COVID, Kidney, Disease & SARS-CoV-2

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An Overlooked, Possibly Fatal Coronavirus Crisis: A Dire Need for Kidney Dialysis

Ventilators aren’t the only machines in intensive care units that are in short supply. Doctors have been confronting an unexpected rise in patients with failing kidneys.
CKD & COVID-19
Italy (Brescia)

- 643 dialysis patients
- 94 (15%) SARS-CoV-2 positive
- 57 (61%) required hospitalization
- Mortality 29%

Alberici et al., KI, 2020
High risk of severe Covid-19 in patients with Chronic Kidney Disease

- All patients on maintenance hemodialysis in Wuhan, China (n = 7154)
- Incidence of Covid-19 $\sim 2.2\%$

**Comorbidities**

- Mild/moderate
- Severe

**Mortality [%]**

- 7/25
- 6/23

Xiong et al. *J Am Soc Nephrol* 2020

COVID-19 in Germany

Up to June 2, 2020

• 182,028 cases
  (2,775 cases in the last 7 days)

• 8,522 deaths

Cumulative incidence per 100,000 persons

Robert Koch Institut, https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Fallzahlen.html
COVID-19 Registry of the German Society of Nephrology
Data available for approx. 14’000 dialysis patients

- SARS-CoV-2 Patients (% of dialysis patients)
- Hospitalization (% of SARS-CoV-2 patients)
- Clearance of SARS-CoV-2 (Cumulative, % of SARS-CoV-2 patients)
- Mortality (Cumulative, % of SARS-CoV-2 patients)
Patients with kidney disease are particularly vulnerable to COVID-19

- Older age, common comorbidities, increased mortality risk
- Impairment of immune system (because of ESKD, the underlying disease or its treatment)
- No home-isolation possible (esp. in-center dialysis patients)
AKI & COVID-19
Renal involvement in Covid-19 patients is frequent and predicts mortality.

Acute kidney injury (AKI) in patients hospitalized with COVID-19

**Methods & Cohort**
- Retrospective cohort
- 13 hospitals in New York
- SARS-CoV-2 positive
- N = 5449
  - Age = 64 (52, 75)
- March 1 – April 5, 2020

**Results**

<table>
<thead>
<tr>
<th>All AKI</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,993 (37%)</td>
<td>47%</td>
<td>22%</td>
<td>31%</td>
</tr>
</tbody>
</table>

**Independent risk factors for AKI**
- Older age
- Black race
- Hypertension
- Diabetes mellitus
- Cardiovascular disease
- Vasopressor use
- Need for ventilation*

*OR=10.7 (95%CI 6.8 -16.7)

**Disposition of patients with AKI**
- Still admitted: 780 (39%)
- Discharged: 519 (26%)
- Died: 694 (35%)

**Conclusion:**
AKI occurs frequently among patients with COVID-19. It occurs early and in temporal association with respiratory failure. AKI in COVID-19 is associated with a poor prognosis.
Acute kidney injury in COVID-19 patients

<table>
<thead>
<tr>
<th>No use of invasive mechanical ventilation (N=4259)</th>
<th>Required invasive mechanical ventilation (N=1190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AKI</td>
<td></td>
</tr>
<tr>
<td>3334 (78.3%)</td>
<td>122 (10.3%)</td>
</tr>
<tr>
<td>AKI, any stage</td>
<td></td>
</tr>
<tr>
<td>925 (21.7%)</td>
<td>1068 (89.7%)</td>
</tr>
<tr>
<td>AKI stage 1</td>
<td></td>
</tr>
<tr>
<td>639 (15.0%)</td>
<td>288 (24.2%)</td>
</tr>
<tr>
<td>AKI stage 2</td>
<td></td>
</tr>
<tr>
<td>185 (4.3%)</td>
<td>262 (22.0%)</td>
</tr>
<tr>
<td>AKI stage 3</td>
<td></td>
</tr>
<tr>
<td>101 (2.4%)</td>
<td>518 (43.5%)</td>
</tr>
<tr>
<td>Required renal replacement therapy</td>
<td></td>
</tr>
<tr>
<td>9 (0.2%)</td>
<td>276 (23.2%)</td>
</tr>
</tbody>
</table>

Hirsch et al., KI, 2020
Akute Kidney Injury in Covid-19 patients

Metaanalysis of 9 studies (mostly China) with ~2800 patients.

JASN study not yet included

Experience from UKE ICU: 25-30%

Renal involvement in Covid-19 patients is frequent and predicts mortality

333 hospitalized patients with Covid-19 pneumonia, single center, China

Acute kidney injury in COVID-19 patients

- Acute tubule injury
- Endothelial damage
- Secondary damage (drug-induced, ischemic injury, secondary infections, rhabdomyolysis, etc.)
- Virulence of SARS-CoV-2 in the kidney? (tubular epithelium, podocytes, other glomerular cells)

Su et al., KI, 2020
Farkash et al., JASN 2020
Varga et al., Lancet 2020
SARS-CoV-2 & Kidney
Multiorgan- and Renal tropism of SARS-CoV-2

Teams Microbiology, Legal Medicine, Nephrology
Patients dying from COVID-19 have a high number of co-morbidities
Multiorgan- and Renal tropism of SARS-CoV-2

Higher number of co-morbidities associates with multiorgan tropism
Multiorgan- and Renal tropism of SARS-CoV-2

Particularly, kidney tropism increases with co-morbidities

<table>
<thead>
<tr>
<th>No. of coexisting conditions</th>
<th>Heart PCR</th>
<th>Liver PCR</th>
<th>Brain PCR</th>
<th>Kidney PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(-)</td>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
</tr>
<tr>
<td>1-2</td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>1 (25%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>3-5</td>
<td>4 (24%)</td>
<td>13 (76%)</td>
<td>12 (71%)</td>
<td>5 (29%)</td>
</tr>
</tbody>
</table>

Puelles et al., NEJM 2020
Renal tropism of SARS-CoV-2

Table S3. This table summarizes renal tropism of SARS-CoV-2 [Kidney PCR (+)] in the presence or absence of reported chronic kidney disease (CKD).

<table>
<thead>
<tr>
<th>CKD history</th>
<th>N of cases</th>
<th>(-)</th>
<th>(+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With history of CKD</td>
<td>8</td>
<td>4 (50%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>Without history of CKD</td>
<td>10</td>
<td>1 (10%)</td>
<td>9 (90%)</td>
</tr>
</tbody>
</table>

In patients with preexisting CKD, there seems to be less kidney tropism
Renal tropism of SARS-CoV-2

After the respiratory tract, kidneys exhibit the highest viral load.

Puelles et al., NEJM 2020
Kidneys do express SARS-CoV-2 adhesion and facilitator genes.
Renal tropism of SARS-CoV-2

ISH detects SARS-CoV-2 RNA in the kidney

Puelles et al., NEJM 2020
Renal tropism of SARS-CoV-2

IF confirms SARS-CoV-2 protein in the kidney

Puelles et al., NEJM 2020
Renal tropism of SARS-CoV-2

Puelles et al., NEJM 2020
Renal tropism of SARS-CoV-2

Puelles et al., NEJM 2020
Enrichment of SARS-CoV-2 in the glomerular compartment
SARS-CoV-2 & Kidney Outlook
Can urine abnormalities serve as outcome predictors in COVID-19 patients?
