



## 2. Bölüm

# COVID-19 ve Kardiyovasküler Sistem

Melek Didem KEMALOĞLU<sup>1</sup>

Zehra ERKAL<sup>2</sup>

2019 yılında Çin'in Wuhan kentinde başlayan hızla yayılan koronavirüs hastalığı (COVID-19) global bir pandemidir ve Dünya Sağlık Örgütü verilerine göre 13 Mayıs 2021 itibariyle küresel olarak 160 milyon pozitif vaka ve 3,3 milyon ölü sayısı ile halen yaşanmaktadır (1). COVID-19'un neden olduğu enfeksiyon Ciddi Akut Respiratuvar Sendrom-2 (SARS-CoV-2) olarak adlandırılmaktadır ve soğuk algınlığına neden olduğu bilinen diğer koronavirüs enfeksiyonlarından farklıdır. 2002 yılından tanıdığımız Zoonotik Ciddi Akut Respiratuvar Sendromu (SARS-CoV) ve 2012 yılından tanıdığımız Middle East Respiratuvar Sendromu (MERS) ile benzer özellikler göstermektedir(2). Tıpkı SARS ve MERS gibi SARS-CoV-2' nin yarasalardan ara konak olan Malayan Pangolinleri'ne, onlardan da insana taşındığına inanılmaktadır. SARS-CoV-2'nin ayırt edici bir özelliği MERS ve SARS'a kıyasla daha kapsamlı bir kardiyak tutulum yapmasıdır (3).

### ETYOPATOGENEZ

COVID-19 kardiyovasküler sistemi çeşitli derecelerde etkilemekte, altta yatan kardiyovasküler hastalığı olanlarda daha ağır seyrtemekte, miyokard hasarı ve disfonksiyonuna neden olmaktadır. SARS-CoV-2 enfeksiyonu kalbe hem doğrudan hem de dolaylı yollardan hasar verebilmektedir (4).

<sup>1</sup> Uzm. Dr. Antalya Atatürk Devlet Hastanesi, Kardiyoloji Kliniği, mdidemdenkli@gmail.com

<sup>2</sup> Uzm. Dr. Sağlık Bilimleri Üniversitesi, Antalya Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, zehraerkalkard@hotmail.com

hastalıktır (64). COVID-19 hastalığında gözlenen inflamatuvar sendrom ile Kawasaki hastalığı arasında benzerlikler bulunmaktadır (65-66).

Bu otoimmün hastalık koroner arter anevrizmasına neden olabilir. Bu durum gözden kaçarsa ya da tedavi gecikirse koroner arter trombozu, miyokardiyal iskemi ve infarkta sebep olur (64). Bu çocukların bir kısmında akut miyokardiyal disfonksiyon veya sistemik hiperinflamasyona bağlı olarak şok gelişebilir. Tanı ve tedavi gecikirse istenmeyen kardiyak olaylarla (koroner arter dilatasyonu, anevrizması, aritmi) sonuçlanabilir (67-68).

## KAYNAKLAR

1. Dong E, Du H and Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis*. Feb 19, 2020. doi: 10.1016/S1473-3099(20)30120-1. [epub ahead of print] Accessed 3/21/20.
2. Badawi A and Ryou SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *Int J Infect Dis*. 2016;49:129-133.
3. Zhang T WQ, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. *Curr Biol*. March 13, 2020. doi: 10.1016/j.cub.2020.03.022. [epub ahead of print]
4. Azevedo RB, Botelho BG, Hollanda JGÇ et al. Covid 19 and the cardiovascular system; a comprehensive review. *Journal of human hypertension*.
5. Bermejo JAP, Kang S, Rockwood SJ et al. SARS-CoV-2 infection of human iPSC-derived cardiac cells predicts novel cytopathic features in hearts of COVID-19 patients. Now published in *Science Translational Medicine* doi: 10.1126/scitranslmed.abf7872
6. A. Sharma, Garcia G, Wang Y et al. *Cell Rep. Med*. 10.1016/j.xcrm.2020.100052(2020).
7. Topol EJ. COVID-19 can affect the heart. *Science* 10.1126/science.abe2813(2020).
8. Turner, A. J., Hiscox, J. A. & Hooper, N. M. ACE2: from vasopeptidase to SARS virus receptor. *Trends Pharmacol. Sci*. 25, 291–294 (2004)
9. Hoffmann M, Kleine-Weber H, Schroeder S et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*. March 5, 2020. doi: 10.1016/j.cell.2020.02.052. [epub ahead of print].
10. Tikellis C and Thomas MC. Angiotensin-Converting Enzyme 2 (ACE2) Is a Key Modulator of the Renin Angiotensin System in Health and Disease. *Int J Pept*. 2012;2012:256294-256294. 9.
11. Zhang H, Penninger JM, Li Y, Zhong N et al. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive Care Med*. March 3, 2020. doi: 10.1007/s00134-020-05985-9. [epub ahead of print].
12. Zheng YY, Ma YT, Zhang JY. Covid-19 and the cardiovascular system. *Nature reviews, Cardiology*.
13. Ackermann M, Verleden SE, Kuehnel M et al. (2020) Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in COVID-19. *N. Engl. J. Med*. 383, 120–128
14. Varga Z, Flammer AJ, Steiger P et al. (2020) Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 395, 1417–1418
15. Teuwen LA, Geldhof V, Pasut A et al. (2020) COVID-19: the vasculature unleashed. *Nat. Rev. Immunol*. 20, 389–391

16. Panigada M, Bottino N, Tagliabue P et al. (2020) Hypercoagulability of COVID-19 patients in intensive care unit: A report of thromboelastography findings and other parameters of hemostasis. *J. Thromb. Haemost.* 18, 1738–1742
17. Tomar B, Anders HJ, Desai J et al. (2020) Neutrophils and neutrophil extracellular traps drive necroinflammation in COVID-19. *Cells* 9, 1383
18. Zuo Y, Yalavarthi S, Shi H et al. (2020) Neutrophil extracellular traps in COVID-19. *JCI Insight* 5, e138999
19. Middleton EA, He XY, Denorme F et al. (2020) Neutrophil extracellular traps contribute to immunothrombosis in COVID-19 acute respiratory distress syndrome. *Blood* 136, 1169
20. Channappanavar, R. and Perlman, S. (2017) Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Semin. Immunopathol.* 39, 529–539
21. Li D, Chen Y, Jia Y et al. (2020) SARS-CoV-2-induced immune dysregulation and myocardial injury risk in China: insight from the ERSCoVID-19 study. *Circ. Res.* 127, 397–399
22. Bermejo- Martin JF, Lejarazu RO, Pumarola T et al. (2009) Th1 and Th17 hypercytokinemia as early host response signature in severe pandemic influenza. *Crit. Care* 13, R201
23. Kindler E, Thiel V, Weber F. (2016) Interaction of SARS and MERS coronaviruses with the antiviral interferon response. *Adv. Virus Res.* 96, 219–243
24. Blanco-Melo D, Payant BEN, Liu WC et al. (2020) Imbalanced host response to SARS-CoV-2 drives development of COVID-19. *Cell* 181, 1036–1045
25. Wu C, Hu X, Song J et al. (2020) Heart injury signs are associated with higher and earlier mortality in coronavirus disease 2019 (COVID-19). *MedRxiv* Published online February 29, 2020. <https://doi.org/10.1101/2020.02.26.20028589>
26. Cummings MJ, Baldwin MR, Abrams D et al. (2020) Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 395, 1763–1770
27. Tanaka T, Nazaraki M, Kishimoto T et al. (2016) Immunotherapeutic implications of IL-6 blockade for cytokine storm. *Immunotherapy* 8, 959–970
28. Chang WT, Toh HS, Liao CT et al. Cardiac involvement of COVID-19: A comprehensive review. *Am J Med Sci* 2021; 361(1): 14–22.
29. Madjid M, Safavi-Naeini P, Solomon SD et al. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. *JAMA Cardiol* 2020 Mar 27. [Epub ahead of print], doi: 10.1001/jamacardio.2020.1286.
30. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497–506.
31. Baba poor-Farrokhran S, Gill D, Walker J, RT et al. Myocardial injury and COVID-19: Possible mechanisms. *Life Sci.* 2020 Jul 15;253:117723.
32. Pulmonary and Cardiac Pathology in COVID-19: The First Autopsy Series from New Orleans. Available at: <https://www.medrxiv.org/content/10.1101/2020.04.06.20050575v1.full.pdf>. Accessed Apr 27, 2020.
33. Wang, D., B. Hu, C. Hu, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *Jama.* 2020 Feb 323(11):1061–1069.
34. Chen, N., M. Zhou, X. Dong, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020 Feb 15;395(10223):507–513
35. Tajbakhsh A, Hayat SMG, Taghizadeh H, Akbari A et al. Covid 19 and cardiac injury: clinical manifestations, biomarkers, mechanisms, diagnosis, treatment and follow up. Expert review of anti-infective therapy.

36. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* Feb 24 2020. <https://doi.org/10.1001/jama.2020.2648> [Epub ahead of print].
37. Welt FGP, Shah PB, Aronow HD. From the American College of Cardiology's (ACC) Interventional Council and the Society of Cardiovascular Angiography and Intervention (SCAI), et al. Catheterization laboratory considerations during the coronavirus (COVID-19) pandemic: from ACC's Interventional Council and SCAI. *JACC* 2020. <https://doi.org/10.1016/j.jacc.2020.03.021>.
38. Wei, Z.Y. and H.Y. Qian. [Myocardial injury in patients with COVID-19 pneumonia]. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2020 Mar 2;48(0):E006.
39. Kwong JC, Schwartz KL, Campitelli MA, et al. Acute myocardial infarction after laboratory-confirmed influenza infection. *N Engl J Med* 2018;378:345–53.
40. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5:1–6. <https://doi.org/10.1001/jamacardio.2020.1096>.
41. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020 Feb 28. [Epub ahead of print], doi: 10.1056/NEJMoa2002032.
42. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020 Mar 28;395:1054–62.
43. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020 Feb 7. [Epub ahead of print], doi: 10.1001/jama.2020.1585.
44. Guo T, Y Fan, M. Chen, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol*. 2020 Mar 27;5(7):1-8.
45. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020;30:269–71.
46. Traebert M, Dumotier B, Meister L, Hoffmann P, Dominguez-Estevéz M, Suter W. Inhibition of hERG K<sup>+</sup> currents by antimalarial drugs in stably transfected HEK293 cells. *Eur J Pharmacol*. 2004;484(1):41–48.
47. Demaziere J, Fourcade JM, Busseuil CT, Adeleine P, Meyer SM, Saissy JM. The hazards of chloroquine self prescription in west Africa. *J Toxicol Clin Toxicol*. 1995;33(4):369–370.
48. Cervera A, Espinosa G, Font J, Ingelmo M. Cardiac toxicity secondary to long term treatment with chloroquine. *Ann Rheum Dis*. 2001;60(3):301
49. Wu CI, Postema PG, Arbelo E, Behr ER, Bezzina CR, Napolitano C, et al. SARS-CoV-2, COVID-19 and inherited arrhythmia syndromes. *Heart Rhythm*. 2020 Mar 31. pii: S1547-5271(20)30285-X. doi: 10.1016/j.hrthm.2020.03.024. [Epub ahead of et al. print]] uyarlanmıştır
50. Türk Kardiyoloji Derneği Uzlaşma Raporu: COVID-19 Pandemisi ve Kardiyovasküler Hastalıklar Konusunda Bilinmesi Gerekenler (13 Mayıs 2020) Dr. Meryem Aktöz,1 Dr. Hakan Altay,2 Dr. Emre Aslanger,3 Dr. Enver Atalar,4
51. Buzon J, Roignot O, Lemoine S, et al. Takotsubo cardiomyopathy triggered by influenza A virus. *Intern Med*. 2015;54(16):2017–2019.
52. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062.

53. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020;368:m1091. <https://doi.org/10.1136/bmj.m1091>.
54. 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(7):726–730.
55. Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. *Cardiovasc Res*. 2020;116(6):1097–1100.
56. Liu, J., S. Li, J. Liu, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine*. 2020 May;55:102763.
57. Siripanthong B, Nazarian S, Muser D, Deo R, Santangeli P, Mohammed Y et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. *Heart Rhythm*. 2020;S1547-5271:30422–7.
58. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.
59. Wang T, Chen R, Liu C, Liang W, Guan W, Tang R, et al. Attention should be paid to venous thromboembolism prophylaxis in the management of COVID-19. *Lancet Haematol* 2020;7:e362–e3.
60. Chang JC. TTP-like syndrome: novel concept and molecular pathogenesis of endotheliopathy-associated vascular microthrombotic disease. *Thromb J* 2018;16:20.
61. Lin L, Lu L, Cao W, Li T. Hypothesis for potential pathogenesis of SARS-CoV-2 infection—a review of immune changes in patients with viral pneumonia. *Emerg Microbes Infect* 2020;9:727–32.
62. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. *J Thromb Haemost* 2020 Apr 9. [Epub ahead of print], doi: 10.1111/jth.14830.
63. COVID-19 and Coagulopathy: Frequently Asked Questions. Available at: <https://www.hematology.org/COVID-19/COVID-19-and-coagulopathy>. Accessed May 5, 2020.
64. McCrindle BW, Cifra B. The role of echocardiography in Kawasaki disease. *Int J Rheum Dis*. 2018;21:50–55.
65. Ronconi G, Teté G, Kritas SK, et al. SARS-CoV-2, which induces COVID-19, causes kawasaki-like disease in children: role of pro-inflammatory and anti-inflammatory cytokines. *J Biol Regul Homeost Agents*. 2020 Jun 1;34(3). <https://doi.org/10.23812/EDITORIAL-RONCONI-E-59>.
66. Loomba RS, Villarreal EG, Flores S. COVID-19 and hyperinflammatory syndrome in children: kawasaki disease with macrophage activation syndrome in disguise. *Cureus*. 2020;12(8):e9515.
67. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis*. 2020 Aug 17. [https://doi.org/10.1016/S1473-3099\(20\)30651-4](https://doi.org/10.1016/S1473-3099(20)30651-4). S1473-3099(20) 30651-4.
68. Sperotto F, Friedman KG, Son MBF, VanderPluym CJ, Newburger JW, Dionne A. Cardiac manifestations in SARS-CoV-2-associated multisystem inflammatory syndrome in children: a comprehensive review and proposed clinical approach. *Eur J Pediatr*. 2020 Aug 15:1–16. <https://doi.org/10.1007/s00431-020-03766-6>.