The pathogenesis of SARS-CoV-2 infection in humans manifests itself as mild symptoms to severe respiratory failure. On binding to epithelial cells in the respiratory tract, SARS-CoV-2 starts replicating and migrating down to the airways and enters alveolar epithelial cells in the lungs. The rapid replication of SARS-CoV-2 in the lungs may trigger a strong immune response. Cytokine storm syndrome causes acute respiratory distress syndrome and respiratory failure, which is considered the main cause of death in patients with COVID-19 (REFS[60,61]). Patients of older age (≥60 years) and with serious pre-existing diseases have a greater risk of developing acute respiratory distress syndrome and death[62-64] (FIG. 4). Multiple organ failure has also been reported in some COVID-19 cases[9,13,65].

Histopathological changes in patients with COVID-19 occur mainly in the lungs. Histopathology analyses showed bilateral diffused alveolar damage, hyaline membrane formation, desquamation of pneumocytes and fibrin deposits in lungs of patients with severe COVID-19. Exudative inflammation was also observed in some cases. Immunohistochemistry assays detected SARS-CoV-2 antigen in the upper airway, bronchial epithelium and submucosal gland epithelium, as well as in type I and type II pneumocytes, alveolar macrophages and hyaline membranes in the lungs[13,60,6467].

Animal models used for studying SARS-CoV-2 infection pathogenesis include non-human primates (rhesus macaques, cynomolgus monkeys, marmosets and African green monkeys), mice (wild-type mice (with mouse-adapted virus) and human ACE2-transgenic or human ACE2-knock-in mice), ferrets and golden hamsters[43,48,68–74]. In non-human primate models, most species display clinical features similar to patients with COVID-19, including strong shedding, virus replication and host response to SARS-CoV-2 infection[69,72,73]. For example, in the rhesus macaque model, high viral loads were detected in the upper and