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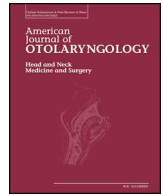
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Otolaryngology during COVID-19: Preventive care and precautionary measures

Chen Zhao^{a,*}, Alonço Viana Jr^{b,c,1}, Yan Wang^a, Hong-quan Wei^a, Ai-hui Yan^a, Robson Capasso^d

^a Department of Otolaryngology, the First Affiliated Hospital of China Medical University, Shenyang, China

^b Department of Otorhinolaryngology, Marçilio Dias Naval Hospital, Rio de Janeiro, Brazil

^c Graduate Program of Neurology, Federal University of the State of Rio de Janeiro (UNIRIO), Rio de Janeiro, Brazil

^d Department of Otolaryngology - Head & Neck Surgery, Stanford University Medical Center, Stanford, CA, United States of America

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ABSTRACT

Since the outbreak of novel coronavirus disease (COVID-19) in December 2019, it has spread to various regions and countries, forming a global pandemic. Reducing nosocomial infection is a new issue and challenge for all healthcare systems. Otolaryngology is a high-risk specialty as it close contact with upper respiratory tract mucous, secretions, droplets and aerosols during procedures and surgery. Therefore, infection prevention and control measures for this specialty are essential. Literatures on the epidemiology, clinical characteristics and infection control measures of COVID-19 were reviewed, practical knowledge from first-line otolaryngologists in China, the United States, and Brazil were reviewed and collated. It was recommended that otolaryngology professionals should improve screening in suspected patients with relevant nasal and pharyngeal symptoms and signs, suspend non-emergency consultations and examinations in clinics, and rearrange the working procedures in operating rooms. The guidelines of personal protective equipment for swab sampling, endoscopy and surgery were listed. Indications for tracheotomy during the pandemic should be carefully considered to avoid unnecessary airway opening and aerosol-generation; precautions during surgery to reduce the risk of exposure and infection were illustrated. This review aimed to provide recommendations for otolaryngologists to enhance personal protection against COVID-19 and reduce the risk of nosocomial infection.

1. Introduction

In December 2019, a novel coronavirus infection broke out in Wuhan, China [1]. This virus has spread rapidly across the country and is now a global pandemic [2,3]. The virus is named SARS-CoV-2, and the disease caused by the virus is called 2019 novel coronavirus disease (COVID-19) [4]. SARS-CoV-2 belongs to lineage B of genus Betacoronavirus [5], shares 96% homology to a bat coronavirus and 79.6% homology to SARS-CoV at the whole genome level [6], but is less similar to the MERS-CoV [7]. By March 2020, COVID-19 caused by SARS-CoV-2 has more than 82,000 cases in China and more than 1,347,000 all around the world [8]. Pneumonia is its main manifestation, although most cases are mild, but 14% of cases present severe symptoms such as dyspnea, reduced blood oxygen saturation, 5% turn to critical with acute respiratory distress syndrome (ARDS) and shock [2], 1.4–4.3% to death [9,10]. However, due to the abruptness of COVID-19, its rapid

increase in the number of infected populations has placed a heavy load on local healthcare systems, due especially to the high requirement for intensive care unit (ICU) and invasive ventilation [11]. As a result, the mortality rate at the center of the national epidemic storm tends to be more severe (7.2–15%) [1,12]. After the outbreak, the specialties that usually need to be in close contact with patients or to deal with the airway management, such as ophthalmology [13], stomatology [14], anesthesiology [15], have issued relevant infection control and prevention measures for COVID-19. Therefore, this review summarized the experiences in China, the United States, and Brazil, thus providing practical guidance for otolaryngologists under this pandemic.

2. Risk for otolaryngologic professionals

Human to human transmission of SARS-CoV-2 has been confirmed [16], and the infection is highly contagious with about 2.2–3.6 basic

* Corresponding author at: Department of Otolaryngology, the First Affiliated Hospital of China Medical University, No. 155, the North Nanjing Street, Shenyang 110001, Liaoning, China.

E-mail address: zhaochen@cmu.edu.cn (C. Zhao).

¹ These authors contributed equally to this work.

reproductive number that is slightly higher than SARS-CoV, but lower than MERS-CoV [17–19]. Direct contact, airborne and droplet are the most common transmission routes. Although SARS-CoV-2 mainly invades the lower respiratory tract, nasopharynx and oropharynx have been proved to have virus shedding [20,21]. For otolaryngologists, most examinations and treatments require inevitable contact with upper airway mucosa and face to face position, and any reflex coughing or sneezing during procedures will cause a direct contamination to medical staffs. Some aerosol generating procedures such as nasal endoscopy and laryngoscopy will increase virus infectivity and contribute to working environment contamination up to several days [22–24]. Generally, otolaryngology is in a high-risk level during this pandemic. Since nosocomial transmission has been confirmed and more than 3000 health care personnel have been infected in China during the epidemic [10], it is important for otolaryngologic staffs to enhance personal protection against nosocomial infections based on current experience and lessons learned from SARS epidemic [25].

3. Preventive measures

3.1. Patients' screening

Identifying infected or suspicious patients is the first step that will help both medical staffs and patients to quickly enter standard COVID-19 infection prevent and control management procedures and avoid unnecessary risks of nosocomial transmission [26]. Otolaryngologists should pay attention to symptoms. Although common discomforts in COVID-19 patients are fever, cough, shortness of breath and sometimes associated with sputum, fatigue, myalgia, some patients also have regular ENT complaints such as sore throat (13.9–60%), rhinorrhea (4–6%) and nasal obstruction (4.8%) [1,9,12,27], 2.1% has tonsil swelling and 1.7% has throat congestion [9]. In other countries, such as Brazil, the USA and Europe, COVID-19 has also been associated with other changes such as anosmia and dysgeusia [28,29]. These symptoms in an isolated form also constitute criteria for quarantine. Abdominal pain and skin rash have also been reported, and can be confusing symptoms in countries where dengue, chikungunya and measles are already epidemic [30]. Epidemiological contact history in about 7 days is another key to assess a suspicious infection [17]. Early in China's experience, 72.3% patients had had contact with people in the original city, Wuhan, and 31.3% had shown travel history [9]. However, with rapid global widespread and infection increase in communities, not only travel history but also any contact or staying in an enclosed environment with people who have been confirmed or suspected with respiratory illness in the previous 14 days should be noted. In China, many people have been infected while caring for sick family members, thus infections transmission in families cannot be ignored [16].

3.2. Examination suggestion

Asymptomatic transmission is an important characteristic of COVID-19 [31,32], there is 1.8% potential infectivity among population with negative symptoms screening result [33]. Therefore, for suspected patients without typical symptoms, necessary examinations should be performed to exclude potential infection. Chest X-radiography or CT is recommended firstly, and pulmonary ground-glass opacity (GGO) and bilateral infiltration manifestation usually indicate SARS-CoV-2 related infection [34]. Blood test will provide additional support for diagnosis, confirmed patients often have lymphopenia and elevated CRP level, or leukopenia or thrombocytopenia [10]. SARS-CoV-2 real-time reverse transcriptase–polymerase chain reaction (RT-PCR) test is the clinical diagnostic criteria [35]. Recently, antibody test was applied and elevated IgM after 5 days of symptom indicated early infection [36]. But the clinical use of the latter two depends on the detection capability of local healthcare system.

3.3. Medical service management

Given the severity of virus transmission and the rapid growth in the number of infected patients, healthcare services should be adjusted accordingly to reduce the accumulation of patients in hospitals, reduce the risk of nosocomial transmission to staffs and other patients, and ensure enough medical services and supplies to respond outbreaks of respiratory infective disease [37]. In the Chinese experience, during the early outbreak, ENT clinic, routine endoscopy and surgeries were suspended, only emergency cases were seen and surgeries were performed until the epidemic was well controlled. Elderly medical staff or with comorbidities such as cardiovascular disease, hypertension, diabetes and cancer, who are susceptible to more severe infection and worse prognosis [2,38], were suggested to avoid engaging with high infection risk medical procedures.

We also suggest the restriction in the necessary number of assistants during procedures and segregate into smaller teams or individuals to cover entire services, with the goal to keep as many physicians and residents home each day as possible, to minimize the chance of transmission between providers if someone gets exposed or infected.

In the author's (C.Z.) hospital, telemedicine has been implemented during pandemic. Patients can make appointments through a mobile app and have text consultation with doctors. After an initial evaluation, the doctor can decide if an in presence consultation is needed and permitted to visit in hospital. Meanwhile, most postoperative patients can get remote recovery instructions. The service is currently free during the outbreak.

3.4. Personal protective equipment (PPE) for otolaryngology

In addition to strict airborne and contact precautions, PPE is necessity for health care staff against SARS-CoV-2 [39,40]. Otolaryngologists should choose appropriate protective equipment based on medical operations, respectively. Routine inquiry or simple examination, such as anterior rhinoscopy and oropharyngeal inspection, require basic protection, including surgical cap, NIOSH-certified disposable N95 filtering respirator, goggles, gown and gloves. If the procedures is likely to have close contact with respiratory droplets or aerosols caused by involuntary coughing, sneezing and deeply breathing, such as throat swabs, endoscopy for nose and larynx, treatment for nasal bleeding and foreign body in pharynx, in our experience more protection should be utilized, including wearing coveralls inside the gown, water-resistant boot covers, face shield outside the goggle (Fig. 1a), aiming to minimize skin exposure. Double-layer gloves are recommended in case of a tearing accident, while the inner layer can provide greater security while putting off the external equipment. Invasive airway procedures such as tracheotomy are at the highest risk and require powered air purifying respirator (PAPR) to provide seamless resistance to aerosols (Fig. 1b).

On the one hand, it should be noted that most nosocomial infections do not occur with careful protection, but when protective equipment is removed while hands, eyes, nose accidentally touch the contaminated surface of the protective equipment. On the other hand, unlike the department of infectious disease, emergency, intensive care medicine, otolaryngology has less knowledge and training on how to use PPE, which increases the risk of nosocomial infections. Practical training and exercises prior to clinical use should be conducted.

4. Treatment

Regarding treatment, there is still no concrete information. There are reports about the use of hydroxychloroquine and azithromycin in severe cases [41], for rescue, in the hospital environment. However, there are records of indiscriminate use of hydroxychloroquine by the population, without any form of risk control. Reports of cardiovascular toxic manifestations (hypotension, suppression of myocardial function,



Fig. 1. (a) Personal protection with surgical mask, N95 filtering respirator (under facial mask), goggle, face shield, coveralls, gown, gloves, water-resistant boot covers as high risk operation will be performed, such as throat swab, endoscopy. (b) Powered air purifying respirator (PAPR) substitute for face shield to provide more sufficient protection for invasive airway operation such as tracheotomy.

cardiac arrhythmias and cardiac arrest) have been recorded among these patients in indiscriminate use. Hydroxychloroquine is used to treat rheumatoid arthritis, systemic lupus erythematosus, malaria, among other diseases. The use of topical and systemic corticosteroids has been contraindicated. Use of vasoconstrictors to control nasal symptoms and nasal lavage with small volumes to avoid swallowing. Antipyretics, oxygen supplementation and, in cases with severe dyspnea, use of respiratory ventilators.

4.1. Tracheotomy consideration during pandemic

Tracheotomy is a routine operation to otolaryngologist [42], but it is an invasive open airway surgery with aerosolization [43]. When patients infected by SARS-CoV-2 undergo the procedure, aerosol mixed with secretions and blood will constitute a high risk to medical staffs, therefore it should be decided and performed with caution. During this epidemic, tracheostomy is most likely to be performed to severe or

critical patients who have undergone endotracheal intubation and mechanical ventilation because of unsustainable blood oxygen saturation and long ICU stay. Whether tracheotomy is needed and when is the optimal timing are still controversial issues. Some studies suggest that early tracheotomy (usually 5-7 days after intubation), in patients with respiratory failure can reduce ventilation dead space, airway resistance, sedation usage [44], decrease the incidence of sepsis and mechanical ventilation-related pneumonia [45], reduce duration of mechanical ventilation and ICU stay [46], increase the chance of discharge [47,48]. However, other studies show that early tracheotomy is only beneficial for some selected ICU patients [49], especially for traumatized patients [50,51]. Pneumonia and consequent ARDS are the main problems for COVID-19 patients with intubation [52,53]. For pneumonia, several meta-analyses demonstrate that there is insufficient evidence for early tracheotomy to reduce incidence of mechanical ventilation-associated pneumonia [54,55]. For ARDS, early tracheostomy should not be performed or only performed to limited patients according to some clinical

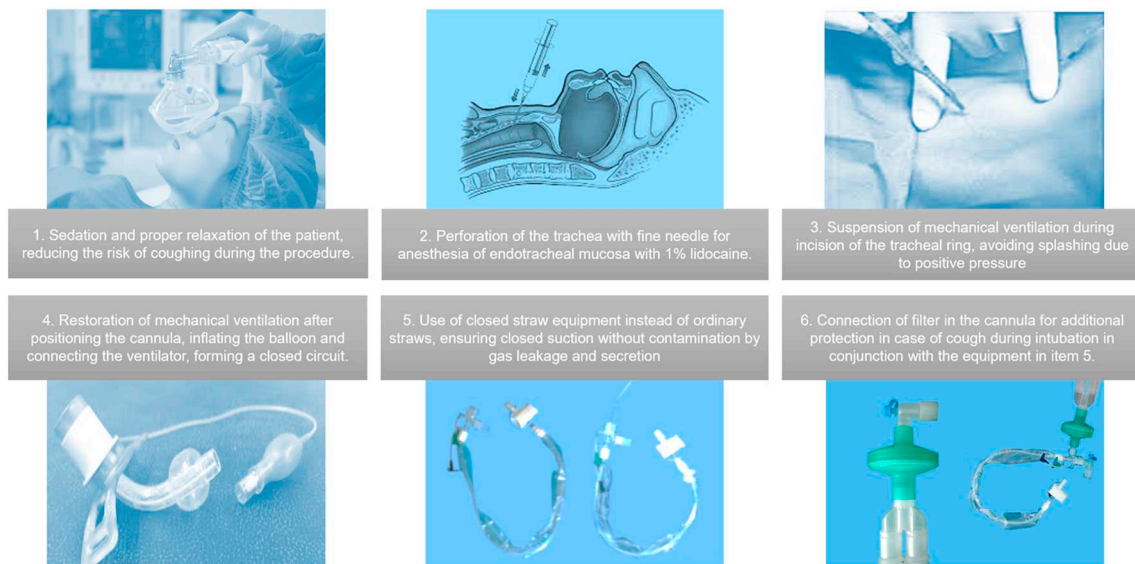


Fig. 2. 1. Communicating with the anesthesiologist to ensure adequately sedated and relaxed to reduce coughing. 2. Performing extra endotracheal mucosal anesthesia. 3. Suspending mechanical ventilation while trachea ring is incised. 4. Restoring mechanical ventilation until forming a closed circuit. 5. Using enclosed straws equipment instead of ordinary straws. 6. Attaching a filter to provide additional protection.

guidelines [56,57]. Once ventilation for more than 2 weeks, the mortality and disability will eventually increase with or without tracheotomy [58]. Therefore, tracheotomy should be evaluated carefully in intubated COVID-19 patients and only be performed with exact benefit expectation. Patients with apparent intolerance to transoral intubation or high muscle load due to increased airway resistance may be an appropriate indication [59].

However, in practical terms, ENT surgeons seldom decide whether to perform a tracheotomy to COVID-19 patients, instead, they usually act in concert with the plan decided by ICU, infectious disease and respiratory specialists. Therefore, otolaryngologists should be prepared for the procedure, including the highest level of personal protection, as described above, and operating skills to reduce aerosol infection (Fig. 2). For experienced surgeons, tracheostomy in COVID-19 patients receiving extracorporeal membrane oxygenation (ECMO) does not significantly increase the risk of bleeding and death, the use of anticoagulants is not a contraindication [60].

5. Conclusions

The epidemic of COVID-19 has spread globally and the pandemic situation is very grim. Otolaryngology medical staff, as high-risk exposed professionals, should enhance protection awareness. Screening patients carefully, conducting advanced training on PPE, preparing appropriate personal protection while performing high-risk operations will help reduce the incidence of nosocomial infections. With the progression of the disease to other populations, new clinical changes have been registered and deserve the constant attention of professionals.

Ethics approval and consent to participate

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Availability of data and materials

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Authors' contributions

CZ, AV, YW, HQW, AHY, RC collected and analyzed the material. CZ and AV were major contributors in writing the manuscript. RC was major supervision. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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References

- [1] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- [2] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.2648>. Feb 24.
- [3] World Health Organization. 2020 coronavirus disease (COVID-19) situation reports. Geneva: World Health Organization; 2020 <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>, Accessed date: 7 April 2020.
- [4] World Health Organization. WHO Director General's remarks at the media briefing on 2019 nCoV on 11 February 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020>, Accessed date: 7 April 2020.
- [5] Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020;395(10224):565–74.
- [6] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579(7798):270–3.
- [7] Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. *Cell Host Microbe* 2020;27(3):325–8.
- [8] John's Hopkins University Medicine. Coronavirus resource center. <https://coronavirus.jhu.edu/map.html>, Accessed date: 7 April 2020.
- [9] Guan WJ, Ni ZY, Hu Y, Liang WH, Qu CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020 Feb 28. <https://doi.org/10.1056/NEJMoa2002032>.
- [10] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020 Feb 7. <https://doi.org/10.1001/jama.2020.1585>.
- [11] Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020. [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5). Feb 24. pii: S2213-2600(20)30079-5.
- [12] Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.4683>. Mar 23.
- [13] Lai TH, Tang EWH, Chau SKY, Fung KSC, Li KKW, et al. Stepping up infection control measures in ophthalmology during the novel coronavirus outbreak: an experience from Hong Kong. *Graefes Arch Clin Exp Ophthalmol* 2020. <https://doi.org/10.1007/s00417-020-04641-8>. Mar 3.
- [14] Peng X, Xu X, Li Y, Cheng L, Zhou X, Ren B, et al. Transmission routes of 2019-nCoV and controls in dental practice. *Int J Oral Sci* 2020;12(1):9.
- [15] Wax RS, Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. *Can J Anaesth* 2020. <https://doi.org/10.1007/s12630-020-01591-x>. Feb 12.
- [16] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395(10223):514–23.
- [17] Li Q, Guan X, Wu P, Wang XY, Zhou L, Tong YQ, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020;382(13):1199–207.
- [18] Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. *Int J Infect Dis* 2020;92:214–7.
- [19] Zhou T, Liu Q, Yang Z, Liao J, Yang K, Bai W, et al. Preliminary prediction of the basic reproduction number of the Wuhan novel coronavirus 2019-nCoV. *J Evid Based Med* 2020;13(1):3–7.
- [20] Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med* 2020;382(12):1177–9.
- [21] Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.3786>. Mar 11.
- [22] van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med* 2020. <https://doi.org/10.1056/NEJMc2004973>. March 17.
- [23] Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. *JAMA* 2020 Mar 4. <https://doi.org/10.1001/jama.2020.3227>.
- [24] Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. *J Hosp Infect* 2020;104(3):246–51.
- [25] Chan JYK, Wong Ewy, Lam W. Practical aspects of otolaryngologic clinical services during the 2019 novel coronavirus epidemic: an experience in Hong Kong. *JAMA Otolaryngol Head Neck Surg* 2020. <https://doi.org/10.1001/jamaoto.2020.0488>. Mar 20.
- [26] World Health Organization. Interim guidance: infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected. [https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-\(ncov\)-infection-is-suspected-20200125](https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125), Accessed date: 7 April 2020.
- [27] Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.3204>. Mar 3.
- [28] AAO-HNS. Anosmia, hyposmia, and dysgeusia symptoms of coronavirus disease. <https://www.entnet.org/content/aaohns-anosmia-hyposmia-and-dysgeusia>

- symptoms-coronavirus-disease, Accessed date: 7 April 2020.
- [29] Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host-virus interaction, and proposed neurotropic mechanisms. *ACS Chem Neurosci* 2020. <https://doi.org/10.1021/acscchemneuro.0c00122>. Mar 13.
- [30] Joob B, Wiwanitkit V. COVID-19 can present with a rash and be mistaken for Dengue. *J Am Acad Dermatol* 2020. <https://doi.org/10.1016/j.jaad.2020.03.036>. Mar 22. pii: S0190-9622 (20)30454-0.
- [31] Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, et al. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.2565>. February 21.
- [32] Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. *N Engl J Med* 2020;382(10):970–1. <https://doi.org/10.1056/NEJMc2001468>. Mar 5.
- [33] Hoehl S, Rabenau H, Berger A, Kortenbusch M, Cinatl J, Bojkova D, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. *N Engl J Med* 2020;382(13):1278–80.
- [34] Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology* 2020. <https://doi.org/10.1148/radiol.2020200463>. Feb 20. 200463. [Epub ahead of print]. <https://doi.org/10.1148/radiol.2020200463>.
- [35] Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020;25(3). <https://doi.org/10.2807/1560-7917.ES.2020.25.3.2000045>.
- [36] Guo L, Ren L, Yang S, Chang Xiao M, Yang F, et al. Profiling early humoral response to diagnose novel coronavirus disease (COVID-19). *Clin Infect Dis* 2020 Mar 21. <https://doi.org/10.1093/cid/ciaa310>. pii: ciaa 310.
- [37] Megan LR, Valerie G, Ashish KJ. Critical supply shortages-the need for ventilators and personal protective equipment during the Covid-19 pandemic. *N Engl J Med* 2020. <https://doi.org/10.1056/NEJMp2006141>. March 25.
- [38] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21(3):335–7.
- [39] Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for patients with known or patients under investigation for 2019 novel coronavirus (2019-nCoV) in a healthcare setting Updated February 21, 2020 <https://www.cdc.gov/coronavirus/2019-nCoV/hcp/infection-control.html>, Accessed date: 7 April 2020.
- [40] World Health Organization. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care: WHO guidelines. <http://apps.who.int/iris/handle/10665/112656>, Accessed date: 7 April 2020.
- [41] Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents* 2020. <https://doi.org/10.1016/j.ijantimicag.2020.105949>. Mar 20. 105949. [Epub ahead of print].
- [42] de Kleijn BJ, Wedman J, Zijlstra JG, Dijkers FG, van der Laan BFAM. Short- and long-term complications of surgical and percutaneous dilatation tracheotomies: a large single-centre retrospective cohort study. *Eur Arch Otorhinolaryngol* 2019;276(6):1823–8.
- [43] Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One* 2012;7(4):e35797 <https://doi.org/10.1371/journal.pone.0035797>.
- [44] Kaese S, Zander MC, Lebiez P. Successful use of early percutaneous dilatational tracheotomy and the no sedation concept in respiratory failure in critically ill obese subjects. *Respir Care* 2016;61(5):615–20.
- [45] Villwock J, Jones K. Outcomes of early versus late tracheostomy: 2008–2010. *Laryngoscope* 2014;124(8):1801–6.
- [46] Adly A, Youssef TA, El-Beghermy MM, Younis HM. Timing of tracheostomy in patients with prolonged endotracheal intubation: a systematic review. *Eur Arch Otorhinolaryngol* 2018;275(3):679–90.
- [47] Mehta AB, Cooke CR, Wiener RS, Walkey AJ. Hospital variation in early tracheostomy in the United States: a population-based study. *Crit Care Med* 2016;44(8):1506–14.
- [48] Patel SA, Plowman EK, Halum S, Merati AL, Sardesai MG. Late tracheostomy is associated with higher morbidity and mortality in mechanically ventilated patients. *Laryngoscope* 2015;125(9):2134–8.
- [49] Blot F, Similowski T, Trouillet JL, Chardon P, Korach JM, Costa MA, et al. Early tracheostomy versus prolonged endotracheal intubation in unselected severely ill ICU patients. *Intensive Care Med* 2008;34(10):1779–87.
- [50] Aquino Esperanza J, Pelosi P, Blanch L. What's new in intensive care: tracheostomy-what is known and what remains to be determined. *Intensive Care Med* 2019;45(11):1619–21.
- [51] Young D, Harrison DA, Cuthbertson BH, Rowan K. Effect of early vs late tracheostomy placement on survival in patients receiving mechanical ventilation: the TracMan randomized trial. *JAMA* 2013;309(20):2121–9.
- [52] Sweeney RM, McAuley DF. Acute respiratory distress syndrome. *Lancet* 2016;388(10058):2416–30.
- [53] Luks AM. Ventilatory strategies and supportive care in acute respiratory distress syndrome. *Influenza Other Respi Viruses* 2013;7(Suppl. 3):8–17.
- [54] Andriolo BN, Andriolo RB, Saconato H, Atallah AN, Valente O. Early versus late tracheostomy for critically ill patients. *Cochrane Database Syst Rev* 2015 Jan 12;1:CD007271 <https://doi.org/10.1002/14651858.CD007271.pub3>.
- [55] Shan L, Hao P, Xu F, Chen YG. Benefits of early tracheotomy: a meta-analysis based on 6 observational studies. *Respir Care* 2013;58(11):1856–62.
- [56] Hashimoto S, Sanui M, Egi M, Ohshimo S, Shiotsuka J, Seo R, et al. The clinical practice guideline for the management of ARDS in Japan. *J Intensive Care* 2017 Jul 25;5:50. <https://doi.org/10.1186/s40560-017-0222-3>.
- [57] Cho YJ, Moon JY, Shin ES, Kim JH, Jung H, Park SY, et al. Clinical practice guideline of acute respiratory distress syndrome. *Tuberc Respir Dis (Seoul)* 2016;79(4):214–33.
- [58] Herridge MS, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, et al. The RECOVER program: disability risk groups and 1-year outcome after 7 or more days of mechanical ventilation. *Am J Respir Crit Care Med* 2016;194(7):831–44.
- [59] MacIntyre NR, Cook DJ, Ely Jr. EW, Epstein SK, Fink JB, Heffner JE. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest* 2001;120(6 Suppl). (375S-95S).
- [60] Yeo HJ, Yoon SH, Lee SE, Jeon D, Kim YS, Cho WH, et al. Safety of surgical tracheostomy during extracorporeal membrane oxygenation. *Korean J Crit Care Med* 2017;32(2):197–204.