Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Guide for surgical procedures in oral and maxillofacial areas during coronavirus disease 2019 pandemic

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1. Guide

1.1. Positioning

The coronavirus disease 2019 (COVID-19), was confirmed in China in December 2019 [1] and rapidly spread worldwide. As of January 2021, the cumulative number of infected individuals in the world was 80 million, with more than 1.8 million deaths (according to the World Health Organization(WHO)). The pandemic has affected not only the daily life but also clinical practice. The virus is transmitted from person to person through droplet infection or contact infection. In Japan, outbreaks of the infection (clusters) have been reported in general hospitals and nursing care facilities. Thus, during the period from March to May 2020, the so-called first wave, many dental clinics and hospitals limited the outpatient and inpatient care, to prevent the spread of infection. Although the number of newly infected patients transiently decreased from June 2020, it increased again from August and November 2020. In December 2020, the presumably highly transmissible variant (VOC-202012/01) that was spreading in the United Kingdom was also detected in Japan, and the infection is still spreading.

Oral and maxillofacial surgeons, who examine and treat the oral cavity and its surrounding structures in daily clinical practice, are always exposed to the risk of infection through exposure to saliva, droplets, and aerosols containing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus. Fortunately, there have been no reports of transmission from patients to medical professionals during surgical procedures or treatment in oral and maxillofacial areas. However, in neurosurgery, cases in which medical professionals were infected during transnasal pituitary surgery have been reported [2]. The risk associated with surgical procedures and treatment among medical professionals of oral and maxillofacial areas is not necessarily revealed because sufficient data have not been accumulated. Given the incidence of infection during surgery in associated clinical fields, to promote prevention of infection, as well as provide sufficient attention to and control against exposure to the virus, in oral and maxillofacial surgeons, we present guide that should be referred when surgical procedures in oral and maxillofacial areas are performed.

The guide includes items on preoperative preparation, preoperative assessment, decision on the performance of surgery,

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intraoperative equipment, and operating room environment. The guide intends to be used by all dentists and surgeons who perform surgical procedures of oral and maxillofacial areas in Japan, including the general practitioners and those working at general hospitals, medical, and dental school hospitals. The guide is applicable to all surgical procedures performed in the oral and maxillofacial surgery including tooth extraction, trauma, infection, tumor, inflammation, and congenital and acquired morphological abnormalities, regardless of the use or type of anesthesia.

Because evidence has not been established on many aspects of COVID-19, this guide is not evidence-based treatment guidelines. Instead, they provide a summary of information and recommendations based on information that the Japanese Society of Oral and Maxillofacial Surgeons collected through extensive search.

1.2. Definitions of terms

1.2.1. Preoperative preparation

1.2.1.1. Cough etiquette. Practice of "cough etiquette" is considered important for the prevention of influenza and other infectious diseases transmitted through droplets generated by coughing or sneezing. Specifically, people should cover their mouth and nose with a mask, paper tissue, handkerchief, the front piece of a jacket, or a sleeve when they cough or sneeze. In the case of COVID-19, cough etiquette alone is insufficient to prevent infection because viral transmission from asymptomatic or pre-symptomatic patients has been reported. For this reason, "universal (community) masking," in which people always wear a mask regardless of whether they are symptomatic or asymptomatic to reduce the amount of droplets generated by infected individuals, is relevant. Although non-woven fabric is a preferable material for a mask, a double-or more-layered fabric mask is considered effective to a certain extent. In addition, proper wearing of a mask is important. For example, the nose should be covered, and a mask should be attached to the face without any gaps.

1.2.1.2. Hand hygiene. Hand hygiene is divided into two categories: "hand disinfection" with rubbing-type alcohol-based hand sanitizers and "handwashing" with running water and liquid soap. In ordinary situations, hand hygiene should be practiced with "hand disinfection." When the hands are contaminated or suspected to be contaminated, "handwashing" should be performed. Appropriate rubbing-type alcohol-based hand sanitizers should be selected because some products may cause 'dry skin' depending on the effect of the emollient contained. Individuals who have trouble with the use of alcohol-based sanitizers because of allergy and other reasons should practice "handwashing."

1.2.1.3. Gargling. In this guide, gargling means "gargle" and "mouth wash/mouth rinse." Gargle is defined as "cleaning the pharynx and oral cavity by rumbling with liquid, which is spitted out afterward." The mouth wash/mouth rinse is defined as rinsing of the oral cavity; in other words, "cleaning the oral cavity by swishing liquid, which is quietly spitted out afterward." Because gargle is associated with the risk of accidental ingestion, the elderly and other people who are not accustomed to gargle should not be forced to practice gargle. When either gargle or mouth wash/mouth rinse is performed, caution should be exercised to avoid contaminating the surrounding environment with the spit.

1.2.1.4. Mouth wash/mouth rinse. Refer to Gargling.

1.2.2. Preoperative assessment

1.2.2.1. Interview of COVID-19 symptoms. Assessment of infection risk. Assess all patients scheduled for surgery. Interview them for features including fever with axillary temperature of $\geq$37.5 °C, cold/respiratory symptoms, history of traveling overseas within the previous 2 weeks, history of contact with a patient with COVID-19, and taste/smell disorder. If any of the features is present, we examine the applicable symptoms or situations in detail. When the possibility of contracting COVID-19 cannot be ruled out, the assessment result is positive.

1.2.2.2. PCR test. PCR (polymerase chain reaction) test is performed to detect the SARS-CoV -2 gene. In principle, a nasopharyngeal swab sample should be used. This test is performed to screen for COVID-19 in regions in the epidemic phase. With detection of the gene, the test result is considered positive.

1.2.2.3. Intraoperative equipment.

1.2.2.3.1. Aerosols. Aerosols generally refer to the dispersion of liquid or solid microparticles in the air. In terms of size, microparticles vary from approximately 1 nm to 100 μm. Aerosols measuring $\leq$2 to 3 μm are so light that they may not fall on the ground immediately but may float in the air for several hours. If microparticles contain pathogens, inhaling them through the mouth or nose may cause infection.

1.2.2.3.2. Personal Protection Equipment (PPE) with an N95 respirator. Wear an N95 respirator, face shield/goggles covering the eyes, gown with long sleeves covering up to the wrists, surgical cap covering the ears, and surgical gloves. Avoid exposure of the skin as much as possible. Wearing an N95 respirator prevents the inhalation of droplets and aerosols. Medical-grade masks of KN95 should be regarded equivalent to N95 respirators.

1.2.2.3.3. Simple PPE. Wear PPE without an N95 respirator. Wear a conventional surgical mask, face shield/goggles covering the eyes, gown with long sleeves covering up to the wrists, surgical cap covering the ears, and surgical gloves. A simple PPE corresponds to PPE for surgery in conventional conditions.

1.2.3. Operating room environment

1.2.3.1. Laminar flow setting. According to the operating room standards, a laminar flow ventilation system should be installed in an operating room beforehand. In an operating room with laminar flow ventilation, the surgeons and other medical professionals are exposed to a reduced risk of inhaling droplets and aerosols generated from the operative field. The surgeons and the assistants should stand more upwind than patients. It is essential to ensure that exhaust air containing aerosols does not reenter the operating room.

1.2.3.2. Intraoral suction. Use intraoral (or surgical) suction devices to suck and dispose fluid waste, droplets, and aerosols generated during surgery. When intraoral (or surgical) suction devices are built into the facility, it is essential that they do not allow reentry of exhaust air containing aerosols into the operating room, and that their structure ensures safe disposal of fluid waste. When mobile devices are used, it is essential that their structure ensures safe dispersion of exhaust air through high-efficiency particulate air (HEPA) or other equivalent filters and safe disposal of fluid waste. HEPA filters need to be replaced regularly according to the specified usage.

1.2.3.3. Extraoral vacuum. Use extraoral vacuum devices to suck and dispose scattered substances, droplets, and aerosols generated during surgery. When extraoral vacuum devices are built into the facility, it is essential that they do not allow reentry of exhaust air containing aerosols into the operating room, and that their structure ensures safe disposal of collected scattered substances. When mobile devices are used, it is essential that their structure ensures safe dispersion of exhaust air through HEPA or other equivalent filters and safe disposal of collected scattered substances. HEPA filters need to be replaced regularly according to the specified usage.

1.3. Algorithm

Refer to the figures: Preoperative assessment and surgical decision algorithm should be performed.

1.4. Overview of the guide

1.4.1. Preoperative preparation (from 2 weeks before surgery to the day of surgery)

Two weeks before surgery, instruct the patient on infection control practices, such as avoidance of non-essential outings, maximal avoidance of conversation, meeting, and eating without proper wearing of a mask in proximity with people other than family members living together, and avoidance of places with a high infection risk, such as hot spots. Instruct the patient to thoroughly practice cough etiquette, hand hygiene, and gargling after outings.

On the day of surgery, let the patient perform "mouth wash/mouth rinse" with povidone-iodine at the shortest possible interval before surgery unless the patient is allergic (refer to 6. Appendix: Precautions for gargling)

1.4.2. Regional risk assessment (from 3 days before surgery to the day of surgery)

When preoperative assessment is performed, the area where the patient lives, works, or studies is classified as a potential zone, epidemic zone, or high community-transmission zone, according to the incidence of infection.

1.4.2.1. Potential zone. It is an area where patients with COVID-19 may potentially exist, although encountering those with COVID-19 is infrequent in daily clinical practice. As a guide, a potential zone is defined as a prefecture where the cumulative number of newly infected individuals* per 100,000 persons is <0.3, within the preceding week.

1.4.2.2. Epidemic zone. It is an area with a high possibility of encountering patients with COVID-19 in daily clinical practice. As a guide, the epidemic zone is defined as a prefecture where the cumulative number of newly infected individuals* per 100,000 persons is ≥0.3, within the preceding week, but where a state of emergency is not declared.

1.4.2.3. High community-transmission zone. It is an area where the risk of nosocomial infection through surgery is high because a high incidence of community-acquired infections increases encounter with patients with COVID-19 requiring surgery in daily clinical practice. As a guide, the high community-transmission zone is defined as a prefecture where the government declares a state of emergency or issues an equivalent travel restriction.

* The number of PCR-positive individuals per 100,000 persons in the preceding week, as reported by the Ministry of Health, Labour and Welfare (by prefecture) https://www.mhlw.go.jp/stf/seisakunitsuite/newpage_00035.html

When the area, where a patient works or studies, differs from the resident area, an area with a higher incidence of infection should be selected. In principle, the incidence of infection should be assessed at the prefectural level. However, if the incidence varies significantly within a prefecture, these criteria can be flexibly applied according to the actual situation.

1.4.3. Preoperative assessment (from 3 days before surgery to the day of surgery)

*Refer to figure: Preoperative assessment to be performed.

Start performing preoperative assessment for COVID-19 3 days before surgery. Select the exact contents of preoperative assessment according to regional risk assessment. Classify the assessment results as positive or negative. When the preoperative assessment cannot be done, or when the results of their assessment are unavailable, such cases should be designated as untested.

Perform only the interview of COVID-19 symptoms (refer to 1.2. Definition of terms) for patients from a potential zone. When features suggesting the risk of developing COVID-19 are present, the result of preoperative assessment is positive.

Perform both the interview for COVID-19 and PCR testing for SARS-CoV-2 detection in patients from epidemic or high community-transmission zone. When the result of either test is positive, the result of the preoperative assessment is considered positive. In principle, PCR testing should be performed with nasopharyngeal swab samples. Alternative tests include quantitative antigen tests using nasopharyngeal swab samples. Other available testing methods include loop-mediated isothermal amplification (LAMP) tests. Either of the two tests have lower sensitivity than the PCR testing; therefore, caution should be exercised (refer to the "Guidelines for Testing of the Pathogen Causing Coronavirus Disease 2019 (COVID-19)" by Ministry of Health, Labour and Welfare of Japan for details of the tests).

Preoperative assessments are preferably performed at the shortest possible interval before surgery. However, performing preoperative assessment approximately 3 days before surgery may be acceptable, depending on the prevailing circumstances in patients or hospitals. After preoperative assessment, patients should be thoroughly instructed to practice not only mask wearing and hand hygiene, but also voluntary restraint on outings and other infection control practices in order to prevent new infections. Meanwhile, patients with history of COVID-19 and those with history of positive PCR test results should be treated as patients with positive assessment results, even if the latest PCR test result is negative, until findings accumulate on the infection risk associated with oral surgical care of previously infected patients.

1.4.4. Decision on go or no-go of surgery (day of surgery)

* Refer to figure: Surgical decision algorithm.

When patients from a potential or epidemic zone have a positive assessment result, elective surgery should be postponed, or alternative treatment should be considered. When surgery cannot be postponed for emergency reasons (e.g., imminent danger to life due to massive hemorrhage, severe infection, airway obstruction; malignant tumor; trauma including skin/mucosal laceration requiring suture, maxillary or mandible fracture, alveolar fracture, and tooth dislocation/fracture), surgery should be performed as an "inevitable choice" for as short operative duration as possible.

Patients with an untested result should be treated as patients with a positive assessment result.

When the assessment result is negative, surgery should be performed.

When patients from a high community-transmission zone have positive assessment results, elective surgery should be postponed, or alternative treatment should be considered. When surgery cannot be postponed for emergency reasons (e.g., imminent danger to life due to massive hemorrhage, severe infection, airway obstruction; malignant tumor; trauma including skin/mucosal laceration requiring suture, maxillary or mandible fracture, alveolar fracture, and tooth dislocation/fracture), surgery should be performed as an "inevitable choice" for as short operative duration as possible.

Patients with untested results should be treated as patients with positive assessment results.

Even if the assessment result is negative, as the number of infected individuals increases, the number of patients with negative assessment results who actually have the virus, in other words, "false negative" patients, increases, and the probability of encountering false-negative patients in daily clinical practice also increases. Thus, when surgery is not urgent but can be postponed,

surgery should be postponed until community transmission subsides, or alternative treatment should be considered. Only surgeries that are highly needed should be performed.

1.4.5. Intraoperative equipment (day of surgery)

* Refer to figure: Surgical decision algorithm.

When surgery is performed for patients with positive assessment results from a potential or epidemic zone, the surgeons and assistants should properly wear PPE with N95 respirators to prevent infection through aerosols and droplets.

When surgery is performed for patients with untested results, surgeons and assistants, should properly wear PPE with N95 respirators to prevent infection through aerosols and droplets. However, when PPE with an N95 respirator is unavailable, simple PPE should be worn properly as an inevitable option. In such cases, the following conditions for the operating room environment should be implemented to perform surgery.

When the assessment result is negative, surgeons and assistants should properly wear simple PPE to perform surgery.

When surgery is performed for patients from a high community-transmission zone who have a positive assessment result or untested result, surgeons and assistants should properly wear PPE with N95 respirators to prevent infection through aerosols and droplets.

As the number of infected individuals increases, the number of patients with negative assessment results who actually have the virus, in other words, "false negative" patients, increases, and the probability of encountering false-negative patients in daily clinical practice also increases. When surgery is performed for patients even with a negative assessment result, proper wearing of PPE with N95 respirators is preferable. When the N95 respirator is unavailable, performing surgery with proper wearing of simple PPE is acceptable. In such a case, the following conditions for the operating room environment should be implemented to perform surgery.

Furthermore, to prevent infection, it is very important to properly wear and remove PPE, including N95 respirators, surgical masks, and other equipment. It is necessary for medical professionals to know how to wear and remove PPE by referring to 6. Appendix: Proper ways to wear and remove an N95 respirators and PPE or other references.

1.4.6. Operating room environment (day of surgery)

* Refer to figure: Surgical decision algorithm.

Surgical procedures in oral and maxillofacial areas are characterized by operations in the operative field where saliva, blood, and irrigation water exist; therefore, all procedures are performed on the basis of the proper application of intraoral suction.

When surgery is performed for patients with positive assessment results from a potential or epidemic zone, an operating room with laminar flow ventilation (laminar flow setting) should be used.

When surgery is performed for patients with an untested result, an operating room with laminar flow ventilation or extraoral vacuum devices should be used to minimize the exposure of surgeons and assistants to droplets and aerosols.

In consideration of the possibility of a "false negative" result, in which patients with a negative assessment result actually have the virus, surgery for patients with a negative assessment result should be performed in an operating room with laminar flow ventilation (laminar flow setting) or with extraoral vacuum devices if possible.

When surgery is performed for patients with positive assessment results from a high community-transmission zone, an operating room with laminar flow ventilation (laminar flow setting) should be used.

For patients with an untested result, surgery should be performed in an operating room with laminar flow ventilation. When the use of an operating room without laminar flow ventilation is necessary, extraoral vacuum devices should be used to minimize the exposure of surgeons and assistants to droplets and aerosols.

In a high community-transmission zone, as the number of infected individuals increases, the probability of encountering false-negative patients in daily clinical practice also increases. Even when surgery is performed for patients even with negative assessment results, an operating room with laminar flow ventilation or extraoral vacuum devices should be used.

As for intraoral suction and extraoral vacuum, waste fluid should be handled as an infectious hazardous material, and safety precautions should be properly observed to dispose it. The devices should be properly maintained according to the specified usage. If they are equipped with HEPA filters, the filters should be replaced periodically.

After each performed surgical procedure, the operating room should be thoroughly ventilated to eliminate aerosols and droplets generated during surgery (refer to 6. Appendix: Indication of ventilation). Whenever surgery is performed, the operating table, the dental unit, and peripheral equipment should be sterilized, disinfected, or wiped (refer to 6. Appendix: Disinfection and cleaning of equipment). While preparing the operating room, attention should be paid to the transmissibility of waste materials. Those performing these tasks should wear a surgical mask, surgical gloves, face shield/goggles, long-sleeved gown, and surgical cap.

1.5. References

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2. Formulation organization and process

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2.2. Methods

The working group of the Subcommittee on the Development of Measures against COVID-19, the Japanese Society of Oral and Maxillofacial Surgeons, considered the summary of the guide and formulated clinical questions (CQs) based on the contents of the guide. For each CQ, a systematic review (SR) team was established to perform an SR.

For the SR, PubMed was searched for keywords to select articles for review. Although the keyword search was difficult because the COVID-19 is an emerging infectious disease, randomized controlled trials (RCTs) and SRs were mainly searched. For each CQ, two members independently performed literature searches. In each SR team, the identified articles were screened in two stages (i.e., the first and second screening). Hand searches were added if necessary. Since the number of selected articles was small, quantitative SR was difficult; therefore, qualitative SR was performed.

Each SR team assessed the evidence levels according to the following criteria:

A (high): The effect estimate is strongly convincing (based on RCTs alone).

B (moderate): The effect estimate is moderately convincing.

C (low): The conviction based on the effect estimate is limited (based on observational studies [e.g., cohort and case-control studies] alone).

D (very low): The effect estimate is almost unconvincing (based only on case reports and case series studies)

Based on these criteria, the working group of the Subcommittee on the Development of Measures against COVID-19 categorized the recommended grades as follows:

Strongly recommended.

Weakly recommended.

Not particularly recommendable.

In the assessment, views that were agreed on by ≥70 % of the members were regarded as the views of the entire group. Voting was repeated until this level of agreement was obtained.

The Working Group prepared the guide and algorithms for the performance of surgical procedures in oral and maxillofacial areas, based on the recommended grades for the CQs. The draft prepared by the Working Group was confirmed by the supervisors and accepted as the final version.

The Working Group, Secretary-general, and Supervisors of the Subcommittee on the Development of Measures against COVID-19, the Japanese Society of Oral and Maxillofacial Surgeons, confirmed that there is no conflict of interest that could inappropriately affect the impartiality required for the production of the guide.

2.3. Timeline

The first meeting took place on July 22, 2020: Review of the summary of the guide.

The second meeting on July 29, 2020: Formulation of the CQs

The third meeting on September 24, 2020: Review of the contents of articles retrieved by the literature search.

The fourth meeting on October 15, 2020: Review of the contents of the SR

The fifth meeting on January 12, 2021: Decision on the recommendations and confirmation of the draft

On January 15, 2021: Approval by the Supervisors

3. Scope targeted by the guide

3.1. Overview of coronavirus disease 2019

COVID-19 is an infection caused by the new coronavirus, SARS-CoV-2. COVID-19 was identified in Wuhan City, Hubei Province, in the People's Republic of China in December 2019. The WHO declared a "Public Health Emergency of International Concern (PHEIC)" for the COVID-19 on January 30, 2020, and subsequently stated on March 11, 2020, that it could be characterized as a pandemic (global outbreak).

While there are many asymptomatic cases of COVID-19, the main symptoms include fever, physical weakness, cough, myalgia, and dyspnea. Characteristically, many patients complain of dysosmia and dysgeusia. In a telephone survey, 202 patients with COVID-19 were asked whether they noticed any abnormalities or changes in smell or taste perception, and they graded the abnormalities or changes into six grades. The results showed that 130 of the 202 patients noticed some changes, while 45 patients reported nasal congestion. C

hanges in smell and taste perception have been suggested as potential indicators of contraction of COVID-19 [1].

A common chest computed tomography (CT) finding in patients with COVID-19 is ground glass opacity. Ground glass opacity is often observed in one area in patients aged <35 years and in multiple areas in those aged ≥60 years [2].

At first, patients develop symptoms such as cold, smell disorder, and taste disorder. In approximately 80 % of patients, their symptoms remain mild and are cured in approximately one week after the onset. In approximately 20 % of the patients, their symptoms of pneumonia are exacerbated by one week to 10 days after the onset, and hospitalization is necessary. Furthermore, from the tenth day after the onset, approximately 5% develop severe conditions requiring mechanical ventilation and other treatments, and 2%–3% develop critical conditions [3].

As for the pathogenic mechanism, SARS-CoV-2 is known to use angiotensin-converting enzyme 2 (ACE2) to enter a cell. When SARS-CoV-2 infects humans, it first binds to the ACE2 receptor, a receptor present on the surface of a target cell. When the spike protein (S protein) of SARS-CoV-2 binds to the ACE2 receptor, the virus begins to enter the cell. The S protein needs to be cleaved by a protease present in the host cell, called transmembrane protease serine2 (TMPRSS2). ACE2 is usually involved in blood pressure regulation; therefore, the findings that have been reported include the following: SARS-CoV-2 may induce cardiovascular disorders by binding to ACE2 receptors; the kidney tubules, which highly express ACE2 receptors, are a high-risk organ for viral invasion, and cancer patients are likely to develop severe conditions [4].

With regard to the transmissibility of SARS-CoV-2, a study with artificially aerosolized SARS-CoV-2 showed that SARS-CoV-2 remained transmissible for up to 3 h in aerosols and 72 h on plastic and stainless steel [5]. When SARS-CoV-2 was cultured in viral transport media, the transmissible virus was almost stable for 2 weeks at 4 °C but became undetectable on the second day at 37 °C, within 30 min at 56 °C, and within 5 min at 70 °C. With regard to the stability of SARS-CoV-2, its transmissibility was evaluated with a cultured virus that was applied to various environments (substances) in the form of a 5-μL drop and collected over time. The transmissible virus was undetectable on paper and tissue paper at 3 h after application; on wood and fabric by the second day; on glass and paper currency until the fourth day; and on plastic and stainless steel until the seventh day. On the external surface of a mask, the transmissible virus was detected even on the seventh day [6]. However, sufficient data on the transmissibility of the virus in the oral cavity or saliva of patients with COVID-19 or on the transmissibility and stability of the virus in aerosols generated in the oral cavity have not been accumulated. The results and data from future studies are awaited.

3.2. Characteristics of surgical procedures in oral and maxillofacial areas

Oral and maxillofacial surgery is a clinical field that treats congenital and acquired diseases occurring in the oral cavity, jaw, face, and adjacent tissues (refer to the home page of the Japanese Society of Oral and Maxillofacial Surgeons [https://www.jsoms.or.jp/]. This guide scopes all surgery associated with the treatment of oral and maxillofacial areas. The range of treatment varies widely, including tooth extraction, dental implant placement, incisional drainage of intraoral and extraoral abscesses, resection of jaw cysts, resection of oral cancer, jaw fracture surgery, maxillary and mandibular osteotomy, mandibular joint surgery, and cleft lip/cleft palate surgery.

During the surgical procedures in oral and maxillofacial areas, surgeons and assistants may be exposed to SARS-CoV-2 through contact with the oral cavity, nasal cavity, or body fluid. Furthermore, those surgical procedures are performed with devices that may generate aerosols. For example, a dental high-speed turbine/micromotor handpiece used for extraction of impacted teeth; implanter (dental implant motor) used for dental implant place-

ment; bone saw, bone drill, and ultrasonic bone scalpel used for osteotomy; electrocautery/laser used for incision of soft tissue and hemostasis in the surgery of tumors and other procedures. There are concerns that because aerosols generated by these devices are easily mixed with saliva, blood, or other fluids of patients, the resultant aerosols may contaminate the air and objects in the vicinity and increase the risk of nosocomial infection of COVID-19. As described above, the field of oral and maxillofacial surgery is exposed to greater risk of COVID-19 than other clinical fields. Therefore, appropriate risk management is essential.

3.3. Range covered with the guide

This guide is based on the SRs of academic articles that were conducted as of September 7, 2020 and have been prepared in consideration of information from related academic societies, the government, and media reports on the epidemic situation and the virus.

Although we took all possible measures to ensure the accuracy of information available at the time of preparation of this guide, the Japanese Society of Oral and Maxillofacial Surgeons shall not be liable for any damages or disadvantages caused by the consideration/implementation of various measures based on this guide (including lost benefits and various expenses).

3.4. References

[1] Spinato G, Fabbris C, Polesel J, Cazzador D, Borsetto D, Hopkins C et al. Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection JAMA, 323 (2020), pp. 2089–2090

[2] Fan N, Fan W, Li Z, Shi M, Liang Y Imaging characteristics of initial chest computed tomography and clinical manifestations of patients with COVID-19 pneumonia Jpn J Radiol, 38 (2020) pp. 533–538

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[4] Li H, Liu Z, Ge J Scientific research progress of COVID-19/SARS-CoV-2 in the first five months J Cell Mol Med, 24 (2020), pp. 6558–6570

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[6] Chin AWH, Chu JTS, Perera MRA, Hui KPY, Yen HL, Chan MCW et al. Stability of SARS-CoV-2 in different environment conditions Lancet Microbe, 1 (2020), pp. e10.

4. Recommendations

4.1. CQ1: Is SARS-CoV-2 in saliva transmissible?

4.1.1. Recommendation

Saliva contains transmissible SARS-CoV-2.

4.1.2. Evidence level and recommended grade

Evidence level: D (very low)

Recommended grade: Weakly recommended

4.1.3. Comment

None of the 25 articles identified by the search strategy indicated that transmissible SARS-CoV-2 was detected in saliva. All accessed articles indicated that the nucleic acid of SARS-CoV-2 was amplified from saliva samples by PCR, instead of detection of transmissible virus [1–9]. All those articles reported a comparison of the positive rate and sensitivity of PCR test for the detection of nucleic acid of SARS-CoV-2 between saliva and nasopharyngeal swab samples. In addition, no study described in this SR met the requirements for an RCT. However, given that the PCR test for the detection of viral nucleic acids in nasopharyngeal swab samples is the standard test to confirm infection with SARS-CoV-2 even before the COVID-19 pandemic, those articles may provide indirect evidence that the viral load in saliva is comparable with that in a nasopharyngeal swab sample.

In the report of a study conducted including 70 patients with confirmed COVID-19, the number of RNA copies (expressed as the logarithmic value) of SARS-CoV-2 was 5.58 in 1 mL of saliva collected by the patients themselves and 4.93 in nasopharyngeal swab samples. This study showed that the amount of SARS-CoV-2 contained in saliva might be comparable with or exceed the amount contained in nasopharyngeal swab samples [1].

Similarly, a study comparing the cycle threshold (Ct) values, which are derived from the number of PCR cycles, suggested that the amount of viral nucleic acid contained in saliva is comparable with that contained in nasopharyngeal swab samples [2]. On the other hand, among reports on PCR testing using nasopharyngeal swab samples, a study using cultured Vero E6 cells to detect transmissible SARS-CoV-2 showed that the detection rate of transmissible SARS-CoV-2 with a Ct value of >35 decreased to 8.3 %. This suggests that a low Ct value corresponds to a large amount of transmissible SARS-CoV-2 [10]. When PCR test was performed with saliva samples, the Ct values were 25–30 in many cases [2]. This may indicate the presence of transmissible SARS-CoV-2 in saliva.

In a study that included 103 Japanese patients with COVID-19 (88 symptomatic and 15 asymptomatic patients), 81.6 % had positive PCR test using saliva samples [6]. In this study, an antigen test for SARS-CoV-2 was simultaneously performed with saliva samples and yielded a positive rate of 11.7 %. Despite the low detection rate, detection of antigens may suggest the presence of viable virus in the saliva.

The positive rates for PCR testing using saliva samples were 64 % in asymptomatic patients and 81 % in symptomatic patients, whereas the positive rates for PCR testing using nasopharyngeal swab samples were 62 % in asymptomatic patients and 100 % in symptomatic patients. While PCR testing using saliva samples is as sensitive as PCR testing using nasopharyngeal swab samples, the viral load in saliva is suggested to be higher in symptomatic patients than in asymptomatic patients [8].

In addition, when the PCR test was performed with supernatant from Vero cells dissolved by adding patient samples (urine, saliva, and feces), “transmissible” SARS-CoV-2 was detected in the saliva samples from two of five patients with COVID-19 [11]. Despite the small sample size, this study may have demonstrated the presence of transmissible SARS-CoV-2 in saliva.

If SARS-CoV-2 exists in saliva, there is the question of which part of the oral cavity the virus is localized in.

According to an article that was not selected during this search [12], by immunostaining, it was demonstrated that the protein of ACE2 receptor, the receptor used by SARS-CoV-2 to bind to and invade the human cells, is expressed in human labial and submandibular glands. This suggests that SARS-CoV-2 is excreted in the saliva. Although this article indicated that ACE2 receptors were not expressed in the epithelial cells of the human lingual mucosa, another article [13] reported that genetic analysis showed expression of ACE2 receptor gene in the cells of the gingiva, buccal mucosa, and tongue. In summary, saliva may satisfy the conditions for accumulation of SARS-CoV-2.

4.1.4. Systematic review

Database: PubMed

Number of identified articles: 250

Date of search: September 7, 2020

Search strategy:

((Bites OR bitten OR spit OR spat OR spitting OR saliva)) and (((coronavirus OR "corona virus" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak))) OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) or ((sars-cov2 or covid-19) and saliva) or ((sars-cov2 or covid-19) ace2 mouth)

Screening

Article	Study Design	P	I	C	O	Comment
Wyllie AL et al. Saliva or Nasopharyngeal Swab Specimens for Detection of SARS-CoV-2. N Engl J Med. 2020 Aug 28. doi: https://doi.org/10.1056/NEJMc2016359.	Case control	* 70 symptomatic patients with positive PCR results from nasopharyngeal swab samples. * 495 asymptomatic health care workers.	Saliva collected by patients	Nasopharyngeal swab	* The number of viral copies (logarithmic value) is higher in saliva (5.58 vs 4.93). * The positive rates for the first 10 days after the diagnosis were 81 % for saliva and 71 % for nasopharyngeal swab. * Variation in viral load due to sample collection was smaller for saliva. * Of 495 patients, 13 had positive saliva, and 9 had positive nasopharyngeal swab.	This article indicates that saliva is more effective for viral detection than nasopharyngeal swab. The presence of viral nucleic acid in saliva of COVID-19 patients was demonstrated. However, the article does not indicate whether the virus is transmissible.
Rao M et al. Comparing nasopharyngeal swab and early morning saliva for the identification of SARS-CoV-2. Clin Infect Dis. 2020 Aug 6:ciaa1156. doi: https://doi.org/10.1093/cid/ciaa1156.	prospective case control	217 asymptomatic men aged ≥18 years who tested positive by nasopharyngeal swab at a quarantine center of one hospital	2 mL self-collected Saliva before gargling or breakfast in the morning. Saliva was pooled in the pharynx and expectorated.	Nasopharyngeal swab (NPS)	Of 217 men, 160 tested positive by either saliva or NPS. Of 160 men, the positive detection rate was higher for saliva (93.1 %) than for NPS (52.5 %). * Based on Ct values, saliva contained a larger amount of viral nucleic acid.	The conclusion that saliva is associated with a higher detection rate than NPS is indicative of the viral presence in saliva. However, the samples used were described as deep throat saliva, which was not considered as genuine oral saliva.
Landry ML et al. Challenges in use of saliva for detection of SARS CoV-2 RNA in symptomatic outpatients. J Clin Virol. 2020 Jul 31;130:104567. doi: https://doi.org/10.1016/j.jcv.2020.104567.	Prospective observational study	124 American patients with respiratory symptoms (drive-through)	Viral detection in saliva samples	Viral detection in nasopharyngeal swab samples	The sensitivity was 94.3 % for nasopharyngeal swab (33/35) and 85.7 % for saliva (30/35).	The sample size is small, and the study is not an RCT.
Lai CKC et al. Prospectivestudy comparing deep-throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease (COVID-19). J Infect Dis. 2020 Aug 1:jiaa487. doi:https://doi.org/10.1093/infdis/jiaa487	Prospective observational study	50 positive patients in Hong Kong:	Viral detection in saliva samples (deep throat saliva) and sputum: longitudinal collection of multiple, parallel samples for ≥23 days e after the onset	Nasopharyngeal swab samples: longitudinal collection of multiple, parallel samples for ≥23 days after the onset	The saliva samples showed the lowest positive rate of 68.7 % (89.4 % for sputum and 80.9 % for nasopharyngeal swab). They also showed the lowest viral load. The viral load in saliva correlated with that in sputum. The false-negative rate for saliva was estimated to be 31.3 %, which was 2.7 times higher than the false-negative rate for sputum.	The study is not an RCT. Sample collection was synchronized across saliva, nasopharyngeal swab, and sputum samples in approximately 1/3 of the patients.
Jeong HW et al. Viable SARS-CoV-2 in various specimens from COVID-19 patients. Clin Microbiol Infect. 2020 Nov;26(11):1520–1524. doi: https://doi.org/10.1016/j.cmi.2020.07.020.	Prospective observational study	5 COVID-19-positive Chinese patients	Swab, saliva, urine, fecal, and serum samples were collected on days 8, 11, 13, 15, and 30 and examined for the transmissibility of the virus.	Swab, saliva, urine, fecal, and serum samples were collected on days 8, 11, 13, 15, and 30 and examined for the transmissibility of the virus.	The viral loads in urine, saliva, and feces were comparable with or higher than the viral load in nasal swab. Transmissible virus was detected in the nasal cavity and saliva during the period from day 11–15.	The sample size is small, and the study is not an RCT. However, it is one of a few studies on transmissibility.

Fakheran O et al. Saliva as a diagnostic specimen for detection of SARS-CoV-2 in suspected patients: a scoping review. Infect Dis Poverty. 2020 Jul 22;9(1):100. doi: https://doi.org/10.1186/s40249-020-00728-w.	Systematic review	305 articles → 9 articles	Saliva was compared with nasal swab to determine the usefulness of saliva.	The detection rate was compared between saliva and nasal swab.	No significant difference in detection rate was observed between saliva and sputum samples.	This basically small-scale systematic review included 9 articles of prospective observational studies. In this review, neither disease stage nor severity was taken into account.
Nagura-Ikeda M et al. Clinical Evaluation of Self-Collected Saliva by Quantitative Reverse Transcription-PCR (RT-qPCR), Direct RT-qPCR, Reverse Transcription-Loop-Mediated Isothermal Amplification, and a Rapid Antigen Test To Diagnose COVID-19. J Clin Microbiol. 2020 Aug 24;58(9):e01438-20. doi: https://doi.org/10.1128/JCM.01438-20.	Prospective observational study	103 COVID-19-positive Japanese patients	Saliva samples collected on admission and at each disease stage (i.e., asymptomatic, early, and late [from 9 days after the onset] stages)	The sensitivity was compared among real time (RT) PCR, laboratory-developed test (LDT), cobas SARS-CoV-2 test, direct RT-quantitative PCR (qPCR), LAMP test, and rapid antigen test. The detection rate was compared among disease stages.	The detection rates for reverse transcription (RT)-PCR-based tests were 50.5%–81.6%. The detection rate for antigen test was 11.7%. The highest detection rate was observed within the first 9 days after the onset (65.6 %–93.4 %), and the rate started decreasing on day 10 (22.2 %–66.7 %). Asymptomatic patients accounted for 40%–66.7%.	The study is not an RCT.
Jamal AJ et al. Sensitivity of nasopharyngeal swabs and saliva for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Clin Infect Dis. 2020 Jun 25:ciaa848. doi: https://doi.org/10.1093/cid/ciaa848.	Prospective study of unknown type	91 COVID-19 patients admitted to 6 hospitals in Toronto	Saliva samples were consecutively collected 4 times with a 3 -h interval, and the viral positive rate of RT-PCR was assessed.	Airway samples (nasopharyngeal swabs) were collected in pairs with saliva samples for comparison of the positive rate.	The sensitivity of viral detection in nasopharyngeal swab and saliva was 89 % and 72 %, respectively. The greatest difference in sensitivity was observed in the late stage of infection.	
Chau NVV et al. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection Clin Infect Dis. 2020 Jun 4:ciaa711. doi: https://doi.org/10.1093/cid/ciaa711.	Prospective study	30 hospitalized patients with confirmed COVID-19 who consented to the study	RT-PCR was performed with nasopharyngeal swab and saliva samples to detect SARS-CoV-2 RNA.	As the nasopharyngeal swab was used as a control, symptomatic and asymptomatic patients were compared.	SARS-CoV -2 RNA was detected in 20 of 27 available saliva samples (74 %). It was detectable in 64 % of asymptomatic patients and 81 % of symptomatic patients. It was detected in 25 of 30 nasopharyngeal swab samples (83.3 %). It was detectable in 62 % of asymptomatic patients and 100 % of symptomatic patients.	
Pasomsub E et al. Saliva sample as a non-invasive specimen for the diagnosis of coronavirus disease 2019: a cross-sectional study. Clin Microbiol Infect. 2020 May 15:S1198-743X(20)30278-0. doi:https://doi.org/10.1016/j.cmi.2020.05.001.	Prospective observational study	200 Thai patients with acute respiratory symptoms	Viral detection in saliva samples (RT-PCR).	Viral detection in nasopharyngeal swab samples (RT-PCR)	For saliva, the sensitivity was 84.2 %, and the specificity was 98.9 %. The concordance rate with nasopharyngeal swab was 97.5 %.	This study is not an RCT but shows that a saliva sample is useful for detection of COVID-19.
To KK et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis. 2020 May;20(5):565–574. doi: https://doi.org/10.1016/S1473-3099(20)30196-1.	Retrospective observational study	23 COVID-19 patients in Hong Kong	Viral detection in oropharyngeal saliva samples (RT-PCR).	Serum samples. (Detection of anti-SARS-CoV-2 nucleocapsid protein [NP] antibody or anti-SARS-CoV-2 pyrrolobenzodi-azepine [RBD] antibody)	COVID-19 was detected in 87 % of the patients (20/23). The highest viral load was observed during the first week of hospitalization. The seropositive rates at ≥14 days after symptom onset were 94 % for anti-NP immunoglobulin (Ig) G, 88 % for anti-NP IgM, and 100 % for anti-NP IgM.	The sample size is small, and the study is not an RCT.

Czumbel LM et al. Saliva as a Candidate for COVID-19 Diagnostic Testing: A Meta-Analysis. Front Med (Lausanne). 2020 Aug 4;7:465. doi: https://doi.org/10.3389/fmed.2020.00465.	Meta-analysis	96 articles → 6 articles; 123 COVID-19 patients	Viral detection in saliva samples	Viral detection in nasopharyngeal swab samples	The sensitivity of test using saliva was 91 %.	The meta-analysis did not include any RCT. It included only case reports and prospective/retrospective observational studies. The authors were unable to construct any 2 × 2 contingency table for calculation of sensitivity and specificity. In other words, they stated that the specificity was unknown. (2 articles showed a specificity of approximately 98 %.)

Systematic review	
Clinical context	Refer to the Comment (Section 4.1.3).
Summary on indirectness	There are few reports of direct studies on transmissibility, and direct assessment of transmissibility is a future issue.
Summary on the bias risk	The accumulation of findings is so limited that selection bias and other bias risks cannot be avoided.
Summary on the inconsistency and other issues	No apparent inconsistency was found.
Comment	None.

4.1.5. References

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[3] Landry ML, Criscuolo J, Peaper DR Challenges in use of saliva for detection of SARS CoV-2 RNA in symptomatic outpatients J Clin Virol, 130 (2020), pp.104567

[4] Lai CKC, Chen Z, Lui G, Ling L, Li T, Wong MCS et al. Prospectivestudy comparing deep-throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease (COVID-19) J Infect Dis, 222 (2020), pp.1612–1619

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[8] Chau NVV, Thanh Lam V, Thanh Dung N, Yen LM, Minh NNQ, Hung LM et al. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection Clin Infect Dis, 71 (2020), pp. 2679–2687

[9] Pasomsub E, Watcharananan SP, Boonyawat K, Janchompoo P, Wongtabtim G, Suksuwan W et al. Saliva sample as a non-invasive specimen for the diagnosis of coronavirus disease 2019: a cross-sectional study Clin Microbiol Infect, 285 (2021), pp. 285.e1–285.e4

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[11] Jeong HW, Kim SM, Kim HS, Kim YI, Kim JH, Cho JY et al. Viable SARS-CoV-2 in various specimens from COVID-19 patients Clin Microbiol Infect, 26 (2020), pp.1520–1524

[12] Usami Y, Hirose K, Okumura M, Toyosawa S, et al. Immunohistochemical detection of ACE2 in human salivary gland Oral Sci Int, (2020), pp.10.1002/osi2.1085

[13] Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa Int J Oral Sci, 12 (2020), pp.8

[14] Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals Nature, 582 (2020), pp. 557-560.

4.2. CQ2: How many days should pass after contracting COVID-19 before surgical procedures in oral and maxillofacial areas can be performed for COVID-19-infected patients without the concern of hospital-acquired infection?

4.2.1. Recommendation

Until findings accumulate on the loss of transmissibility of SARS-CoV-2 in the oral cavity and the safety of oral and maxillofacial surgery, patients with history of COVID-19 or those with history of a positive PCR test result for SARS-CoV-2 should be treated as patients with COVID-19, regardless of the latest assessment result.

4.2.2. Evidence level and recommended grade

Evidence level: D (very low)

Recommended grade: Strongly recommended

4.2.3. Comment

There are no articles that correspond to this CQ. Thus, the evidence level is D (low), and the effect estimate is almost unconvincing. The latent period of SARS-CoV-2 ranges from 1 to 14 days, and symptoms often appear approximately 5 days after exposure [1]. SARS-CoV-2 appears to proliferate in the upper and lower respiratory tracts. In severe cases, the viral load is high, and the viral shedding duration also tends to be long. Detection of pathogenic genes at 3–4 weeks after onset is not rare [2]. However, the detection of pathogenic genes is not synonymous with the presence of transmissible virus. The infectious period is assumed to be from 2 days before the onset to approximately 7–10 days after the

onset (or before isolation in strict epidemiological studies) [2]. In fact, according to the "Guidelines for the Treatment of Coronavirus Disease 2019 (COVID-19), version 4.1" (https://www.mhlw.go.jp/content/000712473.pdf) [3] issued by the Japanese Ministry of Health, Labor, and Welfare, the target day for hospital discharge is set as the tenth day after the onset. It is considered that viral transmissions in daily life should have reduced or stopped by this time.

However, perceptions on the infective potential differ between that in daily life conditions and in the field of oral surgery, where medical professionals may directly touch the oral cavity or saliva of patients and be exposed to aerosolized transmissible virus generated during treatment or surgery. At present, there are no articles that clearly indicate the duration of transmissibility in treatment and procedures of oral and maxillofacial surgery. Thus, in terms of ensuring safety, we have concluded that it is preferable to regard previously infected patients as patients with COVID-19, in other words, those with a positive result of COVID-19, regardless of the latest assessment result, until findings accumulate. Despite the lack of articles corresponding to the CQ, we consider that the benefits of strict infection control in surgical procedures in oral and maxillofacial surgery outweigh the risks associated with reduced opportunities for patients to undergo surgery due to rigorous compliance with conditions for safe performance of surgery. Thus, we regarded the recommended grade as strongly recommended.

4.2.4. Systematic review

Database: PubMed

Number of identified articles: 218

Date of search: September 7, 2020

Filters: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Systematic Review, English

Search strategy:

(((coronavirus OR "corona virus" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak))) OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) AND (("pathogenicity" [Subheading] OR infectivity[Text Word]) OR (transmissibility))) or ((covid 19 or sars-cov-2) and (viral load detection infectivity))

Screening: There were no relevant articles identified by the second screening.

Systematic review: No SR was conducted because of the lack of articles identified by the second screening.

4.2.5. References

[1] US Centers for Disease Control and Prevention (CDC)-related home page: Incubation period https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html#:-:text=The%20incubation%20period%20for%20COVID,from%20exposure%20to%20symptoms%20onset.&text=One%20study%20reported%20that%2097.5,SARS%2DCoV%2D2%20infection.

[2] WHO-related home page: Transmission of SARS-CoV-2: Implications for infection prevention precautions Scientific Brief July 9 2020 https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions

[3] The Guidelines for the Treatment of the Novel Coronavirus Disease 2019 (COVID-19), version 4.1https://www.mhlw.go.jp/content/000712473.pdf

4.3. CQ3: Are SARS-CoV-2 PCR tests and/or chest CT useful for preoperative assessment for surgical procedures in oral and maxillofacial areas?

4.3.1. Recommendation

Real-time PCR or quantitative antigen test using nasopharyngeal swab samples is a useful method to determine whether patients are infected with COVID-19 before surgical procedures in oral and maxillofacial areas.

4.3.2. Evidence level and recommended grade

Evidence level: B (moderate)

Recommended grade: Strongly recommended

4.3.3. Comment

When a patient is from an epidemic zone or may be infected with COVID-19, it is necessary to examine such before surgical procedures and treatment of oral and maxillofacial areas, whether they are infected with the virus. The applicable tests include nucleic acid detection tests (e.g., real-time PCR and LAMP tests), antigen tests, antibody tests, and chest CT. According to the latest "Guidelines for Testing of the Pathogen Causing Coronavirus Disease 2019 (COVID-19) (Version 1)" [1], PCR is a very reliable test for the detection of SARS-CoV-2 at present, followed by the LAMP test. A quantitative antigen test is also considered practicable. Although the sensitivity and specificity vary among different types of PCR tests, they are generally considered to have a sensitivity of ≥90 % and a specificity of almost 100 % [2–4].

For symptomatic patients, it is recommended to perform nucleic acid detection tests or quantitative antigen tests with nasopharyngeal swab, nasal swab, or saliva samples [1]. However, when these tests are performed with saliva samples, attention should be paid to the low detection rate of these tests from 10 days after the onset.

For asymptomatic patients, it is recommended to perform PCR test or quantitative antigen test with nasopharyngeal swab or saliva samples [1]. Nasal swabs are not recommended. The LAMP test is reported to yield false-positive results depending on the type of samples, such as saliva.

Although saliva is an easy-to-use sample for the dentists and oral surgeons, the test results may be affected by eating, drinking, toothbrushing, and gargling. It is preferable to avoid the collection of saliva immediately after gargling. After eating, drinking, and toothbrushing, it is preferable to allow an interval of approximately 30 min before the collection of saliva, if possible [1].

Chest CT is used for the screening of COVID-19 because even asymptomatic patients with COVID-19 frequently present with characteristic findings. However, based on meta-analyses of patients with confirmed or suspected COVID-19, CT is reported to have a high sensitivity of 62 % to ≥90 %, but a low specificity of 25%–46% [4–13]. Because of the high false-positive rate, CT is commonly viewed as unsuitable for the screening of infected patients. In addition, a study of asymptomatic hospitalized patients in a non-endemic area reported that both the sensitivity and positive predictive value were 0% [14]. Based on these results, screening with chest CT is not recommended, especially in non-endemic areas.

Preoperative tests should preferably be performed at the shortest possible interval before surgery.

4.3.4. Systematic review

Database: PubMed

Number of identified articles: 212

Date of search: September 7, 2020

Filters: Meta-Analysis, Randomized Controlled Trial, Systematic Review, English

Search strategy:

((((coronavirus OR "corona virus" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak))) OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) and ((molecular diagnostic techniques/) or (exp Nucleic Acid Amplification Techniques/) or (PCR or (Polymerase and "Chain Reaction") or nucleic acid) or (radiography, thoracic/ or exp Tomography, X-Ray Computed/ or (radiograph or tomograph or x ray or xray or chest ct or ct imag or ct scan)) or (imaging and (feature or finding)) or (exp diagnosis/)) or ((COVID-19 diagnostic testing and (PCR or CT)) or ((covid 19 or sars-cov-2) PCR CT effectiveness diagnosis)

Screening

Article	Study Design	P	I	C	O	Comment
Tsikala Vafea M et al. Chest CT findings in asymptomatic cases with COVID-19: a systematic review and meta-analysis. Clin Radiol. 2020 Nov;75(11):876.e33–876.e39. doi: https://doi.org/10.1016/j.crad.2020.07.025.	Systematic review & meta-analysis	231 early asymptomatic patients positive for COVID-19. (they are only described as test-positive patients. It is unknown which test, PCR or antibody test, was performed.)	CT		63 % of early asymptomatic patients (95 % confidence interval [CI]: 44 %–78 %) had positive CT scans. 62% of late asymptomatic patients (95% CI: 38 %–81 %) had positive CT scans. 90% of late asymptomatic patients (95% CI: 49 %–99 %) had positive CT scans. CT is recommended for the diagnosis of COVID-19 because positive CT scans are frequently observed even in asymptomatic patients.	Of 1781 studies, 7 studies with 231 patients were analyzed. Studies targeting only early asymptomatic patients were evaluated.
Awulachew E et al. Computed Tomography (CT) Imaging Features of Patients with COVID-19: Systematic Review and Meta-Analysis. Radiol Res Pract. 2020 Jul 23;2020:1023506. doi: https://doi.org/10.1155/2020/1023506.	Systematic review & meta-analysis	5041 COVID-19-positive patients (unknown whether the positivity was determined by PCR)	CT		98 % of COVID-19-positive patients had some abnormal CT findings. 65 % showed ground glass opacity (GGO). 18 % showed mixed pattern GGO. 22 % of patients with COVID-19 pneumonia showed consolidation. The bilateral onset is common.	Of 241 studies, 60 were included in meta-analysis. Analyses were performed based on the presence or absence of CT findings and frequency of each CT finding in COVID-19-positive patients.
Kumar J et al. Radiological Findings of COVID-19 in Children: A Systematic Review and Meta-Analysis. J Trop Pediatr. 2020 Jul 21:fmaa045. doi: https://doi.org/10.1093/tropej/fmaa045.	Systematic review & meta-analysis	923 patients aged <19 years who were diagnosed with COVID-19 (unknown which test was performed)	CT	Chest radiography and chest ultrasonography (US)	Chest CT was the most common modality (96.1 %), followed by chest radiography (8.2 %) and chest US (3%). Chest CT showed no abnormal findings in 1/3 of patients and 19 % of even symptomatic patients.	The systematic review included 46 of 1984 articles. The frequency of various imaging examinations was compared in children with COVID-19.
Böger B et al. Systematic review with meta-analysis of the accuracy of diagnostic tests for COVID-19. Am J Infect Control. 2020. https://doi.org/10.1016/j.ajic.2020.07.011	Systematic review & meta-analysis	2229 COVID-19 patients	CT and PCR	Antibody test	CT showed a high sensitivity of 91.9 % (low specificity of 25.1 %). The sensitivity of antibody test is 84.5 % for IgM and 91.6 % for IgG. PCR test using sputum showed the highest sensitivity of 97.2%.	Of 1534 articles, 16 were analyzed. PCR using sputum is the gold standard.
Shao JM et al. Systematic Review of CT Chest in COVID-19 Diagnosis and its Potential Application in a Surgical Setting. The Association of Coloproctology of Great Britain and Ireland, 2020;22:993–1001.	Systematic review	3186 patients with suspected COVID-19	CT	PCR	Overall sensitivity of CT scan ranged from 57 %–100 % for symptomatic and 46 %–100 % for asymptomatic COVID-19 patients, while that of RT-PCR ranged from 39 %–89 %.	Of 290 articles, 20 were analyzed. This systematic review aimed to verify the superiority of CT to PCR. CT is not recommended for asymptomatic patients because the sensitivity of CT is higher in symptomatic patients but lower in asymptomatic patients than the sensitivity of PCR.

Altmayer S et al. Comparison of the computed tomography findings in COVID-19 and other viral pneumonia in immunocompetent adults: a systematic review and meta-analysis. Eur Radiol. 2020 Dec;30(12):6485–6496. doi: https://doi.org/10.1007/s00330-020-07018-x.	Systematic review & meta-analysis	1911 patients with viral pneumonia (COVID-19, n = 934; non-COVID-19, n = 977)	CT	In both patients with COVID-19 pneumonia and those with non-COVID-19 pneumonia, common findings are GGO, mixed pattern GGO, and consolidation. These findings overlap.	Of 2936 articles, 33 were analyzed. Findings commonly appear in the upper and middle lobes in COVID-19 pneumonia and in the lower lobe in non-COVID-19 pneumonia. However, because many findings overlap, caution should be exercised when CT is performed as a first-line test.
Shelmerdine SC et al. Coronavirus disease 2019 (COVID-19) in children: a systematic review of imaging findings Pediatr Radiol. 2020; 50(9): 1217–1230.	Systematic review	Only 431 patients aged <18 years (confirmed diagnosis from a positive PCR result)	CT	CT was performed in 421 of 431 patients (97.7 %). Normal CT findings were observed in 143/421 patients (34.0 %).	This systematic review included 22 articles. CT is not recommended for children, except those with severe conditions.
Waller JV et al. The Limited Sensitivity of Chest Computed Tomography Relative to Reverse Transcription Polymerase Chain Reaction for Severe Acute Respiratory Syndrome Coronavirus-2 Infection: A Systematic Review on COVID-19 Diagnostics. Invest Radiol. 2020;55(12):754–761.	Systematic review & meta-analysis	9610 patients with COVID-19 detected by CT or PCR (Asymptomatic patients were included. Studies on only children were excluded.)	CT and PCR performed in COVID-19 patients	The sensitivity reported by biased studies was 70 % for PCR (4 studies) and 94 % for CT (24 studies). The sensitivity reported by unbiased studies was 78 % for PCR and 75% for CT.	Meta-analysis was performed on 37 of 641 studies (including 4 unbiased studies on PCR and 10 unbiased studies on CT).
Adams HJA et al. Systematic Review and Meta-Analysis on the Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19): Sol Scientiae, Illustra Nos. AJR Am J Roentgenol. 2020 Dec;215(6):1342–1350.	Systematic review & meta-analysis	1431 high-risk patients with clinically suspected COVID-19	CT performed in COVID-19 patients	The COVID-19-positive patients accounted for 47.9 %. The sensitivity was 94.6 % (92.9 %–97.0 %), and the specificity was 46.0% (25.0 %–71.9 %). In symptomatic patients at high risk of COVID-19, the sensitivity was high, but the specificity was low.	Meta-analysis included 6 articles.
Xu B et al. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. Eur Radiol. 2020 Oct;30(10):5720–5727.	Systematic review & meta-analysis	3186 patients with COVID-19 detected by CT or PCR	CT and PCR performed in COVID-19 patients	The sensitivity was 92 % (95 % CI: 86 %–96 %). The specificity reported by 2 studies was 25% (95% CI: 22 %–30 %) and 33% (95% CI: 23 %–44 %).	16 articles were reviewed. There are descriptions of 36 patients who were found negative by PCR and positive by CT.
Kim H et al. Diagnostic Performance of CT and Reverse Transcriptase Polymerase Chain Reaction for Coronavirus Disease 2019: A Meta-Analysis. Radiology. 2020 Sep;296(3):E145-E155.	Systematic review & meta-analysis	COVID-19 patients (6218 patients detected by CT and 1502 patients detected by PCR)	CT performed in COVID-19 patients	The sensitivity was 94 % (95 % CI: 91 %–96 %; I2 = 95%) for CT and 89% (95% CI: 81 %–94 %; I2 = 90%) for PCR. The specificity of CT was 37% (95% CI: 26 %–50 %; I2 = 83%). Chest CT is not recommended for initial screening in areas with a low prevalence of COVID-19 because of its false-positive rate.	63 articles on CT and 19 articles on PCR were reviewed.

Duarte ML et al. Reverse-transcriptase polymerase chain reaction versus chest computed tomography for detecting early symptoms of COVID-19. diagnostic accuracy systematic review and meta-analysis. Sao Paulo Med J. 2020;138(5):422–432.	Meta-analysis	1204 patients (5 articles) with suspected COVID-19 who underwent chest CT and RT-PCR during the first week after symptom onset (quoted as follows: "The participants were men and women of all ages with suspected COVID-19 who underwent chest CT and RT-PCR during their first week of symptoms.")	Chest CT was performed.	RT-PCR was performed.	The sensitivity was favorable.	RT-PCR had a sensitivity of 81.4 %, a specificity of 100 %, and an accuracy of 92.3 %, whereas chest CT had a sensitivity of 95.3 %, a specificity of 43.8 %, and an accuracy of 63.3 %. Although the sensitivity is higher for chest CT, attention should be paid to its low specificity.

Systematic review

Clinical context	Refer to the Comment (Section 4.3.3).
Summary on indirectness	Because there are no studies on patients undergoing surgical procedures in oral and maxillofacial areas, the issue of indirectness remains.
Summary on the bias risk	The accumulation of findings is so limited that the risk of selective outcome reporting and other risks cannot be avoided.
Summary on the inconsistency and other issues	No apparent inconsistency was found.
Comment	None.

4.3.5. References

[1] Guidelines for Testing of the Pathogen Causing Coronavirus Disease 2019 (COVID-19) (Version 1).https://www.mhlw.go.jp/content/000678571.pdf (December 7, 2020)

[2] Kazuhiro T. COVID-19 testing methods and interpretation of results. Retrieved from 12 2020 http://www.kansensho.or.jp/uploads/files/topics/2019ncov/covid19_kensakekka_201012.pdf.

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[6] Awulachew E, Diriba K, Anja A, Getu E, Belayneh F Computed Tomography (CT) Imaging Features of Patients with COVID-19: Systematic Review and Meta-Analysis Radiol Res Pract, (2020), pp.1023506

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[8] Shelmerdine SC, Lovrenski J, Caro-Domínguez P, Toso S; Collaborators of the European Society of Paediatric Radiology Cardiothoracic Imaging Taskforce Coronavirus disease 2019 (COVID-19) in children: a systematic review of imaging findings Pediatr Radiol, 50 (2020), pp.1217–1230

[9] Waller JV, Allen IE, Lin KK, Diaz MJ, Henry TS, Hope MD The Limited Sensitivity of Chest Computed Tomography Relative to Reverse Transcription Polymerase Chain Reaction for Severe Acute Respiratory Syndrome Coronavirus-2 Infection: A Systematic Review on COVID-19 Diagnostics Invest Radiol, 55 (2020), pp.754–761

[10] Adams HJA, Kwee TC, Yakar D, Hope MD, Kwee RM Systematic Review and Meta-Analysis on the Value of Chest CT in the Diagnosis of Coronavirus Disease (COVID-19): Sol Scientiae, Illustra Nos. AJR Am J Roentgenol, 215 (2020), pp.1342–1350

[11] Xu B, Xing Y, Peng J, Zheng Z, Tang W, Sun Y et al. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy Eur Radiol, 30 (2020), pp.5720–5727

[12] Kim H, Hong H, Yoon SH Diagnostic Performance of CT and Reverse Transcriptase Polymerase Chain Reaction for Coronavirus Disease 2019: A Meta-Analysis Radiology, 296 (2020), pp. E145-E155

[13] Duarte ML, Santos LRD, Contenças ACS, Iared W, Peccin MS, Atallah ÁN Reverse-transcriptase polymerase chain reaction versus chest computed tomography for detecting early symptoms of COVID-19. A diagnostic accuracy systematic review and meta-analysis Sao Paulo Med J, 138 (2020), pp.422–432

[14] Uchida S, Uno S, Uwamino Y, Hashimoto M, Matsumoto S, Obara H et al. CT screening for COVID-19 in asymptomatic patients before hospital admission J Infect Chemother, 27(2021), pp.232-236

4.4. CQ4: Is mouth wash/mouth rinse with povidone-iodine immediately before surgical procedures in oral and maxillofacial areas effective for reducing the risk of COVID-19 transmission?

4.4.1. Recommendation

To reduce the risk of contracting COVID-19 for surgeons and assistants, patients should wash/rinse their mouth with povidone-iodine immediately before surgery.

4.4.2. Evidence level and recommended grade

Evidence level: D (very low)

Recommended grade: Weakly recommended

4.4.3. Comment

At present, it is unknown to what extent povidone-iodine mouth wash/mouth rinse performed by patients immediately before surgery contributes to the prevention of viral transmission from patients with COVID-19 to surgeons and assistants. In the SR conducted by the subcommittee, no research articles providing direct answers were found. However, we decided to "weakly recommend" mouth wash/mouth rinse with povidone-iodine because it is easy

and cheap, is associated with low risk, and may transiently reduce the viral load in saliva. We provide evidence for our decision as follows.

It has been demonstrated that mouth wash/mouth rinse with an antimicrobial solution (e.g., chlorhexidine gluconate, essential oil-containing mouth wash/mouth rinse, or cetylpyridinium chloride) before dental treatment reduces the bacterial load in aerosols (note: not viral load) [1]. Aerosols generated during dental treatment contain oral bacteria, and these bacteria are reduced by mouth wash/mouth rinse with an antimicrobial solution before dental treatment. Thus, mouth wash/mouth rinse with an antiviral solution against SARS-CoV-2 in saliva may reduce aerosolized SARS-CoV-2.

SARS-CoV-2, which has an envelope, is generally sensitive to disinfectants. Among disinfectants available as mouth wash/mouth rinse, povidone-iodine is the first-choice agent that is expected to have an antiviral effect. Povidone-iodine is a gargle that can be prescribed and has been widely used in Japan. Except for patients who are allergic to it, it appears to be safe to use for a "single application" such as preoperative mouth wash/mouth rinse.

Multicenter in vitro studies have demonstrated the antiviral activity of povidone-iodine on SARS-CoV-2 [2–5]. Although the concentration and duration of action of povidone-iodine varied among studies, the results showed that "SARS-CoV-2 was completely inactivated by the contact with 0.5 % povidone-iodine for 15 s." Povidone-iodine is also expected to be clinically effective. In Japan, the concentration of povidone-iodine gargle solution that can be prescribed is 7%, and this solution is diluted 15-to 30 folds (by diluting 2–4 mL of the solution with 60 mL of water) before use. Although antiviral activity has been confirmed in the 30-fold diluted solution (0.23 %), the concentration, dose, duration of action (mouth wash/mouth rinse), and temperature of the solution are issues for future studies.

In addition to povidone-iodine, the US Centers for Disease Control and Prevention (CDC) guidelines [6] issued after the outbreak of COVID-19 recommend the use of chlorhexidine gluconate, essential oil, and cetylpyridinium chloride as mouth wash/mouth rinse before dental treatment, while the American Dental Association (ADA) guidelines [7] recommend povidone-iodine (0.2 %) and hydrogen peroxide solution (1.5 %). Although povidone-iodine is used in Japan, Hong Kong, Korea, Taiwan, Singapore, Malaysia, and the Philippines, among others, its use is not common in Europe and the United States. A possible reason why the US CDC [6] and ADA [7]) guidelines recommended other drugs in addition to povidone-iodine is because povidone-iodine is not widely used.

As with other disinfectants, the presence of contaminants including proteins, such as food residues, dental plaque, tongue coating, and blood, markedly weakens the antiseptic effect of povidone-iodine. Thus, cleansing of the oral cavity "before" mouth wash/mouth rinse is fundamental (refer to Section 6. Appendix: Precautions for gargling) Furthermore, the "duration" of antiviral activity, which is clinically very important, is also unknown. The expression of ACE2 receptors, to which SARS-CoV-2 binds, has been confirmed in the duct of the salivary gland in addition to the tongue and gingival mucosa. Even if povidone-iodine is effective on SARS-CoV-2 in the saliva that is excreted in the oral cavity, its effect on saliva excreted after mouth wash/mouth rinse is unknown. In other words, its antiviral activity against SARS-CoV-2 in the saliva contained in the duct, is unknown. This issue needs to be investigated.

A negative view of preoperative mouth wash/mouth rinse is that because SARS-CoV-2 exists not only in saliva but also rather abundantly in the nasal cavity and pharynx, mouth wash/mouth rinse alone is insufficient. There is another view that mouth wash/mouth rinse should be performed in combination with gargle or nasal lavage (so-called nasal irrigation). However, patients without a gargle habit may have a risk of accidental ingestion. If stimulation of gargle or nasal lavage induces sneezing or coughing, highly transmissible droplets will be generated abundantly. This should be taken into consideration.

Thus, when surgical procedures in oral and maxillofacial areas are performed in the epidemic stage and under other conditions with a high possibility to encounter asymptomatic patients with COVID-19, mouth wash/mouth rinse performed by patients without allergy to povidone-iodine or any other safety issues can be expected to transiently reduce the amount of aerosolized SARS-CoV-2, and to lower the risk of infection in surgeons and assistants during surgery.

4.4.4. Systematic review

Database: PubMed

Number of identified articles: 75

Date of search: September 7, 2020

Filters: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Review, Systematic Review, English

Search strategy:

("Mouthwashes"[MeSH Terms] OR "Mouthwashes"[Pharmacological Action] OR "administration, topical"[MeSH Terms] OR ("rinse*"[Title/Abstract] OR "rinsing"[Title/Abstract] OR "mouthrins*"[Title/Abstract] OR "mouthwash*"[Title/Abstract] OR "wash*"[Title/Abstract] OR "gargl*"[Title/Abstract] OR "spray*"[Title/Abstract] OR "topical*"[Title/Abstract])) AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields] OR "coronaviruses"[All Fields] OR "corona virus"[All Fields] OR ("coronaviridae"[MeSH Terms] OR "coronaviridae"[All Fields] OR "coronavirinae"[All Fields]) OR ("coronaviridae"[MeSH Terms] OR "coronaviridae"[All Fields]) OR ("betacoronavirus"[MeSH Terms] OR "betacoronavirus"[All Fields] OR "betacoronaviruses"[All Fields]) OR ("COVID-19"[Supplementary Concept] OR "COVID-19"[All Fields] OR "covid19"[All Fields]) OR "COVID-19"[All Fields] OR "nCoV"[All Fields] OR "CoV 2"[All Fields] OR "CoV2"[All Fields] OR "sarscov2"[All Fields] OR "2019nCoV"[All Fields] OR "novel CoV"[All Fields] OR "wuhan virus"[All Fields] OR (("wuhan"[All Fields] OR "hubei"[All Fields] OR "huanan"[All Fields]) AND ("severe acute respiratory"[All Fields] OR ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumoniae"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae s"[All Fields])) AND ("disease outbreaks"[MeSH Terms] OR ("disease"[All Fields] AND "outbreaks"[All Fields]) OR "disease outbreaks"[All Fields] OR "outbreak"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "outbreaks"[All Fields] OR "outbreak s"[All Fields])) OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept])) or ((COIVD-19 and mouthwash) or ((sars-cov2 or covid-19) mouth rinse) or ((sars-cov2 or covid-19) povidone iodine) or ((sars-cov2 or covid-19) mouth rinse))

Screening

Article	Study Design	P	I	C	O	Comment
Vergara-Buenaventura A et al. Use of mouthwashes against COVID-19 in dentistry. Br J Oral Maxillofac Surg. 2020 Oct;58(8):924–927. doi: https://doi.org/10.1016/j.bjoms.2020.08.016.	Presumed systematic review	Articles on mouth wash with chlorhexidine gluconate (CHX), cetylpyridinium chloride (CPC), povidone-iodine (PVP-I), and hydrogen peroxide (H2O2)	Literature review on the inhibitory effect of mouth wash used in dentistry on SARS-CoV-2	None	Against SARS-CoV-2, gargle with 0.2 %, 0.4 %, and 0.5 % PVP-I for 30 s is recommended.	
Dev Kumar G et al. Novel Antimicrobial Agents for the Mitigation of Coronaviruses. Front Microbiol. 2020 Jun 23;11:1351. doi: https://doi.org/10.3389/fmicb.2020.01351.	in vitro study	Mouth rinse	Povidone-iodine	Hypoiodous acid and alcohol-based products	Povidone-iodine oral spray is described as effective for SARS-CoV-2.	
Kelly N et al. Can oral rinses play a role in preventing transmission of Covid 19 infection? Evid Based Dent. 2020 Jun;21(2):42–43. doi: https://doi.org/10.1038/s41432-020-0099-1.	review	Mouth wash	Povidone-iodine	Hydrogen peroxide and chlorhexidine	Povidone-iodine gargle has an antiviral effect on SARS-CoV, but its effect on SARS-CoV-2 is not mentioned.	

Systematic review

Clinical context	Refer to the Comment (Section 4.4.3).
Summary on indirectness	Because there are no studies on patients undergoing oral surgical procedures, the issue of indirectness remains.
Summary on the bias risk	The accumulation of findings is so limited that the selection bias and other bias risks cannot be avoided.
Summary on the inconsistency and other issues	No apparent inconsistency was found.
Comment	None.

4.4.5. References

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[2] Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B Rapid In-Vitro Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Using Povidone-Iodine Oral Antiseptic Rinse J Prosthodont, 2020 Jul;29(6):529–533

[3] Bidra AS, Pelletier JS, Westover JB, Frank S, Brown SM, Tessema B Comparison of In Vitro Inactivation of SARS CoV-2 with Hydrogen Peroxide and Povidone-Iodine Oral Antiseptic Rinses J Prosthodont, 29(2020), pp.599–603

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4.5. CQ5: Should appropriate personal protection equipment (PPE) be used even when simple incision (biopsy) or tooth extraction is performed?

4.5.1. Recommendation

Appropriate PPE should be used to perform even simple incisions (e.g., biopsy) or tooth extraction with the use of forceps/an elevator.

4.5.2. Evidence level and recommended grade

Evidence level: D (very low)

Recommended grade: Strongly recommended

4.5.3. Comment

There are currently no studies showing the extent of aerosol generation by each procedure, such as by simple incision (biopsy) or tooth extraction. Meanwhile, SARS-CoV-2 has been suggested to exist in the oral mucosal epithelium, salivary duct epithelium, and saliva [1–8]. There are also reports of massive aerosol generation through conversation and speech [9–11]. Based on these reports, it cannot be ruled out that oral and maxillofacial surgeons, who perform therapeutic procedures near the oral cavity of patients, may be exposed to aerosols generated in the oral cavity of patients even when the surgeon is performing a simple incision for biopsy or tooth extraction with the use of forceps/an elevator. Thus, all surgical procedures in oral and maxillofacial areas should be considered to be associated with a risk of SARS-CoV-2 infection. The use of appropriate PPE, such as a cap, mask (an N95 respirator should be selected depending on the situation), face shield, gloves, and gown, and thorough practice of hand hygiene after the procedures, are important.

Despite the lack of articles corresponding to the CQ, we considered that the benefits of strict infection control in surgical procedures of oral and maxillofacial areas outweigh the economic burden on medical professionals. Thus, we regarded the recommended grade as strongly recommended.

4.5.4. Systematic review

Database: PubMed

Number of identified articles: 256

Date of search: September 7, 2020

Search strategy:

(((coronavirus OR "corona virus" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak))) OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) AND (((aerosol) OR (splatter) OR (aerosols) OR (airborne) OR (bioaerosol) OR (bioaerosols) OR (spatter) OR (droplet) OR (droplets)) AND ((dental practice) OR (dental procedure) OR (ultrasonic dental scaling) OR (ultrasonic dental) OR (ultrasonic dental unit) OR (tooth grinding) OR (tooth restoration) OR (tooth scaling) OR (teeth scaling) OR (teeth grinding) OR (rotary dental instruments) OR (bracket debonding) OR (orthodontic debonding) OR (composite removal) OR (resin removal) OR (adhesive removal) OR (dental unit waterline) OR (DUWL) OR dentistry OR oral OR maxillofacial)))

Screening: The second screening identified no relevant articles.

Systematic review: No SR was conducted because of the lack of articles identified by the second screening.

4.5.5. References

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[2] Shamsoddin E Saliva: a diagnostic option and a transmission route for 2019-nCoV Evid Based Dent, 21 (2020), pp.68–70

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[9] Netz RR Mechanisms of Airborne Infection via Evaporating and Sedimenting Droplets Produced by Speaking J Phys Chem B, 124 (2020), pp.7093–7101

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[11] Anfinrud P, Stadnytskyi V, Bax CE, Bax A Visualizing Speech-Generated Oral Fluid Droplets with Laser Light Scattering N Engl J Med, 382 (2020), pp. 2061-2063

4.6. CQ6: Does the use of N95 respirators prevent infection with aerosolized SARS-CoV-2 for operators and assistants in oral and maxillofacial surgery?

4.6.1. Recommendation

The use of N95 respirators by operators and assistants in oral and maxillofacial surgery is effective for the prevention of infection with aerosolized SARS-CoV-2.

4.6.2. Evidence level and recommended grade

Evidence level: C (low)

Recommended grade: Strongly recommended

4.6.3. Comment

Of the 27 articles selected for the second screening, two SRs [1, 2] were included in the analysis. Both reviews indicate that N95 respirators may reduce the risk of infection better than the surgical masks, but they concluded that the evidence level is low. Chu et al. reported that, in contact with patients with coronavirus infectious disease, including those caused by SARS-CoV-2, SARS-CoV, or Middle East respiratory syndrome coronavirus (MERS-CoV), the use of N95 respirators and conventional surgical masks reduces the risk of infection (relative risk: 0.34). Furthermore, the use of N95 respirators is more effective at preventing infection, particularly in medical professionals, than the use of conventional surgical masks (adjusted odds ratio: 0.04 vs. 0.33). They suggested that the use of N95 respirators may reduce the risk of infection [1]. Iannone et al. suggested that the use of N95 respirators reduces the risk of infection better than with the use of conventional surgical masks across infectious respiratory diseases not limited to infection with SARS-CoV-2 (relative risk 0.73) [2].

Medical grade masks of KN95 can be substituted for N95 respirators. The KN95 mask was tested by the Chinese State Administration of Work Safety (SAWS) and meets the GB2626-2006 standard, which is considered equivalent to the N95 standard of the United States. Among the KN95 masks, those with the No. GB19083-2010 met the standards for medical equipment. During the spread of COVID-19 in 2020, the CDC expressed the view that KN95 masks can be an appropriate substitute for an insufficient supply of N95 respirators [3]. Subsequently, the US Food and Drug Administration (FDA) approved the use of KN95 masks. The Japanese Ministry of Health, Labour and Welfare states that, "among medical-grade masks such as KN95 masks, those granted an Emergency Use Authorization (EUA) by the FDA should be used as masks equivalent to N95 respirators" [4].

Despite the small number of articles corresponding to the CQ, we considered that the benefits of an increased possibility of infection prevention outweigh the economic burden on medical professionals. Thus, we regarded the recommended grade as strongly recommended.

4.6.4. Systematic review

Database: PubMed

Number of identified articles: 60

Date of search: September 16, 2020

Filters: Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Systematic Review

Search strategy:

((TITLE-ABSTRACT((coronavirus OR "corona viru" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak))) OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept]) AND (facemask OR face mask OR surgical facemasks OR medical

mask OR medical-grade masks OR medical facemask OR medical face masks OR surgical masks OR surgical facemask OR surgical face mask OR N95 OR respirator OR respiratory protection OR respiratory protective device OR respiratory protective devices)) or (((sars-cov2 or covid-19) N95 masks) or ((sars-cov2 or covid-19) N95 masks aerosols))

Screening

Article	Study Design	P	I	C	O	Comment
Chu DK, et al. COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020 Jun 27;395(10242):1973–1987. doi: https://doi.org/10.1016/S0140-6736(20)31142-9.	Systematic review (4 RCTs)	Four RCTs involving 172 studies from 16 countries	N95 mask	Surgical Mask	The use of masks may substantially reduce the risk of infection.	
Iannone, et al. The need of health policy perspective to protect Healthcare Workers during COVID-19 pandemic. A GRADE rapid review on the N95 respirators effectiveness. PLoS One. 2020 Jun 3;15(6):e0234025. doi: https://doi.org/10.1371/journal.pone.0234025.	Systematic review (4 RCTs)	Four RCTs involving 8736 Healthcare Workers (HCWs)	N95 mask	Surgical Mask	N95 masks protect the HCWs better than surgical masks (based on the low evidence).	

Systematic review

Clinical context	Refer to the Comment (Section 4.6.3).
Summary on indirectness	Because there are no studies on patients undergoing oral surgical procedures, the issue of indirectness remains.
Summary on the bias risk	The accumulation of findings is so limited that the risk of selective outcome reporting and other risks cannot be avoided.
Summary on the inconsistency and other issues	No apparent inconsistency was found.
Comment	None.

4.6.5. References

[1] Chu DK, Akl EA, Duda S, Solo K, Yaacoub S, Schünemann HJ et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis Lancet, 395 (2020), pp.1973–1987

[2] Iannone P, Castellini G, Coclite D, Napoletano A, Fauci AJ, Iacorossi L et al. The need of health policy perspective to protect Healthcare Workers during COVID-19 pandemic. A GRADE rapid review on the N95 respirators effectiveness PLoS One, 15 (2020), pp. e0234025

[3] CDC-related home page: Strategies for Optimizing the Supply of N95 Respirators https://www.cdc.gov/coronavirus/2019-ncov/hcp/ppe-strategy/index.htmlN95.

[4] Administrative notice issued by the Japanese Ministry of Health, Labor and Welfare on April 10, 2020: Exceptional use of masks. https://www.mhlw.go.jp/content/000621007.pdf.

4.7. CQ7: Is the combination of intraoral suction and extraoral vacuum effective for reducing the risk of COVID-19 transmission during surgical procedures in oral and maxillofacial areas?

4.7.1. Recommendation

To reduce the risk of COVID-19 transmission, the combination of intraoral suction and extraoral vacuum is recommended.

4.7.2. Evidence level and recommended grade

Evidence level: D (very low)

Recommended grade: Weakly recommended

4.7.3. Comment

Of the 37 articles selected for the second screening, one article [1] was included in the analysis. This article describes an experimental study on a simulation model using a dental mannequin that was conducted to evaluate the usefulness of extraoral vacuum and other techniques. The results showed that the combination of high-volume suction (intraoral suction) and extraoral vacuum reduced the contamination of the operative field with droplets. It also reduced the exposure of the surgeons and assistants to droplets (reducing the frequency of contamination of the operative field by 20 % and the average contamination intensity by 75 %). This study suggested that the combination of intraoral and extraoral suction might be effective for reducing the risk of contracting COVID-19 [1]. An article not selected at the second screening indicates that aerosols are contaminated by blood from the oral cavity of patients, in the real-world setting. This also suggests the usefulness of extraoral vacuum [2].

Because this recommendation is based on an exploratory study reported by a single group, the evidence level is D (very low).

4.7.4. Systematic review

Database: PubMed

Number of identified articles: 114

Date of search: September 16, 2020

Search strategy:

(TITLE-ABSTRACT((coronavirus OR “corona virus” OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR “covid 19” OR nCoV OR “CoV 2” OR CoV2 OR sarscov2 OR 2019nCoV OR “novel CoV” OR “wuhan virus”) OR ((wuhan OR hubei OR huanan) AND (“severe acute respiratory” OR pneumonia) AND (outbreak))) OR “COVID-19” [Supplementary Concept] OR “severe acute respiratory syndrome coronavirus 2” [Supplementary Concept]) AND (suction OR suctioning OR vacuum OR evacuator)) or ((sars-cov2 or covid-19) vacuum) or ((sars-cov2 or covid-19) suction) or ((sars-cov2 or covid-19)extraoral))

Screening

Article	Study Design	P	I	C	O	Comment
Shahdad S et al. The efficacy of an extraoral scavenging device on reduction of splatter contamination during dental aerosol generating procedures: an exploratory study. Br Dent J. 2020 Sep 11. doi: https://doi.org/10.1038/s41415-020-2112-7	Intervention (experimental) study	Various dental procedures generating aerosols (model-based simulation)	Use of extraoral scavengers (EOSs) in combination with intraoral vacuum and saliva ejector	Use of intraoral vacuum and saliva ejector (without EOS)	The use of EOS reduced the exposure of surgeons and assistants to contaminated substances and contamination of the operative field.	The concomitant use of extraoral vacuum reduced the frequency of contamination of the surgical field by 20 % and the average contamination intensity by 75 %.

Systematic review

Clinical context	Refer to the Comment (Section 4.7.3).
Summary on indirectness	Because there are no studies on patients undergoing oral surgical procedures, the issue of indirectness remains.
Summary on the bias risk	The accumulation of findings is so limited that bias risks, such as the selection and performance biases, cannot be avoided.
Summary on the inconsistency and other issues	No apparent inconsistency was found.
Comment	None.

4.7.5. References

[1] Shahdad S, Patel T, Hindocha A, Cagney N, Mueller JD, Seoudi N et al. The efficacy of an extraoral scavenging device on reduction of splatter contamination during dental aerosol generating procedures: an exploratory study Br Dent J. 11 (2020), pp.1–10

[2] Ishihama K, Koizumi H, Wada T, Iida S, Tanaka S, Yamanishi T et al. Evidence of aerosolised floating blood mist during oral surgery J Hosp Infect, 71 (2009), pp.359-364

5. Activities after publication

To accumulate findings on COVID-19, the Subcommittee on the Development of Measures Against COVID-19 of the Japanese Society of Oral and Maxillofacial Surgeons will collect information on cases of COVID-19 associated with oral surgery that occur in medical institutions and clinics. The subcommittee will analyze the cases and reflect the results in these guidelines as needed.

In areas with limited accumulation of findings, particularly on measures against aerosols, the Japanese Society of Oral and Maxillofacial Surgeons will separately conduct publicly solicited studies and reflect their findings in the contents of the guide as appropriate. Currently, the Japanese Society of Oral and Maxillofacial Surgeons offers the “Research Grant for Studies on Aerosol Generation in Surgical Procedures of Oral And Maxillofacial Areas”

When the contents of the guide need to be changed in consideration of the extent of spread of infection, data issued by the government, current status of medical care, and new findings from articles published in journals or presented at academic conferences, will be used by the subcommittee to revise the guide as necessary (Fig. 1).

Appendix

Precautions for gargling

When povidone-iodine or other disinfectants are used for gargling, attention should be paid to the appropriate concentration and duration of action of disinfectants, and also to possible contaminants. The presence of many contaminants, mainly proteins, in the oral cavity markedly weakens the effect of disinfectants. When gargling is performed in two sessions (first session with 5 cc of solution for 10 s and the second session with 15 cc for 20 s), contaminants are neutralized and diluted in the first session “with 5 cc for 10 s”. Gargling in this manner is far more effective than gargling “in one session with 20 cc for 30 s”.

Indication of ventilation

It is preferable, but not essential, to use negative-air-pressure for the examination rooms, and inpatient wards that are used for patients with COVID-19 (including suspected cases). Rooms with adequate ventilation are sufficient. It is recommended to check the ventilation conditions (e.g., ventilation frequency) in facilities before use. If possible, radiography or CT scans should be performed for patients with COVID-19, after all those without COVID-19 on the same day finished their examinations. The risk of secondary infection may be reduced by encouraging patients to wear masks and by performing environmental disinfection and ventilation for approximately 30 min after imaging examination.

(Guidelines for the Treatment of Coronavirus Diseases 2019 (COVID-19), version 4.1 https://www.mhlw.go.jp/content/000712473.pdf)

Proper ways to wear and remove an N95 respirator and PPE

Before using an N95 repirator, a user must perform a seal check. To wear PPE to treat patients with suspected or confirmed COVID-19, the necessary training must have been completed beforehand. The specific important instructions include the following: always wear PPE before entering the patient area and to keep the PPE properly worn while staying in the contaminated area. The removing of the PPE is associated with a high risk of infection; therefore, PPE should be slowly removed in the specified order after leaving the contaminated area. Posting a sign indicating the procedure and precautions for removal of PPE in the undressing area contributes to better compliance with the procedure.

(Bureau of Social Welfare and Public Health, Tokyo Metropolitan Government Instructions and videos on how to wear and remove personal protection equipment
https://www.fukushihoken.metro.tokyo.lg.jp/smph/iryo/kansen/shingatainflu/cyakudatsu.html)

Disinfection and cleaning of equipment

The following information on cases suitable for the use of disinfectants for SARS-CoV-2 is posted on the home page of the Infectious Disease Surveillance Center of the National Institute of Infectious Diseases. The use of disinfectants for SARS-CoV-2 should also be determined in accordance with this information.

1. Items suitable for heat sterilization

(1) High-pressure steam (autoclave) sterilization (121 °C for 20 min)

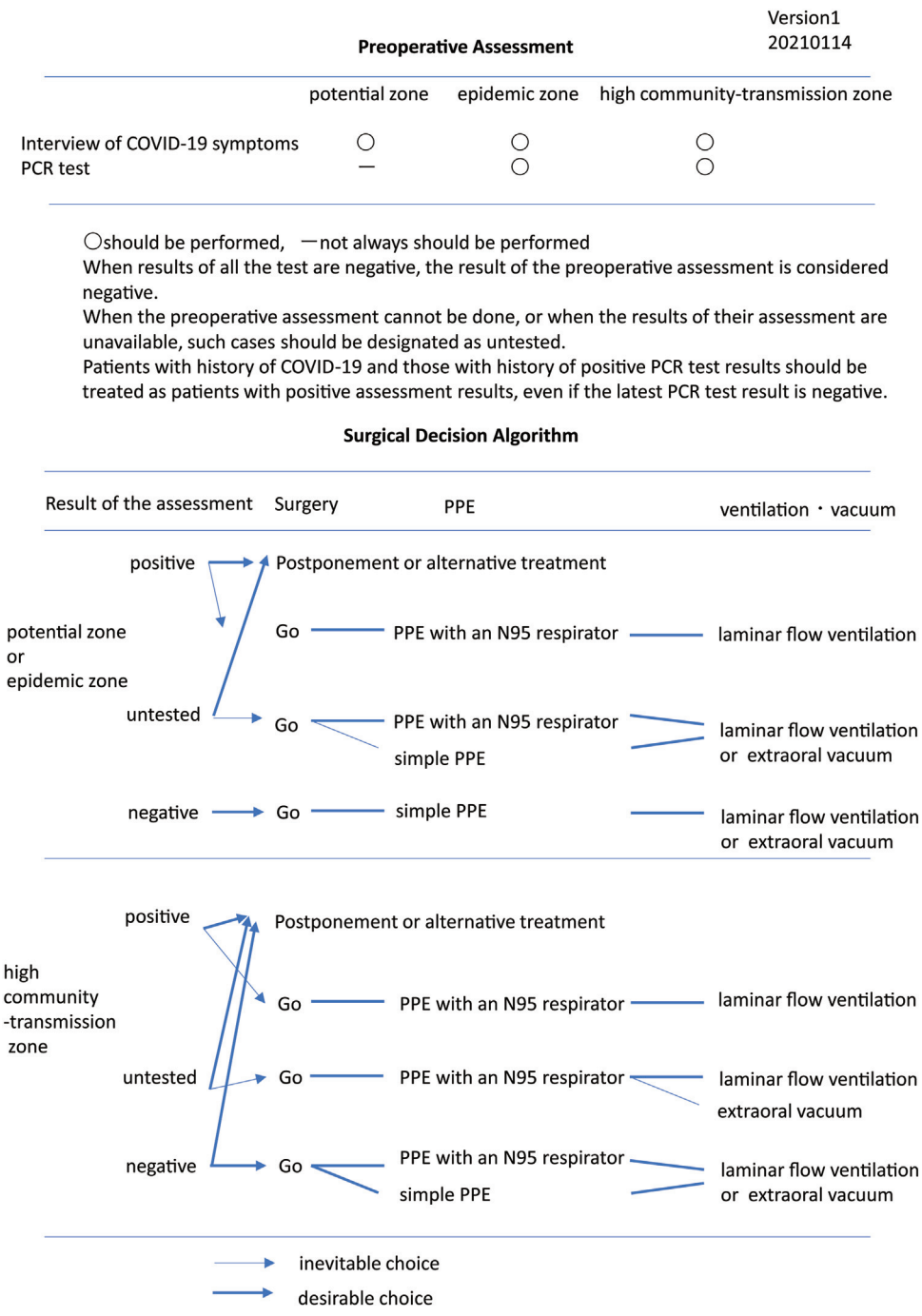

Fig. 1. Preoperative assessment to be performed; Surgical decision algorithm.

(2) Dry heat sterilization (180–200 °C for 1 h or 160–170 °C for 2 h)

(3) Boiling sterilization (≥98 °C for ≥15 min)

2. Items unsuitable for heat sterilization

(1) Sodium hypochlorite: Although it is commonly used for sterilization by immersion in a solution with an effective chlorine concentration of 0.02 % to 0.05 % (200–500 ppm) for ≥1 h, immersion in a sodium hypochlorite solution with a concentration of ≥0.1 % (1,000 ppm) for ≥30 min is needed to achieve a reliable virucidal effect. Sodium hypochlorite is corrosive to fabric and metal, and is less effective when organic compounds are attached. It cannot be used on the human body. Linens should be soaked in a 0.1 % solution (1,000 ppm) for 30 min and then washed with water. Dishes and other utensils should be soaked in a 0.01 % to 0.02 % solution (100–200 ppm) for ≥5 min after they are washed with water. For the disinfection of excrement, a concentration of 0.1%–1% (1,000–10,000 ppm) is effective.

(2) Ethanol for disinfection (approximately 80 %): Ethanol is less toxic to the human body and suitable for disinfection of the hands and fingers. Unless it is stored in an airtight container, the alcohol content may evaporate. Thus, the alcohol concentration decreases; therefore, the ethanol dramatically loses its effect. The alcohol may cause degreasing; so attention should be paid on skin care. Ethanol cannot be applied to the mucosal surfaces. Although isopropanol (70 %) may be used as an alcohol-based disinfectant, its antiviral effect is inferior to that of ethanol. Quick-drying skin disinfectants (e.g., brand names: Welpas and Hibiscol; ingredients: benzalkonium chloride or chlorhexidine gluconate, ethanol, surfactants, and

humectants) are frequently used for hand disinfection. When blood and other substances contaminate the skin, the disinfectants may not reach the skin surface. The hands and fingers should be washed, because alcohol-based disinfectants are flammable; therefore, their use requires caution, and they are unsuitable for spraying over a wide area. In addition, their use is regulated by the Fire Service Act.

(3) Peracetic acid: It is effective at a low concentration (0.001 %–0.2 %) against all microorganisms, including spores. It is even effective in the presence of organic compounds. It is eventually degraded to water, oxygen, and acetic acid, but has no hazardous remnant. Peracetic acid corrodes some metals and has an irritating smell.

(4) Glutaraldehyde (2%, pH 8): Glutaraldehyde is a chemical with protein denaturing and bactericidal activities and is so potent that it can kill all microorganisms. It cannot be used on the human body because it induces severe irritation. To disinfect devices, blood and body fluids should be thoroughly eliminated. Then, the devices should be soaked in a glutaraldehyde solution (2%, pH 8) for one h and thoroughly washed with water. For disinfection of excrement and body fluids, immersion for ≥2 h is reliable. To disinfect the floor, it should be wiped with a 0.2 % solution, left untouched for ≥30 min, and then wiped with water. The procedure to disinfect endoscopes and other devices may include immersion in a 3% solution for 15 min. Disinfection with glutaraldehyde requires the use of protective equipment and ventilation.

(5) Formaldehyde (liquid: immersion in a 1 %–5 % solution; gas: spraying or humidifying with formaldehyde at ≥15 mL/m^3 along with ≥40 mL of water for 7−24 h). The formaldehyde solution is used for disinfection of medical devices by immersion or wiping. Although formaldehyde can be gasified to be used for disinfection of rooms, its gaseous form is very toxic and irritating.

(6) Ethylene oxide gas: It is applied at a concentration of approximately 500 mg/L at 55–60 °C for ≥3 h. It is used to sterilize heat-labile devices in the central supply room. Caution should be exercised to ensure the absence of residual gas after sterilization. Inhalation of the gas causes airway inflammation, nausea, dizziness, and neurological symptoms; and the gas is also reported to be associated with risks of teratogenicity and carcinogenicity. Thus, adequate ventilation is necessary.

(7) Iodine-based disinfectant (iodophor): Iodophor is a solution that contains iodine complexed with a carrier (non-ionic surfactant). When Iodophor becomes alkaline, it is ineffective. Iodophor becomes less effective when mixed with organic compounds; or when there is sputum or blood. Iodophor is corrosive to common metals and stains the skin, mucosa, and fabric. A 10 % solution is used for skin disinfection of the surgical site. A 7.5 % scrub solution is used for disinfecting the hands, fingers, and skin. A 10 % gel is used for disinfection of wounds. To use for gargling, a 7% solution is diluted according to the instructions in the package insert. High-concentration iodine-based disinfectants are irritating to the skin and may cause iodine hypersensitivity.

(8) Benzalkonium chloride, chlorhexidine, and surfactants may also have antiseptic properties, but their effects may be inadequate. Thus, at present, the methods of disinfection described above (1. Items suitable for heat sterilization and 2. Items unsuitable for heat sterilization), are recommended for disinfection of SARS-CoV-2.

(Refer to the home page of the Infectious Disease Surveillance Center (nih.go.jp):
http://idsc.nih.go.jp/disease/sars/desinfect04a.html).