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Can adhesive capsulitis of the shoulder be a consequence of COVID-19? Case series of 12 patients

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Keywords: Shoulder adhesive capsulitis; frozen shoulder; COVID-19; SARS-CoV-2; shoulder inflammation; synovial fibrosis; musculoskeletal manifestations of COVID-19

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) has spread explosively throughout the world, resulting in a pandemic new respiratory disease identified as coronavirus disease 2019 (COVID-19). Since March 2020, the viral infection has affected at least 192 countries or regions, causing about 2.5 million deaths and infecting more than 112 million people.²⁵

Patients with COVID-19 can be classified into 3 groups according to the severity of the viral infection: (1) asymptomatic and mild COVID-19 patients, who account for the majority of cases (approximately 80%), (2) severely ill patients (14%), and (3) critical patients (6%).^{13,43}

COVID-19 symptoms differ in the 3 groups.⁴³ Patients with mild symptoms generally suffer from nasal congestion, fever, anosmia and dysgeusia, a sore throat, cough, headache, malaise, and myalgia. Patients with a severe presentation frequently require hospitalization owing to pneumonia and acute respiratory distress syndrome. The

symptoms in critical patients include respiratory failure, septic shock, multiorgan dysfunction syndrome, and disseminated intravascular coagulation.⁴³

Systemic manifestations of COVID-19 result from a combination of the direct effects of the SARS-CoV-2 on infected target cells and of the indirect effects due to the host's inflammatory response to the virus. In particular, the indirect effects are associated with a cytokine storm and a systemic inflammation that involve any organ or system, including the musculoskeletal system.^{4,21}

The main musculoskeletal manifestations that as of this writing have been associated with COVID-19 are myalgias and generalized weakness, which are reported as early, transient features in 15%–45% of symptomatic patients and resolve on average within 10–15 days.^{19,34,44} Arthralgia is another common symptom, which is often combined with myalgias.⁷ Lastly, high blood creatinine kinase levels are often present in severe and critical patients.^{7,21}

Less is known about joint symptoms, with no studies having yet been published on inflammation of the synovial tissue or joint fibrosis related to COVID-19.

Among the inflammatory diseases involving the shoulder and associated with an overexpression of inflammatory cytokines is adhesive capsulitis (AC).²⁸ Described for the

According to our country's law, this case series did not require ethics committee approval.

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first time in 1872 by Duplay⁹ and subsequently also defined as frozen shoulder by Codman,⁵ AC is characterized by shoulder pain and stiffness combined with reduced active and passive range of motion and may severely impair a person's quality of life.

Several studies^{16,26,28,33,36} have shown that the beginning of the pathologic process in AC is characterized by a glenohumeral inflammation followed by synovial and periarthritic fibrosis.^{16,26,28,33,36} Based on reports that the inflammatory reaction in AC^{28,36} shows several similarities to that in COVID-19, and that synovial cells may be targeted by the SARS-CoV-2,^{6,23,40,46} we hypothesized that COVID-19 might be related to the development of AC in the shoulder. Here, we present our case series of patients with AC evaluated at our hospital.

Materials and methods

The study group included 12 consecutive, prospectively enrolled, subjects with AC. The diagnosis, which was made by the senior author (C.A.) after clinical and radiologic examination, was based on a reduction in both active and passive range of motion (ROM) of the shoulder, evaluated in the sitting and supine positions; no strength reduction in intra-extrarotation; exclusion of the posterosuperior^{18,24,27,29,35,42} and anterior^{1,11,41} rotator cuff tendon tears; a radiographic evaluation, that is, true anteroposterior view (with the central ray tangential to the glenoid surface) and a Velpeau axillary view (with the patient's arm held in internal rotation, the ray is superior to inferior and the patient leaning backward); and an MRI of the involved shoulder.

All the patients were evaluated between November 15, 2020, and January 15, 2021, at the shoulder surgery unit at our hospital, and all reported shoulder stiffness and pain arising after COVID-19, with no apparent cause.

At the time of our examination, none of the patients enrolled reported the following: a recent shoulder trauma; previous diagnosis of AC in either shoulder; a previous ROM limitation or a rotator cuff tear; severe glenohumeral osteoarthritis; cervical spine symptoms and rheumatologic and/or autoimmune pathologies.

The total number of patients and those with AC evaluated during the study period were noted. Clinical information on gender, age, affected side, time of AC onset after COVID-19 diagnosis, severity of COVID-19, shoulder functional limitation, and pain intensity was recorded. All comorbidities, as possible risk factors for development of AC, were noted.

Passive shoulder ROM was evaluated in terms of forward elevation, abduction, and external rotation (with the arm at the side and elbow flexed at 90°). The visual analog scale (VAS) was used to assess pain intensity.²²

All the patients signed an informed consent form in accordance with the Declaration of Helsinki.

Results

During the study period, a total of 1120 patients were evaluated at our shoulder surgery unit. Of these, 146 had an AC of the shoulder. The study sample was composed of 12 patients: 8 female and 4 male. The patients' mean age was 57 years (range: 42-73). All the clinical data are presented in Table I.

The right shoulder was involved in 5 subjects and the left shoulder in 6 subjects, whereas 1 patient reported symptoms in both shoulders. AC arose 1.5-3 months after the COVID-19 diagnosis (mean time to onset: 2 months).

According to severity, COVID-19 in 7 of the patients was asymptomatic, whereas in the remaining 5 patients symptoms were mild. None of the patients were severely or critical ill. As for other comorbidities, 2 patients had well-compensated diabetes mellitus.

Table I Clinical data of the study sample

Pt no.	Sex	Age	Side	AC onset*	COVID-19 severity	Passive ROM†			VAS score
						FE	Abd	ER	
1	F	73	L	2	Mild	100 (60)	90 (60)	10 (35)	5
2	F	42	R	2	Asymptomatic	70 (110)	50 (130)	0 (50)	8
3	F	50	R	2.5	Asymptomatic	110 (60)	80 (90)	10 (30)	6
4	M	49	L	3	Mild	150 (25)	100 (80)	20 (25)	4
5	F	54	R	3	Asymptomatic	140 (40)	100 (75)	10 (40)	5
6	F	57	R	2	Mild	160 (10)	130 (40)	30 (10)	3
7	M	59	L	1.5	Asymptomatic	70 (95)	40 (120)	0 (40)	8
8	F	61	R	3	Asymptomatic	170 (10)	150 (25)	35 (15)	3
9	F	65	L	2	Mild	130 (35)	100 (60)	15 (25)	6
10	M	57	Both	1.5	Asymptomatic	R: 100; L: 110	R: 90; L: 90	R: 10; L: 15	7
11	M	62	L	2.5	Mild	120 (50)	100 (70)	30 (15)	5
12	F	51	L	2	Asymptomatic	80 (100)	40 (140)	5 (45)	7

Pt, patient; F, female; M, male; L, left; R, right; AC, adhesive capsulitis; ROM, range of motion; FE, forward elevation; Abd, abduction; ER, external rotation (with the arm at the side and elbow flexed at 90°); VAS, visual analog scale for pain.

* AC onset after COVID-19 diagnosis in terms of months.

† Reduction of motion compared with the uninjured contralateral side. Values are in degrees, expressed as mean (reduction of motion compared with the uninjured contralateral side).

The decrease in range of motion was as follows: mean forward elevation of the affected side was 116° (range: 70°-170°), with a mean reduction compared with the uninjured shoulder of 54° (range: 10°-110°); the mean abduction was 89° (range: 40°-150°) and mean external rotation was 15° (range: 0°-35°), with a mean reduction compared with the contralateral side of 81° (range: 25°-140°) and 30° (range: 10°-50°), respectively. The mean pain intensity was 5.6 (range: 3-8).

Table II shows all the mean ROM and VAS values in the patients with asymptomatic and mild-symptomatic COVID-19.

Discussion

The initial pathologic process in AC is known to be a synovial inflammation associated with a hypervascular hyperplasia. This is followed by fibroblast hyperactivity and subsequent fibrosis in the synovium and glenohumeral capsular tissue,^{28,36} located above all in the coracohumeral ligament and to the rotator interval area.^{2,15-17,26,33}

Active and passive motion limitations are characteristic in patients with AC and occur with varying degrees of severity.³⁷ Shoulder pain intensity appears to be higher in the first 3 months following symptoms onset, in patients with a more severe range of motion impairment and in females.³ Lastly, the pain in AC is most frequently reported in the anterior surface of the shoulder with irradiation downward, to the antero-lateral aspect of the arm as far as its distal third (dermatomes C5-C6).³

In our series, the asymptomatic patients displayed a greater ROM impairment and a greater intensity of pain than mild-symptomatic patients, though a statistical evaluation is unreliable owing to the limited size of the sample.

As regards the correlation between COVID-19 and the frozen shoulder, we hypothesize that both direct and indirect effects of the viral disease may contribute to the pathogenesis of AC.

Cellular penetration of SARS-CoV-2 occurs via the angiotensin-converting enzyme 2 (ACE2) receptor and the serine protease TMPRSS2 (transmembrane protease, serine 2).²⁰ Following receptor binding, TMPRSS2 permits

mixing of human and viral membranes by proteolytic cleavage of the viral S protein, thus allowing entry into the cell of the viral RNA.¹⁰ After the release of the coronavirus RNA into the cytoplasm, translation of viral proteins and replication of viral RNA may occur.

Subsequently, many proteins translated by viral RNA may interact with different human cellular proteins, significantly impairing their function. Among the human proteins and the systemic pathways affected most by SARS-CoV-2 are those involved in the inflammatory cascade.^{12,14,39}

During infection, the first system to be affected by SARS-CoV-2 is the respiratory tract owing to the presence of target cells, and in particular of type II pneumocytes of the alveolar epithelial lining, which express both ACE2 receptors and TMPRSS2.⁴

Subsequently to the infection, the alveolar cells can rapidly deteriorate and undergo apoptosis. As a result, the epithelial barrier is compromised and may be crossed by the virus, which may in turn lead to viremia.⁸ At this point, the virus can reach all organ systems and directly infect target cells in which its specific membrane receptors are present.

With regard to human skeletal muscle tissue, many cells express TMPRSS2, including smooth muscle cells, muscle stem cells, pericytes, vascular cells, and endothelial cells. However, among these, only pericytes and smooth muscle cells express the ACE2 receptor.

By contrast, several cells in the synovium, including fibroblasts and monocytes, express both ACE2 and TMPRSS2.^{6,23,40,46} Although SARSCoV-2 has not been specifically detected in such tissues, these observations suggest that the synovium is a potential site of direct virus infection.⁷ This finding may be one of the main direct effects of the SARSCoV-2 on the synovium and fibroblasts and, therefore, be related to fibrosis of the capsular and pericapsular tissues in the AC.

In addition to direct infection of the cells outside of the respiratory tract, COVID-19 is characterized by indirect effects resulting from the host's response to the viral infection. These indirect effects are associated with a cytokine storm and a systemic inflammation that may impact nearly every organ system, including the musculoskeletal tissues.^{4,21} In particular, circulating levels of signaling molecules and

Table II ROM and pain intensity in asymptomatic and mild symptomatic COVID-19 patients

	Passive ROM*			VAS score, mean
	FE	Abd	ER	
Asymptomatic patients (n = 7)	106 (69)	80 (97)	11 (37)	6.3
Mild patients (n = 5)	132 (36)	104 (62)	21 (22)	4.6

ROM, range of motion; FE, forward elevation; Abd, abduction; ER, external rotation (with the arm at the side and elbow flexed at 90°); VAS, visual analog scale for pain.

* Reduction of motion compared with the uninjured contralateral side. Values are in degrees, expressed as mean (reduction of motion compared with the uninjured contralateral side).

proinflammatory cytokines, including interleukin 1 beta (IL-1b), IL-6, IL-8, IL-17, tumor necrosis factor alpha (TNF- α), granulocyte colony-stimulating factor, interferon gamma (IFN- γ), and other chemokines, are very high.^{21,30,45}

In strong analogy with COVID-19, the inflammatory cascade implicated in abnormal tissue repair and fibrosis of the shoulder AC is supported by similar cytokines and growth factors, particularly IL-1, IL-6, and TNF- α .^{28,36} Moreover, several authors^{28,32} have shown that expression levels of TNF- α , IL-1, and IL-6 are high in the joint capsule, in the subacromial bursa, and in joint fluid in patients with frozen shoulder. These data lend support to the hypothesis that indirect effects of viral infection may be involved in the development of AC.

Lastly, it should be borne in mind that, in addition to the direct and indirect effects of SARS-CoV-2, viral infection may be related to the development of AC resulting from the marked changes in lifestyle induced by the pandemic, especially those due to quarantine. Indeed, we believe that a sedentary lifestyle is associated with a number of side effects, as is confirmed by extensive reports indicating that lack of physical activity results in and exacerbates musculoskeletal discomfort and pain.^{31,38}

The main limitations of our study are as follows: the limited size of the study group, although it should be borne in mind that we enrolled highly selected patients who had recently suffered from COVID-19 and who had AC of the shoulder with no other apparent causes; SARSCoV-2 was not specifically detected in the shoulder tissues of our patients, nor can we provide incontrovertible data supporting the correlation between overexpression of inflammatory mediators of COVID-19 and the development of AC of the shoulder; the lack of a short- and long-term evaluation of patients regarding the evolution and treatment of AC; the absence of a control group consisting of patients with AC that did not occur after COVID-19.

Despite the possibility that there may be a correlation between COVID-19 and AC for the reasons we have provided, this case series cannot describe a cause-and-effect relationship.

Conclusion

We present our series of 12 patients with AC of the shoulder that developed shortly after COVID-19. We hypothesize that AC may be related to the infectious disease and that both direct and indirect effects of SARS-CoV-2 infection may be involved in its development, as may the sedentary lifestyle forced on these patients by this disease.

Future research will be needed to evaluate the short- and long-term natural history and treatment of these patients as well as to compare them with patients with AC that did not occur concurrently with COVID-19.

Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

References

1. Barth JR, Burkhart SS, De Beer JF. The bear-hug test: a new and sensitive test for diagnosing a subscapularis tear. *Arthroscopy* 2006; 22:1076-84. <https://doi.org/10.1016/j.arthro.2006.05.005>
2. Bunker TD, Reilly J, Baird KS, Hamblen DL. Expression of growth factors, cytokines and matrix metalloproteinases in frozen shoulder. *J Bone Joint Surg Br* 2000;82:768-73.
3. Candela V, Giannicola G, Passaretti D, Venditto T, Gumina S. Adhesive capsulitis of the shoulder: pain intensity and distribution. *Musculoskelet Surg* 2017;101:153-8. <https://doi.org/10.1007/s12306-017-0488-6>
4. Cheng H, Wang Y, Wang GQ. Organ-protective effect of angiotensin-converting enzyme 2 and its effect on the prognosis of COVID-19. *J Med Virol* 2020;92:726-30. <https://doi.org/10.1002/jmv.25785>
5. Codman EA. *The shoulder. Rupture of the supraspinatus tendon and other lesions in or about the subacromial bursa*. Boston: Thomas Todd; 1934. p. 216-24.
6. De Micheli AJ, Spector JA, Elemento O, Cosgrove BD. A reference single-cell transcriptomic atlas of human skeletal muscle tissue reveals bifurcated muscle stem cell populations. *Skelet Muscle* 2020;10:19. <https://doi.org/10.1186/s13395-020-00236-3>
7. Disser NP, De Micheli AJ, Schonk MM, Konnaris MA, Piacentini AN, Edon DL, et al. Musculoskeletal Consequences of COVID-19. *J Bone Joint Surg Am* 2020;102:1197-204. <https://doi.org/10.2106/JBJS.20.00847>
8. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci U S A* 2020;117:9490-6. <https://doi.org/10.1073/pnas.2004168117>
9. Duplay S. Scapulo-humeral peri-arthritis and shoulder stiffness resulting from it. *Arch Gen Med* 1872;20:513-42 [in French].
10. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. *Methods Mol Biol* 2015;1282:1-23. https://doi.org/10.1007/978-1-4939-2438-7_1
11. Gerber C, Hersche O, Farron A. Isolated rupture of the subscapularis tendon. *J Bone Joint Surg Am* 1996;78:1015-23.
12. Gordon DE, Jang GM, Bouhaddou M, Xu J, Obernier K, White KM, et al. A SARS-CoV-2 protein interaction map reveals targets for drug repurposing. *Nature* 2020;583:459-68. <https://doi.org/10.1038/s41586-020-2286-9>
13. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708-20. <https://doi.org/10.1056/NEJMoa2002032>
14. Guzzi PH, Mercatelli D, Ceraolo C, Giorgi FM. Master regulator analysis of the SARS-CoV-2/human interactome. *J Clin Med* 2020;9:982. <https://doi.org/10.3390/jcm9040982>
15. Hand C, Clipsham K, Rees JL, Carr AJ. Long-term outcome of frozen shoulder. *J Shoulder Elbow Surg* 2008;17:231-6. <https://doi.org/10.1016/j.jse.2007.05.009>
16. Hand GC, Athanasou NA, Matthews T, Carr AJ. The pathology of frozen shoulder. *J Bone Joint Surg Br* 2007;89:928-32. <https://doi.org/10.1302/0301-620X.89B7.19097>

17. Hannafin JA, Chiaia TA. Adhesive capsulitis. A treatment approach. *Clin Orthop Relat Res* 2000;372:95-109.
18. Hertel R, Ballmer FT, Lombert SM, Gerber C. Lag signs in the diagnosis of rotator cuff rupture. *J Shoulder Elbow Surg* 1996;5:307-13.
19. Heydari K, Rismantab S, Shamshirian A, Lotfi P, Shadmehri N, Houshmand P, et al. Clinical and paraclinical characteristics of COVID-19 patients: a systematic review and meta-analysis. *medRxiv* 2020. <https://doi.org/10.1101/2020.03.26.20044057>
20. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* 2020;181:271-80.e8. <https://doi.org/10.1016/j.cell.2020.02.052>
21. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
22. Jensen MP, Karoly P. Pain-specific beliefs, perceived symptom severity, and adjustment to chronic pain. *Clin J Pain* 1992;8:123-30.
23. Ji Q, Zheng Y, Zhang G, Hu Y, Fan X, Hou Y, et al. Single-cell RNA-seq analysis reveals the progression of human osteoarthritis. *Ann Rheum Dis* 2019;78:100-10. <https://doi.org/10.1136/annrheumdis-2017-212863>
24. Jobe FW, Jobe CM. Painful athletic injuries of the shoulder. *Clin Orthop Relat Res* 1983;173:117-24.
25. Johns Hopkins University. Coronavirus resource center. Available at: <https://coronavirus.jhu.edu>. Accessed February 22, 2021.
26. Kanbe K, Inoue K, Inoue Y, Chen Q. Inducement of mitogen-activated protein kinases in frozen shoulders. *J Orthop Sci* 2009;14:56-61. <https://doi.org/10.1007/s00776-008-1295-6>
27. Kelly BT, Kadrmas WR, Speer KP. The manual muscle examination for rotator cuff strength. An electromyographic investigation. *Am J Sports Med* 1996;24:581-8.
28. Lho YM, Ha E, Cho CH, Song KS, Min BW, Bae KC, et al. Inflammatory cytokines are overexpressed in the subacromial bursa of frozen shoulder. *J Shoulder Elbow Surg* 2013;22:666-72. <https://doi.org/10.1016/j.jse.2012.06.014>
29. Litaker D, Piro M, El Bilbeisi H, Brems J. Returning to the bedside: using the history and physical examination to identify rotator cuff tears. *J Am Geriatr Soc* 2000;48:1633-7.
30. Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine* 2020;55:102763. <https://doi.org/10.1016/j.ebiom.2020.102763>
31. Memari A, Shariat A, Anastasio AT. Rising incidence of musculoskeletal discomfort in the wake of the COVID-19 crisis. *Work* 2020;66:751-3. <https://doi.org/10.3233/WOR-203221>
32. Mullett H, Byrne D, Colville J. Adhesive capsulitis: human fibroblast response to shoulder joint aspirate from patients with stage II disease. *J Shoulder Elbow Surg* 2007;16:290-4. <https://doi.org/10.1016/j.jse.2006.08.001>
33. Nago M, Mitsui Y, Gotoh M, Nakama K, Shirachi I, Higuchi F, et al. Hyaluronan modulates cell proliferation and mRNA expression of adhesion-related procollagens and cytokines in glenohumeral synovial/capsular fibroblasts in adhesive capsulitis. *J Orthop Res* 2010;28:726-31. <https://doi.org/10.1002/jor.21075>
34. Nasiri MJ, Haddadi S, Tahvildari A, Farsi Y, Arbabi M, Hasanzadeh S, et al. COVID-19 clinical characteristics, and sex-specific risk of mortality: systematic review and meta-analysis. *Front Med (Lausanne)* 2020;7:459. <https://doi.org/10.3389/fmed.2020.00459>
35. Patte D, Goutallier D, Monpierre H, Debeyre J. Etude des lésions étendues [Over-extension lesions]. *Rev Chir Orthop Reparatrice Appar Mot* 1988;74:314-8 [in French].
36. Rodeo SA, Hannafin JA, Tom J, Warren RF, Wickiewicz TL. Immunolocalization of cytokines and their receptors in adhesive capsulitis of the shoulder. *J Orthop Res* 1997;15:427-36.
37. Schellingerhout JM, Verhagen AP, Thomas S, Koes BW. Lack of uniformity in diagnostic labeling of shoulder pain: time for a different approach. *Man Ther* 2008;13:478-83. <https://doi.org/10.1016/j.math.2008.04.005>
38. Shariat A, Cardoso JR, Cleland JA, Danaee M, Ansari NN, Kargarfard M, et al. Prevalence rate of neck, shoulder and lower back pain in association with age, body mass index and gender among Malaysian office workers. *Work* 2018;60:191-9. <https://doi.org/10.3233/WOR-2738>
39. Srinivasan S, Cui H, Gao Z, Liu M, Lu S, Mkandawire W, et al. Structural genomics of SARS-CoV-2 indicates evolutionary conserved functional regions of viral proteins. *Viruses* 2020;12:360. <https://doi.org/10.3390/v12040360>
40. Sun H, Wen X, Li H, Wu P, Gu M, Zhao X, et al. Single-cell RNA-seq analysis identifies meniscus progenitors and reveals the progression of meniscus degeneration. *Ann Rheum Dis* 2020;79:408-17. <https://doi.org/10.1136/annrheumdis-2019-215926>
41. Tifford CD, Plancher KD. Nonsurgical treatment of rotator cuff tears. In: Norris T, editor. *Orthopaedic knowledge update; shoulder and elbow*. Rosemont, IL: American Academy of Orthopaedic Surgeons; 1997. p. 135.
42. Walch G. The chronic painful shoulder exam program. *Shoulder day Lyonnaise*. Lyon. *Clinique de chirurgie orthopédique et traumatologique*; 1993. p. 169-89 [in French].
43. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323:1239-42. <https://doi.org/10.1001/jama.2020.2648>
44. Xu P, Sun GD, Li ZZ. Clinical characteristics of two human to human transmitted coronaviruses: corona virus disease 2019 versus Middle East respiratory syndrome coronavirus. *Eur Rev Med Pharmacol Sci* 2020;24:5797-809. https://doi.org/10.26355/eurrev_202005_21374
45. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the "Cytokine storm" in COVID-19. *J Infect* 2020;80:607-13. <https://doi.org/10.1016/j.jinf.2020.03.037>
46. Zhang F, Wei K, Slowikowski K, Fonseka CY, Rao DA, Kelly S, et al. Defining inflammatory cell states in rheumatoid arthritis joint synovial tissues by integrating single-cell transcriptomics and mass cytometry. *Nat Immunol* 2019;20:928-42. <https://doi.org/10.1038/s41590-019-0378-1>