

No potential conflict of interest relevant to this letter was reported.

1. Rudwaleit M, van der Heijde D, Landewé R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann Rheum Dis* 2009;68:777-83.
2. Rudwaleit M, van der Heijde D, Khan MA, Braun J, Sieper J. How to diagnose axial spondyloarthritis early. *Ann Rheum Dis* 2004;63:535-43.
3. Aggarwal R, Ringold S, Khanna D, et al. Distinctions between diagnostic and classification criteria? *Arthritis Care Res (Hoboken)* 2015;67:891-7.
4. Radner H, Neogi T, Smolen JS, Aletaha D. Performance of the 2010 ACR/EULAR classification criteria for rheumatoid arthritis: a systematic literature review. *Ann Rheum Dis* 2014;73:114-23.
DOI: 10.1056/NEJMc1609622

THE AUTHORS REPLY: Campochiaro and Caruso are correct that mention of cardiovascular associations with ankylosing spondylitis and axial spondyloarthritis, including specific conduction-system lesions and aortic-root lesions, was largely absent from our review of spondyloarthritis. These specific lesions are uncommon and tend to occur late in the disease course, as does the other more common but less specific cardiovascular illness mentioned in their letter. The focus of our article was on early diagnosis and clinical management of the axial disease, and this priority, along with space and citation limitations, precluded our describing specific cardiovascular manifestations.

Rudwaleit and colleagues make the important point that diagnosis in clinical practice cannot be based solely on fulfillment of classification criteria. We tried to make this point in the article, but perhaps our wording conveyed some unintended ambiguity. In order to introduce the new concept of axial spondyloarthritis, we described the classification criteria for this entity proposed by the ASAS in 2009. In discussing this concept, including the critical role of MRI, we referred to

this entity as a diagnosis, in the sense of its being a defined medical condition. We did not intend by this to imply that one can rely strictly on these criteria to establish a diagnosis in clinical practice. In fact, we stated explicitly, “These classification criteria have limited use outside the arena of clinical research,” to introduce the algorithm (in Fig. 2 of our article) for use in clinical practice.

The algorithm itself is a modification of one published by the correspondents and their colleagues,¹ but it was modified specifically to further emphasize the importance of weighing clinical data and post-test probabilities² and of applying clinical judgment to the diagnostic process. Moreover, the discussion of MRI findings includes mention of lesions that are not part of the classification criteria but that can be helpful in supporting a diagnosis in clinical practice. Finally, the Summary section in our article reemphasizes the potential difficulty in accurately establishing or ruling out a diagnosis of axial spondyloarthritis, with no mention of criteria.

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Since publication of their article, the authors report no further potential conflict of interest.

1. van den Berg R, de Hooze M, Rudwaleit M, et al. ASAS modification of the Berlin algorithm for diagnosing axial spondyloarthritis: results from the SPondyloArthritis Caught Early (SPACE)-cohort and from the Assessment of SpondyloArthritis international Society (ASAS)-cohort. *Ann Rheum Dis* 2013;72:1646-53.
2. Feldtkeller E, Rudwaleit M, Zeidler H. Easy probability estimation of the diagnosis of early axial spondyloarthritis by summing up scores. *Rheumatology (Oxford)* 2013;52:1648-50.

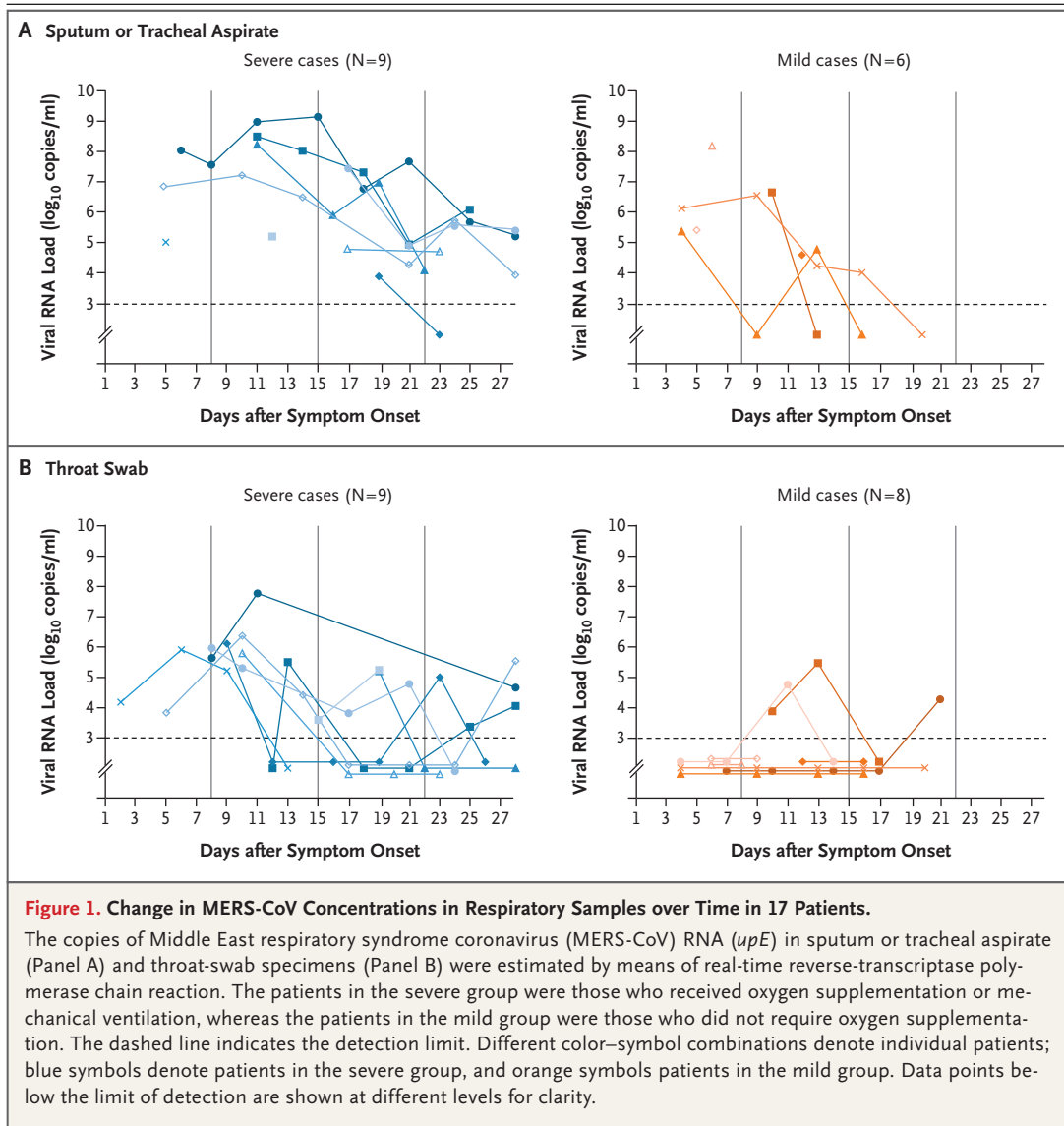
DOI: 10.1056/NEJMc1609622

Viral Load Kinetics of MERS Coronavirus Infection

TO THE EDITOR: The outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) infection in South Korea involved 186 patients and resulted in 38 deaths, with four large hospital outbreaks accounting for 82% of the total cases.^{1,2} Here, we report changes in viral load over time in patients with MERS.

We included all patients who were admitted

to three Seoul National University–affiliated hospitals; the institutional review boards of these hospitals approved this study and waived the need for written informed consent on public health grounds. The patients were categorized into a group with severe disease (severe group) or a group with mild disease (mild group), depending on whether oxygen supplementation was



used during the hospital stay.³ Chest radiographs were scored as described previously (higher scores indicate greater involvement; see the Supplementary Appendix, available with the full text of this letter at NEJM.org).⁴ Quantitative real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) for the envelope gene (*vpE*) was performed with the PowerChek MERS Real-time PCR kit (Kogenbiotech). A generalized mixed model with binary outcome was used to compare repeated samples.

A total of 17 patients were included in the study. The median incubation period was 7 days (range, 2 to 14). Nine patients were categorized into the severe group; in these patients, the chest radiograph score increased abruptly during

week 2 and reached a peak at approximately day 14 (Fig. S1A in the Supplementary Appendix). The copies of MERS-CoV RNA detected by rRT-PCR in respiratory samples peaked during week 2, and the median value was 7.21 \log_{10} copies per milliliter in the severe group and 5.54 \log_{10} copies per milliliter in the mild group ($P=0.06$). The peak in viral load in sputum or tracheal aspirate was higher and occurred later in the severe group than in the mild group (Fig. 1A). An RNA level exceeding 10^5 copies per milliliter in throat-swab samples was found in all 9 patients in the severe group and in 1 of 8 patients (12%) in the mild group ($P<0.001$) (Fig. 1B). At the time of the initial presentation, MERS-CoV RNA was detected in the nasopharyngeal-swab specimens from 5 of

17 patients (29%) and in the throat-swab specimens of 10 of 17 patients (59%) ($P=0.03$) (Fig. 1B, and Fig. S1B in the Supplementary Appendix). Among paired swab specimens obtained from the nasopharynxes and throats of the 17 patients, MERS-CoV RNA was detected in 8 of 70 (11%) nasopharyngeal-swab specimens and in 29 of 70 (41%) throat-swab specimens ($P<0.001$). Viral RNA was detected in serum samples from 3 of 9 patients (33%) in the severe group and in 1 of 8 patients (12%) in the mild group at initial presentation ($P=0.58$) (Fig. S1C in the Supplementary Appendix).

We found that the viral loads in the severe group were higher than those in the mild group. The patients in the severe group also had more prolonged viral shedding in respiratory secretions, beyond 21 days after the onset of symptoms, whereas viral RNA was no longer detected by 21 days in the mild group. A similar association between higher viral load and worse outcome was observed in the severe acute respiratory syndrome (SARS).⁵

In conclusion, MERS-CoV concentrations peaked during the second week of illness. Lower respiratory tract specimens had higher and more prolonged levels of MERS-CoV RNA as detected by rRT-PCR; throat swabs may be an alternative source of diagnostic samples, especially when sputum cannot be obtained.

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Supported by a grant from the Clinical Research Institute, Seoul National University Hospital (2015-1980), and a National Research Foundation of Korea grant funded by the South Korean government (2012R1A5A2A44671346).

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Korea Centers for Disease Control and Prevention. Middle East respiratory syndrome coronavirus outbreak in the Republic of Korea, 2015. *Osong Public Health Res Perspect* 2015;6:269-78.

2. Oh MD, Choe PG, Oh HS, et al. Middle East respiratory syndrome coronavirus superspreading event involving 81 persons, Korea 2015. *J Korean Med Sci* 2015;30:1701-5.

3. Park WB, Perera RA, Choe PG, et al. Kinetics of serologic responses to MERS coronavirus infection in humans, South Korea. *Emerg Infect Dis* 2015;21:2186-9.

4. Das KM, Lee EY, Al Jawder SE, et al. Acute Middle East respiratory syndrome coronavirus: temporal lung changes observed on the chest radiographs of 55 patients. *AJR Am J Roentgenol* 2015;205:W267-74.

5. Peiris JS, Guan Y, Yuen KY. Severe acute respiratory syndrome. *Nat Med* 2004;10:Suppl:S88-97.

DOI: 10.1056/NEJMc1511695

Stellar Quake

Sometimes there's a rift in the skin
of a neutron star caused by a quake
below its gravity-hard crust.
Superfluid protons spew out
with other exotic blood
if only for a few moments
before intense magnetic fields
suture the star shut. Yet it still spins
on its axis, pulses with precision,
before the next burst. It's amazing

what one can learn about stars
from a television in a hospital room.
The good doctor, making his rounds
like clockwork, stands at the door
with his clipboard, for a moment
— a silhouette in frazzled glow
of hall light — before coming in
with the news. I sensed the tangled light
in his eyes. And I knew the hardened
skin of my heart would break tonight

in the darkness of my own universe.

John C. Mannone, M.S.