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Article

Risk and Protective Factors of Long COVID Incidence in the Borriana COVID-19 Cohort from 2020 to 2023: A Prospective Population-Based Cohort Study

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Abstract

Background and Objective: After a SARS-CoV-2 infection, a Long COVID (LC) syndrome occurred in a high proportion of patients with affecting their health. Estimating the incidence, risk and protective factors of LC was the aim of our study. **Material and Methods:** We performed a prospective population-based cohort study on the Borriana COVID-19 cohort (Castellon province, Valencia Community, Spain) from May 2020 to August 2023 with a follow-up of 40 months, and considering the LC definition from the World Health Organization. We used inverse probability weighted regression. **Results:** With a response rate of 63.8% of a total of 722 participants, the average age was 37.7±17.4 years with 460 (62.3%) females, 644 had suffered a SARS-CoV-2 infection, and 184 suffered LC with a cumulative incidence of 28.6%. A total of 135 patients with LC remained affected, and a death associated with the syndrome occurred in 0.54% of them. Significant risk factors for LC were older age, female, chronic disease, SARS-CoV-2 exposure, reinfections and severity. Asymptomatic cases and SARS-CoV-2 vaccinations were significantly protective factors. **Conclusions:** A high incidence of LC was found with low recovery rate, and several risk and protective factors. Continued follow-up for non-recovered LC patients, surveillance of infections, and a SARS-CoV-2 vaccination for an at-risk population can be recommended.

Keywords: COVID-19; SARS-CoV-2 infection; long COVID; cumulative incidence; prospective cohort; population-based; risk factors; SARS-CoV-2 vaccines

1. Introduction

After the COVID-19 pandemic, a high incidence of sequelae has observed in patients who suffered the disease, and it has been denominated post-COVID-19 syndrome or long COVID

syndrome, a syndrome with many clinical variations and different grades of severity. The causes of the syndrome are not well known [1–3].

In the study of long COVID, an operational definition of the syndrome has been proposed by the World Health Organization [4], but other definitions have been presented [5,6]. In cohort studies, the incidence of long COVID showed significant variations, between 2% and 69% in COVID-19 patients, considering different approaches [7,8], and determination of risk and protective factors of long COVID is an essential step of the syndrome's prevention. In addition, a follow-up for these patients is needed to establish effective measures for recovery and prevention [9,10].

The prospective cohort study is an appropriated design for this research, considering that risk and protective factors need to be measured before the onset of the long COVID [11,12]. In addition, a population-based approach could be representative of the general population [13,14]. However, prospective cohort studies on the incidence of long COVID in non-hospitalized patients are few. In contrast, the study of long COVID in hospitalized patients is more frequent, but it could produce selection bias, compromising the generalization of its results [15,16].

In this context, a big outbreak of the COVID-19 pandemic occurred during the Fallas festival in Borriana, a city of 35.052 inhabitants in Castellon province (Valencia Community, Spain) during March 2020, allowing us to begin the study of the Borriana COVID-19 cohort in May 2020 [17]. After 6 months of the onset of COVID-19 disease, complications were studied in this cohort, considering the symptoms of disease and risk factors [18], and it continues with two surveys in 2022, and a follow-up until 2023 [19].

We have settled the estimation of incidence of long COVID in the Borriana COVID-19 cohort, and their related risk and protective factors during the period 2020 to 2023 as objectives for the present study.

2. Materials and Methods

2.1. Presentation

The study was designed as prospective population-based cohort study of the Borriana COVID-19 cohort from May 2020 to August 2023 and a the follow-up period of about 40 months. All COVID-19 cases had a confirmatory laboratory test of SARS-CoV-2 infection, including detection of antibodies against SARS-CoV-2 nucleocapsid protein N by electrochemiluminescence immunoassay (ECLIA Roche Diagnostics, Mannheim, Germany) [20], anti-SARS-CoV-2 spike IgG antibodies and IgG and IgM anti-nucleocapsid antibodies via chemiluminescence microparticle immunoassay (CLIA AlinityI series, Abbot, Chicago, IL, USA) [21], and SARS-CoV-2 virus detection by reverse transcription–polymerase chain reaction (RT-PCR) as well as rapid antigen tests (RATs). In addition, determination of blood groups of participants was implemented. All these tests were performed by the Laboratory of Microbiology Service of the University Hospital de la Plana (Vila-real, Spain), and RATs by the participants at home. More detailed information about laboratory tests is indicated in Domènech and coauthors [19].

For the long COVID-19 syndrome, we used the definition the World Health Organization: “The post-COVID-19 condition 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” [4]. The definition of recovery from long COVID syndrome was: a participant who indicated their health was completely recovered or that no sequelae were present.

2.2. Surveys

Three surveys were performed in May 2020, in October 2020, and in June 2022. In addition, a follow-up of participants was implemented using the register of primary health care with the computer application outpatient care of the Valencia Health Agency (ABUCASIS) from January 2020 up to August 2023, to detect new COVID-19 cases, reinfections, clinical evolution, and long COVID

syndromes. In these surveys, information was obtained through specific questionnaires about participants' demographic and education level; lifestyle, including smoking habits, alcohol consumption, and physical exercise; SARS-CoV-2 exposure, and history prior SARS-CoV-2 infections, and medical assistance and hospitalizations. Face-to-face interviews and telephone surveys were conducted by health staff from Primary Care of the Health Center of Vila-real, the Emergency Service of University Hospital de la Plana, and the Public Health Center of Castellon. Information about the SARS-COV-2 vaccination status of the participants was obtained by consulting the population-based Valencia Region Vaccine Information System (VIS).

2.3. Statistical Analysis

Cumulative incidence of COVID-19 was estimated by dividing the number of COVID-19 patients by the number of total participants. The cumulative incidence of long COVID was estimated by dividing the long COVID patients by the number of participants who suffered from COVID-19 disease. Prevalence of long COVID was estimated by dividing the number of patients who still suffered from long COVID during the study period by the total of patients who suffered from long COVID. It is assumed a binomial distribution for the estimation of 95% confidence intervals (CI). The Chi2 and Fisher exact tests were used for the comparison of qualitative variables and the Kruskal-Wallis test for the comparison of quantitative variables.

Univariable and multivariable models were performed by the inverse probability weighted regression [22]. In addition, robust Poisson regression models were used when independent variables were quantitative. The outcome was to suffer long COVID-19 syndrome, and predictor variables included exposures to SARS-CoV-2 infection, considering attendance mass gathering events (MGE), and observed coughing a person at MGE, a COVID-19 case in the family, demographic factors, blood groups, education level, lifestyle, chronic disease, onset of SARS-CoV-2 infection, severity, medical assistance, hospitalizations, reinfections and SARS-CoV-2 vaccines administered. Crude and adjusted relative risk (cRR and aRR) were estimated with a 95% CI. To adjust for potential confounding factors, the directed acyclic graphs (DAGs) method was followed [23]. Crude and adjusted relative risk (RR and aRR) were calculated with 95% confidence intervals (CI). Stata® version 14 was used in the statistical analysis.

2.3. Ethical Issue

The study was approved by the Ethics Committee of University Hospital de la Plana (14 October 2021; registry number: 2961). All participants, or their parents in the case of minors, provided informed written consent to be included in the study.

3. Results

In the survey of June 2022, 722 individuals from the initial cohort of May 2020 with confirmatory laboratory tests of SARS-CoV-2 infection took part, with a participation rate of 63.8% (722/1132). The average age of participants was 39.7±17.4 years (range 3-82), 450 were female (62.3%) and 272 male (37.7%). In the total of participants, 644 COVID-19 cases occurred, three participants did not have a laboratory confirmation test, and 75 participants had not suffered the infection. The duration of the follow-up of the cohort was 1210 days, from May 2020 to August 2023, and the cumulative incidence of COVID-19 was 89.6% (CI 95% 87.1-91.7) (644/719).

Of 644 COVID-19 cases, 184 participants suffered from long COVID during the study period, with a cumulative incidence of long COVID of 28.6% (CI 95% 25.1-32.2) (184/644). Among long COVID patients, 135 patients remained affected by the syndrome (73.4%), and 49 patients recovered (26.6%). At the moment of this study, the long COVID-19 prevalence was 21.0% (CI 95% 17.9-24.3) (135/644) on the total number of cases, and 73.4% (95% CI 66.4-79.6) (135/184) on long COVID patients. When considering the first period of the pandemic before October 2020, 147 participants suffered from long COVID and 387 participants suffered from COVID-19 disease; the

cumulative incidence of long COVID was 38.0% (95% CI 33.1-43.0) (147/387). In the second period with the Omicron variant predominantly circulating, 37 participants suffered from long COVID and 257 suffered from COVID-19 disease; the cumulative incidence of long COVID was 14.4% (95% CI 10.3-19.2).

The duration of the long COVID without considering the first three months after the onset of the SARS-CoV-2 infection was 433.8 days±289 days on average, and 365 days (ranks 60-950 days) as median. The frequencies of the main sequelae of the 184 patients who suffered long COVID were as follows:

Fatigue (25.6%); alterations in taste and smell (18.0%), hair lost (12.5%), dyspnea (9.8%), cough (7.7%), headache (7.7%), weakness (7.1%), memory lost (7.1%), anxiety (6.5%), joint pain (4.9%), nose and throat disorders (4.9%), eye disorders (4.4%), muscle pain (3.8%), digestive disorders (3.3%), skin disorders (2.8%), sleep disorders (2.2%), menstrual disorders (2.2%), palpitations (1.6%), thrombosis (1.6%), and other disorders with a frequency less than 1.5%. Highlighting a death among the patients with long COVID, a 73-year-old woman died from myelodysplastic syndrome and chronic kidney failure, and it can be considered associated with SARS-CoV-2 infection with a 0.5% mortality long COVID (1/184).

We present in Table 1, the distribution and characteristics of long COVID patients, non-long COVID cases and non-COVID-19 cases participants. Long COVID had a higher incidence during the first period of the pandemic than the Omicron period, 79.9% versus 20.1%. Long COVID patients were older than non-long COVID patients. Children and adolescents had the lowest cumulative incidence of long COVID at 8.8% (6/68) with a progressive increase among older age groups: 34.7% (87/251) for the 45-64-year-old group, and 32.3% (10/31) for 65 years old and above. Females were more affected by long COVID than males, 31.5% versus 23.4%, respectively. Fewer family members and smoking habit were higher in the long COVID patients. BMI, obesity, chronic disease, and B blood group were higher in the long COVID patients. Exposures for SARS-CoV-2 infections such as attendance at mass gathering events, observing persons with cough, and families with COVID-19 cases were higher in the long COVID patients. Three doses of SARS-CoV-2 vaccine before the onset of the infection were protective against long COVID. With respect to COVID-19 disease, duration of the illness (13.4±18.3 days versus 5.9±10.8 days), medical assistance (87.5% versus 64.3%), hospitalization (7.6% versus 2.4%), and SARS-CoV-2 reinfections were higher in the long COVID patients (33.9% versus 21.6%). Asymptomatic infections were higher in the non-long COVID patients (23.0% versus 3.3%).

Table 1. Distribution and characteristics of incidence of long COVID cases, non-long COVID cases and non-COVID-19 cases.

Variables	COVID-19 cases		No COVID-19	
	Long COVID	No-Long COVID	No-Cases	p-value
	Incidence N=184	N=460	N=75	
	N (%)	N (%)	N (%)	
Infection before October 2020	147 (79.9)	240(52.2)		0.000
Infection after October 2020	37 (20.1)	220 (47.8)		
Age years±SD [†]	43.8 ±14.9	37.3±17.8	44.8±17.6	0.001
0-14	6 (3.3)	62 (13.5)	6 (8.0)	
15-24	18 (9.8)	83 (18.0)	7 (9.3)	
25-34	26 (14.1)	53 (11.5)	9 (12.0)	
35-44	37 (20.1)	77 (16.7)	4 (5.3)	
45-64	87 (47.3)	164 (35.7)	42 (56.0)	
65 years and above	10 (5.4)	21 (4.6)	7 (9.3)	

Age-50 years and above	69 (37.8)	128 (27.8)	41 (54.7)	0.000
Male	55 (29.9)	180 (39.1)	37 (49.3)	0.009
Female	129 (70.1)	280 (60.9)	38 (50.7)	
Family members	3.1±1.1	3.4±1.1	2.9±1.1	0.004
Education ²				
Primary	30 (16.7)	94 (21.1)	19 (26.4)	0.192
Secondary	83 (46.1)	178 (40.0)	33 (45.8)	0.303
Superior (University)	67 (37.2)	173 (38.9)	20 (26.4)	0.198
Smoking habit ³				
No smoking	99 (54.1)	294 (64.4)	30 (40.5)	0.000
Ex-smoker	48 (26.2)	77 (17.0)	13 (17.6)	
Current smoking	36 (19.7)	82 (18.1)	31 (41.9)	
Alcohol consumption ⁴	43 (23.4)	81 (17.9)	15 (20.3)	0.278
Physical exercise ⁵	102(55.4)	265 (58.4)	34(47.2)	0.199
Body mass index (BMI) ⁶	26.0±5.0	24.7±5.3	24.8±4.9	0.016
Obesity (BMI≥30.0) ⁶	39 (21.3)	77 (16.9)	11(14.9)	0.342
Chronic disease ⁷	80 (43.5)	139(30.4)	23 (31.5)	0.006
Blood groups ⁸				
O	70 (38.3)	213 (46.6)	34(45.3)	0.155
A	83 (45.4)	195 (42.7)	33 (44.0)	0.825
B	25 (13.7)	34 (7.4)	5 (6.7)	0.045
AB	5 (2.7)	15 (3.3)	3 (4.0)	0.808
SARS-CoV-2 exposure				
Mass gathering events ≥ 2	119 (64.7)	210 (45.7)	22 (29.3)	0.000
Observations persons with cough ⁹	95 (52.2)	156 (34.6)	17 (23.0)	0.000
Family COVID-19 case ¹⁰	166 (92.7)	401 (90.3)	57 (80.3)	0.020
Number of family members	3.1±1.1	3.4±1.1	2.9±1.1	0.002
Family member 1-2 ¹¹	55 (30.4)	87 (19.3)	25 (35.7)	0.001
SARS-CoV-2 vaccination status				
0 doses (Not vaccinated)	3 (1.6)	15 (3.2)	0 (0.0)	0.004
1 doses	9 (4.9)	28 (6.1)	0 (0.0)	
2 doses	63 (34.2)	126 (27.4)	12 (16.0)	
3 doses	108 (58.7)	290 (63.0)	63 (84.0)	
4 doses	1 (0.5)	1 (0.2)	0 (0.0)	
SARS-Vaccines before ≥14 days of onset of infection	N=32	N=207	N=75	
No vaccinated or 1dose	7	31	0	0.000
2 doses	21	77	12	
3 doses	4	99	63	
SARS-CoV-2 vaccines				

No vaccinated, or 1,2 doses	32 (87.5)	108 (52.2)	12 (16.0)	0.000
Vaccinated 3,4 doses	4 (12.5)	99 (47.8)	63 (84.0)	
COVID-19 disease				
Duration illness (days) ¹²	13.4±18.3	5.9±10.8	-	0.000
Median (rank)	7(0-122)	3 (0-110)	-	0.000
Medical assistance ¹³	161 (87.5)	268 (64.3)		0.000
Hospitalized	14 (7.6)	11 (2.4)	-	0.005
Asymptomatic infection	6 (3.3)	106 (23.0)		0.000
SARS-CoV-2 reinfections ¹⁴	59 (33.9)	106 (21.6)		0.002

¹ SD= standard deviation.² Missing information 22 participants.³ Missing information 9 participants.⁴ Missing information 8 participants.⁵ Missing information 9 participants. ⁶ Missing information 7 participants. ⁷ Missing information 4 participants.⁸ Missing information 4 participants. ⁹ Missing information 12 participants. ¹⁰ Missing information 25 participants. ¹¹ Missing information 17 participants.¹² Missing information 18 participants.¹³ Missing information 18 participants.¹⁴ Missing information 10 participants. .

In Table 2, crude and adjusted relative risks of several factors of incidence of long COVID comparing patients who suffered the syndrome with non-long COVID patients are presented. Risk of long COVID was significantly higher when the infection onset occurred before October 2020 (aRR= 2.57; 95% CI 1.85-3.55). Long COVID risk increased with age; children up to fifteen years of age have the lowest incidence, and there was a significant increase in older age groups. Patients 50 years old and above had more risk than those under 50 years old (aRR=1.41; 95% CI 1.11-1.81). Males presented a lower risk than females (aRR= 0.68; 95% CI 0.52-0.89). Education levels, smoking habit, physical exercise, alcohol consumption, and obesity were not significant risk factors of long COVID. However, chronic disease and B blood group were risk factors of long COVID (aRR=1.33; 95% CI1.03-1.75), and (aRR= 1.77; 95% CI 1.24-2.53), respectively. Exposures to SARS-CoV-2 increased the risk of long COVID, such as attendance at mass gathering events (aRR = 1.53; 95% CI 1.18-2.00) and observing people with cough (aRR =1.59; 95% CI 1.23-2.04). Families with a COVID-19 case did not increase significantly the risk (aRR= 1.41; 95% CI 0.85-2.36), and only one or two family members wer a risk factor (aRR = 1.35; 95% CI1.04-1.77).

Regarding the SARS-CoV-2 vaccination 14 or more days before the onset of SARS-CoV-2 infection: three doses were protective of long COVID (aRR= 0.16; 95% CI 0.04-0.37), and three or four doses versus unvaccinated or vaccinated with one or two doses (aRR= 0.15; 95% CI 0.05-0.45). Considering the COVID-19 disease, duration of illness ((aRR=1.01; 95% CI 1.01-1.01), duration of illness above the median (aRR=1.62; 95% CI 1.24-2.12), hospitalization (aRR= 2.10; 95% CI 1.68-2.61), and SARS-CoV-2 reinfections (aRR=1.38; 95% CI 1.07-1.69) were significant risk factors of long COVID. Asymptomatic infections were protective factors (aRR= 0.18; 95% CI 0.08-0.40).

Table 2. Risk and protective factors of incidence of long COVID (n=184) compared with COVID-19 cases who have not suffered from long COVID (n=460). Crude and adjusted relative risk (RR) 95% Confidence interval (CI).

Variables			Crude RR 95% CI	p-value	Adjusted RR 95% CI	p-value
Infection onset	before	October 2020 ¹	2.64 (1.91-3.65)	0.000	2.57 (1.85-3.55)	0.000
Age (years)	^{2,3}		1.02 (1.01-1.02)	0.000	1.02 (1.01-1.02)	0.000
0-14			1.00		1.00	
15-24			1.83 (0.76-4.44)	0.181	1.54 (0.63-3.77)	0.341
24-34			3.92 (1.72-8.90)	0.001	3.35 (1.47-7.64)	0.004

35-44	3.68 (1.64-8.26)	0.002	3.35. (1.50-7.51)	0.003
45-64	3.93 (1.80-8.59)	0.001	3.69 (1.69-8.07)	0.001
65 and above	3.66 (1.46-9.16)	0.006	3.40 (1.36-8.53)	0.009
Age years 50 and above	1.36 (1.06-1.74)	0.014	1.41 (1.11-1.81)	0.006
Male ⁴	0.74 (0.57-0.97)	0.031	0.68 (0.52-0.89)	0.006
Education ⁵				
Low	1.00			
Mean	1.31 (0.92-1.88)	0.135	1.40 (0.99-2.00)	0.060
University	1.15 (0.80-1.67)	0.451	1.14 (0.79-1.66)	0.479
Smoking ⁶				
No	1.00		1.00	
Ex-smoker	1.52 (1.15-2.02)	0.003	1.34 (0.94-1.91)	0.107
Current smoking	1.21 (0.88-1.67)	0.243	1.11 (0.80-1.55)	0.524
Alcohol consumption ⁷	1.26 (0.95-1.67)	0.102	1.30 (0.97-1.76)	0.081
Physical exercise ⁸	0.92 (0.72-1.17)	0.496	0.97 (0.76-1.24)	0.832
Body Mass Index (BMI) ^{9,3}	1.03 (1.01-1.05)	0.004	1.01 (0.98-1.04)	0.383
Obesity (BMI≥30.0) ⁹ .	1.22 (0.91-1.62)	0.183	1.19 (0.88-1.60)	0.262
Chronic disease ¹⁰	1.49 (1.17-1.89)	0.001	1.33 (1.03-1.75)	0.032
Blood groups ⁴				
O	1.00		1.00	
A	1.20 (0.92-1.58)	0.174	1.20 (0.92-1.56)	0.186
B	1.71 (1.19-2.46)	0.003	1.77 (1.24-2.53)	0.002
AB	1.01 (0.46-2.22)	0.979	1.06 (0.48-2.35)	0.890
SARS-CoV-2 exposure				
Mass gathering events ≥ 2 ¹¹	1.75 (1.35-2.27)	0.000	1.53 (1.18-2.00)	0.002
Observations persons with cough ¹²	1.66 (1.30-2.12)	0.000	1.59 (1.23-2.04)	0.000
Family COVID-19 case ¹³	1.26 (0.77-2.07)	0.298	1.41 (0.85-2.36)	0.184
Family members 1-2 ¹⁴	1.51 (1.17-1.95)	0.002	1.35 (1.04-1.77)	0.026
SARS-Vaccination before ≥14 days of onset of infection ¹⁵				
No vaccinated or 1dose	1.00		1.00	
2 doses	1.16 (0.54-2.51)	0.700	0.79 (0.46-1.35)	0.336
3 doses	0.21 (0.07-0.68)	0.009	0.16 (0.04-0.37)	0.000
No vaccinated, or 1,2 doses	1.00		1.00	
Vaccinated 3,4 doses	0.19 (0.07-0.52)	0.001	0.15 (0.05-0.45)	0.001
COVID-19 disease				
Duration illness (days) ^{16,3}	1.02 (1.01-1.02)	0.000	1.01(1.01-1.01)	0.000
Duration illness above median ¹⁶	1.77 (1.37-2.29)	0.000	1.62 (1.24-2.12)	0.001
Medical assistance ¹⁷	3.21 (2.10-4.89)	0.000	1.68 (0.94-2.99)	0.078

Hospitalized ¹⁸	2.04 (1.41-2.95)	0.001	2.10 (1.68-2.61)	0.000
Asymptomatic infection ¹⁹	0.16 (0.07-0.35)	0.000	0.18 (0.08-0.40)	0.000
SARS-CoV-2 reinfections ²⁰	1.53 (1.19-1.97)	0.001	1.38 (1.07-1.69)	0.014

¹Adjusted for age sex.² Adjusted for sex.³ Robust Poisson regression models.⁴ Adjusted for age.⁵ Adjusted for age sex.⁶Adjusted for age, sex, education, obesity, alcohol consumption, physical exercise.⁷ Adjusted for age, sex, education, obesity, smoking habit, physical exercise.⁸ Adjusted for age, sex, education, smoking habit, obesity, alcohol consumption.⁹ Adjusted for age, sex, education, smoking habit, physical exercise, alcohol consumption.¹⁰Adjusted for age, sex, blood groups, education, smoking habit, physical exercise, alcohol consumption, obesity.¹¹Adjusted for age, sex, chronic disease, education, smoking habit, physical exercise, alcohol consumption, obesity, family members, family COVID-19 case, observation person cough.¹²Adjusted for age, sex, chronic disease, education, smoking habit, physical exercise, alcohol consumption, obesity, family members, family COVID-19 case, mass gathering events.¹³Adjusted for age, sex, chronic disease, education, smoking habit, physical exercise, alcohol consumption, obesity, family members, observation person cough, mass gathering events.¹⁴Adjusted for age, sex, chronic disease, education, smoking habit, physical exercise, alcohol consumption, obesity, family COVID-19 case, observation person cough, mass gathering events.¹⁵Adjusted for age, sex, chronic disease, smoking habit, physical exercise, alcohol consumption, obesity.¹⁶Adjusted for age, sex, blood groups, reinfection, smoking habit, physical exercise, alcohol consumption, obesity, education, chronic disease, medical assistance.¹⁷ Adjusted for age, sex, blood groups, reinfection, smoking habit, physical exercise, alcohol consumption obesity, education, chronic disease, duration illness.¹⁸Adjusted for age, sex, blood groups, reinfection, smoking habit, physical exercise, alcohol consumption, obesity, education, chronic disease, medical assistance.¹⁹Adjusted for age, sex, blood groups, smoking habit, physical exercise, alcohol consumption, obesity, education, chronic disease.²⁰Adjusted for age, sex, smoking habit, physical exercise, alcohol consumption, obesity, mass gathering events, family members family COVID-19 case, observation person cough.

4. Discussion

With a considerable follow-up time, up to 40 months, the cumulative incidence of long COVID in our cohort was 28.6%. However, the evolution of the COVID-19 pandemic is clearly reflected in the difference between the cumulative incidences of 38.0% in the pre-Omicron, March 2020 to October 2021, and 14.4% in Omicron wave, November 2021 to August 2023. Recovery of long COVID was low with only a third of patients recovered. Persistent symptoms such as fatigue, alterations in taste and smell alterations, loss of hair, dyspnea, and neurologic symptoms are consistent with other studies [8,13,14]. The rate of death was lower compared with the acute phase of the pandemic [24].

Several significant risk factors of long COVID were found in our cohort, including female sex, older age, chronic disease, B blood group, SARS-CoV-2 exposure, COVID-19 severity, SARS-CoV-2 reinfections, and SARS-CoV-2 infection during the first period of the pandemic. Asymptomatic infections and vaccination against SARS-CoV-2 were significantly protective factors.

The estimated cumulative incidence of long COVID is consistent with other cohort studies and its decrease in the Omicron period [25,26]. However, large variations of cumulative incidence of long COVID have been reported due to differences between methods, time of follow-ups, and populations of study[7,8,27–33]. Also, the incidence in children and adolescents was low in consistency with other studies [34,35].

In our cohort, the reduction of susceptible participants, lower SARS-CoV-2 exposures associated with preventive measures, vaccination against SARS-CoV-2, and changes in virulence of the Omicron variant could explain this pattern. The low recovery rate of the cohort is consistent with other studies [36–40].

In line with other studies of long COVID incidence, these risk factors include female sex, older age, chronic diseases, severity of COVID-19 infection, onset of infection in the period of pre-Omicron, SARS-CoV-2 reinfections and hospitalizations [41–43]. Exposures of SARS- CoV-2 during the first wave of the pandemic virus incremented the risk of long COVID, consistent with studies on

professions with high exposure of this infection which had a higher incidence of long COVID [44,45]. Asymptomatic cases presented less risk of long COVID with a probable innate immunity. In addition, patients with B blood group and two or one family member had more risk of long COVID than O group and families with 3 or more members, respectively. These risks are not found in other studies [41,46,47].

In contrast to some studies, low education level, obesity, and smoking were not risk factors in our cohort [48–50]. Current smoking was a risk factor in our first study of COVID-19 complications but not in this study [18].

In accordance with our previous study of prevalence of long COVID [51], vaccination against SARS-CoV-2 was a protective factor of long COVID in patients vaccinated before the onset of SARS-CoV-2 infection, and it corresponds with the Omicron variant period, in line with several studies [52–54]. The exact mechanism of this effect is not well understood, but it could be associated with a lower incidence of severe SARS-CoV-2 infection in the vaccinated population, and an increase in immune response and a decrease in autoantibodies [55,56].

Strengths of this study include its prospective population-based cohort design, a long follow-up time of the cohort, measured exposures before the syndrome occurred, and a control of potential confounding factors by the inverse probability weighted regression.

Thus the study has some limitations, including a self-reported of long COVID and its persistence with potential information bias, losses from the initial cohort, a definition of long COVID without laboratory confirmation, residual confounding could be presented, no information about SARS-CoV-2 variants, and as a new syndrome some aspects could be not considered in the study.

Maintaining the follow-up of this cohort with medical care for non-recovery long COVID patients is needed to obtain a completed recovery of the syndrome. In addition, continuing the research of long COVID to understand the biologic mechanisms of production is important considering the high prevalence and the low recovery rate of patients [57,58]. Research of new SARS-CoV-2 vaccines with few side effects deserves attention. In addition, epidemiological surveillance of SARS-CoV-2 infections in the population with detection and control of outbreaks, measures for infection's prevention, including health education, and SARS-CoV-2 vaccination at-risk population are recommended.

5. Conclusions

A high incidence of long COVID syndrome was found in the Borriana COVID-19 cohort after 40 months of follow-up with a low recovery rate, and several risk and protective factors were found. Continued follow-up of non-recovery long COVID patients, surveillance of the SARS-CoV-2 infections, and SARS-CoV-2 vaccination at risk population can be recommended.

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References

1. Cogliandro, V.; Bonfanti, P. Long COVID: lights and shadows on the clinical characterization of this emerging pathology. *New Microbiol.* **2024**, *47*, 15-27.
2. Pazukhina, E.; Garcia-Gallo, E.; Reyes, L.F.; Kildal, A.B.; Jassat, W.; Dryden, M.; Holter, J.C.; Chatterjee, A.; Gomez, K.; Søråas, A., et al. Long Covid: a global health issue - a prospective, cohort study set in four continents. *BMJ Glob Health.* **2024**, *9*, e015245.
3. Sharma, S.K.; Mohan, A.; Upadhyay, V. Long COVID syndrome: An unfolding enigma. *Indian J Med Res.* **2024**, *159*, 585-600.
4. Soriano, J.B.; Murthy, S.; Marshall, J.C.; Relan, P.; Diaz, J.V.; WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis.* **2022**, *22*, e102-e107.
5. Thaweethai, T.; Jolley, S.E.; Karlson, E.W.; RECOVER Consortium. Development of a definition of postacute sequelae of SARS-CoV-2 infection. *JAMA.* **2023**, *329*, 1934-1946.
6. Geng, L.N.; Erlandson, K.M.; Hornig, M. RECOVER Consortium. 2024 Update of the RECOVER-Adult Long COVID Research Index. *JAMA.* **2025**, *333*, 694-700.
7. Saheb Sharif-Askari, F.; Ali Hussain Alsayed, H.; Saheb Sharif-Askari, N.; Saddik, B.; Al Sayed Hussain, A.; Halwani, R. Risk factors and early preventive measures for long COVID in non-hospitalized patients: analysis of a large cohort in the United Arab Emirates. *Public Health.* **2024**, *230*, 198-206.
8. Bai, F.; Tomasoni, D.; Falcinella, C.; Barbanotti, D.; Castoldi, R.; Mulè, G.; Augello, M.; Mondatore, D.; Allegrini, M.; Cona, A.; et al. Female gender is associated with long COVID syndrome: a prospective cohort study. *Clin Microbiol Infect.* **2022**, *28*, 611.e9-611.e16.
9. Peluso, M.J.; Deeks, S.G. Mechanisms of long COVID and the path toward therapeutics. *Cell.* **2024**, *187*, 5500-5529.
10. Gheorghita, R.; Soldanescu, I.; Lobiuc, A.; Caliman Sturdza, O.A.; Filip, R.; Constantinescu-Bercu, A.; Dimian, M.; Mangul, S.; Covasa, M. The knowns and unknowns of long COVID-19: from mechanisms to therapeutical approaches. *Front Immunol.* **2024**, *15*, 1344086.
11. Shabnam, S.; Razieh, C.; Dambha-Miller, H.; Yates, T.; Gillies, C.; Chudasama, Y.V.; Pareek, M.; Banerjee, A.; Kawachi, I.; Lacey, B.; et al. Socioeconomic inequalities of Long COVID: a retrospective population-based cohort study in the United Kingdom. *J R Soc Med.* **2023**, *116*, 263-273.
12. Salci, M.A.; Carreira, L.; Oliveira, N.N.; Pereira, N.D.; Covre, E.R.; Pesce, G.B.; Oliveira, R.R.; Höring, C.F.; Baccon, W.C.; Puente Alcaraz, J.; et al. Long COVID among Brazilian Adults and Elders 12 Months after Hospital Discharge: A Population-Based Cohort Study. *Healthcare (Basel).* **2024**, *12*, 1443.
13. Bahmer, T.; Borzikowsky, C.; Lieb, W.; Horn, A.; Krist, L.; Fricke, J.; Scheibenbogen, C.; Rabe, K.F.; Maetzler, W.; Maetzler, C.; et al. Severity, predictors and clinical correlates of Post-COVID syndrome (PCS) in Germany: A prospective, multi-centre, population-based cohort study. *EClinicalMedicine.* **2022**, *51*, 101549.
14. Ellingjord-Dale, M.; Nygaard, A.B.; Støer, N.C.; Bø, R.; Landrø, N.I.; Brunvoll, S.H.; Istre, M.; Kalleberg, K.T.; Dahl, J.A.; Geng, L., et al. Temporal trajectories of long-COVID symptoms in adults with 22 months follow-up in a prospective cohort study in Norway. *Int J Infect Dis.* **2024**, *149*, 107263.
15. Sigfrid, L.; Drake, T.M.; Pauley, E.; Jesudason, E.C.; Olliaro, P.; Lim, W.S.; Gillesen, A.; Berry, C.; Lowe, D.J.; McPeake, J.; et al. Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. *Lancet Reg Health Eur.* **2021**, *8*, 100186.

16. Boglione, L.; Meli, G.; Poletti, F.; Rostagno, R.; Moglia, R.; Cantone, M.; Esposito, M.; Scianguetta, C.; Domenicale, B.; Di Pasquale, F.; et al. Risk factors and incidence of long-COVID syndrome in hospitalized patients: does remdesivir have a protective effect? *QJM*. **2022**, *114*, 865-871.
17. Domènech-Montoliu, S.; Pac-Sa, M.R.; Vidal-Utrillas, P.; Latorre-Poveda, M.; Del Rio-González, A.; Ferrando-Rubert, S.; Ferrer-Abad, G.; Sánchez-Urbano, M.; Aparisi-Esteve, L.; Badenes-Marques G.; et al. "Mass gathering events and COVID-19 transmission in Borriana (Spain): A retrospective cohort study". *PLoS One*. **2021**, *16*, e0256747.
18. Domènech-Montoliu, S.; Puig-Barberà, J.; Pac-Sa, M.R.; Vidal-Utrillas, P.; Latorre-Poveda, M.; Del Rio-González, A.; Ferrando-Rubert, S.; Ferrer-Abad, G.; Sánchez-Urbano, M.; Aparisi-Esteve, L.; et al. Complications post-COVID-19 and risk factors among patients after six months of a SARS-CoV-2 infection: A population-based prospective cohort study. *Epidemiologia (Basel)*. **2022**, *3*, 49-67.
19. Domènech-Montoliu, S.; Pérez-Olaso, Ó.; Sala-Trull, D.; Del Rio-Gonzalez, A.; López-Diago, L.; Aleixandre-Goriz, I.; Pac-Sa, M.R.; Sánchez-Urbano, M.; Satorres-Martinez, P.; Notari-Rodriguez, C.; et al. SARS-CoV-2 mRNA vaccine effectiveness in the Borriana COVID-19 cohort: A prospective population-based cohort study. *Epidemiologia (Basel)*. **2025**, *7*, 1.
20. Egger, M.; Bundschuh, C.; Wiesinger, K.; Gabriel, C.; Clodi, M.; Mueller, T.; Dieplinger, B. Comparison of the Elecsys® Anti-SARS-CoV-2 immunoassay with the EDI™ enzyme linked immunosorbent assays for the detection of SARS-CoV-2 antibodies in human plasma. *Clin Chim Acta*. **2020**, *509*, 18-21.
21. Narasimhan, M.; Mahimainathan, L.; Araj, E.; Clark, A.E.; Markantonis, J.; Green, A.; Xu, J.; SoRelle, J.A.; Alexis, C.; Fankhauser, K.; et al. Clinical evaluation of the Abbott Alinity SARS-CoV-2 spike-specific quantitative IgG and IgM assays among infected, recovered, and vaccinated groups. *J Clin Microbiol*. **2021**, *59*, e0038821.
22. Robins, J.M.; Hernán, M.A.; Brumback, B. Marginal structural models and causal inference in epidemiology. *Epidemiology*. **2000**, *11*, 550-60.
23. Textor, J.; van der Zander, B.; Gilthorpe, M.S.; Liskiewicz, M.; Ellison, G.T. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. **2016**, *45*, 1887-1894.
24. Lippi, G.; Sanchis-Gomar, F. Mortality of post-COVID-19 condition: 2025 update. *COVID* **2025**, *5*, 11.
25. Antonelli, M.; Pujol, J.C.; Spector, T.D.; Ourselin, S.; Steves, C.J. Risk of long COVID associated with delta versus omicron variants of SARS-CoV-2. *Lancet*. **2022**, *399*, 2263-2264.
26. Du, M.; Ma, Y.; Deng, J.; Liu, M.; Liu, J. Comparison of long COVID-19 caused by different SARS-CoV-2 strains: A systematic review and meta-analysis. *Int J Environ Res Public Health*. **2022**, *19*, 16010.
27. Pérez-González, A.; Araújo-Ameijeiras, A.; Fernández-Villar, A.; Crespo, M.; Poveda, E.; Cohort COVID-19 of the Galicia Sur Health Research Institute. Long COVID in hospitalized and non-hospitalized patients in a large cohort in Northwest Spain, a prospective cohort study. *Sci Rep*. **2022**, *12*, 3369.
28. Di Gennaro, F.; Belati, A.; Tulone, O.; Diella, L.; Fiore Bavaro, D.; Bonica, R.; Genna, V.; Smith, L.; Trott, M.; Bruyere, O.; et al. Incidence of long COVID-19 in people with previous SARS-Cov2 infection: a systematic review and meta-analysis of 120,970 patients. *Intern Emerg Med*. **2023**, *18*, 1573-1581.
29. Jeffrey, K.; Hammersley, V.; Maini, R.; Crawford, A.; Woolford, L.; Batchelor, A.; Weatherill, D.; White, C.; Millington, T.; Kerr, R.; et al. Deriving and validating a risk prediction model for long COVID: a population-based, retrospective cohort study in Scotland. *J R Soc Med*. **2024**, *117*, 402-414.
30. Ruiyin, W.; Qi, J.; Tingting, W.; Yuqin, Y.; Yan, J.; Kun, P. Long COVID outcomes following omicron wave in non-hospital population. *Front Public Health*. **2024**, *12*, 1377866.
31. Kogevinas, M.; Karachaliou, M.; Espinosa, A.; Iraola-Guzmán, S.; Castaño-Vinyals, G.; Delgado-Ortiz, L.; Farré, X.; Blay, N.; Pearce, N.; Bosch de Basea, M.; et al. Risk, determinants, and persistence of long-COVID in a population-based cohort study in Catalonia. *BMC Med*. **2025**, *23*, 140.
32. Dosbayeva, A.; Serikbayev, A.; Sharapiyeva, A.; Amrenova, K.; Krykpayeva, A.; Kairkhanova, Y.; Dyussupov, A.; Seitkabylov, A.; Zhumanbayeva, Z. Post-COVID-19 syndrome: Incidence, biomarkers, and clinical patterns in Kazakhstan. *Georgian Med News*. **2025**, *363*, 184-192.

33. Gottlieb, M.; Yu, H.; Chen, J.; Spatz, E.S.; Gentile, N.L.; Geyer, R.E.; Santangelo, M.; Malicki, C.; Gatling, K.; Saydah, S.; et al. Differences in Long COVID severity by duration of illness, symptom evolution, and vaccination: a longitudinal cohort study from the INSPIRE group. *Lancet Reg Health Am.* **2025**, *44*, 101026.
34. Asghar, A.F.; Enderle, J.; Salazar, J.H.; Esani, M. Predictors of post-acute sequelae of coronavirus disease 2019 and long COVID in adults and children: a retrospective cohort study using us electronic health record data. *J Public Health (Oxf).* **2026**, *48*, 185-194.
35. Mandel, H. Yoo, Y.J.; Allen, A.J.; Abedian, S.; Verzani, Z.; Karlson, E.W.; Kleinman, L.C.; Mudumbi, P.C.; Oliveira, C.R.; Muszynski, J.A.; et al. Long COVID incidence proportion in adults and children between 2020 and 2024: An electronic health record-based study from the RECOVER initiative. *Clin Infect Dis.* **2025**, *80*, 1247-1261.
36. Pazukhina, E.; Andreeva, M.; Spiridonova, E.; Bobkova, P.; Shikhaleva, A.; El-Taravi, Y.; Rumyantsev, M.; Gamirova, A.; Bairashevskaya, A.; Petrova, P.; et al. Prevalence and risk factors of post-COVID-19 condition in adults and children at 6 and 12 months after hospital discharge: a prospective, cohort study in Moscow (StopCOVID). *BMC Med.* **2022**, *20*, 244.
37. Rahmati, M.; Udeh, R.; Yon, D.K.; Lee, S.W.; Dolja-Gore, X.; McEVoy, M.; Kenna, T.; Jacob, L.; López Sánchez, G.F.; Koyanagi, A.; et al. A systematic review and meta-analysis of long-term sequelae of COVID-19 2-year after SARS-CoV-2 infection: A call to action for neurological, physical, and psychological sciences. *J Med Virol.* **2023**, *95*, e28852.
38. Lee, C.; Williams, P.; Abrahams, A.; Darbyshire, J.; Davies, H.E.; De Kock, J.; Esmer, U.; Jones, S.A.; Newey, V.; Scott, J.; et al. What Can We Learn Four Years On? A multi-centre service evaluation exploring symptoms, functional impact, recovery and care pathways in Long Covid. *Health Expect.* **2025**, *28*, e70435.
39. Ávila Nieto, A.; Infante, P.; Barca Durán, F.J. Prevalence and persistence of post-COVID-19 condition after critical care: 32-month follow-up. *J Clin Med.* **2026**, *15*, 711.
40. Shi, Y.; Strobl, R.; Apfelbacher, C.; Bahmer, T.; Geisler, R.; Heuschmann, P.; Horn, A.; Hoven, H.; Keil, T.; Krawczak, M.; et al. Persistent symptoms and risk factors predicting prolonged time to symptom-free after SARS-CoV-2 infection: an analysis of the baseline examination of the German COVIDOM/NAPKON-POP cohort. *Infection.* **2023**, *51*, 1679-1694.
41. Coste, J.; Delpierre, C.; Robineau, O.; Rushyizekera, M.; Richard, J.B.; Alleaume, C.; Gallay, A.; Tebeka, S.; Steichen, O.; Lemogne, C.; et al. A multidimensional network of factors associated with long COVID in the French population. *Commun Med (Lond).* **2025**, *5*, 114.
42. Zemni, I.; Gara, A.; Bennasrallah, C.; Ezzar, S.; Kacem, M.; Chokri, R.; Maatouk, A.; Abroug, H.; Dhoubi, W.; Fredj, M.B.; et al. Incidence and risk factors of post COVID-19 syndrome: a Tunisian cohort study. *BMC Infect Dis.* **2024**, *24*, 461.
43. Shah, D.P.; Thaweethai, T.; Karlson, E.W.; Bonilla, H.; Horne, B.D.; Mullington, J.M.; Wisnivesky, J.P.; Hornig, M.; Shinnick, D.J.; Klein, J.D.; et al. Sex Differences in Long COVID. *JAMA Netw Open.* **2025**, *8*, e2455430.
44. De Matteis, S.; Consonni, D.; Espinosa, A.; de Cid, R.; Magriña, N.B.; Castaño-Vinyals, G.; Karachaliou, M.; Alba Hidalgo, M.A.; Papantoniou, K.; Garcia, J.; et al. Occupational determinants of Long COVID in the population-based COVICAT cohort. *Occup Environ Med.* **2026**, *82*, 579-588.
45. Rushyizekera, M.; Delpierre, C.; Makovski, T.T.; Coste, J. Occupational and non-occupational factors of post-COVID-19 condition: a cross-sectional survey in the French general working population. *BMJ Public Health.* **2025**, *3*, e001613.
46. Guzman-Esquivel, J.; Mendoza-Hernandez, M.A.; Guzman-Solorzano, H.P.; Sarmiento-Hernandez, K.A.; Rodriguez-Sanchez, J.P.; Martinez-Fierro, M.L.; Paz-Michel, B.A.; Murillo-Zamora, E.; Rojas-Larios, F.; Lugo-Trampe, A.; et al. Clinical characteristics in the acute phase of COVID-19 that predict long COVID: tachycardia, myalgias, severity, and use of antibiotics as main risk factors, while education and blood group B are protective. *Healthcare (Basel).* **2023**, *11*, 197.
47. Soriano, J.B.; Peláez, A.; Busquets, X.; Rodrigo-García, M.; Pérez-Urría, E.Á.; Alonso, T.; Girón, R.; Valenzuela, C.; Marcos, C.; García-Castillo, E.; et al. ABO blood group as a determinant of COVID-19 and Long COVID: An observational, longitudinal, large study. *PLoS One.* **2023**, *18*, e0286769.

48. 48 Subramanian, A.; Nirantharakumar, K.; Hughes, S.; Myles, P.; Williams, T.; Gokhale, K.M.; Taverner, T.; Chandan, J.S.; Brown, K.; Simms-Williams, N.; et al. Symptoms and risk factors for long COVID in non-hospitalized adults. *Nat Med.* **2022**, *28*, 1706-1714.
49. 49. Adebisi, Y.A.; Ogunkola, I.O.; Jimoh, N.D.; Alshahrani, N.Z.; Shomuyiwa, D.O.; Alaran, A.J.; Lucero-Prisno, D.E 3rd. Tobacco smoking and the risk of Long COVID: a prospective cohort study with mediation analysis. *J Epidemiol Popul Health.* **2025**, *73*, 203142.
50. 50. Feldman, C.H.; Santacroce, L.; Bassett, I.V.; Thaweethai, T.; Alicic, R.; Atchley-Challenner, R.; Chung, A.; Goldberg, M.P.; Horowitz, C.R.; Jacobson, K.B.; et al. Social determinants of health and risk for Long COVID in the U.S. RECOVER-Adult Cohort. *Ann Intern Med.* **2025**, *178*, 1287-1297.
51. 51. Domènech-Montoliu, S.; Puig-Barberà, J.; Badenes-Marques, G.; Gil-Fortuño, M.; Orrico-Sánchez, A.; Pac-Sa, M.R.; Perez-Olaso, O.; Sala-Trull, D.; Sánchez-Urbano, M.; Arnedo-Pena, A. Long COVID Prevalence and the Impact of the Third SARS-CoV-2 Vaccine Dose: A Cross-Sectional Analysis from the Third Follow-Up of the Borriana Cohort, Valencia, Spain (2020-2022). *Vaccines (Basel).* **2023**, *11*, 1590.
52. 52. Abul, Y.; Harris, D.A.; Chachlani, P.; Hayes, K.N.; Zullo, A.R.; Mor, V.; Gravenstein, S. Incidence of long COVID diagnoses in 3.6 million U.S. Medicare beneficiaries with COVID-19. *J Gerontol A Biol Sci Med Sci.* **2025**, *80*, glaf108.
53. 53. Byambasuren, O.; Stehlik, P.; Clark, J.; Alcorn, K.; Glasziou, P. Effect of covid-19 vaccination on long covid: systematic review. *BMJ Med.* **2023**, *2*, e000385.
54. 54. Català, M.; Mercadé-Besora, N.; Kolde, R.; Trinh, N.T.H.; Roel, E.; Burn, E.; Rathod-Mistry, T.; Kostka, K.; Man, W.Y.; Delmestri, A.; et al. The effectiveness of COVID-19 vaccines to prevent long COVID symptoms: staggered cohort study of data from the UK, Spain, and Estonia. *Lancet Respir Med.* **2024**, *12*, 225-236.
55. 55. Hedberg, P.; van der Werff, S.D.; Naclér, P. The effect of COVID-19 vaccination on the risk of persistent post-COVID-19 condition: Cohort study. *J Infect Dis.* **2025**, *231*, e941-e944.
56. 56. Guimarães, G.N.; Brunetti, N.S.; De Lima, D.G.; Proenca-Modena, J.L.; Farias, A.S. Vaccination and COVID-19: impact on long-COVID. *Front Immunol.* **2025**, *16*, 1686572.
57. 57. Latifi, A.; Flegr, J. Persistent health and cognitive impairments up to four years post-COVID-19 in young students: The impact of virus variants and vaccination timing. *Biomedicines.* **2024**, *13*, 69. .
58. 58. Sardell, J.; Pearson, M.; Chocian, K.; Das, S.; Taylor, K.; Strivens, M.; Gupta, R.; Rochlin, A.; Gardner, S. Reproducibility of genetic risk factors identified for long COVID using combinatorial analysis across US and UK patient cohorts with diverse ancestries. *J Transl Med.* **2025**, *23*, 516.

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