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Review

A comparative overview of COVID-19, MERS and SARS: Review article

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ABSTRACT

Following the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV), a third, highly pathogenic coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appearing at end of 2019 led to a pandemic, increased panic and attracted global attention. This review analyzes the epidemiology, etiology, clinical characteristics, treatment and sequelae of the severe acute respiratory syndrome (SARS), the Middle East respiratory syndrome (MERS) and the 2019 novel coronavirus disease (COVID-19) to help provide direction for further studies that can help understand COVID-19.

1. Introduction

Coronaviruses are enveloped, positive-stranded RNA viruses that negatively influence the respiratory, intestinal, liver and nervous systems of animals and humans [1,2]. Before the discovery of SARS-CoV-2, there were only six human coronaviruses identified. Among these, HCOV-229E, HCOV-NL63, HCOV-OC43 and HCOV-HKU1 mainly led to self-limited, respiratory infections that became serious in infants, immunosuppressed patients and elderly individuals. SARS and MERS belong to the B and C subclasses of β - coronavirus respectively and both can lead to fatal respiratory diseases [3]. SARS-CoV-2, SARS-CoV and MERS-CoV are zoonotic viruses that are highly pathogenic. Diseases caused by these viruses including COVID-19, SARS and MERS significantly impact infected individuals as well as the economies of infected countries. This article presents the epidemiology, etiology, clinical features, laboratory tests, imaging, treatment and sequelae of SARS-CoV-2, SRAS-CoV and MERS-CoV to provide reference for the development of treatment plans and infection-control measures that can be used for COVID-19.

2. Epidemiology

SARS-CoV is the coronavirus causing first-century pandemic that originated in an animal market in Guangdong Province, China in November 2002 and eventually spread to over 30 countries in about 8 months (https://www.who.int/csr/sars/country/table2004_04_21/en/). Ten years later, a second coronavirus, MERS-CoV, originating in the Middle East infected over 2000 of individuals world-wide, with the highest number of cases in Saudi Arabia. Almost all MERS-CoV infected cases reported outside of the Middle East were related to travel in the Arabian Peninsula or closely related to already infected cases (http://www.who.int/emergencies/mers-CoV/en/). At the end of 2019, pneumonia caused by a novel, highly pathogenic human coronavirus, SARS-CoV-2, was discovered in a seafood market in Wuhan, Hubei, China. Subsequently, infection quickly spread to China and around the world. By the 20th of May 2020, COVID-19 infected 499, 3470 of individuals and caused 32, 7738 world-wide (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200522-CoVid-19-sitrep-123.pdf?sfvrsn=5ad1bc3_4).

The most likely natural hosts of SARS-CoV, MERS-CoV and SARS-CoV-2 are bats. Chinese horseshoe bats coronaviruses are closely related to SARS-CoV. Among these, RsSHC014 and Rs3367 from Yunnan horseshoe bats have 95% homology with SARS-CoV [4]. The ORF8 protein SARSr-Rf-BatCoV YNLF_31C and YNLF_34C from greater horseshoe bats has over 80% homology to human SARS-CoV [5]. MERS-CoV has high homology with bat coronavirus HKU4 or HKU5 and its polymerase gene (RdRp) has 90–92% amino acid homology with the bat coronavirus HKU4 or HKU5 [1]. The genomes of SARS-CoV-2 and

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SARS-CoV are similar and have 79.6% identity. The SARS-CoV-2 and bat coronavirus RaTG13 has 96% identity in genome sequence. Given the high homology between SARS-CoV-2 and bats coronaviruses, bats may be the original host of SARS-CoV-2 [6,7]. Intermediate hosts between the three coronaviruses differ. SARS-CoV was isolated from civets, cats, raccoons and ferret badgers in live animal market, suggesting that these animals may serve as intermediate hosts [8]. MERS-CoV was isolated secretions obtained from the nose of a camel and those who were infected with this virus were in close contact with camels, suggesting that camels served as an intermediate host for the transmission of MERS-CoV [9]. Studies on COVID-19 have shown that the pangolin is an intermediate host for promoting the transfer of SARS-CoV-2 to humans [10]. Furthermore, in an animal model of SARS-CoV-2, animals vulnerable to the virus were ferrets and cats, which may also act as intermediate hosts for transmission to humans. The number and array of intermediate hosts for this virus are still uncertain [11]. The transmission of zoonotic coronaviruses to humans through an intermediate host may be related to human consumption of intermediate hosts via their meat, serum or milk or direct contact with these host animals. For example, a patient diagnosed with MERS-CoV infection experienced frequent contact with camels and consumed unpasteurized camel milk before diagnosis [12]. Active markets may provide ideal conditions for the amplification, recombination and transmission of the human coronaviruses to human hosts. During the process of epidemic prevention, public health surveillance in active markets is very important.

The spread of SARS and MERS between individuals is dominated by transmission through health care settings. A study on SARS in Hong Kong showed that 49.3% of infected individuals were related to clinics, hospitals or nursing homes, and health care workers accounted for 23% of infected individuals [13]. In the Toronto study, out of 144 patients diagnosed with SARS, 77% were associated with hospital exposure [14]. The incidence of MERS in health care settings may be high, reaching 100%. Nosocomial outbreaks of SARS and MERS are characterized by highly heterogeneous transmission and marked by super-spreading events. However, the prevalence rate of health-care workers with SARS is higher than MERS [15–17]. Among the first 138 cases of COVID-19, 41% of infections may be hospital-related transmissions [18]. Some secondary transmission cases for the three viruses were through community or family clusters. Among these, the famous Amoy Gardens SARS outbreak was associated to the sewage system failure after fecal pollution in the index case [13]. In the MERS family cluster study, close contact with patients and direct patient-care activities, such as resting in the room of target patients, contact with patient respiration secretions or the removal of human excreta were risk factors for family transmission of MERS [19]. There is a good number of asymptomatic patients with SARS, MERS and COVID-19. In a retrospective study, serological tests revealed asymptomatic SARS patients that composed a small number of cases [20]. There is a larger number of infected MERS and COVID-19 patients that appear to be asymptomatic [21,22]. Some asymptomatic COVID-19 patients continued to test negative through CT [23]. Asymptomatic patients contained high viral loads and long virus shedding times, indicating that transmission potential existed in asymptomatic patients [22,24]. Therefore, asymptomatic patients cannot be ignored in the process of epidemic prevention.

R0 indicates the average number of additional infections among fully susceptible people. In the absence of intervention and control measures, the R0 of SARS was about 3. Without effective public health intervention, the epidemic spread continuously and widely [25]. The R0 of COVID-19 is also large. Designating cases on the Japanese cruise ship Diamond Princess as a group, the R0 value was about 2.28 at the beginning of the outbreak. Another analysis of over 400 cases confirmed in Wuhan estimated that the R0 value was 2.2. Like SARS, COVID-19 has an R0 greater than 1 and is highly contagious [26,27]. The study on the ability of interhuman transmissibility of MERS showed that in most pessimistic scenario, the R0 of MERS in secondary cases was about 0.69 [28], A similar study estimated that without control, the range of R0 values for MERS was 0.8–1.3 [29]. R0 values for MERS was much lower than the epidemic threshold and did not show a trend of a continuous epidemic. However, during hospital outbreaks in Saudi Arabia and South Korea, the R0 of MERS was estimated to be 2–5, possibly since nosocomial infection could be transmitted not only by contact but also by aerosol contrary to community-acquired infection [30]. The above-mentioned R0 is mainly used for human-to-human transmission and R0 varies when used in host-to-human transmission.

3. Etiology

Different host selectivity and tissue toxicity of coronaviruses may depend on differences in spike (S) protein. The spike (S) protein of coronavirus is a type I membrane glycoprotein with multiple functional domains. It binds to the specific cell receptor through its S1 subunit and then mediates the fusion of the virus and the cell membrane through its S2 subunit [2]. SARS-CoV and SARS-CoV-2 enter the target cell through the ACE2 receptor and initiates S protein infection based on the host cell protease TMPRSS2 [31–34]. Compared to SARS-CoV, the RBD of SARS-CoV-2 binds to angiotensin converting enzyme II (ACE2) more closely and RBD residue changes make binding between the virus and receptor more stable [32]. A ten-year structure study based on SARS-CoV shows that the efficiency of SARS-CoV-2 using human ACE2 may be lower than human SARS-CoV (2002) but higher than human SARS-CoV (2003), indicating that COVID-19 has acquired some transmission power between individuals [35]. ACE2 is highly expressed in the lung, gastrointestinal tract, kidney, testis and cardiovascular system, especially in type II alveolar cells and intestinal epithelial cells, which is consistent with symptoms observed in SARS and COVID-19 cases [36,37]. ACE2 plays a role in a variety of biological functions such as regulating blood pressure, heart and kidney function [38,39]. ACE2 can reduce acute lung injury and shows protective effects in the lung [40,41]. CD209L (a transmembrane glycoprotein) is another receptor involved in SARS-CoV infection. However, the efficiency of mediating infection is much lower than that of ACE2 [42].

The MERS-CoV receptor is an exopeptidase dipeptidyl peptidase-IV (DPP IV; also known as CD26), which is a multifunctional type II transmembrane glycoprotein. DPP IV is highly expressed in the liver, kidney, intestinal epithelial cells and prostate. DPP IV also has a wide range of effects such as reducing intestinal insulin degradation. It also plays a role in lymphocyte immune functions and tumor transformation [43].

The cellular susceptibility of the three coronaviruses differs. In 9 different cell tests, SARS-CoV-2 and SARS-CoV showed similar tissue tendency and replicated stably in the lung cells, intestinal cells, hepatocytes and kidney cells. The replication ability of SARS-CoV-2 in the lung and intestine was opposite to what was observed for SARS-CoV. Moreover, SARS-CoV-2 had the ability to replicate in neuronal cells [44]. In a sensitivity study including 28 cell lines, MERS had the ability to effectively replicate in 17 cell types. In addition to respiratory tract infection, the viral load of MERS in the kidney, intestine, hepatocytes, tissue cells, neurons, monocytes and T lymphocytes increased significantly, showing a greater tissue tendency than SARS [45].

The peak viral load of SARS appeared on the 10th day and the peak viral load of MERS appeared during the second week of the disease [46,47]. Compared to SARS and MERS, the viral peak of COVID-19 appeared earlier, and the salivary viral load was the highest in the first week after symptom onset [48,49]. The viral load of the three viruses in severe cases was higher than that in mild groups [46,47,50]. In severe MERS-CoV infections, the time for virus shedding in respiratory secretions was also significantly longer than in mild patients [51]. Some studies had shown that there was a positive correlation between age and peak viral load in both SARS and COVID-19 cases [49,52]. Also, the initial viral load of people infected with SARS-CoV was independently correlated with poor prognosis [50].

4. Clinical features

The initial symptoms of MERS, SARS or COVID-19 infection are non-specific. Fever and cough are the most familiar and dry cough is the main symptom. Other communal symptoms include myalgia, shortness of breath or dyspnea, chills and gastrointestinal symptoms. Gastrointestinal symptoms (diarrhea, nausea and vomiting) are the first symptoms observed in some patients and most patients show potential complications. Severe cases will progress from no hypoxemia to acute respiratory distress syndrome, multiple organ failure or even death [13–15,18,19,24,46,53–67]. A corresponding summary is presented in Table 1.

Factors related to the progression of SARS and COVID-19 differ. Age and chronic hepatitis B virus infection were shown to be important independent risk factors for the progression of SARS to ARDS. Immunity of patients diagnosed with hepatitis B infection may not be able to resist coronavirus infection. Advanced age was a predictor of adverse outcomes for SARS [46]. Besides age, neutropenia, organ and coagulation dysfunctions also are associated with the progression of COVID-19 to ARDS and even the progression of ARDS to death. Among COVID-19 patients, patients with high fever are more likely to develop ARDS but have a lower risk of death [62].

Severe coronavirus cases show characteristics of advanced age, diabetes, hypertension, chronic heart disease and other chronic complications and greater APACHE-II and SOFA scores at admission. The main reason for entering the ICU may be that mechanical ventilation treatment is needed for ARDS [13,14,55,59,68–71]. It is possible that patients with these complications are more likely to trigger the release of a large number of cytokines during coronavirus infection. In SARS cases, tachycardia and elevated creatine kinase were associated with poor prognosis. Bilateral X-ray pulmonary infiltration was more common in patients who subsequently needed ICU care [55]. Central tachycardia is the score content of APACHE II in critically ill patients. Severe MERS patients required more renal replacement therapy than SARS and COVID-19 and showed extrapulmonary organ dysfunction [64,68,72]. Critically ill MERS patients were more likely to be treated with vasopressors. The need for vasopressors was an independent risk factor for death in MERS patients [69]. The use of vasopressor may indicate tissue perfusion disorders. Severe COVID-19 cases were also more likely to develop a sore throat, dyspnea, dizziness, abdominal pain and anorexia [70].

Table 1
Clinical and laboratory features of COVID-19, SARS and MERS.

	SARS [13,14,46,52] [53–55]	MERS [15,19] [24,56–58]	COVID-19 [18,59–66]
Demographic and general characteristics			
Male	25%–60%	65%–83%	43%–73%
Health care personnel	23%–51%	8.3–13%	29%
Infected by medical and health care	50%–77%	55.7%–98%	41%
Clinical characters			
fever	99%–100%	40%–98%	65%–99%
cough	29%–100%	18%–87%	22%–82%
Myalgia	20%–60%	7%–32%	11%–44%
shortness of breath	20%–60%	27%–72%	4%–35%
dyspnea	42%–44%	5%–15%	17%–40%
chills	15%–74%	7%–87%	7%–17%
diarrhea	10%–50%	7%–44%	1%–10%
vomiting or nausea	10%–35%	7%–21%	1%–13%
chest pain	30%	15%	2%
headache	15%–70%	5%–13%	4%–8%
sore throat	11%–30%	4%–11%	4%–26%
runny nose	2%–24%	4%	4%
Laboratory findings			
Leukopenia $<4 \times 10^9$	7%–34%	6%–14%	17%–25%
Lymphopenia $<1 \times 10^9$	54%–75%	35%	35%–70%
Thrombocytopenia	20%–44.8%	17%–36%	21%
Elevated lactate dehydrogenase	71%–87%	47%–49%	40%–98%
Elevated alanine transaminase	23%–56%	11%	17%–31%
Elevated aspartate transaminase	32%–78%	15%–53%	30%–37%
Complications			
diabetes	5%–40%	28%–87%	6%–34%
hypertension	11%–30%	22%–34%	19%–57%
Chronic lung disease	1%	26%–43%	2%–17%
heart disease	8%–10%	22%–53%	8%–18%
Chronic renal insufficiency	1%–5%	5%–53%	1%–8.5%
smoking	5%–20%	13%–23%	6%–15.6%
malignant disease	6%	2%–23%	0.5%–7%
Abnormal chest radiograph	70%–100%	87%–100%	100%
Treatment received			
Critically ill patients	20%–23%	53%–89%	14%–32%
Mechanical ventilation support	13%–50%	70%–78%	29%–89%
Mortality rate	3.6%–30%	60%–65%	4%–28%

SARS, the severe acute respiratory syndrome; MERS, the Middle East respiratory syndrome; COVID-19, 2019 novel coronavirus disease.

5. Laboratory examination

The most common laboratory tests for COVID-19, MERS and SARS measure lymphocytopenia, elevated lactate dehydrogenase and elevated liver transaminase. Thrombocytopenia and elevated creatine kinase can also be analyzed in some patients [13–15,18,19,24,46,53–67]. Elevated lactate dehydrogenase levels are associated with tissue injury. High or peak LDH levels were associated with ICU or death in SARS and COVID-19 patients [13,53,62]. This could predict pulmonary fibrosis in patients with MERS and SARS after discharged from the hospital [73,74]. In some SARS and COVID-19 cases, coagulation disorders were observed such as increased levels of D-dimer, prolonged prothrombin time or activated partial thromboplastin time [53,60]. In hospitalized COVID-19 patients, D-dimer levels greater than 1 μg/mL were associated with increased mortality [60]. In addition, hypoproteinemia was an independent risk factor for severe MERS infections [24].

6. Imaging

The abnormal rate of chest X-rays for coronaviruses is over 70% and the abnormal rate of chest X-ray in MERS and COVID-19 is greater than SARS [13–15,18,19,24,46,53–67]. Air-space opacity is an abnormality observed in SARS chest radiographs. After an initial, normal chest radiograph, it may develop into focal consolidation or bilateral, multifocal consolidation, primarily in the middle and lower regions of the lung and surrounding tissues without pleural effusion, cavitation or hilar lymph node enlargement [53,75–77]. A chest computed tomography (CT) is more sensitive to the changes of disease than a chest radiograph. Thin sliced CT for SARS was often manifested as ground glass opacity or ground glass opacity combined with consolidation. Interlobular septal thickening, interlobular interstitial thickening, the crazy-paving mode and bronchiectasis were also identified [78].

MERS chest radiographs showed that common changes included surrounding ground glass followed by consolidation, patchy consolidation, confluence or a round nodular shadow. In the late stage of the disease, more patients exhibited pleural effusion and pneumothorax. Pleural effusion and higher chest X-ray or chest CT scores were associated with poor prognosis and short-term mortality [69,79,80]. The chest CT of COVID-19 is very similar to the other two viruses. Most of the lesions involve bilateral lungs, showing multiple patchy ground glass opacity or consolidation, distributed in the surrounding tissues and some patients exhibited nodular lesions [66,67]. In early stages, multifocal incidence was greater than what was observed in the other two viruses. COVID-19 and MERS were more visible than SARS in pleural effusion and the pneumothorax [67,77,79].

7. Treatment

At present, there is no effective prevention or targeted treatment for the three coronaviruses but symptomatic support is available. Frequently used drugs to treat symptoms include antibiotics, antiviral drugs (ribavirin, oseltamivir, lopinavir/ritonavir, interferon) and steroids. Empirical antibiotic therapy is widely used since patients may have bacterial infections or complications cannot be ruled out.

7.1. Ribavirin

Ribavirin is a ribonucleoside analog that shows antiviral activity against a variety of DNA and RNA viruses. Its antiviral effect is directly related to its mutagenic activity in the treatment of poliomyelitis [81]. Even though ribavirin has widely been used in the treatment of coronaviruses, its efficacy has been controversial. In a retrospective cohort study investigating MERS, ribavirin combined with interferon-alpha significantly improved the 14-day survival rate of patients [82]. Another retrospective study investigating critically ill patients with MERS suggested that ribavirin/interferon may not lead to quicker RNA clearance of MERS-CoV and was associated with higher 90-day mortality in critically ill patients [83]. Ribavirin and glucocorticoids were widely used as a first-line treatment in critically ill SARS patients, but treatment outcomes suggested that the combination of ribavirin and glucocorticoids did not significantly benefit SARS [84]. Ribavirin shows obvious signs of toxicity and the use of high doses of ribavirin in critically ill patients can lead to progressive hemolytic anemia, bradycardia and hypomagnesemia [85]. The exact effects of ribavirin are unknown due to the mixed-use of multiple drugs. In the treatment of COVID-19, there have been many clinical trials for ribavirin, but the exact results are unknown.

7.2. Remdesivir

Remdesivir shows broad-spectrum, anti-coronavirus activity and can inhibit the replication of SARS-CoV and MERS-CoV in human epithelial cells, improve lung function and reduce viral load [86]. Remdesivir was effective in controlling SARS-CoV-2 infection *in vitro* [87]. However, evidence is needed through a large number of clinical trials to validate the role of Remdesivir in COVID-19.

7.3. Corticosteroids

Corticosteroids have anti-inflammatory effects and can improve lung injury and reduce mortality in ARDS [88]. The three coronaviruses can cause patients to develop ARDS and the body produced a large number of inflammatory factors. Thus, immune regulation of corticosteroids may be suitable for the treatment of these viruses, but this is controversial [61,89,90]. Corticosteroids may be effective in relieving symptoms of SARS and the use of glucocorticoids was recommended [91]. In ARDS patients diagnosed with COVID-19, methylprednisolone treatment reduced risk of death [62]. However, in a trial evaluating the efficacy and safety of corticosteroids for ARDS treatment, methylprednisolone was found to increase risk of death after use of corticosteroids, although the cardiopulmonary function of patients improved [92]. Corticosteroid treatment could significantly delay the clearance of MERS-CoV RNA in respiratory secretions or SARS-CoV in the blood, probably through immunosuppressive effects [93,94].

7.4. Lopinavir/ritonavir

Lopinavir/ritonavir is a protease inhibitor and may serve as a broad-spectrum anti-coronavirus inhibitor. The antiviral ability of ritonavir is weak, mainly inhibiting the metabolism of CYP3A-mediated lopinavir and increasing its serum concentration. *In vitro* tests show that 4 μ g/ml of lopinavir had antiviral effects on SRAS-CoV [95]. SARS patients initially treated with lopinavir/ritonavir showed reduced use of steroids, viral load, overall mortality and intubation rates [95,96]. In an *in vitro* study for MERS, a low concentration of lopinavir inhibited the replication of MERS-CoV and the inhibitory effect could reach 89% at the dose of 12 μM [97]. However, for SARS-CoV-2, lopinavir/ritonavir did not lead to a relevant decrease in viral load or significant clinical improvement and was more likely to cause gastrointestinal adverse events, including anorexia and nausea [98].

7.5. Chloroquine

Chloroquine/hydroxychloroquine is an anti-malarial drug showing direct antiviral and immunomodulatory effects [99]. *In vitro* experiments revealed that chloroquine was effective in the prevention and treatment of SARS-CoV infection. The addition of chloroquine before SARS infection showed that cells were not sensitive to SRAS-CoV infection [100,101]. Chloroquine inhibited MERS-CoV replication in a dose-dependent manner, with a 50% effective concentration of 3.0 μM [97]. The role of chloroquine in SRAS-CoV-2 is similar to SARS-CoV [87]. Another randomized trial of COVID-19 showed that hydroxychloroquine significantly shortened clinical recovery time and promoted the absorption of pneumonia [102].

7.6. Plasma

Plasma in the recovery phase contains antibodies. Passive immunotherapy can suppress viremia and neutralize pathogens [103]. In early stage SARS patients, the recovery period plasma prognosis was more optimal and the discharge rate was greater [104]. Compared to continuous use of high-dose methylprednisolone, hospital stays were shorter and the mortality rate was lower [105]. Five critically ill patients with COVID-19 given convalescent plasma resulted in decreased viral load and improved prognosis [106]. However, there are some uncertainties and limitations in the use of restored plasma, such as the lack of randomized clinical trials, the risk of transmitting the infection to transfusion service personnel and the appropriate choice of donors for high neutralizing antibody titers [103]. Therefore, considerations are needed during plasma transfusions.

7.7. Vaccines

Spike protein and its fragments are the key targets for developing a highly effective coronavirus vaccine, which will be a long process.

There are many vaccines under development for SARS, such as an inactivated or whole-killed virus vaccine, recombinant vector vaccines, subunit vaccines, DNA vaccines or attenuated vaccines. However, the effects of the vaccine for protecting humans from clinical symptoms and lung injury is still uncertain [107]. A study investigating the safety and efficacy of a modified vaccine based on the expression of SARS-CoV spike protein or nucleocapsid protein found that when vaccinated ferrets were exposed to SARS-CoV, liver tissue damage was significantly stronger than what was observed in the unvaccinated group [108]. Also, the candidate vaccines developed by MERS were similar to SARS. Among these, the MERS-CoV RBD-based subunit vaccine showed strong safety and effectiveness in protecting transgenic mice from MERS-CoV attack. Most vaccine studies on MERS are under preclinical development [109,110]. Vaccines against human SARS and MERS have not yet been approved. Presently, there are many countries working towards COVID-19 vaccine development. The vaccine development platform is similar to the previous two viruses. Some vaccines have rapidly entered into the clinical trial stage and the effectiveness and safety of the vaccines need to be seriously considered [111].

In conclusion, various drugs used for COVID-19 need to be confirmed by high-quality clinical trials.

7.8. Surgery and surgeons

Surgical thresholds during the SARS-CoV-2 pandemic should be higher than normal. A cohort study involving 24 countries showed that half of patients with perioperative COVID-19 patients had postoperative pulmonary complications, and were associated with high mortality [112]; Another study in Italy estimated that the surgical complications in COVID-19 patients with cancer was 13 times higher than that in the control group [113]. During the COVID-19 pandemic, surgeons need to balance the risks of delayed emergency surgery against the increased morbidity and mortality associated with SARS-CoV-2 infection.

For surgeons, standard personal protective equipment is absolutely necessary, specially performing operations related to aerosol generating procedures [114]. In addition, in order to minimize the risk of infection for patients and health care workers, surgeons should consider another clinical practice that limits time-in-hospital and promotes telemedicine to follow patients when needed [114,115].

7.9. Sequelae

During follow-ups for patients who have recovered from SARS and MERS, permanent damage to the lungs, commonly pulmonary fibrosis, was observed [73,74]. In an 8-month follow-up study of SARS patients, most patients showed focal, multifocal fibrosis through chest high-resolution computed tomography (HRCT). A total of 7% showed mild restrictive lung injury and 38% showed reduced diffusivity [116]. Since COVID-19 is a new outbreak, it is worrisome that follow-up results and sequelae may be assessed at a later time.

8. Summary

Presently, COVID-19 has resulted in a global pandemic, posing a major threat to public health. There is no effective treatment for COVID-19. Infected individuals are asked to stay in isolation while receiving treatment for their symptoms. Since all three zoonotic coronaviruses are similar, it is important to learn from SARS and MERS to understand how these may be related to this new outbreak. To further understand the pathogenesis and therapeutic targets of COVID-19, a larger number of animal studies and clinical trials are required.

Ethical approval

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Author contribution

Qingping Wu and Wanli Xie designed and conceived the paper. Jie Liu wrote the manuscript. Yanting Wang, Yue Xiong, Shiqiang Chen, Jingjing Han revised the manuscript. All authors read and approved the final manuscript.

Data statement

The data presented in the article may be requested by consulting the correspondence author.

Declaration of competing interest

None.

Acknowledgments

None.

List of Abbreviations

SARS-CoV	the severe acute respiratory syndrome coronavirus
MERS-CoV	the Middle East respiratory syndrome coronavirus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SARS	the severe acute respiratory syndrome
MERS	the Middle East respiratory syndrome
COVID-19	2019 novel coronavirus disease
HCoV-229E	human coronavirus 229E
HCoV-NL63	human coronavirus NL63
HCoV-OC43	human coronavirus OC43
HCoV-HKU1	human coronavirus HKU1
ACE2	angiotensin converting enzyme II
DPP IV	dipeptidyl peptidase-IV
CT	computed tomography

References

[1] J.F.W. Chan, K.S.M. Li, K.K.W. To, V.C.C. Cheng, H. Chen, K.-Y. Yuen, Is the discovery of the novel human betacoronavirus 2c EMC/2012 (HCoV-EMC) the beginning of another SARS-like pandemic? J. Infect. 65 (6) (2012) 477–489.

[2] T.M. Gallagher, M.J. Buchmeier, Coronavirus spike proteins in viral entry and pathogenesis, Virology 279 (2) (2001) 371–374.

[3] N. Kin, F. Miszczak, W. Lin, M.A. Gouilh, A. Vabret, Genomic analysis of 15 human coronaviruses OC43 (HCoV-OC43s) circulating in France from 2001 to 2013 reveals a high intra-specific diversity with new recombinant genotypes, Viruses 7 (5) (2015) 2358–2377.

[4] X.-Y. Ge, J.-L. Li, X.-L. Yang, A.A. Chmura, G. Zhu, J.H. Epstein, et al., Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor, Nature 503 (7477) (2013) 535–538.

[5] S.K.P. Lau, Y. Feng, H. Chen, H.K.H. Luk, W.-H. Yang, K.S.M. Li, et al., Severe acute respiratory syndrome (SARS) coronavirus ORF8 protein is acquired from SARS-related coronavirus from greater horseshoe bats through recombination, J. Virol. 89 (20) (2015) 10532–10547.

[6] P. Zhou, X.-L. Yang, X.-G. Wang, B. Hu, L. Zhang, W. Zhang, et al., A pneumonia outbreak associated with a new coronavirus of probable bat origin, Nature 579 (7798) (2020) 270–273.

[7] Z.J. Cheng, J. Shan, Novel coronavirus: where we are and what we know, Infection 48 (2) (2019) 155–163, 2020.

[8] Y. Guan, B.J. Zheng, Y.Q. He, X.L. Liu, Z.X. Zhuang, C.L. Cheung, et al., Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China, Science (New York, NY) 302 (5643) (2003) 276–278.

[9] E.I. Azhar, S.A. El-Kafrawy, S.A. Farraj, A.M. Hassan, M.S. Al-Saeed, A. M. Hashem, et al., Evidence for camel-to-human transmission of MERS coronavirus, N. Engl. J. Med. 370 (26) (2014) 2499–2505.

[10] T.T.-Y. Lam, M.H.-H. Shum, H.-C. Zhu, Y.-G. Tong, X.-B. Ni, Y.-S. Liao, et al., Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins, Nature 583 (7815) (2020) 282–285.

[11] J. Shi, Z. Wen, G. Zhong, H. Yang, C. Wang, B. Huang, et al., Susceptibility of Ferrets, Cats, Dogs, and Other Domesticated Animals to SARS-Coronavirus 2, Science, New York, NY, 2020.
[12] Z.A. Memish, M. Cotten, B. Meyer, S.J. Watson, A.J. Alsahafi, A.A. Al Rabeeah, et al., Human infection with MERS coronavirus after exposure to infected camels, Saudi Arabia, Emerg. Infect. Dis. 20 (6) (2013) 1012–1015, 2014.
[13] G.M. Leung, A.J. Hedley, L.-M. Ho, P. Chau, I.O.L. Wong, T.Q. Thach, et al., The epidemiology of severe acute respiratory syndrome in the 2003 Hong Kong epidemic: an analysis of all 1755 patients, Ann. Intern. Med. 141 (9) (2004) 662–673.
[14] C.M. Booth, L.M. Matukas, G.A. Tomlinson, A.R. Rachlis, D.B. Rose, H.A. Dwosh, et al., Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area, J. Am. Med. Assoc. 289 (21) (2003) 2801–2809.
[15] A. Assiri, A. McGeer, T.M. Perl, C.S. Price, A.A. Al Rabeeah, D.A.T. Cummings, et al., Hospital outbreak of Middle East respiratory syndrome coronavirus, N. Engl. J. Med. 369 (5) (2013) 407–416.
[16] C. Drosten, D. Muth, V.M. Corman, R. Hussain, M. Al Masri, W. HajOmar, et al., An observational, laboratory-based study of outbreaks of middle East respiratory syndrome coronavirus in Jeddah and Riyadh, kingdom of Saudi Arabia, Clin. Infect. Dis. : an official publication of the Infectious Diseases Society of America 60 (3) (2014) 369–377, 2015.
[17] G. Chowell, F. Abdirizak, S. Lee, J. Lee, E. Jung, H. Nishiura, et al., Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study, BMC Med. 13 (2015) 210.
[18] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in wuhan, China, J. Am. Med. Assoc. 323 (11) (2020) 1061–1069.
[19] M.A. Arwady, B. Alraddadi, C. Basler, E.I. Azhar, E. Abuelzein, A.I. Sindy, et al., Middle East respiratory syndrome coronavirus transmission in extended family, Saudi Arabia, Emerg. Infect. Dis. 22 (8) (2014) 1395–1402, 2016.
[20] X-y Che, B. Di, G-p Zhao, Y-d Wang, L-w Qiu, W. Hao, et al., A patient with asymptomatic severe acute respiratory syndrome (SARS) and antigenemia from the 2003-2004 community outbreak of SARS in Guangzhou, China. Clinical infectious diseases 43, an official publication of the Infectious Diseases Society of America, 2006, pp. e1–e5, 1.
[21] R. Grant, M.R. Malik, A. Elkholy, M.D. Van Kerkhove, A review of asymptomatic and subclinical Middle East respiratory syndrome coronavirus infections, Epidemiol. Rev. 41 (1) (2019) 69–81.
[22] C. Rothe, M. Schunk, P. Sothmann, G. Bretzel, G. Froeschl, C. Wallrauch, et al., Transmission of 2019-nCoV infection from an asymptomatic contact in Germany, N. Engl. J. Med. 382 (10) (2020) 970–971.
[23] Z. Ling, X. Xu, Q. Gan, L. Zhang, L. Luo, X. Tang, et al., Asymptomatic SARS-CoV-2 infected patients with persistent negative CT findings, Eur. J. Radiol. 126 (2020) 108956.
[24] M. Saad, A.S. Omrani, K. Baig, A. Bahloul, F. Elzein, M.A. Matin, et al., Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia, Int. J. Infect. Dis. : IJID : official publication of the International Society for Infectious Diseases 29 (2014) 301–306.
[25] M. Lipsitch, T. Cohen, B. Cooper, J.M. Robins, S. Ma, L. James, et al., Transmission dynamics and control of severe acute respiratory syndrome, Science (New York, NY) 300 (5627) (2003) 1966–1970.
[26] S. Zhang, M. Diao, W. Yu, L. Pei, Z. Lin, D. Chen, Estimation of the reproductive number of novel coronavirus (COVID-19) and the probable outbreak size on the Diamond Princess cruise ship: a data-driven analysis, Int. J. Infect. Dis. : IJID : official publication of the International Society for Infectious Diseases 93 (2020) 201–204.
[27] Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, et al., Early transmission dynamics in wuhan, China, of novel coronavirus-infected pneumonia, N. Engl. J. Med. 382 (13) (2020) 1199–1207.
[28] R. Breban, J. Riou, A. Fontanet, Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk, Lancet 382 (9893) (2013) 694–699.
[29] S. Cauchemez, C. Fraser, M.D. Van Kerkhove, C.A. Donnelly, S. Riley, A. Rambaut, et al., Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility, Lancet Infect. Dis. 14 (1) (2014) 50–56.
[30] S. Choi, E. Jung, B.Y. Choi, Y.J. Hur, M. Ki, High reproduction number of Middle East respiratory syndrome coronavirus in nosocomial outbreaks: mathematical modelling in Saudi Arabia and South Korea, J. Hosp. Infect. 99 (2) (2018) 162–168.
[31] W. Li, M.J. Moore, N. Vasilieva, J. Sui, S.K. Wong, M.A. Berne, et al., Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus, Nature 426 (6965) (2003) 450–454.
[32] J. Shang, G. Ye, K. Shi, Y. Wan, C. Luo, H. Aihara, et al., Structural basis of receptor recognition by SARS-CoV-2, Nature 581 (7807) (2020) 221–224.
[33] M. Hoffmann, H. Kleine-Weber, S. Schroeder, N. Krüger, T. Herrler, S. Erichsen, et al., SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor, Cell 181 (2) (2020) 271–280.
[34] S. Matsuyama, N. Nagata, K. Shirato, M. Kawase, M. Takeda, F. Taguchi, Efficient activation of the severe acute respiratory syndrome coronavirus spike protein by the transmembrane protease TMPRSS2, J. Virol. 84 (24) (2010) 12658–12664.
[35] Y. Wan, J. Shang, R. Graham, R.S. Baric, F. Li, Receptor recognition by the novel coronavirus from wuhan: an analysis based on decade-long structural studies of SARS coronavirus, J. Virol. 94 (7) (2020).
[36] I. Hamming, W. Timens, M.L.C. Bulthuis, A.T. Lely, G.J. Navis, H. van Goor, Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis, J. Pathol. 203 (2) (2004) 631–637.
[37] D. Harmer, M. Gilbert, R. Borman, K.L. Clark, Quantitative mRNA expression profiling of ACE 2, a novel homologue of angiotensin converting enzyme, FEBS Lett. 532 (1–2) (2002) 107–110.
[38] U. Danilczyk, J.M. Penninger, Angiotensin-converting enzyme II in the heart and the kidney, Circ. Res. 98 (4) (2006) 463–471.
[39] U. Danilczyk, U. Eriksson, G.Y. Oudit, J.M. Penninger, Physiological roles of angiotensin-converting enzyme 2, Cell. Mol. Life Sci. : CM 61 (21) (2004) 2714–2719.
[40] Y. Imai, K. Kuba, J.M. Penninger, The discovery of angiotensin-converting enzyme 2 and its role in acute lung injury in mice, Exp. Physiol. 93 (5) (2008) 543–548.
[41] K. Kuba, Y. Imai, S. Rao, H. Gao, F. Guo, B. Guan, et al., A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury, Nat. Med. 11 (8) (2005) 875–879.
[42] S.A. Jeffers, S.M. Tusell, L. Gillim-Ross, E.M. Hemmila, J.E. Achenbach, G. J. Babcock, et al., CD209L (L-SIGN) is a receptor for severe acute respiratory syndrome coronavirus, Proc. Natl. Acad. Sci. U. S. A. 101 (44) (2004) 15748–15753.
[43] A.-M. Lambeir, C. Durinx, S. Scharpé, I. De Meester, Dipeptidyl-peptidase IV from bench to bedside: an update on structural properties, functions, and clinical aspects of the enzyme DPP IV, Crit. Rev. Clin. Lab Sci. 40 (3) (2003) 209–294.
[44] H. Chu, J.F.-W. Chan, T.T.-T. Yuen, H. Shuai, S. Yuan, Y. Wang, et al., Comparative tropism, replication kinetics, and cell damage profiling of SARS-CoV-2 and SARS-CoV with implications for clinical manifestations, transmissibility, and laboratory studies of COVID-19: an observational study, The Lancet Microbe 1 (1) (2020) e14–e23.
[45] J.F.-W. Chan, K.-H. Chan, G.K.-Y. Choi, K.K.-W. To, H. Tse, J.-P. Cai, et al., Differential cell line susceptibility to the emerging novel human betacoronavirus 2c EMC/2012: implications for disease pathogenesis and clinical manifestation, J. Infect. Dis. 207 (11) (2013) 1743–1752.
[46] J.S.M. Peiris, C.M. Chu, V.C.C. Cheng, K.S. Chan, I.F.N. Hung, L.L.M. Poon, et al., Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study, Lancet 361 (9371) (2003) 1767–1772.
[47] M.-D. Oh, W.B. Park, P.G. Choe, S.-J. Choi, J.-I. Kim, J. Chae, et al., Viral load kinetics of MERS coronavirus infection, N. Engl. J. Med. 375 (13) (2016) 1303–1305.
[48] K.K.-W. To, O.T.-Y. Tsang, W.-S. Leung, A.R. Tam, T.-C. Wu, D.C. Lung, 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. 20 (5) (2020) 565–574.
[49] R. Wölfel, V.M. Corman, W. Guggemos, M. Seilmaier, S. Zange, M.A. Müller, et al., Virological assessment of hospitalized patients with COVID-2019, Nature 581 (7809) (2020) 465–469.
[50] C.-M. Chu, L.L.M. Poon, V.C.C. Cheng, K.-S. Chan, I.F.N. Hung, M.M.L. Wong, et al., Initial viral load and the outcomes of SARS, CMAJ (Can. Med. Assoc. J.) : Canadian Medical Association journal = journal de l'Association medicale canadienne 171 (11) (2004) 1349–1352.
[51] M-d Oh, W.B. Park, P.G. Choe, S.-J. Choi, J.-I. Kim, J. Chae, et al., Viral load kinetics of MERS coronavirus infection 375 (13) (2016) 1303–1305.
[52] W.-J. Chen, J.-Y. Yang, J.-H. Lin, C.S.J. Fann, V. Osyetrov, C.-C. King, et al., Nasopharyngeal shedding of severe acute respiratory syndrome-associated coronavirus is associated with genetic polymorphisms, Clin. Infect. Dis. : an official publication of the Infectious Diseases Society of America 42 (11) (2006) 1561–1569.
[53] N. Lee, D. Hui, A. Wu, P. Chan, P. Cameron, G.M. Joynt, et al., A major outbreak of severe acute respiratory syndrome in Hong Kong 348 (20) (2003) 1986–1994.
[54] L.-Y. Hsu, C.-C. Lee, J.A. Green, B. Ang, N.I. Paton, L. Lee, et al., Severe acute respiratory syndrome (SARS) in Singapore: clinical features of index patient and initial contacts, Emerg. Infect. Dis. 9 (6) (2003) 713–717.
[55] R.A. Fowler, S.E. Lapinsky, D. Hallett, A.S. Detsky, W.J. Sibbald, A.S. Slutsky, et al., Critically ill patients with severe acute respiratory syndrome, J. Am. Med. Assoc. 290 (3) (2003) 367–373.
[56] J.S.M. Peiris, S.T. Lai, L.L.M. Poon, Y. Guan, L.Y.C. Yam, W. Lim, et al., Coronavirus as a possible cause of severe acute respiratory syndrome, Lancet 361 (9366) (2003) 1319–1325.
[57] A. Assiri, J.A. Al-Tawfiq, A.A. Al-Rabeeah, F.A. Al-Rabiah, S. Al-Hajjar, A. Al-Barrak, et al., Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study, Lancet Infect. Dis. 13 (9) (2013) 752–761.
[58] J.A. Al-Tawfiq, K. Hinedi, J. Ghandour, H. Khairalla, S. Musleh, A. Ujayli, et al., Middle East respiratory syndrome coronavirus: a case-control study of hospitalized patients, Clin. Infect. Dis. : an official publication of the Infectious Diseases Society of America 59 (2) (2014) 160–165.
[59] Korea Centers for Disease C, Prevention, Middle East respiratory syndrome coronavirus outbreak in the Republic of Korea, Osong public health and research perspectives 6 (4) (2015) 269–278, 2015.
[60] F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, et al., Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, Lancet 395 (10229) (2020) 1054–1062.

[61] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Lancet 395 (10223) (2020) 497–506.

[62] C. Wu, X. Chen, Y. Cai, Ja Xia, X. Zhou, S. Xu, et al., Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in wuhan, China, JAMA internal medicine 180 (7) (2020) 1–11.

[63] K.K.-W. To, O.T.-Y. Tsang, W.-S. Leung, A.R. Tam, T.-C. Wu, D.C. Lung, 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. 20 (5) (2020) 565–574.

[64] S. Richardson, J.S. Hirsch, M. Narasimhan, J.M. Crawford, T. McGinn, K. W. Davidson, et al., Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area, J. Am. Med. Assoc. (2020), e206775.

[65] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, et al., Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, Lancet 395 (10223) (2020) 507–513.

[66] X. Li, W. Zeng, X. Li, H. Chen, L. Shi, X. Li, et al., CT imaging changes of corona virus disease 2019(COVID-19): a multi-center study in Southwest China, J. Transl. Med. 18 (1) (2020) 154.

[67] X. Xu, C. Yu, J. Qu, L. Zhang, S. Jiang, D. Huang, et al., Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2, Eur. J. Nucl. Med. Mol. Imag. 47 (5) (2020) 1275–1280.

[68] Y.M. Arabi, A.A. Arifi, H.H. Balkhy, H. Najm, A.S. Aldawood, A. Ghabashi, et al., Clinical course and outcomes of critically ill patients with Middle East respiratory syndrome coronavirus infection, Ann. Intern. Med. 160 (6) (2014) 389–397.

[69] G.A. Almekhlafi, M.M. Albarrak, Y. Mandourah, S. Hassan, A. Alwan, A. Abudayah, et al., Presentation and outcome of Middle East respiratory syndrome in Saudi intensive care unit patients, Crit. Care 20 (1) (2016) 123.

[70] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, et al., Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in wuhan, China, J. Am. Med. Assoc. 323 (11) (2020) 1061–1069.

[71] E.H.Y. Lau, C.A. Hsiung, B.J. Cowling, C.-H. Chen, L.-M. Ho, T. Tsang, et al., A comparative epidemiologic analysis of SARS in Hong Kong, Beijing and Taiwan, BMC Infect. Dis. 10 (2010) 50.

[72] X. Yang, Y. Yu, J. Xu, H. Shu, Ja Xia, H. Liu, et al., Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study, The Lancet Respiratory medicine 8 (5) (2020) 475–481.

[73] G.E. Antonio, K.T. Wong, D.S.C. Hui, A. Wu, N. Lee, E.H.Y. Yuen, et al., Thin-section CT in patients with severe acute respiratory syndrome following hospital discharge: preliminary experience, Radiology 228 (3) (2003) 810–815.

[74] K.M. Das, E.Y. Lee, R. Singh, M.A. Enani, K. Al Dossari, K. Van Gorkom, et al., Follow-up chest radiographic findings in patients with MERS-CoV after recovery, Indian J. Radiol. Imag. 27 (3) (2017) 342–349.

[75] N.S. Paul, H. Roberts, J. Butany, T. Chung, W. Gold, S. Mehta, et al., Radiologic pattern of disease in patients with severe acute respiratory syndrome: the Toronto experience, Radiographics : a review publication of the Radiological Society of North America, Inc 24 (2) (2004) 553–563.

[76] L. Grinblat, H. Shulman, A. Glickman, L. Matukas, N. Paul, Severe acute respiratory syndrome: radiographic review of 40 probable cases in Toronto, Canada, Radiology 228 (3) (2003) 802–809.

[77] K.T. Wong, G.E. Antonio, D.S.C. Hui, N. Lee, E.H.Y. Yuen, A. Wu, et al., Severe acute respiratory syndrome: radiographic appearances and pattern of progression in 138 patients 228 (2) (2003) 401–406.

[78] K.T. Wong, G.E. Antonio, D.S.C. Hui, N. Lee, E.H.Y. Yuen, A. Wu, et al., Thin-section CT of severe acute respiratory syndrome: evaluation of 73 patients exposed to or with the disease, Radiology 228 (2) (2003) 395–400.

[79] K.M. Das, E.Y. Lee, S.E. Al Jawder, M.A. Enani, R. Singh, L. Skakni, et al., Acute Middle East respiratory syndrome coronavirus: temporal lung changes observed on the chest radiographs of 55 patients, AJR American journal of roentgenology 205 (3) (2015) W267–W274.

[80] K.M. Das, E.Y. Lee, M.A. Enani, S.E. AlJawder, R. Singh, S. Bashir, et al., CT correlation with outcomes in 15 patients with acute Middle East respiratory syndrome coronavirus, AJR American journal of roentgenology 204 (4) (2015) 736–742.

[81] S. Crotty, D. Maag, J.J. Arnold, W. Zhong, J.Y. Lau, Z. Hong, et al., The broad-spectrum antiviral ribonucleoside ribavirin is an RNA virus mutagen, Nat. Med. 6 (12) (2000) 1375–1379.

[82] A.S. Omrani, M.M. Saad, K. Baig, A. Bahloul, M. Abdul-Matin, A.Y. Alaidaroos, et al., Ribavirin and interferon alfa-2a for severe Middle East respiratory syndrome coronavirus infection: a retrospective cohort study, Lancet Infect. Dis. 14 (11) (2014) 1090–1095.

[83] Y.M. Arabi, S. Shalhoub, Y. Mandourah, F. Al-Hameed, A. Al-Omari, E. Al Qasim, et al., Ribavirin and interferon therapy for critically ill patients with Middle East respiratory syndrome: a multicenter observational study, Clin. Infect. Dis. : an official publication of the Infectious Diseases Society of America 70 (9) (2020) 1837–1844.

[84] E.H.Y. Lau, B.J. Cowling, M.P. Muller, L.-M. Ho, T. Tsang, S.-V. Lo, et al., Effectiveness of ribavirin and corticosteroids for severe acute respiratory syndrome, Am. J. Med. 122 (12) (2009), 1150.e11-.e21.

[85] M.P. Muller, L. Dresser, J. Raboud, A. McGeer, E. Rea, S.E. Richardson, et al., Adverse events associated with high-dose ribavirin: evidence from the Toronto outbreak of severe acute respiratory syndrome, Pharmacotherapy 27 (4) (2007) 494–503.

[86] T.P. Sheahan, A.C. Sims, R.L. Graham, V.D. Menachery, L.E. Gralinski, J.B. Case, et al., Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses, Sci. Transl. Med. 9 (396) (2017).

[87] M. Wang, R. Cao, L. Zhang, X. Yang, J. Liu, M. Xu, et al., Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro, Cell Res. 30 (3) (2020) 269–271.

[88] Meduri Gu, A.S. Headley, E. Golden, S.J. Carson, R.A. Umberger, T. Kelso, et al., Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial, J. Am. Med. Assoc. 280 (2) (1998) 159–165.

[89] C.K. Wong, C.W.K. Lam, A.K.L. Wu, W.K. Ip, N.L.S. Lee, I.H.S. Chan, et al., Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome, Clin. Exp. Immunol. 136 (1) (2004).

[90] W.H. Mahallawi, O.F. Khabour, Q. Zhang, H.M. Makhdoum, B.A. Suliman, MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile, Cytokine 104 (2018).

[91] Z. Zhao, F. Zhang, M. Xu, K. Huang, W. Zhong, W. Cai, et al., Description and clinical treatment of an early outbreak of severe acute respiratory syndrome (SARS) in Guangzhou, PR China, J. Med. Microbiol. 52 (Pt 8) (2003) 715–720.

[92] K.P. Steinberg, L.D. Hudson, R.B. Goodman, C.L. Hough, P.N. Lanken, R. Hyzy, et al., Efficacy and safety of corticosteroids for persistent acute respiratory distress syndrome, N. Engl. J. Med. 354 (16) (2006) 1671–1684.

[93] Y.M. Arabi, Y. Mandourah, F. Al-Hameed, A.A. Sindi, G.A. Almekhlafi, M. A. Hussein, et al., Corticosteroid therapy for critically ill patients with Middle East respiratory syndrome, Am. J. Respir. Crit. Care Med. 197 (6) (2018) 757–767.

[94] N. Lee, K.C. Allen Chan, D.S. Hui, E.K.O. Ng, A. Wu, R.W.K. Chiu, et al., Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients, J. Clin. Virol. : the official publication of the Pan American Society for Clinical Virology 31 (4) (2004) 304–309.

[95] C.M. Chu, V.C.C. Cheng, I.F.N. Hung, M.M.L. Wong, K.H. Chan, K.S. Chan, et al., Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings, Thorax 59 (3) (2004) 252–256.

[96] K.S. Chan, S.T. Lai, C.M. Chu, E. Tsui, C.Y. Tam, M.M. Wong, et al., Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicentre retrospective matched cohort study, Hong Kong Med. J. 9 (6) (2003) 399–406.

[97] A.H. de Wilde, D. Jochmans, C.C. Posthuma, J.C. Zevenhoven-Dobbe, S. van Nieuwkoop, T.M. Bestebroer, et al., Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture, Antimicrob. Agents Chemother. 58 (8) (2014) 4875–4884.

[98] B. Cao, Y. Wang, D. Wen, W. Liu, J. Wang, G. Fan, et al., A trial of lopinavir-ritonavir in adults hospitalized with severe covid-19, N. Engl. J. Med. 382 (19) (2020) 1787–1799.

[99] A. Savarino, J.R. Boelaert, A. Cassone, G. Majori, R. Cauda, Effects of chloroquine on viral infections: an old drug against today's diseases? Lancet Infect. Dis. 3 (11) (2003) 722–727.

[100] M.J. Vincent, E. Bergeron, S. Benjannet, B.R. Erickson, P.E. Rollin, T.G. Ksiazek, et al., Chloroquine is a potent inhibitor of SARS coronavirus infection and spread, Virol. J. 2 (2005) 69.

[101] E. Keyaerts, L. Vijgen, P. Maes, J. Neyts, M. Van Ranst, In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine, Biochem. Biophys. Res. Commun. 323 (1) (2004) 264–268.

[102] Z. Chen, J. Hu, Z. Zhang, S. Jiang, S. Han, D. Yan, et al., Efficacy of Hydroxychloroquine in Patients with COVID-19: Results of a Randomized Clinical Trial, 2020.

[103] G. Marano, S. Vaglio, S. Pupella, G. Facco, L. Catalano, G.M. Liumbruno, et al., Convalescent plasma: new evidence for an old therapeutic tool? Blood transfusion = Trasfusione del sangue 14 (2) (2016) 152–157.

[104] Y. Cheng, R. Wong, Y.O.Y. Soo, W.S. Wong, C.K. Lee, M.H.L. Ng, et al., Use of convalescent plasma therapy in SARS patients in Hong Kong, Eur. J. Clin. Microbiol. Infect. Dis. : official publication of the European Society of Clinical Microbiology 24 (1) (2005) 44–46.

[105] Y.O.Y. Soo, Y. Cheng, R. Wong, D.S. Hui, C.K. Lee, K.K.S. Tsang, et al., Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients, Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 10 (7) (2004) 676–678.

[106] C. Shen, Z. Wang, F. Zhao, Y. Yang, J. Li, J. Yuan, et al., Treatment of 5 critically ill patients with COVID-19 with convalescent plasma, J. Am. Med. Assoc. 323 (16) (2020) 1582–1589.

[107] R.L. Roper, K.E. Rehm, SARS vaccines: where are we? Expet Rev. Vaccine 8 (7) (2009) 887–898.

[108] M. Czub, H. Weingartl, S. Czub, R. He, J. Cao, Evaluation of modified vaccinia virus Ankara based recombinant SARS vaccine in ferrets, Vaccine 23 (17–18) (2005) 2273–2279.

[109] L. Du, S. Jiang, Middle East respiratory syndrome: current status and future prospects for vaccine development, Expet Opin. Biol. Ther. 15 (11) (2015) 1647–1651.

[110] Y. Zhou, S. Jiang, L. Du, Prospects for a MERS-CoV spike vaccine, Expet Rev. Vaccine 17 (8) (2018) 677–686.

[111] T. Thanh Le, Z. Andreadakis, A. Kumar, R. Gómez Román, S. Tollefsen, M. Saville, et al., The COVID-19 vaccine development landscape, Nat. Rev. Drug Discov. 19 (5) (2020) 305–306.

[112] Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study, Lancet 396 (10243) (2020) 27–38.

[113] E.V. Robilotti, N.E. Babady, P.A. Mead, T. Rolling, R. Perez-Johnston, M. Bernardes, et al., Determinants of COVID-19 disease severity in patients with cancer, Nat. Med. (2020), https://doi.org/10.1038/s41591-020-0979-0.
[114] A. Barry, S. Apisarnthanarax, G.M. O'Kane, G. Sapisochin, R. Beecroft, R. Salem, et al., Management of primary hepatic malignancies during the COVID-19 pandemic: recommendations for risk mitigation from a multidisciplinary perspective, Lancet Gastroenterol Hepatol 5 (8) (2020) 765–775.
[115] J. Raskin, M. Lebeer, C. De Bondt, R. Wener, A. Janssens, J.P. van Meerbeeck, Cancer in the time of COVID-19: expert opinion on how to adapt current practice, Eur. Respir. J. 55 (5) (2020).
[116] C.-H. Chiang, J.-F. Shih, W.-J. Su, R.-P. Perng, Eight-month prospective study of 14 patients with hospital-acquired severe acute respiratory syndrome, Mayo Clin. Proc. 79 (11) (2004) 1372–1379.