ACC-CCA Webinar Notes 3.18.20 (Epidemiology, CVD Treatment & Management)

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As China is getting close to declare victory over COVID-19 (only 10-20 new cases a day across the country), here are some important lessons learned from the Chinese experience:

****Chinese Guidelines for Diagnosis and Treatment of COVID-19 (7th Edition)****

Virology and Epidemiology

- SARS-CoV-2 → β genus, diameter 60-140 nm
- Shares 79% of nuclear identity of SARS-CoV-1 and 52% of that of MERS
- ACE-2 is the host cell receptor
- Affects alveolar type II cells primarily → lung pathology very similar to SARS and MERS (bilateral diffuse alveolar damage with cellular fibromyxoid exudates)
- Can also affect the heart, the liver, and the kidney
- Disinfection by Ethanol and UV light, not inactivated by Chlorhexidine
- Epidemic started in China, now Europe is the epicenter
- Mortality in China 2.3%, but ~5% in Italy
- Median incubation period 4 – 5.2 days (95% percentile is 12.5 days)
- Main source of infection is asymptomatic infected people
- Route of transmission is respiratory droplets, close contact with asymptomatic infected people, long-term environmental exposure to high viral aerosolized load, possibly fecal transmission too
- R_0 2.2 – 2.95 (i.e. one infected person infects on average 2-3 healthy individuals)

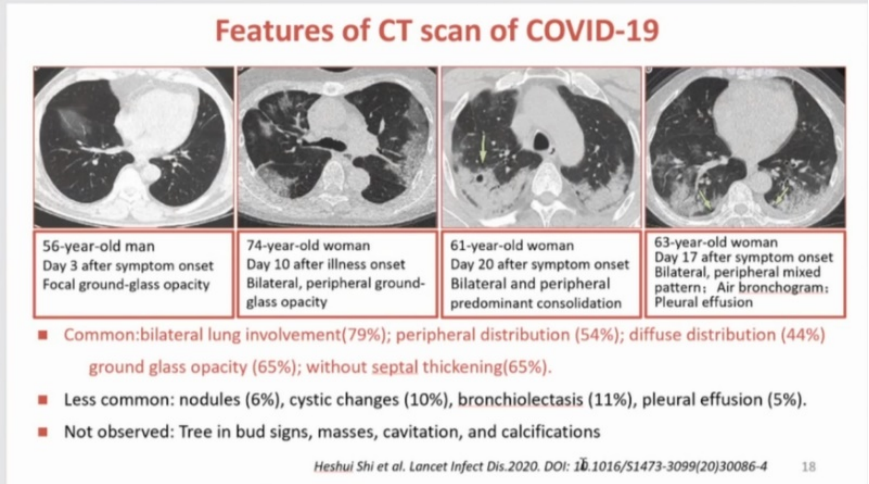
Clinical Findings

- WHO diagnostic criteria (one epidemiological + 2 clinical findings OR 3 clinical findings)
    - Epidemiological criteria:
        - H/o travel to (or residence in) high risk areas
        - H/o contact with a confirmed or suspected case
        - Attendance of events where clusters of cases were reported
    - Clinical criteria:
        - Fever
        - Respiratory symptoms (e.g. cough and dyspnea)
        - Leucopenia/ Lymphopenia (unclear etiology but very characteristic with COVID-19)
- Frequency of symptoms and complications:
    - Fever 98%
    - Cough 76% (mostly dry)
    - Lymphopenia 63% - lowest at day 7, prolonged lymphopenia poor prognostic sign
    - Diarrhea 3%
    - Complications: ARDS 29%, acute cardiac injury 12%, AKI 7%, septic shock 7%, secondary bacterial infection 10%
- Average duration of dyspnea is 13 days, 45% of survivors still had cough on discharge

- Median duration of viral shedding is 20 days (up to 37 days)
- COVID vs Influenza
    - Similar constellation of symptoms – recommend evaluation with RVP
    - Clinically, onset of COVID is slower than influenza which tends to be more abrupt
    - Additionally there appears to be less sputum production in COVID as compared to influenza
- Important observations from the Chinese experience:
    - D-dimer > 1µg/ml → independent risk factor for in-hospital death
    - Very high D-dimer and FDP levels in severe cases → extensive intravascular microthrombi on autopsy (possibly related to high ACE-2 expression in vascular endothelial cells) → **Anticoagulation should be started in severe COVID-19 cases if no contraindication (Chinese Expert opinion – no supporting evidence)**
    - Red flags for severity:
        - Progressive lymphopenia
        - Progressive increase in inflammatory biomarkers (IL-6 and CRP)
        - Progressive worsening infiltrates on CT scan
        - Elevated troponin and D-dimer

Diagnostic Tests

- RNA detection (RT-PCR) from nasopharyngeal swab, sputum, lower respiratory tract samples (best yield), blood and feces
- Serum antibody detection (IgM and IgG)
    - RNA testing alone has high false negative
    - When RNA testing + serum Ab testing → 98% sensitivity
    - Some cases tested positive for RNA again after discharge with negative test (unclear significance for now)
- Chest CT
    - Bilateral lung involvement
    - Peripheral distribution
    - Diffuse distribution
    - Ground glass opacities (can appear before the clinical onset of illness)
    - No septal thickening



Treatment

- **Isolation**
    - All confirmed and suspected cases (did not specify but seems that they used airborne given use of N95 and mention of negative pressure rooms)
    - PPE for healthcare workers → N95 when taking care of suspected or confirmed cases / Surgical masks everywhere else in the hospital (ALL THE TIME)
- **Supportive therapy**

    - Sufficient caloric intake (many patients had hypoproteinemia)
    - Water and electrolytes
- **Antiviral therapy**
    - So far, no specific antiviral for SARS-CoV-2
    - Clinically evaluated antivirals:
        - Lopinavir-ritonavir monotherapy (LOTUS China, trial completed, just published, no therapeutic benefit observed beyond standard care https://www.nejm.org/doi/full/10.1056/NEJMoa2001282?query=TOC) – **1st line therapy in China during the epidemic surge**
        - Remdesivir (CAP China Remdesivir 1 and 2, ongoing trials for mild-mod and severe pneumonia)
    - Other antimicrobials without supportive clinical data:
        - Ribavirin
        - Chloroquine
        - Arbidol
        - Convalescent plasma therapy
        - Favipiravir (favilavir)
- **Immune therapy**
    - Targeting the host immune response to the virus
    - Tocilizumab – IL-6 monoclonal antibody – for severe cases
- **Steroids**
    - Controversial
    - Central role for inflammation has been determined in the pathophysiology of COVID-19
    - Used for rapid deterioration in oxygenation and radiologic findings
    - Low to moderate doses only – max 1-2 mg/kg/day of methylprednisone
    - For 3-5 days only

Discharge Criteria

- Normal temperature for >3 days
- Improvement of respiratory symptoms
- 2 consecutive negative respiratory specimens at least 24 hours apart

****COVID-19 and Cardiovascular Disease****

COVID-19 patients with underlying cardiovascular disease have the highest fatality rate (10.5%)

Pathology of Cardiac Damage

- Mononuclear inflammatory infiltrate
- Endothelial shedding
- Intravascular thrombosis
- SARS-CoV-2 inclusions can be seen

Mechanisms of Acute Cardiac Damage

- ACE-2-mediated direct cellular damage
- Hypoxia-induced myocardial damage
- Microvascular damage
- SIRS

Clinical Presentations and Complications

- Arrhythmias (17%)
- Acute cardiac injury (elevated high-sensitivity troponin) (12%)
- Elevated regular troponin or CK-MB (7.2%) → occurs in severe cases (mostly negative in mild and moderate cases) → mortality 49%
- Fulminant myocarditis can occur (they presented a case with regional STE [inferior leads], negative coronary angiogram, initial drop in EF to 27%, and complete recovery with supportive therapy)
- STEMI can also occur as a complication
- Important observations:
    - ↓ pericardial adipose tissue correlates with COVID-19 severity
    - There may be evidence of chronic cardiovascular damage following COVID-19

Management of Cardiac Medications

- ACEI/ ARBs → dilemma:
    - The good: ACEI/ARBs → ↓Angiotensin II activity → improvement of lung inflammatory response
    - The bad: ACEI/ARBs → ↑ACE-2 activity → increase viral cellular bindings and facilitate infection
    - CV perspective:
        - They are essential medications from a cardiovascular standpoint
        - For COVID-19 mortality, HTN had an OR of 3.05
        - ➔ The current Chinese recommendation is NOT to stop them in COVID-19 patients
- Antiplatelets → continue
- Statins → continue and monitor liver functions closely
- BB → selective B1 blockers are recommended in the absence of airways spasm

Important Considerations with Antiviral Medications

- Antiviral interaction with cardiovascular drugs (……I missed the examples….)
- Lopinavir/ritonavir (the first-line antiviral therapy in China) can cause complete heart block and dilated cardiomyopathy

Management of Acute MI and Protection of Cardiologists during COVID-19

Important general rules:

- Nearby therapy (treat at the nearest medical center – avoid transfers as possible)
- Safe protection (if fever or suspicion of COVID-19 in AMI patients → test immediately → isolate)
- Travel and exposure history should be assessed in all STEMI patients

- Thrombolysis first (rather than primary PCI) in confirmed or suspected COVID-19 patients. *Remember: PCI less widely available in China than in US, and thus thrombolysis remains a more standard therapy there.*
- Coronary angiography for suspected or confirmed COVID-19 patients should be in designated Cath labs (with negative pressure if available)
- In suspected or confirmed COVID-19 cases who need cardiology input → use remote cardiology consultation as possible (virtual or telephone)
- Avoid unnecessary hospitalizations

Important Final Remarks

- The most dangerous thing about this epidemic from the Chinese perspective is *the transmission by asymptomatic or mildly symptomatic infected individuals.*
- We learned from Wuhan and Italy that *young healthy people can also get severe disease and die*
- *Many infections in healthcare professionals* (in China → 3.8% of the cases are HC workers, of those, 15% were severe/critically ill, 5 deaths)
- Observation from Wuhan is that the rate of *co-infection with other respiratory viruses especially influenza is high.* Dr Bin Cao said "*As if they always came together"* when referring to influenza pneumonia and COVID-19. This has huge implications since many US hospital protocols now say that if RVP is +ve then no need to test for SARS-CoV-2.
- Best way to prepare from a hospital perspective is DIAGNOSIS *(you need to know who's infected and who's not once they present to clinic or ED → RNA testing IMMEDIATELY*) – to ensure proper isolation and admission to appropriate wards/ICU.
- Changes to hospitals workflow in Wuhan:
    - *All outpatient clinics were closed during the epidemic surge*
    - *All outpatient visits were performed virtually or by telephone (if medical attention is needed → ED)*
    - *Marked increase in the use of thrombolysis (vs primary PCI) for STEMI*
- Social isolation/ distancing is EFFECTIVE → needs to be done for *at least 2-4 weeks*
- Best way to think about the situation now is: *No more normal life, it's COVID-19 pandemic life* (things that are not normally acceptable or feasible should be now, to face the pandemic)