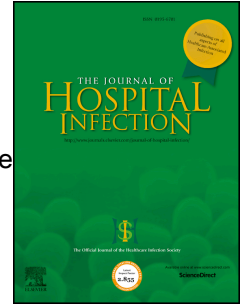


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Duration of quarantine in hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection: a question needing an answer

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1 **RUNNING TITLE: Hospital quarantine for COVID-19**

2 **Duration of quarantine in hospitalized patients with severe acute respiratory**
3 **syndrome coronavirus 2 (SARS-CoV-2) infection: a question needing an answer**

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15 In December 2019 a new form of pneumonia was observed in the Chinese province
16 of Hubei.[1] The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
17 was subsequently identified as responsible of this condition, defined coronavirus
18 disease (COVID-19).[2] The virus has now spread outside Chinese borders with
19 82,297 cases and 2,804 deaths worldwide at the 26th of February.[3] After infection,
20 symptoms appear after an incubation time of 3-5 days, with 80% of those infected
21 developing a mild disease, 15% a severe disease and 5% will require support in
22 intensive care unit (ICU).[4] Overall, the estimated case-fatality rate is comprised
23 between 0.4% and 2.9% and the basic reproduction number is approximately
24 3.28.[4,5] SARS-CoV-2 is a new pathogen for humankind and any type of immune
25 protection exist, thus everybody can be potentially infected. Moreover, no primary
26 prophylaxis measures (vaccination) nor effective treatments are available. If the
27 above represented percentages are applied to the worldwide populations, it appears
28 clear why any measure should be considered to avoid a further diffusion of the virus
29 and prevent the saturation and collapse of health systems and the most catastrophic
30 pandemic since 1919 Spanish flu.

31 Isolation of those affected and the use of personal protective equipment (PPE) are
32 the mainstay to block transmission of this pathogen, which is presumed through
33 respiratory droplets. A 14 days quarantine is applied to subjects coming from
34 endemic areas or who had contact with confirmed cases. It is assumed that, if in this
35 period the subject does not develop any sign or symptoms compatible with COVID-

36 19, he is not infected and thus the quarantine can be removed, and the subject
37 returned to the community. Domiciliary quarantine of 14 days since a positive test is
38 applied also for patients with a diagnosed mild disease who did not need medical
39 support.

40 These rules are effective in controlling infections in the community, but several
41 doubts arise when it is necessary to transpose them in the hospital setting. Hospitals
42 are indeed a delicate place in epidemics: they collect fragile persons who can be
43 exposed to the virus and are subsequently readmitted to the community thus
44 spreading the infection. Indeed, the ongoing outbreak in Northern Italy has been
45 linked to a single infected patient who accessed to a community hospital where he
46 transmitted the virus to several other patients and health-care operators.[6]
47 Moreover, the isolation of patients in the hospital setting impose a significant burden
48 in terms of PPE used by the health-care operators, space dedicated and time
49 employed in their management. Even more complex is the situation of patients in
50 ICU, where viral spreading is facilitated by endotracheal tubes and manoeuvres
51 performed on the respiratory tract. Therefore, a clear definition of the infectiousness
52 timing and intensity of viral spreading is mandatory to alleviate the burden on the
53 health-care system.

54 Unfortunately, the data available on the topic are scarce and composed only of
55 measurements of viral shedding, without an assessment of the infectivity. Kim et
56 al.[7] assessed the viral load kinetics of SARS-CoV-2 in upper and lower respiratory

57 tract materials in the first two confirmed patients in Korea. They employed real-time
58 reverse transcriptase polymerase chain reaction (rRT-PCR) to detect SARS-CoV-2
59 and converted cycle threshold (CT) values of rRT-PCR into RNA copy number. The
60 detection limit of rRT-PCR was 2,690 copies/mL. Overall, viral load above detection
61 limit was detected until 14 and 25 days after symptoms onset and for 13 and 11 days
62 after the first detection, respectively.[7] Of note, both patients received treatment
63 with lopinavir/ritonavir. Instead, Zou and colleagues analysed viral load in repeated
64 nasal and throat swabs obtained from the 17 symptomatic patients.[8] They also
65 employed rRT-PCR and considered a CT of 40 as detection limit. Higher viral loads
66 were observed in nasal swabs and in samples collected soon after symptoms onset.
67 Overall, only two patients presented positive samples, and only in nasal swab, 14
68 days after symptoms onset, and with low viral load.

69 In conclusion, a larger amount of data about duration of viral spreading and
70 infectivity in hospitalized patients, especially in ICU, is badly needed to better define
71 quarantine period and avoid nosocomial transmission. Before their availability, the
72 canonical 14 days period of quarantine should be respected.

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