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MYOCARDIAL INJURY IN COVID-19 AND THE ROLE OF TROPONIN TESTING

By Daniel Menza

Evidence to Date

Outside of the typical presentation of COVID-19, cardiac injury has been observed as a feature of the disease in some patients. The etiology is not completely clear, but increased demand on the heart, exacerbation of underlying cardiovascular disease and myocarditis caused by the virus have both been observed. The biomarker for cardiac injury, high sensitivity cardiac troponins, have been found to be highly predictive of who will progress to severe disease, with one study finding an odds ratio for death higher than any other biomarker studied. Currently, the American College of Cardiology does not recommend checking troponins in COVID-19 patients unless acute myocardial infarction is being considered. However, some authors have suggested that this test could be useful in predicting who will progress to severe disease and therefore triaging patients and helping clinicians determine who to treat more aggressively.

Details

Myocardial injury, as defined by elevation of troponin above the 99% percentile, has been seen in anywhere from 8-27% of patients presenting with COVID-19 [1,2,3]. Several mechanisms of injury have been hypothesized. The first is that the hypoxia that can be caused by COVID-19 combined with the increased strain on the heart in severe infection lead to insufficient myocardial oxygen supply, or a type 2 myocardial infarction [1,4,5,9]. The second is that the increased systemic inflammation due to COVID-19 infection can lead to atherosclerotic plaque instability and rupture, leading to a type 1 myocardial infarction [1,4,9]. Lastly, direct attack of cardiac myocytes leading to myocarditis has been observed in COVID-19 [3,4,9]. Cardiac myocytes express ACE2, the likely receptor SARS-CoV-2 uses to enter cells, so there exists a mechanism the virus would use to attack these cells [5]. Viral RNA has been found in hearts of 35% of COVID-19 patients on autopsy in one study, and other autopsy reports have found infiltration of the heart by interstitial mononuclear inflammatory cells, which suggests that this process certainly occurs [4,5].

The patients who are at risk for myocardial injury in COVID-19 tend to be older and more likely to have comorbidities, especially prior cardiovascular disease [1]. One study of 187 COVID-19 patients in Wuhan, China found that patients with myocardial injury were older (mean age 71.4 vs 53.5), more likely to be male (65.4% vs 42.2%), and had higher rates of comorbidities like hypertension (63.5% vs 20.5%), coronary heart disease (32.7% vs 3%), and diabetes (30.8% vs 8.9%) [4]. However, some of the patients with myocardial injury have been younger and without comorbidities. A case report from Italy describes a 53-year-old woman with no comorbidities presenting with elevated troponins and reduced ejection fraction [6].

Elevated troponins have been found to be a marker of severe disease and are strongly associated with poor outcomes. One study of 191 COVID-19 patients found that the odds ratio for death in patients with elevated troponin compared to those without was 80.1, which was higher than any other biomarker they looked at in this study [7]. Another study of 416 patients found that patients with elevated troponins were significantly more likely to require invasive ventilation (22% vs 4%), non-invasive ventilation (46% vs 4%), develop ARDS (59% vs 15%) and die (51% vs 5%). Many other studies have found similar results linking elevated troponins and risk of severe disease and death [3,4,8].

There has been some debate over how to use troponins in COVID-19 patients. Due to the prognostic value of troponins seen in the studies previously referenced, some authors feel that his test could be very useful in both initial evaluation of patients and in following patients. It could help identify patients who are at risk for bad outcomes and who therefore should be followed more closely and treated more aggressively [2,7]. However, the American College of Cardiology has recommended against checking troponins in...
COVID-19 patients unless acute myocardial infarction is being considered on clinical grounds. This is because of the high frequency of patients with elevated troponins and the non-specific nature of the abnormality in these patients [9].

References

Is there a Genetic Predisposition to Severe Illness with COVID-19 Infection?
By Katherine Veltri

Introduction
A recent case report from Iran identified fatal cases of COVID-19 in three brothers, ages 54-66, who lived separately and had no known underlying conditions. As similar cases around the world have been reported, as well as high variation of disease severity among middle-aged adults, it is hypothesized that there could be a genetic predisposition that leaves some individuals at increased risk for severe or fatal disease. [4]

Similarly to SARS-CoV, COVID-19 uses a spike (S) protein to enter human tissue through the angiotensin-converting enzyme-2 (ACE2) receptor. The ACE2 receptor is encoded by the ACE2 gene, and it is possible that genetic variation in ACE2 can contribute to susceptibility and/or resistance to viral infection.

Evidence to Date
ACE2 Expression:
ACE2 is found throughout the body, such as in the lungs, intestines, kidneys, liver etc. Since COVID-19 is known to spread through mucus membranes, Xu et al. explored ACE2 expression in the oral cavity. The study found that ACE2 is expressed on the mucosa of the oral cavity, and is more concentrated in the tongue than in the buccal or gingival tissues. While the study did not explore genetic differences in ACE2 expression in the oral cavity, they conclude that those with increased expression of ACE2 in their oral cavity could be vulnerable to COVID-19 infection. [3]

ACE2 Variation:
The S protein is a trimeric glycoprotein on the surface of COVID-19 that is used to gain entry into host cells via the ACE2 receptor. The receptor binding domain (RBD) of the S protein mediates receptor recognition and membrane fusion. Recent studies found evidence that ACE2 residues near lysine 31 and tyrosine 41, 82-84, 353-357 interact with the S protein. [2]

Renieri et al. hypothesize that genetic variation in the ACE2 receptor could modulate virion intake and thus disease severity [2]. This preprint study explored ACE2 genetic variation in the Italian population using the Network of Italian Genomes (NIG). They found three areas of genetic variation near the residues on ACE2 that interact with the S protein on COVID-19. These areas of variation, identified as p.Asn720Asp, p.Lys26Arg, p.Gly211Arg were moderately expressed in Italian and European non-Finnish populations, but had very low allele frequency in the Eastern Asian population. The study concluded that these variations could contribute to the increased severity of disease found in the
Italian and European-non Finnish population at the time the study was being prepared. Interestingly, they also found an extremely low rate of homozygous variants in females, which they attribute to the impact of X-inactivation. The study concludes that this could be one of many reasons why females are experiencing less morbidity and mortality compared to males. A limitation of this study is that the morbidity and mortality in the Italian and European-non Finnish population compared to the morbidity and mortality in other populations without these specific genetic variations is changing every day. [2]

Hussain et al. propose that genetic variation in spatial orientation of key binding residues on ACE2 can interfere with S protein binding. The study explored how genetic variation in the binding protein on ACE2 receptor affected S protein entry into cells. To do this, they used comparative modeling and generated docking poses by superimposition of ACE2 variants over ACE2-SARS-CoV-2 complex structure. Based off this modeling, they predict that ACE2 variants rs73653825 (S19P) and rs143936283 (E329G) have the lowest binding affinity with the S protein and may offer some level of resistance to viral infection. [1]

Conclusion

Since COVID-19 gains entry into host cells through the ACE2 receptor, current research suggests that genetic variation in the ACE2 receptor can lead to increased vulnerability or resistance against infection.

Limitations

It is hard to determine the clinical significance of the genetic variants identified in these studies. Renieri et al. used a genetic database to identify three genetic variants of ACE2 in the Italian population. With these findings, they suggest that these variants attribute to the severity of disease seen in Italy, without matching the variants to clinical outcomes in individuals. Hussain et al. identified genetic variants that may offer resistance to infection using a comparative modeling approach. These genetic variants should be matched to clinical outcomes in individuals before we can confirm that they offer any resistance to infection. Due to these limitations, it is premature to come to conclusions about what these variants mean on an individual level, especially as these studies were looking at broad populations. More research is needed to explore how these genetic variants influence the clinical course of disease.

References

Duration of Viral Shedding in Recovery Period: When Can Healthcare Workers Return to Work?
By Candace Pattillo

Evidence to Date

Duration of viral shedding in a patient recovering from COVID-19 is important to understand when considering the return of healthcare workers to clinical duties after being infected. While presence of viral RNA may not necessarily indicate infectivity, there is concern about infectious potential during recovery given the fact that asymptomatic carriers are able to transmit the disease.[1] Recent studies have shown that viral shedding begins prior to symptoms developing, but also seems to peak around 3-5 days of illness in upper respiratory tract samples with similar viral loads in asymptomatic and symptomatic patients.[2,3] At this time, the evidence varies for duration of viral shedding based on severity of the disease and specific risk factors, but there is no clear consensus. Review of the current literature about viral shedding may help update guidelines for return of healthcare workers to their clinical duties.

One study compared two different diagnostic tests, digital droplet PCR (ddPCR) and reverse transcriptase PCR (RT-PCR) while also assessing changes in viral load of different tissue samples (nasal, throat, sputum, blood, and urine) with disease progression. They found that the average number of days from symptom onset to recovery phase was 20 days (ranging from 10-33). The recovery phase was determined by gradual decrease of pulmonary lesions on CT scan and clinical cure was defined as fever-free for 3 days, improvement in respiratory symptoms, absorption of pulmonary lesions on CT scan, and two consecutive negative RT-PCR tests at least 24 hours apart. They found that ddPCR and RT-PCR were both reliable for high viral load and negative samples, but that ddPCR was better at detecting lower viral loads. In addition, the study revealed that viral load and rate of positive sample was significantly higher in sputum samples compared to throat and nasal swabs while using ddPCR. The results also demonstrated that for two patients who entered the recovery phase, they continued to have low levels of viral load for more than 9 days before having a negative test.[4]

Another study analyzing 28 patients from Korea, none of whom required oxygen therapy with invasive ventilation or any intensive care unit treatments, found that viral shedding was higher in upper respiratory samples compared to lower respiratory samples at 5 days using RT-PCR. They also found that viral shedding began to decline after 7 days as measured by cycle threshold (Ct) value.[2] They noted that 78.6% of cases were mild or asymptomatic. Overall, the median time to resolution of fever was 9 days (range 3-10) after symptom onset and 18.5 days (range 11-27) until the patients were off isolation, but they did not mention criteria for off-isolation. While this is a small sample size with primarily mild or asymptomatic cases, they found that viral shedding in upper respiratory samples was higher than in lower respiratory early in the disease course.

Other studies report varying durations of viral shedding. For instance, one study of 18 patients in Singapore revealed that average duration of viral shedding from first positive nasopharyngeal test to last was 12 days (range 1-24).[5] Another report of 16 people with mild cases found that the mean duration of symptoms was 8 days with half remaining viral positive after resolution of symptoms for an average of 2.5 days (range 1-8) as detected by throat swabs using RT-PCR.[6] In addition, a larger retrospective cohort study (n =191) analyzing risk factors for mortality found that among the 137 survivors, the average duration of viral shedding was 20 days (IQR 17-24) from illness onset using RT-PCR throat swabs. It was also found to be 19 days (range 17-22) in patients with severe disease and 24 days (22-30) in patients with critical disease.[7] Furthermore, studies have shown that viral shedding can persist longer in fecal samples with one particular report noting that fecal samples remained positive for 7 days (range 6-10) after nasopharyngeal swabs were negative and regardless of disease severity.[8] Overall, the RT-PCR results of nasopharyngeal and throat swabs, which may be appropriate for diagnostic purposes given the high upper respiratory viral shedding early in disease progression, but may not be as useful as lower respiratory samples or fecal for viral shedding in the convalescent period.

Risk Factors for Prolonged Viral RNA Shedding

A retrospective study analyzed factors that were associated with prolonged viral RNA shedding in 113 symptomatic patients.[9] Duration of viral RNA shedding was defined as the number of days from symptom onset to the first negative test of respiratory samples. This study purposefully analyzed viral RNA clearance only within 21 days and found that 84 patients achieved clearance within 21 days with the median being 15 days. Prolonged viral RNA shedding was defined as longer than 15 days. They found that male patients, delayed admission to hospital after onset of illness, and invasive mechanical ventilation, were independent risk factors for prolonged viral RNA shedding. Disease severity and use of corticosteroids were also found to be associated. The viral RNA was detected using RT-PCR with daily samples mostly from sputum, endotracheal aspirate, or bronchoalveolar lavage fluid. Less than 10% of the samples came from nasopharyngeal and throat swabs since lower respiratory tract samples were preferred. They classified patients based on illness severity with severe cases including severe pneumonia, ARDS, sepsis or septic shock. The ratio of severe patients on admission with prolonged viral shedding was larger than in the group with early viral clearance (<15 days). However, these results could be confounded by the fact that patients admitted to the hospital closer to when symptoms began received antiviral treatments earlier than patients who were admitted later (>5 days after symptoms began). Another important distinction to make is that viral RNA shedding is not the same as viral shedding and its effects on infectivity are not known. Overall, the study explores the possibility that specific risk factors related to disease severity can affect its duration.
factors, such as mechanical ventilation, can be associated with prolonged viral shedding.

Healthcare Workers Return to Work

The Centers for Disease Control and Prevention (CDC) includes a test-based and a non-test-based strategy for healthcare workers to return to work after being infected with COVID-19. The test-based strategy includes resolution of fever without anti-pyretics, improvement in respiratory symptoms, and 2 negative consecutive nasopharyngeal swabs at least 24 hours apart. The non-test-based strategy requires at least 3 days since resolution of fever without the use of antipyretics, improvement in respiratory symptoms, and at least 7 days since onset of symptoms. They also specify that after a healthcare worker returns to work, they should “wear a facemask at all times while in the healthcare facility until all symptoms are completely resolved or until 14 days after illness onset, whichever is longer” as well as to restrict contact from immunocompromised patients until 14 days after illness onset.[10]

Since there is no clear consensus about viral shedding in the recovery period and it seems to differ per sample and disease severity, a test-based strategy for return of healthcare workers to work should be preferred. The CDC prefers use of nasopharyngeal swabs, but it is possible that lower respiratory samples may be more accurate for detecting viral shedding in the recovery period.[4,8] While the data is inconclusive, it has shown that individuals can shed the virus for more than 14 days in respiratory samples and even longer in fecal samples.[8] Furthermore, patients can have subsequent positive tests for more than 7 days after improvement and resolution of symptoms. Therefore, 7 days since onset of symptoms for a non-test-based strategy may not be enough time to clear the virus. Further caution should be used if healthcare workers are returning to work with any symptoms given the higher ability to transmit the disease when symptomatic. However, one major limitation to current research is that no studies have examined infectivity of individuals in the recovery phase, but it does pose as a concern given the ability of asymptomatic carriers to infect others. If healthcare facilities are going to employ a non-test-based strategy, they should consider a duration longer than 7 days before returning from work given the likelihood that there is probably still relatively high viral shedding at that time since average peak in viral load is 3-5 days and duration of viral shedding can last longer than 14 days.

Conclusion

Current research regarding viral shedding during recovery has several collective limitations including small sample sizes, varying use of antivirals, tests from different manufacturers, and different samples used for those tests. None of the studies have assessed infectivity during this period. Furthermore, duration of viral shedding could vary based on disease severity and specific risk factors, but more information is needed. In terms of applying this information to practical settings, test-based strategies would be preferred healthcare workers to return to work after being infected with COVID-19, but more information about which tests and samples should be used as well as how this confers infectivity is needed to better inform this decision. For non-test-based strategies, healthcare facilities may want to consider the possibility of extending the duration before returning to work longer than 7 days since onset of symptoms if it is feasible given the high possibility that viral shedding may occur longer than 7-14 days and even after resolution of symptoms. However, due to the lack of medical personnel in many hospitals, difficulties in acquiring tests, length of time it takes to obtain test results, and inconclusive nature of the present data, it would be best to adhere to current CDC recommendations. Furthermore, there have been no documented cases of healthcare workers transmitting COVID-19 to others in their recovery period and if healthcare workers continue to maintain good hand hygiene as well as universal masking, this potential risk would be even lower. Overall, viral shedding in the recovery phase is a concern, particularly for infected healthcare workers, because asymptomatic individuals have been shown to transmit COVID-19, but more information is needed regarding the actual infectious potential of individuals in this period in order to best inform when healthcare workers can return to work after being infected with COVID-19.

References

Summary

Tracheostomy is a recognized aerosol generating procedure that was associated with increased risk of SARS infection. Techniques are being developed to mitigate risk of COVID-19 transmission while performing tracheostomy. Foster et al suggest a setup using an Ecolab Scope Pillow Warmer with Buffalo Filter smoke evacuator tubing during tracheostomy to provide a droplet barrier and air filtration while maintaining good visualization and relatively easy access to the surgical field. Vargas et al suggest the use of double lumen endotracheal tubes with flexible fiber-optic bronchoscopes and inflation of the cuff at the level of the carina to prevent aerosol spread. This was explored using a percutaneous technique, which was avoided during the SARS outbreak due to increased aerosolization risk, and current methods and risks regarding infection and aerosol have not been examined in the literature.

Evidence to Date

Aerosol generating procedures (AGPs) have been approached with great caution since the advent of COVID-19 and providers have been urged to wear proper PPE when performing them. One specific AGP that has been examined at length is that of the tracheostomy, which was associated with increased risk of SARS infection in healthcare workers.[1] This review aims to discuss possible improvements for tracheostomy procedures to protect healthcare workers by limiting the spreading of aerosol during the procedure.

When performing surgical tracheostomy under general anesthesia, the endotracheal tube is withdrawn to remove the cuff of the tube from the surgical field prior to making the tracheal stoma. When this incision is made, ventilation is lost which requires the stoma to be created and the tracheostomy tube inserted in a short amount of time.[2] A large spread of aerosol may occur during this procedure. Tracheal tube removal and tracheal cannula insertion has been identified as the most hazardous step with respect to spreading infection due to creation of droplets and aerosol.[3]

Foster et al have suggested a technique involving an Ecolab Scope Pillow Warmer Drape. After placing the table supine and draping them in the usual fashion, Omni-Tract retractor is mounted at the level of the abdomen with its retractor arms placed in a wide V configuration over the upper body. The Ecolab Scope Pillow Warmer Drape is stretched over the retractor arms to serve as a droplet barrier between the operative field and the surgeon while allowing for good...
visualization. Buffalo Filter smoke evacuator tubing is connected with two heat and moisture exchange (HME) filters in series and placed under the drape to provide air filtration of the operative field. This setup has been proposed to minimize the risk of exposure to the surgical team. It was tested in several dry runs and used successfully in one actual patient.[4]

Vargas et al suggest a technique that involves a double lumen endotracheal tube (DLET) containing a flexible fiber-optic bronchoscope (FFB) in the upper lumen with the lower lumen dedicated solely to ventilation. They recommend pushing the endotracheal tube as caudally as possible beyond the site chosen for the tracheal stoma to prevent cuff incision. However, they have observed in the past that the endotracheal tube and the tracheal cannula can be simultaneously inserted within the trachea when using a DLET.[5] They propose that cuffing the endotracheal tube at the level of the carina after confirmation with FFB can avoid spread of aerosol while performing the procedure as the DLET is not removed until the cannula is correctly positioned under direct visualization.

However, Vargas et al’s technique was explored using percutaneous dilational tracheostomy, which requires more extensive airway manipulation and results in increased generation of aerosol.[6] Open tracheostomies were preferred during the SARS outbreak for these reasons.[7] Percutaneous techniques have advanced since then but the considerations, safety and PPE requirements for them in an infected, aerosolized setting have not been established in the literature.

The above recommendations have emerged given the increased risk to healthcare workers during the COVID-19 pandemic. Tracheostomy indications may increase if patients with COVID-19 remain ventilated for extended periods of time. Preventing nosocomial infection should be a priority during this pandemic, and the previously outlined techniques attempt to address this issue.

References

Remdesivir Update
By Kevin Brandecker

Summary
This paper looks at the outcomes of 53 out of the 61 patients that had received their first dose of Remdesivir by March 7, 2020, on a compassionate use basis. Seven patients were excluded due to missing post-baseline information and one for an incorrect starting date. All patients were hospitalized, Covid-19 positive via reverse transcriptase-polymerase chain reaction and had an oxygen saturation of less than 94% on room air or need oxygen support. Patients were treated with Remdesivir for up to 10 days and were then followed for the next 28 days or until discharge or death if sooner. By day 18, 68% had improvement in the degree of oxygen supported needed while 15% had worsened. Among those who were receiving mechanical ventilation, 57% were extubated and 75% of those on ECMO were stopped. By day 28, 84% of patients either had improved by ≥2 points on the ordinal scale or were discharged alive with 13% having died after completing the 10-day course. This is lower mortality then reported in a lopinavir-ritonavir trial which found a mortality of 22% and studies out of Wuhan, China showing a 22% mortality overall in hospitalized patients and 66% among those receiving mechanical ventilation. It is important to note that Gilead Science, makers of Remdesivir, designed the program and collected the data as well as employed a writer who wrote the initial draft along with one of the authors with input from all of the other authors.

Background
This study conducted by Gilead Science looked at the outcomes of patients treated with Remdesivir on a compassionate use basis. Criteria for treatment with Remdesivir included hospitalization with Covid-19 confirmed via reverse transcriptase-polymerase chain reaction assay with oxygen saturation less than 94 % on room air or who need oxygen support. Patients were also required to have a creatine clearance above 30 mL/minute, a serum level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) less than 5 times the upper limit and agree not to use any other investigational agents for Covid-19.

They were treated with a 10-day course of Remdesivir, 200 mg loading dose IV on day 1, then 100 mg daily for the next 9 days. They were then followed for the next 28 days or until discharge or death. Sixty-one patients had received a dose of Remdesivir by March 7, 2020. In that group, 7 patients were excluded due to missing post-baseline information and 1 due to an incorrect start date. This left 53 patients of which 40 patients (57 %) received the full 10 days, 10 patients (19%) received 5-9 days of treatment and 3 patients (6 %) fewer than 5 days. Clinical improvement was defined as live discharge or a decrease by ≥ 2 from baseline on a modified ordinal scale.

<table>
<thead>
<tr>
<th>Score</th>
<th>Condition</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Not hospitalized</td>
</tr>
<tr>
<td>2</td>
<td>hospitalized, not requiring supplemental oxygen</td>
</tr>
<tr>
<td>3</td>
<td>hospitalized, requiring supplemental oxygen</td>
</tr>
<tr>
<td>4</td>
<td>hospitalized, requiring nasal high-flow oxygen therapy, noninvasive mechanical ventilation, or both</td>
</tr>
<tr>
<td>5</td>
<td>hospitalized, requiring invasive mechanical ventilation, ECMO, or both</td>
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<td>6</td>
<td>death</td>
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The median timeframe from symptoms to the initiation of Remdesivir was 12 days. At the initiation of the trial 30 patients (57%) were receiving invasive mechanical ventilation and 4 patients (8%) were on ECMO. Those receiving invasive ventilation tended to be older, male, and have preexisting medical conditions.

By day 18, 68% of patients showed an improvement in the degree of oxygen support needed while 15% had worsened. Among those who were receiving mechanical ventilation, 57% were extubated and 75% of those on ECMO were stopped. By day 28, 84% of patients either had improved by ≥2 points on the ordinal scale or were discharged alive. Seven patients (13%) died after completing the 10-day course of Remdesivir; of which 6 were receiving invasive mechanical ventilation and 1 non-invasive oxygen support at the start of the trial.

Increased hepatic enzymes, diarrhea, rash, renal impairment, and hypotension were the most common adverse events and occurred more often in those receiving invasive mechanical ventilation. During the study 12 patients (23%), who were all receiving invasive mechanical ventilation, had serious adverse events including; multi organ dysfunction syndromes, septic shock, acute kidney injury, and hypotension. Remdesivir was discontinued in 4 patients (8%) due to; one for worsening preexisting renal failure, one due to multi organ failure, and two due to elevated aminotransferase of which one developed a maculopapular rash.

With a median follow up of 18 days 68% of patients were found to have an improvement in their oxygen saturation with an overall mortality of 13%. They compared this to a randomized control trial of lopinavir-ritonavir in hospitalized patients which showed a mortality of 22%. They note that in the lopinavir-ritonavir trial only 1 of 199 patients was receiving invasive mechanical ventilation at baseline. Another study showed a 22% mortality overall in hospitalized patients and 66% among those receiving mechanical ventilation in Wuhan, China. There are currently several clinical trials being...
performed with Remdesivir in both critically and moderately ill patients to assess its efficacy in the treatment of Covid-19. But the initial data from those treated with Remdesivir as part of compassionate care show that Remdesivir may be a successful pharmacological option for the treatment of Covid-19.

During the trial, no data was collected on viral load to assess Remdesivir antiviral function. They note that the study is limited due to small size, short follow up periods, lack of information on the 8 patients initially treated, and the lack of a control group. Gilead Science, makers of Remdesivir, designed the program and collected the data as well as employed a writer who wrote the initial draft along with one of the authors with input from all of the other authors.

Reference


Clinical Discharge Guidelines for COVID-19
By Kevin Brandecker

Evidence to Date

Currently the CDC guidance states that COVID-19 patients can be discharged “when clinically indicated.” This is distinct from the criteria which are used to decide when the patient can be discontinued from transmission-based precautions. The indications for discontinuing transmission-based precautions are divided into a test based and a non-test-based strategy. The test-based strategy means the patient must have resolution of their fever without anti-pyretic medications, an improvement in their respiratory symptoms, and two negative nasal swab test results over 24 hours apart. The non-test-based strategy means the patient must be fever free for 3 days without anti-pyretic medications, have an improvement in their respiratory symptoms and 7 days must have passed since symptoms first appeared. If the clinical team feels that the patient is ready for discharge prior to these criteria being met, the patient can be discharged if they will be able to successfully home isolate and the local public health department should be involved in the decision making [1].

The discharge criteria the Chinese have been using has also been published. They require the body temperature return to normal for 3 days, significant improvement in respiratory symptoms, marked improvement in exudative lesions on pulmonary imaging, and two negative nucleic acid tests on respiratory specimens over 24 hours apart [2].

There has not been much discussion of whether patients are clinically ready to be discharged, rather the controversial portion of these guidelines is if and how much the patients will still be actively shedding virus. One study from China reported 25 patients who met the above specified discharge criteria, but were then found to be virus positive again between 2 and 13 days later without new onset of symptoms [3]. Another Chinese study of 7 patients discharged after meeting the criteria found that 3 of them were found to be virus positive again between 5-7 days later with no new symptoms [4]. These studies highlight the challenges in discharging COVID-19 patients, who may be clinically ready to go home but are still shedding virus.

Another study in China followed 172 Covid-19 patients after discharge from the hospital with repeat cloacal and nasopharyngeal swabs. At the time of discharge, all patients had met the criteria for discharge in China including two consecutively negative RT-PCR tests separated by at least 24 hours. Upon returning home patients had cloacal and nasopharyngeal swab samples collected every 3 days. It was found that 25 patients retested positive, 14 via cloacal swab
and 11 via nasopharyngeal, for Covid-19 after returning home. There was no mention if any of these patients developed previous or additional symptoms, but the positive tests were considered unexpected by the researchers. The average time from the last negative to new positive was 7.32 ±3.86 days. The median age of this group was 28 and contained 6 children under the age of 12 which does not accurately reflect the age of the average hospitalized Covid-19 patient, no age range was given for group that remained negative. The authors recommend that the time period between swabs be increased to 48 hours as well as looking at immunological parameters like D-dimer and absolute lymphocyte count in order to support that the conclusion that the Covid-19 has been cleared. This is due to a correlation found between there level and the chance of having a delayed positive test [5].

References