Delaying Surgery for Patients Recovering from COVID-19

A rapid review commissioned by RACS

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Version Number	Date Changed	Reason for Change
1	December 2020	Original version
2	March 2021	Inclusion of findings regarding the optimal timing of surgery following SARS-CoV-2 infection from the newly-published GlobalSurg-COVIDSurg Week study Update of Recommendation #5 based on findings from GlobalSurg-COVIDSurg Week Study
3	30 November 2021	Disclaimer and exclusion of liability added.

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Executive summary:

Introduction:

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The median time from symptom onset to clinical recovery is approximately two weeks for mild cases and three to six weeks for severe or critical disease. However, many patients have a variety of symptoms that persist for an extended period of time following recovery from their acute infectious illness. With the cautious resumption of elective surgery, it is important to consider the potential chronic health issues of patients who have recovered from acute COVID-19 but may still harbour unexpected or occult disease that could affect surgical outcomes. Therefore, this rapid review aimed to identify current evidence on the following two questions:

1. What are the long-term pathophysiological and functional sequelae of COVID-19 in patients who have recovered from the acute illness?
2. What is the impact of prior COVID-19 infection on postoperative surgical outcomes in patients who have recovered from the acute illness?

Methods:

A rapid review methodology was used to evaluate relevant published literature identified through comprehensive searches of the Medline and medRxiv databases and grey literature, including various international health networks, guideline repositories, surgical and anaesthesia societies and other relevant websites. Additional articles were identified by screening the reference lists of retrieved full-text articles. The relevant findings from included papers were extracted and synthesised narratively.

Results:

Research question 1:

One case-control (level III-2 evidence) and 18 case series studies (level IV evidence) met the inclusion criteria for research question 1. The evidence indicated that COVID-19 symptoms can persist up to 16 weeks after initial symptom onset. These range from minor persistent cough to more insidious, debilitating fatigue, lung impairment and cardiac damage. There is also evidence to suggest the presence of ongoing cognitive changes, inflammation and derangement of blood clotting and immune response in recovered patients.

Research question 2:

One prospective multicentre cohort study (level III-2 evidence) met the inclusion criteria for research question 2. The study found that patients with cancer who are recovering from COVID-19 were more likely to experience a postoperative pulmonary complication than those who had not been infected with SARS-CoV-2. When split by time from diagnosis to surgery, both pulmonary complications and mortality rates were lowest at least four weeks after a positive nasopharyngeal swab. Additionally, current expert opinion from four guidance documents recognised the multi-system, and sometimes long-lasting, effects of COVID-19, which may be difficult to measure and could adversely affect postoperative outcomes if not properly assessed prior to surgery.

Conclusions:

The effect of COVID-19 on the postoperative outcomes of recovered patients is currently unknown. However, there is evidence that overt and occult effects across multiple systems (particularly cardiorespiratory), that could affect a patient's surgical risk, can persist for between two and four months after the initial onset of symptoms. A pragmatic approach to the preoperative assessment of patients recovering from COVID-19 would likely include assessment of cardiorespiratory, inflammatory, immunological and coagulation function, depending on the degree and type of surgery planned.

Recommendations:

1. Ensure COVID-19 swab negative
2. Ensure adequate informed consent; if memory issues may need relatives present
3. Assess degree of cardiac, respiratory, immunological and coagulation abnormalities during the acute illness
4. If minor surgery four weeks delay to surgery may be adequate
5. If major deferrable surgery then recommend waiting ≥7 weeks if possible; if severe illness at time of acute infection or ongoing long COVID-19 symptoms suggest physician review (preoperative review may include stress echocardiography, brain natriuretic peptide (BNP) levels, respiratory function tests, immune and clotting status review), and potentially high dependency or critical care in the immediate postoperative period.

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Severe cases follow a typical symptomatic pattern: anosmia, fever and cough in the first two days, developing into severe respiratory disease after a week that often requires hospitalisation.[2] While most patients infected with SARS-CoV-2 have relatively mild disease, up to 14% of cases are severe, and 6% experience respiratory failure, septic shock and/or multiple organ dysfunction or failure.[3] Median time from symptom onset to clinical recovery is approximately two weeks for mild cases and three to six weeks for severe or critical disease.[3, 4] However, many patients, even those with mild disease, have a variety of symptoms that may persist over an extended period.[2, 4]

As of 17 October 2020 there were 24,936 Australians who had recovered from COVID-19, however limited data exist on their long-term outcomes.[5] A recent study from the United States[6] found that 35% of people did not return to their previous level of health 14 to 21 days after a positive SARS-CoV-2 test—for young adults with no chronic medical conditions the rate was 26%—and around 10% of all patients remained unwell for much longer.[7] In contrast, over 90% of outpatients with influenza largely recover within approximately two weeks.[6] The reasons for this are unclear, but may include the presence of ongoing viral infection, relapse or reinfection, deconditioning, new or relapsing inflammation or other immune reactions, mental factors and treatment side effects.[7, 8] Even patients who had mild COVID-19 report persistent cough, low-grade fever and fatigue similar to chronic fatigue syndrome, which sometimes display a relapsing and remitting course.[7] These residual symptoms are known as “post-COVID syndrome”, “long-COVID” or “chronic COVID-19”.[9, 10]

COVID-19 has been associated with cardiac injury,[11], neurologic effects[1], acute kidney injury[12], gastrointestinal manifestations[13], liver injury[13, 14], thromboembolic complications and haemorrhagic stroke.[15-19] In addition to the lingering effects of these conditions, patients may not receive adequate physical and occupational therapy during the recovery phase due to concerns over disease transmission and lack of available medical personnel and resources, which can prolong persisting functional loss and debility.[18, 19]

With the cautious resumption of elective surgery, it is important to consider the longer term effects of COVID-19 on patients’ surgical risk. Contracting COVID-19 in the immediate perioperative period or within 30 days of undergoing surgery increases 30-day postoperative mortality, particularly among men aged 70 years or older and those undergoing emergency or oncological surgery.[20] Consequently, there are increasing concerns about the potential chronic health issues of patients who have recovered from acute COVID-19, but may still harbour symptomatic or occult disease, that need to be taken into account when considering surgery.

Interim guidance from the Royal Australasian College of Surgeons (RACS) Victorian State Committee, which was endorsed by five other colleges and societies, recommends that patients recovering from COVID-19 be symptom free for a minimum of eight weeks before undergoing all but minor elective surgical procedures.[21] Prior to surgery, an assessment of the cardiac and respiratory systems should be undertaken, particularly in patients who were hospitalised with COVID-19 and have persisting symptoms. Data are limited about the natural history of post-acute and chronic COVID-19, and most published guidance currently available relies on extrapolations from longer-term data on other coronavirus infections.[22] Therefore, the RACS Victoria State Committee and the National COVID-19 Taskforce are updating their guidance on when it is safe to perform surgery in patients who have

recovered from the acute SARS-CoV-2 infection by reviewing current evidence on the following two questions:

1. What are the long-term pathophysiological and functional sequelae of COVID-19 in patients who have recovered from the acute illness?
2. What is the impact of prior SARS-CoV-2 infection on postoperative surgical outcomes in patients who have recovered from the acute illness?

Methods

A rapid review methodology[23] was used to identify and synthesise the published literature on the two research questions above. An information specialist conducted searches of the Medline and medRxiv databases to identify English-language articles of any type published between 31 December 2019 and 4 October 2020, with consideration of the World Health Organization's (WHO) identification of the novel coronavirus.[24] Grey literature searches were conducted according to the Grey Matters checklist[25] and included various international health networks (e.g. the United Kingdom National Health Service and the United States Centers for Disease Control and Prevention), guideline repositories, the COVID-19 Evidence Accelerator (https://www.evidenceaccelerator.org/), surgical and anaesthesia societies, and the United States Food and Drug Administration website. Additional articles were identified by screening the reference lists of any full-text articles retrieved. The search strategy is provided in Appendix A and will be repeated at the designated revision to update this review to incorporate contemporary evidence.

The abstract screening and study selection were conducted by one ASERNIP-S researcher according to the criteria listed in Table 1.

Table 1. General inclusion criteria for research questions 1 and 2

	Research Question 1	Research Question 2
Population	• All populations (including children) undergoing surgery who have contracted and recovered from SARS-CoV-2 infection • The post-acute phase of recovery was defined as >21 days from the onset of first COVID-19 symptoms[7] or from the time of the first positive nucleic acid test	
Intervention	Any elective or emergency surgery	
Comparator	Not applicable	Patients undergoing surgery who are considered SARS-CoV-2 naïve
Outcomes	• Patient outcomes (e.g. exercise capacity, acute lung injury, cardiovascular or cerebrovascular events, limb ischaemia, and psychiatric complications) • Laboratory findings (e.g. cytokine profiles, blood clotting profile) • Pulmonary function tests • Imaging results	• Postoperative mortality • Serious life-threatening postoperative complications (e.g. acute lung injury, cardiac events, and stroke) • Postoperative hospital or intensive care admission
Study type	• Studies of any design	
Exclusions	• Case reports • Studies including mixed population groups where <75% were in the post-acute phase of recovery as defined above	

	Research Question 1	Research Question 2
	• Studies pertaining to other coronavirus-related illnesses, such as Middle East Respiratory Syndrome • Post-mortem findings	

COVID-19: coronavirus disease 2019; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

Relevant findings from included papers were extracted and synthesised narratively. Where possible, data for research question 2 were analysed according to surgery type (elective/emergent; specialty; major/minor). Quality assessment of the included studies was not performed due to time constraints, but the level of evidence was categorised according to the National Health and Medical Research Council evidence hierarchy.[26]

Results

The electronic search yielded an initial pool of 1,020 citations. After screening the titles and abstracts, this pool was refined to 94 potentially relevant articles, for which full-text versions were retrieved. Information deemed pertinent in 20 articles was synthesised along with findings from the targeted searches to produce the following sections of this review.

Research question 1: Long-term sequelae of COVID-19 in recovered patients

After full-text examination of potentially relevant articles identified in the abstract screening process, one case-control (level III-2 evidence) and 18 case series studies (level IV evidence) met the inclusion criteria for research question 1. Of these, 12 were peer-reviewed publications (Table 2) and seven were non-peer-reviewed publications or conference abstracts (Table 5). Relevant information from these articles is synthesised in the following sections.

Peer-reviewed data

The single case-control study identified[27] (level III-2 evidence) compared the serum immunological and peripheral mononuclear cell profiles of 49 patients from a German and a Chinese cohort 1.5 months (median 41 days) and 3.5 months (median 112 days, range 60-136) after diagnosis with those of 27 age- and sex-matched individuals who were SARS-CoV-2 naïve. The results from the cohort with the longest follow up (n=30) indicated that while most components of cellular immunity had returned to normal at least two months after the first diagnosis in patients who had mild to moderate COVID-19, numbers of invariant natural killer T cells and natural killer T-like cells were still significantly lower than in uninfected persons. Long-term suppression of the cytotoxic potential of T cells was also evident. The authors concluded that the immune system is likely to still be compromised at least two months after diagnosis in patients recovering from COVID-19.

Table 2: Summary of peer-reviewed studies for research question 1

Study/Country	Patients	Study Details	Length of FU
Liu et al.[27] China, Germany	N=30 Adults hospitalised (43%) or outpatient-managed with mild (17%) or moderate COVID-19 Age: mean 37 years Men: 11% Age- and sex-matched unexposed cohort: N=21	Prospective concurrent case-control study (level III-2 evidence) Recruitment type unclear Multi-centre	Median 112 days (range 60-136) after first diagnosis

Study/Country	Patients	Study Details	Length of FU
Carfi et al.[28] Italy	N=143 Adults hospitalised with COVID-19: mean LOS 14 (SD 9.7) days Age: mean 57 years (SD 14.6, range 19-84) Men: 63%	Retrospective case series (level IV evidence) Consecutive recruitment Single centre	Mean 60 (SD 13.6) days after symptom onset
Chiesa-Estomba et al.[29] Europe	N=701 Adults (age >18 years) hospitalised (% not stated) or outpatient-managed with mild COVID-19 who had dysgeusia Age: mean 40 years (SD 13.0) Men: 33%	Prospective case series (level IV evidence) Consecutive recruitment Multi-centre	Mean 63 (SD 9.0) days (range 60-76) after symptom onset
Ding et al.[30] China	N=53 Patients hospitalised with COVID-19 pneumonia Age: mean 56 years (range 12-89) Men: 46%	Retrospective case series (level IV evidence) Non-consecutive recruitment Multi-centre	>28 days after the onset of symptoms
Garrigues et al.[31] France	N=120 Patients hospitalised (20% in ICU) with COVID-19: mean LOS 11 (SD 13.4) days Age: mean 63 years (SD 15.7) Men: 63%	Retrospective case series (level IV evidence) Non-consecutive recruitment Single centre	Mean 111 (SD 11.1) days after hospital admission
Halpin et al.[32] United Kingdom	N=100 Adults (age ≥18 years) hospitalised (32% in ICU) with COVID-19; median LOS 6.5 days for non-ICU and 12 for ICU patients Age: range 20-93 years Men: 54%	Retrospective case series (level IV evidence) Non-consecutive recruitment Multi-centre	Mean 48 (SD 10.3) days (range 29-71) after hospital discharge
Huang et al.[33] China	N=26 Adults hospitalised with COVID-19 who had cardiac symptoms; median LOS not reported Age: mean 38 (range 32-45) years Men: 38%	Retrospective case series (level IV evidence) Non-consecutive recruitment Single centre	Median 47 (IQR 36-58) days after onset of cardiac symptoms
Li et al.[34] China	N=145 Patients with COVID-19 Age: mean 49 years (range 13-80) Men: 39%	Prospective case series (level IV evidence) Recruitment type unclear Multi-centre	Median 62 days (range 25–95) after symptom onset
Otte et al.[35] Germany	N=91 Adults (age ≥18 years) outpatient-managed with COVID-19	Prospective case series (level IV evidence)	Mean 58 (SD 1.4) days after symptom onset

Study/Country	Patients	Study Details	Length of FU
	Age: mean 43 years (SD 12.7) Men: 51%	Consecutive recruitment Single centre	
Patelli et al.[36] Italy	N=20 Patients hospitalised with COVID-19 Age: mean 58 years (SD 10.0, range 35-86) Sex: not reported	Retrospective case series (level IV evidence) Recruitment type unclear Single centre	Mean 40 (SD 13) days after fever remission
Puntmann et al.[37] Germany	N=100 Patients hospitalised (33%) or outpatient-managed with COVID-19 Age: mean 49 years (SD 14.0) Men: 53%	Prospective case series (level IV evidence) Non-consecutive recruitment Single centre	Median 71 (IQR 64-92) days after diagnosis
Zhao et al.[38] China	N=55 Adults (age ≥18 years) hospitalised with COVID-19: median LOS, 5 days (IQR 2-8) Age: mean 48 years (SD 15.5) Men: 58%	Retrospective case series (level IV evidence) Consecutive recruitment Multi-centre	64-93 days after hospital discharge

COVID-19: coronavirus disease 2019; FU: follow up; ICU: intensive care unit; IQR: interquartile range; LOS: length of stay; SD: standard deviation

Of the 11 peer-reviewed case series studies, seven[28, 30-33, 36, 38] reported data exclusively on a combined total of 517 patients who had been hospitalised with COVID-19. The other four included either a mixed population of hospitalised and outpatient-managed patients (n=801),[29, 37] outpatients alone (n=91)[35] or did not report the degree of care required during the acute phase of the disease (n=145).[34] Two studies included adolescent patients,[30, 34] although none included patients younger than 12 years. The follow-up periods ranged from four to approximately 16 weeks, with most studies (64%) defining follow-up as starting either from first diagnosis or symptom onset.

Up to 87% (n=143) of patients exhibited at least one ongoing symptom at a mean of two months after the acute phase of COVID-19 (Table 3). Respiratory symptoms such as persistent cough and breathlessness were the most commonly reported across the studies. Abnormal lung function was present in 26% (n=55) of patients 13 weeks after hospital discharge, and abnormalities on chest computed tomography scan were evident in up to 56% (most commonly ground glass opacity, interstitial thickening and crazy paving).[38] One in six patients still had dysfunctional or absent taste or smell, and nearly a third reported lingering gastrointestinal symptoms and memory, attention and sleep issues at least two months into recovery. Chest pain was reported by 11 to 42% of patients, with heart damage (as indicated on magnetic resonance imaging [MRI]) being evident in up to 54% of patients who had cardiac symptoms during their hospitalisation.[33]

Table 3. Summary of post-recovery symptoms reported in peer-reviewed case series studies (level IV evidence) of previously hospitalised patients

Post-Recovery Symptom	Proportion of Patients (N; Length of FU)
At least one ongoing symptom	87% (N =143; mean 60 days)[28]
Cough	12% (N =120; mean 111 days)[31] 2% (N =55; 64-93 days)[38]
Breathlessness	43% (N =143; mean 60 days)[28] 42% (N =120; mean 111 days) [31] 50% (N =100; mean 48 days)[32] 40% (N=20; mean 40 days)[36] 15% (N =55; 64-93 days)[38]
New[a] or excessive fatigue	53% (N=143; mean 60 days)[28] 55% (N=120; mean 111 days)[31] 64% (N=100; mean 48 days)[32] 16% (N=55; 64-93 days)[38]
Memory disorder	34% (N=120; mean 111 days)[31]
Attention disorder	27% (N=120; mean 111 days)[31]
Sleep disorder	31% (N=120; mean 111 days)[31]
Anosmia	15% (N=143; mean 60 days)[28] 13% (N=120; mean 111 days) [31]
Ageusia or dysgeusia	10% (N=143; mean 60 days)[28] 11% (N=120; mean 111 days)[31] 4% (N=55; 64-93 days)[38]
Swallowing problem	8% (N=100; mean 48 days)[32]
Headache	9% (N=143; mean 60 days)[28] 18% (N=55; 64-93 days)[38]
Myalgia	5% (N=143; mean 60 days)[28]
Arthralgia	27% (N=143; mean 60 days)[28]
Gastrointestinal symptoms	31% (N=55; 64-93 days)[38]
Diarrhoea	2% (N=143; mean 60 days)[28]
New bowel or bladder incontinence	13% (N=100; mean 48 days)[32]
Chest pain	22% (N=143; mean 60 days)[28] 11% (N=120; mean 111 days)[31] 42% (N=26; median 47 days)[33]
Myocardial oedema and/or fibrosis (MRI)	54% (N=26; median 47 days)[33]
Abnormal left ventricular ejection fraction	4% (N=26; median 47 days)[33]
Lung fibrosis (CT)	40% (N=20; mean 40 days)[36]
Abnormal lung function	26% (N=55; 64-93 days)[38]
Abnormal lung CT scan	98% (N=52; >28 days)[30] 56% (N=55; 64-93 days)[38]
Pneumothorax	4% (N=52; >28 days)[30]
Pleural effusion	15% (N=52; >28 days)[30]
Bronchiectasia	45% (N=52; >28 days)[30]

[a]Compared with pre-COVID-19 levels; CT: computed tomography; FU: follow up; MRI: magnetic resonance imaging

Among patients who experienced milder COVID-19 that generally did not require hospitalisation, breathlessness and cardiac symptoms were the most commonly reported health issues at least two months into recovery, closely followed by a disordered sense of taste or smell (Table 4).

Table 4. Summary of post-recovery symptoms reported in peer-reviewed case series studies (level IV evidence) of mixed hospitalised and outpatient-managed patient groups

Post-Recovery Symptoms	Proportion of Patients (n; Length of FU)
Breathlessness	36% (N=100; median 71 days)[37]
Anosmia or hyposmia	11% (N=145; median 62 days)[34] 45% (N=80 who had the symptom during acute phase)[35]
Ageusia or hypogeusia	9% (N=701 who had the symptom during acute phase; 60-76 days)[29]
Olfactory loss (hyposmia and/or hypogeusia)	39% (N=84; mean 58 days)[35]
Chest pain	17% (N=100; median 71 days)[37]
Myocardial inflammation	60% (N=100; median 71 days)[37]

FU: follow up

Additional unpublished and non-peer-reviewed data

Of the seven unpublished case series studies (level IV evidence) on adult patients, three (four publications)[22, 39-41] reported data exclusively on 348 patients who had been hospitalised with COVID-19 (Table 5). The other four included either a mixed population of hospitalised and outpatient-managed patients (n=240)[42, 43] or only outpatients (n=48).[44, 45] The follow-up period ranged from 3 to 12 weeks and was variously defined as starting from hospital discharge,[39-41, 43] symptom onset,[22, 45] diagnosis[44] or two consecutive negative test results.[42]

Table 5: Summary of non-peer-reviewed case series studies (level IV evidence) for research question 1

Study/Country	Patients	Study Details	Length of FU
Arnold et al.[22] United Kingdom	N=110 Adults (age ≥18 years) hospitalised with COVID-19: median LOS, 5 days (IQR 2-8) Age: median 60 years (IQR 46-73) Men: 56%	Prospective Consecutive recruitment Single centre	Median 83 (IQR 74-88) days after hospital admission Median 90 days (IQR 80-97) after symptom onset
Clark et al.[44] USA	N=22 Adult (age >18 years) collegiate athletes outpatient-managed with mild or asymptomatic COVID-19 Age: mean 20 years Men: 41%	Retrospective Recruitment type unclear Single centre	Median 52 days from infection
Klein et al.[42] Israel	N=112 Adults (age ≥18 years) hospitalised (5%) or outpatient-managed with mild COVID-19 Age: mean 35 years (SD 12.0) Men: 64%	Retrospective Non-consecutive recruitment Single centre	6 weeks after two consecutive negative COVID-19 tests
O'Keefe and Cellai[45] USA	N=26 Adult outpatient-managed with mild or asymptomatic COVID-19	Retrospective	Median 38 days (range 21-49) after symptom onset

Study/Country	Patients	Study Details	Length of FU
	Age: median 47.5 years (range 23-78) Men: 33%	Non-consecutive recruitment Single centre	
Sahanic et al.[39, 40] Austria	N=86 Patients hospitalised with COVID-19: mean LOS, 13 days Age: mean 61 years Men: 65%	Prospective Recruitment type unclear Multi-centre	6 and 12 weeks after discharge
Townsend et al.[43] Ireland	N=128 Patients hospitalised (56%) or outpatient-managed with COVID-19 Age: mean 50 years (SD 15.0) Men: 48%	Retrospective Consecutive recruitment Single centre	Median 72 (IQR 62-87) days after hospital discharge or a 14-day timepoint after diagnosis for outpatients
Weerahandi et al.[41] USA	N=152 Adults (age ≥18 years) hospitalised with severe COVID-19: median LOS, 18 days (IQR 10-31) Age: median 62 years (IQR 50-67) Men: 63%	Retrospective Consecutive recruitment Multi-centre	Median 37 days (range 30-43) after hospital discharge

COVID-19: coronavirus disease 2019; FU: follow up; IQR: interquartile range; LOS: length of stay; SD: standard deviation

The pattern and frequency of symptoms reported in the unpublished studies on hospitalised patients were similar to that reported in the published case series data (Table 6). Sahanic et al[39, 40] reported left ventricular diastolic dysfunction in 59% of patients (n=86) six weeks after hospital discharge (mean 13-day length of stay), in addition to elevated serum markers of heart damage, inflammation and coagulation abnormalities.

Table 6. Summary of post-recovery symptoms reported in unpublished case series studies (level IV evidence) of previously hospitalised patients

Post-Recovery Symptom	Proportion of Patients (N; Length of FU)
Cough	15% (N=86; 12 weeks)[40]
Breathlessness	39% (N=86; 12 weeks)[40]
New ongoing need for home oxygen	14% (N=152; median 37 days)[41]
New[a] or excessive fatigue	43% (N=152; median 37 days)[41]
Left ventricular diastolic dysfunction	59% (N=86; 6 weeks)[40]
Lung impairment	20% (N=86; 12 weeks)[40]
Abnormal lung CT scan	22% (N=86; 12 weeks)[40]
Reduced diffusion capacity	22% (N=86; 12 weeks)[40]
Hyperinflation	38% (N=82; 6 weeks)[39]
Ongoing lymphopenia	2% (N=110; median 83 days)[22]
C-reactive protein >10 mg/L	2% (N=110; median 83 days)[22]

[a]Compared with pre-COVID-19 levels; CT: computed tomography

Arnold et al.[22] stratified patients according to the degree of acute COVID-19 experienced during hospitalisation (Table 7). While the pattern and frequency of symptoms in the entire patient group at a median of 90 days after onset were similar to that reported in the published and unpublished case

series data, patients who had moderate to severe COVID-19 were more likely to report subsequent longstanding breathlessness, fatigue and lung impairment than those who had mild COVID-19. In addition, patients recovering from severe disease were more likely to have persistent sleep disturbance, myalgia and arthralgia. However, between group differences were not statistically analysed.

Table 7: Post-recovery symptoms at median of 90 days after onset stratified by degree of acute disease in patients previously hospitalised with COVID-19[22]

Post-Recovery Symptoms	All Patients (N=110)	Mild COVID-19[a] (n=27)	Moderate COVID-19 (n=65)	Severe COVID-19 (n=18)
At least one ongoing symptom	74%	59%	75%	89%
Fever	1%	0%	2%	0%
Cough	12%	7%	15%	6%
Breathlessness	39%	26%	40%	56%
Excessive fatigue	39%	26%	40%	56%
Sleep disorder	24%	22%	17%	50%
Anosmia	12%	11%	9%	22%
Headache	2%	4%	2%	0%
Myalgia	23%	15%	22%	39%
Arthralgia	5%	4%	2%	16%
Chest pain	13%	7%	15%	11%
Diarrhoea	1%	0%	2%	0%
Abdominal pain	2%	2%	2%	0%
Restrictive pattern spirometry	10%	0%	12%	17%
Significant desaturation on STS	14%	0%	15%	28%

COVID-19: coronavirus disease 2019; STS: 1-minute sit-to-stand test

[a]Mild COVID-19: no requirement for oxygen or enhanced care during hospital stay; Moderate COVID-19: requirement for oxygen during hospital stay; Severe COVID-19: requirement for non-invasive ventilation, intensive care or high dependency unit admission

Among patients who experienced milder COVID-19 that generally did not require hospitalisation, more than one in two patients reported at least one ongoing symptom a median 72 days after the acute phase of the disease (Table 8). Respiratory symptoms, fatigue, gastrointestinal problems and palpitation were the most commonly reported at least 6 weeks into recovery.

A retrospective case series study by Clark et al.[44] evaluated 22 collegiate athletes recovering from mild (77%) or asymptomatic (23%) COVID-19 detected during mandatory screening. Even after mild disease, 9% of these young, previously fit individuals had persistent myocardial inflammation or fibrosis at a median 52 days after infection identified by cardiac MRI. However, the effect of this on athletic performance was not assessed.

Table 8. Summary of post-recovery symptoms reported in unpublished case series studies (level IV evidence) of mixed hospitalised and outpatient-managed patient groups

Post-Recovery Symptoms	Proportion of Patients (N; Length of FU)
At least one ongoing symptom	57% (N=128; median 72 days)[43]
Respiratory symptoms	92% (N =26; median 38 days)[45]
Cough	1% (N =112; 6 weeks)[42]
Breathlessness	9% (N =112; 6 weeks)[42]
Low-grade fever	12% (N =26; median 38 days)[45]
New[a] or excessive fatigue	21% (N =112; 6 weeks)[42] 65% (N =26; median 38 days)[45] 52% (N =128; median 72 days)[43]
Memory disorder	5% (N =112; 6 weeks)[42]
Attention disorder	1% (N =112; 6 weeks)[42]
Anosmia or hyposmia	14% (N =112; 6 weeks)[42]
Ageusia or hypogeusia	7% (N =112; 6 weeks)[42]
Headache	4% (N =112; 6 weeks)[42] 50% (N =26; median 38 days)[45]
Myalgia	5% (N =112; 6 weeks)[42]
Myocardial inflammation or fibrosis	9% (N =22; median 52 days)[44]
Palpitations	23% (N =26; median 38 days)[45]
Chest pain	1% (N =112; 6 weeks)[42]
Gastrointestinal problems	35% (N =26; median 38 days)[45]
Diarrhoea	1% (N =112; 6 weeks)[42]
Abdominal pain	1% (N =112; 6 weeks)[42]

[a]Compared with pre-COVID levels; CT: computed tomography

Research question 2: Effect of infection with SARS-CoV-2 on postoperative outcomes in recovered patients

One prospective multicentre cohort study[46] (level III-2 evidence) met the inclusion criteria for research question 2. The COVIDSurg-Cancer study compared 122 patients recovering from COVID-19 who underwent curative elective cancer surgery with a propensity score matched group of 448 persons who had not been infected with SARS-CoV-2. Among the patients with COVID-19, 22% (n=27) underwent surgery within two weeks of diagnosis, 49% (n=60) between two and four weeks and 28% (n=35) after four weeks. Overall, patients who had been previously infected with SARS-CoV-2 were more likely to experience a postoperative pulmonary complication than those who had not been infected (11% versus 4%; adjusted odds ratio 3·84: 95% confidence interval 1·51-9·74, p = 0·004). Although higher rates of pulmonary complications were observed amongst recovering patients undergoing major versus minor surgery, the difference was not statistically significant (p=0.09). However, most of the patients (71% of 122) had surgery within four weeks of being diagnosed with SARS-CoV-2 infection. When examined by time from diagnosis to surgery, no pulmonary complications

or mortalities were recorded if surgery was performed at least four weeks after a positive swab test. Consequently, the authors concluded that patients with cancer who are recovering from COVID-19 should delay their elective surgery for at least four weeks after a positive swab test.

As of March 2021, the GlobalSurg-COVIDSurg Week study has been completed, and their important findings regarding the optimal timing of surgery following SARS-CoV-2 infection published online in *Anaesthesia*.[47] From 140,231 patients across 116 countries, the study investigated 3,127 patients (2.2%) that had a preoperative diagnosis of SARS-CoV-2. In these patients, mortality was increased for patients having surgery within 0–2 weeks, 3-4 weeks and 5-6 weeks of diagnosis, however operations performed ≥7 weeks was associated with a similar mortality risk to baseline. The study also found that after a ≥7 week delay following SARS-CoV-2 infection, surgical patients with ongoing symptoms had a higher mortality than those whose symptoms had resolved or who had been asymptomatic. Therefore, the study concluded that where possible, surgery should be delayed for at least 7 weeks following SARS-CoV-2 infection, and patients with ongoing symptoms at ≥7 weeks may benefit from further delay.

Furthermore, four guidance documents, in addition to that produced by RACS,[21] mentioned the consideration of long-term effects of COVID-19 in recovered patients undergoing surgery (Table 9). However, this very general guidance is based on expert opinion.

Table 9: Relevant statements reported in guidance documents

Source	Statement
American College of Surgeons American Society of Anesthesiologists Association of perioperative Registered Nurses American Hospital Association[48]	Given the multi-system and sometimes long-lasting ill effects after coronavirus infection, special attention and re-evaluation are needed if the patient has had COVID-19 disease.
Anesthesia Patient Safety Foundation[49] USA	If a patient tests positive for SARS-CoV-2, elective surgical procedures should be delayed until the patient is no longer infectious and has demonstrated recovery from COVID-19. Recommendations regarding the definition of sufficient recovery from the physiologic changes from SARS-CoV-2 cannot be made at this time; however, evaluation should include an assessment of the patient's exercise capacity (metabolic equivalents [METs]).
Healthcare Improvement Scotland[50]	A positive screen result should lead to deferral of surgery until the patient has recovered from SARS-CoV-2 infection (minimum of 10 days post-test).
Patel et al.[51] USA	For patients recently recovered from COVID-19, we recommend delaying cardiac surgery for at least two to four weeks after the positive SARS-CoV-2 test.

COVID-19: coronavirus disease 2019; SARS-Cov-2: severe acute respiratory syndrome coronavirus 2

A further guidance document, the Stanford Hall consensus statement, provided recommendations on the rehabilitation of active individuals (e.g. military personnel and athletes) with post COVID-19

syndrome.[52] Although the main focus of this document is treatment programmes, there were some recommendations pertaining to the assessment of individuals with ongoing symptoms (Table 10).

Table 10: Recommended assessments for patients with post-COVID syndrome[52]

Assessment Type	Statement
General	Post COVID-19 medical sequelae should be considered in all patients. Post-acute assessment should include a full medical history and if indicated, an examination and panel of blood markers. In post-COVID-19 patients with new-onset shortness of breath or chest pain, life-threatening medical complications should be considered.
Pulmonary	Respiratory complications should be considered in post-COVID-19 patients as they may present with some degree of impairment and functional limitation, including but not exclusively, due to decreased respiratory function.
Cardiac	Cardiac sequelae should be considered in all patients post-COVID-19, regardless of severity, and all patients should have an assessment of their cardiac symptoms, recovery, function and potential impairments. Depending on the patient's initial assessment and symptoms, specialist advice should be sought, and further investigations may include a specialist blood panel, ECG, 24-hour ECG, echocardiogram, cardiopulmonary exercise testing and/or cardiac MRI.
Musculoskeletal	All patients requiring rehabilitation following COVID-19 should have a functional assessment to determine residual musculoskeletal impairments.
Neurological	All patients with COVID-19 should be reviewed for any neurological symptoms, as symptoms can be immediate (at time of active infection) or delayed (in the weeks following COVID-19). Consider a cognitive screen for those at risk (postcritical care or with residual cognitive impairment).
Hepatic and renal	It is important to check liver function tests, including amylase, during recovery, so persistent abnormalities can be identified and either managed or referred on for management. It is important to check renal function where indicated during the recovery phase to identify persistent abnormalities and need for further investigation.

COVID-19: coronavirus disease 2019; ECG: electrocardiogram; MRI: magnetic resonance imaging

Discussion

To date, most of the concerns regarding surgery in patients recovering from COVID-19 have centred around personnel and patient safety during the post-symptomatic infectious period. However, the risks imposed by post-COVID-19 sequelae on postoperative outcomes in newly recovered patients is beginning to gain attention as health systems start to resume elective surgeries.

This rapid review indicates that COVID-19 may result in symptoms and identifiable organ changes that can persist at least 16 weeks after initial symptom onset. Current expert opinion recognises the multi-system and sometimes long-lasting ill effects of COVID-19, which may be difficult to measure and could adversely affect postoperative outcomes if not adequately assessed prior to surgery.[48-51] The single study available on patients undergoing surgery while recovering from COVID-19 indicated that rates of pulmonary complications and mortality were lowest when surgery was performed at least four weeks after a positive swab test.[46] The persisting symptoms of COVID-19 range from minor cough to more insidious, debilitating fatigue, lung impairment and cardiac damage. Regarding assessment of cardiac damage, brain natriuretic peptide (BNP) can be used as a marker in patients who have been previously infected with COVID-19.[53, 54] There is also some evidence to suggest the presence of ongoing

inflammation and derangement of blood clotting and immune response in recovered patients. These results from the medical literature have been affirmed by patient-centred studies such as Banda et al.[55] (unpublished), which reviewed information from the largest publicly available COVID-19 Twitter chatter dataset posted more than 60 days after the start of the pandemic using the hashtags #longcovid and #chroniccovid. The 10 most common symptoms reported among 107 users experiencing post-COVID syndrome were malaise and fatigue (62%), dyspnoea (19%), tachycardia or palpitations (13%), chest pain (13%), insomnia or sleep disorders (10%), cough (9%), headache (7%) and joint pain, fever and unspecified pain (6% each). Less commonly reported symptoms included ear, nose and throat issues (tinnitus, anosmia, chronic sinusitis, parageusia and aphonia), neuropsychological problems (amnesia, neuralgia or neuropathy, visual disturbance, cognitive impairment and disorientation), myalgia and skin pruritus or rash.

The symptoms of post-COVID syndrome, where the effects of COVID-19 persist for weeks to months even in patients who experienced mild or asymptomatic disease, can significantly affect a patient's surgical risk profile. For example, acute respiratory infection in the month preceding surgery is an independent risk factor for postoperative pulmonary complications.[56] In addition, the often significant derangement of the haematopoietic system during acute COVID-19, which can result in anaemia, vasculopathy and venous thromboembolism, may have serious consequences if not resolved before a recovered patient undergoes surgery.[52] At present, there are imprecise tools to accurately determine the surgical risk for persons undergoing surgery, and the risks are likely to vary depending on the type of surgery (elective/emergent; specialty; major/minor), the organs targeted, and the patient's general health.[57] As surgery and anaesthesia have become safer, patient factors have become more important in determining perioperative risk.[58] Patients who are frail, have at least one comorbidity, have survived a recent infection or have experienced recent hospitalisation or significant periods of bed rest or convalescence are at high risk for poor surgical outcomes.[57, 59] Respiratory, cardiovascular and cerebrovascular disease and cirrhosis are associated with the highest 30-day mortality rates among surgical patients.[60] Consequently, cardiorespiratory fitness, serological markers of inflammation and existing cardiovascular disease are important clinical factors in assessing a patient's fitness for surgery.[61]

COVID-19 is associated with high rates of cardiopulmonary complications, some of which are only evident on imaging studies. These complications occur not only in patients with pre-existing cardiovascular disease but also in young, previously fit patients. There is evidence that these symptoms, along with ongoing inflammation and impaired blood clotting and immune response, can persist for up to 16 weeks after hospital admission, and are often present in non-hospitalised patients.[7, 18, 19, 31] In addition, patients hospitalised with COVID-19 may experience a prolonged period of bed rest and convalescence, leading to profound deconditioning that can affect a patient's fitness for surgery.[62] This can also occur in patients who have ongoing breathlessness and fatigue even after a mild episode of COVID-19.[57]

The data in this review raise important questions on the timing of surgery after asymptomatic and symptomatic COVID-19 infections. However, the current evidence base does not provide sufficient data for meaningful or generalisable conclusions to be drawn. It is limited by heterogeneity among the studies with respect to defining the starting point of the follow-up period, the generally small sample sizes and short study periods and the low level of evidence. However, this is understandable given that COVID-19 is a novel disease. The literature is also limited in generally only addressing outcomes in

adult patients. Consequently, there was no information available on the newly recognised multisystem inflammatory syndrome in children that has been associated with SARS-CoV-2 infection. This syndrome tends to appear weeks (mean 45 days[63]) after infection with COVID-19 and produces symptoms similar to toxic shock syndrome or Kawasaki disease.[64-66]

It is currently unclear what factors play a role in the type and severity of residual symptoms in patients recovering from COVID-19. Age, genetic makeup, comorbidities, history of cigarette smoking, length of hospital admission, severity of COVID-19 and type of medications administered may all be important.[67] It is clear that any patients recovering from COVID-19 should be reassessed before undergoing surgery, taking into account variables related to the infection that may have increased surgical risk, such as cardiopulmonary changes, radiological and immunological abnormalities and presence of inflammation.[68] Guidance on these aspects is particularly important given the variability exhibited among surgeons within the same speciality, and even among anaesthetists and intensivists, when assessing surgical risk.[69] It is not currently possible to determine which patients recovering from COVID-19 are most likely to develop long-term abnormalities that will increase their surgical risk, or whether such sequelae will resolve, worsen or become permanent.[8] Large ongoing studies have recently been commissioned that will provide a more comprehensive picture of the long-term effects of COVID-19 and help answer these questions.[70-72]

Conclusion

The effect of COVID-19 on postoperative outcomes in recovered patients is currently unknown. However, there is evidence that overt and occult effects across multiple systems (particularly cardiorespiratory), that could affect a patient's surgical risk, can persist for between two and four months after the initial onset of illness in a significant number of patients. A pragmatic approach to the preoperative assessment of patients recovering from COVID-19 would likely include assessment of cardiorespiratory, inflammatory and immune function and coagulation, depending on the degree and type of surgery planned. Any definition of "recovery" after COVID-19 should include duration, severity and fluctuation of symptoms. As more data become available from ongoing studies, identifying and mapping the long-term sequalae of COVID-19 to potential risk factors for postoperative mortality and life-threatening complications will be an important next step.

Limitations of the review

Since the literature selection and data extraction were all conducted by one researcher, there was no opportunity to double-check for errors in these processes. In addition, the limited literature searches undertaken to identify peer-reviewed publications may have overlooked some articles, and the expedited publication of peer-reviewed articles within the literature means that the evidence base may change rapidly. However, screening the reference lists of retrieved full-text articles would have mitigated the potential of missing relevant literature. Also, throughout the process of developing this rapid review, iterative engagement with a working group of expert clinicians was maintained in order to optimise the clinical relevance of the presented evidence.

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Appendix A: Search Strategy

#	Searches	Results (4 Oct 2020)
1	*Coronavirus Infections/	28966
2	(COVID-19 OR COVID19).mp.	55103
3	((pneumonia OR COVID* OR coronavirus* OR corona virus* OR ncov* OR 2019-ncov OR sars*) AND (hubei OR wuhan OR beijing OR shanghai)).ti,kf.	925
4	Wuhan virus*.ti,kf.	8
5	(19nCoV OR 2019-nCoV OR 2019nCoV).ti,kf.	726
6	(nCoV* OR n-CoV*).ti,kf.	804
7	("CoV 2" OR CoV2).ti,kf.	13275
8	(OC43 OR NL63 OR 229E OR HKU1 OR HCoV* OR Sars-coronavirus*).ti,kf.	1343
9	(2019-novel CoV OR Sars-coronavirus2 OR Sars-coronavirus-2 OR SARS-like coronavirus* OR ((novel OR new OR nouveau) adj2 (CoV OR nCoV OR COVID OR coronavirus* OR corona virus OR Pandemi*2)) OR (coronavirus* AND pneumonia)).ti,kf.	3334
10	COVID-19.rx,px,ox. OR severe acute respiratory syndrome coronavirus 2.os.	26764
11	severe acute respiratory syndrome coronavirus 2.ti,kf.	1245
12	(SARSCoV* OR SARS-CoV* OR SARS2 OR SARS-2).ti,kf.	14065
13	(novel coronavirus* OR novel corona virus* OR novel CoV).ti,kf.	2086
14	((coronavirus* OR corona virus*) adj2 "2019").ti,kf.	5035
15	((coronavirus* OR corona virus*) adj2 "19").ti,kf.	940
16	(coronavirus 2 OR corona virus 2).ti,kf.	1371
17	COVID*.ti,kf.	48101
18	OR/1-17	63813
19	(201911* OR 202*).dp. OR 20191101:20301231.(ep). OR 20191101:20301231.(dt).	1400591
20	18 AND 19	58365
21	*Coronavirus Infections/su [surgery]	44
22	exp *Specialties, Surgical/	156391
23	exp *Surgical Procedures, Operative/	2012842
24	(intraoperat* OR intra-operat* OR operation? OR operative* OR preoperat* OR pre-operat* OR peroperat* OR per-operat* OR perioperat* OR peri-operat* OR postoperat* OR post-operat* OR presurg* OR pre-surg* OR perisurg* OR peri-surg* OR postsurg* OR post-surg* OR reoperat* OR re-operat* OR surgeries OR surgery OR surgeon? OR surgical*).ti,kf.	1017840
25	OR/21-24	2666199
26	*Failure to Rescue, Health Care/ OR *Hospitalization/ OR exp *Intensive Care Units/ OR exp *Mortality/ OR *Patient Admission/	151536

27	exp *Specialties, Surgical/ae, co, mo [adverse effects, complications, mortality]	1154
28	exp *Surgical Procedures, Operative/ae, co, mo [adverse effects, complications, mortality]	256808
29	(admission? OR admitted OR admitting OR adverse* OR complication? OR complicat* OR death* OR fatal OR fatalit* OR hospitalis* OR hospitaliz* OR icu? OR ((coronary OR intensive* OR respiratory) adj2 (care OR unit?)) OR mortalit*).ti,kf.	789014
30	(ae OR co OR mo).fs.	3929637
31	OR/26-30	4397057
32	*Brain Ischemia/ OR exp *Intracranial Hemorrhages/ OR exp *Stroke/ OR *Stroke Rehabilitation/	178858
33	(stroke* OR poststroke? OR post-stroke? OR CVA OR CVAs).ti,kf.	123321
34	((cerebrovascular* OR cerebro-vascular* OR cerebral vascular*) adj2 (apoplex* OR accident* OR infarct*)).ti,kf.	2235
35	((brain OR cerebral OR intracerebral OR intra-cerebral OR arachnoid OR subarachnoid OR sub-arachnoid OR intracranial* OR intra-cranial* OR cranial*) adj2 (infarct* OR isch?emi* OR h?emorrhag*)).ti,kf.	60590
36	((postacute OR post-acute OR chronic) adj5 (stroke* OR poststroke? OR post-stroke?)).ti,kf.	2513
37	(((postacute OR post-acute OR chronic) adj5 (hemipare* OR paretic OR paresis OR phase? OR stage? OR state? OR condition? OR paraly* OR spastic*)) AND (stroke* OR poststroke? OR post-stroke?)).ti,kf.	363
38	exp *Heart Diseases/	967223
39	((cardiac* OR heart? OR myocardia* OR myo-cardia*) adj2 (attack? OR event? OR failure? OR infarct* OR ruptur*)).ti,kf.	193632
40	*Lung/pa, pp	24203
41	exp *Lung Injury/	33043
42	((lung? adj2 (damag* OR injur*)) OR pulmonary function*).ti,kf.	25199
43	*Respiratory Distress Syndrome, Adult/	15345
44	(((acute OR syndrome?) adj (respiratory distress OR respiratory failure)) OR ARDS OR ARDSS).ti,kf.	12995
45	*Venous Thrombosis/ OR *Upper Extremity Deep Vein Thrombosis/	20802
46	((deep adj (vein OR venous) adj (thrombos?s OR thrombus)) OR deep thrombophlebitis OR deep thrombo-phlebitis OR DVT OR DVTs).ti,kf.	12115
47	exp *Pulmonary Embolism/	28762
48	((lung? OR pulmonary) adj (embol* OR infarct* OR micro-embol* OR microembol* OR thrombo-embol* OR thromboembol*)).ti,kf.	23406
49	OR/26-48	5216331
50	exp *Intraoperative Complications/	25785
51	exp *Postoperative Complications/	291232
52	OR/50-51	309653
53	exp animals/	23471581

54	exp animal experimentation/ OR exp animal experiment/	9487
55	exp models animal/	573370
56	nonhuman/	0
57	exp vertebrate/ OR exp vertebrates/	22807589
58	OR/53-57	23473525
59	exp humans/	18732734
60	exp human experimentation/ OR exp human experiment/	12488
61	OR/59-60	18733389
62	58 NOT 61	4740761
63	(20 AND 52) OR (20 AND 25 AND 49)	796
64	63 NOT 62	795
65	limit 64 to English language	767
66	*Long Term Adverse Effects/	373
67	((duration? OR follow-up* OR followup* OR long-term* OR longterm* OR persistent* OR post-recover* OR postrecover*) adj2 (complication? OR consequence? OR (adverse* adj effect?) OR implication? OR outcome? OR sequelae OR symptom?)).ti,kf.	27460
68	*Recovery of Function/	12977
69	((recover* OR return*) adj2 (baseline? OR base-line? OR disease? OR function* OR health* OR patient* OR usual)).ti,kf.	9251
70	OR/66-69	47842
71	20 AND 70	126
72	71 NOT 62	126
73	limit 72 to English language	125