

COVID-19 u. kardiale Komplikationen

Myokarditis – Arrhythmien – Impfassozierte Probleme – kardiozirkulatorische Manifestationen von Long-Covid (= Post-acute Sequelae of SARS-CoV2; PASC), Fatigue /ME-CFS und Dysautonomien /POTS

Prof. Dr. med. Thomas Klingenheben



Conflict of interest statement

Between 2018 and 2022 Thomas Klingenheben has received speaker honoraria from the following companies:

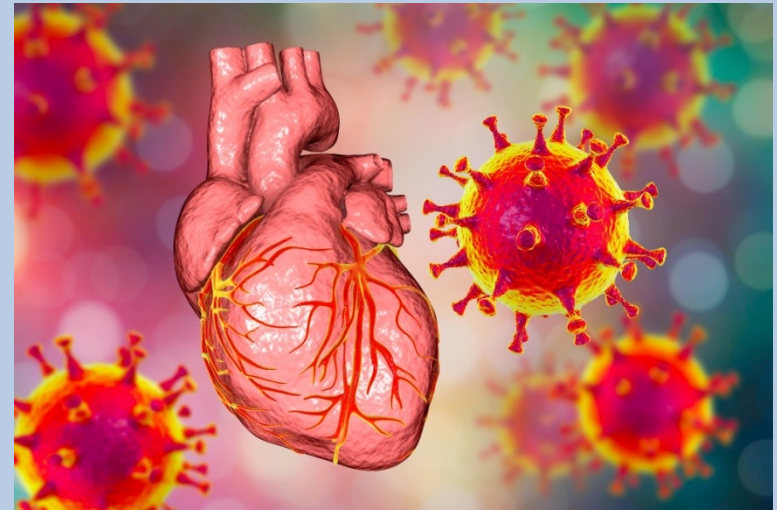
*Astra-Zeneca; BAYER vital; Berlin-Chemie; Boehringer Ingelheim;
Daiichi-Sankyo; Pfizer; Sanofi; Servier*



Covid-19 und Cardiovasculäres System

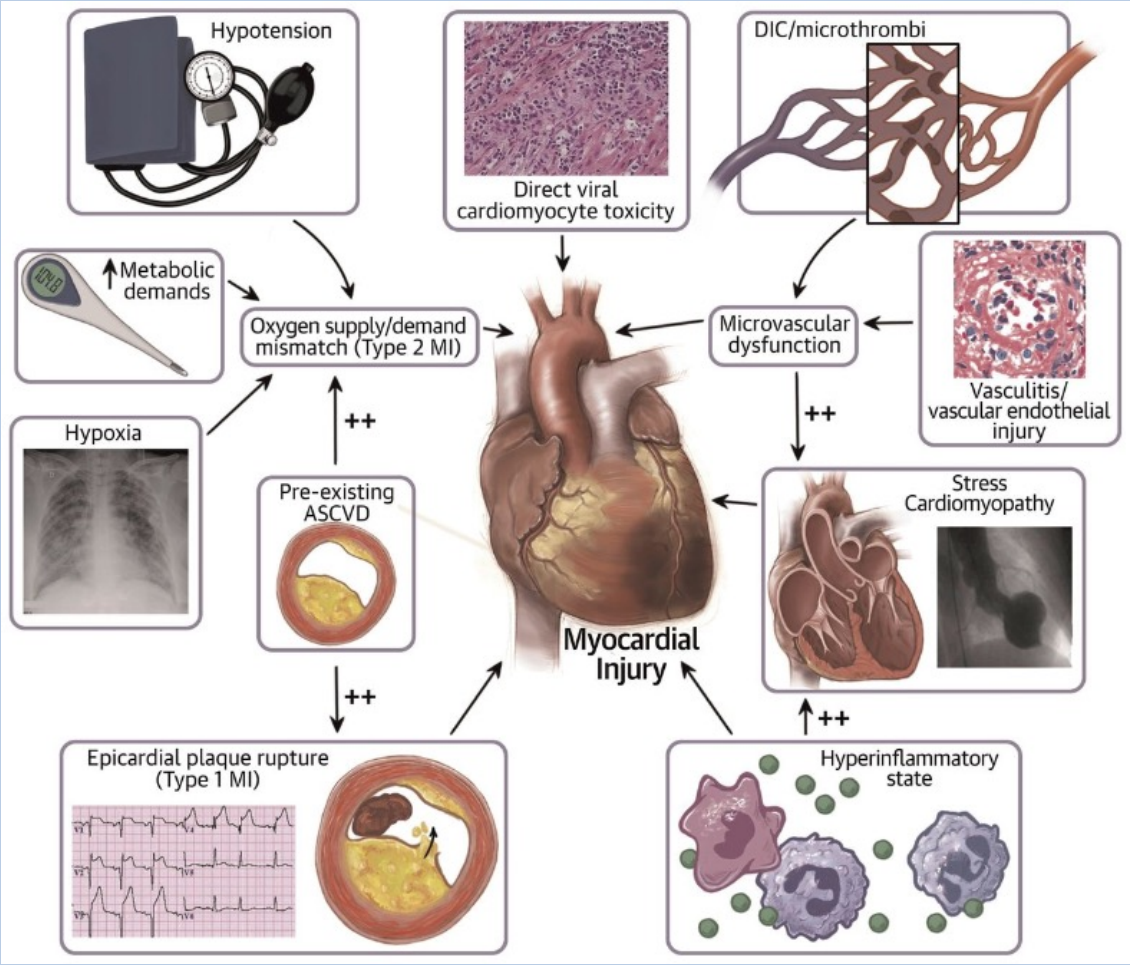
Welche Manifestationen ?

- *Myokarditis*
- *Herzinsuffizienz*
- *Rhythmusstörungen*
- *Autonome Funktionsstörungen*
(u.a. POTS, Fatigue, ...)
- *Covid-assoziiert*
- *„Long- (post) Covid“ – assoziiert*
- *Impf-assoziiert*



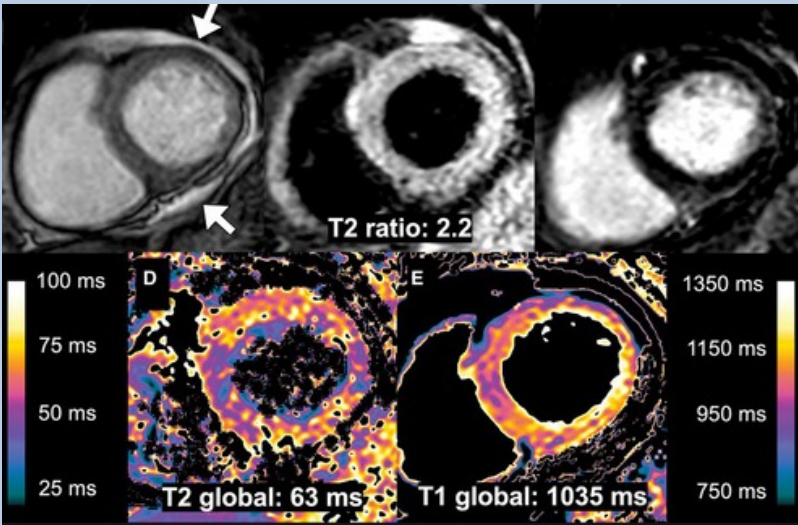
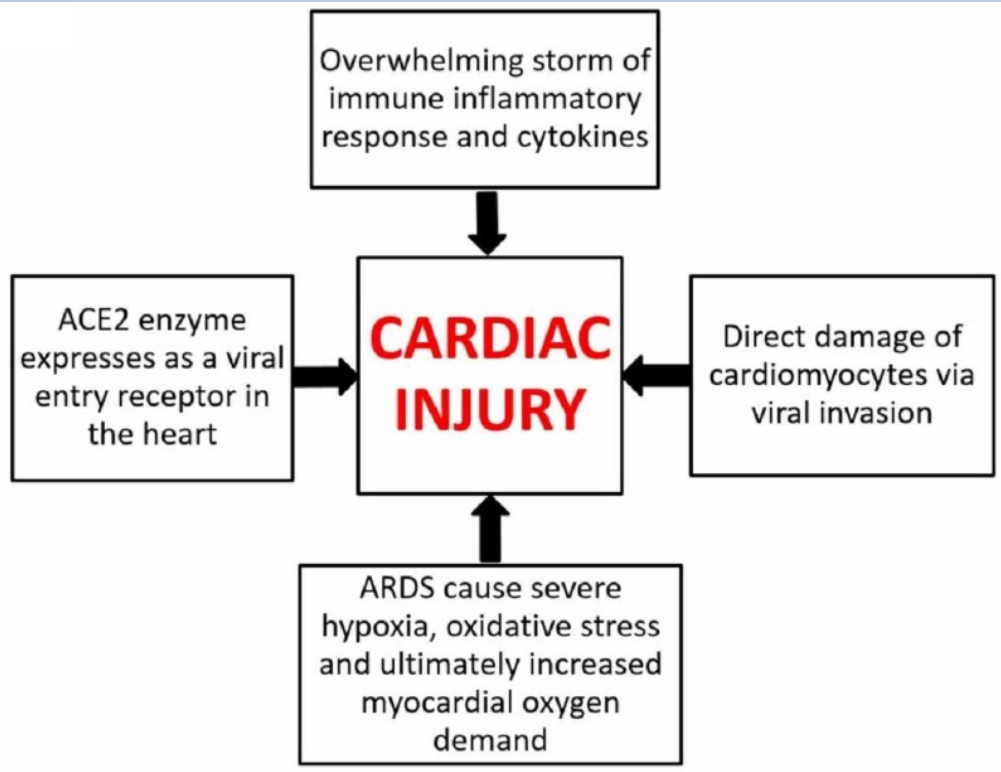
Covid-19 und Cardiovasculäres System

Kardiale Beteiligung bei Covid-19



Covid-19 und Cardiovasculäres System

Wie kommt es zum Myokardschaden



Covid-19 und Cardiovasculäres System

Prognostische Determinanten bei stationären Patienten

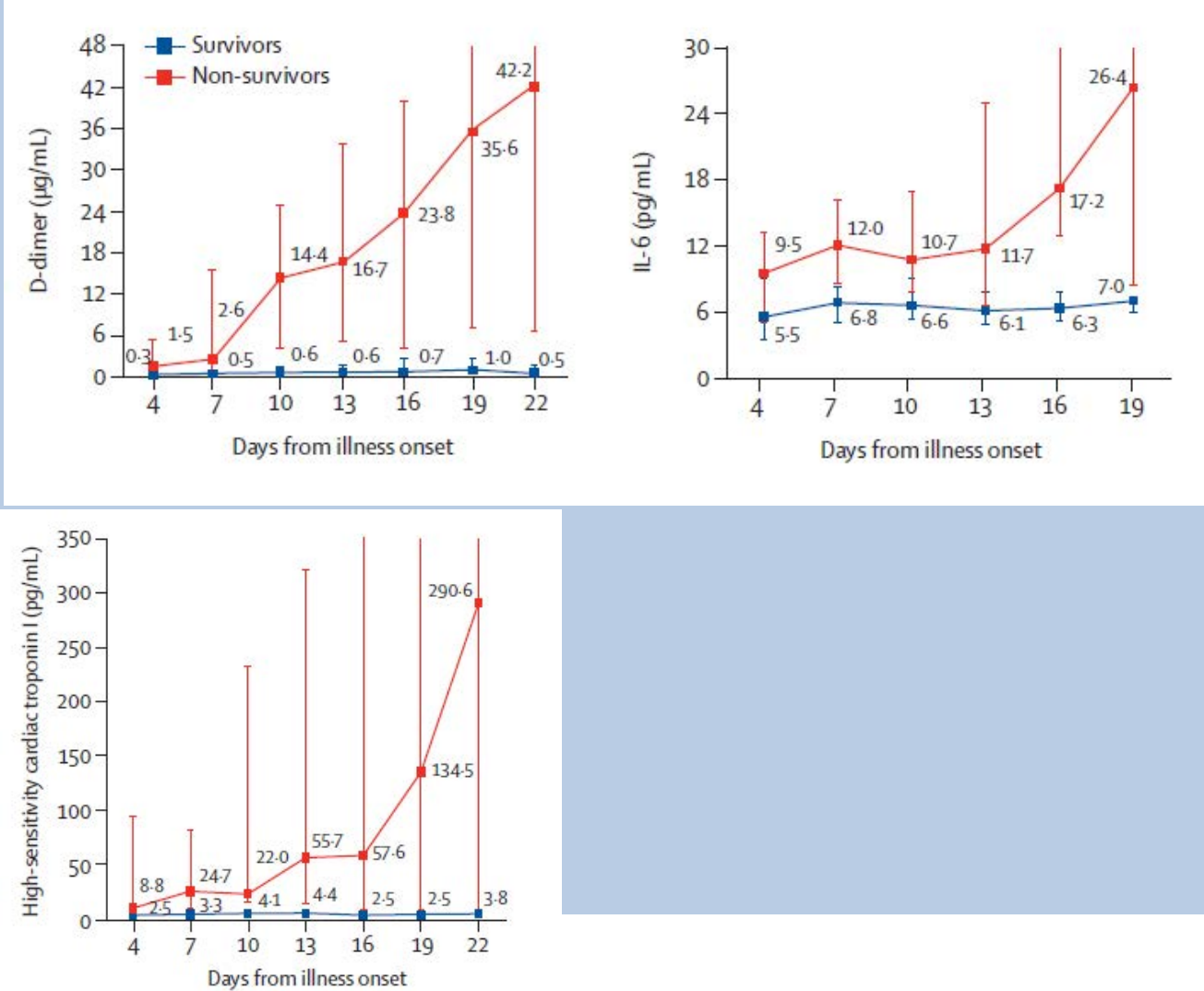
	Total (n=191)	Non-survivor (n=54)	Survivor (n=137)	pvalue
Outcomes				
Sepsis	112 (59%)	54 (100%)	58 (42%)	<0.0001
Respiratory failure	103 (54%)	53 (98%)	50 (36%)	<0.0001
ARDS	59 (31%)	50 (93%)	9 (7%)	<0.0001
Heart failure	44 (23%)	28 (52%)	16 (12%)	<0.0001
Septic shock	38 (20%)	38 (70%)	0	<0.0001
Coagulopathy	37 (19%)	27 (50%)	10 (7%)	<0.0001
Acute cardiac injury	33 (17%)	32 (59%)	1 (1%)	<0.0001
Acute kidney injury	28 (15%)	27 (50%)	1 (1%)	<0.0001
Secondary infection	28 (15%)	27 (50%)	1 (1%)	<0.0001
Hypoproteinaemia	22 (12%)	20 (37%)	2 (1%)	<0.0001
Acidosis	17 (9%)	16 (30%)	1 (1%)	<0.0001
ICU admission	50 (26%)	39 (72%)	11 (8%)	<0.0001

- Troponin-erhöhung 15-20 %
- Herzinsuffizienz 20-25%



Covid-19 und Cardiovasculäres System

Biomarker und Prognose

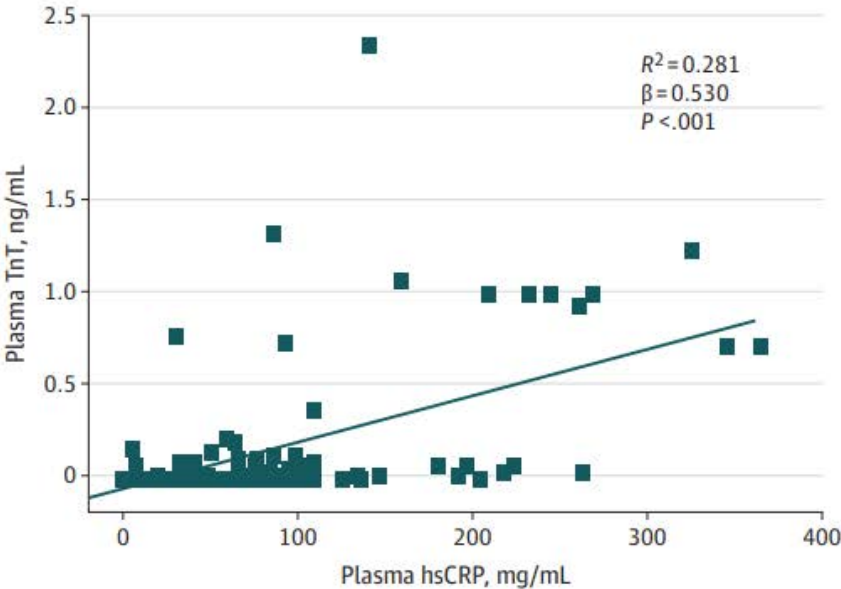


Covid-19 und Cardiovasculäres System

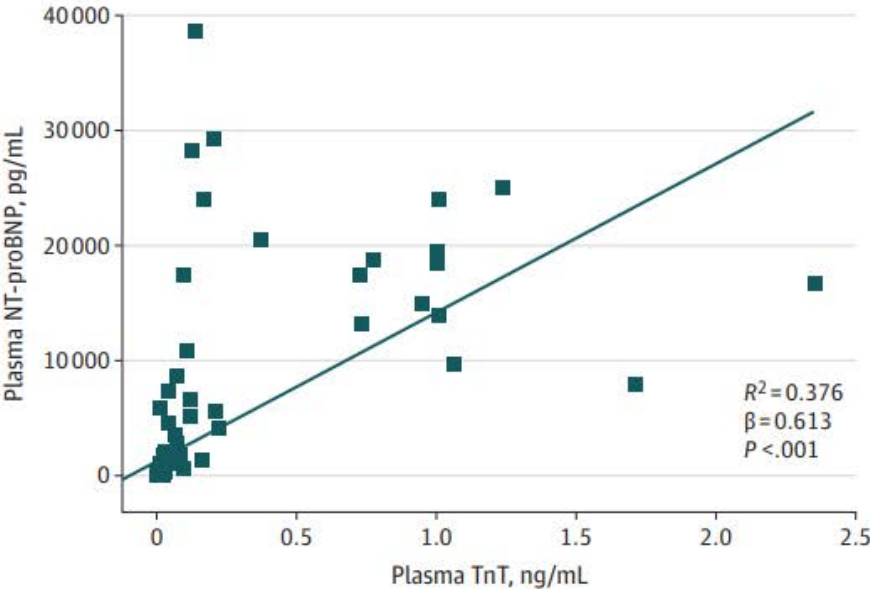
Korrelation v. Biomarkern bei Herzkranken mit Covid-19

Correlation Between Plasma TnT and NT-proBNP With hsCRP

A Plasma TnT (total patients)



B Plasma NT-proBNP (total patients)



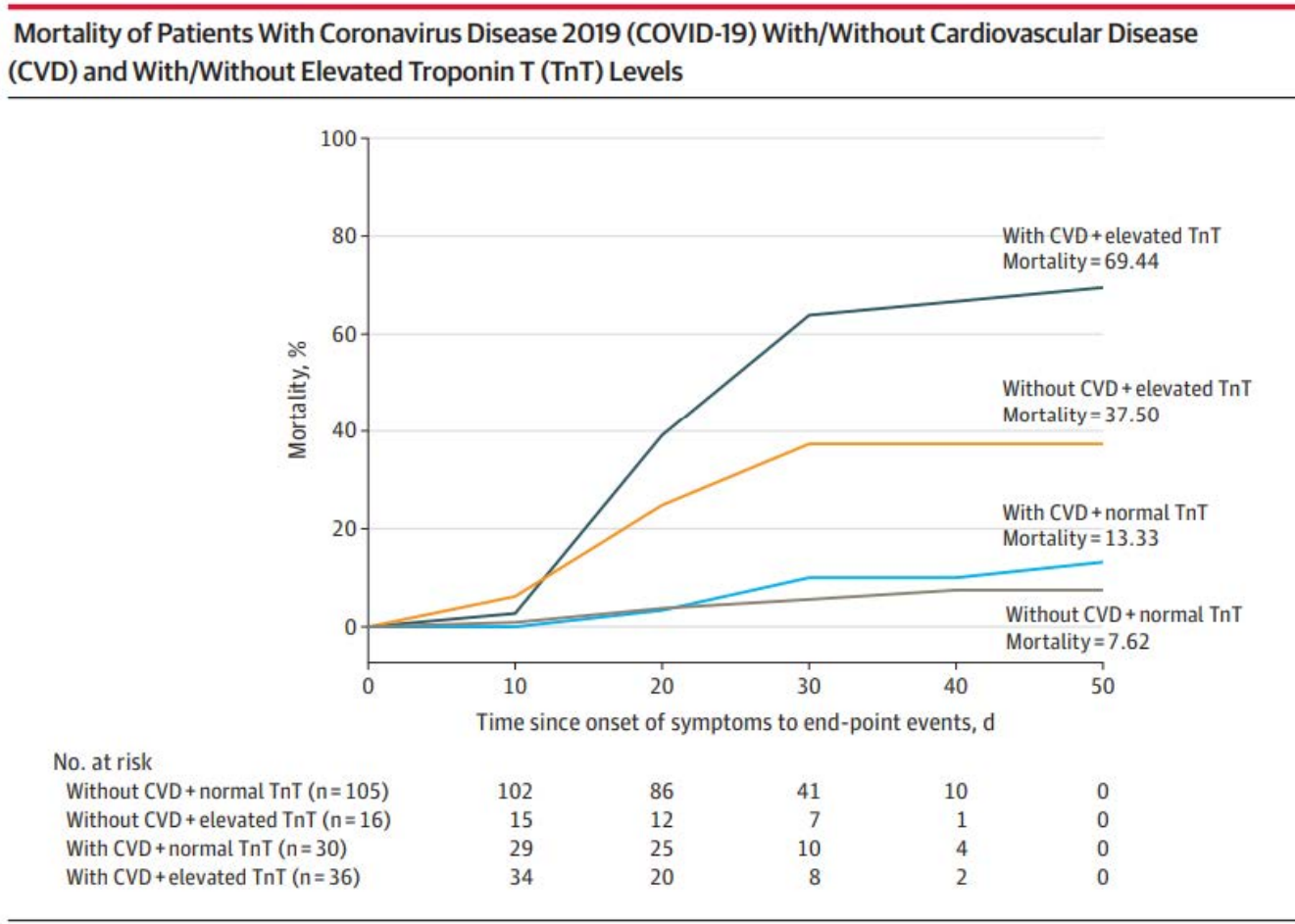
Plasma troponin T (TnT), high-sensitivity C-reactive protein levels (hsCRP), and N-terminal pro-brain natriuretic peptide (NT-pro BNP) collected on admission.

- Troponin-T 54% vs 13% bei Herzgesunden



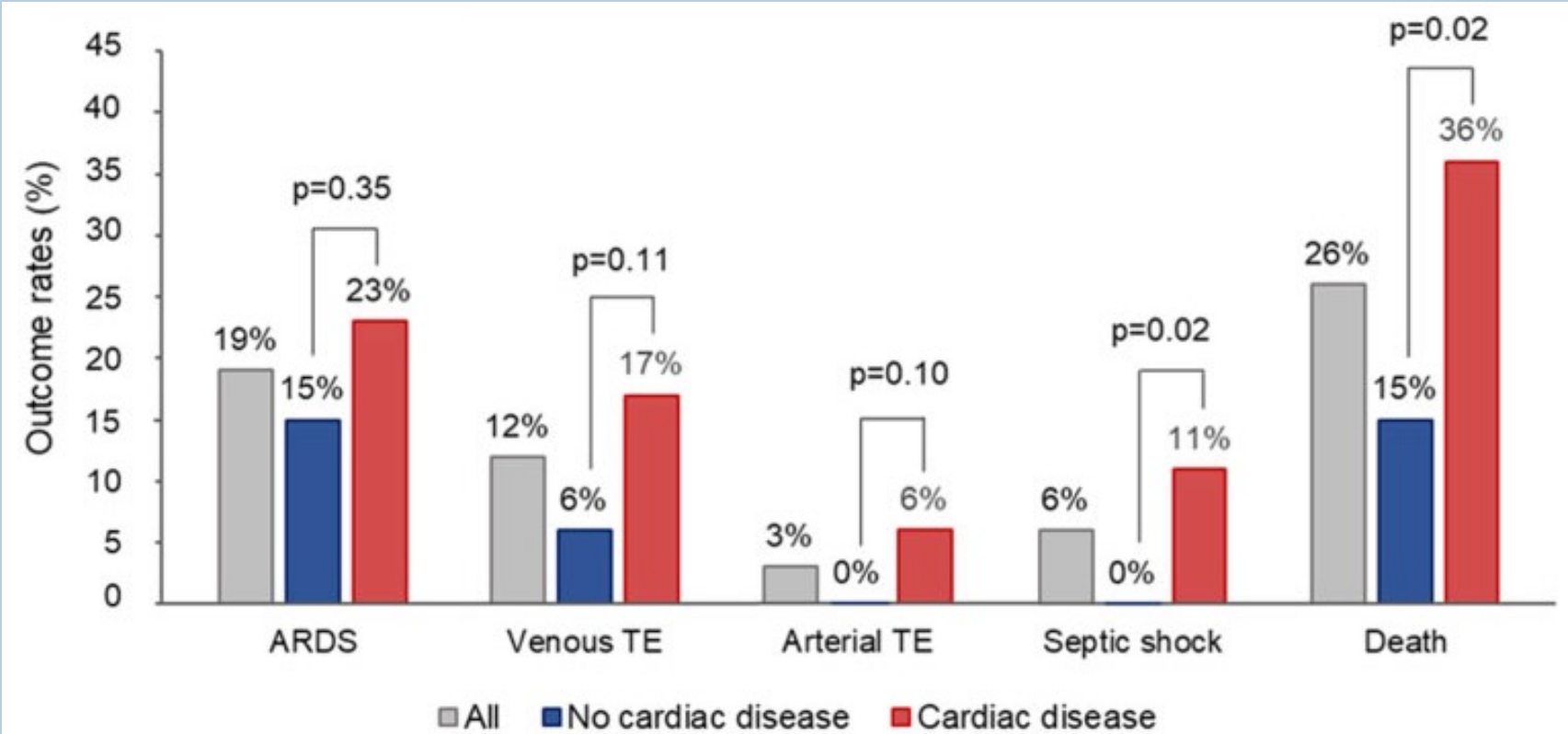
Covid-19 und Cardiovasculäres System

Mortalität in Abh von CVD u. Troponin-I



Covid-19 und Cardiovasculäres System

Vorbestehende Herzerkrankung und Outcome



Covid-19 und Cardiovasculäres System

Kardiovaskuläre Manifestationen

Myokarditis

COVID-assoziierte Myocarditis

Pathophysiologie

- **Virusmyokarditis (allgemein):**
- **Kombination aus direkter Zellschädigung und T-Lymphozyten vermittelter Zytotoxizität**
- **Zytokin-Sturm (IL-6 vermittelt) => weitere inflamm. Mediatoren**
- **SARS-CoV-2 Myokarditis:**
- **Eintritt des Virus in Kardiomyocyten via ACE-2-Rezeptor; dazu ist eine Spaltung des Spike-Proteins an S1/S2 und S2' notwendig, um die Bindung an ACE-2 zu ermöglichen.**

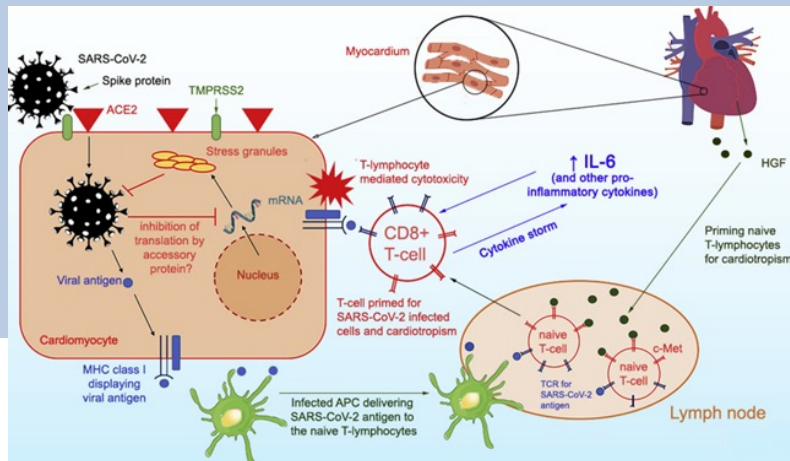


TABLE 1 Diagnostic Tests and Potential Findings in Patients With Acute Myocarditis*

ECG, Holter, or stress test
AV block I-III, bundle branch block, sinus arrest
Extrasystoles
Supraventricular tachycardia, atrial fibrillation
Ventricular tachycardia, ventricular fibrillation, asystole
ST-segment and T-wave changes (ST-segment elevation, T-wave inversion)
Intraventricular conduction delay
New Q waves
Low voltage
Seromarkers for myocardial necrosis
Troponin elevation
Creatine kinase elevation
Cardiac imaging
Echocardiography/angiography
Regional or global systolic or diastolic dysfunction, with or without LV dilatation
Increased wall thickness
Pericardial effusion
Intracavitary thrombi
CMR
Edema
Hyperemia or capillary leak (early gadolinium enhancement)
Irreversible injury (necrosis, scar; late gadolinium enhancement)
Regional or global systolic or diastolic dysfunction, with or without LV dilatation
Increased wall thickness
Pericardial effusion
Intracavitary thrombi

*Clinically suspected myocarditis if ≥ 1 clinical presentation and ≥ 1 diagnostic criteria from different categories, in the absence of: 1) angiographically detectable coronary artery disease (coronary stenosis $\geq 50\%$); 2) known pre-existing cardiovascular disease or extracardiac causes that could explain the syndrome (e.g., valve disease, congenital heart disease, hyperthyroidism). Suspicion is higher with higher number of fulfilled criteria. If the patient is asymptomatic, ≥ 2 diagnostic criteria should be met. Modified with permission from Caforio et al. (12).

AV = atrioventricular; CMR = cardiovascular magnetic resonance; ECG = electrocardiogram; LV = left ventricular.

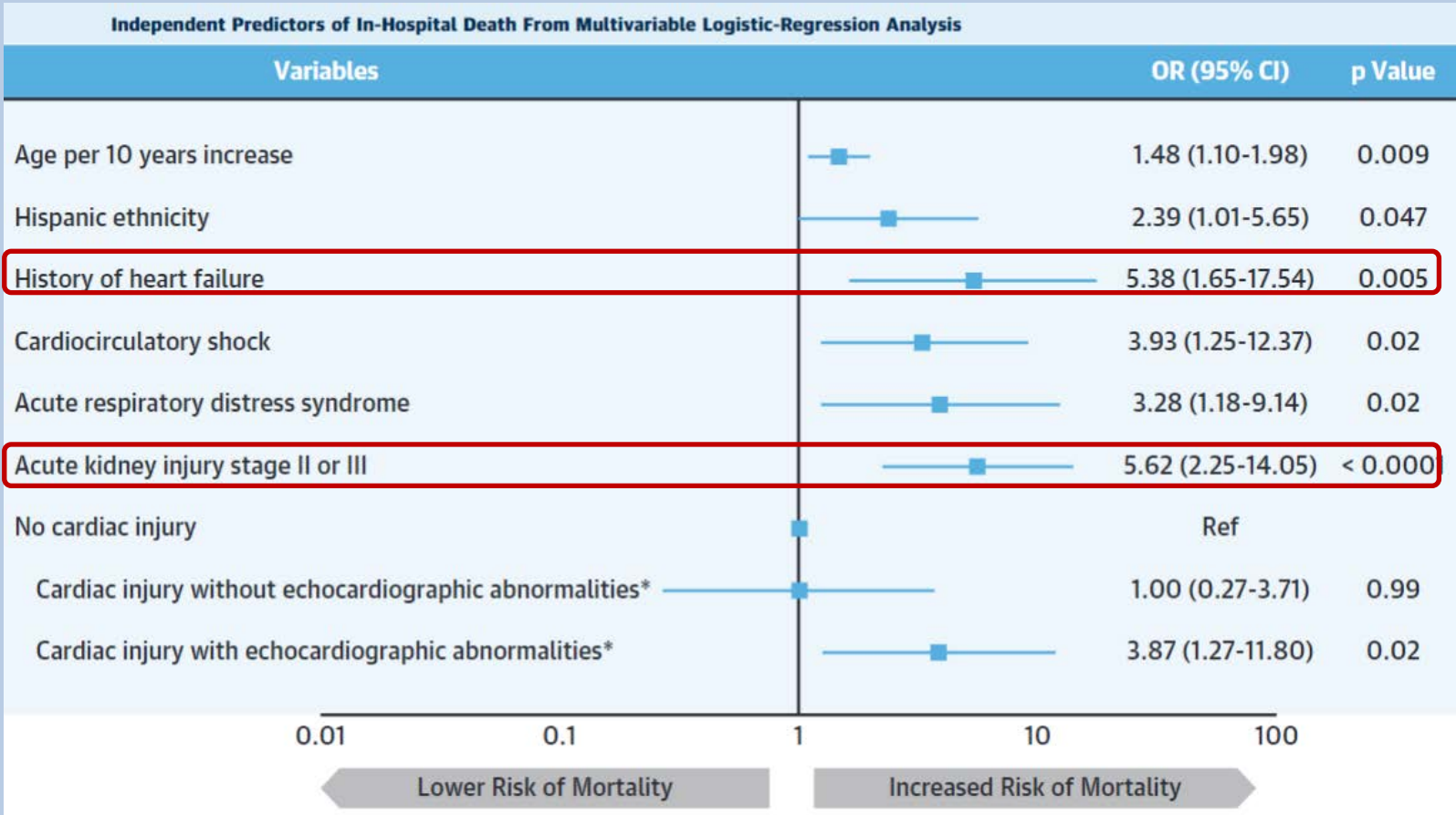
MYOKARDITIS

Diagnostische Kriterien



COVID-assoziierte „myocardial injury“

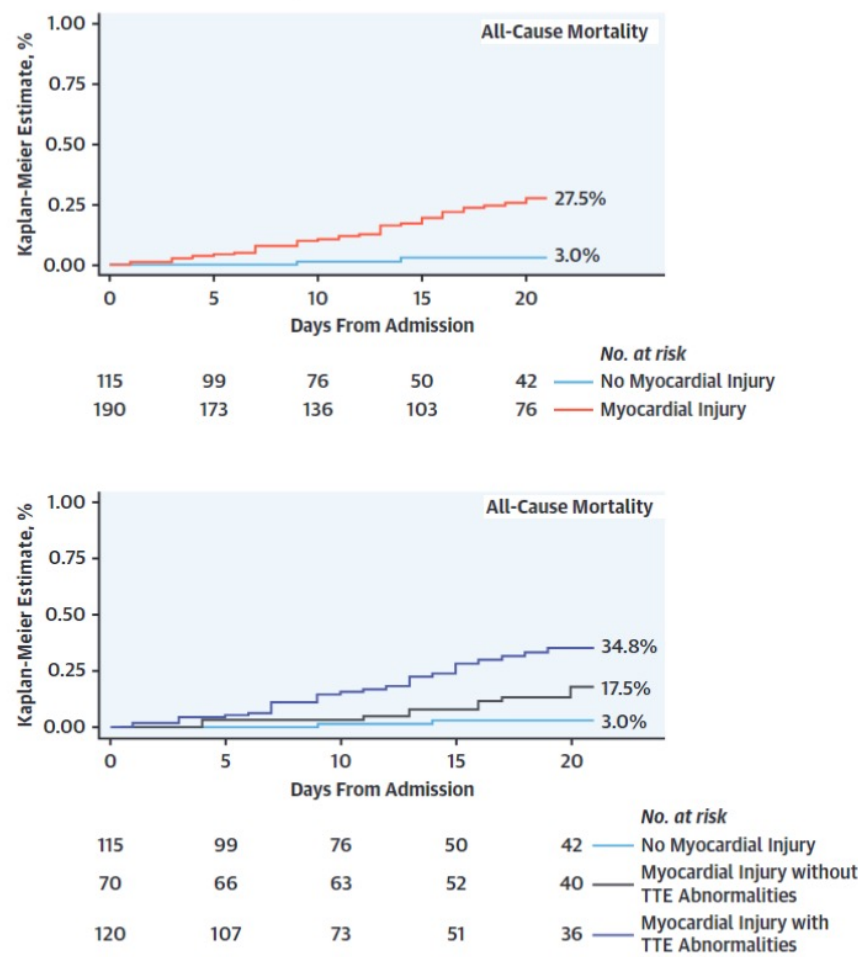
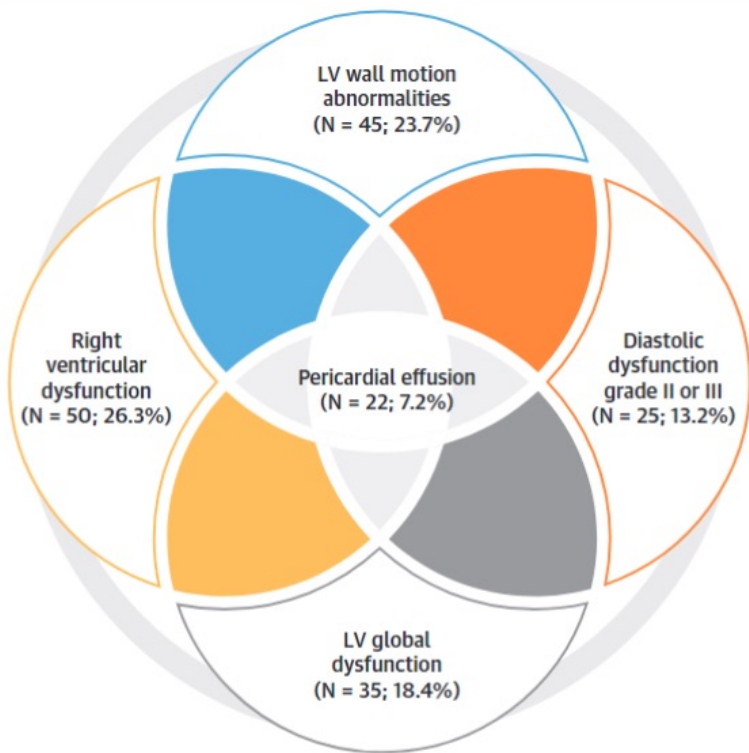
Prognostische Determinanten



COVID-assoziierte „myocardial injury“

Echokardiographie und Prognose bei hospitalisierten Ptn (N=305)

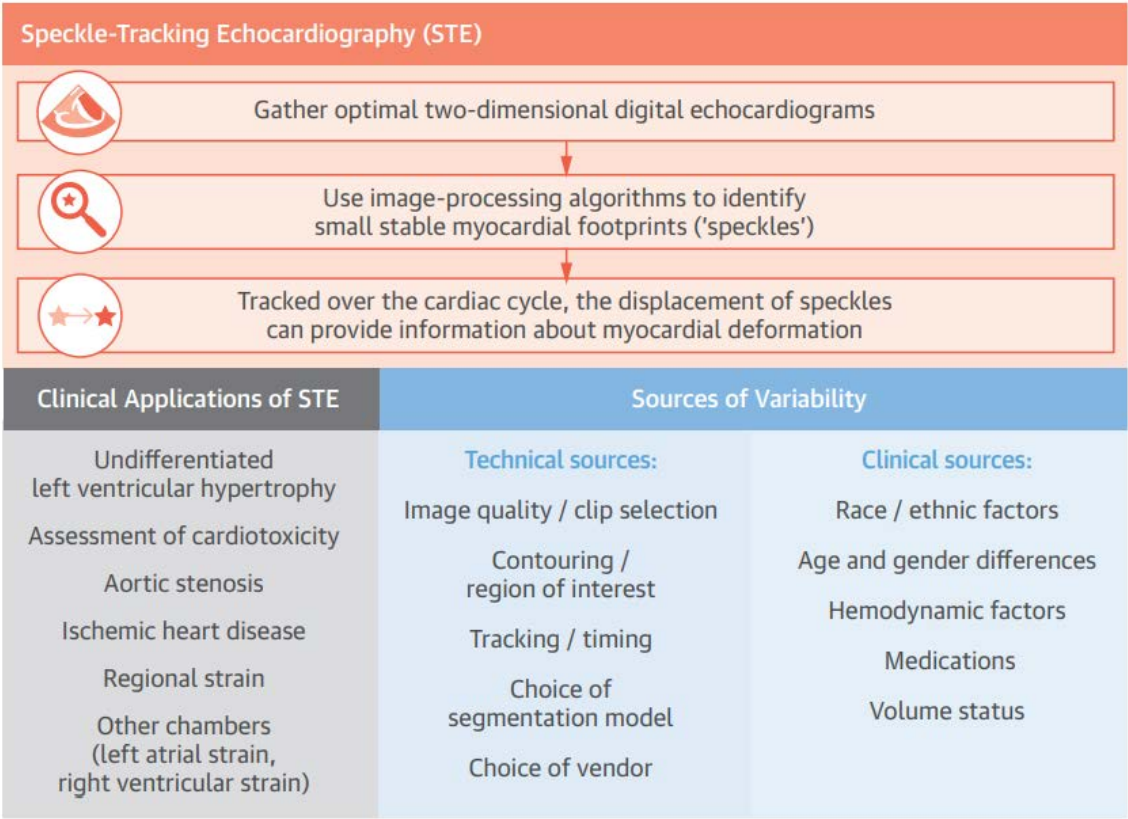
Spectrum of Major Echocardiographic Abnormalities in Patients With Myocardial Injury and COVID-19



Speckle-tracking Echokardiographie (STE): ‚Myocardial strain‘

LV-myokardiale Deformations-Analyse

CENTRAL ILLUSTRATION Speckle-Tracking Strain: Clinical Utility and Future Directions



Collier, P. et al. J Am Coll Cardiol. 2017;69(8):1043-56.

Speckle-tracking strain is an increasingly used echocardiographic technology that can provide additional (if not potentially incremental) clinical utility. Interpretation of speckle-tracking strain must take into consideration both technical and clinical sources of variability. This technology is a focus of much current research, with the prospect of exciting future developments that are eagerly awaited. 3D = 3-dimensional.



Speckle-tracking echocardiography (STE)

Critically (N=52) vs. Non-critically (N=166) ill Covid-19 patients

	Total (n = 218)	Noncritical (n = 166)	Critical (n = 52)	P value ^a
Demographic				
Age (years)	62 (54.8, 69.3)	61 (53, 68)	64 (58, 73)	0.017
Male, n (%)	118 (49.6)	78 (47)	33 (68.5)	0.046
Signs				
SBP (mmHg)	135.0 ± 18.0	134.1 ± 17.8	137.7 ± 18.4	0.021
DBP (mmHg)	81.8 ± 11.5	81.2 ± 12.0	83.9 ± 9.3	0.103
HR (beat/min)	90 ± 15	89 ± 16	95 ± 13	0.011
SpO ₂ (%)	90 ± 9	93 ± 4	81 ± 12	<0.001
Blood and chemical tests				
WBC count (10 ⁹ /L)	6.7 (5.1, 9.8)	6.2 (4.8, 8.1)	10.3 (6.6, 13.4)	<0.001
Neutrophil (%)	72.9 (60.1, 85.8)	66.9 (57.6, 79.9)	88.3 (80.3, 91.3)	<0.001
Lymphocyte (%)	15.9 (7.7, 27.0)	20.6 (11.0, 30.1)	6.9 (4.1, 10.4)	<0.001
Albumin (g/L)	35.0 ± 6.6	36.3 ± 6.6	31.3 ± 4.8	<0.001
Creatinine (mmol/L)	69.1 ± 24.2	66.5 ± 21.7	77.4 ± 29.7	0.017
Biomarkers for MI				
Peak cTnI (pg/mL)	4.5 (1.9, 15.7)	3.2 (1.9, 10.8)	15.6 (6.2, 58.4)	<0.001
>34.2 pg/mL, n (%)	23 (10.8)	8 (5.0)	15 (28.8)	<0.001
>34.2 and <100 pg/mL, n (%)	15 (6.8)	8 (5.0)	7 (13.5)	<0.001
Peak NT-proBNP (pg/mL)	173 (53, 563)	108 (36.5, 336.5)	582 (192.5, 1703)	0.004
>900 pg/mL, n (%)	32 (15.3)	14 (8.9)	18 (34.6)	<0.001
Creatine kinase (U/L)	54 (34, 89.5)	54 (36, 87)	55.5 (25, 145.8)	0.981
Inflammatory markers				
hsCRP (mg/L)	16.6 (2.6, 66.3)	6.4 (1.7, 45.6)	67 (41.2, 199.7)	<0.001
ESR (mm/h)	30 (14, 67)	19 (7.5, 55.5)	56 (30.5, 78)	<0.001
IL-6 (pg/mL)	6.1 (2.2, 23.9)	3.8 (1.6, 11.8)	32.7 (9.5, 109.9)	0.045
IL-10 (pg/mL)	5 (5, 7.7)	5 (5, 5.6)	7.1 (5, 14.3)	0.179
TNF-α (pg/mL)	8.5 (6.3, 11.3)	8.2 (6.2, 11)	10.2 (7.3, 16.2)	0.002
>50% involvement of chest CT, n (%)	137 (62.8)	89 (53.6)	48 (92.3)	<0.001
Outcomes				
Hospital length (days)	28 (16, 43)	27 (14, 43)	40 (28, 45)	<0.001
Death, n (%)	2 (0.9)	0 (0)	2 (3.4)	<0.001
^b GLS < -21.0%, n (%)	181 (83.0)	130 (78.3)	51 (98)	<0.001
EF < 50%, n (%)	48 (22)	18 (10.8)	30 (57.6)	<0.001



Speckle-tracking echocardiography (STE)

Critically vs. Non-critically ill Covid-19 patients

Table Univariate and multivariate analysis to test the association between GLS and different clinical parameters and medical treatments.

Variables	Univariate		Multivariable ^a	
	Relative risk (95% CI)	P value	Relative risk (95% CI)	P value
Age	0.18	0.007	–	–
Male	–0.10	0.142	–	–
cTnl	–0.56	<0.0001	–0.58	<0.0001
NT-proBNP	–0.37	<0.0001	–0.37	<0.0001
SpO ₂	0.43	<0.0001	0.42	<0.0001
hsCRP	–0.23	0.0002	–0.20	0.006
ESR	–0.15	0.094	–0.15	0.116
IL-6	–0.23	0.001	–0.21	0.003
IL-10	–0.13	0.079	–0.12	0.096
TNF-α	–0.19	0.006	–0.16	0.022
Antiviral treatment	–0.71	0.723	–0.73	0.344
Intravenous corticosteroid	–0.62	0.093	–0.59	0.027
Oral corticosteroid	–0.47	0.521	–0.48	0.346
Dopamine/norepinephrine	–0.16	>0.999	–63.3	1.000

^aCorrection for age and sex.

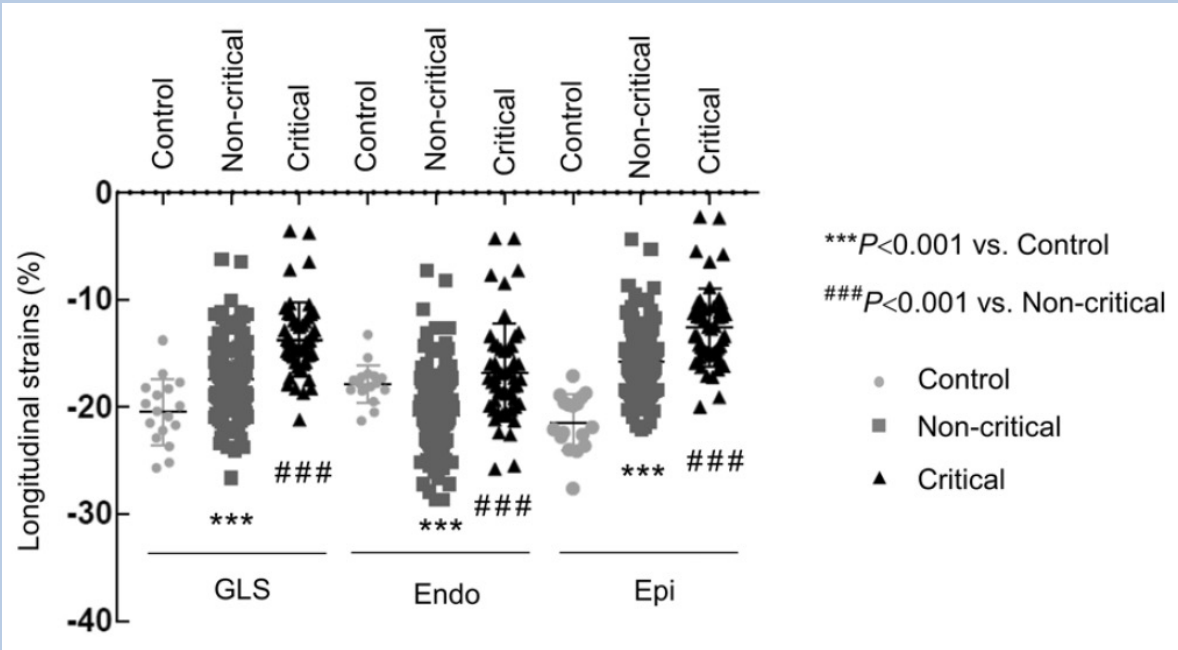


Fig. Comparison of GLSs, longitudinal strains in the subendocardium and longitudinal strains in the subepicardium in normal subjects, noncritical patients with COVID-19 and critical patients with COVID-19. GLSs global longitudinal strains, Endo subendocardium, Epi subepicardium. ***P value vs. control; ###P value vs. noncritical.



Speckle-tracking echocardiography (STE)

Critically vs. Non-critically ill Covid-19 patients

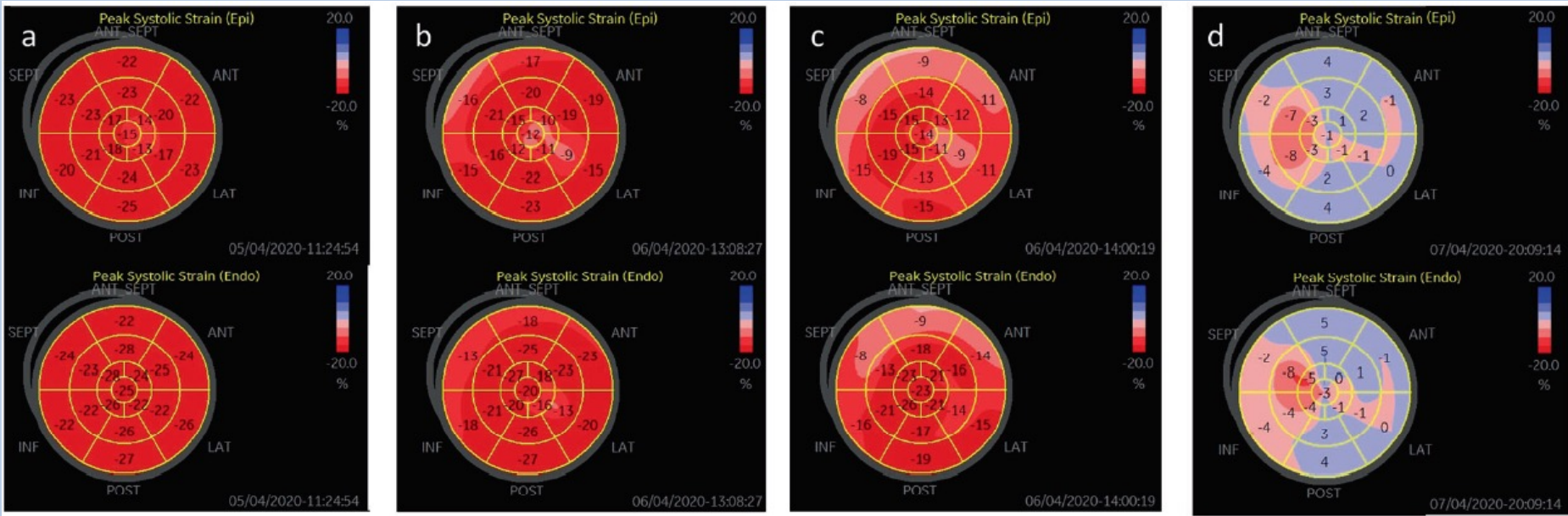


Fig. Representative images of GLS presented as "bull's-eye". (a) The subepicardium and the subendocardium images of a normal subject, (b) the subepicardium and the subendocardium images of a noncritical COVID-19 patient, (c) the subepicardium and the subendocardium images of a critical COVID-19 patient, (d) the subepicardium and the subendocardium images of a critical COVID-19 patient who died. The top line shows images of the subepicardium, and the bottom line shows images of the subendocardium. Alterations in layer-specific longitudinal strains were preferentially seen in the subepicardial layer of the myocardium. Endo subendocardium, Epi subepicardium.



Myocardial inflammation and dysfunction in COVID

Echo (STE)-Bildgebung bei Ptn mit erhöhtem Troponin-Spiegel

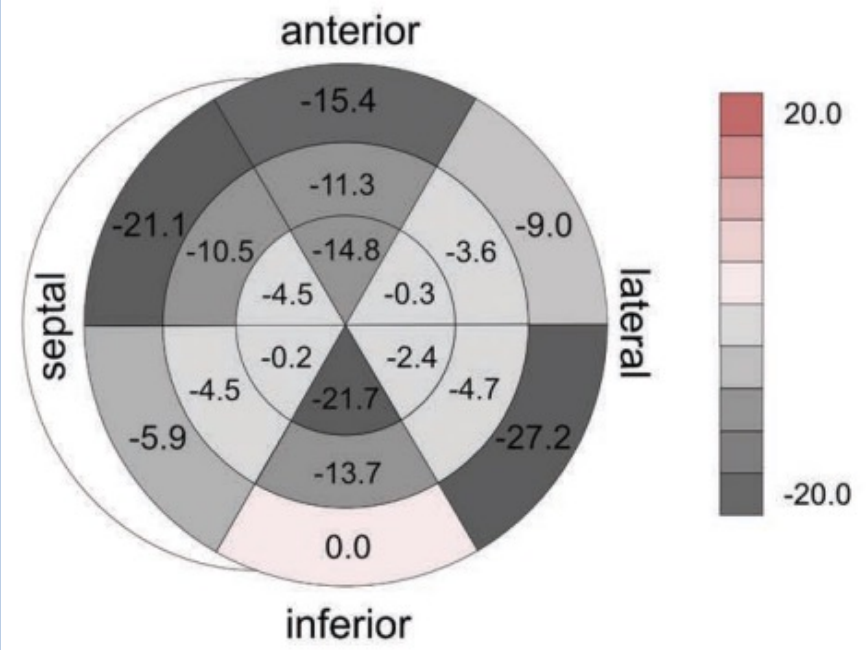
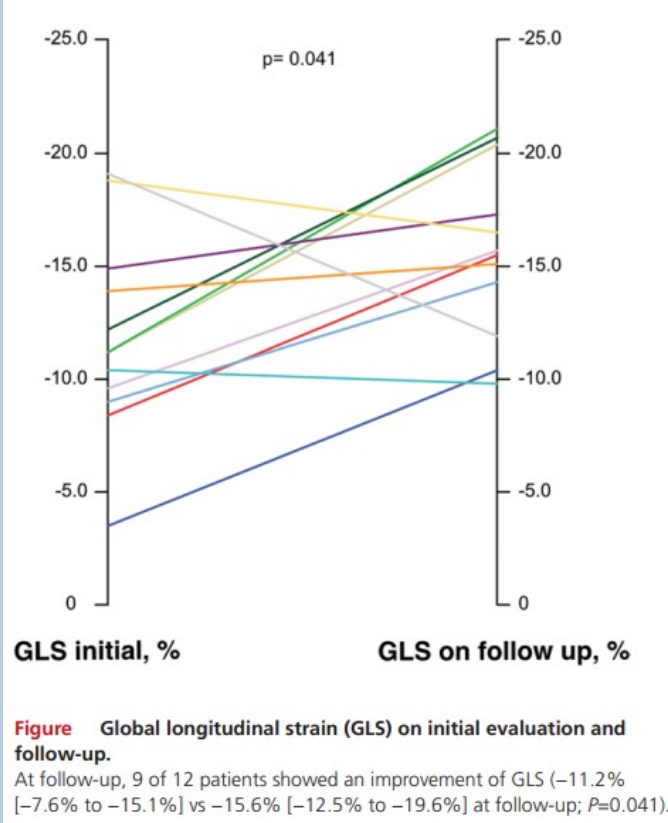


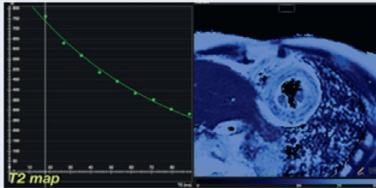
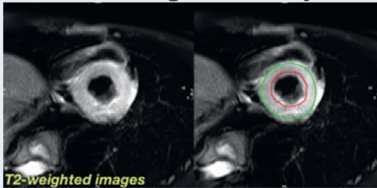
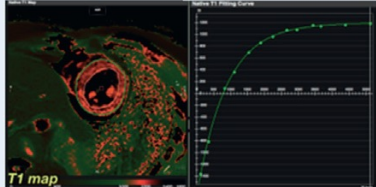
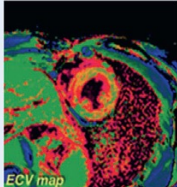
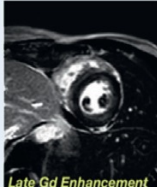
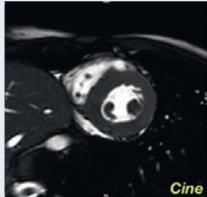
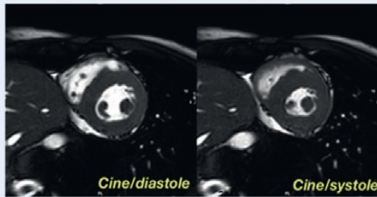
Figure 2. Cardiac phenotyping of patients with coronavirus disease 2019 (COVID-19). **A,** Representative bull's-eye view of global longitudinal strain of patient 9.

Echo: Verlauf Longitudinal Strain



MYOKARDITIS

Diagnostische Kriterien

2018 Lake Louise Criteria		CMR Image Examples	
Main Criteria	Myocardial Edema (T2-mapping or T2W images)	Regional or global increase of native T2 	Regional or global increase of T2 signal intensity 
	Non-ischemic Myocardial Injury (Abnormal T1, ECV, or LGE)	Regional or global increase of native T1 	Regional or global increase of ECV  or Regional LGE signal increase 
Supportive Criteria	Pericarditis (Effusion in cine images or abnormal LGE, T2, or T1)	Pericardial effusion 	Regional or global hypokinesis 
	Systolic LV Dysfunction (Regional or global wall motion abnormality)		



Myocardial inflammation and dysfunction in COVID

MRI-Bildgebung bei Ptn mit erhöhtem Troponin-Spiegel

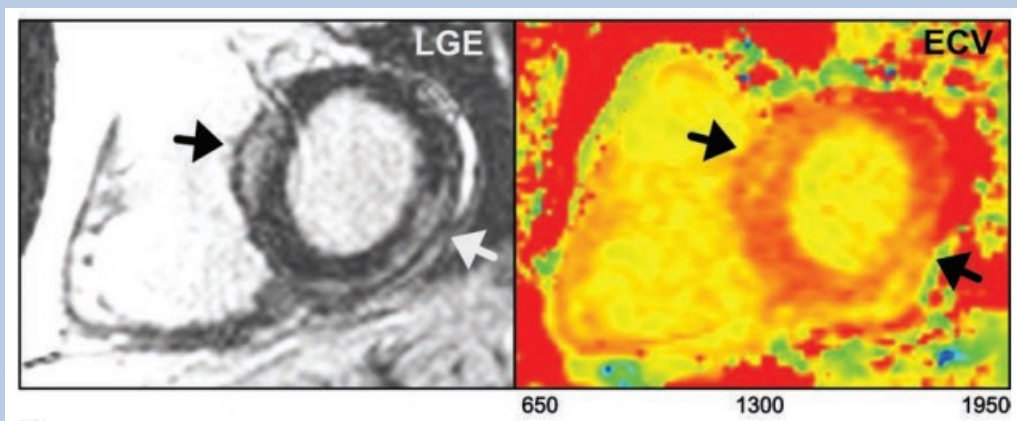


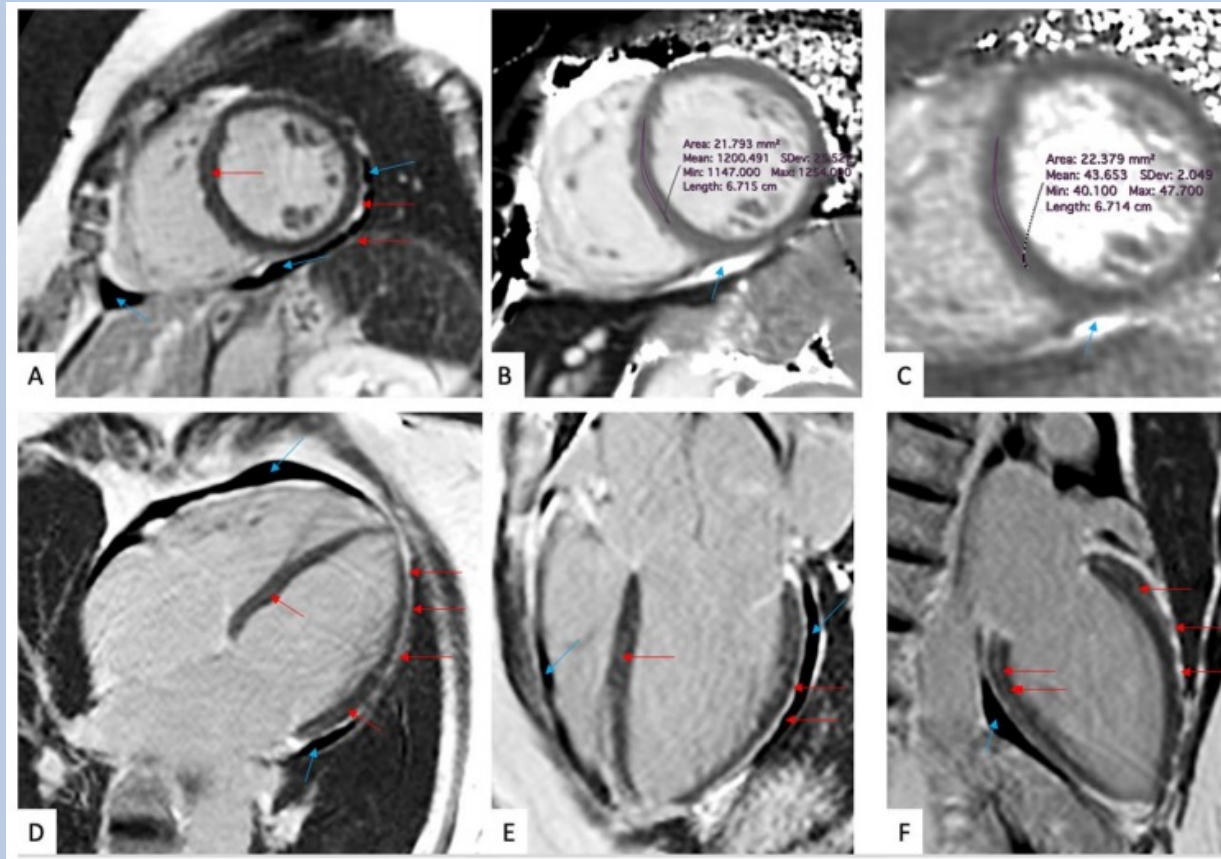
Figure Cardiac phenotyping of patients with coronavirus disease 2019 (COVID-19).
B. Representative cardiac magnetic resonance images of patient 14. Images show late gadolinium enhancement (LGE), extracellular volume (ECV), T2, and T1 as indicated. Arrows point areas of myocardial tissue injury (in LGE, ECV, and T1), as well as edema (T2).

MRT-Befunde

CMR	Study population (n=18)
	n (%) or median (IQR)
LVEF, %	59.5 (54.5–62.8)
LVEDV, mL	121.0 (107.3–162.8)
LVESV, mL	45.5 (42.0–75.8)
SV, mL	72.5 (51.8–77.5)
Myocardial edema	7 (38.9)
T2 mapping	5/17 (27.8)
T2W images	3/5 (16.7)
Myocardial tissue injury	15 (83.3)
Native T1 (>2.5 SD)	12/17 (66.7)
Native T1 (>5 SD)	6/17 (33.3)
ECV	10/15 (55.6)
LGE	12/16 (66.7)
Lake-Louise criteria for acute myocarditis	7 (38.9)



„Subtile Myocarditis“ als eine Ursache von „long-Covid“ ?



Extended Data Fig. | Representative magnetic resonance images of a symptomatic patient. (a-f) Late gadolinium enhancement imaging (A, D-F) and Native T1 (B) and T2 (C) mapping measurements of a 57-year-old woman evaluated 201 days after COVID-19 infection. This individual reported dyspnea, palpitations, and chest pain, worsening on minimal exertion. Late gadolinium enhancement imaging allows to visualize regional accumulation of the gadolinium-based contrast agent along the outer rim of the myocardial free wall (red arrows), as well as within the thickened pericardial layers, separated by small amounts of pericardial effusion (blue arrows).



COVID-assoziierte Myocarditis

Therapie

- **Herzinsuffizienz:** Therapie gem. ESC-guidelines CHF
- **assoz. Rhythmusstörungen:** Therapie gem. ESC-guidelines AF / VTA
- **schwere LV-Dysfunktion:** MCS / ECMO (Klasse IIa-Empfehlung)
- **Antivirale Therapie**
- **Immunmodulierende Therapie**
- **Off-label / Studien:** Colchizin , u.a.
- **Monitoring bzgl. Langzeitschäden bei Ptn mit Post-Acute Sequelae of Sars-Cov-2 (PASC) oder "Long COVID"-Syndrom**

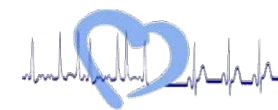




COVID-19 Treatment Guidelines



Coronavirus Disease 2019 (COVID-19) Treatment Guidelines



COVID-19 Treatment guidelines

NIH – Empfehlungen: antivirale Therapie

Summary Recommendations

Remdesivir is the only antiviral drug that is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19. Ritonavir-boosted nirmatrelvir (Paxlovid), molnupiravir, and certain anti-SARS-CoV-2 monoclonal antibodies (mAbs) have received Emergency Use Authorizations from the FDA for the treatment of COVID-19.

This section focuses on the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations for using small-molecule antiviral drugs to treat COVID-19. These recommendations are based on the available data. For recommendations and information regarding the use of anti-SARS-CoV-2 mAbs, see [Anti-SARS-CoV-2 Monoclonal Antibodies](#).

Recommendations for Treating Nonhospitalized Patients

- The Panel recommends the following anti-SARS-CoV-2 therapies as preferred treatments for COVID-19. These drugs are listed in order of preference:
 - Ritonavir-boosted nirmatrelvir (Paxlovid) (AIIa)
 - Remdesivir (BIIa)
- The Panel recommends the following anti-SARS-CoV-2 therapies as alternative treatments for COVID-19. These drugs should **ONLY** be used when neither of the preferred treatments are available, feasible to use, or clinically appropriate. These drugs are listed in alphabetical order:
 - Bebtelovimab (CIII)
 - Molnupiravir (CIIa)
- See [Therapeutic Management of Nonhospitalized Adults With COVID-19](#) for detailed recommendations.

Recommendations for Treating Hospitalized Patients

- See [Therapeutic Management of Hospitalized Adults With COVID-19](#) for the Panel's recommendations on using remdesivir with or without immunomodulators in certain hospitalized patients.

Antiviral Drugs That the Panel Recommends Against

- The Panel **recommends against** the use of the following drugs for the treatment of COVID-19, except in a clinical trial:
 - Interferons for nonhospitalized patients (AIIa)
 - Interferon alfa or lambda for hospitalized patients (AIIa)
 - Ivermectin (AIIa)
 - Nitazoxanide (BIIa)
- The Panel **recommends against** the use of the following drugs for the treatment of COVID-19:
 - Chloroquine or hydroxychloroquine and/or azithromycin for hospitalized (AI) and nonhospitalized patients (AIIa)
 - Lopinavir/ritonavir and other HIV protease inhibitors for hospitalized (AI) and nonhospitalized patients (AIII)
 - Systemic interferon beta for hospitalized patients (AI)

The sections on [Chloroquine or Hydroxychloroquine and/or Azithromycin](#), [Lopinavir/Ritonavir and Other HIV Protease Inhibitors](#), and [Nitazoxanide](#) have been archived. The Panel will no longer be updating the information on these therapies.



COVID-19 Treatment guidelines

NIH – Empfehlungen: Immunmodulierende Therapie

Summary Recommendations
The hyperactive inflammatory response to SARS-CoV-2 infection plays a central role in the pathogenesis of COVID-19. See Therapeutic Management of Hospitalized Adults With COVID-19 for the COVID-19 Treatment Guidelines Panel's (the Panel) recommendations on the use of the following immunomodulators for hospitalized patients according to their disease severity: • Corticosteroids: dexamethasone • Interleukin-6 inhibitors: tocilizumab (or sarilumab) • Janus kinase (JAK) inhibitors: baricitinib (or tofacitinib) There is insufficient evidence for the Panel to recommend either for or against the use of the following immunomodulators for the treatment of COVID-19: • Anakinra • Fluvoxamine • Granulocyte-macrophage colony-stimulating factor inhibitors for hospitalized patients • Inhaled corticosteroids The Panel recommends against the use of the following immunomodulators for the treatment of COVID-19, except in a clinical trial: • Baricitinib plus tocilizumab (AIII) • Canakinumab (BIIa) • Colchicine for nonhospitalized patients (BIIa) • Intravenous immunoglobulin (IVIG) (non-SARS-CoV-2-specific) for the treatment of patients with acute COVID-19 (AIII). This recommendation should not preclude the use of IVIG for multisystem inflammatory syndrome in children (MIS-C) or when it is otherwise indicated. • Bruton's tyrosine kinase inhibitors (e.g., acalabrutinib, ibrutinib, zanubrutinib) (AIII) • JAK inhibitors other than baricitinib and tofacitinib (e.g., ruxolitinib) (AIII) • Siltuximab (BIII) The Panel recommends against the use of the following immunomodulators for the treatment of COVID-19: • Colchicine for hospitalized patients (AI)



Covid-19 und Cardiovasculäres System

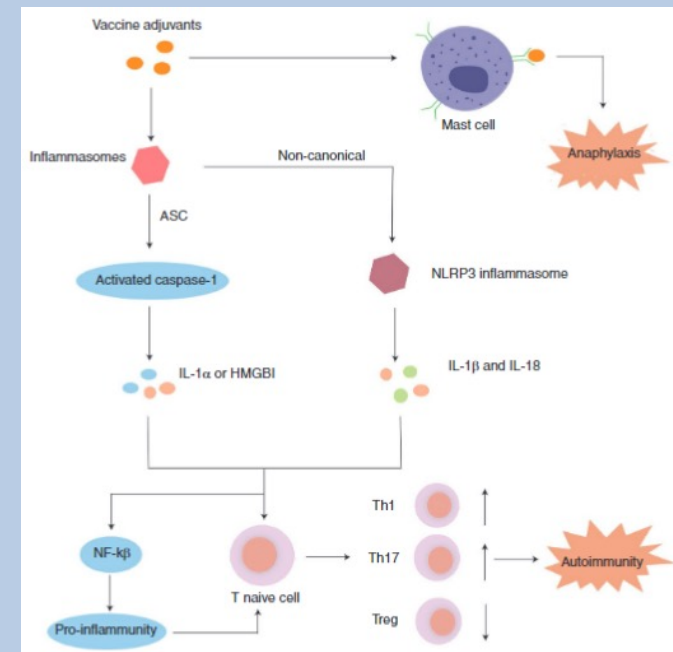
Kardiovaskuläre Manifestationen

Impfassozierte Komplikationen

CoV-Impfung: kardiovaskuläre Effekte

Autoimmun-Aktivierung: potentielle Mechanismen

- „molecular mimicry“
- Kreuzreaktionen pulmonal (z.B. teilen sich Cov-2 Spikeprotein und pulmonale surfactant Proteine 13/24 pentapeptide)
- Kreuzreaktion CoV-2 Proteine u. Gewebe-Antigenen (Autoimmun-Reaktion gegen Bindegewebe, das kardiovaskuläre-, gastrointestinale- und Nerven-System)
- Adjuvanzen im Impfstoff



CoV-Impfung: kardiovaskuläre Effekte

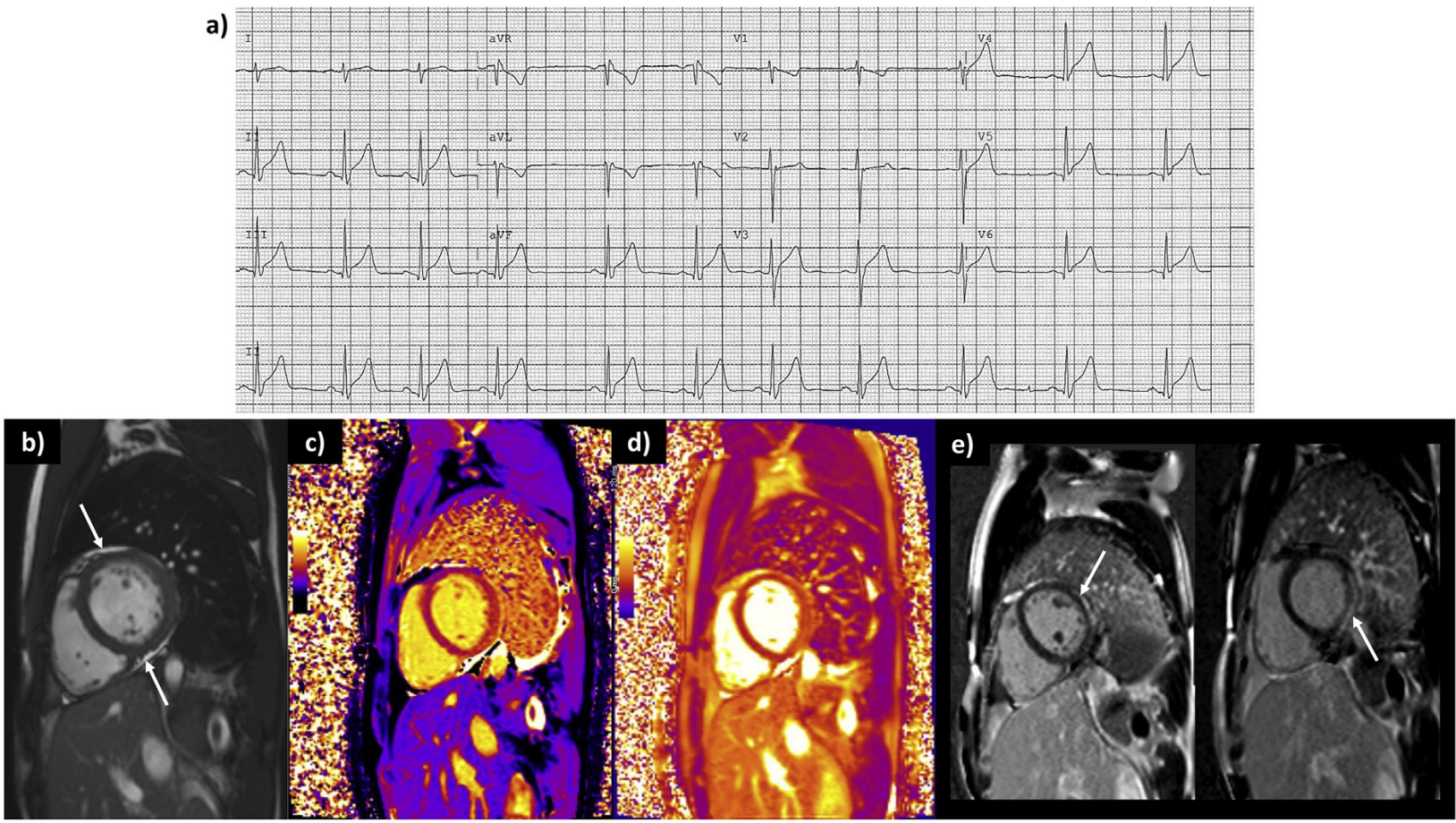


Figure Electrocardiogram and cardiac resonance imaging in an example case of myocarditis following mRNA vaccine. A 16-year-old male presented with typical central chest pain with onset 2 days post second dose of mRNA vaccination. The ECG was consistent with myopericarditis with supporting peak troponin I of 19,322 ng/L. Non-sustained ventricular tachycardia was recorded on telemetry. Echocardiography demonstrated normal LV size with mildly reduced systolic function (ejection fraction 51%) with mid-septal regional wall motion abnormalities. Global longitudinal strain was 18.2%. Inpatient CMR identified a small pericardial effusion and myocardial oedema with mid-wall LGE confirming acute myocarditis. Though there were no preceding viral symptoms, a viral screen for other causes was performed and was negative.

- a) 12-lead ECG demonstrating myopericarditis with diffuse ST segment elevation and PR depression.
- b) Short axis CMR imaging at the mid left ventricular level demonstrating pericardial effusion (arrows).
- c) Native T1 mapping showing elevated values in the lateral segments consistent with myocardial inflammation. Normal T1 values were identified in the remote myocardium.
- d) T2 mapping showing elevated T2 values in the lateral segments consistent with myocardial oedema. Normal T2 values were identified in the remote myocardium.
- e) Late gadolinium enhancement images at basal and mid ventricular levels showing a sub-epicardial to mid-wall pattern of regional fibrosis, as typically seen in myocarditis (arrows).

Abbreviations: ECG, electrocardiography; CMR, cardiac magnetic resonance; LV, left ventricular; LGE, late gadolinium enhancement.

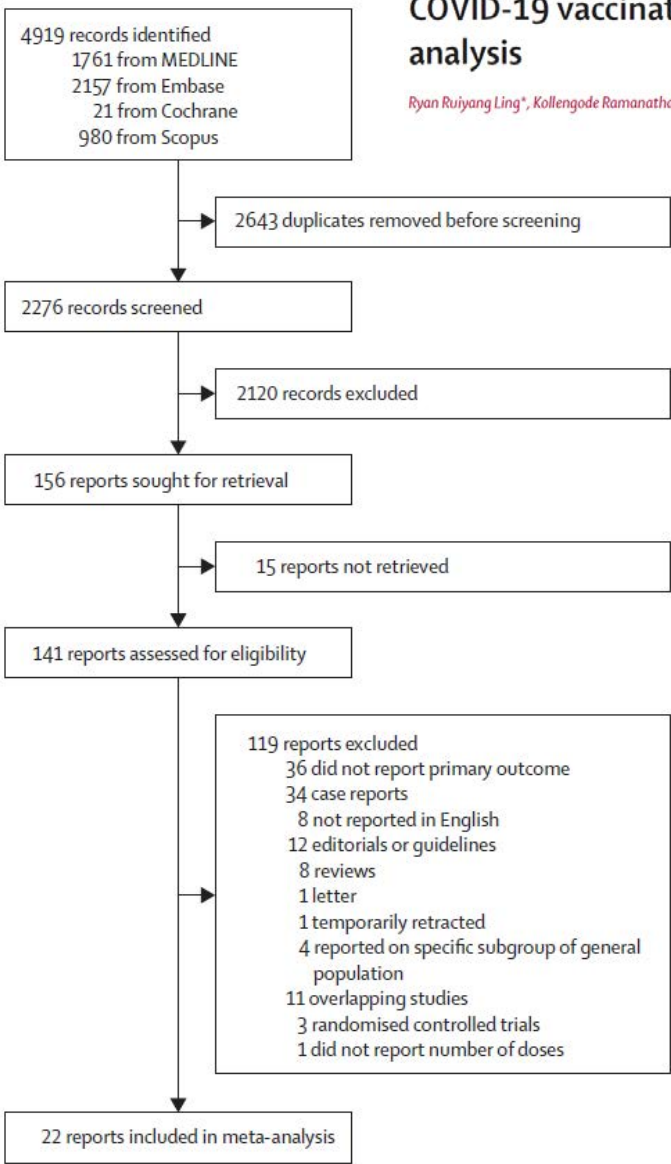


CoV-Impfung: kardiovaskuläre Effekte

Myopericarditis following COVID-19 vaccination and non-COVID-19 vaccination: a systematic review and meta-analysis

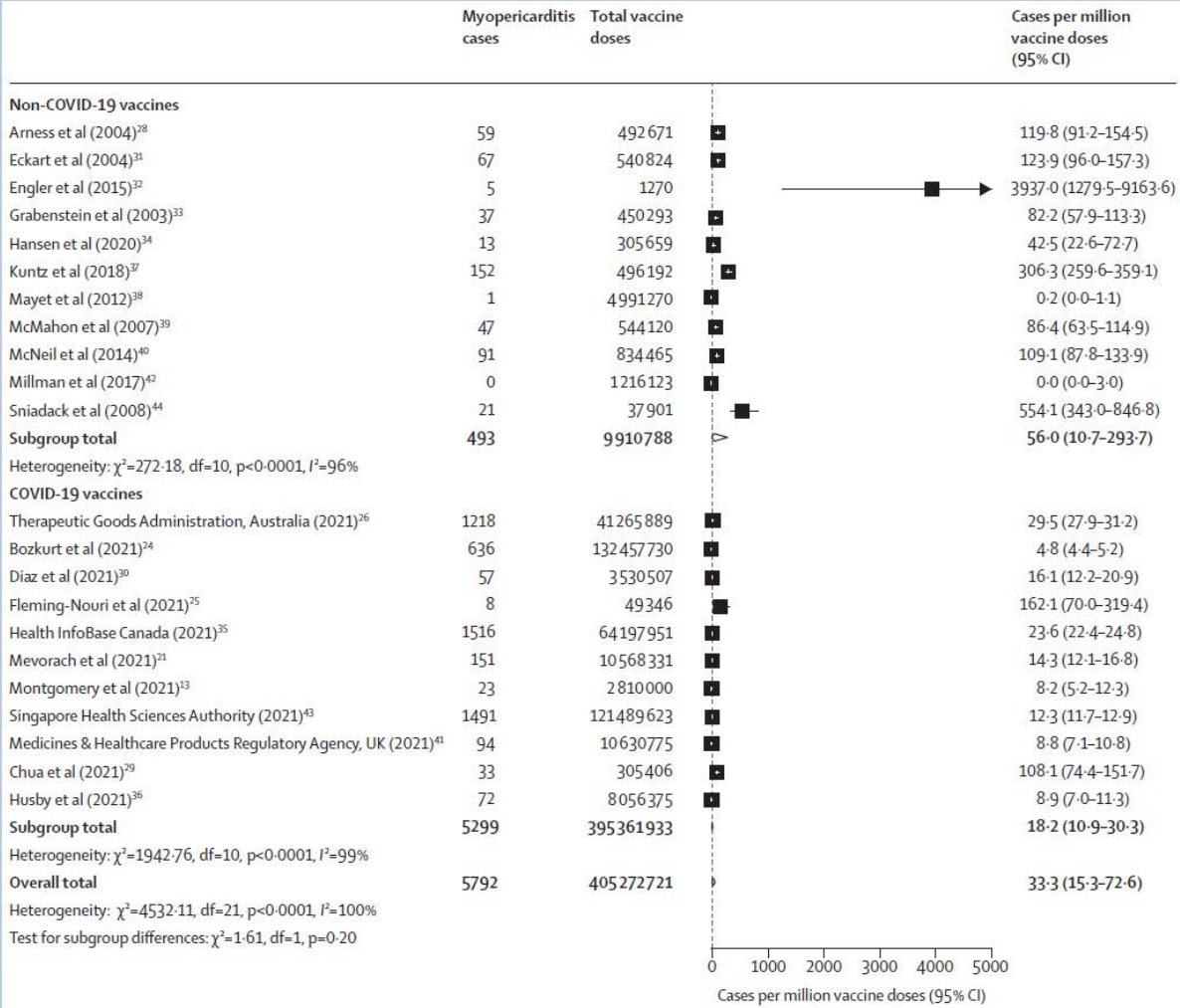
Ryan Ruiyang Ling*, Kollengode Ramanathan*, Felicia Liying Tan, Bee Choo Tai, Jyoti Somani, Dale Fisher, Graeme MacLaren

 
Lancet Respir Med 2022;
10: 679-88
Published Online
April 11, 2022
[https://doi.org/10.1016/S2213-2600\(22\)00059-5](https://doi.org/10.1016/S2213-2600(22)00059-5)



CoV-Impfung: kardiovaskuläre Effekte

Myokarditis



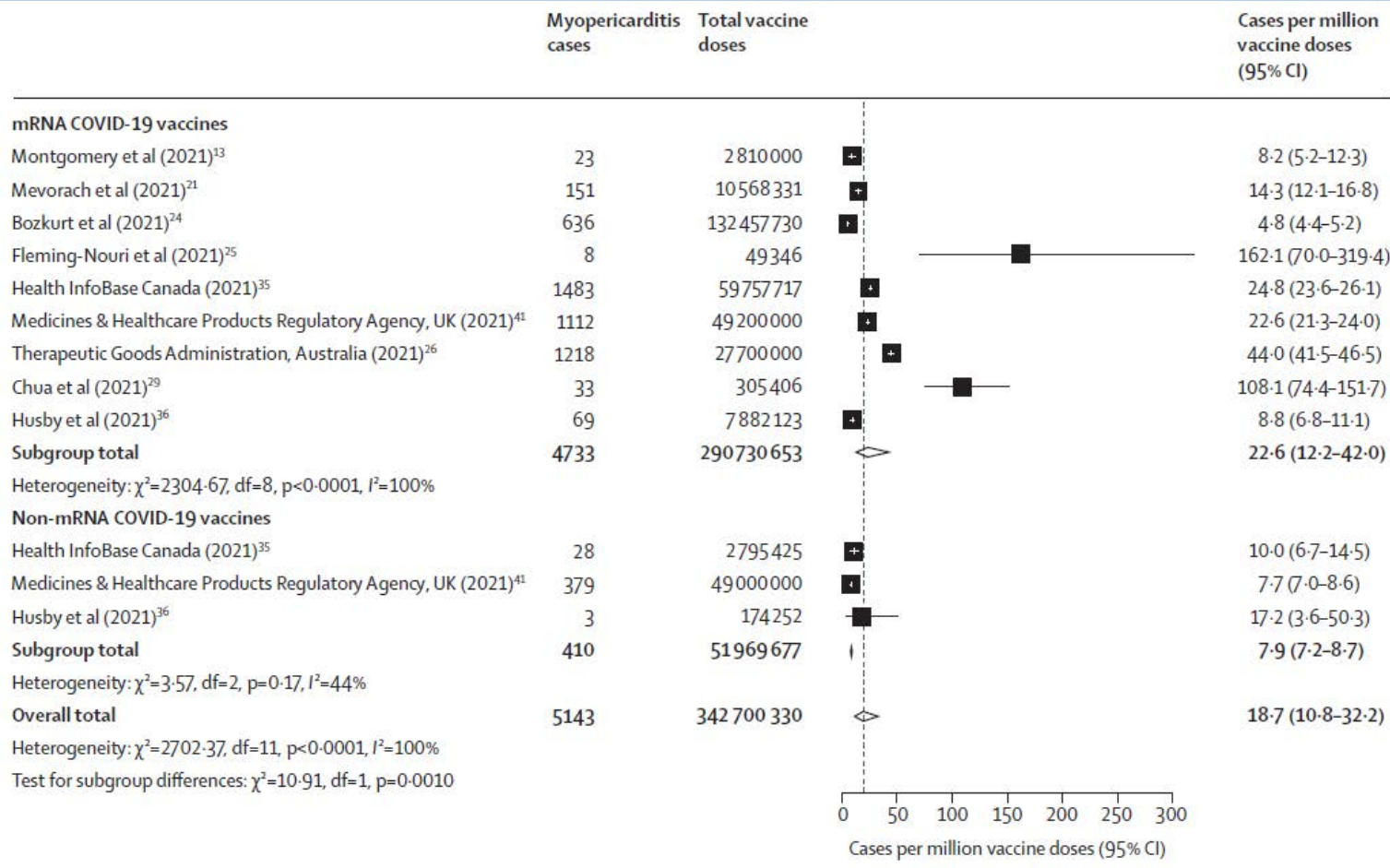
Incidence of myopericarditis following vaccination in studies investigating COVID-19 and non-COVID-19 vaccines

The pooled incidence of myopericarditis following vaccination was 18.2 cases per million doses of COVID-19 vaccine and 56.0 cases per million doses of non-COVID-19 vaccine ($p=0.20$).



CoV-Impfung: kardiovaskuläre Effekte

Myokarditis



Incidence of myopericarditis following vaccination in studies investigating mRNA and non-mRNA COVID-19 vaccines

The pooled incidence of myopericarditis following COVID-19 vaccination was 22.6 cases per million doses of mRNA vaccine and 7.9 cases per million doses of non-mRNA vaccine ($p=0.0010$).



CoV-Impfung: kardiovaskuläre Effekte

	Studies, n	Vaccine doses, n	Myopericarditis cases per million vaccine doses (95% CI)	p value
Type of vaccine	..	..	..	0.0010
mRNA	9 ^{13,21,24,25,26,29,35,36,41}	290 730 653	22.6 (12.2–42.0)	..
non-mRNA	3 ^{35,36,41}	51 969 677	7.9 (7.2–8.7)	..
Age*	..	..	..	<0.0001
≥30 years	3 ^{21,24,26}	143 154 756	2.9 (1.8–4.7)	..
<30 years	5 ^{21,24,25,26,29}	30 564 464	40.9 (18.4–90.9)	..
Dosing*	..	..	..	<0.0001
First dose	8 ^{13,21,25,26,29,30,35,36}	54 971 473	7.2 (3.8–14.0)	..
Second dose	8 ^{13,21,25,26,29,30,35,36}	46 754 686	31.3 (14.1–69.8)	..
Third dose	1 ³⁵	2 643 203	3.0 (1.5–6.1)	..
Sex*	..	..	..	0.0019
Female	5 ^{21,24,26,35,29}	123 336 615	5.1 (2.3–11.5)	..
Male	5 ^{21,24,26,35,29}	110 454 182	23.0 (8.9–59.4)	..
Sex by age group*				
Age <30 years	..	..	..	<0.0001
Male	5 ^{21,24,25,26,29}	14 532 527	59.7 (29.8–119.4)	..
Female	4 ^{21,24,26,29}	16 161 957	5.3 (3.6–8.0)	..
Age ≥30 years	..	..	..	0.034
Male	3 ^{21,24,26}	66 729 801	4.0 (2.4–6.8)	..
Female	3 ^{21,24,26}	76 424 955	1.7 (0.9–3.1)	..

Forest plots of the studies included in these subgroup analyses are provided in the appendix (pp 25–29). *Data extracted from the Therapeutic Goods Administration (Australian Government Department of Health)²⁶ on Dec 31, 2021, were not amenable for these analyses; therefore, we opted to use data from our previous most recent update (Oct 15, 2021), in which data of sufficient granularity were provided; all other analyses were conducted on the basis of data extracted on Dec 31, 2021.

Table: Subgroup analyses among people who received COVID-19 vaccines



CoV-Impfung: kardiale Effekte

Zusammenfassung : Myokarditis nach CoV-mRNA Impfung...

- *ist nicht häufiger, als Myokarditis nach non-CoV19-Impfung !*
- *betrifft überwiegend mRNA-Impfstoffe*
- *betrifft meist jüngere Männer*
- *i.d.R. milder Verlauf, und rapide Erholung*
- *kritische Klinik selten; CAVE Entwicklung von Herzinsuffizienz !!*
-
- *Die optimale Therapie der mRNA-Vacc induzierten Myokarditis ist derzeit nicht definiert / standardisiert*



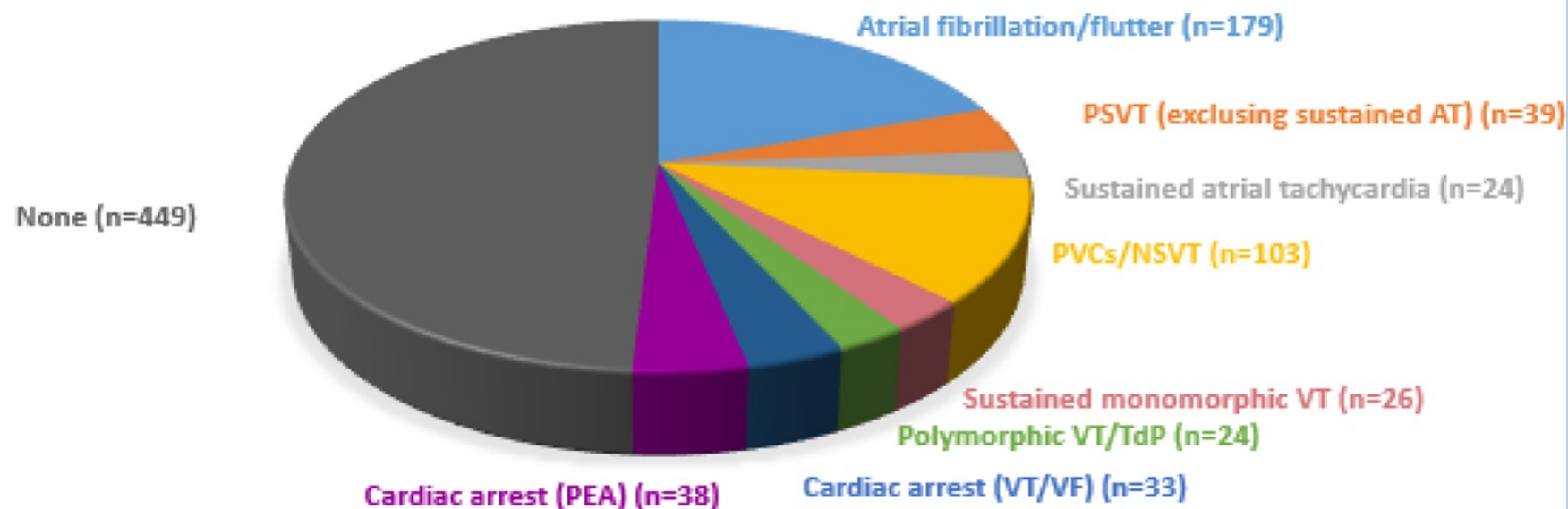
Covid-19 und Cardiovasculäres System

Kardiovaskuläre Manifestationen

***Rhythmus-
störungen***

COVID-19 and cardiac arrhythmias: a global perspective on arrhythmia characteristics and management strategies

WHAT TACHYARRHYTHMIAS HAVE YOU OBSERVED IN COVID-19 POSITIVE PATIENTS?



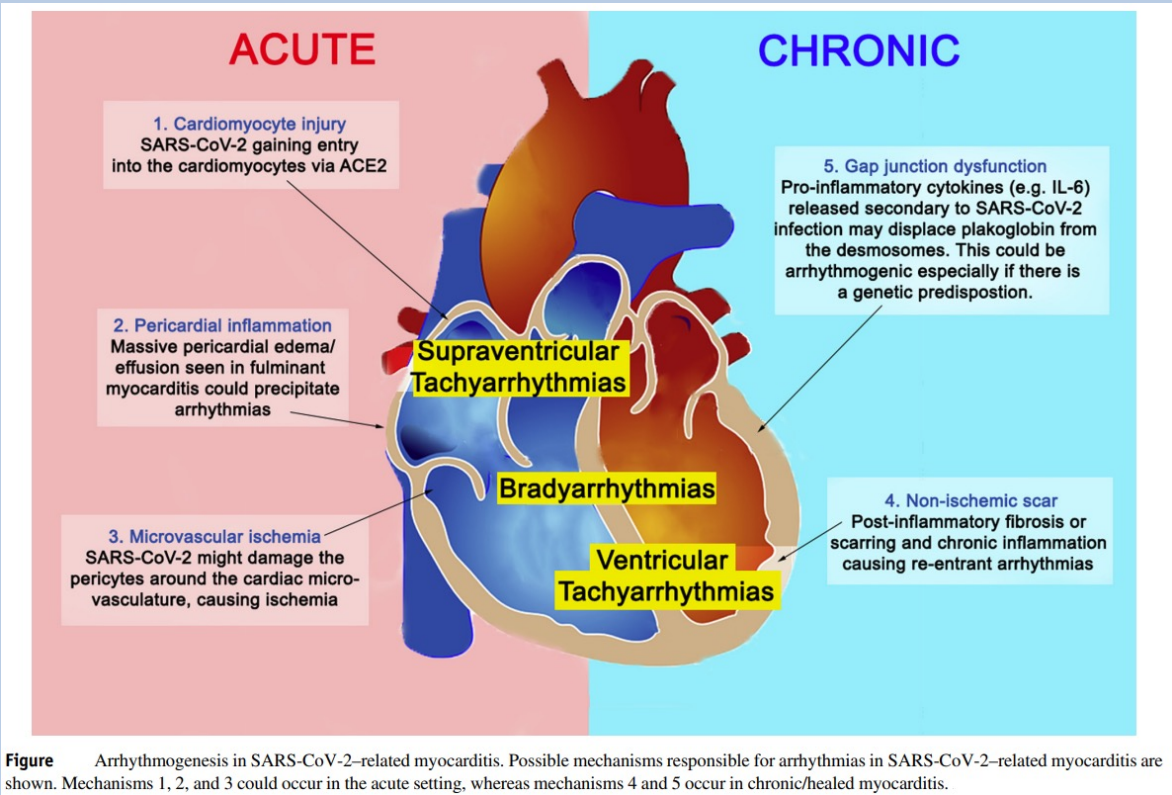
Antiarrhythmic drug use

(mainly amiodarone)
Prophylactic amiodarone use was rare (reported by only 8 (1.7%) of 477 respondents). In COVID-19 patients with ventricular arrhythmias, 250 (57%) of the 441 respondents reported not using any class I, II, or III antiarrhythmic agents whereas 150 (34%) used amiodarone and 64 (14.5%) used lidocaine/mexiletine. Sotalol and dofetilide use was infrequent, reported by 35 (8%) and 10 (2.3%) of survey respondents, respectively.



COVID-assoziierte Myocarditis

Arrhythmie-Prädisposition



Case report

Covid-19 assoziierter „electrical storm“

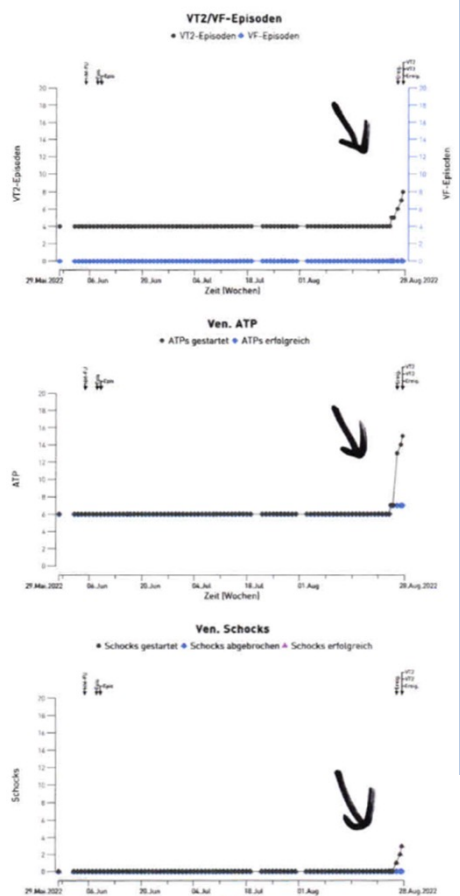
- *Pat W.M., männl., 81 Jahre*
- *Ischämische CMP; 2x HWI 2006 u. 2011 (bei Stentthrombose)*
- *Z.n. endovaskulärem Aorten-Repair bei TAA/BAA*
- *Z.n. früherer Pneumonie (2017)*
- *Ventilationsstörung mit O2-Therapie bei Z.n. UL-Resektion u. Zwerchfellresektion bei Zwerchfellhochstand*
- *Z.n. ICD-Implantation bei VT*
- *Umgehender Anruf bei Pat /Ehefrau => Zusatzinfo: Pat gehe es schlecht – habe Covid u. sei sehr schwach, am Vortag Synkope*
- *Pat umgehend ins kooperierende KH dirigiert*



Case report

Covid-19 assoziierter „electrical storm“

➤ Am 28.8.22 (Sonntag) über HomeMonitoring => Alarmmeldung: mehrere VT-therapien, eskalierend in ICD-Schock bei VF



Implantatstatus	
Status	OK
Batteriestatus	BOS
Batt.-Spannung	3,11 V (26.08.2022)
Ladedauer	9,5 s für 40 J (28.08.2022 09:18:19)

Tachy-Einst.						
	Zonengrenze	1. ATP	2. ATP	1. Schock	2. Schock	3. - n. Schock
VT1	460 ms	AUS	AUS	AUS	---	---
VT2	400 ms	3 * Burst	3 * Rampe	40 J	40 J	6 * 40 J
VF	280 ms	Burst		40 J	40 J	6 * 40 J

Brady-Elektrode		RV-Elektrode	
Stimulationsimpedanz [Ohm]		352	
Reizschwelle [V]		1,2	
Wahrn.-ampl. mtl./min. [mV]		10,7 / 10,0	
Programmiert [V@ms]		2,00 @ 0,40	

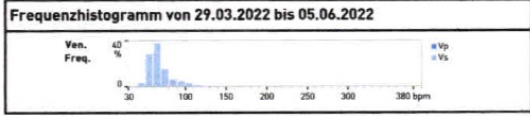
Ven. Arrhythmien seit 29.03.2022		VT1	VT2	VF
Therapieepisoden		0	4	0
ATP gestartet/erfolgr.		9 / 1		1 / 0
Schocks gestartet/abgebr./erfolgr.		3 / 0 / 3		
Letzte Episode: VT2 [28.08.2022 09:18:03]				

Atriale Arrhythmien seit 29.03.2022	
SVT-Episoden	1

Befunde	
VT2 detektiert	
Ven. Epis. mit Beschl. des ven. Rhythmus	
Details wurden für Arrhythmieepisode empfangen	

Brady-Einstellungen	
Modus	VVI
Grundfrequenz	40 bpm

Schockelektrode	
Schockimpedanz [Ohm]	88
Impedanz letzter Schock [Ohm]	68 (28.08.22)

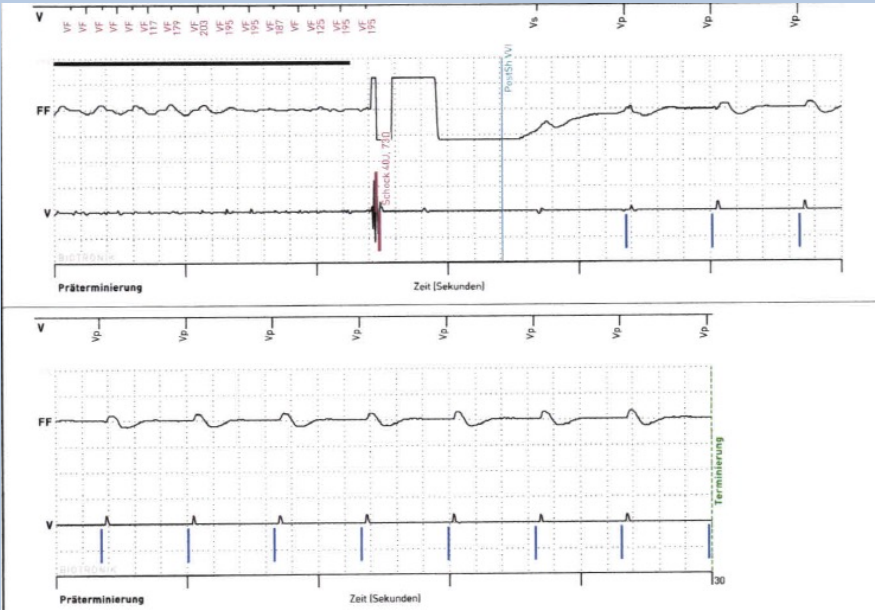
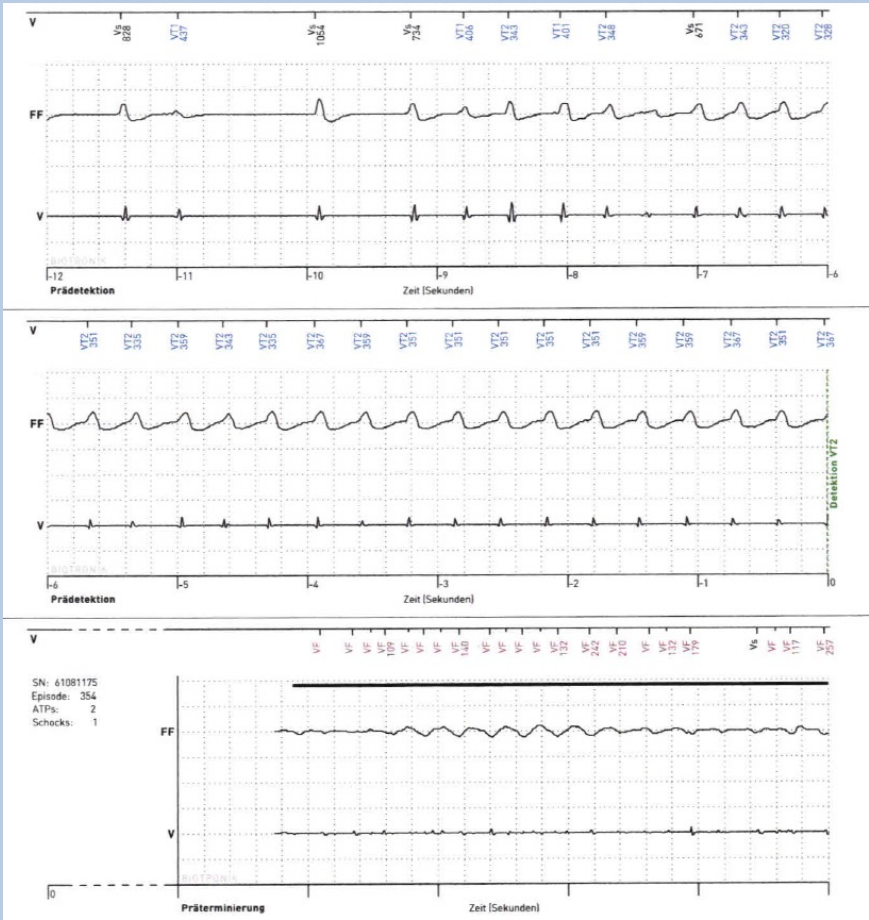


Ereignisepisoden seit 29.03.2022 (Mittelwert)	
Stimulation	
RVp	0 %



Case report

Covid-19 assoziierter „electrical storm“



Case report

Covid-19 assoziierter „electrical storm“

Diagnosen:

Z.n. ICD-Schockabgabe bei Kammerflimmern
- Electrical Storming unter Covid-19-Infektion

SARS-CoV-2-Infektion
- Erkrankung seit 19.08.2022

- Dexamethason 6mg seit 02.09.2022 bis 12.09.2022 (10 Tage gemäß LL)

V.a. bilaterale Pneumonie
- Blutkulturen vom 28.08.2022: ausstehend
- antibiotische Therapie mit Piperacillin/Tazobactam seit 28.08.2022

Mittelgradig reduzierte Pumpfunktion im Z.n. altem Hinterwandinfarkt (LVEF 38%)

- Optimierung der Herzinsuffizienz Medikation: Valsartan, Spironolacton + Forxiga seit 06.09.2022

Beginnendes Aneurysma der Aorta ascendens (43mm)

Vordiagnosen:

Koronare Herzerkrankung

- Z.n. Hinterwandinfarkt 07/2006 und 03/2011
- Z.n. RCA-PCI mit BMS 08.03.2011, Rekanalisation bei Stent-Thrombose 10.03.2011
- Z.n. Implantation eines DES in RCA 10/2020

Ischämische Kardiomyopathie

- Z.n. ICD-Implantation (05/2014)
- Z.n. ICD-Aggregatwechsel bei Batterieerschöpfung 09/2019
- Z.n. wiederholten VT-Episoden mit erfolgreicher ATP-Überstimulation
- zuletzt 09/2020

Arterielle Hypertonie

Nicht stenosierende Carotis-Sklerose beidseits

Thorako-abdominelles Aortenaneurysma

- max. Diameter Aorta ascendens 4,5 cm; infrarenal max. 5,5 cm
- Z.n. endovaskulärem Aorten-Repair 10/2021 (UKB)
- Z.n. Endoprothese A. iliaca externa beidseits

Ausgeprägter Zwerchfellhochstand rechts mit ausgeprägter restriktiver Ventilationsstörung

- Sauerstofflangzeit-Therapie
- Z.n. Zwerchfellteilresektion mit Dopplung, Raffung und Kelresektion rechter Unterlappen 04/2016
- Z.n. Re-Thorakotomie mit erneuter Zwerchfellraffung sowie Netzplastik 09/2016

COPD GOLD I

Z.n. Pneumonie 06/2017

Z.n. Lungenembolie 01/2017

Dissoziative Tetanie/Hyperventilationstetanien
vorbestehend Myoklonien unklarer Genese

Polyneuropathie

CVRP:

arterielle Hypertonie, Nikotin ex(pack years),

Allergien: nach Angaben gegen:Nickel, Chrom

Voroperationen:

Z.n. ICD-Implantation (05/2014)
Z.n. ICD-Aggregatwechsel bei Batterieerschöpfung 09/2019
Z.n. endovaskulärem Aorten-Repair 10/2021 (UKB)
Z.n. Endoprothese A. iliaca externa beidseits
Z.n. Zwerchfellteilresektion mit Dopplung, Raffung und Kelresektion rechter Unterlappen 04/2016
Z.n. Re-Thorakotomie mit erneuter Zwerchfellraffung sowie Netzplastik 09/2016
Z.n. Hüft-TEP links 2006
Z.n. Revision-OP Hüft-TEP links 2008
Z.n. Sigmaresektion



Case report

Laborverlauf

Bezeichnung	Ref.-Bereich	Einheit	30.10.19 10:07	28.8.22 10:36	28.8.22 11:26	29.8.22 05:00	5.9.22 00:58
Auftragsinfo				* Bem.			
SARS-CoV-2 (COVID-19) PCR				* positiv ^{††}			
Blutsenkung	3 - 8	mm	21 [†]				
Erythrozyten	4.0 - 5.7	10 ⁶ /μL	3.9 [↓]		3.4 [↓]	3.3 [↓]	3.6 [↓]
Leucocyten	3.6 - 10.5	10 ³ /μL	4.9		5.9	5.3	7.8
Hämoglobin	12.5 - 17.2	g/dL	12.5 [↓]		10.9 [↓]	10.6 [↓]	11.8 [↓]
Hämatokrit	37.0 - 49.0	%	37.6 [↓]		32.1 [↓]	32.2 [↓]	35.3 [↓]
MCV	80 - 101	fL	97.0		95.3	98.2	98.1
MCH	27.0 - 34.0	pg	32.2		32.3	32.3	32.8
MCHC	31.5 - 36.0	g/dL	33.2		34.0	32.9	33.4
RDW		fL			48.1		
RDW-CV		%	13.6		13.4		
Thrombo	160 - 370	10 ³ /μL	177		184	164	266
Lymphozyten abs.	1.1 - 4.0				0.9 [↓]		
Neutrophile abs.	1.5 - 7.7				4.4		
Eosinophile abs.	0.0 - 0.5				0.0		
Basophile abs.	0.0 - 0.2				0.0		
Monozyten abs.	0.1 - 0.9				0.5		
Eosinophile	0.5 - 5.5	%	2.7		0.9		
Basophile	0.0 - 1.8	%	0.6		0.3		
Monozyten	2.0 - 9.5	%	8.2		9.2		
Lymphocyten	20 - 44	%	30.1		14.8 [↓]		
Neutrophile	42 - 77	%	58.4		74.8		
Quick	70 - 130	%	67 [↓]		103		
INR-Wert			1.23		1.00		
Fibrinogen	210-400	mg/dL	363.03				
aPTT (partielle TPZ)	21.8 - 28	sec	25.8		21.6 [↓]		
Thrombinzeit/TZ	14 - 21	sec	17.3				
C-reaktives Prot. quant.	< 0.5	mg/dL	<0.5		11.36 [†]	12.41 [†]	0.92
Troponin I (high sensitiv)	< 26.2	pg/mL			* 44.2 ^{††}	* 22.3	
B-Typ natriuretisches Peptid (BNP)	< 121	pg/mL	73.5				
NT-proBNP	< 450.0	pg/mL			*		
					1260.1 ^{††}		

Bezeichnung	Ref.-Bereich	Einheit	30.10.19 10:07	28.8.22 10:36	28.8.22 11:26	29.8.22 05:00	5.9.22 00:58
Natrium	136 - 146	mmol/L	137		137	138	141
Kalium	3.5 - 5.1	mmol/L	3.7		3.1 [↓]	3.9	4.7
Calcium	2.2 - 2.65	mmol/L	2.39		2.17 [↓]		
Chlorid	96 - 109	mmol/L			95 [↓]		
Magnesium	0.73 - 1.06	mmol/L	0.85				
Kreatinin	0.67 - 1.17	mg/dL	1.47 [†]		1.04	1.00	1.08
eGFR (CKD-EPI)	> 90	ml/min/1.73	* 45.0		* 67.0 [↓]	* 70.3 [↓]	* 64.0 [↓]
Glom. Filtrationsrate (MDRD,	> 60	ml/min/1.73	* 49.24		* 72.85	* 76.22	* 69.75



Covid-19 – assoziierte Arrhythmien

Determinanten eines Arrhythmie-Risikos

- *Progress der Covid-Infektion / Inflammation
=> Covid-assoziiierter Myokardschaden*
- *Zugrundeliegende strukturelle HE*
- *Polypharmakotherapie*



Covid-19 – assoziierte Arrhythmien

Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy

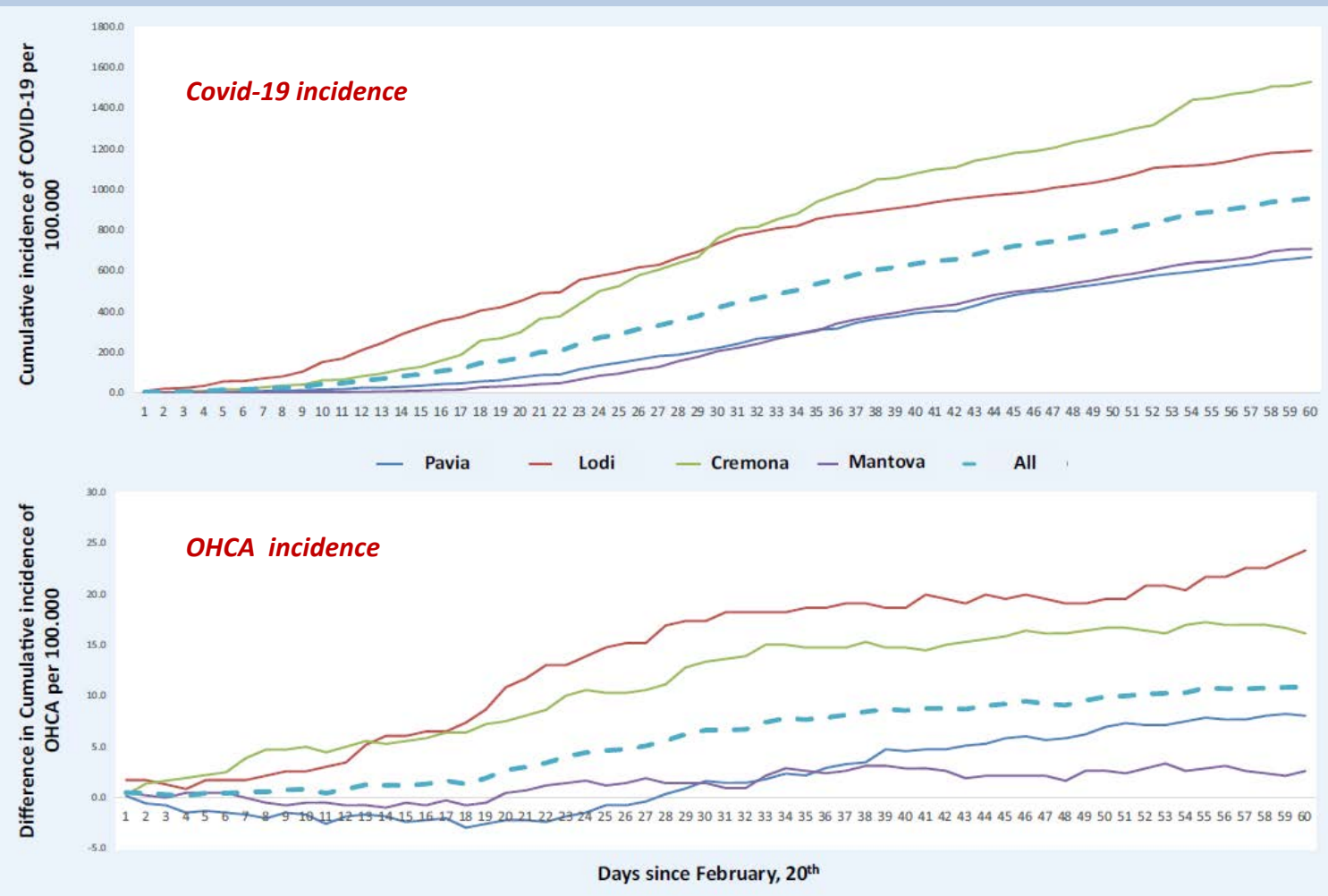
Relationship of COVID-19 per 100 000 inhabitants and OHCA difference between 2020 and 2019 cumulative incidences per 100 000 from days 1 to 60

Description				Model with fractional polynomials			
Province	Cumulative incidence per 100 000		% increase	Cumulative incidence per 100 000 COVID-19	Spearman's ρ	95% CI	P-value
	2020 OHCA	2019 OHCA					
All*	31.7	20.8	+52%	956	0.87	0.84–0.9	<0.001
Lodi	38.7	14.4	+169%	1,190	0.98	0.97–0.99	<0.001
Cremona	31.5	15.3	+106%	1,529	0.98	0.97–0.99	<0.001
Pavia	34.1	26	+31%	667	0.88	0.8–0.92	<0.001
Mantova	24.7	22.1	+12%	706	0.81	0.7–0.88	<0.001

*P for interaction with province <0.001.



Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy



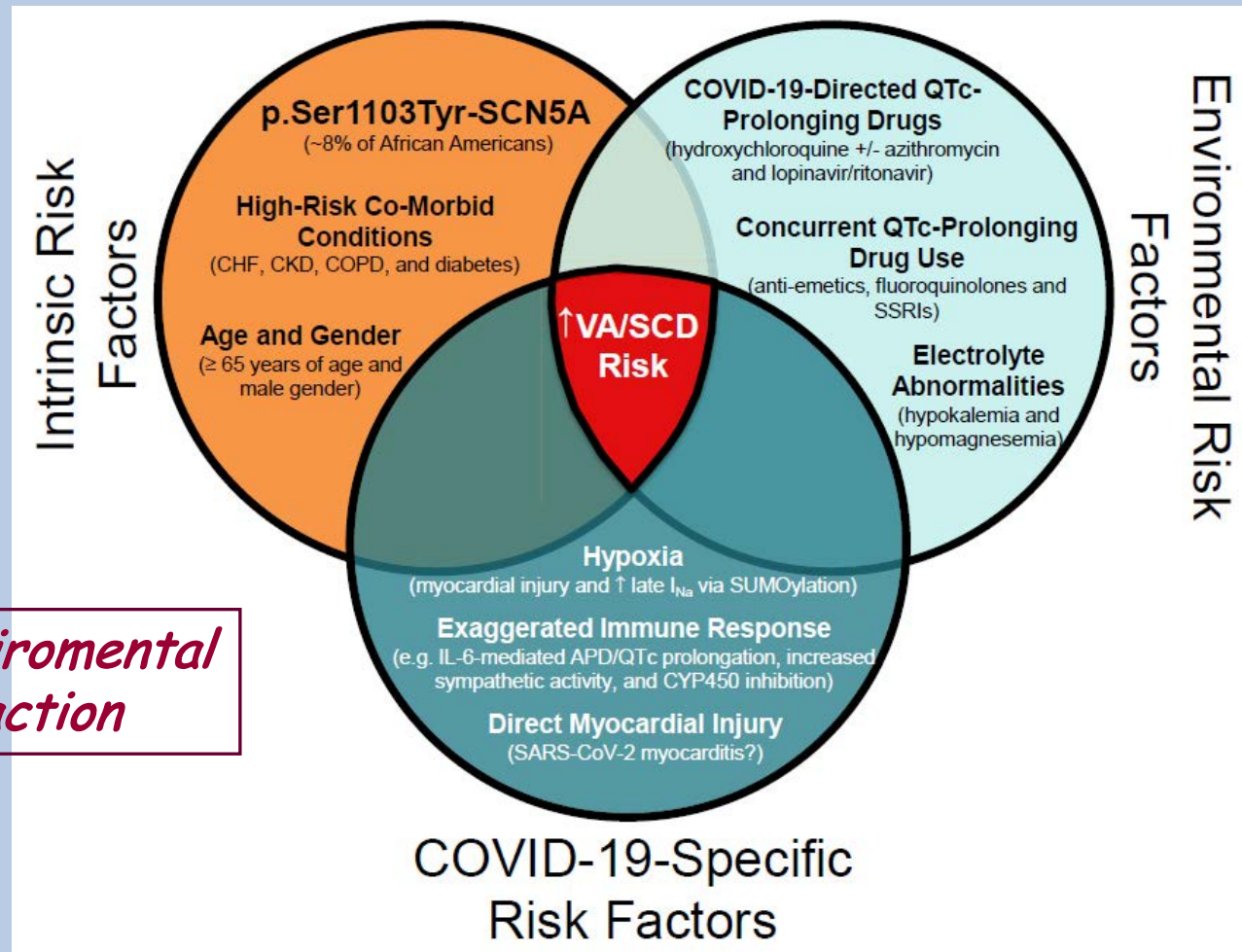
Baldi E, et al (Lombardia CARE Researchers); NEJM 2020;383:5

Eur Heart J 2020; doi:10.1093/eurheartj/ehaa508



Covid-19 – assoziierte Arrhythmien

Prädisposition für CoV-19 assoziierte ventr. TAA u. SCD



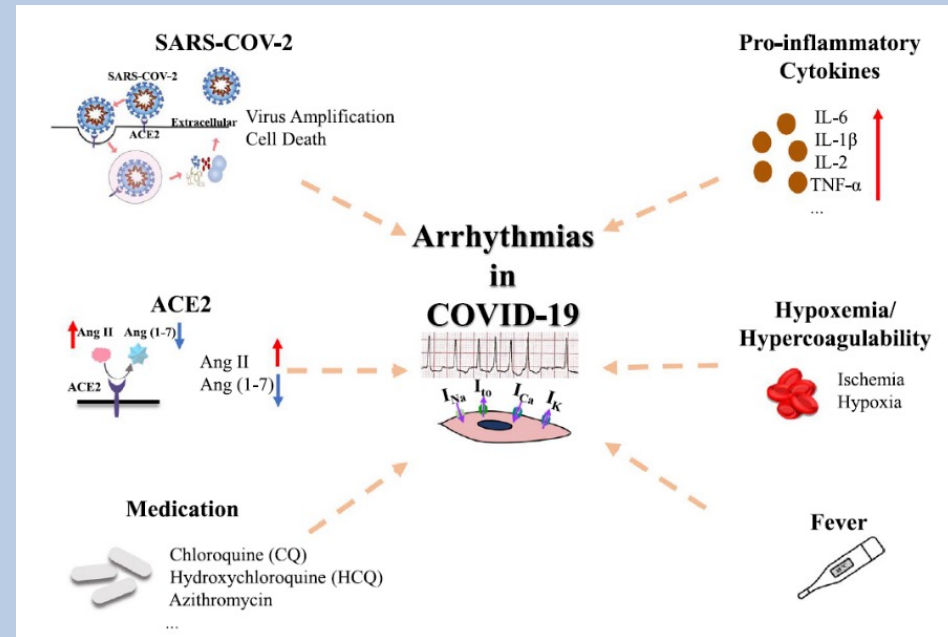
Gene-environmental interaction



Covid-19 – assoziierte Arrhythmien

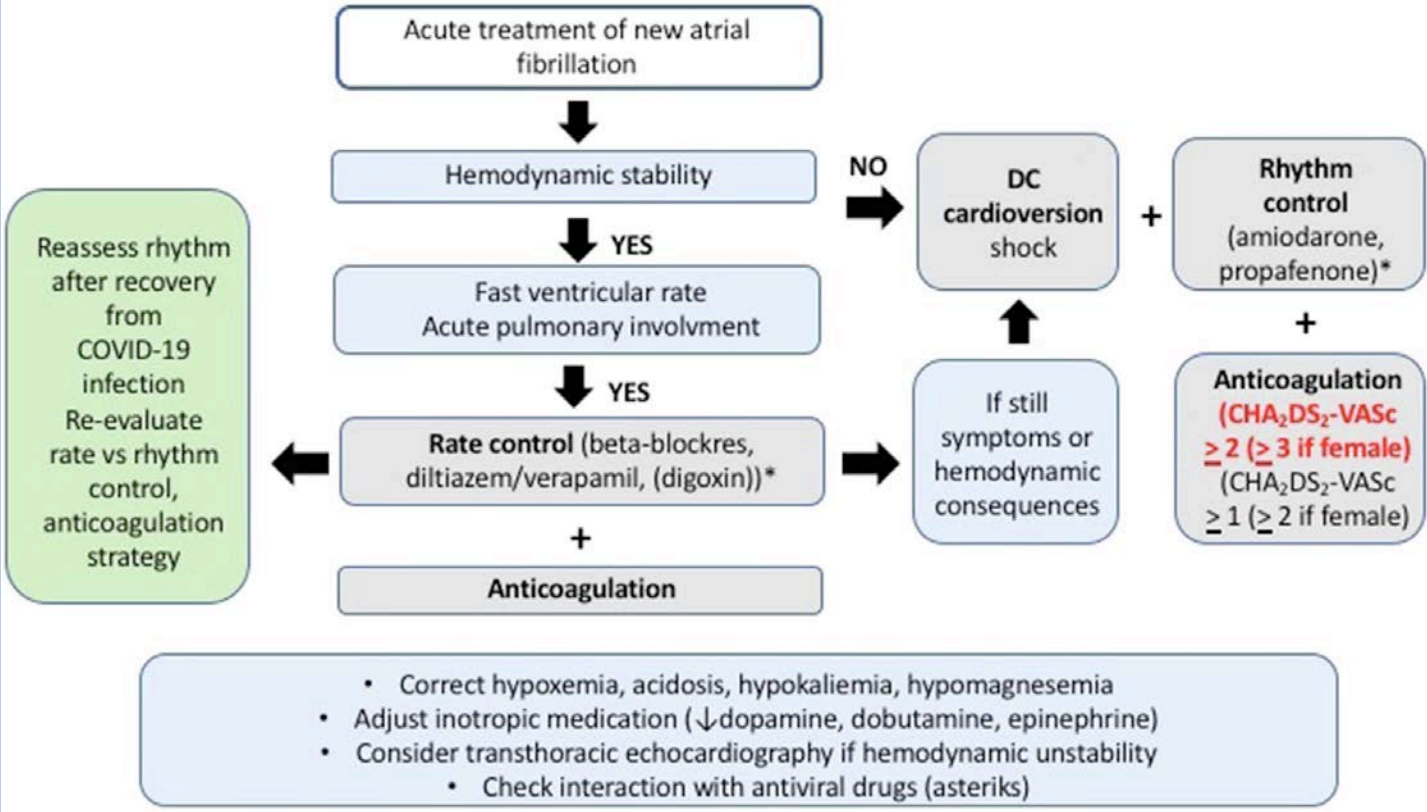
Pathogenese CoV-assoziierter ventrikulärer Rhythmusstörungen

- Direct cardiomyocyte injury (affecting mRNA expression of pore forming subunit of I_{to})
- „Cytokine-storm“ => Hypoxia / myocardial damage / Microthrombogenesis
- SARS-Co2-induzierter Zelltod.
- Synergistischer Effekt multipler QTc-verlängernder Medikamente
- Sympathikusaktivierung
- Alter - Begleiterkrankungen - Polypharmakotherapie



Covid-19 – assoziierte Arrhythmien

Flowchart of acute AF management in CoV-19-Patients



Covid-19 – assoziierte Arrhythmien

New-onset AF bei hospitalisierten CoV19-Patienten

[AHA Covid-19 Cardiovascular registry]

	No AF (n=26 115)	New-onset AF (n=1517)	P value
Age, y; median (interquartile range)	61 (48–73)	73 (64–82)	<0.0001
Male sex, %	12 532 (48%)	915 (60.3%)	<0.0001
Weight, kg	84 (71–102)	85 (64–82)	0.52
Body mass index	29.8 (25.5–35.5)	29.2 (25.0–35.0)	0.01

	No AF	New-onset AF	P value
Temperature >38 °C (>100.4 °F)	4868 (19.3%)	263 (18.2%)	0.32
Heart rate >100 beats/min	8643 (34.0%)	532 (36.4%)	0.06
Systolic blood pressure <90 mm Hg	539 (2.1%)	61 (4.2%)	<0.0001
Documented oxygen saturation <94%	8444 (34.1%)	612 (42.6%)	<0.0001
BNP	53 (20–162)	158 (52–436)	<0.0001
NT-proBNP	224 (63–885)	1320 (427–3876)	<0.0001
CRP	6.0 (1.6–11.9)	9.1 (2.9–17)	<0.0001
D-dimer	852 (456–1658)	1171 (641–3000)	<0.0001



Covid-19 – assoziierte Arrhythmien

Vorhofflimmern: Mechanismen

Preexisting medical comorbidities			
Prior CVD	5116 (19.6%)	495 (32.6%)	<0.0001
Ischemic heart disease			
Prior CABG	707 (2.7%)	69 (4.6%)	<0.0001
Prior MI	1322 (5.1%)	129 (8.5%)	<0.0001
Prior PCI	1052 (4.0%)	98 (6.5%)	<0.0001
CVA	2095 (8.0%)	181 (11.9%)	<0.0001
PAD	608 (2.3%)	52 (3.4%)	0.006
Congestive heart failure	2234 (8.5%)	264 (17.4%)	<0.0001
Hypertension	14822 (56.8%)	1099 (72.5%)	<0.0001
Diabetes	9072 (34.7%)	580 (38.2%)	0.006
Hyperlipidemia	8724 (33.4%)	673 (44.4%)	<0.0001
Tobacco use	1790 (6.9%)	126 (8.3%)	0.03
DVT/PE			
Pulmonary embolism	585 (2.2%)	40 (2.6%)	0.31
DVT	856 (3.3%)	65 (4.3%)	0.03
Renal disease	3008 (11.5%)	283 (18.7%)	<0.0001
Dialysis	3176 (12.2%)	294 (19.4%)	<0.0001
Chronic lung disease			
ILD	105 (0.4%)	5 (0.3%)	0.66
COPD	2159 (8.3%)	208 (13.7%)	<0.0001
Asthma	2467 (9.5%)	103 (6.8%)	0.0005
Cancer	3132 (12.0%)	271 (17.9%)	<0.0001



Covid-19 – assoziierte Arrhythmien

Vorhofflimmern: Outcomes Tod u. MACE

	No AF	New-onset AF	P value
Death	3111 (11.9%)	684 (45.2%)	<0.0001
ICU patients	2183 (30.1%)	562 (57.6%)	<0.0001
Non-ICU	924 (4.9%)	121 (22.5%)	<0.0001
MACE	1691 (6.5%)	361 (23.8%)	<0.0001
ICU patients	1229 (16.9%)	304 (31.1%)	<0.0001
Non-ICU	460 (2.4%)	57 (10.6%)	<0.0001



Covid-19 – assoziierte Arrhythmien

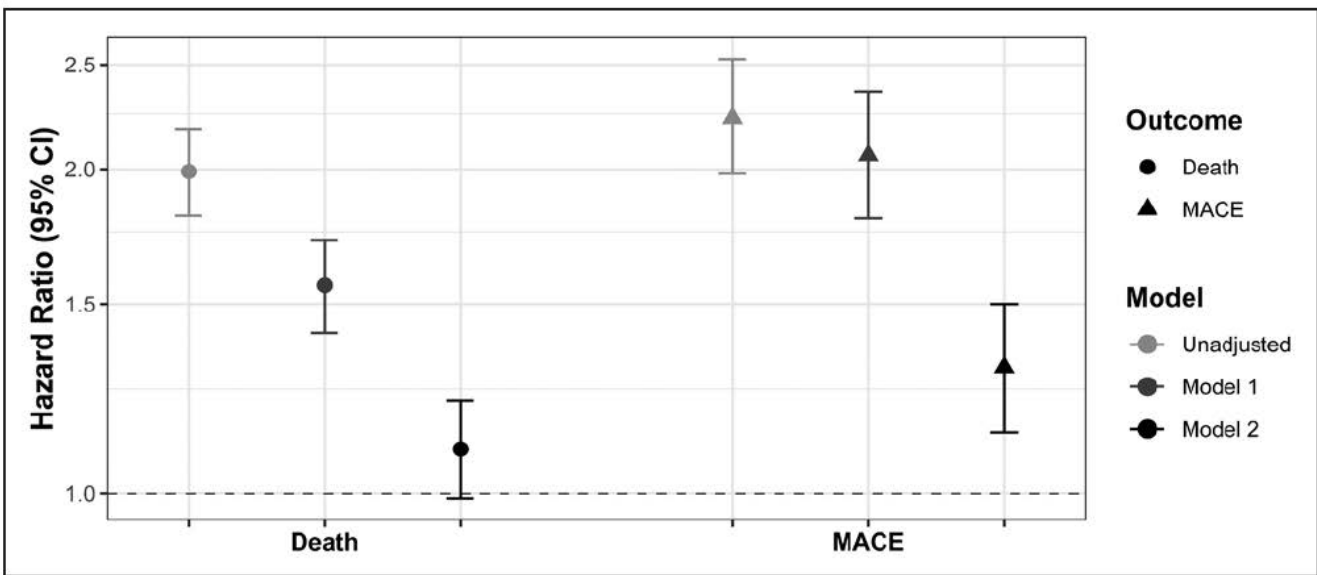
Vorhofflimmern: Prognose adjustiert nach Co-Morbiditäten

WHAT IS KNOWN?

- Atrial fibrillation is common in critically ill patients and is associated with higher morbidity and mortality.
- COVID-19 has a wide range of cardiac complications including atrial fibrillation.

WHAT THE STUDY ADDS

- One in 20 patients hospitalized with COVID-19 developed new-onset atrial fibrillation.
- New-onset atrial fibrillation was strongly associated with increased in-hospital mortality and major adverse cardiovascular events.
- The association between new-onset atrial fibrillation and increased risk of death completely attenuated after multivariable adjustment for in-hospital factors and underlying comorbidities, suggesting atrial fibrillation is a marker of disease severity rather than an independent driver of mortality.



Unadjusted and adjusted hazard ratios of primary and secondary outcome with 95% CIs.

Model 1 adjusted for age, race, sex, and clinical comorbidities. Model 2 adjusted for clinical factors in model 1 and disease severity. MACE indicates major adverse cardiovascular events.



Covid-19 und Cardiovasculäres System

Kardiovaskuläre Manifestationen

Long-Covid

Jeder achte Corona-Infizierte erkrankt an Long Covid

Eine niederländische Studie zeigt, wie weit Long-Covid-Symptome nach einer Corona-Infektion verbreitet sind. 12,7 Prozent leiden demnach an Langzeitbeschwerden.



Long Covid Syndrom

Terminologie / Definition ?

Reference	Terms	Description
[4]	Long COVID	Long-term COVID-19 illness that is cyclical, progressive, and multiphasic.
[5,6,7]	Long-hauler COVID-19	Multi-organ symptoms that persist for months after acute COVID-19.
	Long-COVID	
	Chronic COVID syndrome	
[8]	Long-haul COVID	Symptoms lasting for > 100 days.
	Long-tail COVID	
[9,10]	Long COVID	Symptoms lasting for > 2 months.
[11,12,13]	Late sequelae of SARS-CoV-2 infection	Symptoms lasting for > 4 weeks after the initial infection or diagnosis.
	Long-haulers	
	Long-COVID	
[14]	Post-acute COVID-19 syndrome	Symptoms lasting for > 4 weeks after the first symptom onset.
[15]	Acute post-COVID symptoms	Symptoms lasting for 5-12 weeks.
	Long post-COVID symptoms	Symptoms lasting for 12-24 weeks.
	Persistent post-COVID symptoms	Symptoms lasting for > 24 weeks.
[16, 17,7]	Post-acute COVID-19	Symptoms lasting for 1-3 months from the first symptom onset.
	On-going symptomatic COVID-19	
	Chronic COVID-19	Symptoms lasting for > 3 months from the first symptom onset.
	Long COVID	
	Post-COVID-19 syndrome	



Long Covid Syndrom



AWMF-Registernummer: 020-027

AWMF S1-Leitlinie Long/ Post-COVID

(Stand 17.8.2022)

- 1 Deutsche Gesellschaft f. Pneumologie und Beatmungsmedizin e.V. (DGP)
- 2 Deutsche gesetzliche Unfallversicherung (DGUV)
- 3 Deutsche Gesellschaft f. Allgemeinmedizin und Familienmedizin (DEGAM)
- 4 Deutsche Gesellschaft f. Psychosomatische Medizin und Ärztliche Psychotherapie (DGPM)
- 5 Deutsche Dermatologische Gesellschaft (DDG)
- 6 Deutsche Gesellschaft f. Neurologie (DGN)
- 7 Deutsche Gesellschaft f. Kardiologie – Herz- und Kreislaufforschung (DGK)
- 8 Deutsche Gesellschaft f. Neurorehabilitation (DGNR) und Redaktionskomitee S2k-LL SARS-CoV-2, COVID-19 und (Früh-) Rehabilitation
- 9 Berufsverband der Pneumologen (BdP)
- 10 Deutsche Gesellschaft f. Gastroenterologie, Verdauungs- und Stoffwechselerkrankungen (DGVS), Deutsche Gesellschaft f. Infektiologie (DGI)
- 11 Gesellschaft für Pädiatrische Pneumologie (GPP)
- 12 Paul Ehrlich Gesellschaft für Chemotherapie e.V. (PEG) / Sektion Infektiologie
- 13 Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V. (DGHNO)
- 14 Österreichische Gesellschaft für Pneumologie (ÖGP)
- 15 Deutsches Kollegium für Psychosomatische Medizin (DKPM)
- 16 Charité Fatigue Centrum, Charité Berlin

- 17 Deutsche Schmerzgesellschaft e.V.
- 18 Chronische Fatigue Centrum, Klinikum rechts der Isar der Technischen Universität München
- 19 Deutsche Gesellschaft für Gynäkologie und Geburtshilfe e.V. (DGGG)
- 20 Deutscher Bundesverband für Logopädie e.V. (DBL)
- 21 Gesellschaft für Neuropsychologie e.V. (GNP)
- 22 Deutsche Gesellschaft für Kinder- und Jugendmedizin (DGKJ)
- 23 Deutsche Gesellschaft für Reproduktionsmedizin e.V. (DGRM)
- 24 Deutscher Verband für Gesundheitssport und Sporttherapie e.V. (DVGS)
- 25 Deutsche Ophthalmologische Gesellschaft (DOG)
- 26 Deutsche Gesellschaft für Pädiatrische Infektiologie (DGPI)
- 27 Deutsche Gesellschaft für Rehabilitationswissenschaften (DGRW)
- 28 Deutsche Gesellschaft für Klinische Psychotherapie, Prävention und Psychosomatische Rehabilitation (DGPPR)



Long Covid Syndrom

Überblick über COVID-19 Nomenklatur

(nach National Institute for Health Care Excellence (NICE))

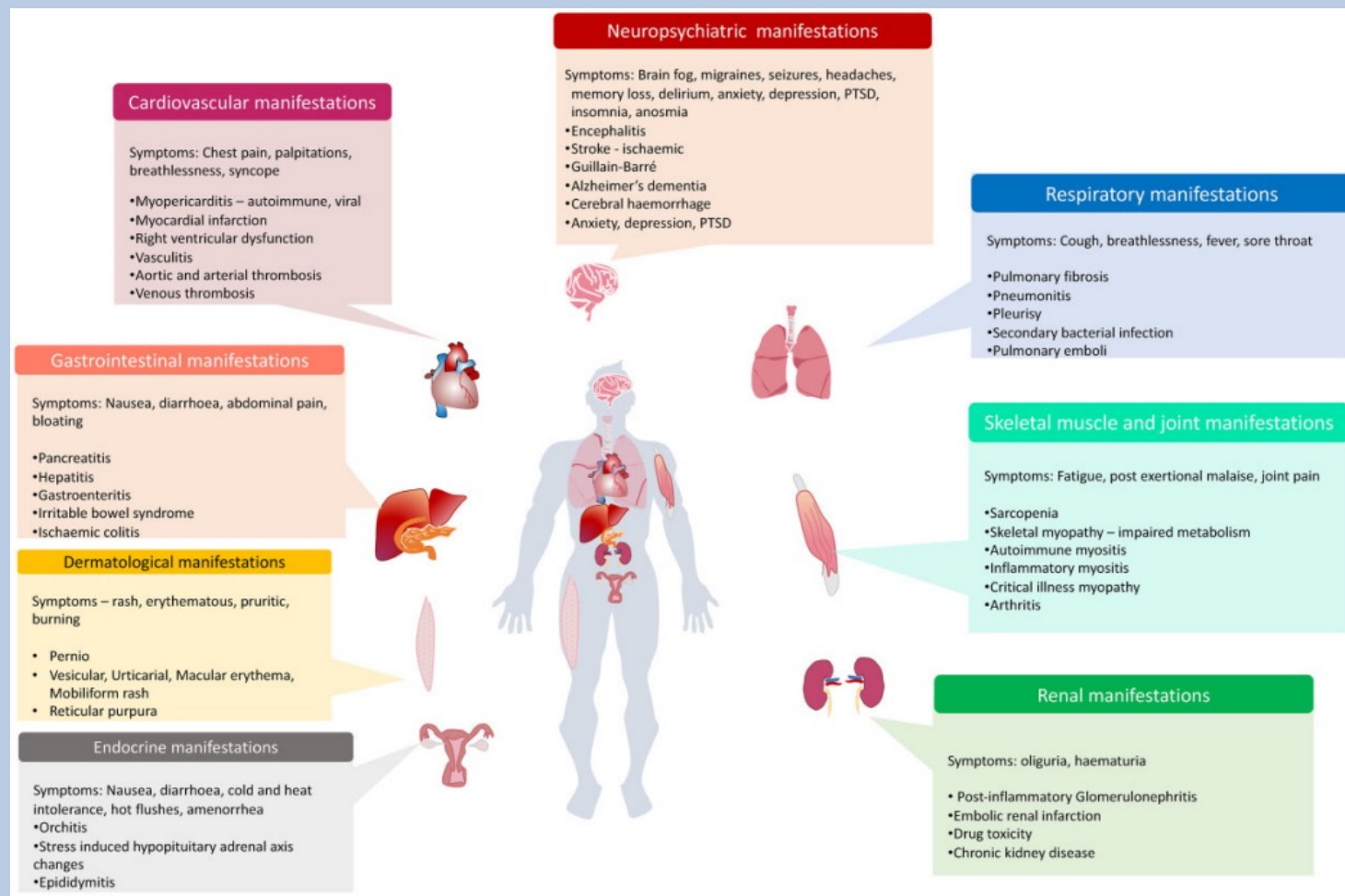


Zudem wurden in der Literatur weitere Begriffe wie z.B. „post-acute sequelae of COVID-19“ (PASC), „post-acute COVID syndrome“ (PACS), „chronic COVID syndrome“ (CCS) oder „COVID-19 long-hauler“ beschrieben. In Anlehnung an den Cochrane Rehabilitation-Review [16] und eine internationale Delphi-Konferenz unter Beteiligung der WHO [17] kann eine der folgenden drei Kategorien herangezogen werden, um ein Long/Post-COVID-Syndrom zu diagnostizieren:

- 1) Symptome, die nach der akuten COVID-19 oder deren Behandlung fortbestehen,
- 2) neue Symptome, die nach dem Ende der akuten Phase auftreten, aber als Folge der SARS-CoV-2-Infektion verstanden werden können,
- 3) Verschlechterung einer vorbestehenden Erkrankung in Folge einer SARS-CoV-2-Infektion.



Long Covid: Post-acute sequelae of Covid-19 with a cardiovascular focus



Long Covid Syndrom

Pragmatische Einteilung der Symptommhäufigkeit von Long-/Post COVID nach aktueller Literatur ohne Anspruch auf Vollständigkeit

Sehr häufig

- Fatigue
- Dyspnoe (Ruhe –Belastung)
- Leistungs-/Aktivitätseinschränkung
- Kopfschmerzen
- Muskel- und Gelenkschmerzen
- Riech- und Schmeckstörungen

häufig

- Husten
- Schlafstörungen
- Depressive Verstimmung
- Angstsymptomatik
- PTBS Symptome
- Allg. Schmerzen
- Verändertes Atemmuster
- Kognitive Einschränkungen
- Zwangshandlungen
- Haarausfall
- Stress

selten

- Lähmungen und Sensibilitätsstörungen
- Schwindel
- Übelkeit
- Diarrhoe
- Appetitverlust
- Tinnitus
- Ohrenschmerzen
- Stimmverlust
- Palpitationen
- Tachykardie



Long Covid Syndrom

Klinische Manifestationen ?

Participant and clinical characteristics	Follow-up duration	Symptom (% prevalence)
N = 110; median age = 60; 44% females; 100% inpatients; 24.5% had mild disease; 59% had moderate disease; 16.4% had severe disease; Bristol, England.	Median of 83 days after hospital discharge.	• ≥1 symptom (74%) • Dyspnoea (39%) • Fatigue (39%) • Insomnia (24%) • Myalgia (22%) • Cough (11%) • Anosmia (11%) • Arthralgia, headache, abdominal pain, diarrhoea (<5%).
N = 238; median age = 61; 40.3% females; 100% inpatients; 72.3% needed supplemental O ₂ ; 11.8% admitted to ICU; 8.8% needed MV; Novara, Italy.	4 months after hospital discharge.	• Post-traumatic stress symptoms (17%) • Arthralgia (5.9%) • Myalgia (5.9%) • Dyspnoea (5.5%) • Ageusia, anosmia, cough, diarrhoea, and chest pain (≤5%)
N = 143; 56.5 ± 14.6 years; 37.1% females; 100% inpatients; 53.8% needed supplemental O ₂ ; 12.6% admitted to ICU; 14.7% needed non-invasive ventilation; 4.9% needed MV; Rome, Italy.	Mean of 60 days after hospital discharge.	• ≥1 symptom (87.4%) • Fatigue (53.1%) • Dyspnoea (43.4%) • Worsened quality of life (44.1%) • Joint pain (27.3%) • Chest pain (21.7%)
N = 21,359 (only 233 were COVID-19 survivors; 96.6% outpatients); median age = 56; 63.6% females; 83.7% Europeans.	90 days after symptom onset.	• Symptom lasting for >30 days (42.3%). • Symptom lasting for >60 days (33.8%). • Symptom lasting for >90 days (24.1%). • Symptoms: concentration and memory problems, anosmia, ageusia, dyspnoea, headache, heart palpitations, chest pain, tachycardia, and cough.
*N = 3,762; age groups of 18-29 (8%), 30-39 (26.1%), 40-49 (33.7%), 50-59 (27.1%), 60-69 (11%), 70-79 (2.5%), 80+ (0.4%) years; 78.9% females; 56.7% did not seek hospital care; 34.9% outpatients; 8.43% were hospitalized; 56 countries (41.6% from U.S.).	6-7 months after symptom onset.	• Fatigue (80%) • Post-exertional malaise (73.3%) • Cognitive dysfunction (58.4%) • Sensorimotor symptoms (55.7%) • Headaches (53.6%) • Memory issues (51.0%) • Insomnia, heart palpitations, and muscle aches (40-50%) • Dyspnoea, dizziness and balance issues, speech and language issues, joint pain, tachycardia, and other sleep issues (30-40%) • Reduced work schedule (45.2%) • Unable to work (22.3%)



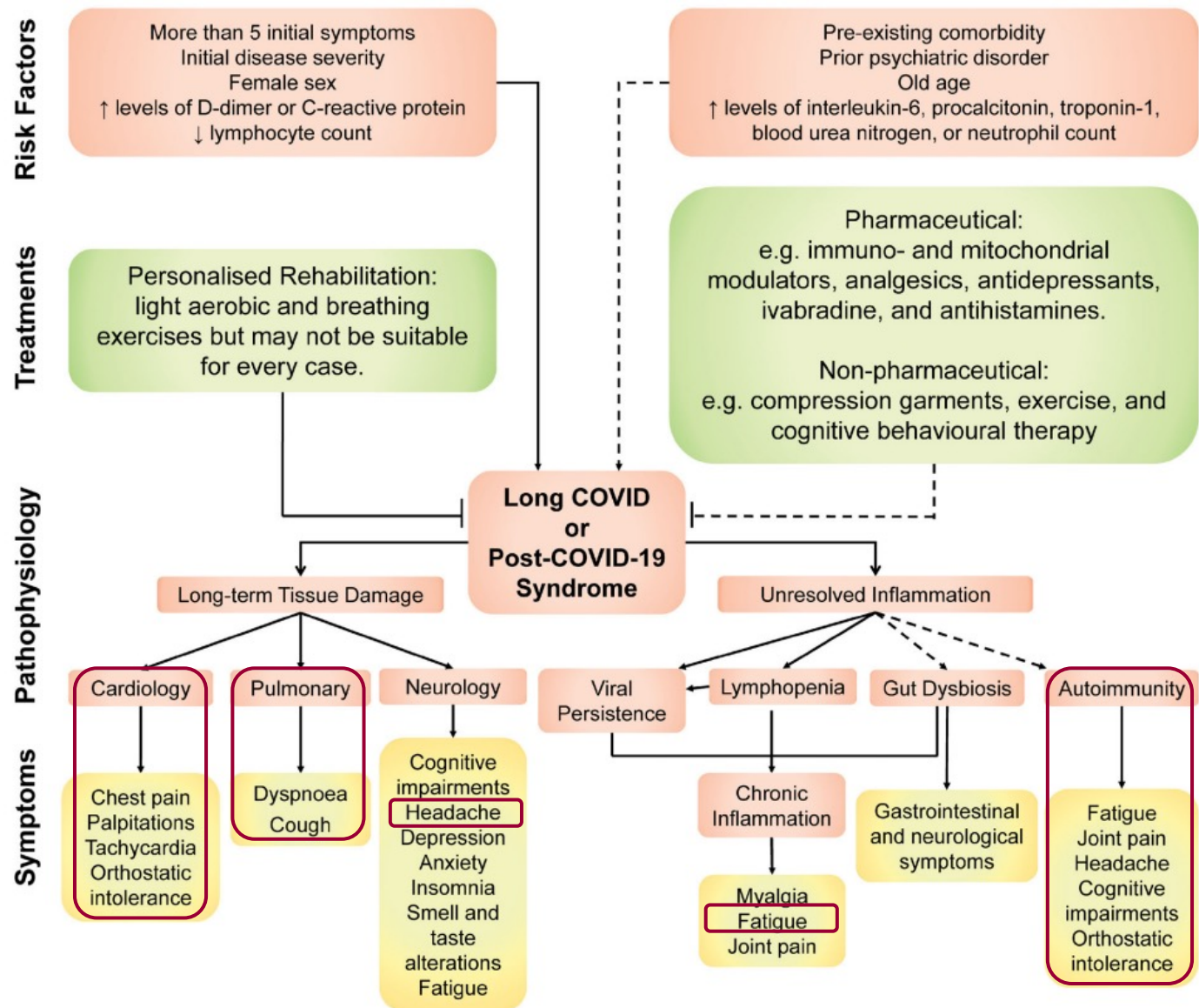


Figure An overview of the symptoms, putative pathophysiology, associated risk factors, and potential treatments involved in long COVID. Note: Dashed lines represent areas where evidence is relatively lacking compared to non-dashed lines. (Color online only).



Long Covid Syndrom

Pathophysiologie ?

- SARS-CoV-2 particles may become active again, causing symptoms to reappear.
- **Overactive immune cells may release high levels of inflammatory substances that can injure organs and tissues.**
- The infection may cause the immune system to start making autoantibodies that attack a person's own organs and tissues.



Long Covid Syndrom

Factors anticipating PACS

- Latente EBV Reaktivierung und SARS-CoV2-RNAemia zu Beginn einer Covid-Erkrankung antizipieren PACS
- Diverse Autoantikörper (z.B. SLE-assoziierte ANAs; anti-IFN- α 2; u.a.m.) antikorrelieren mit SARS-CoV2-Antikörpern
- T-Zellen Dynamik (z.B. ungewöhnliche Expansion von zytotox. CD4+ T-Zellen sind mit gastrointestinaler Form von PACS assoziiert).
- CMV-spezifische T-Zellen 'bystander' Aktivierung mit GI –PACS assoziiert.
- Pat mit **vorbestehenden Autoimmunerkrankungen** sind mutmaßlich **anfälliger für Long Covid**



Covid-19 und Cardiovasculäres System

Kardiovaskuläre Manifestationen

***Fatigue Syndrom u.
autonome
Funktionsstörungen***

Fatigue Syndrom CORONA-PANDEMIE

häufiger als bisher gedacht ?



Folgen des Coronavirus

Ein Fünftel chronisch erschöpft

Eine Vergleichsstudie liefert weitere Erkenntnisse über das Fatigue-Syndrom nach einer Corona-Erkrankung. Ein knappes Fünftel der Infizierten hat demnach nach mehr als sechs Monaten noch Beschwerden.



ME / CFS

(Myalgische Enzephalomyelitis / Chronic fatigue Syndrom)

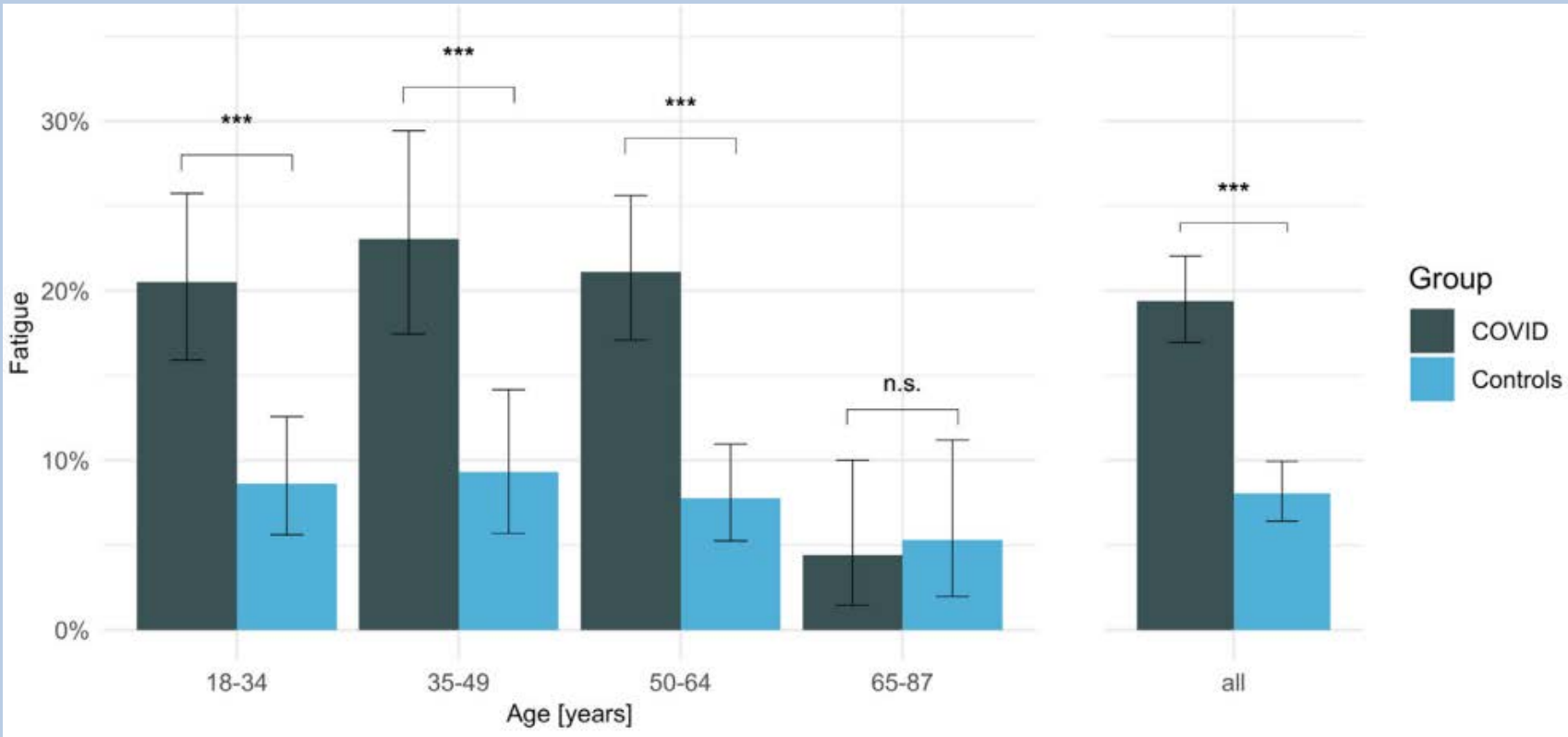
- vermutlich neuro-immunologische Systemerkrankung
- Leitsymptom: schnelle körperliche u. geistige Erschöpfbarkeit; Gedächtnisstörungen, Kopfschmerzen, Grippeähnliche Symptome; ggf später auch psychische Beeinträchtigungen
- oft schwere Einschränkung der Lebensqualität; 25% verlassen das Haus kaum; bis zu 60% AU !
- Pat mit **vorbestehenden Autoimmunerkrankungen** sind mutmaßlich **anfälliger für Long Covid**



Fatigue and cognitive impairment after COVID-19: A prospective multicentre study

Tim J. Hartung,^{a,b,†} Christian Neumann,^{c,†} Thomas Bahmer,^{d,e} Irina Chaplinskaya-Sobol,^f Matthias Endres,^{a,g,h,i,j} Johanna Geritz,^c Karl Georg Haeusler,^k Peter U. Heuschmann,^{l,m} Hanna Hildesheim,^c Andreas Hinz,^b Sina Hopff,ⁿ Anna Horn,[†] Michael Krawczak,^o Lillian Krist,^p Jennifer Kudelka,^c Wolfgang Lieb,^q Corina Maetzler,^c Anja Mehnert-Theuerkauf,^b Felipe A. Montellano,^{l,k,r} Caroline Morbach,^s Sein Schmidt,[†] Stefan Schreiber,^u Flo Steigerwald,^a Stefan Störk,^{v,w} Walter Maetzler,^{c,†} and Carsten Finke^{a,†,*}

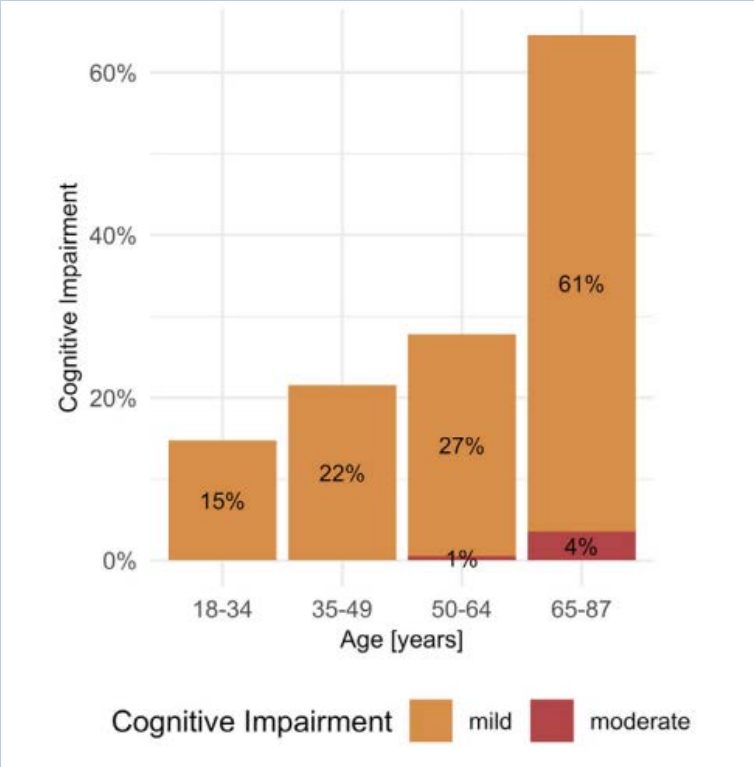
eClinicalMedicine
2022;53: 101651
Published online xxx
<https://doi.org/10.1016/j.eclinm.2022.101651>



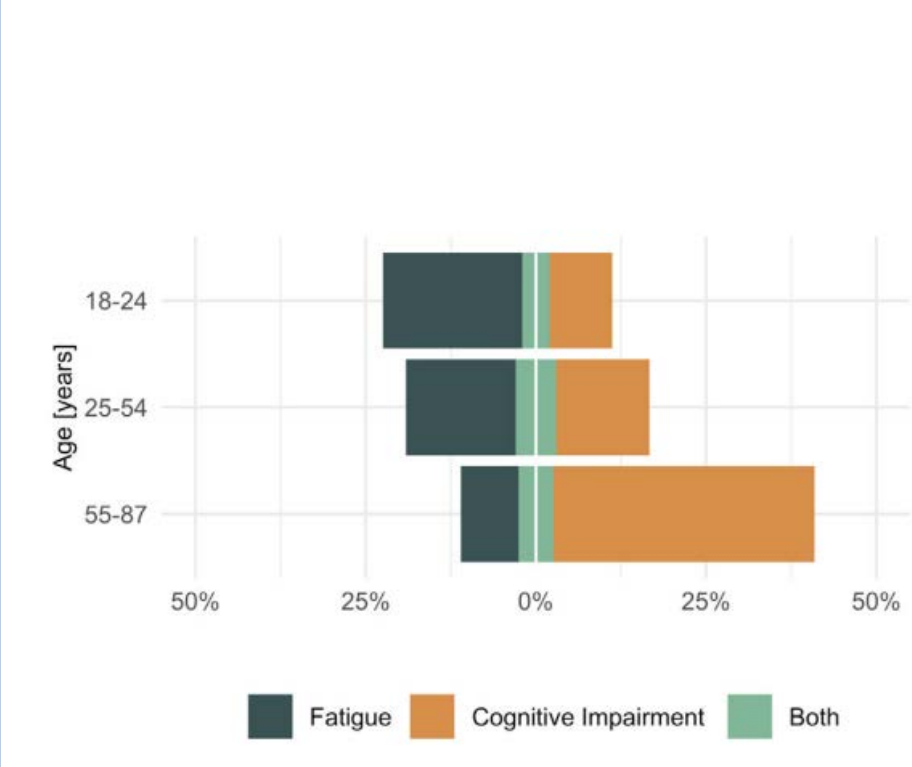
Frequency of fatigue by age in patients ≥ 6 months after SARS-CoV-2 infection (n = 969) and matched general population controls (n = 969), *** p < 0.001, n.s. non-significant



Fatigue Syndrom *und / oder* kognitive Störungen



Frequency of mild and moderate cognitive impairment in n = 969 patients by age

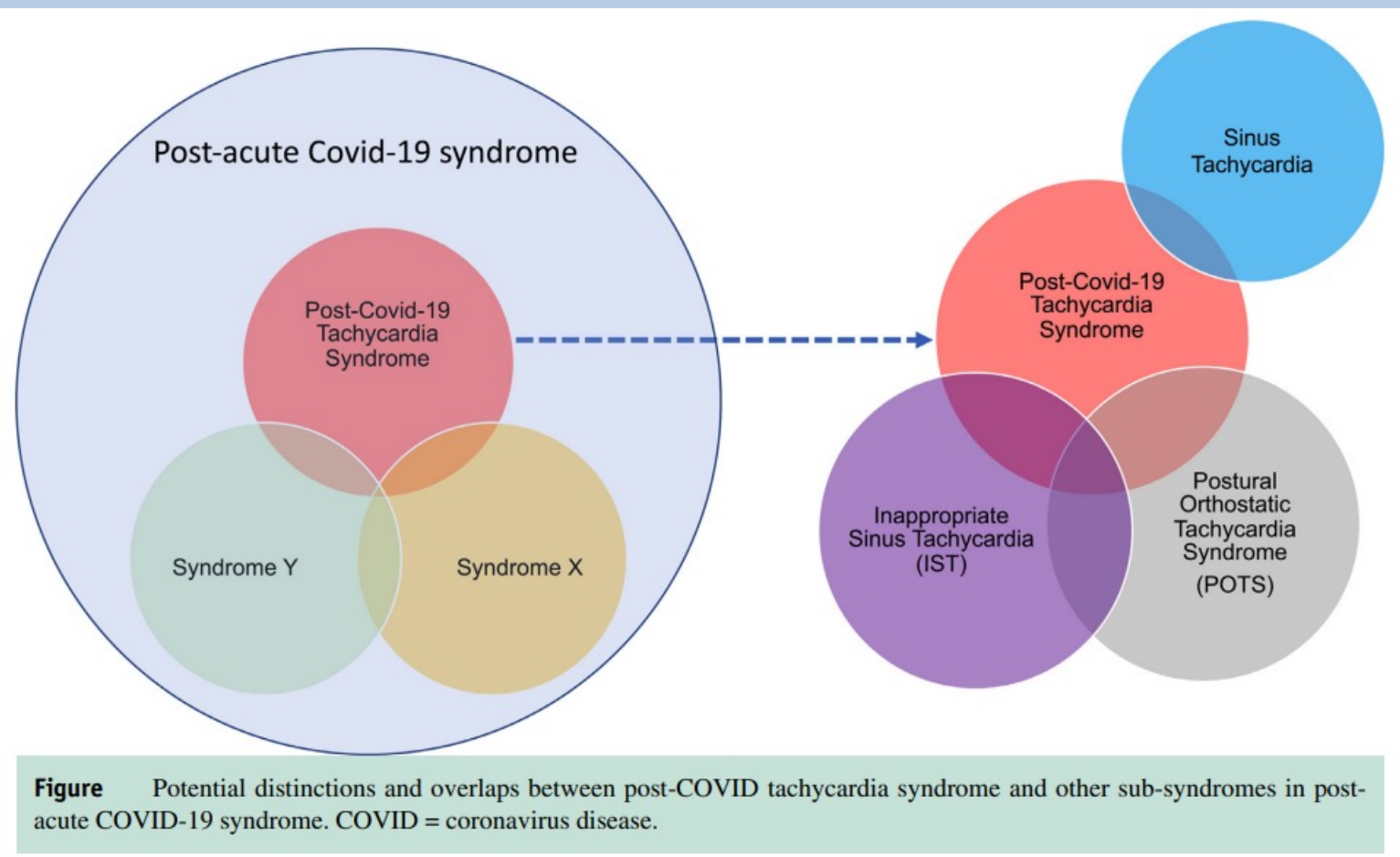


Fatigue was more common in younger patients, compared to cognitive impairment, which was more common in older patients. Between 4% and 6% of patients suffered from both fatigue and cognitive impairment.



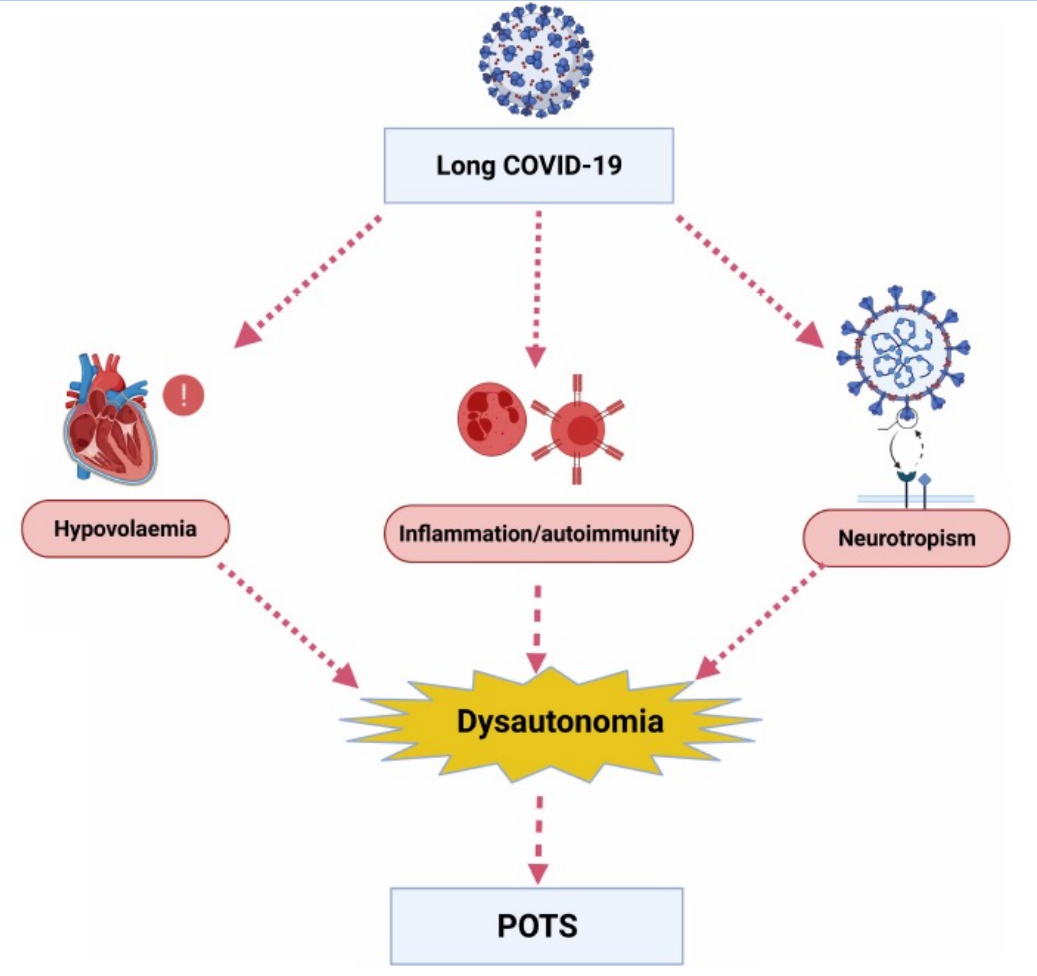
Autonomic dysfunction in Long Covid

"Post-Covid Tachycardia Syndrome"



Autonomic dysfunction in Long Covid

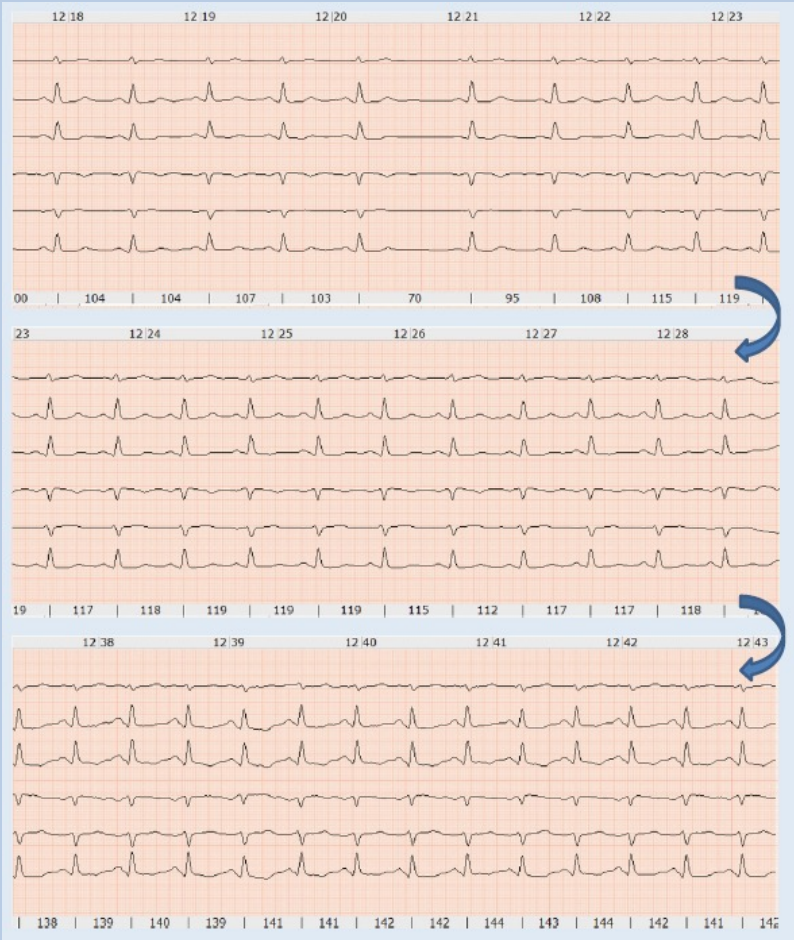
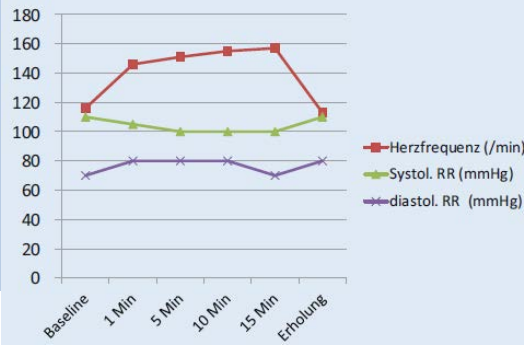
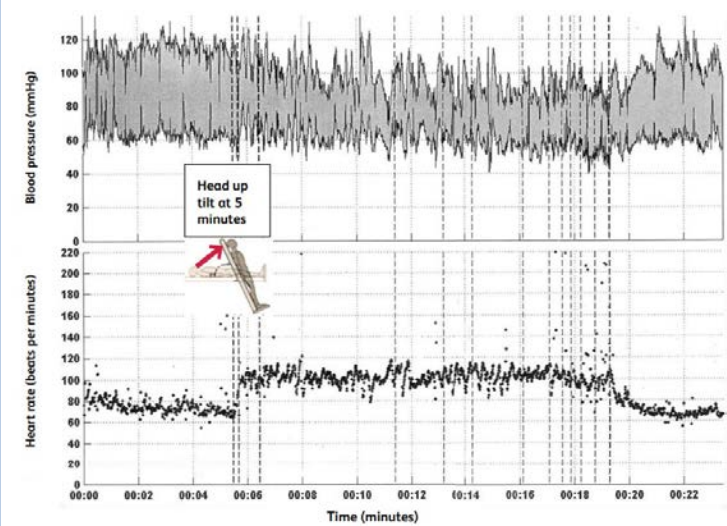
Pathophysiologie



Autonomic dysfunction in Long Covid

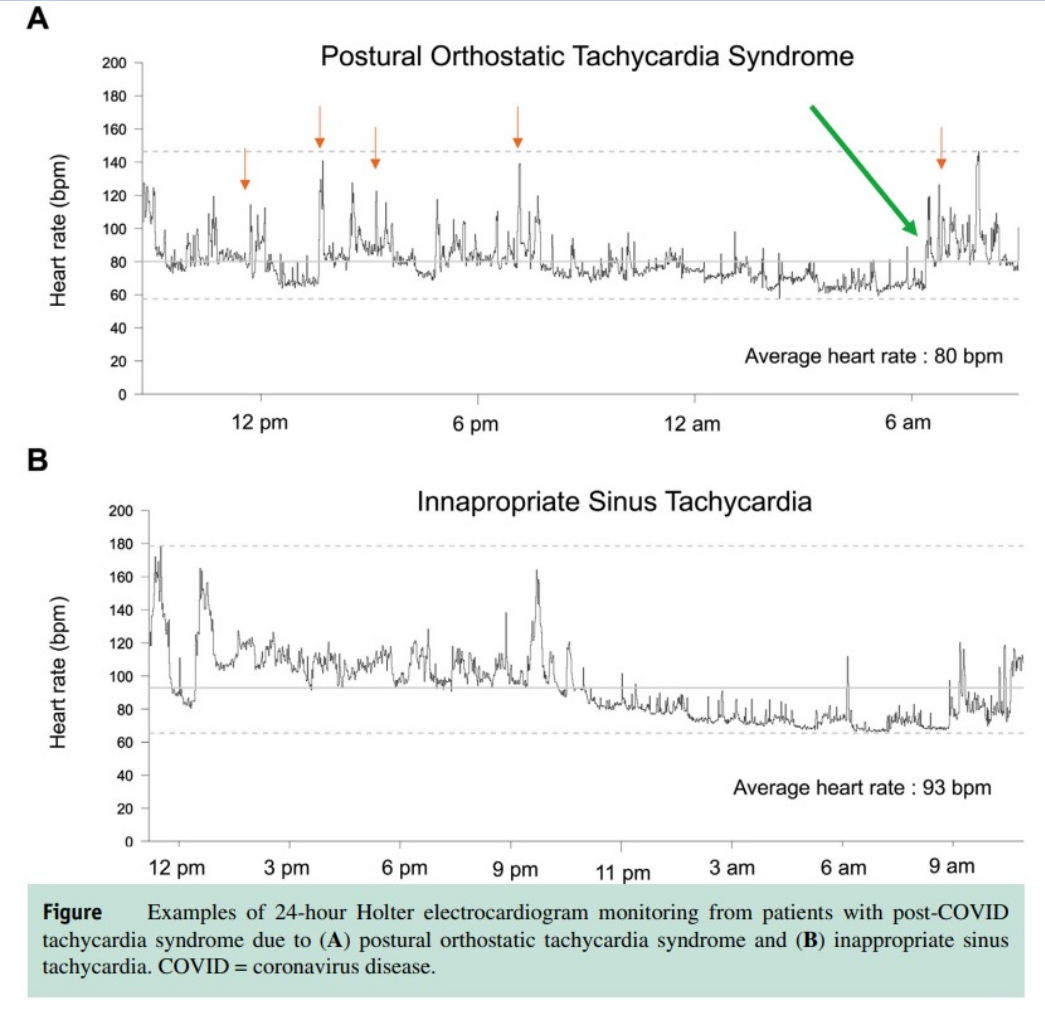
Klinische Probleme

- **Orthostatische Intoleranz / - Hypotonie**
- **POTS (posturales Tachykardie-Syndrom)**



Autonomic dysfunction in Long Covid

"Post-Covid Tachycardia Syndrome" (POTS / IAST)



Autonomic dysfunction in Long Covid

Therapie ?

Isometric exercises . Simple physical isometric counter-manoeuvres can be taught to those with orthostatic hypotension. These simple exercises involve sustained tensing of muscles which increases venous return to the heart and raises blood pressure. These counter-pressure manoeuvres include tensing thigh and buttock muscles, crossing arms and legs, folding arms and leaning forward, squatting, or raising a leg and placing the foot on a stool.

Compression garments . In orthostatic hypotension, compression garments extending up to the waist, or abdominal binders, are effective and tolerable

Orthstatic intolerance:

- Flüssigkeit 2-3 l täglich
- Kochsalz 2-3 g täglich (z.B. als Kapsel)
- Fludrocortison 0,1 mg /d
- Midodrin 2 mg Tbl 1-2x/d

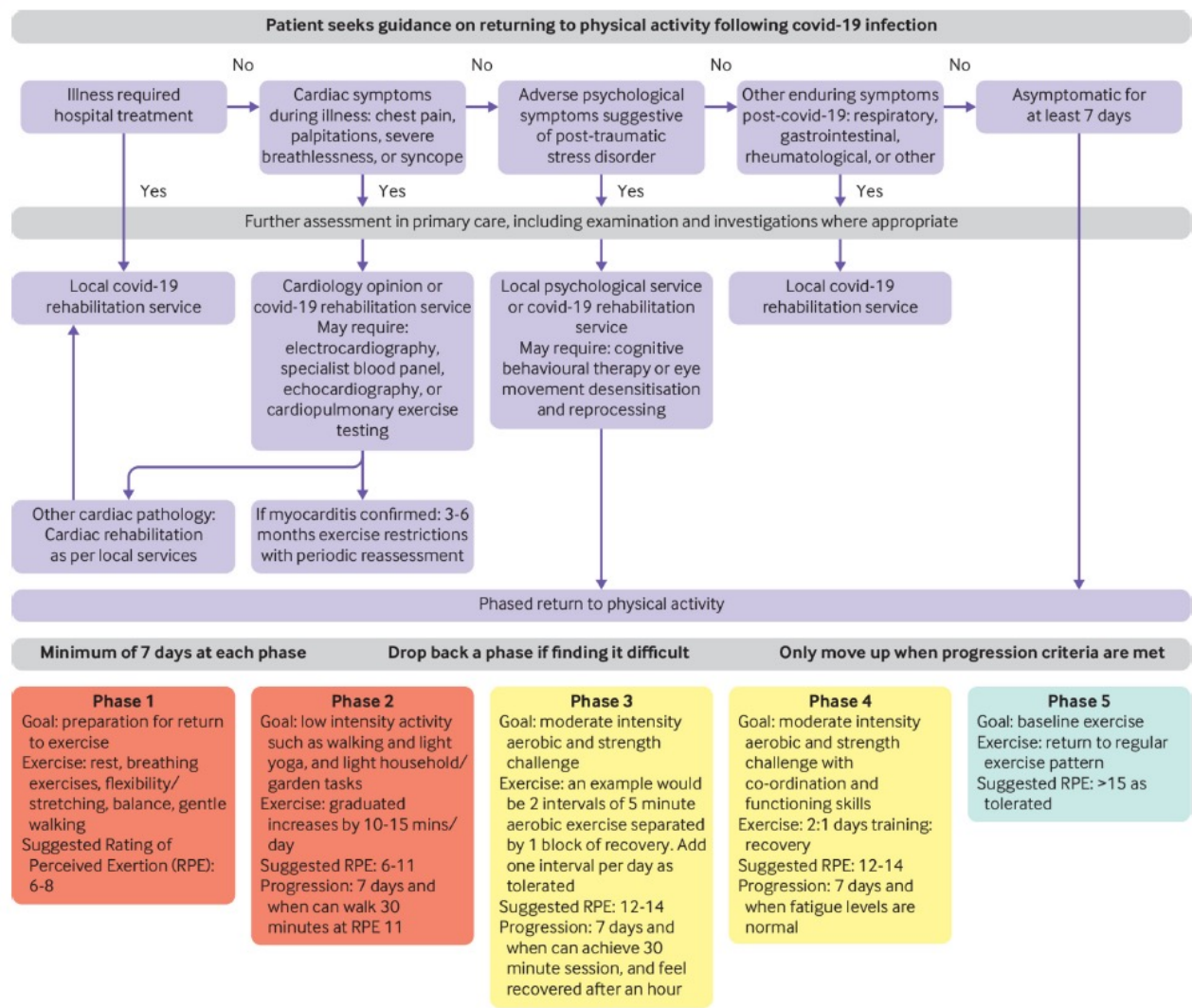
POTS

- leichter Konditionssport
- low-dose β -Blocker
- Ivabradin (ggf. in Kombination mit β BL)



Nach Covid-19 Infektion / Long Covid

Wiedereinstieg in körperliche Aktivität – Bedeutung der REHA



Kardiovaskuläre Manifestationen bei CoV19-Infektion

Zusammenfassung and Take-home (I)

- *Eine kardiale Mitbeteiligung bei Covid-19 verschlechtert die Prognose*
- *Auch nach klinischer Erholung können - selbst bei Fehlen von inflammatorischen Parametern - myokardiale Alterationen nachweisbar sein (STE / myocardial strain; MRI).*
- *Die Prognose korreliert jedoch vor allem mit der Schwere der Inflammation - und damit dem Nachweis inflammatorischer Aktivität.*
- *Alter - Begleiterkrankungen - Polypharmakotherapie*



Kardiovaskuläre Manifestationen bei CoV19-Infektion

Zusammenfassung and Take-home (II)

- *Vorhofflimmern stellt die häufigste Arrhythmie bei Covid dar, und ist -wenn neu-aufgetreten - ein prognostischer Marker.*
- *Vor allem bei ausgeprägtem „myocardial injury“ und LV-Dysfunktion auch erhöhtes Risiko für ventr. Arrhythmien.*
- *Long-Covid / post-Covid betrifft nicht nur schwer kranke Patienten sondern kann bei vielen Betroffenen die klinische Hauptmanifestation der Infektion sein.*
- *Neben diversen Organbeteiligungen und Symptomen spielen CFS und autonome Kreislaufdysregulation (POTS / OI) in der kardiolog. Praxis eine Rolle.*



A digital illustration of a human torso, primarily in shades of blue and purple, with a glowing red heart visible in the center. The image is overlaid with several blue, wireframe virus particles, some of which are larger and more prominent than others. The text "VIELEN DANK" is written in large, white, sans-serif capital letters across the middle of the image, partially overlapping the virus particles and the torso.

VIELEN
DANK



COVID-19 Treatment Guidelines



Coronavirus Disease 2019 (COVID-19) Treatment Guidelines

