This article has been accepted for publication in Neurosurgery published by Oxford University Press.

PRECAUTIONS FOR ENDOSCOPIC TRANSNASAL SKULL BASE SURGERY DURING THE COVID-19 PANDEMIC

Key Words: COVID-19, coronavirus, transmission, endoscopic surgery, extended endoscopic skull base surgery, personal protective equipment (PPE), Powered Air Purifying Respirators (PAPR)

Zara M. Patel, MD; Juan Fernandez-Miranda, MD; Peter H. Hwang, MD; Jayakar V. Nayak, MD, PhD; Robert Dodd, MD, PhD; Hamed Sajjadi, MD; Robert K. Jackler, MD

Stanford University School of Medicine Departments of Otolaryngology-Head & Neck Surgery and Neurosurgery

On March 12, 2020 the World Health Organization (WHO) officially announced the COVID-19 outbreak a pandemic, where to date there have been over 381,000 cases resulting in over 16,500 deaths worldwide.¹ The COVID-19 pandemic is accelerating within the United States, and any information that we can gain from our international colleagues who have already experienced this, or are currently going through it, should be utilized to protect our patients, our hospital teams and ourselves.

The compilation of information below is anecdotal, based primarily on personal communication with international colleagues reporting their individual experiences, and more data is needed before strict policies are set. There is no scientific evidence in this report. However, based on the preliminary observations summarized below and the fast course of events, it would be prudent to exercise an abundance of caution as more data accumulates. Our goal with this preliminary, rapid article is to alert surgeons of the need to temporarily alter their practices to avoid repeating the unfortunate experience of the early period of the epidemic.

Personal communication with colleagues deployed in Wuhan, China to combat the COVID-19 outbreak, have warned us about the potential risks of endonasal endoscopic surgery in COVID -19 symptomatic patients. From their reports, a patient with mild flu-like symptoms underwent transphenoidal pituitary surgery in early January 2020, before the severity of this pandemic was well established. Multiple members (>14 by report) of the patient care team, both within and outside of the operating room, became infected from what became recognized as human-tohuman transmission of COVID-19.² Testing for COVID-19 prior to that time was scarce. A second case of intraoperative transmission of COVID-19 occurred later on January 2020, at the peak of the pandemic in Wuhan province. A young patient with a known pituitary adenoma developed fever and acute vision changes and was diagnosed with pituitary apoplexy and suspected viral pneumonia based on imaging studies. The surgical team was aware of the potential risks of infection, but given the acuity of symptoms proceeded with transphenoidal surgery using personal protective equipment (PPE). The neurosurgeon and two OR nurses employed N95 masks and the anesthesiologist reportedly used a "home-made" positive pressure helmet. The operation was completed successfully without incident and the surgical team was quarantined after surgery. Within 3-4 days, all of them developed fever and respiratory

symptoms compatible with pneumonia, except the anesthesiologist. Fortunately, all recovered with no sequelae. The patient, however, required prolonged intubation, but finally recovered.

A significant number of doctors who became infected and even died in Wuhan, China were anesthesiologists/critical care doctors, ophthalmologists, and otolaryngologists, possibly due to the high viral shedding from the nasal and oropharyngeal cavity.³ Healthcare providers are at high risk of infection when taking care of COVID-19 patients without PPE. High risk procedures include intubation and procedures involving the upper respiratory tract and gastrointestinal tract with risk for aerosolization, such as endoscopy, bronchoscopy, and laryngoscopy.

From our colleagues in Iran, Dr. Ebrahim Razmpa, Professor of Otolaryngology at Tehran University Medical Sciences, Dr. Saee Atighechi, Associate Professor of Otolaryngology at Yazd University School of Medicine, and Dr. Mohammed Hossein Baradanfar, Professor and Chairman of Otolaryngology Yazd University School of Medicine, we have additionally heard that at least 20 otolaryngologists in Iran are currently hospitalized with COVID-19, with 20 more in isolation at home. They are testing only people who have been admitted to the hospital, so those twenty at home are not confirmed, but have classic symptoms. A previously healthy 60 year old facial plastic surgeon died from COVID-19 three days ago. A young, otherwise healthy otolaryngology chief resident had a short prodrome, rapidly decompensated and died from what was found to be acute myocarditis and cardiac arrest. It was recently confirmed from these colleagues that he did also test positive for COVID-19.

The British Association of Otorhinolaryngology has now also stated two of its consultants are on ventilators and being treated for COVID-19.⁷ In Athens, 21 staff members of the Athens General Hospital "Hippocrates" are quarantined, as a doctor at the Otolaryngology Clinic reportedly tested positive for COVID-19.⁸

Our colleague Dr. Puya Deghani-Mobaraki, in Italy, also reports otolaryngologists being affected adversely, but his information is about the possible loss of smell and taste that this virus brings. They are not only seeing it in their patients, but they have noticed it within their own ranks, in otherwise healthy asymptomatic doctors, at rates far above what could be considered normal. This observation has also been reported in the media regarding patients, as an under-reported aspect of this disease process.^{9,10} In fact, this symptom has been seen now so commonly in France in association with COVID-19 that the government has issued an official statement instructing citizens with this symptom to contact their physicians, who may advise self-quarantine or to come in and be tested, depending on individual evaluation.¹¹

Based on this information, and until we know more, we are performing only urgent/emergent surgery at Stanford University at this time. Due to this apparent high risk with endoscopic transnasal surgery on COVID-19 symptomatic patients, in spite of current limitations in testing capacity, our institution has approved testing for COVID-19 in pre-operative patients needing this type of procedure urgently or emergently. This is true even for asymptomatic patients (ie. no cough and/or fever), although the true risk in this cohort of patients is still unknown. If the test is negative and the patient is asymptomatic, we may proceed using normal levels of protective gear; however, the rate of false negative tests is still to be determined, and until this is known , the use of additional levels of PPE, such as N95 and face shields can be considered. If the test is

positive, we defer surgery if at all possible until the infection is cleared, verified by repeat testing. When endonasal surgery cannot be postponed in a COVID-19 positive patient, based on guidelines now being used in China, we have recommended to our institutional officials that we utilize full PAPR (an enclosed powered system with HEPA filter), acknowledging that they have challenging decisions surrounding allocation of limited resources that are urgently needed by our critical care teams taking care COVID-19 patients.¹² Alternatively, a transcranial approach should be considered whenever possible. Because endonasal surgery creates clouds of droplets and aerosols which may permeate the operating environment, anyone in the operating theater requires the same protection when operating on known COVID-19 positives.

The question of whether two separate negative tests are needed before surgery, or if one is sufficient, is under active discussion. The test that we are using, developed at Stanford, is an inhouse assay that uses a real time RT-PCR for SARS-CoV-2. This first screens for the presence of virus envelope protein, and if positive then evaluates for the presence of the RNA-dependent RNA polymerase gene for confirmation (Developed by Benjamin Pinsky MD, Stanford University). Positive results from this test have been demonstrated to be very sensitive and very specific and have been given early approval by the FDA. The Chinese CDC test uses different gene targets and primers and thus may, or may not, have a different accuracy profile. Conservation of precious testing and PPE resources is another reason to limit these operations to the bare minimum at this time. We also recommend use of as minimal an OR team as necessary and that no trainees or observers be allowed in the room both for reasons of safety and to preserve PPE.

In the clinic setting, we have similarly restricted visits to only urgent/emergent patients and have ceased the use of spray anesthetic/decongestants, opting instead for nasal pledgets as needed, but preferably avoiding endoscopy whenever possible. We are using N95 masks, face shields and gowns for all outpatient nasal endoscopies.

Please keep in mind that from the time of this submission, the situation may have evolved, and our policies may have changed. We hope that more hard data becomes available soon upon which to base these important decisions. We follow with tempered optimism the evolution of this pandemic in China, where at this point no new local cases have been reported for several days now, with gradual return to normal surgical activities, including endoscopic endonasal surgery.

We thank our international colleagues who have given us this important information, and we extend wishes of safety and health to all our otolaryngology, neurosurgery, and critical care/anesthesia colleagues at this challenging time.

²China Newsweek. View.inews.qq.com/a/20200125A07TT200?uid=&devid=BDFE70CD-5BF1-4702-91B7-329F20A6E839&qimei=bdfe70cd-5bf1-4702-91b7-329f20a6e839

3https://www.bloomberg.com/news/articles/2020-03-17/europe-s-doctors-getting-sick-like-in-wuhan-chinese-doctors-say?fbclid=IwAR2ds9OWRxQuMHAuy5Gb7ltqUGMZNSojVNtFmq3zzcSLb_bO9aGYr7URxaI

¹John's Hopkins Coronovirus Center. https://coronavirus.jhu.edu/map.html Accessed March 21, 2020

³van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med. 2020 Mar 17. doi: 10.1056/NEJMc2004973. [Epub ahead of print]

⁵5Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. N Engl J Med. 2020 Mar 19;382(12):1177-1179. doi: 10.1056/NEJMc2001737. Epub 2020 Feb 19.

⁶ 6Xu K¹, Lai XQ², Liu Z¹. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2020 Feb 2;55(0):E001. doi: 10.3760/cma.j.issn.1673-0860.2020.0001. [Epub ahead of print] [Suggestions for prevention of 2019 novel coronavirus infection in otolaryngology head and neck surgery medical staff]. [Article in Chinese (translated via Google translator); Abstract available in Chinese from the publisher]

⁷ https://news.sky.com/story/coronavirus-experts-say-new-symptoms-could-be-loss-taste-or-smell-11961439

⁸ 8https://www.euractiv.com/section/politics/news/cracks-appear-in-nordic-response-to-covid-19-crisis/

⁹ 9https://en.radiofarda.com/a/loss-of-sense-of-smell-among-iranians-coinciding-with-coronavirus-epidemic/30478044.html

 $^{10}\,https://www.forbes.com/sites/judystone/2020/03/20/theres-an-unexpected-loss-of-smell-and-taste-in-coronavirus-patients/\#48e2a8c85101$

 $^{11} https://www.sortiraparis.com/news/coronavirus/articles/210162-coronavirus-update-on-the-situation-in-paris-and-ile-de-france-controls-reinforc/lang/en$

¹² Lian, Tingbo (Editor). Handbook of COVID-19 Prevention and Treatment. The First Affiliated Hospital. Zhejiang University School of Medicine. Compiled according to Clinical Experience.