34% mortality rate from SARS in critically ill patients at 28 days in Toronto

Fowler RA, Lapinsky SE, Hallett D, et al. **Critically ill patients with severe acute respiratory syndrome.** JAMA. 2003;290:367-73.

QUESTION

What is the clinical course and mortality rate of critically ill patients with the severe acute respiratory syndrome (SARS)?

DESIGN

Inception cohort followed for 8 weeks.

SETTING

Intensive care units (ICUs) of 13 hospitals (5 university and 8 community) in Toronto, Ontario, Canada.

PATIENTS

38 critically ill patients (mean age 57 y, 61% men) of 196 patients with probable or suspected SARS, defined according to World Health Organization criteria. Suspected SARS was defined by the presence of fever > 38 °C, respiratory symptoms, and history of travel to a location associated with SARS transmission or close contact with a known SARS patient. Probable SARS included the addition of lung infiltrates evident on chest radiograph. Patients were defined as critically ill if they were admitted to the ICU and required mechanical ventilation, inspired oxygen concentration ≥ 60%, or inotropic medication.

ASSESSMENT OF PROGNOSTIC FACTORS

Age, sex, occupation (health care worker [HCW] or non-HCW), duration of fever or respiratory symptoms, comorbid conditions, Acute Physiology and Chronic Health Evaluation II scores, and sepsis-related organ failure assessment scores.

MAIN OUTCOME MEASURES

Mortality at 28 days after ICU admission. Secondary outcomes were proportion of SARS-related critical illness, location and ventilation requirements at day 28, number of tertiary-care ICUs placed under quarantine, and number of HCWs contracting SARS secondary to ICU SARS transmission.

MAIN RESULTS

Among the 38 patients admitted to the ICU, 31 (82%) met criteria for the acute respiratory distress syndrome. 29 patients (76%) required mechanical ventilation. 13 patients (34%) died by day 28. The mortality rate for those on mechanical ventilation was 45%. At day 28, 16% of patients were still in the ICU, 5% were in a hospital ward, and 45% had been discharged. At 8 weeks, 15 patients (39%) had died. Factors associated with a poor outcome were older age, history of diabetes mellitus, admission tachycardia, and elevated creatine kinase level. 2 episodes of SARS transmission by ICU patients to HCWs occurred in 2 of the 5 university hospitals causing 164 HCWs to be quarantined, 35 critical care beds to be closed for 10 days, and 16 HCWs to develop SARS. In 4 of 8 community hospitals, 38 beds were closed because of ICU SARS transmission.

CONCLUSIONS

In critically ill patients with the severe acute respiratory syndrome (SARS), 28-day mortality was 34%. Intensive care unit transmission of SARS to health care workers led to substantial bed closures and health care worker quarantine.

Source of funding: No external funding.

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COMMENTARY

Providing critical care to patients with SARS has many challenges. The optimal therapy and specific type of supportive care needed for the best outcomes are unknown. The close interaction with patients and the increased potential for exposure to respiratory secretions place HCWs who work in critical care units at high risk for nosocomial acquisition of the SARS coronavirus (1).

The studies by Fowler and colleagues and Lew and colleagues of patients critically ill with SARS in Toronto and Singapore, respectively, offer important information about prognosis. Strengths of the study by Fowler and colleagues include a clearly defined inception cohort of critically ill patients and standardized assessment of severity of illness, sepsis-related organ failure, and radiologic progression. The key finding—that one third of patients admitted to the ICU died by 28 days, with a 45% mortality rate in those on mechanical ventilation—is a sobering reminder of why it is important to contain the spread of this virus. Not unexpectedly, older patients were at highest risk for death. Although many other potentially relevant prognostic factors were examined, including duration of fever and respiratory illness before admission to the critical care unit, the small data set limits the number of factors that can be examined in a multivariable model.

Similarly, Lew and colleagues describe a carefully defined cohort of patients with SARS. Follow-up time was longer in this study and again the prognosis was poor—half of critically ill patients died at 13 weeks. There were too few outcome events in this series to clearly define key independent prognostic factors. Given these limitations, a good argument can be made for pooling data from these and other SARS critical care cohort studies in a meta-analysis.

Our understanding of therapy for SARS is limited to small observational studies and anecdotal experience. It is clear that randomized, placebo-controlled trials are needed to establish effective therapy for SARS in case it reappears and that to achieve sufficient power, international clinical trials will be required. The World Health Organization can play a key role in coordinating such efforts. Priority should be given to establishing trials of early therapy. More data about predictors for

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37% mortality rate from SARS in critically ill patients at 28 days in Singapore

Lew TW, Kwek TK, Tai D, et al. **Acute respiratory distress syndrome in critically ill patients with severe acute respiratory syndrome.** JAMA. 2003;290:374-80.

QUESTION

What is the clinical course and mortality rate of critically ill patients with the severe acute respiratory syndrome (SARS)?

DESIGN

Inception cohort followed for 13 weeks.

SETTING

1 acute care general hospital in Singapore.

PATIENTS

46 critically ill patients (mean age 51 y, 52% men) of 199 patients admitted to hospital with probable SARS, defined according to World Health Organization criteria. Patients were critically ill if they were transferred to the intensive care unit (ICU) because of signs and symptoms of respiratory failure, arterial oxygen saturation < 92% despite oxygen therapy with ≥ 50% fraction of inspired oxygen (FIO_2), or if they were transferred with acute respiratory failure from another hospital and had a contact history that was suspicious of SARS.

ASSESSMENT OF PROGNOSTIC FACTORS

Age, sex, patient demographics, Acute Physiology and Chronic Health Evaluation (APACHE) II scores, duration of illness, comorbid conditions, baseline ratio of PaO_2 to FIO_2, and peak serum lactate dehydrogenase level.

MAIN OUTCOME MEASURES

Mortality at 28 days after symptom onset. Deaths were classified as early (< 7 d after ICU admission) or late (≥ 7 d after ICU admission). Patients' clinical course was classified as early recovery (those who survived without need for mechanical ventilation), intermediate recovery (those who required mechanical ventilation ≤ 14 d), or late survival (need for mechanical ventilation > 14 d).

MAIN RESULTS

45 patients met the criteria for acute lung injury (PaO_2–FIO_2 ratio ≤ 300 mm Hg) or the acute respiratory distress syndrome (ARDS) (PaO_2–FIO_2 ratio ≤ 200 mm Hg). 17 patients died by day 28 (37%, 95% CI 23% to 53%). The 13-week mortality rate was 52% (CI 37% to 67%). 5 patients (11%) died within 7 days of ICU admission; 4 of these patients had important comorbid conditions. 84% of late deaths were from complications related to ARDS, multiorgan failure, thromboembolic complications, or septicemic shock. Among the 22 survivors, the 7 patients in the early recovery group had a shorter course of acute lung injury and their FIO_2 requirements peaked at median 8 days; the 9 patients in the intermediate recovery group had improved oxygenation and pulmonary function after 5 days of mechanical ventilation; and the 6 patients in the late survival group had a longer and more severe course of ARDS, needed the most interventions, and had the most complications. Lower APACHE II scores and baseline PaO_2–FIO_2 ratio were associated with early or intermediate recovery.

CONCLUSIONS

In critically ill patients with SARS, 28-day mortality was 37%. Two thirds of patients surviving past 28 days had a protracted, severe course of the acute respiratory distress syndrome and high rates of complications.

Sources of funding: No external funding.

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early disease are needed for these planning efforts. Although reports on the features of SARS were quickly published (2, 3), these data were compiled before the end of the outbreak and therefore are limited by incomplete case ascertainment and follow-up. Additional information about the influence of viral load in prognosis is needed. Unlike other respiratory viral illnesses where the viral load is high initially and then diminishes, viral load tends to increase over the first several days of illness in SARS (4). It would be valuable to assess whether the rate of increase in viral load or whether a high baseline viral load is independently associated with poor prognosis.

SARS has had devastating effects on hospitalized patients and HCWs. We need to be prepared for a recurrence, which means bolstering surveillance and infection control measures. The poor outcomes described in the studies by Fowler and colleagues and Lew and colleagues dramatically illustrate why this is so important.

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