AASLD-NASPGHAN-SPLIT COVID-19 & the Liver: Pediatric Perspective

July 23, 2020
5:00pm – 6:00pm EDT

Moderated by:
Emily J. Rothbaum Perito, MD
Nadia Ovchinsky, MD, MBA

Presenters:
Jaime Chu, MD
Noelle Ebel, MD
Mohit Kehar, MBBS, DNB
Burnett “Beau” S. Kelly, MD

Panelists:
Vicky Lee Ng, MD, FRCPC
Mercedes Martinez, MD
Webinar Agenda

❖ Housekeeping Items – Dr. Nadia Ovchinsky
❖ Presenter Introductions – Dr. Nadia Ovchinsky
❖ Webinar Introduction – Dr. Nadia Ovchinsky / Dr. Emily Perito
❖ Liver manifestations of pediatric COVID-19 infection and MIS-C – Dr. Jaime Chu
❖ COVID-19 Registry: Outcomes in Pediatric Liver Transplant Recipients – Dr. Mohit Kehar & Dr. Noelle Ebel
❖ Re-Entry into Clinical Transplantation during a COVID Pandemic – Dr. Beau Kelly
❖ Panel Discussion / Q&A
Webinar Q&A

Submit your questions in the Q&A box at the top or bottom of your screen.

Questions will be answered at the end of the presentation.
Webinar Moderator

Nadia Ovchinsky, MD, MBA
Director, Pediatric Hepatology
Medical Director, Pediatric Liver Transplant
Associate Professor of Pediatrics,
Children’s Hospital at Montefiore – Albert Einstein College of Medicine
Goryeb Children's Hospital, Morristown NJ
Webinar Moderator

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Associate Medical Director of Pediatric Liver Transplant
Associate Professor of Pediatrics and of Epidemiology and Biostatistics
University of California, San Francisco
Jaime Chu, MD

Associate Chief in the Division of Pediatric Hepatology
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Icahn School of Medicine and the Recanati / Miller Transplantation Institute at Mount Sinai
Webinar Presenter

Mohit Kehar, MBBS, DNB
Pediatric Gastroenterologist and Hepatologist – Kingston Health Science Center
Assistant Professor in the Department of Pediatrics – Queens University
Webinar Presenter

Noelle Ebel, MD

Assistant Professor of Pediatrics

Director the Alagille Syndrome Program

Stanford University
Webinar Presenter

Burnett "Beau" Kelly, MD, MBA, FACS, FAST

Surgical Director and Transplant Surgeon

DCI Donor Services, Inc.
Webinar Panelist

Vicky Lee Ng, MD, FRCPC

Professor of Pediatrics – University of Toronto

Medical Director, Pediatric Liver Transplantation – Hospital for Sick Children
Webinar Panelist

Mercedes Martinez, MD

Associate Professor of Pediatrics – Columbia University Medical Center

Director, Intestinal Transplant Program – Columbia University College of Physicians and Surgeons
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- Co-chair, Oren K. Fix, MD, MSc, FAASLD, Swedish Medical Center (Washington)
- Co-chair, Elizabeth C. Verna, MD, MS, Columbia University (New York)
- Kimberly Brown, MD, Henry Ford Health System (Michigan)
- Jaime Chu, MD, Icahn School of Medicine at Mount Sinai (New York)
- Bilal Hameed, MD, University of California (California)
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- Andrew Reynolds, (Patient Advocate)
- Raymond Chung and K. Rajender Reddy (ex-officio)
AASLD-NASPGHAN-SPLIT COVID-19 & the Liver: Pediatric Perspective

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Joint Webinar
COVID-19 in Children

Kids do get the coronavirus — they just don’t get as sick

By Stephanie Pappas - Live Science Contributor  March 06, 2020

A new study suggests that kids are as likely as adults to be infected with the new coronavirus, but their symptoms tend to be mild.

SARS-CoV-2 Infection in Children

TO THE EDITOR: As of March 10, 2020, the 2019 novel coronavirus (SARS-CoV-2) has been responsible for more than 110,000 infections and 4000 deaths worldwide, but data regarding the epidemiologic characteristics and clinical features of infected children are limited.2 A recent review of 72,314 cases by the Chinese Center for Disease Control and Prevention showed that less than 1% of the cases were in children younger than 10 years of age.2 In order to determine the spectrum of disease in children, we evaluated children infected with SARS-CoV-2 and treated at the Wuhan Children’s Hospital, the only center assigned by the central government for treating infected children under 16 years of age in Wuhan. Both symptomatic and asymptomatic children with known contact with persons having confirmed or suspected SARS-CoV-2 infection were evaluated. Nasopharyngeal or throat swabs were obtained for detection of SARS-CoV-2 RNA by established methods.2 The clinical outcomes were monitored up to March 8, 2020.

Of the 1391 children assessed and tested from January 28 through February 26, 2020, a total of 171 (12.3%) were confirmed to have SARS-CoV-2 infection. Demographic data and clinical features are summarized in Table 1. (Details of the laboratory and radiologic findings are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.) The median age of the infected children was 6.7 years. Fever was present in 41.5% of the children at any time during the illness. Other common signs and symptoms included cough and pharyngeal erythema. A total of 27 patients (15.8%) did not have any symptoms of infection or radiologic features of pneumonia. A total of 12 patients had radiologic features of pneumonia but did not have any symptoms of infection. During the course of hospitalization, 3 patients required intensive care support and invasive mechanical ventilation; all had coexisting conditions (hydropspherosis, leukemia [for which the patient was receiving maintenance chemotherapy], and intussusception]. Lymphopenia (lymphocyte count <1.2×10⁷ per liter) was present in 6 patients (3.5%). The most
COVID-19 in Children

COVID-19 Pediatrics Daily Update: March 20, 2020

- **RECENT CHAM NUMBERS & STATISTICS**
  - As of the morning of March 20, 2020, the Department of Pediatrics has tested 22 children at the Children’s Hospital at Montefiore (CHAM). Of the total 22 tests:
    - 1 test positive
    - 8 tests negative
    - 13 tests pending

- **FIRST COVID-19 CASE**
  - On Thursday, March 19, we confirmed our first COVID-19 positive patient at CHAM. The teams from Pediatric Emergency Medicine (PEM) to our inpatient services did an excellent job screening the patient and appropriately isolating the patient in the emergency department (ED) and throughout her admission until the testing results were available. Thank you for the great teamwork in maintaining a safe environment for our patients and staff.

- **Admiring Nadia Ovchinsky**
  - @D... · 3/28/20
  - Admitting my first liver transplant
  - #covidpositive baby
COVID-19 in Children

15 Children Are Hospitalized With Mysterious Illness Possibly Tied to Covid-19

The health authorities in New York City issued an alert saying that the children had a syndrome that doctors do not yet fully understand.

By Joseph Goldstein
Published May 5, 2020  Updated May 13, 2020

An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study

Laure Vendramin, Angelino Mazzari, Annalisa Gervasini, Laura Martelli, Maurizio Ruggieri, Matteo Gaffrazi, Edo Baravalle, Lorenzo Pignatelli

Summary
Background The Bergamo province, which is extensively affected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic, is a natural observatory of virus manifestations in the general population. In the past month we recorded an outbreak of Kawasaki disease; we aimed to evaluate incidence and features of patients with Kawasaki-like disease diagnosed during the SARS-CoV-2 epidemic.

Methods All patients diagnosed with a Kawasaki-like disease at our centre in the past 5 years were divided according to symptomatic presentation before (group 1) or after (group 2) the beginning of the SARS-CoV-2 epidemic. Kawasaki-like presentations were managed as Kawasaki disease according to the American Heart Association indications. Kawasaki disease shock syndrome (KDSS) was defined by presence of circulatory dysfunction, and macrophage activation syndrome (MAS) by the Paediatric Rheumatology International Trials Organisation criteria. Current or previous infection was sought by reverse-transcriptase quantitative PCR in nasopharyngeal and oropharyngeal swabs, and by serological qualitative test detecting SARS-CoV-2 IgM and IgG, respectively.

Findings Group 1 comprised 19 patients (seven boys, 12 girls; aged 3-0 years [SD 2-5]) diagnosed between Jan 1, 2015, and Feb 17, 2020. Group 2 included ten patients (seven boys, three girls; aged 7-5 years [SD 1-5]) diagnosed between Feb 18 and April 20, 2020; eight of ten were positive for IgG or IgM, or both. The two groups differed in disease incidence (group 1 vs group 2, 6:0-3 vs ten per month, means age (5:6 w 7:5 years), cardiac involvement (two of 19 vs six of ten), KDSS (zero of 19 vs five of ten), MAS (zero of 19 vs five of ten), and need for adjudicial steroid treatment (three of 19 in eight of ten, all p<0-00).

Interpretation In the past month we found a 30-fold increased incidence of Kawasaki-like disease. Children diagnosed after the SARS-CoV-2 epidemic began showed evidence of immune response to the virus, were older, had a higher rate of cardiac involvement, and features of MAS. The SARS-CoV-2 epidemic was associated with high incidence of a severe form of Kawasaki disease. A similar outbreak of Kawasaki-like disease is expected in countries involved in the SARS-CoV-2 epidemic.
Liver manifestations of pediatric COVID-19 infection and MIS-C

Jaime Chu, MD
Associate Chief in the Division of Pediatric Hepatology
Associate Professor of Pediatrics
Icahn School of Medicine and the Recanati / Miller Transplantation Institute at Mount Sinai
Overview

Focus on liver manifestations in COVID-19 and MIS-C in children without known chronic liver disease or transplantation

1. Pathogenesis of liver injury in COVID-19
2. Liver injury in COVID-19
3. Liver injury in Multisystem Inflammatory Syndrome in Children (MIS-C)
Viral pathogenesis of SARS-CoV-2

Adapted from Risitano et al., Nat Rev Immunol, June 2020.
Viral pathogenesis of SARS-CoV-2

1. Viral Entry
   - Spike protein
   - Viral RNA
   - ACE2
   - Endocytosis
   - Genomic RNA release
   - Translational
   - Proteolysis

2. Viral Replication
   - Host cell ribosomes
   - Genomic RNA replication
   - Translation
   - Multiple proteins

3. Inflammation and Immune Dysregulation
   - Acute respiratory distress syndrome
   - Sepsis
   - Hypoxemia
   - Hypovolemia
   - Liver injury
   - Systemic inflammatory response
   - Hypoventilation
   - Intestinal flora disturbances
   - Heart injury
   - Renal injury

Adapted from Risitano et al., Nat Rev Immunol, June 2020.

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Multiple etiologies of liver injury in COVID-19

- Direct injury to liver cells
  - Limited data regarding ACE2 expression in cholangiocytes > hepatocytes
- Secondary to COVID-19 complications:
  - myositis (AST > ALT)
  - cardiac injury
  - ischemia/hypotension
  - cytokine release syndrome
- Drug-induced liver injury
- Multisystem Inflammatory Syndrome in Children (MIS-C)

Burden of COVID-19 in children

Relatively fewer cases of COVID-19 among children compared to cases among adult patients:

- **United States**: 2% of confirmed cases of COVID-19 were <18 years
- **China**: 2.2% were pediatric COVID-19 cases
- **Italy**: 1.2% were pediatric COVID-19 cases
- **Spain**: 0.8% were pediatric COVID-19 cases


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COVID-19 clinical course is less severe in children

N = 2135 pediatric COVID-19 cases, Chinese CDC

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>% of total cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>4%</td>
</tr>
<tr>
<td>Mild</td>
<td>51%</td>
</tr>
<tr>
<td>Moderate</td>
<td>39%</td>
</tr>
<tr>
<td>Severe</td>
<td>5%</td>
</tr>
<tr>
<td>Critical</td>
<td>0.6%</td>
</tr>
</tbody>
</table>
The majority of adult COVID-19 with mild liver injury

Abnormal liver biochemistries in the first 30 days of +COVID test

<table>
<thead>
<tr>
<th>Peak ALT</th>
<th></th>
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<tbody>
<tr>
<td>&lt;ULN</td>
<td>445</td>
</tr>
<tr>
<td>≥1× to &lt;2×ULN</td>
<td>190</td>
</tr>
<tr>
<td>≥2× to &lt;5×ULN</td>
<td>141</td>
</tr>
<tr>
<td>≥5× to &lt;10×ULN</td>
<td>32</td>
</tr>
<tr>
<td>≥10×ULN</td>
<td>8</td>
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</table>

<table>
<thead>
<tr>
<th>Peak ALP</th>
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<tbody>
<tr>
<td>&lt;ULN</td>
<td>747</td>
</tr>
<tr>
<td>≥1× to &lt;2×ULN</td>
<td>65</td>
</tr>
<tr>
<td>≥2× to &lt;5×ULN</td>
<td>4</td>
</tr>
<tr>
<td>≥5× to &lt;10×ULN</td>
<td>0</td>
</tr>
<tr>
<td>≥10×ULN</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Peak total bilirubin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;ULN</td>
<td>391</td>
</tr>
<tr>
<td>≥1× to &lt;2×ULN</td>
<td>339</td>
</tr>
<tr>
<td>≥2× to &lt;5×ULN</td>
<td>79</td>
</tr>
<tr>
<td>≥5× to &lt;10×ULN</td>
<td>6</td>
</tr>
<tr>
<td>≥10×ULN</td>
<td>1</td>
</tr>
</tbody>
</table>
### Pediatric COVID-19 and mild liver injury

Table 2. Difference of Laboratory Findings of Pediatric Patients With Coronavirus Disease 2019 on Admission to Hospital

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Median (IQR)</th>
<th>Mild (n = 60)</th>
<th>Moderate (n = 88)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coagulation function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin time, s</td>
<td>10.9 (10.5-11.3)</td>
<td>10.9 (10.6-11.4)</td>
<td>10.8 (10.5-11.1)</td>
<td>.24</td>
</tr>
<tr>
<td>Fibrinogen, g/L</td>
<td>207 (177-252)</td>
<td>199 (176-231)</td>
<td>214 (178-267)</td>
<td>.26</td>
</tr>
<tr>
<td>Activated partial thromboplastin time, s</td>
<td>30.8 (28.7-33.8)</td>
<td>30.3 (27.8-33.5)</td>
<td>30.9 (28.8-34.2)</td>
<td>.28</td>
</tr>
<tr>
<td>Thrombin time, s</td>
<td>18.4 (17.7-19.4)</td>
<td>18.6 (18.0-19.2)</td>
<td>18.4 (17.5-19.6)</td>
<td>.84</td>
</tr>
<tr>
<td>D-dimer, μg/mL</td>
<td>0.20 (0.14-0.35)</td>
<td>0.16 (0.13-0.26)</td>
<td>0.24 (0.15-0.36)</td>
<td>.02</td>
</tr>
<tr>
<td><strong>Liver function</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.44 (0.32-0.61)</td>
<td>0.51 (0.36-0.67)</td>
<td>0.43 (0.29-0.58)</td>
<td>.04</td>
</tr>
<tr>
<td>Direct bilirubin, mg/dL</td>
<td>0.14 (0.10-0.19)</td>
<td>0.15 (0.10-0.20)</td>
<td>0.13 (0.09-0.19)</td>
<td>.12</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>4.54 (4.32-4.77)</td>
<td>4.56 (4.34-4.82)</td>
<td>4.54 (4.31-4.75)</td>
<td>.27</td>
</tr>
<tr>
<td>Globulin, mean (SD), g/dL</td>
<td>2.30 (0.48)</td>
<td>2.34 (0.37)</td>
<td>2.27 (0.54)</td>
<td>.48</td>
</tr>
<tr>
<td>Alanine aminotransferase, U/L</td>
<td>16.0 (12.0-26.0)</td>
<td>13.0 (11.0-18.8)</td>
<td>18.0 (12.3-33.8)</td>
<td>.001</td>
</tr>
<tr>
<td>γ-glutamyltransferase, U/L</td>
<td>11.0 (9.0-16.0)</td>
<td>10.0 (8.0-13.0)</td>
<td>12.0 (10.0-19.0)</td>
<td>.005</td>
</tr>
<tr>
<td>Aspartate aminotransferase</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level, U/L</td>
<td>30.0 (23.0-41.8)</td>
<td>25.0 (20.3-34.5)</td>
<td>33.0 (24.0-46.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Increased, No. (%)</td>
<td>25 (16.9)</td>
<td>4 (6.7)</td>
<td>21 (23.9)</td>
<td>.007</td>
</tr>
</tbody>
</table>
Emerging evidence suggests increased ALT is associated with more severe COVID-19

- Increased ALT or abnormal liver function on admission is associated with more severe COVID-19
- COVID-19 patients with elevated liver chemistries had increased risk of adverse clinical outcomes and mortality compared to patients without elevated liver chemistries
- Difficult to determine whether the liver injury is directly modulating disease or whether the injury is secondary to COVID-19-related pathologies, DILI, or immune dysregulation

Yip TC-F et al., Gut, June 2020
Mao et al., Lancet Gastroenterol Hepatol, May 2020
Kulkarni et al., Aliment Pharmacol Ther, July 2020
Fan et al., Clin Gastroenterol Hepatol, April 2020
Multisystem Inflammatory Syndrome in Children (MIS-C)
Pediatric Cases of COVID-19 and MIS-C in New York State

MIS-C: CDC definition, 5 criteria

1. Hospitalized patient < 21 years
2. Fever ≥ 24 hours
3. Laboratory evidence of inflammation (CRP, ESR, fibrinogen, procalcitonin, d-dimer, ferritin, LDH, or IL-6, elevated neutrophils, reduced lymphocytes and low albumin)
4. Multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological)
5. Evidence of SARS-CoV-2 infection by RT-PCR, antibody, antigen test; or exposure to a suspected or confirmed COVID-19 case within the last 4 weeks of symptom onset

https://www.cdc.gov/mis-c/hcp/
Children with MIS-C admitted to pediatric ICUs in New York City between April 23 and May 23, 2020

In contrast with the infantile age distribution of Kawasaki disease, MIS-C is predominantly a disease of older children and adolescents (median age 10 years) and is consistent with other centers.
Liver injury is mild in MIS-C

- PICU LOS = 4.7 days
- Hospital LOS 7.8 days
- Mortality 3%
- Rapid, complete clinical and myocardial recovery was almost universal

Table II. Admission laboratory test results of all patients with MIS-C

<table>
<thead>
<tr>
<th>Tests</th>
<th>Value</th>
<th>Reference normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV-2 PCR positive</td>
<td>11 (33)</td>
<td>–</td>
</tr>
<tr>
<td>SARS-CoV-2 antibody positive</td>
<td>27 (81)</td>
<td>–</td>
</tr>
<tr>
<td>SARS CoV-2 PCR and antibody positive</td>
<td>6 (18)</td>
<td>–</td>
</tr>
<tr>
<td>WBC, cells/μL</td>
<td>11,000 (8450-14,400)</td>
<td>4000-11,000/μL</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>11.3 (9.55-12.5)</td>
<td>10.5-14 g/dL</td>
</tr>
<tr>
<td>Platelets, thousands/μL</td>
<td>176 (130.5-282)</td>
<td>150-300 K/μL</td>
</tr>
<tr>
<td>Absolute lymphocyte count, thousands/μL</td>
<td>1.1 (0.6-1.3)</td>
<td>1.0-4.0 K/μL</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>53 (28.2-77.2)</td>
<td>0-10 mm/h</td>
</tr>
<tr>
<td>Serum sodium, mEq/L</td>
<td>136 (135-139)</td>
<td>135-145 mEq/L</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.5 (2.6-3.9)</td>
<td>3.5-4.9 g/dL</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>12 (9-16)</td>
<td>6-23 mg/dL</td>
</tr>
<tr>
<td>Serum creatinine, mg/dL</td>
<td>0.6 (0.4-1.1)</td>
<td>0.7-1.3 mg/dL</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>45 (27-69)</td>
<td>1-35 U/L</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>36 (28-53)</td>
<td>1-45 U/L</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>0.7 (0.4-1.3)</td>
<td>0.1-1.2 mg/dL</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>250 (156-302)</td>
<td>0.0-5.0 mg/L</td>
</tr>
<tr>
<td>C-reactive protein at peak, mg/L</td>
<td>255 (181-310)</td>
<td>0.0-5.0 mg/L</td>
</tr>
<tr>
<td>Procalcitonin, ng/mL</td>
<td>5.4 (1.8-16.7)</td>
<td>&lt;0.1 ng/mL</td>
</tr>
<tr>
<td>Procalcitonin peak, ng/mL</td>
<td>6 (2.7-16.5)</td>
<td>&lt;0.1 ng/mL</td>
</tr>
<tr>
<td>Fibrinogen, mg/dL</td>
<td>627 (455-782)</td>
<td>162-378 mg/dL</td>
</tr>
<tr>
<td>Ferritin, ng/mL</td>
<td>568 (340-954)</td>
<td>80-500 mg/dL</td>
</tr>
<tr>
<td>BNP at admission, pg/mL</td>
<td>388 (75-1086)</td>
<td>0-100 pg/mL</td>
</tr>
</tbody>
</table>
Liver injury is more common in MIS-C than in acute COVID-19

Percentage of MIS-C Patients with ALT ≥ 40 U/L, by Age

- Overall (N=186) 64%
- 13-20 years (N=45) 77%
- 5 - 12 years (N=75) 68%
- < 5 years (N = 66) 51%

186 MIS-C Cases, 26 states
March 15-May 20, 2020

MIS-C ICU cases: persistent but mild liver injury (U.K)

<table>
<thead>
<tr>
<th></th>
<th>Reference ranges</th>
<th>Day 1 (n=78)</th>
<th>Day 2 (n=44)</th>
<th>Day 3 (n=43)</th>
<th>Day 4 (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil count (×10⁶ cells per L)</td>
<td>2-0-7-5</td>
<td>12-3 (10-7-22-9)</td>
<td>13-2 (9-2-17-6)</td>
<td>13-0 (8-9-19-4)</td>
<td>11-9 (7-2-20-0)</td>
</tr>
<tr>
<td>Lymphocyte count (×10⁶ cells per L)</td>
<td>1-5-4-0</td>
<td>0-7 (0-4-1-1)</td>
<td>0-9 (0-7-1-6)</td>
<td>1-2 (0-9-1-7)</td>
<td>1-8 (1-0-2-3)</td>
</tr>
<tr>
<td>Platelet count (×10⁶ cells per L)</td>
<td>150-400</td>
<td>125 (75-178)</td>
<td>179 (115-272)</td>
<td>187 (109-293)</td>
<td>201 (100-358)</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>&lt;5</td>
<td>264 (192-316)</td>
<td>233 (143-308)</td>
<td>191 (77-283)</td>
<td>96 (39-197)</td>
</tr>
<tr>
<td>D-dimer (µg/L)</td>
<td>&lt;500</td>
<td>4030 (2349-7422)</td>
<td>2293 (1319-4638)</td>
<td>3503 (1902-5291)</td>
<td>1659 (646-3792)</td>
</tr>
<tr>
<td>Ferritin (µg/L)</td>
<td>12-200</td>
<td>1042 (538-1746)</td>
<td>1152 (473-1529)</td>
<td>842 (495-1422)</td>
<td>757 (484-1198)</td>
</tr>
<tr>
<td>Troponin (ng/L)</td>
<td>&lt;10</td>
<td>157 (43-810)</td>
<td>232 (70-829)</td>
<td>355 (66-2252)</td>
<td>358 (30-3015)</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>60-120</td>
<td>75 (46-103)</td>
<td>54 (41-77)</td>
<td>48 (34-67)</td>
<td>49 (32-64)</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>10-50</td>
<td>50 (30-93)</td>
<td>51 (27-77)</td>
<td>43 (30-68)</td>
<td>51 (35-71)</td>
</tr>
</tbody>
</table>

Data are median (IQR). PICU=paediatric intensive care unit. ALT=alanine aminotransferase.

Table 2: Laboratory results for the first 4 days of PICU admission
Summary and Recommendations

- Liver injury is common but mild in most pediatric COVID-19 and MIS-C cases
- Etiologies of abnormal liver biochemistries include myositis, ischemia, cardiac injury, DILI, MIS-C
- Monitor for interval change of liver tests, especially in pediatric patients receiving investigational treatments such as remdesivir and tocilizumab
- Longitudinal studies are needed to determine the long-term effects of COVID-19 in children

AASLD-NASPGHAN-SPLIT
COVID-19 & the Liver: Pediatric Perspective

Mohit Kehar, MBBS, DNB
Assistant Professor of Pediatrics
Queen’s University, Canada
Outline

• Introduction
• NASPGHAN-SPLIT COVID-19 Registry

• Review course, treatment and outcome in children with liver disease (native liver) presenting with COVID-19 infection:
  • Demographics
  • Etiology and comorbid conditions
  • Presenting symptoms
  • Laboratory trends
  • Management
  • Outcome
Introduction

• COVID 19: Elevated AST/ALT/Bilirubin

• Information is limited regarding the effects of COVID-19 infection in patients with chronic liver disease

• Few adult studies

• No Pediatric Data
Comparison of mortality risk in patients with cirrhosis and COVID-19 compared with patients with cirrhosis alone and COVID-19 alone: multicentre matched cohort

- **37** patients with cirrhosis+COVID-19
- Matched with **108** patients with COVID-19 and **127** patients with cirrhosis
- Seven sites in USA, Median age 61yrs.
- Mortality
  - Cirrhosis+COVID-19 vs. COVID-19 (30% vs. 13%, p=0.03)
  - Cirrhosis +COVID-19 vs. Cirrhosis (30% vs. 20%, p=0.16)
High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: Preliminary results from an international registry

- N= 152 (103 patients with cirrhosis and 49 with non-cirrhotic CLD)
- Median age 61 yrs.
- Most Common diagnosis : NAFLD
- Death (N=47)
  - COVID-19 lung disease: 78.7%
  - Cardiac-related: 4.3%
  - Liver-related: 12.2%
NASPghan-Split COVID-19 registry

• Joint collaborative effort: NASPghan Hepatology committee and Society of Pediatric Liver Transplantation
• Course and outcome of COVID-19 in children with liver disease and recipients of liver transplantation
• Patient Population: Less than 21 years of age
• Inclusion Criteria: All cases of chronic liver disease, recipients of pediatric liver transplantation ± intestinal transplant/MVT/Other solid organs
NASPGHAN-SPLIT COVID-19 registry

• **Launched:** April 2020

• Weekly report shared through the NASPGHAN GI listserv, the SPLIT COVID listserv and the NASPGHAN website

• Week 12 report shared last week

• International RED cap registry

• Data collection ongoing
Week 12: 45 cases reported
5 countries, **US (majority of cases)**
Demographics of Children: COVID+ Liver Disease (Native Liver)

Median Age: 5 years

Race/Ethnicity:
- White: 41%
- Hispanic: 36%
- Asian: 14%
- Black/African American: 9%

Highest level of care:
- Outpatient: 31%
- Hospital Floor: 30%
- PICU: 39%

N=23 of 45
M/F = 13/10
Etiology and Comorbid Conditions: COVID+ Liver Disease (Native liver)

<table>
<thead>
<tr>
<th>Comorbid conditions</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>5</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>3</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3</td>
</tr>
<tr>
<td>Genetic</td>
<td>2</td>
</tr>
<tr>
<td>Cardiac</td>
<td>2</td>
</tr>
<tr>
<td>Renal/CKD</td>
<td>1</td>
</tr>
<tr>
<td>Endocrine</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine</td>
<td>5</td>
</tr>
<tr>
<td>Steroids</td>
<td>3</td>
</tr>
<tr>
<td>Dose reduced</td>
<td>1</td>
</tr>
<tr>
<td>No changes</td>
<td>4</td>
</tr>
</tbody>
</table>

Etiology

- Biliary Atresia: N=7
- NAFLD: N=5
- Autoimmune hepatitis: N=5
- Metabolic disorders: N=4
- ALF: N=1
- Others: N=4
Presenting Symptoms: COVID+ Liver Disease (Native liver)

- Constitutional: fever, myalgia, fatigue, sore throat, loss of smell/taste
- Respiratory illness
- GI manifestation
- Others
- Asymptomatic

Anorexia, malaise, headache, MIS-C (N=2)
# Laboratory Trends: COVID+ Liver disease (Native liver)

<table>
<thead>
<tr>
<th>Laboratory Variable</th>
<th>Baseline value Median (IQR)</th>
<th>Peak value Median (IQR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count (10X9 cells/L)</td>
<td>10.9 (5.3-14.7)</td>
<td>14.4 (7.9-20.43)</td>
<td>0.002</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>74 (41-143)</td>
<td>146 (53-227)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Bilirubin (mg/dl)</td>
<td>0.85 (0.52-6.4)</td>
<td>3.25 (1-8.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>INR</td>
<td>1.12 (1-1.2)</td>
<td>1.2 (1.18-1.5)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Laboratory Variable</th>
<th>Baseline value Median (IQR)</th>
<th>Nadir value Median (IQR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC count (10X9 cells/L)</td>
<td>10.9 (5.3-14.7)</td>
<td>7.35 (4.1-11.1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.8 (3.4-4.35)</td>
<td>3.1 (2.6-3.4)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Median ALC: 2.48 (0.76-7)k/ul**
Management: COVID+ Liver disease (Native liver)

Treatment

- None: 42%
- IVIG: 19%
- Hydroxychloroquine + Azithromycin: 13%
- Steroids: 10%
- Remdesivir: 10%
- Others: 6%

Others:
- Tocilizumab + Sarilumab (N=2)
- Azithromycin (N=1)
- Convalescent Plasma (N=1)
- Anakinra (N=1)
- Eculizimab (N=1)
Management: COVID+ Liver disease (Native liver)

Respiratory support

- None: 68%
- Nasal cannula/CPAP/BiPAP: 14%
- Mechanical ventilation: 14%
- High Frequency Oscillatory ventilation: 4%

Need for vasoactive agents: 4
Need for RRT: 2

Median days: 6.5 (2-34)
Outcome: COVID+ Liver disease (Native liver)

Outcome:
- Recovery: N=19 (N=1)
- Still active in clinical course: N=2 (N=1)
- Death: N=1
- Unknown: N=1

Liver-related Decompensation events:
- Median (range) to recovery: 7 (2-37) days
- Median (range) of hospitalization: 6.5 (1-37) days
- Median (range) of ICU stay: 6 (4-34) days

Recovery: 5%
Still active in clinical course: 5%
Death: 60%
Unknown: 5%
None: 30%

Ascites: 5%
Portal Hypertension Bleeding: 5%
Infection: 5%
Summary

• First Pediatric specific registry assessing outcome of COVID-19 on liver disease and liver transplantation recipient
• Hospitalization was needed in majority (70%) of children with liver disease (native liver) +COVID 19
• Majority of patients did not receive any specific treatment for COVID-19 or respiratory support
• Over 80% recovered with only one death reported till date in cohort of children with liver disease (native liver) +COVID 19
COVID-19 Registry: Outcomes in Pediatric Liver Transplant Recipients

Noelle Ebel, M.D.
Assistant Professor of Pediatrics
Director, Alagille Syndrome Program
Stanford University
nebel@stanford.edu
Background: COVID+ post-transplant recipients

Median age 59 years, 63% male

COVID-19 in an international European liver transplant recipient cohort

- 57 patients, 70% male, aged 57-70 years
- Co-morbidities: 37% cardiovasc disease, 37% diabetes, 28% renal disease, 23% respiratory disease
- 28% outpatient
- 72% inpatient
  - 10% ICU, intubated
  - 19% ARDS
  - 12% died

Liver transplant (n = 160)

<table>
<thead>
<tr>
<th>Major outcomes</th>
<th>129</th>
<th>81%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalised</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensive care admission</td>
<td>47</td>
<td>29%</td>
</tr>
<tr>
<td>Invasive ventilation</td>
<td>31</td>
<td>19%</td>
</tr>
<tr>
<td>Death</td>
<td>30</td>
<td>19%</td>
</tr>
</tbody>
</table>

https://doi.org/10.1016/S2468-1253(20)30125-4
doi:10.1136/gutjnl-2020-321923
Demographics of COVID+ post-transplant recipients

22 post-liver transplant recipients in the registry

- 45% female (n=10)
- Aged 6 months – 21 years (median 13.5 years old)
- Time out from transplant: 1 week – 19 years (median 4.6 years)
Race of COVID+ post-transplant recipients

22 post-liver transplant recipients in the registry

- White: 52%
- Hispanic: 24%
- Asian: 14%
- Black/African American: 5%
- American Indian or Alaska Native: 5%
Indications for liver transplantation

Comorbidities at time of diagnosis

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td>1 - de novo AIH</td>
</tr>
<tr>
<td></td>
<td>1 - lupus</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1 - IBD</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1 - pacemaker</td>
</tr>
<tr>
<td></td>
<td>1 - hypertension</td>
</tr>
<tr>
<td>Renal/CKD</td>
<td>1</td>
</tr>
<tr>
<td>Endocrine</td>
<td>2 - diabetes</td>
</tr>
</tbody>
</table>
## Presenting symptoms of COVID+ post-transplant recipients

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Liver transplant only (includes liver-kidney) (n=20)</th>
<th>Multivisceral transplant (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>4 (20%)</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>10 (50%)</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory symptoms</td>
<td>6 (30%)</td>
<td>1</td>
</tr>
<tr>
<td>GI symptoms</td>
<td>9 (45%)</td>
<td>1</td>
</tr>
<tr>
<td>Constitutional (loss of smell/taste, myalgia, fatigue, sore throat)</td>
<td>6 (30%)</td>
<td>0</td>
</tr>
</tbody>
</table>
Highest level of care for COVID+ post-transplant recipients

COVID-19 Infection (n=22)
- Inpatient 32% (n=7)
- Outpatient 68% (n=15)

Ward
- 57% (n=4)
- Nasal cannula n=1

PICU
- 43% (n=3)
- CPAP n=1

Outpatient 68% (n=15)
Number of hospital days for COVID+ post-transplant recipients

Patient 1
- ICU: 0 days
- Ward: 8 days

Patient 2
- ICU: 0 days
- Ward: 1 day

Patient 3
- ICU: 1 day
- Ward: 23 days

7 months out from transplant
Multivisceral transplant, 5 years out

Patient 4
- ICU: 1 day
- Ward: 18 days

Patient 5
- ICU: 1 day
- Ward: 22 days

Patient 6
- ICU: 0 days
- Ward: 2 days

Patient 7
- ICU: 0 days
- Ward: 1 day

Fresh post-transplant
Laboratory trends of COVID+ post-transplant recipients

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated ALT (17%)</td>
<td>• ALT 21 -&gt; 174&lt;br&gt;• ALT 44 -&gt; 424&lt;br&gt;• ALT baseline 231 (fresh post-transplant) -&gt; 1215</td>
</tr>
<tr>
<td>Hypoalbuminemia (11%)</td>
<td>• Albumin baseline 2.5 (fresh post-transplant) -&gt; 2.3&lt;br&gt;• Albumin 3 -&gt; 1.6</td>
</tr>
<tr>
<td>Elevated INR (6%)</td>
<td>• INR baseline 2.3 -&gt; 2.8</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>• No reports of significantly elevated bilirubin</td>
</tr>
</tbody>
</table>
## Immunosuppression at time of diagnosis: COVID+ post-transplant recipients

| Single immunosuppression (n=8) | Tacrolimus only (n=6)  
|                              | Sirolimus only (n=1)  
|                              | MMF only (n=1)        |
| Dual immunosuppression (n=8)  | Tacrolimus + MMF (n=4)  
|                              | Tacrolimus + steroids (n=4) |
| Triple immunosuppression (n=4) | Tacrolimus + sirolimus + steroids (n=1)  
|                              | Tacrolimus + MMF + steroids (n=1)  
|                              | Cyclosporine + MMF + steroids (n=1)  
|                              | Tacrolimus + azathioprine + steroids (n=1) |
| Quadruple immunosuppression (n=1) | Tacrolimus + sirolimus + MMF + steroids |
Highest level of care by baseline immunosuppression

Number of patients

- Single immunosuppression
- Double immunosuppression
- Triple immunosuppression
- Quadruple immunosuppression

<table>
<thead>
<tr>
<th>Immunosuppression Level</th>
<th>Outpatient</th>
<th>Ward</th>
<th>PICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Double</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Triple</td>
<td>3</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Quadruple</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Immunosuppression minimization:
**COVID+ post-transplant recipients**

<table>
<thead>
<tr>
<th>Description</th>
<th>MMF stopped (n=6)</th>
<th>Sirolimus stopped (n=1)</th>
<th>All continued on primary immunosuppression (tacrolimus or CSA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunosuppressive medication stopped</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunosuppression decreased (n=9)</td>
<td>Tacrolimus trough goal reduced (n=6)</td>
<td>CSA reduced (n=1)</td>
<td>Steroid dose reduced (n=1)</td>
</tr>
<tr>
<td></td>
<td>MMF reduced (n=1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No changes to immunosuppression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=11)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Primary immunosuppressive medication decreased**  
**AND**  
**Secondary immunosuppressive medication discontinued**

N=6
Directed therapies: COVID+ post-transplant recipients

- Azithromycin
- Steroids
- Hydroxychloroquine and IVIG
- Hydroxychloroquine and favipiravir

Outpatient

PICU CPAP

PICU Multivisceral
Outcomes: COVID+ post-transplant recipients

- Fully recovered (n=17)
- Still active in clinical course (n=5)
- No reported deaths
Summary: COVID+ post-transplant recipients

• No reported deaths or need for mechanical ventilation

• Higher degrees of immunosuppression didn’t necessarily predict more severe COVID courses
Summary: SPLIT and NASP GHAN COVID-19 Registry

Registry link: https://is.gd/naspghansplitliversurvey


NASP GHAN COVID website: https://naspghan.org/professional-resources/covid-19/
Re-Entry in Clinical Transplantation during a COVID Pandemic

Beau Kelly MD MBA FACS FAST
Surgical Director and Transplant Surgeon, DCI Donor Services

July 2020
The Problem with Re-Entry

- Accurate triangulation of the present position
  - Separation of Signal from Noise
- The Attack Angle and Attitude
- “Ionization blackout”
  - Poor communication and messaging
- Balancing “G” forces and Environmental pressures
- Faith in developing consensus on a Program and Design

Just want to return to a safe and “normal” life!
Accurate Position and Communication?

- Increasing rates of new infections in nearly every state!
- Resurgence of cases as mobility increases!
- ~10% Testing COVID +
- Masking, Social distancing, and SIP practices are not uniform
The Result!

- 142.8K COVID-related deaths
- 4.9M COVID +
- 51.7M COVID tests
The “G” Forces and “Heat”

- Healthcare Economic Impact of COVID (Gravity)
  - GDP decline by 5% for every month of partial closure
  - US Hospital financial losses projected at $323B
  - Unemployment spike to 14.7%
    - Hospital employee layoffs, furloughs, and salary reductions
  - Interruption of Medical Education, Training programs, Hospital credentialing, and Certifications

“Adversity introduces us to ourselves!” ~ Albert Einstein
The Angle of Attack and Attitude

- Psychosocial Consequences of “Lock-down” and Social Distancing
  - Increased isolation
  - Increased anxiety and depression
  - Disruptions in family structure
  - Food insecurity and
  - Increased ACE's – predictive determinants of health

- Profound and Lasting Consequences of COVID
  - Despite a “miracle” COVID vaccine, attitudes will persist that shape how we live!
Assumptions and Course Corrections

Way back in March we thought…
• Based on past experiences with H1N1, WNV, Influenza, and SARS:
  • Increased infection rates associated with extent of IS
  • Disproportionately high morbidity and mortality in TXP recipients
  • Vaccination yields protective Ab’s
    • ?Herd immunity
• Testing will yield too many false positives and should be reserved for symptomatic patients.
  • >150 tests used. ~10 tests are FDA reviewed

• CMS deems transplant as an essential health service- Organ donation and transplantation move forward despite geographic variation in healthcare.
Knowing and Assessing Risk

• Risk of COVID transmission in Organ donation and Transplant across the entire process
  • No NBA “Bubble”
  • The Pro’s and Cons of moving forward with a liver donor and transplant

• Infection Risk Circles and Models
  • Cleveland Clinic Online Risk Calculator
  • CHIME
  • CDC Risk Calculator
Relative Risk of Returning to Activity

[Diagram showing activities ranked by relative risk]

1. Opening the mail
2. Visiting an elderly relative or friend in their home
3. Going to a hair salon or barbershop
4. Eating in a restaurant (inside)
5. Going for a walk, run, or bike ride
6. Attending a wedding or funeral
7. Playing basketball
8. Attending a large music concert
9. Traveling by plane
10. Going to a bar
NorCal
~140 liver donors
Decreased DCDs, Living donors
>32 MELD txp’d
Assessing Aggregate Risk/Benefit

Organ Donor

Heart Recipient

Liver Recipient

Kidney Recipients

Procurement Teams

US Measures
- Survey screening
- Temp Checks
- PCR
- IgM/IgG Surveillance
- Quarantine

Other countries
- mandatory serial testing
- risk-stratified isolation algorithms

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# Stratifying Risk of Surgery - MeNTS Score

<table>
<thead>
<tr>
<th>PROCEDURE SCORE</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR Time</td>
<td>&lt;30 min</td>
<td>30-60 min</td>
<td>60-120 min</td>
<td>120-180 min</td>
<td>&gt;180 min</td>
</tr>
<tr>
<td>LOS</td>
<td>Outpt</td>
<td>&lt;24 hours</td>
<td>24-48 hours</td>
<td>2-4 days</td>
<td>&gt;4 days</td>
</tr>
<tr>
<td>Post-Op ICU Need</td>
<td>unlikely</td>
<td>&lt;5%</td>
<td>5-10%</td>
<td>10-25%</td>
<td>&gt;25%</td>
</tr>
<tr>
<td>EBL</td>
<td>&lt;10cc</td>
<td>10-25cc</td>
<td>25-50cc</td>
<td>50-75cc</td>
<td>&gt;75cc</td>
</tr>
<tr>
<td>Surgical Team Size</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Intubation Probability</td>
<td>&lt;1%</td>
<td>1-5%</td>
<td>5-10%</td>
<td>10-25%</td>
<td>&gt;25%</td>
</tr>
<tr>
<td>Surgical Site</td>
<td>Other</td>
<td>MIS Abd Surgery</td>
<td>Open Infraumbilical Abd Surgery</td>
<td>Open Supraumbilical Abd Surgery</td>
<td>OHNS/Upper GI/Thoracic</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DISEASE SCORE</th>
<th>1</th>
<th>3</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Non-Op Option</td>
<td>No Option Available</td>
<td>50% Effective vs. Surgery</td>
<td>Equally Effective</td>
</tr>
<tr>
<td>Non-Op Option Resource/Exposure Risk</td>
<td>Significant</td>
<td>Moderate</td>
<td>Minimal</td>
</tr>
<tr>
<td>Impact on Disease- 2wk Delay</td>
<td>Significant</td>
<td>Moderate</td>
<td>Minimal</td>
</tr>
<tr>
<td>Impact on Surgical Outcome- 2wk Delay</td>
<td>Significant</td>
<td>Moderate</td>
<td>Minimal</td>
</tr>
<tr>
<td>Impact on Disease- 6wk Delay</td>
<td>Significant</td>
<td>Moderate</td>
<td>Minimal</td>
</tr>
<tr>
<td>Impact on Surgical Outcome- 6wk Delay</td>
<td>Significant</td>
<td>Moderate</td>
<td>Minimal</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PATIENT SCORE</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;20 yo</td>
<td>20-40 yo</td>
<td>40-50 yo</td>
<td>50-65 yo</td>
<td>&gt;65 yo</td>
</tr>
<tr>
<td>Lung Disease (Asthma, COPD, CF)</td>
<td>None</td>
<td>Minimal</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>None</td>
<td>Minimal</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>CV Disease (HTN, CHF, CAD)</td>
<td>None</td>
<td>Minimal</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
</tr>
<tr>
<td>Diabetes</td>
<td>None</td>
<td>Minimal</td>
<td>Oral Hypoglycemics Meds</td>
<td>On Insulin</td>
<td>Moderate</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>None</td>
<td>Minimal</td>
<td>Moderate</td>
<td>Severe</td>
<td>YES</td>
</tr>
<tr>
<td>Covid-like Flu Symptoms</td>
<td>None</td>
<td>Minimal</td>
<td>Moderate</td>
<td>Severe</td>
<td>YES</td>
</tr>
<tr>
<td>Exposure to COVID (last 14 days)</td>
<td>None</td>
<td>Probably Not</td>
<td>Probably</td>
<td>More than Likely</td>
<td>YES Definitely</td>
</tr>
</tbody>
</table>

*Higher Scores associated with: Worse Outcomes, Increased Exposure Risk, Higher Resource Utilization*

*Organ donation and liver transplant are at the highest end of scores*

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**Ethical and Efficient estimation of resource scarcity and provider risk.**

Review and application of a stratified scoring system for Operations deferred and performed in March 2020

Prachand, et. al, JACS, April, 2020
Fundamental Considerations for Re-Entry

- Clear Objectives based on available “data!”
- Clear and transparent risk stratification for every step along the path of the patient
  - Customized step-step plan from organ acceptance to patient discharge
  - Minimize risk of COVID exposure (Distancing, masks, hand hygiene, etc.)
  - Optimize Resources
  - Disaster planning team (administration, multidisciplinary team, community, and PARENTS/PATIENTS)
- Frequent Reassessment and Refinement of the Program and Design beyond financial considerations
- Advocate for government support for families in need
- Ask more Questions!
Return to School Special Considerations

- Liver transplant recipients >6 months post-txp.
- Stable/weaning immunosuppression regimens.
- Stable/decreased community COVID incidence (<10% + test rates).
- OK for asymptomatic siblings to return to school.

- Return to athletic programs
- Return to after-school activities
- Return to Colleges
- Siblings living at-home w/ high-risk for exposure

- Recent liver transplant (3-6 months)
- High-dose Immunosuppression regimen
- Rapidly increasing COVID+ (Hotspots!)
- Serious medical conditions or actively managed surgical complications
- Any COVID-like symptoms or acute respiratory illness
- School system does not have adequate resources to foster safe participation

*All decisions and options should be discussed with patient-specific transplant professionals!"
Acknowledgements

• Special Thanks
• Better ______ is on the other side of this adversity
• Not a “re-entry” into the normal of 2019. Those strategies and practices are inadequate for the weight, challenges and goals of today.

• Rather a Re-emergence!
Panel Discussion Q&A

Please submit any remaining questions to the Q&A Chat at this time!
Acknowledgements

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