



Skull Base Surgery During the Covid-19 Pandemic: The Italian Skull Base Society Recommendations

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ABSTRACT

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), which causes coronavirus disease 2019 (Covid-19), is highly contagious with devastating impacts for healthcare systems worldwide. Medical staff are at high risk of viral contamination and it is imperative to know what personal protective equipment is appropriate for each situation. Furthermore, elective clinics and operations have been reduced in order to mobilize manpower to the acute specialties combatting the outbreak; appropriate differentiation between patients who require immediate care and those who can receive telephone consultation or whose treatment might viably be postponed is therefore crucial.

Italy was one of the earliest and hardest-hit European countries and therefore the Italian Skull Base Society board has promulgated specific recommendations based on consensus best practices and the literature, where available. Only urgent surgical operations are recommended and all patients should be tested at least twice (on days 4 and 2 prior to surgery). For *positive patients*, procedures should be postponed until after swab test negativization. If the procedure is vital to the survival of the patient, FFP3 and/or PAPRs devices, goggles, full-face visor, double gloves, water-resistant gowns and protective caps, are mandatory. For *negative patients*, use of at least FFP2 mask is recommended. In all cases the use of drills, which promote the aerosolization of potentially infected mucous particles, should be avoided. Given the potential neurotropism of SARS-CoV-2, dura handling should be minimized. It is only through widely-agreed protocols and teamwork that we will be able to deal with the evolving and complex implications of this new pandemic.

Key Words: skull base, sinus surgery, paranasal sinuses, olfaction, intracranial dura, endoscopic skull base surgery, endoscopic sinus surgery

Introduction

The rapid spread of the coronavirus epidemic has forced epochal changes in our daily habits as well as revolutionizing our usual clinical and surgical practice. Since March 12th, 2020, when the WHO officially announced that the COVID-19 infection represented a real global pandemic, healthcare workers have been implementing strategies to contain the infection whilst protecting their patients' and their own health as much as possible.¹ We are also observing heavy restrictions on healthcare resources, which must be redirected to support the management of the pandemic and therefore removed from normal elective clinical and surgical activities.

In common with many international scientific societies, the Italian Skull Base Society wants to offer clinical and behavioral recommendations to adequately deal with the emergency. Our recommendations are in line with the scientific evidence available to date as well as the concrete experience "in the field" of those who are dealing with the epidemic in the hot areas of the infection.

Olfactory and taste loss

In addition to fever, coughing, wheezing and diarrhea, there are other symptoms that can be helpful in identifying at risk patients. Of these, we would emphasize the importance of hyposmia and dysgeusia, which, as confirmed by much scientific evidence from different countries, are configuring as symptoms associated with SARS-CoV-2 infection.² Moreover, 1 in 6 patients with recent onset anosmia report this as an isolated symptom [Isolated Sudden-Onset Anosmia (ISOA)].³ It is known that post-viral etiologies account for 15% - 40% of smell and taste loss cases.⁴ It is important to investigate this symptom, even in telephone consultations, in order to determine the presence of infection. This might help identify otherwise asymptomatic carriers of disease and trigger targeted testing.⁵

The therapeutic recommendations for patients with sudden onset of olfactory loss are: social isolation in quarantine for at least 14 days, and starting nasal olfactory training as soon as possible.⁶ Omega-3 supplementation might be helpful in recovery after post-viral loss as it was found to be protective against olfactory loss during the recovery period after skull base surgery.⁷ In patients with isolated anosmia, a short course of budesonide nasal irrigations can be prescribed since it has been demonstrated to improve olfactory ability⁸ without compromising the local or systemic immune status.⁹

Other adjuvant treatment options proposed in the past, before Covid-19 outbreak, although without a high level of evidence, might be used to facilitate the recovery of the taste-olfactory function: vitamin A-based nasal drops,¹⁰ oral alpha-lipoic acid, caroverine, minocycline, ginkgo biloba.¹¹ However, the use of oral corticosteroids should be avoided since they could impair viral clearance and therefore interfere with the subsequent course of the infection.¹² Since no clear data are yet available to contraindicate the use of topical nasal steroid therapy, ongoing chronic nasal topical steroid therapy should be continued regularly to avoid exacerbation of allergic and sinonasal symptoms, which could mimic the symptoms of coronavirus infection.³ A recent study seems to indicate that most patients are likely to recover chemosensory function within weeks or months paralleling resolution of other disease-related symptoms.¹³ However, further studies on olfactory function recovery will be necessary to shed more light on this issue.

Precautionary rules for healthcare workers

This infection spreads through droplets and therefore the more the operator is exposed to the patient's airways (e.g. via outpatients, endoscopic diagnostic procedures, surgery), the greater the risk. The viral load of SARS-CoV-2 is higher in the nasal cavity than in the throat, regardless of whether the patient is symptomatic or asymptomatic.¹⁴ Once aerosolized, SARS-CoV-2 particles may stay in the

air for at least three hours. Otolaryngologists and Neurosurgeons are therefore at high risk.¹⁵ The anecdotal evidence of the first case of COVID-19 transmission during an endoscopic transphenoidal pituitary surgery in Wuhan, China, and resulting in cross-contamination of 14 healthcare workers, emphasizes the high potential for hospital-acquired viral infection.¹⁶ This has provoked anxiety towards endonasal endoscopic procedures worldwide. However, recently, Huang et al. provided additional information to clarify that event reporting that the infected healthcare workers were mainly those who were outside the operation room. Therefore the impact of surgical-related exposure in promoting the contamination should be balanced with the equally important role of social interaction between healthcare staff and contaminated surfaces in wards and living areas.¹⁷

No matter the potential contamination pathways, to date, hundreds of healthcare workers have been hospitalized for COVID-19 in China and Europe and some of them, unfortunately, have died. Therefore, the recommendations in managing patients with unknown COVID-19 status (e.g. outpatient service) are to wear appropriate PPE, including disposable FFP2/N95 mask, water-resistant gown, gloves, goggles, cap and full-face visor shield. In addition, for COVID-19 positive patients, FFP3 mask and/or Powered Air Purifying Respirators (PAPRs) should be used.¹⁸

COVID-19 positivity tests

Nasopharyngeal swab tests, based on reverse-transcriptase PCR to identify SARSCoV-2, are currently available, results returning within 24 hours with time variations depending on the institution. Recently, a newer test from Abbott (Abbott Laboratories, Chicago, IL, USA), with results ready within 15 minutes, is being made available to current practice. These tests might be burdened by a non-negligible rate of false negatives, ranging from 4% to 30%, depending on the expertise and training of those performing the swabs.¹⁹ The execution of two nasopharyngeal swabs, distanced by at least 2-4 days, is recommended to improve the sensitivity of the method. Moreover, the accuracy of

the swab test can be increased if complemented with chest imaging showing signs of infection. It was suggested that chest CT could be even more sensitive in detecting COVID-19 than repeated RT-PCR test.²⁰

New immune-assay methods are becoming available for blood determination of specific IgM and IgG antibodies for SARS-CoV-2, which can provide results in about 20-40 minutes.²¹ The rapid IgM-IgG combined antibody test provided by PharmACT (Berlin, Germany) scored a IgM sensitivity of 70% during the early stages of infection (first 4-10 days), which rapidly increases to 92.3% between day 11 and day 24. In the same period of late infection, the IgG component of the test reaches 98.6% of sensitivity. These new methods, in addition to being faster, offer an overall lower rate of false negatives (ranging from 11% to 13%) and probably will be used more frequently in the upcoming months.²²

Additionally, saliva may serve as a potential, non-invasive material for diagnosing COVID-19, with emerging preliminary evidence that it might be considered as a more accurate material to detect the novel coronavirus than nasopharyngeal swab.²³ Saliva could be self-collected by the patient spitting into a sterile container, eliminating the exposure of healthcare services, and subsequently analyzed using nucleic acid extraction and RT-PCR test. Authors from China reported that SARS-CoV-2 was detected in saliva specimens obtained from 91.7% of patients with COVID-19.²⁴ Other studies on this issue are required to better understand the role of saliva in fast diagnosis of SARS-CoV-2 infection.

Outpatient assessments

It is recommended that all elective and non-urgent outpatient procedures be postponed.²⁵ Many consultations and evaluations can be done by telephone or video visits. Telemedicine screening can also be very useful in identifying urgent cases requiring rapid medical care, as well as those patients with alarming symptoms, who need to be directed towards COVID-19 diagnostic and therapeutic

investigations. We recommend wearing appropriate protective devices, encouraging patients to use a surgical mask, maintaining interpersonal distancing of greater than one meter, frequent hand washing and alcoholic disinfection and only admitting patients themselves to consultations (with exceptions made in the cases of minors or disabled patients).^{1,25} In the outpatient setting, use of a barrier such as an intact surgical mask or a modified VENT mask (Valved Endoscopy of the Nose and Throat, according to Workman et al.), which enables endoscopy, significantly reduces aerosol spread.²⁶

Skull base surgery

Data emerging from international clinical experiences show that surgical procedures involving the airways or using them as a surgical corridor, as in transnasal skull base surgery, must be, prudentially considered high-risk procedures, at least as long as further evidences will become available.^{16,18,26,27} Obviously, it is not the endoscopic technique per se which is risky, but the nasal and pharyngeal anatomical site is hazardous, as it may act as a reservoir with a high viral load. Therefore, all endoscopic, microscopic and open surgical procedures involving these anatomical regions must be considered at risk. Likewise surgical procedures on the lateral skull base, given the previous scientific evidences documenting the presence of respiratory viruses in the mucosa of the middle ear.^{1,15}

Our current recommendations are summarized in Figure 1 and described as follows:

- Elective surgical activities and non-urgent procedures must be completely suspended.
- Only urgent surgical operations (severe trauma, bleeding, infections/abscesses) and non-deferrable surgical interventions (malignant tumors with critical local extension to brain, orbit and/or with borderline resectability where a considerable waiting time might be fatal for the prognosis quoad vitam et valetudinem) should be performed. Pituitary tumors or skull base lesions with rapidly worsening vision should receive treatment. Similarly, acoustic neuromas, meningiomas and other tumors presenting with hydrocephalus or symptoms of brainstem

compression should be managed quickly. Conversely, slow-growing tumors associated with progressive symptoms should be evaluated on a case by case basis. Finally, radiation therapy or systemic therapy should be considered as an alternative to surgery whenever possible.²⁸

- There is new evidence for the neurotropism of SARS-CoV-2 and transcribiform route of the SARS-CoV-2 to the brain has been suggested. The isolation of SARS-CoV-2 RNA in the cerebrospinal fluid would be the most conclusive evidence to document the neurovirulence of SARS-CoV-2.²⁹ Therefore, dura handling during skull base surgery should be performed with particular caution, especially in endoscopic endonasal and lateral skull base approaches. Extradural surgery should be advised whenever feasible while transdural approaches should be reserved only for selected cases which are of unavoidable necessity.
- In preoperative setting, whenever feasible, patients scheduled for surgery should be prepared with povidone-iodine (PVP-I) solution delivered by nasal irrigations and oral wash in order to decrease the potential viral load.³⁰
- It is mandatory to test for COVID-19 in all patients who are candidates for surgery (except for emergency procedures), with at least 2 tests, repeated at a distance of 2 - 4 days, in order to minimize the possibility of false negatives. The last test must be performed within 48 hours prior to surgery.
- For *COVID-19 positive patients*, procedures should be postponed until after swab test negativization, when feasible. If the procedure is strictly necessary for the patient's survival, surgery must be performed in dedicated negative-pressure operating theatres with a pre-established allocated run, which should not interfere with the COVID-19-free areas. All medical and nursing staff in the operating room must wear FFP3 and/or PAPRs devices, goggles, full-face visor, double gloves, water-resistant gowns and protective caps, not only for the entire duration of surgery but for the whole of the patient's stay in the operating room.¹⁶

- If testing for *COVID-19 is not available* (emergency procedures such as trauma, major bleeding, abscesses): follow guidelines as for positive patients.
- Surgical procedures in *COVID-19 negative patients*: use the highest individual protection standards (at least FFP2 mask), in consideration of the significant number of false negatives from the swab tests currently used.¹⁶
- In endoscopic transnasal approaches, the use of high speed drills which promote the aerosolization of potentially infected mucous particles (Aerosol Generating Surgery) should be avoided, or at least reduced. Osteotomes such as Kerrison and Citelli rongeurs, circular punches, chisel and hammer should be preferred, where possible, to minimize the bony drilling. On the other hand, cold surgical instruments and shavers/microdebriders seem to have less aerosolization risk.²⁶ However, while this might be true for larger particles, we still do not know if it is the case for smaller aerosolized particles. In selected cases it would be advisable to consider transcranial surgery instead of endonasal whenever feasible without additional morbidity for the patient.¹⁶
- Mastoid drilling creates droplets and aerosolization of particles and should also be considered Aerosol Generating Surgery. It should thus proceed using standard PPE (face shields and N95).^{31,32,33} Moreover, once the mastoid and middle ear are open, topical PVP-I solution should be applied to reduce the mucosal viral load.³⁰
- The whole operating area must be considered at risk, not only for the duration of surgery but for the entirety of the patient's stay. It is therefore advisable to minimize the number of staff in the operating room. Likewise, observers, fellows and residents in training must be excluded from the operating sessions during this period to reduce exposures.¹
- Adequate advice should be provided to COVID-19 negative patients who undergo surgery to adhere to proper hygiene-behavioral rules during the post-operative period to avoid subsequent superinfections: this should include stressing the imperative of accurate and

frequent hand washing, wearing a surgical mask and of social distancing (greater than 1 meter).

These recommendations may require specific patient-tailored and nation-based changes according to available facilities and resources as well as on the future evolution of the pandemic.

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Figure Legend

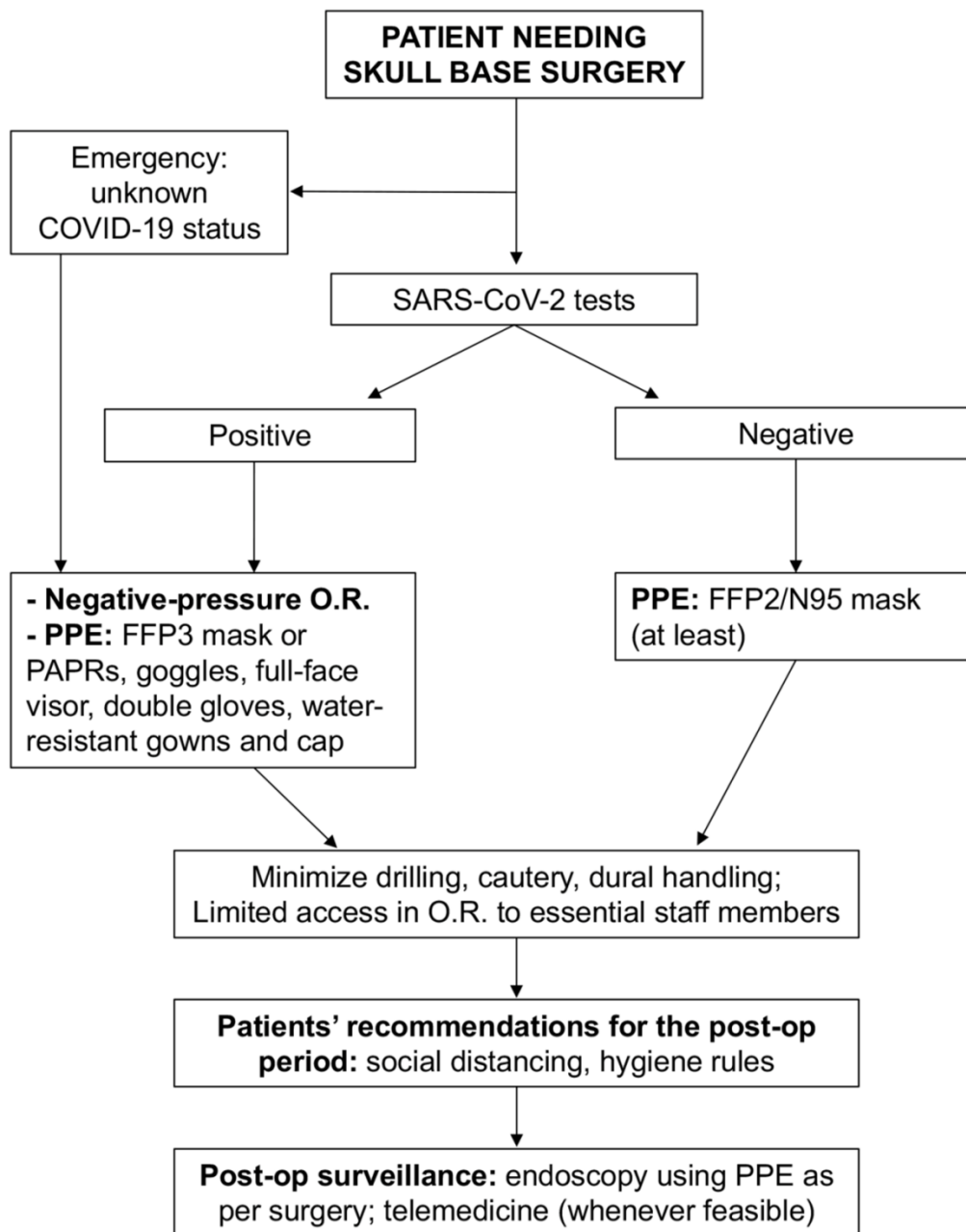


Figure 1. Flow-chart for management of patients who are candidates for skull base surgery during the COVID-19 pandemic. Abbreviations: OR, operating room; PPE, personal protective equipment; PAPRs, powered air purifying respirators.