

# Long Covid in family medicine

Follow-up of a cohort of patients suffering from Long  
Covid in a family practice

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a discovery by rowing,



in patients who are usually quiet



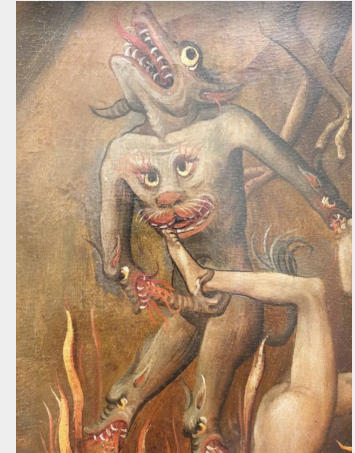
with very strange symptoms,



life turned upside down,



and pain everywhere



Jerome Bosh, Triptych of The Temptation of Saint Anthony (ca. 1520-1530) MBA Brussels





# Plan

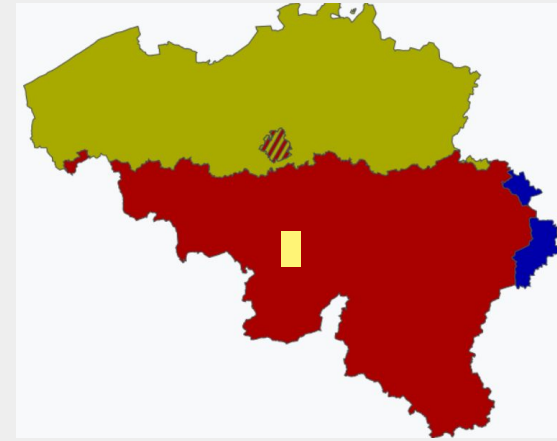
- Introduction: Main issues / lessons from clinical practice
- Methods; narrative/ isotopes / indicators
- Results : follow up of 52 PACS patients
- Discussion ; difficult paths
- Key messages :



Ben Genaux (1911-1996)  
No comment. No date

## Primary care practice setting

- Charleroi, Belgium, Low income area
- Private group practice (fee for service)
- Three GPs, One trainee, Two nurses
- 2000 Patients
- Pandemic time (2020-2022)



# Long Covid

The condition that occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis

CDC. February 11, 2020.

<https://www.cdc.gov/coronavirus/2019-ncov/long-term-effects/index.html>



**Table 1.** Summary of the described manifestations of PCS; (\*) represents the most commonly reported symptoms [4,8,18,20,21,24]. (PCS : Post Covid syndrome)

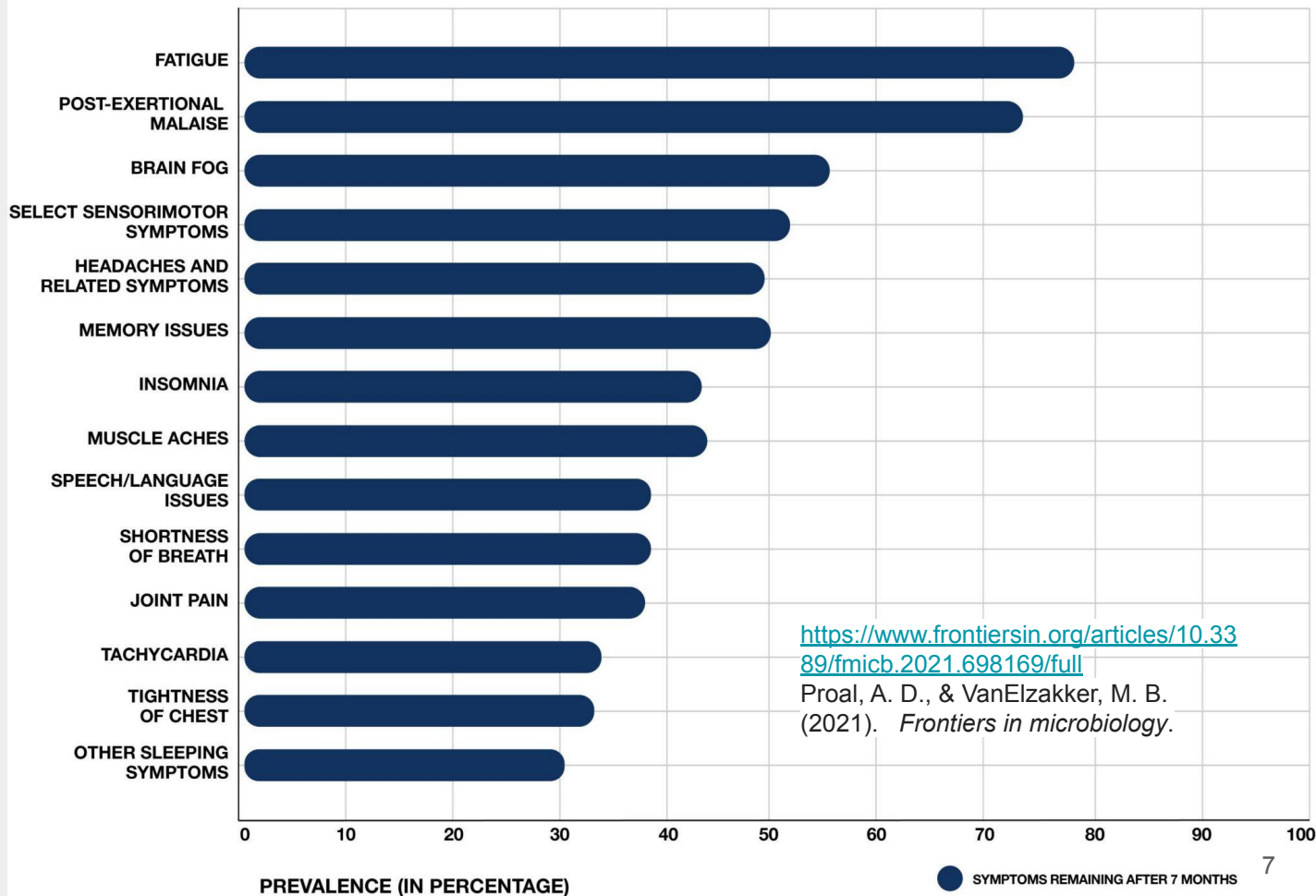
Respiratory sequelae	Dyspnea *, cough, sore throat, altered diffusion capacity, restrictive pattern, obstructive pattern
Cardiac sequelae	Palpitations, chest pain, myocarditis
Gastrointestinal sequelae	Vomiting/nausea, diarrhea
Neurological sequelae	Anosmia, loss of taste, anxiety *, depression, sleeping difficulties, concentration/memory problems *, dizziness, chronic fatigue*, headache
Other sequelae	Joint pain, post-exertional malaise *, increased incidence of pain, antihypertensive, and antidepressant drugs



Long Covid  
multi-systemic  
disabling  
condition with no  
treatment

Six months after a  
coronavirus infection,  
at least one in seven  
people still have some  
symptoms. [KCE  
Reports 344 \(2021\)](#)

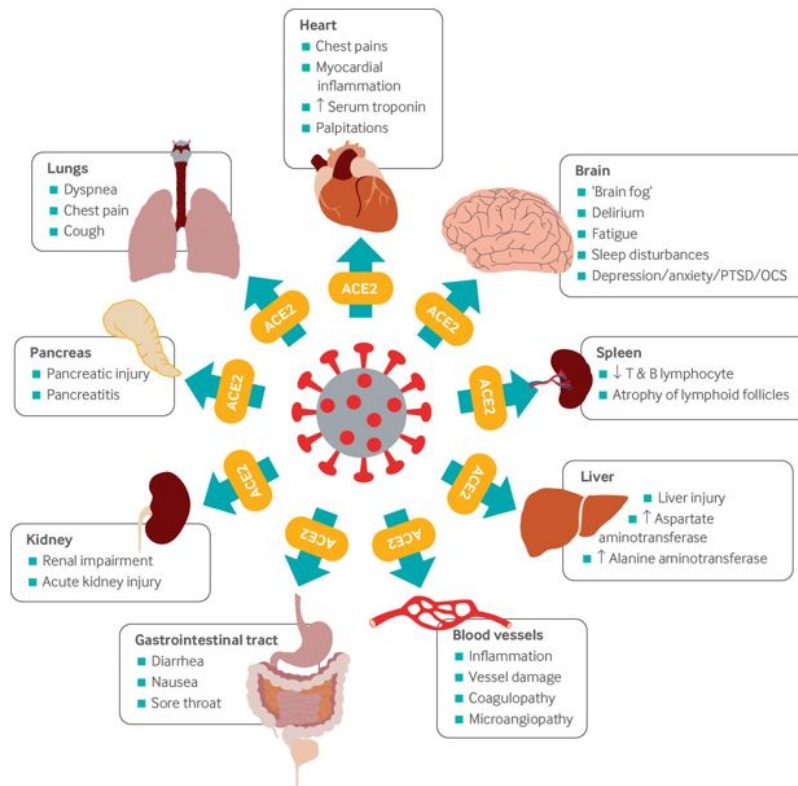
## REMAINING SYMPTOMS AFTER MONTH 7 (PREVALENCE >30%)







## Multi-organ complications of covid-19 and long covid.



Harry Crook et al. BMJ 2021;374:bmj.n1648







# Narrative medicine

when doctors take a medical history they inevitably act as ethnographers, historians, and biographers, required to understand aspects of personhood, personality, social and psychological functioning, and biological and physical phenomena

EMR notes  
Interviews

Greenhalgh T, Hurwitz B. . *BMJ*.  
1999;318(7175):48-50.  
<https://www.bmj.com/content/318/7175/48.1>



# DUSOI WONCA Severity index

Parkerson 1996 DUSOI WONCA  
<https://tinyurl.com/DUSOIWONCAscore>

- (1) symptoms during the past week,
- (2) complications during the past week,
- (3) the prognosis of the problem evolving without treatment during the following six months,
- (4) the possibility of treatment

## \* RAW SCORES

	None	Questionable	Mild	Moderate	Major	
1. <u>Symptoms</u> (past week):	0	1	2	3	4	
2. <u>Complications</u> (past week):	0	1	2	3	4	
<u>Disability</u>						
3. <u>Prognosis</u> (next 6 months, without treatment):	None 0	Mild 1	Moderate 2	Major 3	<u>Threat to Life</u> 4	
<u>Need for Treatment</u>						
4. <u>Treatability</u> :	No 0	Questionable 1	<b>IF YES</b> JJ 2	<u>Expected Response to Treatment</u> Good 2	Questionable 3	Poor 4

## \*\* SEVERITY CODES

Total Raw Score	=	Severity Code	Severity
0	=	0	Zero
1 - 4	=	1	Low
5 - 8	=	2	Intermediate
9 - 12	=	3	High
13 - 16	=	4	Maximum



# Functional indicator COOP WONCA

van Weel et al COOP WONCA  
<https://tinyurl.com/COOPWONCA>

### Feelings

During the past 2 weeks...  
How much have you been bothered by e  
feeling anxious, depressed, irritable or d

### Daily activities

During the past 2 weeks...  
How much difficulty have you had doin  
tasks, both inside and outside the house  
and emotional health?

### Social activities

During the past 2 weeks...  
Has your physical an emotional health limited your social activ  
with family, friends, neighbours or groups?

### Change in health

How would you rate your overall health now com  
2 weeks ago?

### Overall health

During the past 2 weeks...  
How would you rate your health in general?

### Physical fitness

During the past 2 weeks...  
What was the hardest physical activity yo  
2 minutes?

Very heavy, (for example) run, at a fast pace
Heavy, (for example) jog, at a slow pace
Moderate, (for example) walk, at a fast pace
Light, (for example) walk, at a medium
Light, (for example)

Not at all
Slightly
Moderately
Quite a bit
Extremely

No difficulty at all
A little bit of difficulty
Some difficulty
Much difficulty
Could not do

Not at all	
Slightly	
Moderately	
Quite a bit	
Extremely	

Much better	▲▲
A little better	▲
About the same	↔
A little worse	▼
Much worse	▼▼

Excellent	
Very good	
Good	
Fair	
Poor	



52 Long Covid patient carefully followed; data available in Google sheet

SPECT-CT were requested in 29 patients with all 3 of the following criteria:

- Clinical symptoms suggesting a brain disorder in the context of the Covid pandemic
- a degree of severity at 3 or 4 on the DUSOI/WONCA
- a functional status at more than 20 points on the COOP/WONCA



# Nuclear medicine resources



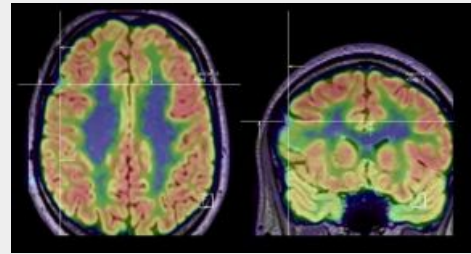
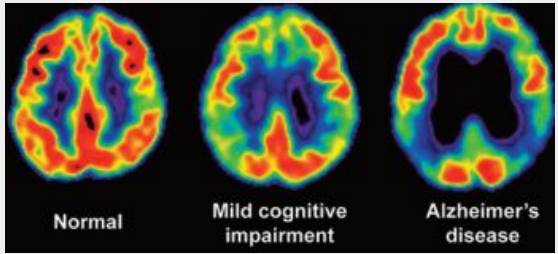
## SPECT CT

- can be prescribed by GP
- lower sensitivity, similar specificity
- less clear images / vascular flow
- reimbursed €222
- high environmental cost



## 8FDG PET

- prescribed by specialist / not reimbursed in COVID
- higher sensitivity, similar specificity
- detailed images / glucose metabolism
- high cost
- very high environmental cost (isotopes produced by cyclotron)

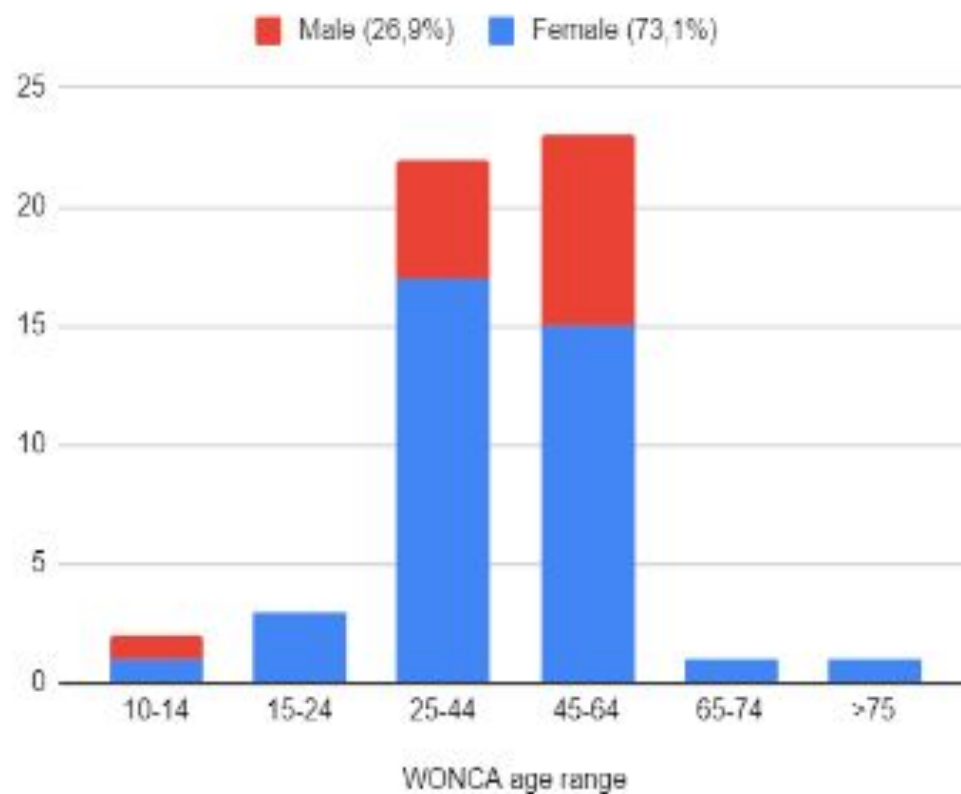




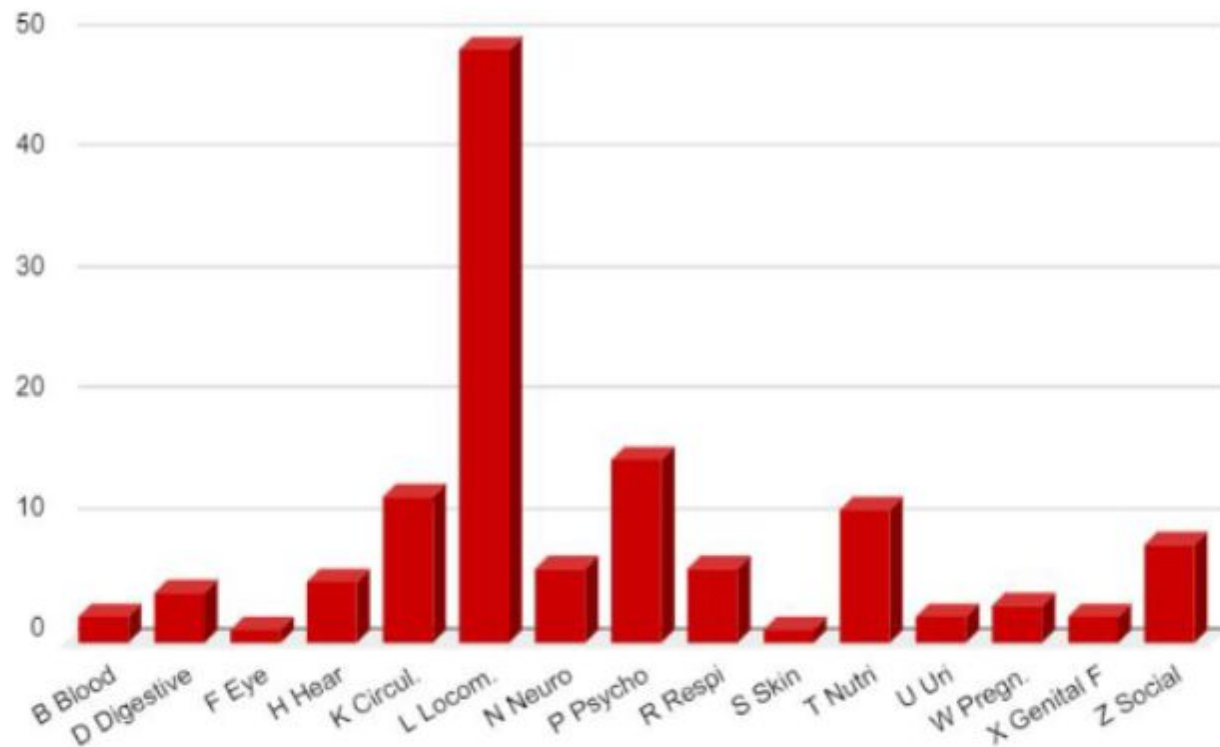


**Table 1.** Patients with clinical PACS met in a general family practice. Main data collected from May 2021 to to June 2022 for 52 patients.

Nr. of patients with clinical PACS	52
Nr. of women	38 (73,1%)
Mean age	43,2 (12 to 79)
Nr. of patients vaccinated	45
Nr. of vaccine by patient	1; once, 16; two, 28; three
Nr. of vaccinated patients with adverse reactions	local 5 / systemic 29
Nr. of patients with no laboratory proof	20
Nr. of available positive PCRs	32
Nr. of cerebral SPECT-CT with altered perfusion	29/31 ordered
Nr. of cerebral SPECT-CT control	7 improve / 6 worsen
Nr. of pat. severe to very severe	47 (DUSOI 3 or 4)
Nr. of pat. with altered to very altered functional status	37 (COOP Charts >20)
Pat. cured without sequel after 6 to 8 months	16
Cured pat. with minor sequels after 12 to 18 months	15
Pat. with persistent encephalopathy after 18 months	21
Mean nr. of months of illness	15 (min 2; max 27)



**Figure 1.** Age-sex distribution of 52 patients clinically identified as having PACS in a family practice.



**Figure 2.** Number of health problems or diagnosis found in the diagnostic index of 34 patients at the time of diagnosis of Long Covid, coded in *ICD-10* chapters. (excluding Long Covid related symptoms and diagnosis)



## The Covid patient's journey

<p>The acute Covid experience</p>	<p><i>Before I got sick with COVID, I was generally feeling fine because I was used to my condition. But when I got Covid, everything became more difficult..." "Before the Covid I was mentally pretty good, a little depressed but not much. But with Covid, I was at my lowest point. A week to ten days later, I became extremely sick and more and more afraid. I could hardly see, I couldn't even hold my phone. I felt like I had no oxygen left in my brain and I had to go to the window to breathe. I had awful headaches. I was thinking, 'I'm going to die, I'm going to die,' 'Why me? Why did I get the Covid?'. I wanted to die. Life seemed very dark to me, and I didn't feel like living, I didn't feel like eating. Even tea, which I usually like to drink, disgusted me. (...) For more than three weeks, I didn't eat, I lost weight, I couldn't sleep, I woke up at night, I cried and cried... I didn't know how to do anything.</i></p>
<p>The Long Covid period</p>	<p><i>For nine months I didn't laugh, I was always tired, I didn't go out, I was always in the chair. I had to eat all the time, I gained 7 kgs. I would have hunger attacks, and when I didn't eat, I would shake. In the morning, when I woke up, I ate, at night, I woke up and ate. Every morning I was waiting for the night to come and every night I waited for the morning. The days were endless because I was sick, I did nothing. I couldn't stand the TV or the noise. Before Covid, I thought I was a beautiful woman but when I looked at myself in the mirror, I said to myself "I am so old, as if I had aged ten years" I forgot a lot. Words, names. I had to repeat to myself "I must not forget, I must not forget". My brain was working backwards. I was angry for no reason. I was wondering "when will I die?</i></p>

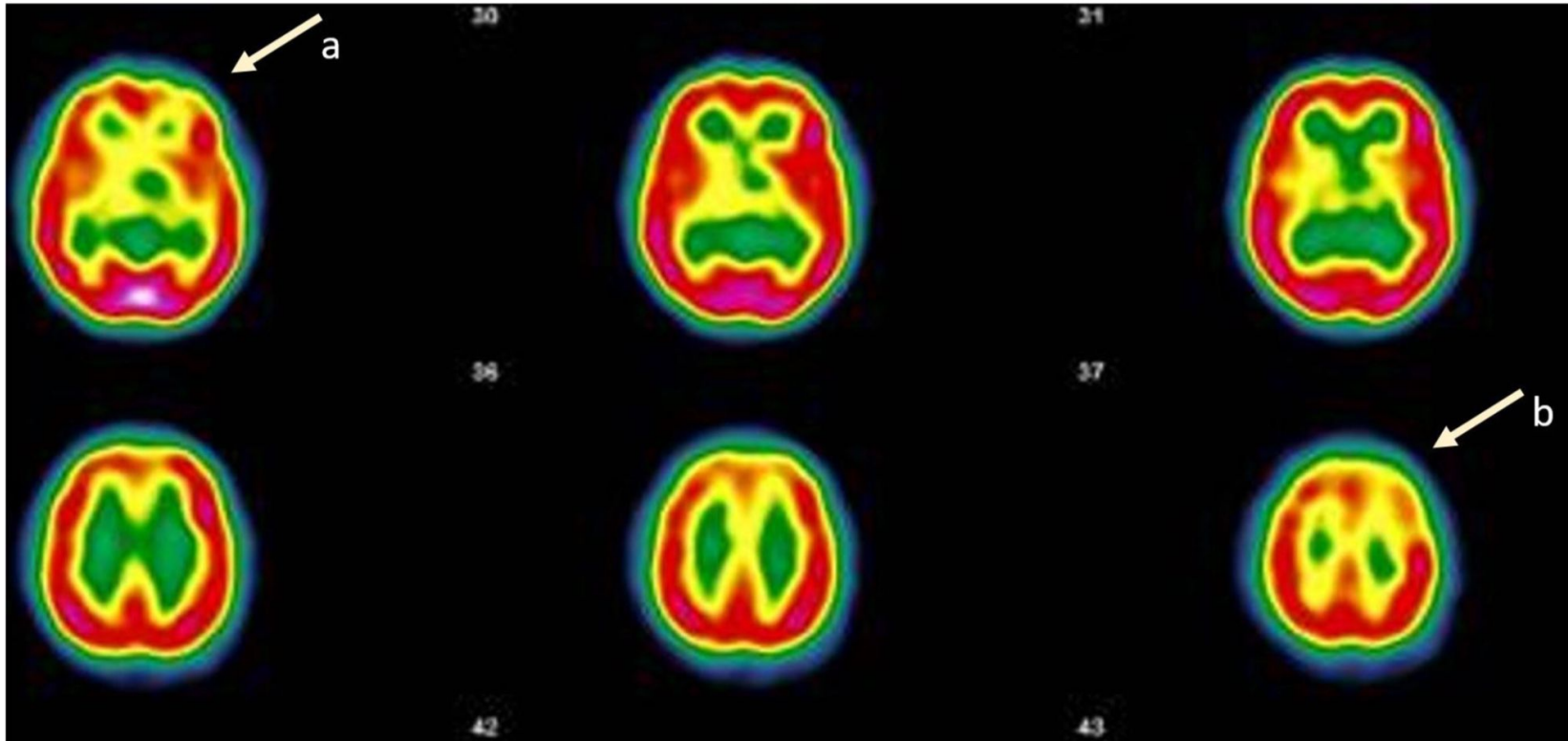


**Table 3.** Patients MGA001 & MGA013 with clinical Long Covid. Age, Sex, date of Acute Covid, date of of suspicion of Long Covid diagnosis, date of first SPECT-CT, EMRs notes, SPECT-CT protocols (Drs Bouazza and Mahy, Vesalius Hospital, ISPPC, Belgium). More de-identified data: <https://tinyurl.com/tablelongCovid>

Acute symptoms	Long lasting symptoms	SPECT-CT protocol
<p>MGA001</p> <p>F. 48, Oct. 13, 2020. ; throat pain, rhinorrhea, achy++, fatigue ++ and headache, but no breathing difficulties, dysgeusia ,anosmia. Stays at home, cured after 12 days. Home care only</p>	<p>Nov.11, 2020.;</p> <p>pain in both eyes, ocular pruritus, rapid ocular fatigue, noise intolerance, memory loss (forgets to pick up her daughter at school); concentration problem; remains isolated in her room; dyspnea at the slightest effort and at speech; almost continuous osteoarticular and muscular pains; often with headaches; abnormal dreams; depressive feeling; fatigue; effort exhaustion</p>	<p>July 27, 2021;</p> <p><i>On the images taken, left fronto-parietal, left frontal and left thalamic hypofixation is observed. No preservation of the sensory motor cortices. The fixation in front of the cerebellum is correct. Conclusion: Scintigraphic examination compatible with a cerebral pathology of the vascular type with clearer left fronto-parietal, left frontal and left thalamic vascular disorders.</i></p>
<p>MGA013</p> <p>F. 39. March 3, 2021 cough; aching; temperature; headache; 20 days in bed; loss of taste; loss of smell; tinnitus +++; 20 days in total; home care</p>	<p>Oct. 5, 2021</p> <p>Hearing loss in right ear; balance always disturbed; dizziness; vision loss; quickly tired; weight gain ++: quickly out of breath; became depressed; pain in left hip every night: post-vaccinations headaches; memory loss; word not found; repeats herself and doesn't realize it; forgets which groceries she went to get; has trouble concentrating ; disseminated myalgia; insomnia; loss of sense of direction</p>	<p>Nov. 17, 2021</p> <p><i>Heterogeneous tracer distribution throughout the cortex, with more marked hypofixation in the bilateral predominantly left superior parietal, left parietal, bilateral medial temporal and bilateral predominantly right parieto-occipital areas. Diffuse subcortical periventricular hypofixation. The basal ganglia and cerebellum show preserved and symmetrical tracer uptake. Scintigraphic image suggestive of vascular damage in the broad sense.</i></p>





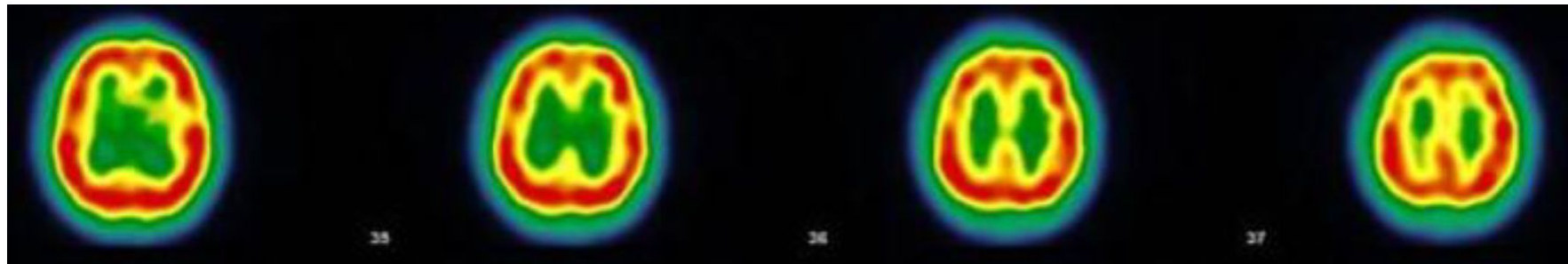


**Fig. 1** Patient MGA001 48. Long Covid persisting 9 months since acute illness with brain fog, abnormal dreams, depressive feeling, irrepressible fatigue, poor exercise tolerance. The brain SPECT CT scan shows hypofixation of the tracer in left cortico-frontal (a) and left fronto-parietal (b) areas. (Courtesy Drs Bouazza & Mahy, Vesale hospital, ISPPC, Belgium)



## Same patient as previous slide; spect ct , control after 6 months, aggravation

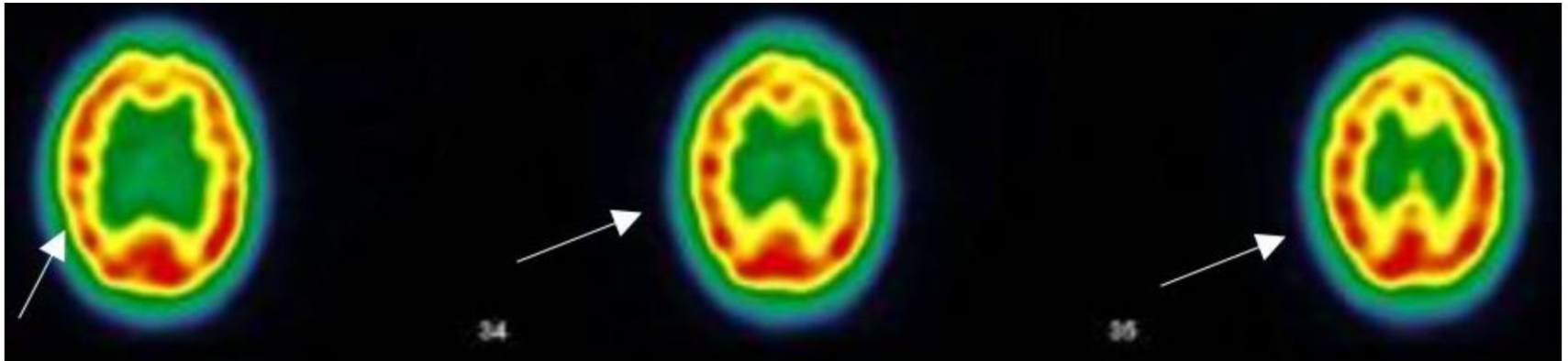
**Figure 7.** Patient MGA001; SPEC-CT (ECD Tc-99m) control at nine months; On the images taken, right parietal, left fronto-parietal, left frontal and left thalamic hypofixation is observed. No preservation of the sensory motor cortices. The fixation in front of the cerebellum is correct. Conclusion: Scintigraphic examination compatible with a cerebral pathology of vascular type. Compared to the previous examination, we note the appearance of a small right parietal hypofixation. The other hypofixations are comparable. (Images and protocol; Drs Bouazza & Mahy, Vesale hospital, ISPPC, Belgium)



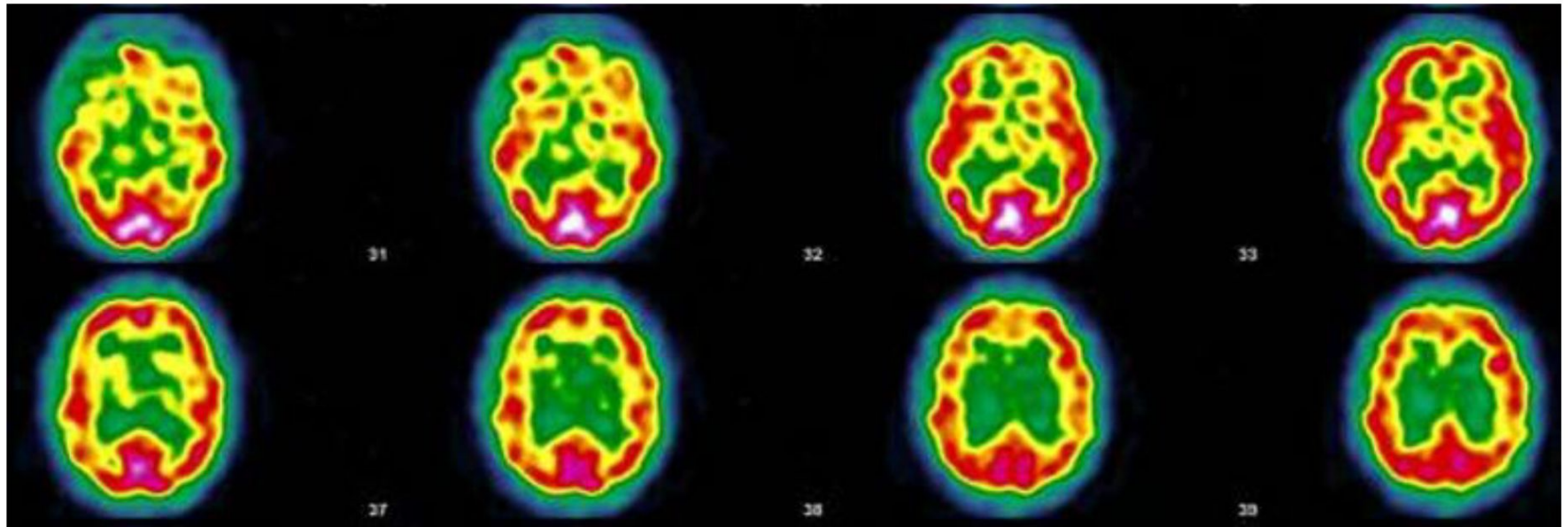




**Figure 4.** Case MGA010, F, 46, May 2021 ; Scintigraphic examination (ECD Tc-99m): heterogeneous tracer fixation with clearer left frontal, left parietal and right parietal hypofixations. No preservation of the sensory-motor cortices. The fixation in front of the grey nuclei and the cerebellum is correct. Presence of periventricular hypofixation. Conclusion: Evidence of heterogeneous tracer fixation and periventricular hypofixation compatible with vascular-type cerebral damage. (Images and protocol: Drs Bouazza and Mahy, Vesalius Hospital, ISPPC, Belgium)



**Figure 5.** Patient MGA017; SPEC-CT (ECD Tc-99m)); heterogeneous tracer fixation with bilateral temporal, bilateral frontal, left posterior parietal, right parieto-occipito-temporal hypofixation. Discrete preservation of the sensory-motor cortices. The fixation in front of the grey nuclei is correct. Right cerebellar hypofixation. Cortico-subcortical atrophy with periventricular hypocaptation as an indirect sign. Conclusion: Scintigraphic examination compatible with a cerebral pathology of vascular type. Moderate cortico-subcortical atrophy. (Images and protocol; Drs Bouazza & Mahy, Vesale hospital, ISPPC, Belgium)







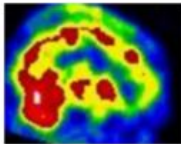
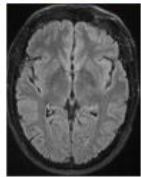
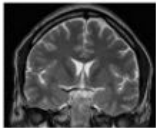
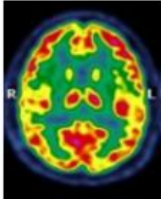
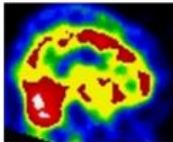
SPECT-CT 13 <sup>th</sup> month	28/04/2021 severe disturbance of cerebral vascular perfusion (very heterogeneous fixation throughout the cortex, area of marked hypofixations left frontoparietal)	
Brain MRI 16 <sup>th</sup> month	05/07/2021 Normal caliber of the ventricular system. Tropicity and normal appearance of the hippocampi. No intracranial expansive process. No recent or sequential haemorrhagic lesion. Conclusion : negative examination.	
Brain SCAN 16 <sup>th</sup> month	06/07/2021 No structural abnormalities. No recent or sequential haemorrhagic lesions. Conclusion : negative examination.	
18FDG PET-CT 16 <sup>th</sup> month	29/07/2021 18FDG brain scan, which shows a discrete hypometabolism, not significant compared to a normal database, in the cerebral cortex in the superior parietal and temporal areas, bilaterally. Conclusion: No formal argument on PET for Alzheimer's dementia	
SPECT CT Control 27 <sup>th</sup> month	27/06/2022 Heterogeneous tracer binding throughout the cerebral cortex. Heterogeneous binding in the basal ganglia and the thalamus. Normal and symmetrical binding of the cerebellum. Conclusion: The scintigraphic aspect of these abnormalities rather pleads for a vascular origin.	

Figure 7.

Case MGA 058, M, 49, senior executive. Acute COVID-19 on March 1, 2020. Persisting cognitive loss and exhausting fatigue, still off work after 27 months. Nuclear imaging shows its value in the follow-up of patients with PACS Brain MRI and CT do not contribute in this case. SPECT-CT highlights the vascular flow problem while 18FDG PET-CT gives an information on the brain metabolism. (Images; courtesy of Dr Fabienne Richelle, St Luc Clinic, Bouge, Belgium)



Evolution; 52 Patients have been followed for max 27 months (June 2022)

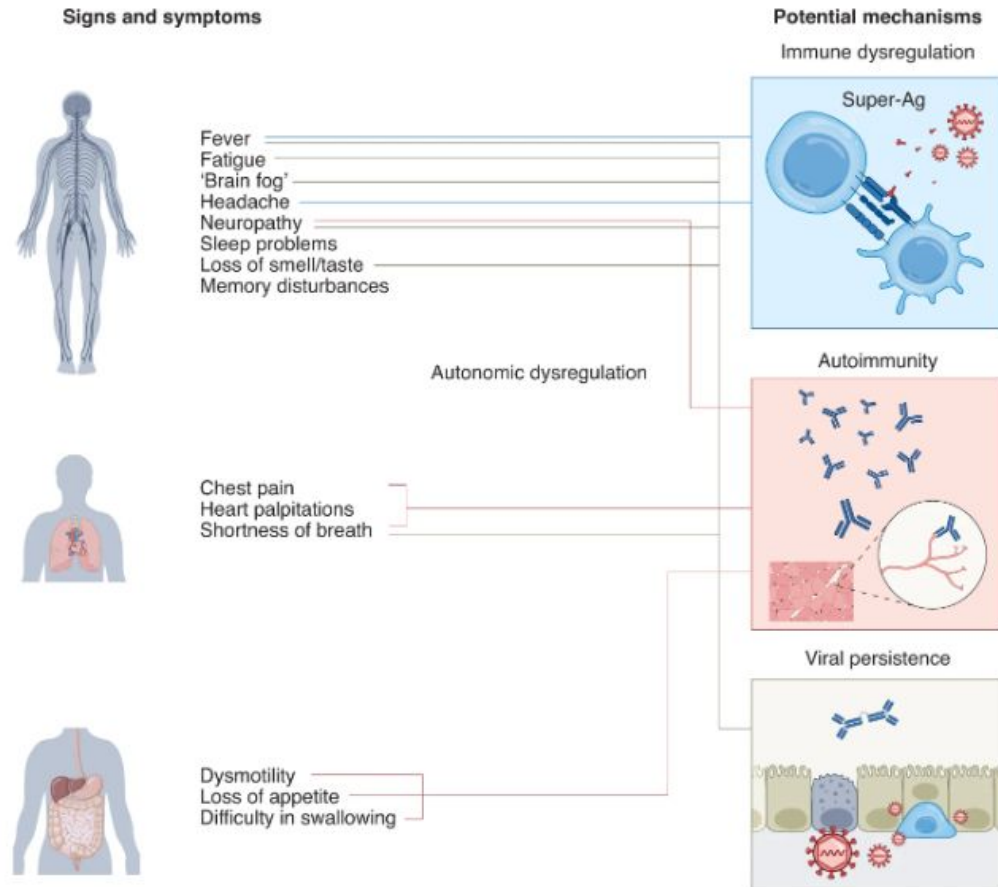
Clinically we can identify three categories (ongoing study)

- 16 patients (9 f,7 m) **Mild Long Covid**;  
disabling but mono or pauci symptomatic  
without cognitive impairment 4 to 6 months  
(with sometimes sequelae)
- 15 patients (12 f,3 m) **Severe Long Covid**  
with cognitive impairment improving after  
6-12 months (with sometimes sequelae)
- 21 patients (17 f,4 m) **Very severe Long  
Covid** with relapse or/and worsening  
cognitive impairment after 18 months

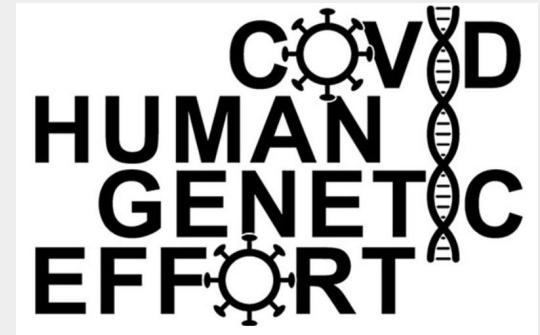


# Fig. 1: Common signs and symptoms and possible causes of long COVID.

From: [Studying severe long COVID to understand post-infectious disorders beyond COVID-19](#)



The patients have been included in a study in genetics and immunology <https://www.covidhge.com/>

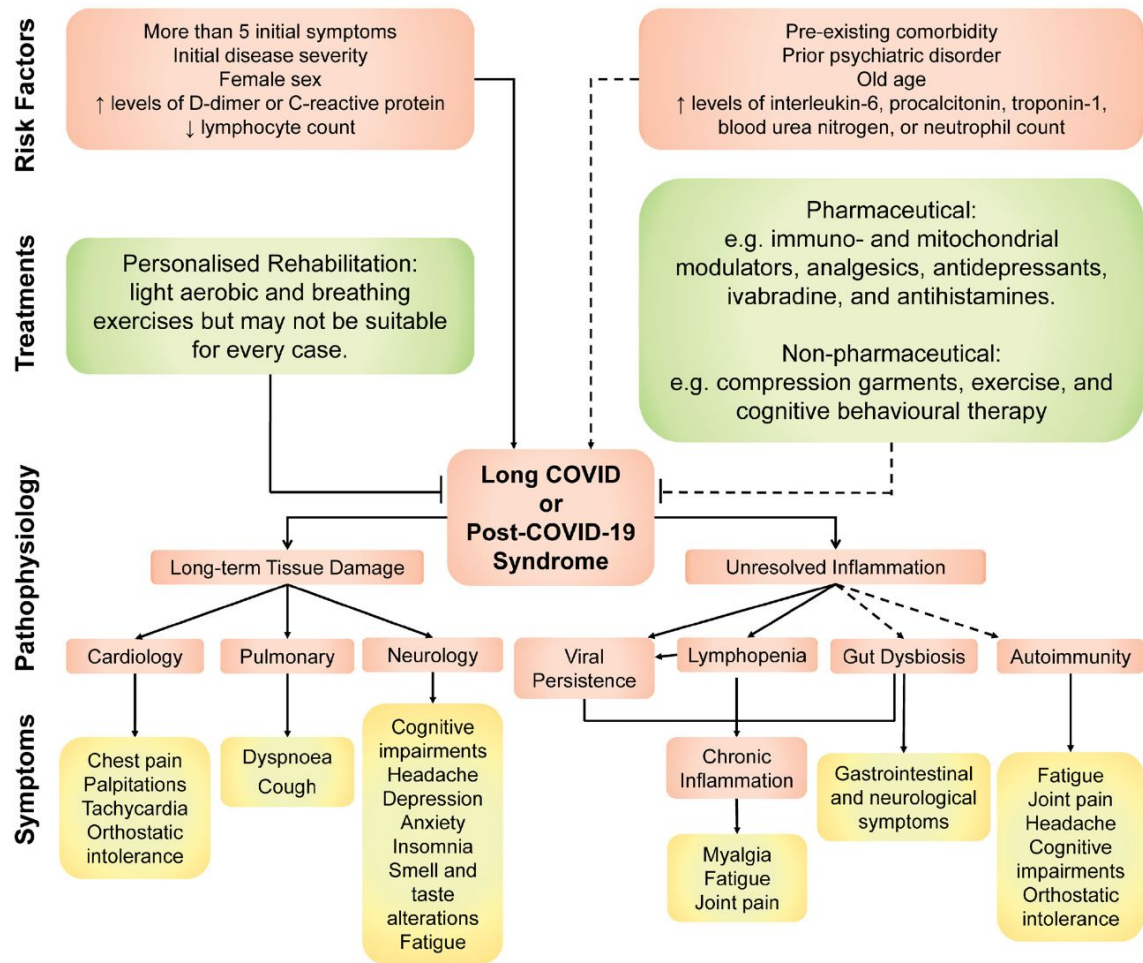


Brodin, P., ... & Casanova, J. L. (2022). *Nature Medicine*, 1-4. <https://www.nature.com/articles/s41591-022-01766-7>

a. Signs and symptoms frequently present or reported in patients with long COVID. b. Hypothetical mechanisms that could explain key signs and symptoms targeted for further investigation. Super-Ag, superantigen. Figure by P.B.



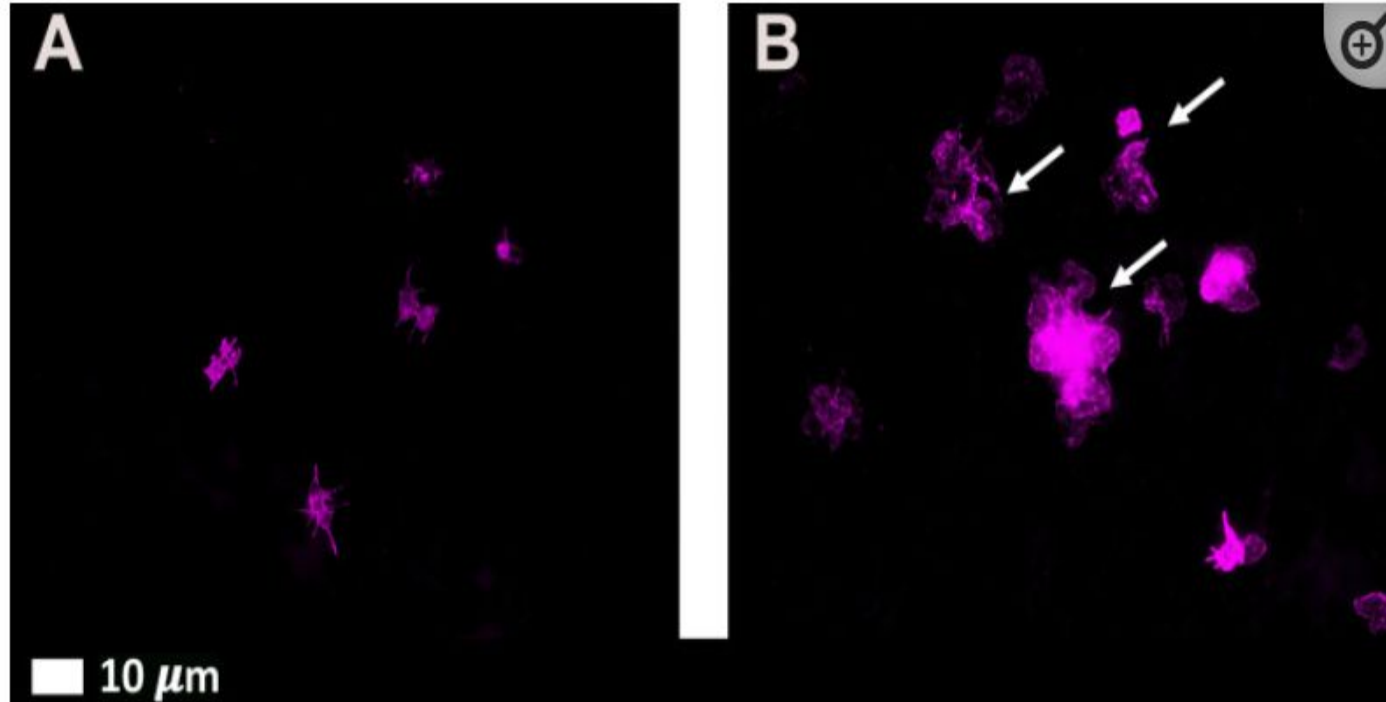
Yong, S. J. (2021). Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infectious diseases*, 53(10), 737-754. <https://pubmed.ncbi.nlm.nih.gov/34024217/>



**Figure 1.** 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).



Parmi les suggestions de physiopathologie ;  
Formation de micro-caillots



Fluorescence microscopy micrographs of platelets, before and after exposure to spike protein

Grobbelaar, L. ... & Pretorius, E.  
(2021). *Bioscience reports*, 41(8).  
<https://doi.org/10.1042/BSR20210611>

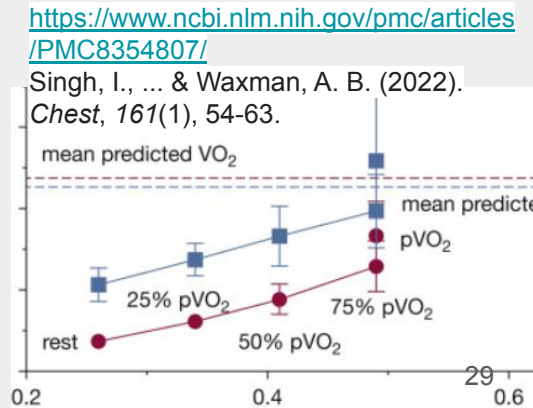




# Identify potential reasons for exercise exhaustion by Invasive cardiopulmonary exercise test (iCET)

- There is an impairment of O<sub>2</sub> extraction
- and an exaggerated hyperventilatory response

This contributes to the reduced aerobic exercise capacity of Long Covid patients.





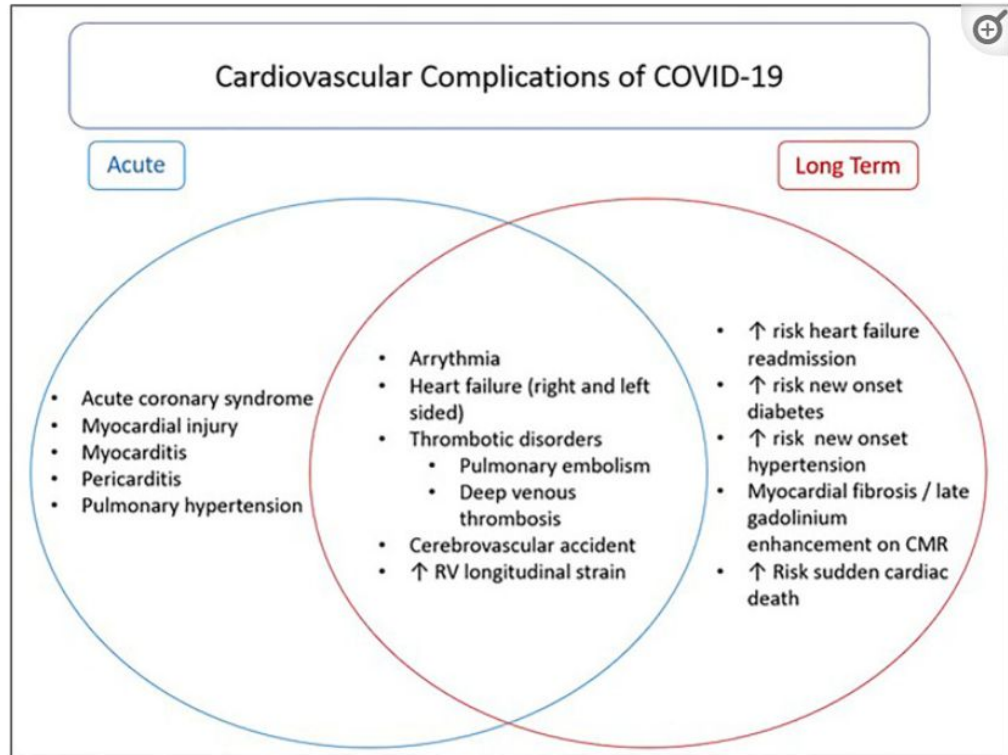
PMc full text:

[Curr Atheroscler Rep. 2022; 24\(7\): 563–570.](#)

Published online 2022 May 4. doi: [10.1007/s11883-022-01032-8](https://doi.org/10.1007/s11883-022-01032-8)

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Fig. 1

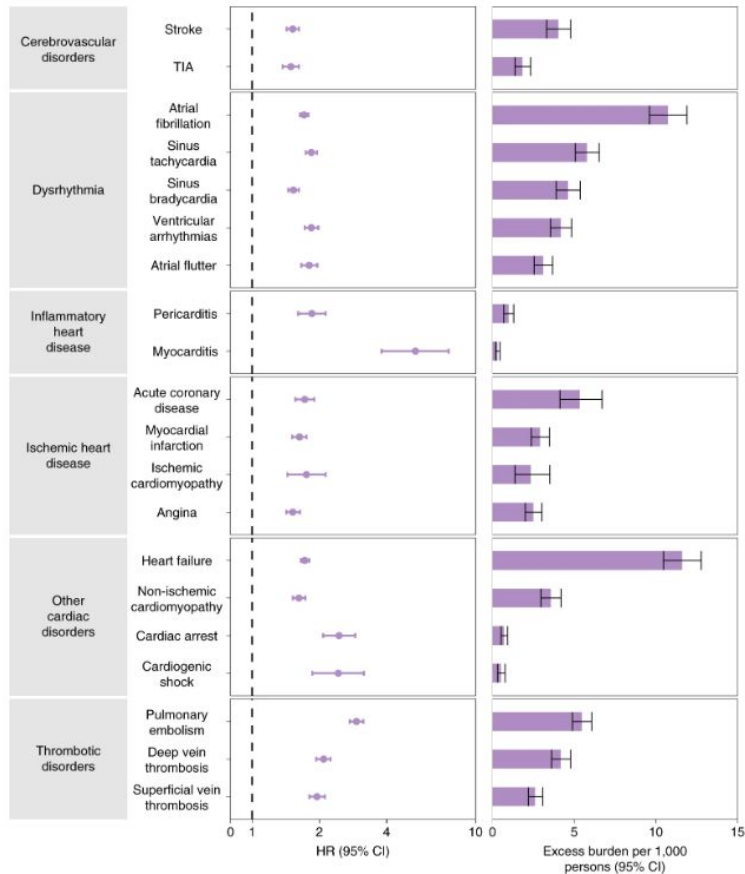


Puntmann VO, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(11):1265–1273. doi:[10.1001/jamacardio.2020.3557](https://doi.org/10.1001/jamacardio.2020.3557)



**Fig. 2: Risks and 12-month burdens of incident post-acute COVID-19 cardiovascular outcomes compared with the contemporary control cohort.**

From: Long-term cardiovascular outcomes of COVID-19



Outcomes were ascertained 30 d after the COVID-19 positive test until the end of follow-up. COVID-19 cohort (n = 153,760) and contemporary control cohort (n = 5,637,647). Adjusted HRs and 95% CIs are presented. The length of the bar represents the excess burden per 1,000 persons at 12 months, and associated 95% CIs are also shown.

Tobler, D.L., et al 2022. Long-Term Cardiovascular Effects of COVID-19: [doi:10.1007/s11883-022-01032-8](https://doi.org/10.1007/s11883-022-01032-8)



## Fugitive or persistent skin lesions



Lésions vasculopathiques acrales

Infections increase the production of thrombin and cause the anticoagulant pathway to malfunction. The thrombin released in this process also increases inflammation. This disrupted cycle evolves into microthrombosis and diffuse intravascular coagulation

<https://onlinelibrary.wiley.com/doi/10.1111/cup.14059>  
Sadeghzadeh-Bazargan, A., ....& Goodarzi, A. (2021).  
*Journal of cutaneous pathology*, 48(10), 1266-1276.



# Long Covid treatment

- Name the disease, listen to the patient
- Neurocognitive revalidation
- Physical revalidation
- Drugs ; Nothing EBM / short corticotherapy/ anticoagulant ; Aspirin /Clopidogrel/  
Piracetam / Oxygenotherapy (hyperbaric) / Cetirizine / Famotidine / Antiviral?



## Take home message

- PACS syndrome has a high prevalence in primary care for those who want to see it.
- Narrative and patient view is important to understand. This needs time, open mindedness and empathy.
- Cerebral hypoperfusion demonstrated by single-photon emission computed tomography (SPECT-CT) seems to correlate with neurological symptoms in a cohort of PACS patients.
- Uncertainty about the primary acute infection is a problem. The participation of 48 patients to the European Consortium for Genetic and Immunological Studies on COVID-19 will probably provide some answers and further questions.
- The impact of PACS is substantial, with many social and economic implications and to date no response from the Belgian health authorities.



# Source; the figures and tables are extracted from :

- Jamouille M. Vascular encephalopathy demonstrated by brain single-photon emission computed tomography (SPECT) in long Covid patients. *J Am Board Fam Med* 2022;35: in press.  
<https://orbi.uliege.be/handle/2268/288290>
- Jamouille M. Kazeneza Mugisha G., Zayane A. Follow-up of a cohort of patients with post-acute COVID-19 syndrome in a Belgian family practice *Viruses*. Submitted, 2022