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SPECIAL TOPIC
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Elective Surgery during SARS-Cov-2/COVID-19 Pandemic: Safety Protocols with Literature Review

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Background: Health care systems worldwide have been affected by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emergence since December 2019. The coronavirus disease 2019 (COVID-19) pandemic caused a steep decrease in elective surgery scheduling, to the extent of complete cancellation without future planning of safe development.
Purpose: We performed a review of the literature and diagnosis data analysis with the aim to reduce the risk of operating a patient infected with SARS-CoV-2/COVID-19 during the incubation period.
Methods: We searched for specific words and phrases about SARS-CoV-2 and COVID-19 in the PubMed database (US National Library of Medicine) from December 2019 to April 2020. A detailed analysis of the clinical picture and existing diagnostic tests for COVID-19 was performed to achieve the desired objectives.
Results: A total of 1273 out of 5930 articles about COVID-19/SARS-CoV-2 did meet the criteria for the searched terms. We reviewed 105 articles, and 60 were selected for analysis. Specific recommendations were described based on our revision.
Conclusions: With the combination of immunoglobulin M and immunoglobulin G antibody tests + real-time polymerase chain reaction for SARS-CoV-2 implemented in different time periods by taking into account the natural history of the disease, it is possible to decrease the risk of operating a patient during the incubation period higher than 93%. Adding other security measures can further increase this percentage. As long as there is no immunity to COVID-19, these measures will help us to perform safer elective surgeries. *(Plast Reconstr Surg Glob Open 2020;8:e2973; doi: 10.1097/GOX.0000000000002973; Published online 27 May 2020.)*

INTRODUCTION

In December 2019, in Wuhan, China, a new kind of respiratory disease surged due to an unknown coronavirus.[1] Because it causes a severe acute respiratory syndrome, the International Committee on Taxonomy of Viruses named it as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resultant disease as coronavirus disease 2019 (COVID-19).[2,3] Dissemination was faster than expected, and cases did multiply 1879 times from January 10 to February 23 among the Chinese population.[4] Around 81% of cases were reported as mild, 14% were reported as severe, and 5% required critical care.[5,6] Mortality was calculated as 2.84% in China and 12% in European countries.[7–9] A meta-analysis displayed a mortality rate of 4.3%.[10] Besides, severe cases were commonly reported amid the elderly, patients with certain comorbidities (eg, diabetes mellitus, hypertension, and lung and/or cardiovascular diseases)[11,12] and obesity.[12–14]

This new illness rapidly extended worldwide and was later declared as an international public health emergency in January 30, 2020.[15] Studies reported the human-to-human transmission by means of droplets but also by aerosols and fomites in contaminated places.[16] The viral genome and phenotype were rapidly identified,[17,18] which allowed researchers to develop specific diagnostic tests and antibody (Ab) detection assays.[19] Due to the easy contagion and resultant brisk increased incidence, several quotidian activities have been restricted all over the world,

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including surgical procedures considered unessential.[20,21] Consequently, almost all elective surgeries were canceled, including plastic surgery.[22,23] Protocols for initiation in the near future were not described and have not been proposed yet. Based on this concern, we decided to report a systematic literature review about SARS-CoV-2/COVID-19 articles, with the aim to create protocols and specific indications to decrease the surgical risk of operating a COVID-19–infected patient during the incubation period.

MATERIALS AND METHODS

We searched for publications about COVID-19 and SARS-CoV-2. The PubMed database (US National Library of Medicine) was used to perform the medical literature research from December 2019, 2020, to April 21, 2020. Documents in any language published in PubMed were included. We regarded for specific words and phrases about COVID-19/SARS-CoV-2 to find the most suitable references for our article's main purpose. The following 10 (MESH) terms were used: "Epidemiology" AND "COVID-19," "Clinical manifestations" AND "COVID-19," "Tests" AND "COVID-19," "Early diagnosis" AND "COVID-19," "Surgical procedures" AND "COVID-19," "Surgical care" AND "COVID 19," "Surgical procedures" AND "suspicious patients" AND "COVID-19," "Intraoperative care" AND "suspicious patients" AND "COVID-19," "Elective Surgery" AND "COVID 19," and "Chest study imaging" AND "COVID 19." Many terms and words were displayed similarly when searching for articles. Words like "intraoperative," "trans-operative," "surgical," and "surgery" showed similar results. The same happened with words like "caution," "care," "precaution," and so forth; in which case, the word with the most frequent results was chosen. The results of the investigated words and phrases were analyzed by quantity and quality. Articles included for analysis fulfilled the objectives of our research based on their main description and summary. The final selected articles were classified into 5 groups to be specifically analyzed by the corresponding author and co-authors. The classification was made into 5 groups: the first 3 groups included all the aspects that could help identify a patient during the incubation period and the last 2 groups included relevant articles and guidelines published by surgical societies for their use during the discussion of the article. Groups were designated as follows: (1) epidemiology and clinical symptoms; (2) diagnostic tests; (3) radiologic evaluation; (4) surgical procedures and/or elective surgeries; and (5) comorbidities and complications. Acting in accordance with the analysis of all the article's content, recommendations were described to meet the objectives of this manuscript.

RESULTS

From December 2019, 2020, to April 21, 2020, a total of 5930 articles about COVID-19/SARS-CoV-2 in the PubMed database were found, with specified MESH terms in 1273 articles. The most referenced term was about epidemiology with 961 articles, followed by the term "tests" with 118 articles. Terms about clinical manifestations and chest imaging studies were very similar, with 64 and 63 articles, respectively. We found 32 articles, including early diagnosis terms. Articles including surgery and COVID-19 terms were the least common (only 26 articles), most of them reporting emergency procedures. Research done by multiple other methods and using comparable words did not show articles about protocols incorporating patients suspected of having COVID-19 infection who underwent elective surgery. Neither we did on articles about asymptomatic patient's care with potential infection (or during the incubation period) undergoing surgery. Complete results for the specific terms and phrases, as well as the articles included in the analysis, are summarized in Table 1.

Sixty of the articles that compied with our study goals were subject to analysis: (1) diagnostic tests (n = 23); (2) epidemiology and clinical symptoms (n = 18); (3) surgical procedures and/or elective surgeries (n = 11); (4) radiologic evaluation (n = 4); and (5) comorbidities and complications (n = 4) (Table 2).

DISCUSSION

Because the COVID-19 pandemic has compelled our institutions to make drastic changes in protocols for everyday in-hospital activities (including surgical procedures), different Medical Societies have reported specific recommendations for elective procedures during these contingency periods.[24,25] The absence of an effective vaccine to provide immunity for everyone, which could take even years to develop[26,27]; in addition to the fact that the rate of asymptomatic or mild symptomatic patients with a positive test for SARS-CoV-2 can be as high as 80%,[28–30] any individual should be now considered as a potential carrier of SARS-CoV-2 until proven otherwise. Significant concern

Table 1. Total Articles Found According to Search Criteria

Words and Phrases Searched	Articles Found (n)
"Epidemiology" and "COVID-19"	961
"Tests" and "COVID-19"	118
"Chest study imaging" and "COVID-19"	63
"Clinical manifestations" and "COVID-19"	64
"Early diagnosis" and "COVID-19"	32
"Surgical procedures" and "COVID-19"	14
"Elective surgery" and "COVID-19"	12
"Surgical care" and "COVID-19"	9
"Surgical procedures" and "suspicious patients" and "COVID-19"	0
"Intraoperative care" and "suspicious patients" and "COVID-19"	0
Total (n)	1273

Table 2. Selected and Analyzed Articles

Articles Content	Analyzed Manuscripts (n)
Diagnostic tests	23
Epidemiology and clinical symptoms	18
Surgical procedures and/or elective surgeries	11
Radiologic evaluation	4
Comorbidities and complications	4
Total (n)	60

has emerged in our profession to perform elective surgeries safely because recent studies have reported the high incidence and severity of complications associated with patients undergoing surgery who were unknown to be carriers of the disease, or were infected after the procedure.[31,32] Although the most radical and simplest solution would be the cancellation of all elective surgeries, that seems far from real. As stated by projections and estimations from transmission models, social distancing may be necessary until 2022 to prevent recurrent outbreaks, and the risks of contagion resurgence may be present until 2024.[33] Somehow, if successful therapeutic and immunity measures do not come to light, the likelihood of intervening unknown COVID-19 patients is going to increase exponentially in the upcoming 4 years.

By now, serologic immunoassays and rapid detection tests are the most effective tools available to determine patients who are infected.[19,34–36] The Coronaviridae are enveloped RNA viruses with the SARS-CoV-2 emerging as a new β-coronavirus that shares 88% of its genomic sequence with the SARS-CoV and a 50% of it with the MERS coronavirus.[37,38] The SARS-CoV-2 genetic material can be detected in an infected individual by means of the real-time reverse transcriptase polymerase chain reaction (qRT-PCR).[34–36] It is a biological and molecular diagnostic test, based on the viral nucleic acid sequence (RNA). This technology combines the reverse transcription of RNA into DNA to achieve polymerase chain reaction amplification in real time, which is also used to detect SARS-CoV and MERS coronavirus from upper (nasal and oropharynx) and lower (sputum, orotracheal, or bronchoalveolar secretions) respiratory tract samples.[39,40] The viral RNA quantity (q) can be measured by means of qRT-PCR, which uses fluorescent markers to calculate the amount of nucleic acids present in a specific sample. Currently, the qRT-PCR is the gold standard diagnostic test for SARS-CoV-2/COVID-19[34–36,41] because it is able to detect affected cells from the moment our body gets in contact with the virus. In contrast, some false-negative cases (asymptomatic infected patients with a negative test) have been reported[42–45] because the sensitivity increases proportionally with the viral load, but also depends on where the sample is taken from (the lower in the respiratory tract, the more sensible the test). The qRT-PCR has a pretest sensitivity of 40% for nasal samples and 50% for oropharyngeal samples, compared with the 80%–100% for samples acquired from bronchoalveolar lavage by bronchoscopy or endotracheal tube.[34,46] Therefore, we could infer that qRT-PCR test for COVID-19 diagnosis may reach a sensitivity of 50–100% depending on "What" protocol was used, "When" and "Where" the sample is obtained from.[34,47] Because the lower respiratory tract samples are usually difficult to collect (specially in asymptomatic patients), Ab detection tests are also available to increase the diagnosis sensitivity. After the virus is detected by the innate immune cells, antigen-presenting cells start the B and T lymphocyte–mediated cellular and humoral response, in which immunoglobulin (Ig)-M and later Ig-G Ab are produced against SARS-CoV-2.[19,34–36,48,49] First-line defense Ig-M Abs are produced 3–6 days after the initial exposure

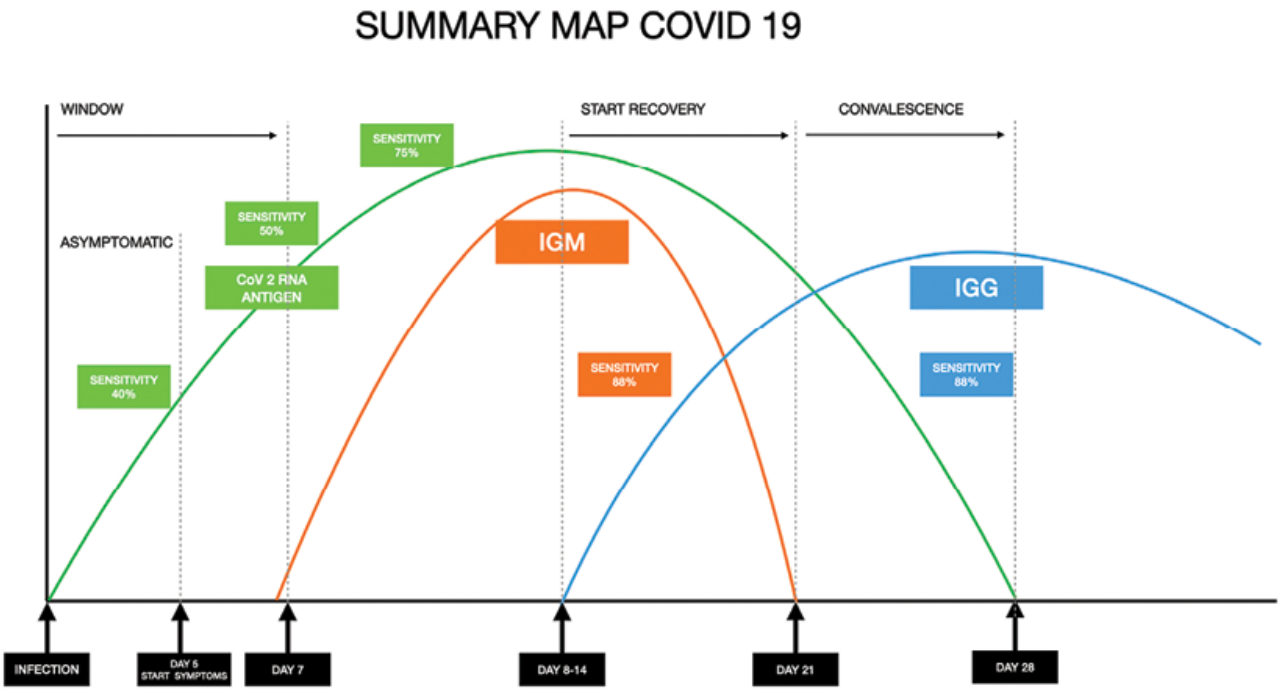

Fig. 1. Detection time for COVID-19 diagnostic tests. The qRT-PCR is the first test to be positive after the first contact with the virus and remains positive until the virus is cleared up from our system, around day 28 (green line). Ig-M Abs are the first-line humoral defense and usually rise between 6 and 8 days after infection and become undetectable around day 21 (orange line). Ig-G Abs are specific and confer long-term immunity (last to appear positive), they rise between the first and second week after infection and data surrounding their permanence are unclear (blue line). Remember that the sensitivity of each test depends on what, when, and where (see Discussion section).

and remain positive for approximately 4 weeks, whereas the specific Ig-G Abs produced by long-term memory cells increase by the eighth to 12th day and remain positive for months to years[45,50–53] (Fig. 1). The rapid results (15 minutes) of Ig-M and Ig-G Abs against SARS-CoV-2 are the main advantage of these tests. Diagnostic time is shortened; no special equipment or training are required and are easily performed. Therefore, they can be applied to asymptomatic patients in a straightforward basis at health care facilities, airports, nursing homes, educational institutions, etc.[50,51,53] In any case, it is important to understand that these tests just indicate that the patient has or did have a contact with the virus; hence, they are neither considered confirmatory tests nor recommended for ruling out acute COVID-19 infection, in which case qRT-PCR must be done.[50,51,53] Some studies have reported the combination of qRT-PCR + Ig-M or Ig-M serology to increase the detection index roughly to a 98% in symptomatic patients,[53] which gives us clinicians a "thumbs up" for early diagnosis, although it is not reported on asymptomatic patients. Regardless, the Igs behavior and the qRT-PCR results have helped us to determine each patient's state of infection (Figs. 2, 3). F2,F3

Tests for Ig-M and Ig-G Ab detection have a very high sensitivity and specificity; they are reported to be 88.7% and 90.6%, respectively.[54] However, statistically there is an 11.3% of patients in whom early diagnosis cannot be made.[54] In the actual pandemic scenario, the sensitivity

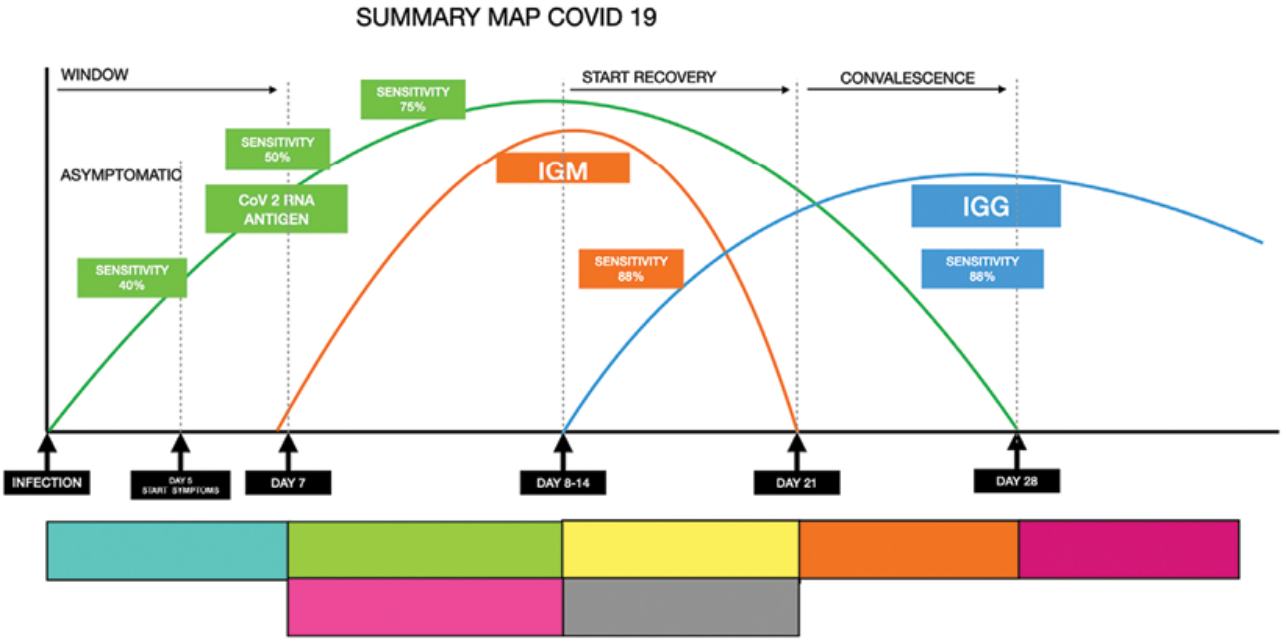

Fig. 2. Diagnostic test behavior. Our recommendations regarding patient safety while undergoing elective surgeries are based on the specific serology and molecular test results. Current patient status can be accurately determined by their results as depicted in the chart (right). Observe that the only possible combination for a patient who is not infected is the 3-negative result (left). Any other combination has a different meaning (right) (see Discussion section for further explanation).

PCR	IGM	IGG	
+	-	-	Patient in infection window
+	+	-	Patient in early stage of infection
+	+	+	Patient in active phase of infection.
+	-	+	Patient in late or recurrent state of infection
-	-	+	Patient with past infection and already recovered.
-	+	-	Initial patient. PCR have low sensitivity and false negatives.
-	+	+	Patient start recovery. PCR have low sensitivity and false negatives.

Fig. 3. Diagnostic test behavior. Our recommendations regarding patient safety while undergoing elective surgeries are based on the specific serology and molecular tests results. Current patient status can be accurately determined by their results as depicted in the chart. Observe that the only possible combination for a patient who is not and was not infected is the 3-negative result. Any other combination has a different meaning (see Discussion section for further explanation). PCR indicates polymerase chain reaction.

of the Ig test means that approximately 12% of infected patients (or patients with positive qRT-PCR for SARS-CoV-2) will have a negative Ig-M test (false negatives), perhaps because Abs are not produced during the first 5–7 days of the disease. Conversely, the specificity of the Ig test means that around 10% of patients without infection will test positive for the Ig-M (false positives).[52] Furthermore, some COVID-19 patients may test negative due to low Ab production secondary to immunologic diseases or brisk decreased Ig-M concentrations 2 weeks after the first contact with the virus.[52] Due to the abundant offer of Ig tests that have emerged in the market, we must consider the validity and precision of the tests for use on this protocol because its success depends on them.

Chest radiologic studies have not shown relevant data during the incubation period (≈7 days); however, they could be useful in early symptomatic patients and/or with advanced disease.[55,56] Having in mind the normal immunologic response, the average timing for Abs to be positive, and the qRT-PCR sensitivity, we could recommend

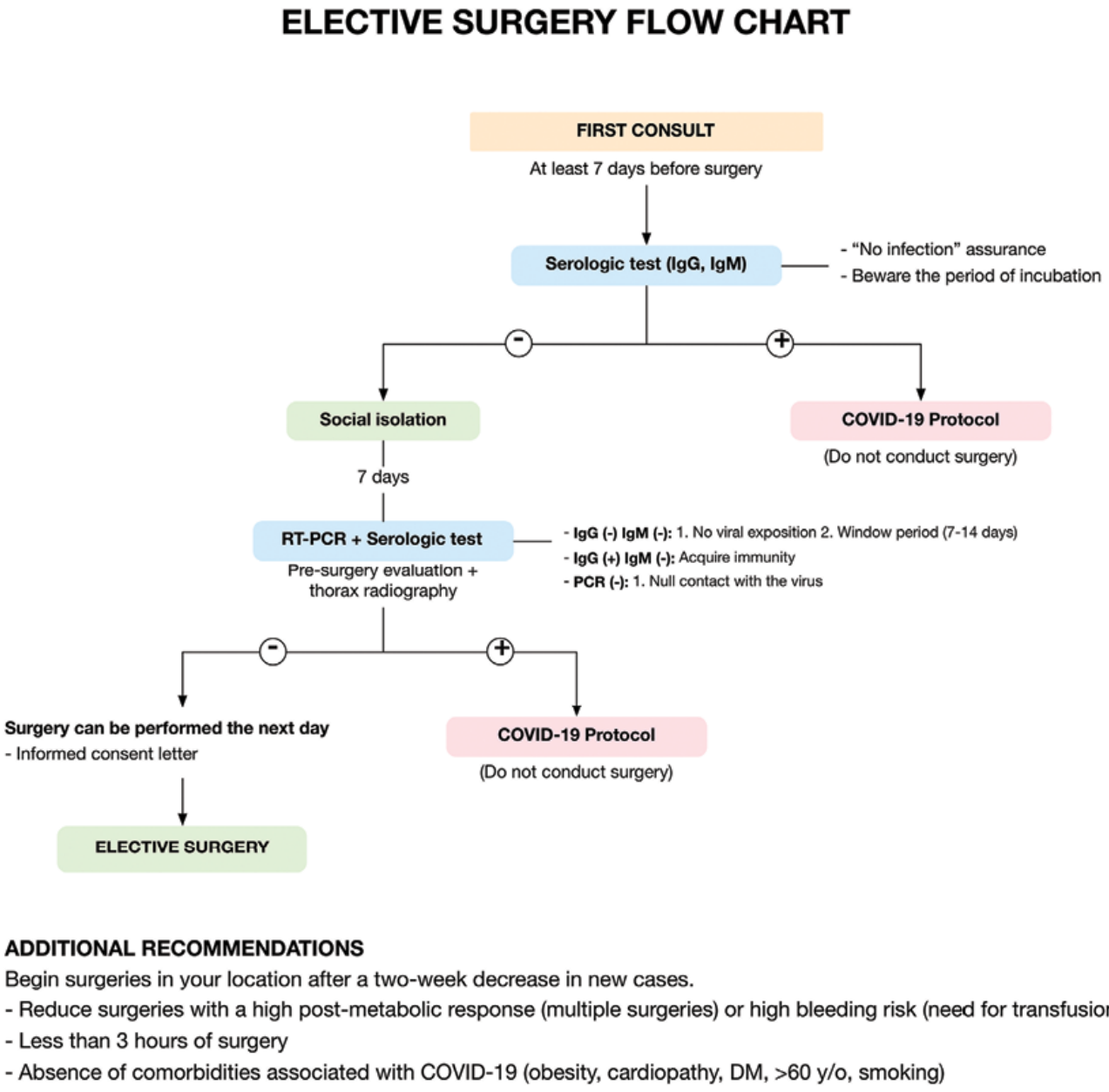

Fig. 4. Elective surgery flow chart. How to increase patient safety for elective surgeries. The correct selection of tests in a determined point in time, in addition to complete individual isolation, will help us to clear patients for elective surgeries but also to exclude high-risk ones. Following the diagram, all patients must be tested 7 days before surgery for Ig-M and Ig-G Abs. If both negative: the day before surgery, they must be tested again for Abs, in addition to a qRT-PCR to rule out any viral load. If both negative: preoperative chest x-ray must be performed and surgery can be scheduled for the next day. Note: be aware that these recommendations are based on a 93% preoperative safety rate according to currently available evidence on SARS-CoV-2/COVID-19 (see Discussion section). DM, diabetes mellitus.

that surgical procedures can be programmed with a specific process with time limitations and scientific support. First step is the evaluation of each patient to rule out active infection or a previously infected patient in actual recovery period. The latter must be tested for Ig-M and Ig-G Abs during the first appointment. If both negative, we can certainly assure that the patient is not infected, but possibly within the window phase (incubation period). This patient must remain in quarantine with standard preventive measures (frequent hand washing, alcohol-based solutions, face mask, etc). Complete isolation aims to avoid any upcoming contact contamination. After 7 days, a second set of Ig Ab test must be done in addition to a qRT-PCR assay. If both negative (Ab tests and qRT-PCR), then we could be certain that there has not been any contact with the SARS-CoV-2 virus (Fig. 4).

Although qRT-PCR and Ab tests are indicated for COVID-19 diagnosis and therefore an elective surgery could be safely performed, there will always be a 10% chance that an actual infected patient might not be detected by those.[54] As a result, additional measures must be implemented to ensure a entirely harmless procedure for the patient. A focused medical record of SARS-CoV-2 infection[10,57,58] in addition to a detailed epidemiologic history (looking for COVID-19 nexus) have to be registered in the patient notes[59] to detect patients at risk.

All elective surgeries, including aesthetic ones, may be resumed at the geographic area where we are going to operate after the incidence of COVID-19 infections has progressively decreased over a 2-week period (or where the patient comes from).[24,60] We should keep to a minimum procedures that may cause a moderate to severe increase in the patient metabolic rate (eg, multiple or combined surgeries) and avoid including patients with comorbidities that could worsen the COVID-19 infection[12–14] (Table 3). Prevention and control strict measures must be implemented in each health care facility where we are planning to schedule surgeries (non-COVID-19 institutions), including periodic serologic tests for employees and regular visitors.

SUMMARY

1. Serologic Ab Ig-M or Ig-G tests have almost 90% of sensitivity and specificity for SARS-CoV-2/COVID-19 diagnosis; however, they can be detected only 6–8 days after the initial viral infection (Ig-M).
2. The diagnostic confirmatory test for COVID-19 is qRT-PCR from respiratory tract secretions. Unfortunately, sensitivity varies (50%–100%) depending on the collecting site of the sample (higher sensitivity for lower respiratory tract compared with that of the upper respiratory tract).
3. Both patient and surgeon must be aware: even though we run every test available (Ig-M and Ig-G + qRT-PCR) for diagnosis, nearly 7% of asymptomatic patients who are infected with SARS-CoV-2 could test negative.
4. Complemented by other preventive measures, patient safety could be even higher.

Table 3. Checklist to Investigate Presurgical Symptoms and Comorbidities Current Symptoms or within the Last Month

Presurgical Symptoms		
Data to Investigate	**Yes**	**No**
Fever >38°C		
Dry and/or wet cough		
Fatigue		
Myalgia		
FIO_2 oximetry <90%		
Dyspnea		
Headache		
Diarrhea		
Skin lesions		
Anosmia		
Dysgeusia		
Vomiting		
Nasal congestion		
Conjunctivitis		
Comorbidities		
Data to Investigate	**Yes**	**No**
Age over 60 y		
Arterial hypertension		
Diabetes mellitus		
Lung diseases		
Obesity		
Chronic smoker		

FIO_2 = fraction of inspired oxygen.

RECOMMENDATIONS

We make the following recommendations with the aim of minimizing the possibility of operating a patient during the incubation period of COVID-19. Due to the rapid evolution of the disease, changes, and new knowledge that are constantly taking place, all the recommendations must be updated according to new scientific evidence.

1. Resume elective surgeries once the incidence of COVID-19 has progressively decreased at the geographic zone where the procedures are going to be held and/or where the patient comes from.
2. Record a focused medical history for COVID-19 signs and symptoms in addition to detailed epidemiologic risk factor assessment (Table 3).
3. Carry out a focused preoperative evaluation led by the attending physician (1 day before surgery).
4. All patients must be tested for Ig-M and Ig-G Abs in the first appointment, and a second test must be repeated after 7 days, in addition to a qRT-PCR test. Only all-test negative patients will be cleared for surgery (Caution: Almost 7% of asymptomatic patients who are infected with SARS-CoV-2 would test negative) (Fig 4).
5. Patient must remain completely isolated for the next 7 days after the initial appointment when scheduled for surgery.
6. Optimize standard preventive measures during and before every appointment.

Note that each country and state must individualize the criteria for elective surgery protocols. This is a general guide for future studies with further clinical data regarding

the associations between the SARS-CoV-2/COVID-19 and elective procedures.

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