令和４年度第３回安全技術調査会
参考資料４－５

2021年06月23日 (水)
17:30-19:00

採血事業 濵口班
第3回 班会議

国立感染症研究所
血液・安全性研究部
濵口 功
(協：水 上 拓 郎)

発症からの感染可能期間と再陽性症例における感染性・二次感染リスクに関するエビデンスのまとめ

2021年2月18日
国立感染症研究所感染症疫学センター

発症10日目以降の症例からの感染リスクについて

- 軽症から中等症の患者において、発症11日目・12日目にそれぞれ1例ずつ感染性のあるウイルスが分離された症例を含む報告があるが、その他では、ウイルスが分離されるのは、発症10日目までであった[2]
  台湾：発症5日以内の接触者では陽性発症者が1%（二次発症率）、6日以降の接触者では二次発症者なし [3]
- 英国：確定症例の発症5日経過後以降の接触者では二次発症者なし [4]。
- 日本：発症9日目の鼻咽頭ぬぐい液、発症13日目の気管吸引物から、感染性ウイルス分離 [5]。症状不明

軽症・中等症においては、発症10日目以降の症例からの感染のリスクは低い

再陽性症例における感染性についてと二次感染リスクについて

- 韓国：再陽性者の感染期の接触者790名から二次感染者なし、再陽性108検体のウイルス培養は陰性 [6]
- 中国：再陽性者は、他の患者と同様の中和抗体価を示し、感染性のあるウイルス株は分離されなかった[7]
- 中国：退院後28日間の経過観察期間中に再陽性となった189名の濃厚接触者から二次感染者なし[8]。

核酸検査再陽性例よりウイルス培養の陽性例（感染性の再燃）はなしや二次感染なし

SARS-CoV-2排泄が長引く場合について

- 感染性ウイルス分離期間の中央値は発症後8日（四分位範囲：5-11、範囲：0-20日）。ウイルス分離可能性は、発症15.2日で5%以下まで低下 [13]。
- 免疫不全患者20名の調査では、発症後20日以降も3名からウイルス培養 [14]。
- 高齢はRNA排泄持続の独立したリスク因子だが、感染性ウイルス排泄が遅延するという報告はない[11, 15]

重症者や免疫不全者では感染性ウイルスの排泄が長引く可能性が示唆

- 軽症・中等症においては、現行の退院基準を満たした症例からの二次感染のリスクは低い
- 重症者は発症15日程度までは一部の症例で感染性ウイルス排泄があり、重度免疫不全者では、それ以降も感染性のあるウイルス排泄が長引く。
- 変異株に関しては感染性に関しての情報が乏しい。

Evaluation of High-Sensitivity Cardiac Troponin T Levels in Japanese Patients Recently Recovered From Coronavirus Disease 2019

Satoshi Ide, MD; Hiromasa Hayama, MD; Yusuke Asai, PhD; Mari Terada; Hidetoshi Nomoto, MD; Satoshi Kutsuna, MD, PhD; Norio Ohmagari, MD, PhD; Yukio Hiroi, MD, PhD

Circulation Journal
Circ J 2021; **85:** 944–947
doi:10.1253/circj.CJ-21-0219

hsTnT >0.003ng/mL

hsTnT陽性者

Table. Comparison of the Characteristics of hsTnT-Positive and -Negative Patients

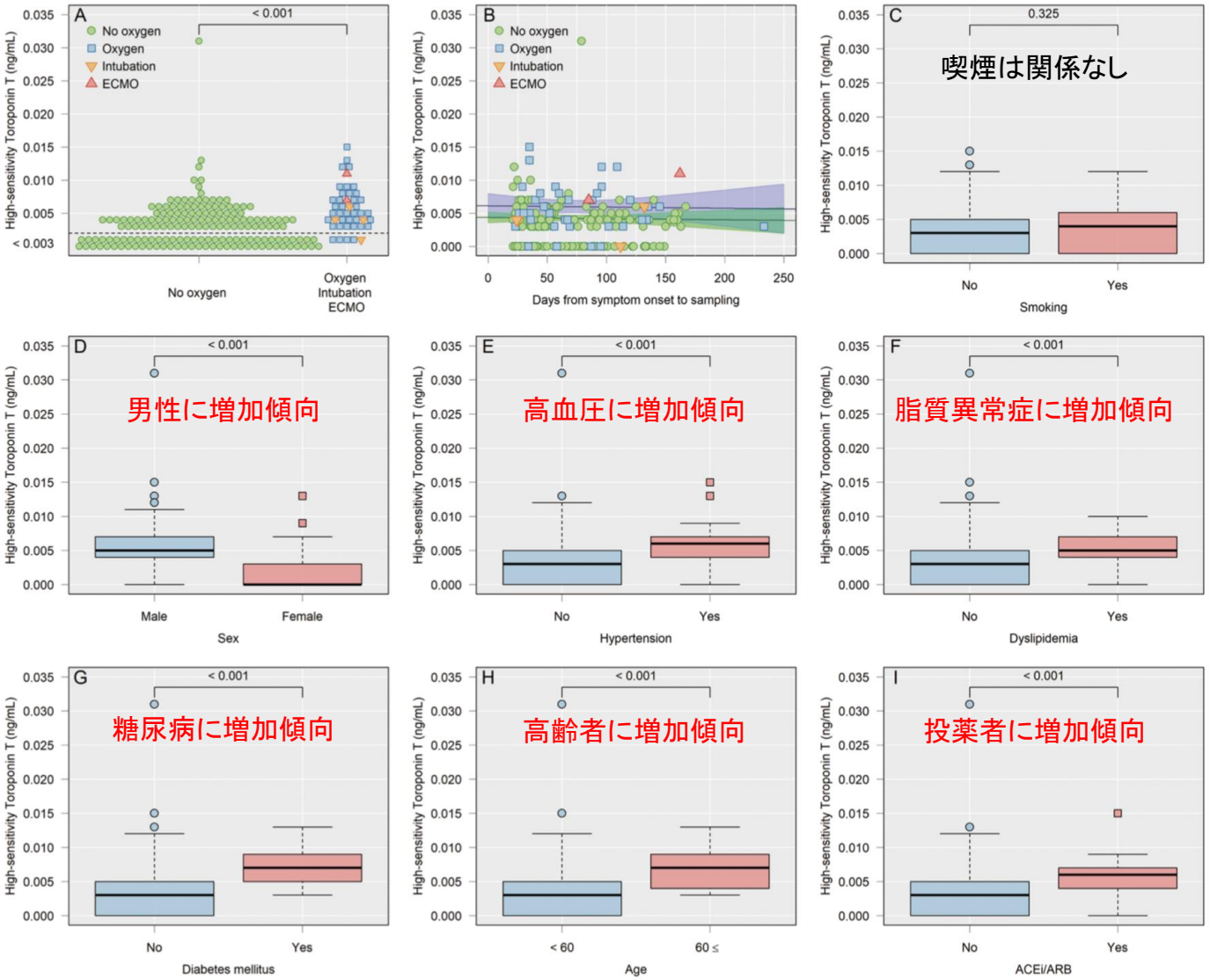
	COVID-19 (n=209)	hsTnT >0.003 ng/mL (n=135)	hsTnT ≤0.003 ng/mL (n=74)	P value[a]
Patient characteristics				
Age, mean (SD) years	45 (19)	50 (42.5–56)	36 (31–45)	<0.001
Male sex, n (%)	106 (51)	93 (69)	13 (18)	<0.001
Days since onset (SD), days	56 (62)	54 (35–97.5)	56.5 (32.3–89.8)	0.507
Comorbidities and medication				
Hypertension, n (%)	33 (16)	30 (22)	3 (4)	<0.001
Diabetes, n (%)	16 (8)	16 (12)	0 (0)	0.002
Dyslipidemia, n (%)	26 (12)	24 (18)	2 (3)	0.002
History of smoking, n (%)	47 (23)	32 (24)	15 (20)	0.608
COPD, n (%)	1 (1)	1 (1)	0 (0)	1
OMI, n (%)	0 (0)	0 (0)	0 (0)	1
CABG, n (%)	0 (0)	0 (0)	0 (0)	1
Arrhythmia, n (%)	4 (2)	4 (3)	0 (0)	0.300
Use of ACEi/ARB, n (%)	24 (12)	23 (17)	1 (1)	<0.001
Use of β-blocker, n (%)	1 (1)	1 (1)	0 (0)	1
Severity of COVID-19				
Non-severe; no oxygen n (%)	165 (79)	96 (71)	69 (93)	<0.001
Severe; inhalation of oxygen, intubation, and ECMO n (%)	44 (21)	39 (28)	4 (5)	<0.001
Laboratory data				
White blood cells, mean (SD), μL	5,310 (1,725)	5,310 (1,630)	5,330 (1,875)	0.652
Hemoglobin, mean (SD), mg/dL	13.7 (2.2)	14.1 (2.1)	13.1 (1.5)	<0.001
Platelets, mean (SD), 10^4/μL	24.6 (7.1)	23.5 (7)	26.0 (5.9)	0.009
Echocardiography				
Ejection fraction, (SD) %	64.9 (6.5)	65.4 (6.5)	63.6 (6.5)	0.069

Evaluation of High-Sensitivity Cardiac Troponin T Levels in Japanese Patients Recently Recovered From Coronavirus Disease 2019

Satoshi Ide, MD; Hiromasa Hayama, MD; Yusuke Asai, PhD;
Mari Terada; Hidetoshi Nomoto, MD; Satoshi Kutsuna, MD, PhD;
Norio Ohmagari, MD, PhD; Yukio Hiroi, MD, PhD

Circulation Journal
Circ J 2021; **85:** 944–947
doi:10.1253/circj.CJ-21-0219

hsTnT陽性者 hsTnT >0.003ng/mL

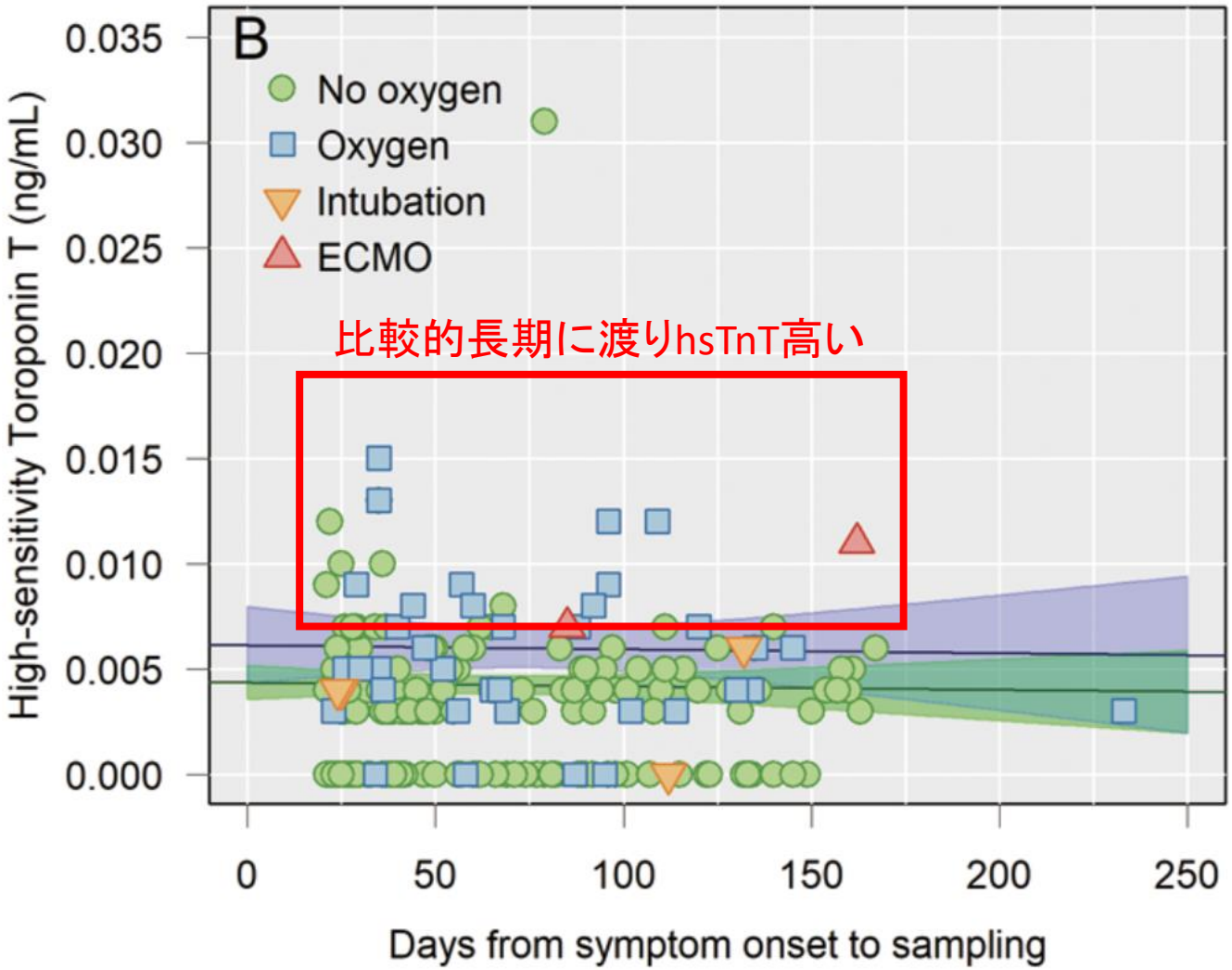


Evaluation of High-Sensitivity Cardiac Troponin T Levels in Japanese Patients Recently Recovered From Coronavirus Disease 2019

Satoshi Ide, MD; Hiromasa Hayama, MD; Yusuke Asai, PhD;
Mari Terada; Hidetoshi Nomoto, MD; Satoshi Kutsuna, MD, PhD;
Norio Ohmagari, MD, PhD; Yukio Hiroi, MD, PhD

Circulation Journal
Circ J 2021; **85:** 944–947
doi:10.1253/circj.CJ-21-0219

hsTnT陽性者 hsTnT >0.003ng/mL



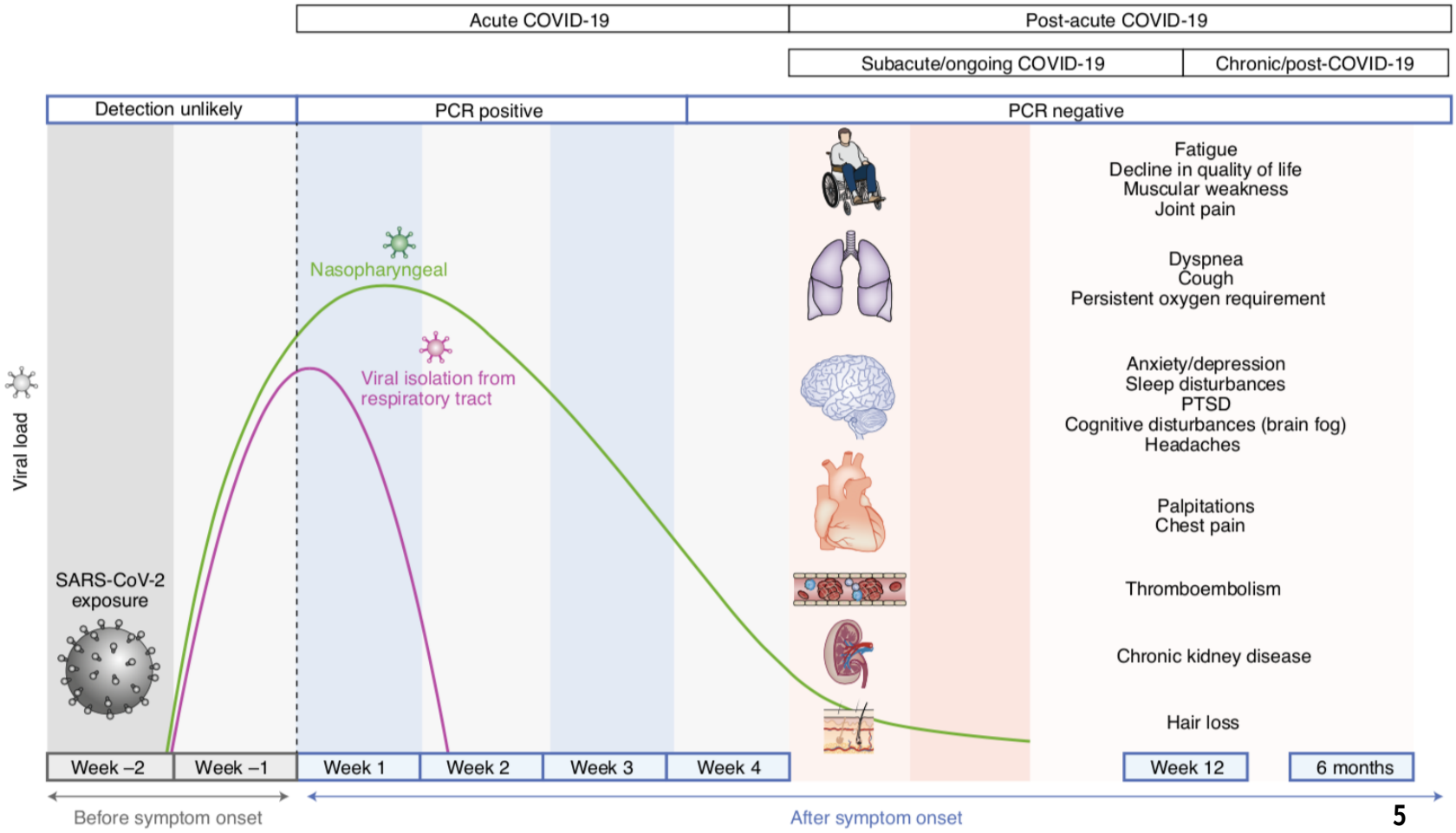
nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

Post-acute COVID-19 syndrome

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

- **COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations.**
- **post-acute COVID-19 : a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms**



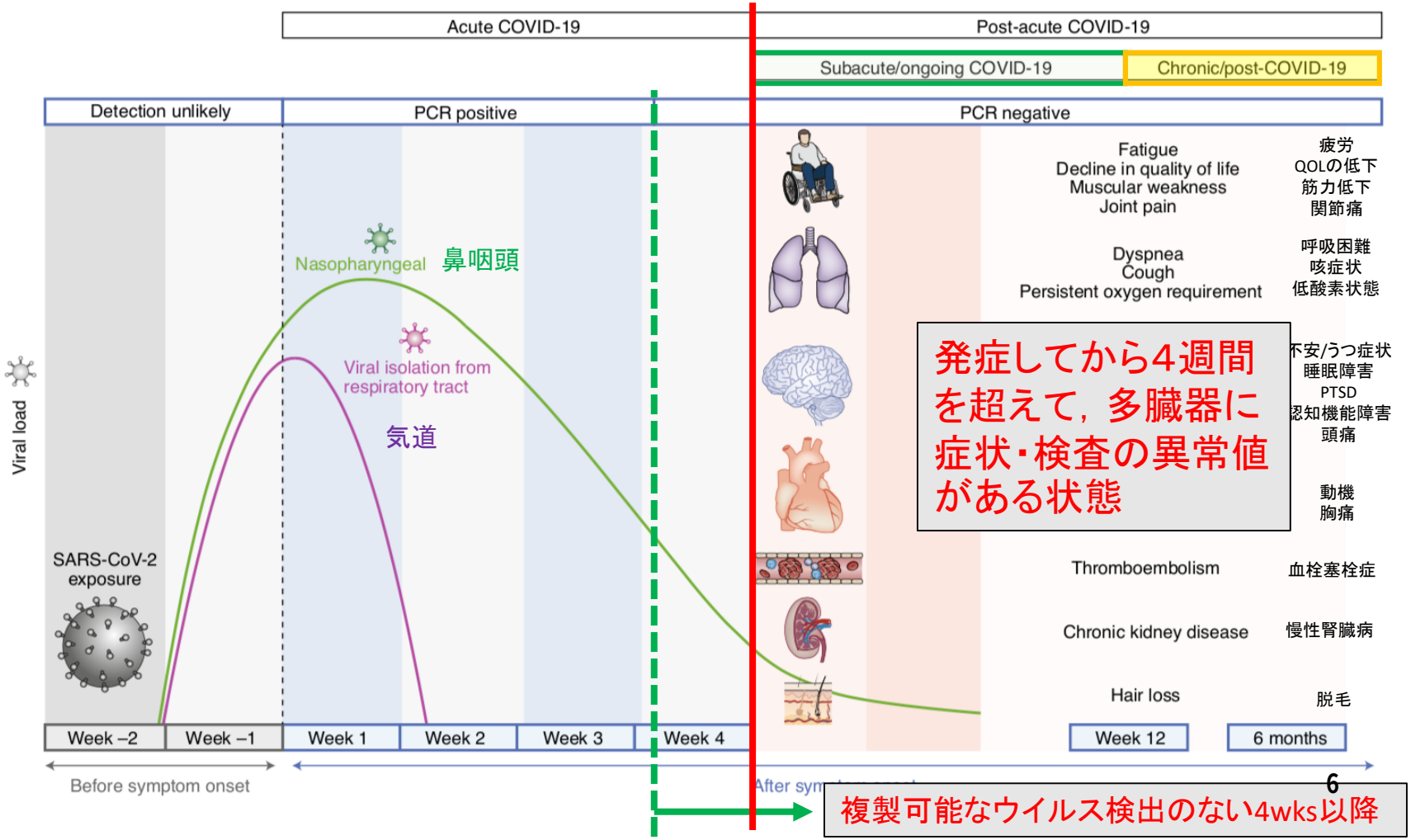
nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

急性COVID-19 後遺症・症候群

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

- COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations.
- post-acute COVID-19 : a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms



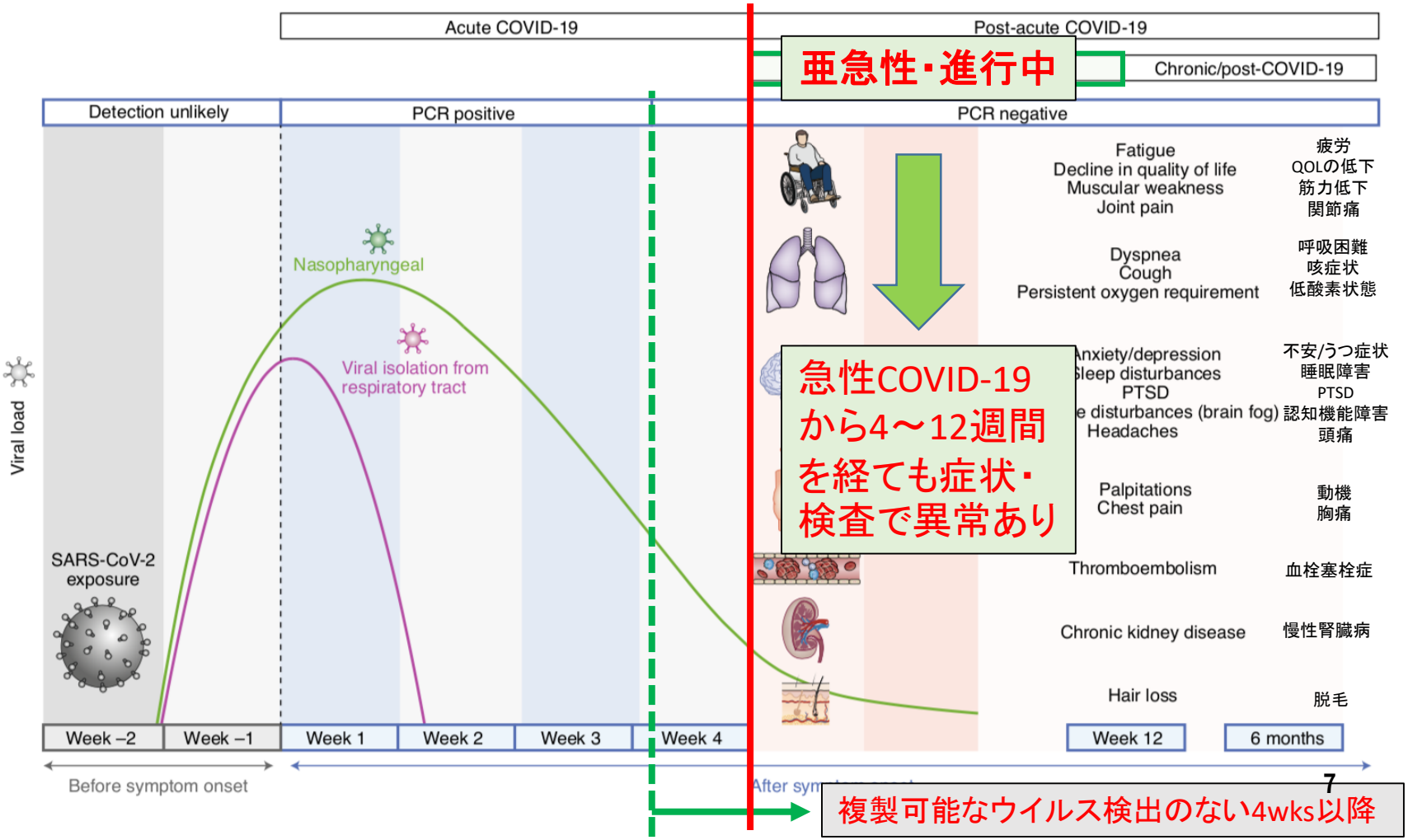
nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

急性COVID-19 後遺症・症候群

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

- COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations.
- post-acute COVID-19 : a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms



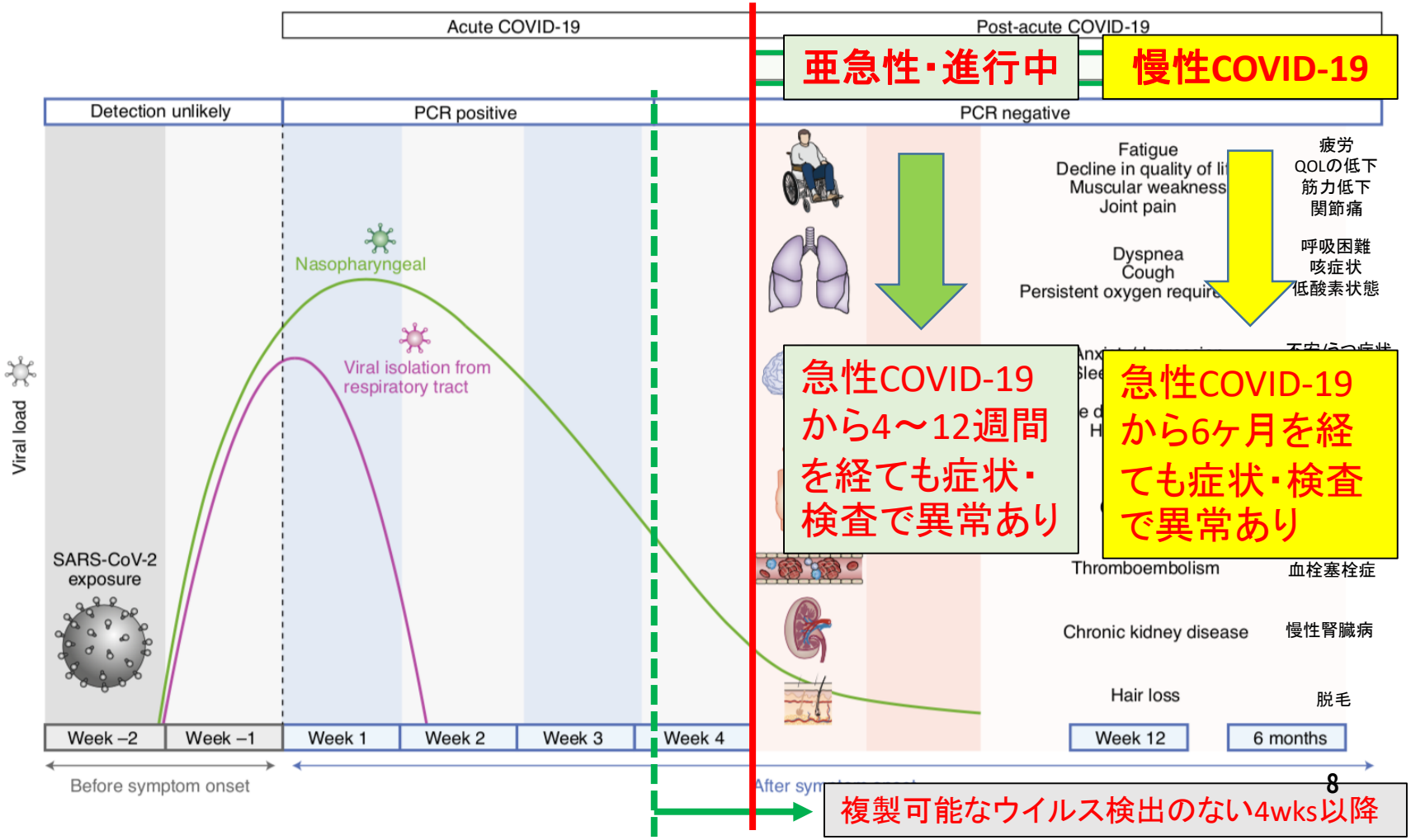
nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

急性COVID-19 後遺症・症候群

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

- COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations.
- post-acute COVID-19 : a syndrome characterized by persistent symptoms and/or delayed or long-term complications beyond 4 weeks from the onset of symptoms



nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

Post-acute COVID-19 syndrome

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Table 1 | Findings from clinical studies on the prevalence of post-acute COVID-19 syndrome

	Carfì et al.[3]	Halpin et al.[24]	Carvalho-Schneider et al.[21]	Chopra et al.[20]	Arnold et al.[22]	Moreno-Pérez et al.[23]	Moreno-Pérez et al.[23]	Garrigues et al.[26]	Huang et al.[5]
Site	Italy	United Kingdom	France	United States	United Kingdom	Spain	Spain	France	China
Number of participants	143	100	150	488	110	277	277	120	1,733
Follow-up									
Duration	2 months post-symptom onset	1–2 months post-discharge	2 months post-symptom onset	2 months post-discharge	3 months post-symptom onset	2–3 months post-COVID-19 onset	4 months post-COVID-19 onset	3–4 months post-admission	6 months post-symptom onset
Mode of follow-up evaluation	In person	Telephone survey	Telephone survey	Telephone survey	In person	In person	In person	Telephone survey	In person
Baseline characteristics									
Age (years)	Mean (s.d.) = 56.5 (14.6)	Median (ward/ICU) = 70.5/58.5	Mean (s.d.) = 45 (15)	NR	Median (IQR) = 60 (44–76)	Median (IQR) = 56 (42–67.5)	Median (IQR) = 56 (42–67.5)	Mean (s.d.) = 63.2 (15.7)	Median (IQR) = 57 (47–65)
Female (%)	37.1	46	56	NR	38.2	47.3	47.3	37.5	48
Acute COVID-19 features									
Oxygen therapy requirement (%)	53.8	78			75.4				75
Non-invasive ventilation (%)	14.7	30							6
Invasive ventilation (%)	4.9	1							1
ICU care (%)	12.6	32	0		16.4	8.7	8.7	20	4
Post-acute COVID-19									
≥1 symptom (%)	87.4		66	32.6	74	50.9			76
≥3 symptoms (%)	55.2								
General sequelae									
Fatigue (%)	53.1	64	40		39	34.8		55	63
Joint pain (%)	27.3		16.3		4.5	19.6			9
Muscular pain (%)						19.6			2
Fever (%)	0		0		0.9	0			0.1
Respiratory sequelae									
Dyspnea (%)	43.4	40	30	22.9	39	34.4	11.1	41.7	23
Cough (%)	~15			15.4	11.8	21.3	2.1	16.7	
Cardiovascular sequelae									
Chest pain (%)	21.7		13.1		12.7			10.8	5
Palpitations (%)			10.9						9
Neuropsychiatric sequelae									
Anxiety/depression (%)									23
Sleep disturbances (%)					24			30.8	26
PTSD (%)		31							
Loss of taste/smell (%)	~15		22.7	13.1	11.8	21.4		10.8–13.3	7–11
Headache (%)	~10				1.8	17.8	5.4		2
Gastrointestinal sequelae									
Diarrhea (%)					0.9	10.5			~5
Dermatologic sequelae									
Hair loss (%)								20	22
Skin rash (%)									3
Quality of life									
Scale	EuroQol visual analog scale	EQ-5D-5L			SF-36	EuroQol visual analog scale		EQ-5D-5L	EuroQol visual analog scale
Decline (percentage of patients reporting or yes/no)	44.1	Yes			Yes	Yes		Yes	Yes

IQR, interquartile range; NR, not reported; s.d., standard deviation; SF-36, 36-Item Short Form Survey.

倦怠感
関節痛

呼吸困難
咳症状
胸部痛

嗅覚・味覚
異常

QOL低下

nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

Post-acute COVID-19 syndrome

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Box 1 | Summary of post-acute COVID-19 by organ system

Pulmonary
- Dyspnea, decreased exercise capacity and hypoxia are commonly persistent symptoms and signs
- Reduced diffusion capacity, restrictive pulmonary physiology, and ground-glass opacities and fibrotic changes on imaging have been noted at follow-up of COVID-19 survivors
- Assessment of progression or recovery of pulmonary disease and function may include home pulse oximetry, 6MWTs, PFTs, high-resolution computed tomography of the chest and computed tomography pulmonary angiogram as clinically appropriate

Hematologic
- Thromboembolic events have been noted to be <5% in post-acute COVID-19 in retrospective studies
- The duration of the hyperinflammatory state induced by infection with SARS-CoV-2 is unknown
- Direct oral anticoagulants and low-molecular-weight heparin may be considered for extended thromboprophylaxis after risk–benefit discussion in patients with predisposing risk factors for immobility, persistently elevated D-dimer levels (greater than twice the upper limit of normal) and other high-risk comorbidities such as cancer

Cardiovascular
- Persistent symptoms may include palpitations, dyspnea and chest pain
- Long-term sequelae may include increased cardiometabolic demand, myocardial fibrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction
- Patients with cardiovascular complications during acute infection or those experiencing persistent cardiac symptoms may be monitored with serial clinical, echocardiogram and electrocardiogram follow-up

Neuropsychiatric
- Persistent abnormalities may include fatigue, myalgia, headache, dysautonomia and cognitive impairment (brain fog)
- Anxiety, depression, sleep disturbances and PTSD have been reported in 30–40% of COVID-19 survivors, similar to survivors of other pathogenic coronaviruses
- The pathophysiology of neuropsychiatric complications is mechanistically diverse and entails immune dysregulation, inflammation, microvascular thrombosis, iatrogenic effects of medications and psychosocial impacts of infection

Renal
- Resolution of AKI during acute COVID-19 occurs in the majority of patients; however, reduced eGFR has been reported at 6 months follow-up
- COVAN may be the predominant pattern of renal injury in individuals of African descent
- COVID-19 survivors with persistent impaired renal function may benefit from early and close follow-up in AKI survivor clinics

Endocrine
- Endocrine sequelae may include new or worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralization
- Patients with newly diagnosed diabetes in the absence of traditional risk factors for type 2 diabetes, suspected hypothalamic–pituitary–adrenal axis suppression or hyperthyroidism should undergo the appropriate laboratory testing and should be referred to endocrinology

Gastrointestinal and hepatobiliary
- Prolonged viral fecal shedding can occur in COVID-19 even after negative nasopharyngeal swab testing
- COVID-19 has the potential to alter the gut microbiome, including enrichment of opportunistic organisms and depletion of beneficial commensals

Dermatologic
- Hair loss is the predominant symptom and has been reported in approximately 20% of COVID-19 survivors

MIS-C
- Diagnostic criteria: <21 years old with fever, elevated inflammatory markers, multiple organ dysfunction, current or recent SARS-CoV-2 infection and exclusion of other plausible diagnoses
- Typically affects children >7 years and disproportionately of African, Afro-Caribbean or Hispanic origin
- Cardiovascular (coronary artery aneurysm) and neurologic (headache, encephalopathy, stroke and seizure) complications can occur

Multisystem inflammatory syndrome in children (MIS-C)

nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

Post-acute COVID-19 syndrome

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Box 1 | Summary of post-acute COVID-19 by organ system

Pulmonary
- Dyspnea, decreased exercise capacity and hypoxia are commonly persistent symptoms and signs
- Reduced diffusion capacity, restrictive pulmonary physiology, and ground-glass opacities and fibrotic changes on imaging have been noted at follow-up of COVID-19 survivors
- Assessment of progression or recovery of pulmonary disease and function may include home pulse oximetry, 6MWTs, PFTs, high-resolution computed tomography of the chest and computed tomography pulmonary angiogram as clinically appropriate

Hematologic
- Thromboembolic events have been noted to be <5% in post-acute COVID-19 in retrospective studies
- The duration of the hyperinflammatory state induced by infection with SARS-CoV-2 is unknown
- Direct oral anticoagulants and low-molecular-weight heparin may be considered for extended thromboprophylaxis after risk–benefit discussion in patients with predisposing risk factors for immobility, persistently elevated D-dimer levels (greater than twice the upper limit of normal) and other high-risk comorbidities such as cancer

Cardiovascular
- Persistent symptoms may include palpitations, dyspnea and chest pain
- Long-term sequelae may include increased cardiometabolic demand, myocardial fibrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction
- Patients with cardiovascular complications during acute infection or those experiencing persistent cardiac symptoms may be monitored with serial clinical, echocardiogram and electrocardiogram follow-up

Neuropsychiatric
- Persistent abnormalities may include fatigue, myalgia, headache, dysautonomia and cognitive impairment (brain fog)
- Anxiety, depression, sleep disturbances and PTSD have been reported in 30–40% of COVID-19 survivors, similar to survivors of other pathogenic coronaviruses
- The pathophysiology of neuropsychiatric complications is mechanistically diverse and entails immune dysregulation, inflammation, microvascular thrombosis, iatrogenic effects of medications and psychosocial impacts of infection

Renal
- Resolution of AKI during acute COVID-19 occurs in the majority of patients; however, reduced eGFR has been reported at 6 months follow-up
- COVAN may be the predominant pattern of renal injury in individuals of African descent
- COVID-19 survivors with persistent impaired renal function may benefit from early and close follow-up in AKI survivor clinics

Endocrine
- Endocrine sequelae may include new or worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralization
- Patients with newly diagnosed diabetes in the absence of traditional risk factors for type 2 diabetes, suspected hypothalamic–pituitary–adrenal axis suppression or hyperthyroidism should undergo the appropriate laboratory testing and should be referred to endocrinology

Gastrointestinal and hepatobiliary
- Prolonged viral fecal shedding can occur in COVID-19 even after negative nasopharyngeal swab testing
- COVID-19 has the potential to alter the gut microbiome, including enrichment of opportunistic organisms and depletion of beneficial commensals

Dermatologic
- Hair loss is the predominant symptom and has been reported in approximately 20% of COVID-19 survivors

MIS-C
- Diagnostic criteria: <21 years old with fever, elevated inflammatory markers, multiple organ dysfunction, current or recent SARS-CoV-2 infection and exclusion of other plausible diagnoses
- Typically affects children >7 years and disproportionately of African, Afro-Caribbean or Hispanic origin
- Cardiovascular (coronary artery aneurysm) and neurologic (headache, encephalopathy, stroke and seizure) complications can occur

- 呼吸困難，運動　能力の低下，低酸素
- 肺拡散機能の低下，スリガラス陰影，線維症の兆候あり
- 6分間平地歩行テスト，PFT，胸部CTなどで確認

- 5%以下に血栓塞栓症
- 過剰炎症の持続期間不明
- 凝固能が高くD-dimer値が2倍以上の場合，経口薬，Heparinが推奨

- 動悸，呼吸困難，胸痛
- 心筋の繊維化，不整脈，頻脈，血圧異常の後遺症
- 心エコー，心電図検査によるモニター

- 倦怠感，筋肉痛，頭痛，不眠，認知機能異常
- 不安，鬱，睡眠障害，PTSDなど30-40%に生じる
- 免疫学的な異常，炎症，血栓，投薬による可能性

- 急性腎機能障害が6ヶ月持続する例もあり
- コロナ関連腎症
- 初期に腎機能があった日は継続的にフォローアップ

- 内分泌関連後遺症，糖尿病の人は悪化の傾向，甲状腺炎，骨脱灰化
- 新規に糖尿病の診断を受けた人は，視床下部-下垂体ー副腎軸の異常，甲状腺機能亢進の可能性

- 鼻咽頭swabで陰性でも糞便中で陽性の例あり
- 腸内細菌叢の変化

- 20%に脱毛

Multisystem inflammatory syndrome in children (MIS-C)
- 21歳以下で発熱・炎症性マーカーの増加，多臓器疾患
- 7歳以下の影響大，人種による偏り
- 新機能・神経系の合併症

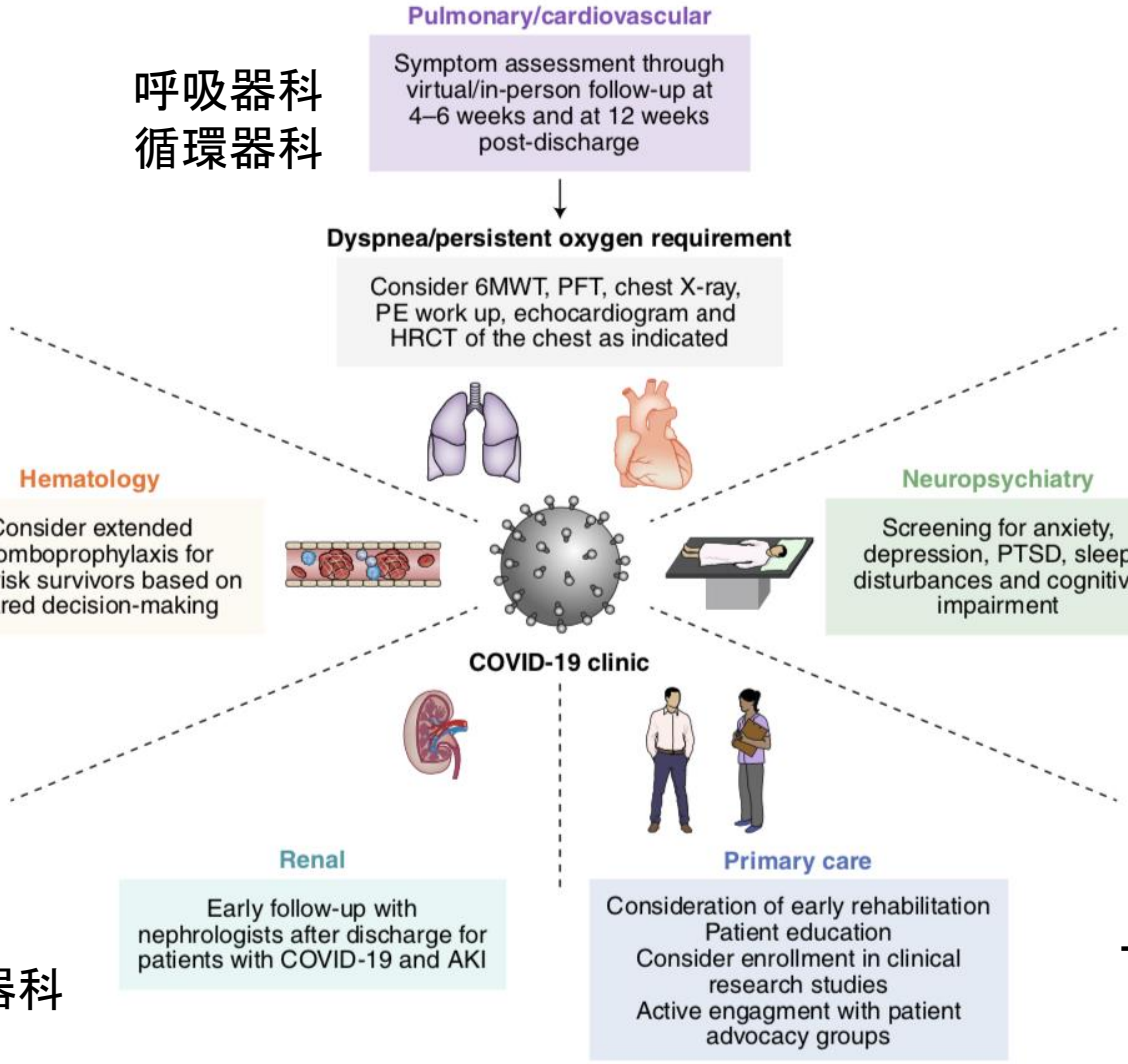
nature medicine
FOCUS | REVIEW ARTICLE
https://doi.org/10.1038/s41591-021-01283-z

Post-acute COVID-19 syndrome

Ani Nalbandian[1,24], Kartik Sehgal[2,3,4,24]✉, Aakriti Gupta[1,5,6], Mahesh V. Madhavan[1,5], Claire McGroder[7], Jacob S. Stevens[8], Joshua R. Cook[9], Anna S. Nordvig[10], Daniel Shalev[11], Tejasav S. Sehrawat[12], Neha Ahluwalia[13], Behnood Bikdeli[4,5,6,14], Donald Dietz[15], Caroline Der-Nigoghossian[16], Nadia Liyanage-Don[17], Gregg F. Rosner[1], Elana J. Bernstein[18], Sumit Mohan[8], Akinpelumi A. Beckley[19], David S. Seres[20], Toni K. Choueiri[2,3,4], Nir Uriel[1], John C. Ausiello[9], Domenico Accili[9], Daniel E. Freedberg[21], Matthew Baldwin[7], Allan Schwartz[1], Daniel Brodie[7], Christine Kim Garcia[7], Mitchell S. V. Elkind[10,22], Jean M. Connors[4,23], John P. Bilezikian[9], Donald W. Landry[8] and Elaine Y. Wan[1]✉

NATURE MEDICINE | VOL 27 | APRIL 2021 | 601–615 | www.nature.com/naturemedicine

Interdisciplinary management in COVID-19 clinics



呼吸器科
循環器科
血液内科
精神科
泌尿器科
一次診療

様々な専門分野の協力によるacute COVID-19ケアが必要