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Risk Factors for Death From COVID-19 Identified in Wuhan Patients

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Patients who did not survive hospitalization for COVID-19 in Wuhan were more likely to be older, have comorbidities, and elevated D-dimer, according to the first study to examine risk factors associated with death among adults hospitalized with COVID-19.

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"Older age, showing signs of sepsis on admission, underlying diseases like high blood pressure and diabetes, and the prolonged use of noninvasive ventilation were important factors in the deaths of these patients," coauthor Zhibo Liu said in a news release. Abnormal blood clotting was part of the clinical picture too.

Fei Zhou, MD, from the Chinese Academy of Medical Sciences, and colleagues conducted a retrospective, observational, multicenter cohort study of 191 patients, 137 of whom were discharged and 54 of whom died in the hospital.

The study, published online today in *The Lancet*, included all adult inpatients with laboratory-confirmed COVID-19 from Jinyintan Hospital and Wuhan Pulmonary Hospital who had been discharged or died by January 31 of this year. Severely ill patients in the province were transferred to these hospitals until February 1.

The researchers compared demographic, clinical, treatment, and laboratory data from electronic medical records between survivors and those who succumbed to the disease. The analysis also tested serial samples for viral RNA.

Overall, 91 (48%) of the 191 patients had comorbidity. Most common was hypertension (30%), followed by diabetes (19%) and coronary heart disease (8%).

The odds of dying in the hospital increased with age (odds ratio 1.10, 95% confidence interval [CI], 1.03 - 1.17, per year increase in age), higher Sequential Organ Failure Assessment (SOFA) score (5.65, 2.61 - 12.23; P < .0001), and D-dimer level exceeding 1 μ g/L on admission.

The SOFA was previously called the "sepsis-related organ failure assessment score" and assesses rate of organ failure in intensive care units. Elevated D-dimer indicates increased risk of abnormal blood clotting, such as deep vein thrombosis.

Nonsurvivors compared with survivors had higher frequencies of respiratory failure (98% vs 36%), sepsis (100%, vs 42%), and secondary infections (50% vs 1%).

The average age of survivors was 52 years compared to 69 for those who died. Liu cited weakening of the immune system and increased inflammation, which damages organs and also promotes viral replication, as explanations for the age effect.

From the time of initial symptoms, median time to discharge from the hospital was 22 days. Average time to death was 18.5 days.

Fever persisted for a median of 12 days among all patients, and cough persisted for a median 19 days; 45% of the survivors were still coughing on discharge. In survivors, shortness of breath improved after 13 days, but persisted until death in the others.

Viral shedding persisted for a median duration of 20 days in survivors, ranging from 8 to 37. The virus (SARS-CoV-2) was detectable in nonsurvivors until death. Antiviral treatment did not curtail viral shedding.

But the viral shedding data come with a caveat. "The extended viral shedding noted in our study has important implications for guiding decisions around isolation precautions and antiviral treatment in patients with confirmed COVID-19 infection. However, we need to be

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clear that viral shedding time should not be confused with other self-isolation guidance for people who may have been exposed to COVID-19 but do not have symptoms, as this guidance is based on the incubation time of the virus," explained co-lead author Bin Cao.

"Older age, elevated d-dimer levels, and high SOFA score could help clinicians to identify at an early stage those patients with COVID-19 who have poor prognosis. Prolonged viral shedding provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future," the researchers conclude.

A limitation in interpreting the findings of the study is that hospitalized patients do not represent the entire infected population. The researchers caution that "the number of deaths does not reflect the true mortality of COVID-19." They also note that they did not have enough genetic material to accurately assess duration of viral shedding.

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