Summary of Research – Natural History and Mortality Data

Compiled by Jessica Gencarelli PGY1 and Alex Pearce PGY1 and Jesse Guscott PGY17
April2, 2020
Jessica.gencarelli@medportal.ca
alex.pearce@medportal.ca
Jesse.guscott@medportal.ca

While there is some data here on outpatients and asymptomatic/minimally symptomatic patients, the goal of this report was to find the best possible data to inform care decisions and conversations for symptomatic hospitalized patients with COVID19.

Straight to the point:

When talking about plans I'm going to tell my patients some variation of this:
"We are working hard to understand who will be able recover from COVID and who will not. Our best evidence tells us that the majority of people who are infected will get better better and will never need to come into hospital. That you need to be admitted tells us that you are sicker then most and your risk is higher. People who get admitted to the ICU have about a 50% survival rate but we have to remember that that includes young healthy people as well older people. People who are over 55 and have medical problems like high blood pressure, diabetes and especially heart disease or stroke, have a much lower chance of surviving COVID infections. In some cases we may consider using a breathing tube and ventilator to help people stay alive long enough to recover but this has not been very successful for COVID. People over 70 almost never survive mechanical ventilation and even younger people who do survive require up to weeks on a ventilator to recover."

In my small N of having this conversation I'm reminded that everyone thinks they are in the "pretty healthy" category but once you start to listing their negative prognostic features as outlined below, they tend to add up quickly.

General natural history of COVID as discussed by Zhou et al., 2020, Zhao et al., 2020 and Guan et al., 2020, Onder 2020:

Of identified COVID positive patients

- 80+% have mild illness and can be managed at home
- 10-20% require hospitalization
- 3.4% die*

*WHO Global Case Fatality Rate (CFR), rates vary from 2% in Chinese reports to 7%in Italian reports

- Of those who require admission:
    - 10-20% go to the ICU
    - 3-10% require intubation

- Of those requiring ICU admission
    - 40-50% are intubated
    - 25-70% mortality in all comers to ICU depending on the study BUT survival heavily skewed to younger patients with less co-morbidities

- Amongst those requiring mechanical ventilation (all studies are small)
    - Yang reported 13% survival though some survivors remained ventilated
    - Zhou reported 3% survival to discharge 97% mortality BUT survivors who had not yet been discharged from hospital were excluded from this study so this represents an underestimate of survival
    - C. Wu reported 21% survived to discharge, 66% died, 13% remained in hospital
    - Bhatra (N=18) reports 50% survival during study period, 22% survival to discharge, ¾ of which were <60 years old. Only 1 of 7 mechanically ventilated patients > 70 survived the ICU

The Bhatra study consisted of 24 ICU patients in Seattle for whom at least 14 days of followup are available. 18 of these patients were mechanically ventilated. The supplement to the Bhatra paper provides individual data for each of these patients. From this data I was able to organize outcomes of mechanically ventilated patients by age.

Table:Outcomes in mechanically ventilated patients from supplement of Bhatra 2020

Age	Died during study period	Survivors Discharged from hospital	Survivors who remain ventilated	Avg # days of M. ventilation amongst extubated survivors
<60	1/4	3/3	-	11.3
60-70	2/7	1/5	3/5	11
70-80	5/5	-	-	-
>80	1/2	1/1	-	11
Total	9/18	5/9		11.1

Factors significantly associated with COVID-19 mortality

- Age>55 with increasing risk with advancing age
- Comorbidities especially Cardiac disease, cerebrovascular disease, hypertension and diabetes
- Need for mechanical ventilation, renal replacement, ECMO
- Secondary Infection
- Elevated inflammatory indicators in blood
- SOFA Score>6

Case Fatality by Age

Riou 2020. This study used mathematical modeling to account for factors such underreporting, sampling bias and delayed mortality. Using the crude (reported) data of >40k Chinese cases, their model provides the following estimates.

Table 1. Estimates of case fatality ratios among SYMPTOMATIC (not necessarily hospitalized) infections (Riou 2020)

Age	Overall	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	>80
Crude	**2.4%**	**0**	**0.25%**	**0.22%**	**0.26%**	**0.48%**	**1.4%**	**3.8%**	**8.5%**	**15%**
Adjusted for unidentified symptomatic cases and delayed mortality	**3.3%**	**0.02%**	**0.046%**	**0.19%**	**0.38%**	**0.82%**	**2.7%**	**9.4%**	**20%**	**36%**

It is believed that the higher average age of the Italian population is contributing to their CFR being 3x higher then China's (7% vs 2%). When you compare CFR across age groups, the numbers are very similar until you get to the >80 age group and especially >90.

Comorbidities

(Wu & McGoogan, 2020) Comparing an overall CFR of 2-3%, the CFR for those with comorbid conditions:

1. 10.5% for cardiovascular disease
2. 7.3% for diabetes
3. 6.3% for chronic respiratory disease
4. 6% for hypertension
5. 5.6% for cancer

The most common complications include:

- Sepsis
- Respiratory failure
- ARDS
- Heart failure
- Arrhythmias
- Renal failure

The median time from illness onset (prior to admission) to discharge was 22 days

- The median time to death was 18.5 days.
- The median onset to invasive mechanical ventilation was 14.5 days

Laboratory parameters as a predictor of prognosis: a study of 127 patients in Wuhan China (Bai et al., 2020) These laboratory parameters were significantly higher in those patients who passed due to COVID-19:

1. Elevation of WBC with decreased lymphocytes
2. Significant elevation of LFT including total bilirubin, direct bilirubin, AST and ALT
3. Decreased albumin
4. Urinalysis showed red blood cells, urine protein and glucose
5. Significant elevation of creatinine and BUN
6. Significantly elevated lactate dehydrogenase (>245IU/L), CK, troponin, PT and d-dimer (>1000ng/L)
7. CRP (>100), ferritin (>300ug/L) were also significantly elevated

Vital signs predictive of a poor prognosis include a respiratory rate > 24, a heart rate >125 and oxygen saturation <90% on room air.

Zhao et al., 2020 and Guan et al., 2020 confirm the same prognostic factors.

Pediatrics

Many summaries report that there have been no deaths under the age of 9, but one study looking at 171 cases found: (Lu et al, 2020)

- The vast majority of children do well; many are asymptomatic; and most can be managed from home
- However, 3/171 COVID+ children required ICU and ventilation
- Their comorbidities included hydronephrosis, leukemia, and intussusception
- 1/171 died 4 weeks later -- a 10mo with intussusception who went on to have multiorgan failure

Prognosis in Critically Ill Patients

Yang (2020) 52 Critically ill patients with pneumonia, defined as those admitted to the intensive care unit (ICU) who required mechanical ventilation or had a fraction of inspired oxygen (FiO2) of at least 60% or more outcome was 28 day survival.

- Average age 59.7, 40% had chronic illness, 32 (61.5%) died

- Only 3 of the 20 patients who were still alive at 28 days had been mechanically ventilated and all remained on invasive ventilation
- 19 of the 22 (86%) patients who were mechanically ventilated died

- Of the 20 patients who “survived”, eight patients were discharged. Three patients were still on invasive ventilation at 28 days, including one patient who was also on ECMO.

A reminder: All ratio data depends on an accurate denominator to represent the population in question. Population denominators are affected by testing policies. The number of asymptomatic carriers, atypical presentations, patients not presenting for care will all contribute significantly to the sampling bias affecting the denominator for population based rates. Take all of these numbers with a grain of salt.
*This review is not exhaustive or systematic.

Resources

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