohl, AC;Bork, U;Fluegen, G;Horch, RE;Schmedding, A;Schnitzbauer, A;Eberbach, H;Schlager, D;Spelsberg, F;Keppler, L;Hecker, A;Wolfer, S;Ronellenfitsch, U;Nitschke, C;Peiper, C;Hakami, I;Welter, S;Nikolaieva, K;Roth, A;Lindert, J;Gousias, K;Rissmann, A;Linz, VC;Rahbari, N;Rassweiler-Seyfried, M-C;Gut, AE;Gempt, J;Reim, D;Wagner, A;Albertsmeier, M;Keppler, AM;Stoleriu, MG;Saier, T;Stadler, J;Kaiser, JC;Brunner, SM;Pfister, K;Herzberg, J;Nowak, K;Reinhard, T;Stavrou, GA;Koenigsrainer, A;Konrads, C;Quante, M;Laban, S;von Pusch, S;Hirschburger, M;Doerner, J;Wiegering, A;Tampaki, EC;Gutierrez Ruiz, A;Rodas, A;Lucia Portilla, A;Recinos, G;Aguilera-Arevalo, M-L;Carrera, J;Duarte, AB;Lowey, M;Barillas, S;Suroy, A;Vaishnav, D;Chowdappa, RG;Madabhavi, I;Bhat, D;Venkatappa, SK;Thakar, S;Jain, K;Kumar, A;Nagar, M;Mishra, T;Sekar, A;Gupta, A;Kaman, L;Karthigeyan, M;Tripathi, M;Rammohan, A;Vayoth, SO;Rajanbabu, A;Subbian, A;Gupta, R;Raut, M;Evelyn R, N;Kannaiyan, L;Matai, A;Misra, S;Bhende, V;Muthu, S;Ghosh, I;Sharma, A;Bajaj, A;Rajan, S;Agarwal, G;Pawar, P;Alexander, P;Vijayakumar, MV;Hameed,

BMZ;Badareesh, L;Chaudhry, NK;Baliarsing, L;Dharap, S;Kulkarni, A;Thyavihally, Y;Sharma, RD;Pramesh, CS;Soni, R;Dube, SK;Sharma, S;Singh, H;Bains, L;Ghodke, R;Kumar, A;Sodhai, V;Maji, S;Basu, S;Mahakalkar, C;Kannan, R;Mehraj, A;Ranganath, N;Phadnis, A;Yadev, I;Kavalaka, A;Mittal, R;Vallam, KC;Akhavizadegan, H;Maleki, ER;Kandevani, NY;Ikele, H;McNestry, C;Fleming, C;O'Brien, S;Abd Elwahab, S;Davis, N;Javadpour, M;McDonnell, B;Connor, CO;Bolger, J;Clancy, C;Croghan, SM;Donlon, N;Cullinane, C;Creavin, B;Muheilan, M;Earley, H;Kabir, SMU;Fahadullah, M;Ryan, E;Connelly, T;Zmora, O;Hashimoto, D;Alqudah, MA;Alajalen, A;Omari, RY;Ayasra, F;Qasem, A;Alawneh, Y;Ahmad, A;Aladawi, O;Alrayes, B;Haidar, H;Husain, S;Qassem, F;Sumadi, A;Abu Salhiyeh, A;Al-Manaseer, BM;Alsunna, Z;Ra'ed, H;Hamad, FRB;Abuleil, A;Abou Chaar, MK;Jimaale, EAM;Abu-Mehsen, M;Olaywah, N;Wafi, O;Ababneh, H;Abu-Ismail, L;Khamees, A;Alkhatib, A;Bolatbekova, R;Kulimbet, M;Nurgozhin, T;Saliev, T;Zhussupov, B;Almabayev, Y;Fakhradiyev, I;Saliev, T;Kaidarova, D;Tamoos, K;Aqeelah, A;Mohammed, AAK;Al Maadany, F;Alkadeeki, G;Gahwagi, M;Aldressi, W;Amnaina, M;Alansari, AHA;Alkaseek, A;Yagoub, G;Ben Amer, A;Salem, M;Almugaddami, A;Burgan, D;Abdelkabir, M;Alshareef, K;Ben Jouira, RAI;Meelad, A;Bouhuwaish, A;Dwaga, SE;Khalifa, H;Almiqlash, B;Suliaman, T;Alawami, M;Elhajdawe, F;Aboazamazem, H;Ellojli, I;Msherghi, A;Saleh, IA;Alayan, M;Roslani, AC;Ndayishyigikiye, MD;Munyika, A;Plarre, P;Borowski, DW;Nashidengo, PR;Noltes, M;Steinkamp, P;Wells, C;Teague, R;Elliott, B;Kieser, D;Mohyieldin, O;Varghese, C;McIntosh, N;Haran, C;Rennie, S;King, J;Ha, J;McGuinness, MJ;Adesanya, O;Olaogun, J;Akinmade, A;Bwala, K;Agbonrofo, P;Afolabi, A;Usang, U;Ekenze, S;Olori, S;Lawal, TA;Seyi-Olajide, J;Okunlola, A;Ekiti, I;Williams, O;Adisa, A;Abdur-Rahman, L;Kache, S;Sale, D;Anyanwu, L-J;Okereke, C;Tolani, MA;Filipce, V;Todorovic, L;Pejkova, S;Stavridis, S;Massoud, JG;Alsibai, S;Sultan, R;Altaf, HN;Bhatti, ABH;Waqar, SH;Aziz, A;Kerawala, AA;Rai, L;Anwer, M;Tariq, A;Ayub, B;Niazi, SU;Naseem, MY;Sarwar, MZ;Khokhar, MI;Zahid, IA;Majid, HJ;Talat, N;Asif, M;Chaudhary, MH;Farooq, U;Ahmad, S;Mabood, W;Bukhari, SI;Tariq, M;Yaqoob, E;Javed, S;Malik, MU;Yaqoob, HN;Cukier, M;Falcon Pacheco, GM;Mas Melendez, R;Paucar Urbina, ADP;Rios Chiuyari, J;Otiniano Alvarado, CE;Rivera Lau, LF;Borda-Luque, G;Niquen-Jimenez, M;Arias, C;Zegarra, S;Betalleluz Pallardel, J;Ugarte Oscco, RA;Mendiola, G;Carpio Colmenares, YT;Zapata, CS;Rosa Ortiz, M;Dione Sacdalan, M;Major, P;Borges, FC;Viveiros, O;Serralheiro, P;Santos-Costa, P;Mendes, F;Melo, MR;Cardoso, P;Soares, A;Azevedo, J;Pereira, RG;Silva, N;Caiado, A;Sacras, ML;Azevedo, P;Almeida-Reis, R;Cunha, MF;Oliveira, J;Nogueiro, J;Sampaio-Alves, M;Costa, LC;Baia, C;Deus, AC;Branquinho, R;Marcal, A;Tojal, A;Zarour, A;Makkai-Popa, ST;Mironescu, A;Grama, F;Toma, EA;Negoi, I;Filipescu, D;Bacalbasa, N;Motas, N;Ionescu, S;Ginghina, O;Costea, R;Zarnescu, NO;Drasovean, R;Bonci, E-A;Dimofte, M-G;Porumb, V;Kirov, M;Molitvin, Y;Litvin, A;Pykhteev, V;Raevskaya, M;Efetov, S;Butyrskii, A;Alshahrani, M;Althumairi, A;Alzerwi, N;Al Ameer, A;Madkhali, T;Almulhim, AS;Ghazwani, S;Ayoub, A;Iskander, O;Ghunaim, M;Alharthi, M;Alzaidi, TM;Althumairi, A;Alyami, M;Al Amri, A;Althumairi, A;AlFakhri, A;Alhefdhi, A;Chowdhury, S;Nouh, T;Alshehri, A;Alzahrani, A;Alalawi, Y;Awad, S;Konate, I;Ndong, A;Tendeng, J;Teo, NZ;Koh, F;Kosir, JA;Bele, U;Aqil, S;Barrena Lopez, C;Sanchez Mozo, A;Rodriguez Infante, A;Caja Vivancos, P;Prieto, M;Alberdi San Roman, I;Gomez Fernandez, L;Munoz Vives, JM;Carreras-Castaner, A;Diaz-Feijoo, B;Sieira-Gil, R;Turrado-Rodriguez, V;Sanchez Lopez, A;Sanchez-Cabus, S;Jimenez Toscano, M;Canals Sin, MP;Garcia Laura, S;Martin Sole, O;Palazon Bellver, P;Perez-Bertolez, S;Prat-Ortells, J;Riba Martinez, M;Rubio-Palau, J;Tarrado, X;Nunez, J;Alonso Mendoza, V;Bescos, C;Espin-Basany, E;Espinosa-Bravo, M;Gil-Sala, D;Gonzalez-Suarez, S;Montferrer Estruch, N;Porteiro Marino, L;Rodriguez-Tesouro, A;Rojas Portilla, F;Tormos Perez, MP;Vives, I;Garcia De Cortazar, U;Tudela, K;Landaluce-Olavarria, A;Estaire Gomez, M;Almoguera, J;Ugarte-Sierra, B;Jimenez, V;Bertrand, M;Cardenas Puiggros, L;Delisau-Puig, O;Garcia-Adamez,