



CONVEGNO
**VIRTUAL
EDITION**
7-8 Giugno 2021

**ASSOCIAZIONE TRA GENERE FEMMINILE E
PERSISTENZA DI SINTOMI DOPO LA GUARIGIONE
DA COVID-19: STUDIO PROSPETTICO DI COORTE**

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«LONG COVID» (UK NICE GUIDELINES)

Ongoing symptomatic COVID-19: signs and symptoms persist from 4 to 12 weeks after acute illness;

Post COVID-19 syndrome: symptoms for more than 12 weeks, without an alternative diagnosis;

(Venkatesan, 2021; Shah et al., 2021; Sivan & Taylor, 2020)

Long COVID, both physical and psychological symptoms observed **from 1-2 to 6-7 months** after the acute phase. Prevalence of **more than half** of patients.

(Huang et al., 2021; Carfì et al., 2020; Venturelli et al., 2021; Davis HE, 2020)

LONG COVID

Physical symptoms

Fatigue and muscle weakness

Shortness of breath or cough

Joint or chest pain

«brain fog»

Possible predictors: lenght of hospital stay (LOS), longer virological clearance, comorbidities.
Disease severity? Gender?

Psychological symptoms

PTSD

Depression

Anxiety

Obsessive-compulsive symptomatology

Insomnia

Worsening of quality of life

References: Carfi et al., 2020; Carvalho-Schneider et al., 2020; Huang et al., 2021; Xiong et al., 2021; Mazza, 2020, Tomasoni et al., 2020

STUDY DESIGN AND METHODS

Primary objective: to verify the possible association between gender and long COVID

Secondary objectives: to identify possible predictors of long COVID among participants.

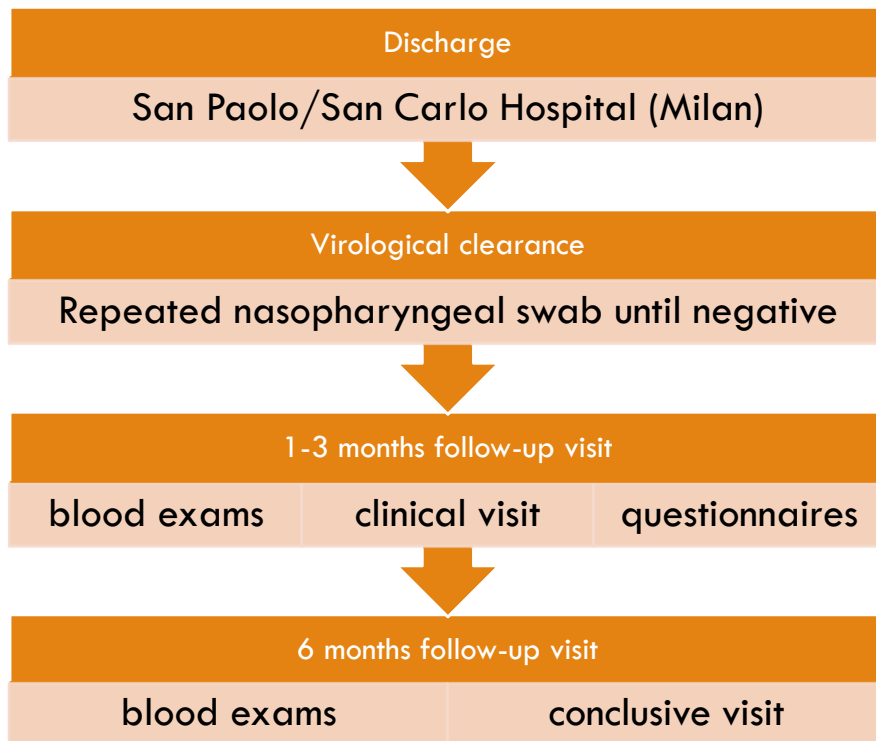
End Point: long COVID, defined as defined as persistence of **at least 1 physical and/or psychological symptom** at follow-up

Cohort study

Inclusion criteria:

- COVID patients
- Discharged from San Paolo/San Carlo Hospitals (Milan)
- From apr/2020 to dec/2020

METHODS



This analysis shows data about the first examination at 1-3 months after virological clearance.

List of **self-reported symptoms** (ongoing; resolved; never)

HADS (anxiety/depression symptoms): pathological if score >8

IES-R (screening of PTSD): pathological if score >33.

METHODS

Mann-Whitney test and Chi-square or Fisher's exact test were used to compare patients diagnosed with long COVID vs patients without persistent symptoms – females vs males

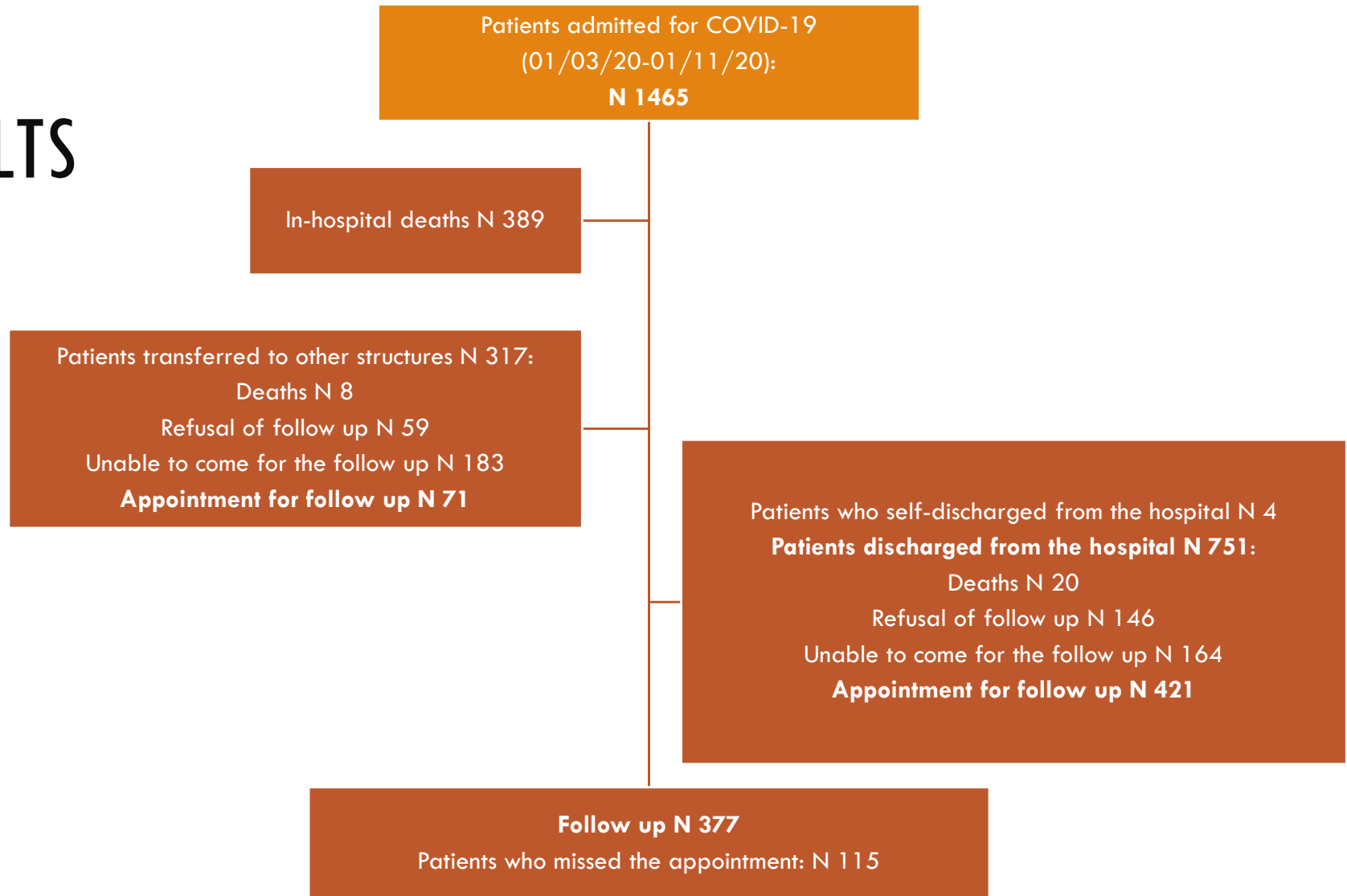
The association between females and long COVID was analysed by fitting a multivariable logistic regression, **adjusting for:**

- Age
- Severity of disease
- Length of hospital stay
- Comorbidities
- BMI
- Smoking
- Time to virological clearance from symptoms onset

Respiratory support as proxy of **disease severity**

- No oxygen therapy
- Low/high flow oxygen therapy
- CPAP
- NIMV
- OTI

RESULTS



STUDY POPULATION

69% of patients (260/377) presented long COVID, as persistence of physical and/or psychological symptoms

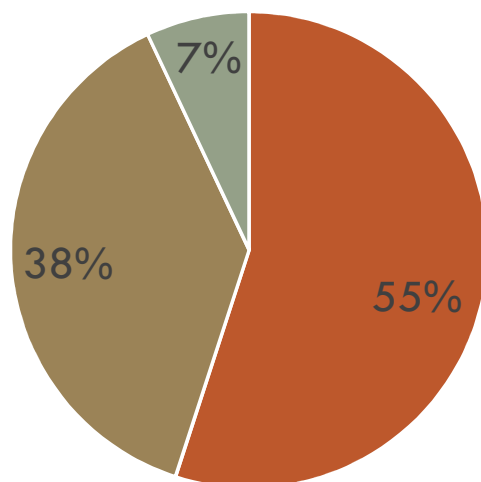
Parameters	Total population (N 377)	No long COVID (N 117)	Long COVID (N 260)	p values
Age, years*	57 (49-68)	56 (42-64)	58 (51-69)	0,008
Gender. males°	240 (63.7%)	92 (78.6%)	148 (56.9%)	<0.0001
Comorbidities°	164 (43,5%)	45 (38,5%)	119 (45,8%)	0,185
Smoking°:				0,046
Never	216 (57,3%)	71 (60,7%)	145 (55,8%)	
Ex smokers	20 (5,3%)	9 (7,7%)	11 (4,2%)	
Active smokers	131 (34,7%)	30 (25,7%)	101 (38,8%)	
Unknown	10 (2,7%)	7 (5,9%)	3 (1,2%)	

Parameters	Total population (N 377)	No long COVID (N 117)	Long COVID (N 260)	p values
Pneumonia:				0,287
Absence of pneumonia	31 (8,2%)	9 (7,7%)	22 (8,5%)	
Pneumonia	346 (91,8%)	108 (92,3%)	238 (91,5%)	
Oxygen therapy^o:				0,879
No O2 therapy	35 (9,3%)	13 (11,1%)	22 (8,4%)	
Low/high flows systems	197 (52,2%)	60 (51,3%)	137 (52,7%)	
CPAP, NIV	115 (30,6%)	35 (29,9%)	80 (30,8%)	
OTI	30 (7,9%)	9 (7,7%)	21 (8,1%)	
Length of hospital days (LOS)*	11 (6-20)	10 (6-16)	12 (7-21)	0,198
Obesity^o				0,017
BMI <30	227 (60,2%)	79 (67,5%)	148 (61,7%)	
BMI ≥30	136 (36,1%)	31 (26,5%)	105 (40,4%)	
Unknown	14 (3,7%)	7 (6%)	7 (2,7%)	
Follow-up visit				
Time since clinical recovery, days*	79 (69-102)	81 (69-108)	79 (69-97)	0,564
Time since virological clearance, days*	56 (47-74)	56 (46-79)	56 (47-74)	0,971
Time since symptoms onset, days*	102 (86-126)	101 (85-131)	103 (86-124)	0,66
Time from symptoms onset to virological clearance, days*	44 (37-53)	43 (35-50)	44 (38-55)	0,078

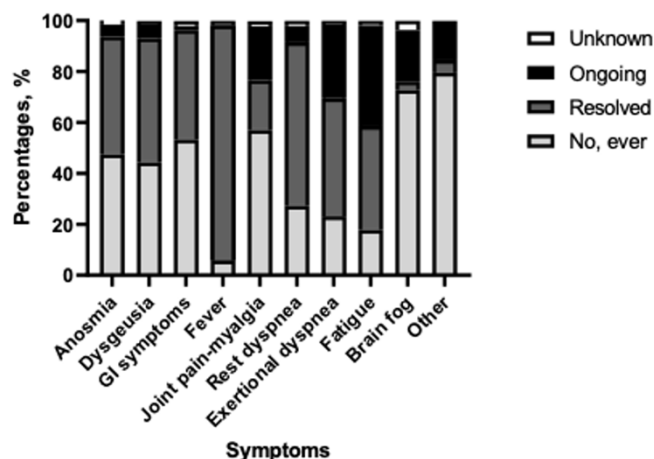
RESULTS

Long COVID symptoms

■ only physical ■ both ■ only psychological



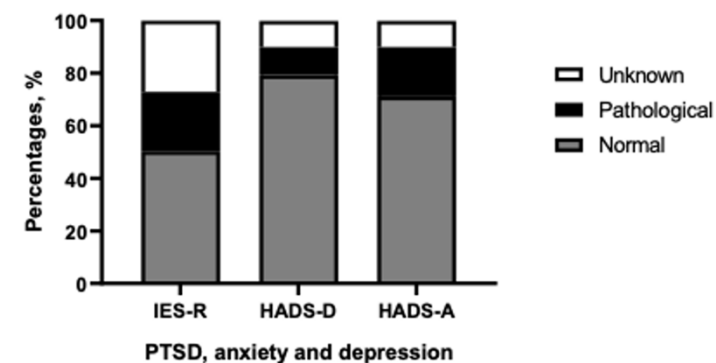
Physical symptoms



Most common physical symptoms:

Fatigue (40%),
exertional dyspnea (29%),
muscle and joint pain (21%),
brain fog (20%).

Psychological symptoms



Most common psychological symptoms:

anxiety (19%),
depression (11%)
PTSD symptoms in 85/275 (31%) of patients

COMPARISON BETWEEN MALES AND FEMALES

Parameters	Females (N 137)	Males (N 240)	p values
Age, years*	58 (50-68)	57 (49-67)	0,741
Comorbidities°	57 (41,6%)	107 (44,6%)	0.575
Smoking°:			0,001
Never	94 (68,6%)	122 (50,8%)	
Ex smokers	10 (7,3%)	10 (4,2%)	
Active smokers	31 (22,6%)	100 (41,7%)	
Unknown	2 (1,5%)	8 (3,3%)	
Ethnicity°:			0,584
White/Caucasian	90 (18,2%)	162 (67,5%)	
Arabic	6 (4,4%)	10 (4,2%)	
Black	2 (1,5%)	0	
Asian	2 (1,5%)	5 (2,1%)	
Hispanic	12 (8,8%)	21 (8,7%)	
Unknown	25 (18,2%)	42 (17,5%)	

Parameters	Females (N 137)	Males (N 240)	p values
During hospitalization			
Pneumonia:			0,751
Absence of pneumonia	11 (8,1%)	20 (8,3%)	
Pneumonia	126 (91,9%)	220 (91,7%)	
Oxygen therapy°:			0,002
No O2 therapy	18 (13,1%)	17 (7,1%)	
Low/high flows systems	79 (57,7%)	118 (49,2%)	
CPAP, NIV	37 (27%)	78 (32,5%)	
OTI	3 (2,2%)	27 (11,2%)	
Length of hospital days (LOS)*	10 (6-16)	12 (7-21)	0,031
Obesity°			0,259
BMI <30	75 (54,7%)	152 (63,4%)	
BMI ≥30	56 (40,9%)	80 (33,3%)	
Unknown	6 (4,4%)	8 (3,3%)	
Follow-up visit			
Time since clinical recovery, days*	85 (69-112)	78 (69-96)	0,201
Time since virological clearance, days*	59 (49-77)	55 (46-72)	0,05
Time since symptoms onset, days*	107 (84-133)	98 (86-122)	0,198
Time from symptoms onset to virological clearance, days*	45 (38-55)	44 (37-52)	0,453

POSSIBLE PREDICTORS

PARAMETERS	OR (95%CI)	p values	AOR (95%CI)	p values
Gender				
Male	1		1	
Female	2,78 (1,68-4,62)	<0,0001	3,32 (1,78-6,17)	<0,0001
Age,				
10 years older	1,03 (1,01-1,04)	0,001	1,03 (1,01-1,05)	0,01
O2 therapy,				
No O2	1		1	
O2 therapy low high flow	0,67 (0,38-1,19)	0,17	0,39 (0,19-0,82)	0,01
CPAP/NIV/IOT	0,97 (0,55-1,71)	0,91	0,67 (0,29-1,55)	0,34
LOS,				
Each day more	1,01 (0,99-1,03)	0,28	0,998 (0,97-1,03)	0,92
Comorbidities,				
No	1	0,19	1	0,87
Yes	1,35 (0,86-2,11)		1,05 (0,597-1,84)	
Smoking,				
Active	1		1	
Unknown	0,13 (0,03-0,52)	0,004	0,16 (0,04-0,75)	0,02
Never	0,61 (0,37-0,997)	0,05	0,56 (0,31-1,01)	0,05
Former	0,36 (0,14-0,96)	0,04	0,19 (0,06-0,62)	0,01
BMI,				
≥30	1		1	
Unknown	0,29 (0,096-0,91)	0,03	0,13 (0,30-0,53)	0,004
<30	0,55 (2,27-5,06)	0,02	0,55 (0,31-0,98)	0,04
Time from symptoms onset to virological clearance, each day more	1,01 (0,99-1,02)	0,64	0,99 (0,98-1,01)	0,47

LIMITATIONS

Possible **selection bias**: patients who died from COVID-19, and patients who missed or refused the follow-up appointments were excluded from this analysis;

Limited **sample size**, especially for patients with severe disease and for female gender.

Lack of **validated tools** to assess symptoms such as dyspnea and fatigue, reducing the possibility of objective comparisons;

Lack of data about anxiety and depression symptoms **before** hospital admission.

The **sixth-month evaluation** of our patients still ongoing, and we are evaluating new patients discharged after November 2020.

TAKE HOME MESSAGES

More than half of patients recovering from COVID-19 developed **long COVID** (defined as ≥ 1 persistent symptom for ≥ 4 weeks after recovery);

Most common persistent symptoms were **physical** (fatigue, exertional dyspnea, brain fog, muscle or joint pain) **or psychological** (anxiety, depression, PTSD)

More than one third of patients with long COVID suffered from **both** physical and psychological symptoms;

Females were at 3-fold higher risk of being diagnosed with long COVID;

Other populations at higher risk were **elderly, obese and active smokers**.

Severity of disease seems **NOT** associated with long COVID in our study.



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