Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Table 2
Results of the univariate and multivariate analyses of mortality and the combined event of respiratory failure and death

Variables	Univariate		Multivariate	
	OR (95%CI)	*P*	OR (95%CI)	*P*
Mortality				
Age	1.096 (1.074-1.118)	< .001	1.089 (1.062-1.116)	< .001
Hypertension	3.850 (2.480-5.977)	< .001		
Diabetes mellitus	2.578 (1.603-4.144)	< .001		
Chronic kidney disease	3.175 (1.611-6.258)	.001		
Heart disease	2.599 (1.531-4.411)	< .001		
$SatO_2$ < 90%	6.172 (3.771-10.099)	< .001	4.998 (2.752-9.078)	< .001
Lymphocytes < 1000/μL	2.388 (1.582-3.604)	< .001		
D-dimer > 500 μg/L	2.305 (1.373-3.869)	.002		
Creatinine > 1.5 mg/dL	9.973 (5.755-17.283)	< .001	7.538 (3.738-15.201)	< .001
C-reactive protein > 10 mg/L	2.728 (1.207-6.166)	.016		
Respiratory failure and death				
Age	1.053 (1.039-1.068)	< .001	1.038 (1.021-1.054)	< .001
Hypertension	3.850 (2.480-5.977)	< .001		
Diabetes mellitus	2.619 (1.637-4.190)	< .001		
Chronic kidney disease	4.044 (1.868-8.755)	< .001		
Heart disease	2.828 (1.646-4.857)	< .001	2.017 (1.050-3.876)	.035
$SatO_2$ < 90%	12.362 (6.625-23.068)	< .001	9.109 (4.703-17.644)	< .001
Lymphocytes < 1000/μL	2.554 (1.791-3.641)	< .001		
D-dimer > 500 μg/L	2.092 (1.392-3.144)	< .001		
Creatinine > 1.5 mg/dL	4.796 (2.700-8.520)	< .001	2.874 (1.415-5.836)	.003
C-reactive protein > 10 mg/L	3.810 (1.972-7.364)	< .001	4.309 (1.704-10.892)	.002

95%CI, 95% confidence interval; OR, odds ratio; SatO2, arterial oxygen saturation.

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Clinical course of COVID-19 in pulmonary arterial hypertension patients

Curso clínico de la COVID-19 en pacientes con hipertensión arterial pulmonar

To the Editor,

The coronavirus disease of 2019 (COVID-19) is an infectious disease caused by severe acute respiratory coronavirus 2 (SARS-CoV-2).[1] Most patients with severe disease develop pneumonia and acute respiratory distress syndrome (ARDS).[1] Patients with previous cardiovascular conditions seem to be at a higher risk for developing severe forms of COVID-19.[1]

Pulmonary arterial hypertension (PAH) is a rare disease with a poor long-term prognosis and a particularly high mortality risk during hospitalizations for noncardiovascular conditions.[2]

By 10 April 2020, 10 out of 350 PAH patients (100% female, 43.3 years [36.0-47.2]) followed up at our center were diagnosed with COVID-19.

All patients had a previous history of PAH (mean pulmonary artery pressure: 51.5 [44-66] mmHg; pulmonary vascular resistance 10.9 [8-18.4] Wood units). Median time from PAH diagnosis to COVID-19 was 3.9 [0.6–11.1] years.

A total of 7 patients (70%) required hospitalization (length of stay 10 [4-16] days), none in the intensive care unit. Five (50%) developed pneumonia, with ARDS features in 2 patients. Five patients (50%) needed oxygen therapy (3 of them were on domiciliary oxygen therapy). Clinical outcome was favorable in all patients (table 1).

We report the clinical characteristics and outcomes of PAH patients with COVID-19. The mortality risk from noncardiovascular processes for PAH patients is particularly high (9.4% for

Table 1
Patients' baseline characteristics before infection and COVID-19 clinical picture

Pt	Sex	Etiology	Years	HTN	Smoker	MPAP mmHg	PVR WU	CI l/min/m^2	ESC risk score	PAH treatment	Picture	T °C	CXR pattern	CRP mg/dL	LDH u/L	ALC mL	DD ng/mL	LoS days	O_2	COVID-19 treatment
1	F	HIV	58	N	N	69	13.7	2.3	Intermediate	PDi ERA PC O_2	SOB	40	MLP	1.9[a]	265[a]	1300	1324[a]	16	HFO[b]	LPV-RTV HCQ
2	F	FPVOD	37	N	N	51	8.5	3.2	Low	PDi ERA O_2	SOB	39	MLP	2.1[a]	293[a]	1200	455	14	NS[b]	LPV-RTV
3	F	RCCB	43	N	N	26	2.7	2.9	Low	CCBs	Flu-like	38	Normal	0.17	168	400[a]	314	4	None	LPV-RTV HCQ
4	F	IPAH	47	Y	Y	28	2.5	3.1	Low	PDi ERA	Flu-like	38.5	Normal	0.65	NA	1650	NA	0	None	-
5	F	IPAH	50	N	N	42	5.6	2.8	Low	PDi ERA PC O_2	SOB	37.8	MLP	0.72	208	1520	266	6	NS[b]	HCQ
6	F	RCCB	35	N	N	29	1.9	3.3	Low	CCBs	None	36	Normal	NA	NA	NA	NA	0	None	-
7	F	CHD	76	N	N	44	5	3.24	Intermediate	None	ARDS	38	MLP	6.5[a]	NA	1050[a]	1300[a]	28	HFO	LPV-RTV HCQ
8	F	CTD	64	N	N	26	2.7	3.2	Low	ERA	ARDS	38	MLP	4.2[a]	228[a]	430[a]	520[a]	20	HFO	LPV-RTV HCQ IL6-A
9	F	HIV	53	N	Y	52	8	2.7	Intermediate	ERA	Flu-like	35.5	Normal	2.03[a]	191	1500	NA	3	None	LPV-RTV[c] HCQ
10	F	FPAH	35	N	N	62	11.2	2.9	Low	PDi ERA PC	Flu-like Diarrhea	38.5	Normal	5.8[a]	223[a]	1300	396	0	None	-

ALC, absolute lymphocyte count; ARDS, acute respiratory distress syndrome; °C, degrees Celsius; CCBs, calcium-channel blockers; CHD, congenital heart disease; CI, cardiac index; CRP, C-reactive protein; CTD, connective tissue disease; CXR, chest X-ray; DD, D-dimer; ERA, endothelin receptor antagonist; ESC, European Society of Cardiology; F, female; FC, functional class (World Health Organization); FPAH, familial pulmonary arterial hypertension; FPVOD, familial pulmonary veno-occlusive disease; HCQ, hydroxychloroquine; HFO, high-flow oxygen; HIV, human immunodeficiency virus; HTN, hypertension; IL6-A, interleukin-6 antagonist; IPAH, idiopathic pulmonary arterial hypertension; LDH, lactate dehydrogenase; LoS, length of stay; LPV-RTV, lopinavir-ritonavir; MLP, multilobar pneumonia; MPAP, mean pulmonary artery pressure; N, no; NS, nasal spectacles; O_2, domiciliary oxygen; PC, prostacyclin analogs or prostacyclin receptor agonists; PDi, phosphodiesterase type 5 inhibitors; pt, Patient; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RCCB, responders to calcium-channel blockers; SOB, shortness of breath; T, temperature; WU, Wood units; Y, yes.

[a] Indicates abnormal levels. Reference levels in local laboratory assays are (CRP $<$ 1 mg/dL; LDH $<$ 220 U/L; lymphocytes $>$ 1200 / mL; D-dimer $<$ 500 (ng/mL).

[b] Patients under domiciliary oxygen.

[c] HIV patient with chronic treatment with LPV-RTV.

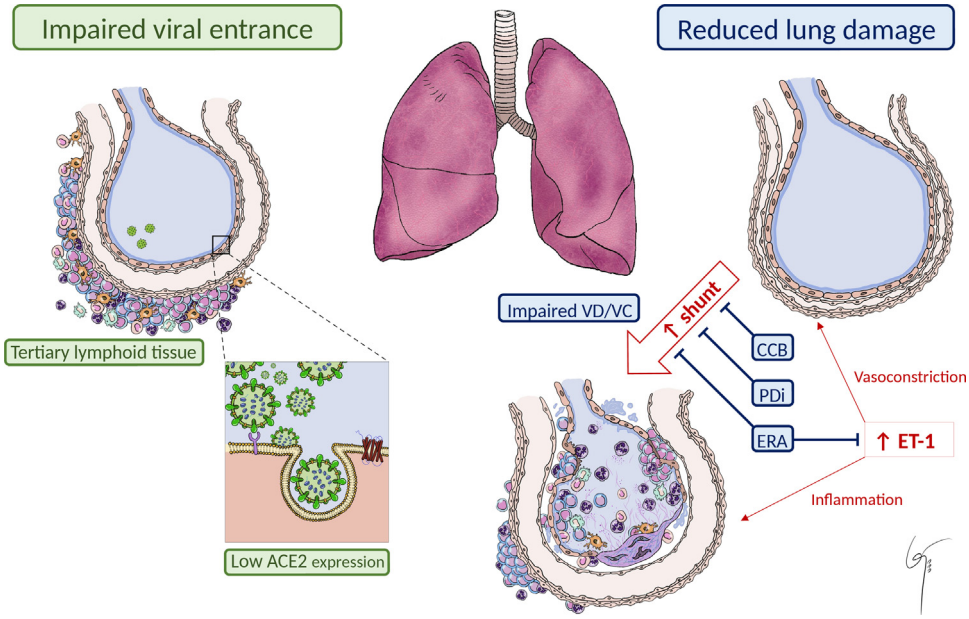

Figure 1. Possible explanations for the benign course of COVID-19 in PAH patients. Impaired viral entrance to pulmonary cells due to the presence of "tertiary lymphoid tissue" and reduced ACE2 expression. Reduced lung damage due to impaired "vasotonic" properties and to PAH vasodilator treatment, minimizing intrapulmonary shunt. Reduced inflammatory response mediated by ET-1 due to the effect of ERA. ACE2, angiotensin-converting enzyme 2; CCB, calcium-channel blocker; ERA, endothelin receptor antagonist; ET-1, endothelin-1; PDi, phosphodiesterase-5 inhibitor; VD/VC, vasodilatation/vasoconstriction.

pneumonia, 21.4% for respiratory failure).[2] Surprisingly, half of our patients only developed mild symptoms and, among those with established pneumonia, a favorable course was the general trend, without need for intensive care or deaths.

We hypothesize that the physiopathological features of PAH and the benefits attributable to specific treatment might lead to a protective effect through the following mechanisms (figure 1):

1. Reduced viral entrance:
   - *Angiotensin-converting enzyme 2 (ACE2):* In PAH patients' blood and lungs, ACE2 expression is decreased.[3] Indeed, recombinant ACE2 has been proposed as a novel therapy for PAH, to reverse vasoconstriction, proliferation, and inflammation.[3] ACE2 is known to act as a receptor for SARS-CoV-2. Experimental studies with SARS-CoV have shown that in ACE2 knockout mice, only a very low quantity of infectious SARS-CoV virus could be recovered.[4] Thus, low ACE2 levels in PAH patients could act as a protective factor at an initial infective phase, avoiding SARS-Cov-2 entrance.
   - *The role of chronic inflammation in PAH:* Chronic pulmonary inflammation is a common finding in PAH patients.[3,5] The immune cell types that infiltrate the lungs of PAH patients include lymphocytes, macrophages, neutrophils, dendritic cells, and mast cells. This different immune cellular landscape in PAH lungs suggests a shift toward the adaptive immune system. Therefore, the so-called tertiary lymphoid tissue is present in the vicinity of bronchioles and could limit viral infection and expansion.

2. Attenuated lung damage: Changes in pulmonary circulation inherent to PAH pathophysiology or related to specific vasodilator treatment might reduce the damage inflicted to the lungs and the consequent severe hypoxemia described in COVID-19 patients.
   - *Changes in lung perfusion*: An atypical form of ARDS has been described among COVID-19 patients. An unusual dissociation between lung mechanical properties (with nearly normal compliance) and severe hypoxemia has been reported,[6] suggesting abnormal hyperperfusion of nonventilated areas as a consequence of impaired lung perfusion regulation and hypoxic vasoconstriction.[6] The basal abnormal lung perfusion present in PAH patients could limit this abrupt perfusion imbalance toward nonventilated areas. Furthermore, chronic vasodilator treatment could prevent a severe hypoxic vasoconstriction response. In this regard, phosphodiesterase-5 inhibitors and even calcium-channel blockers have been proposed as a potential treatment for COVID-19, based on its vasodilator properties and a clinical trial with sildenafil is currently ongoing (NCT:04304313).[1] Thus, pulmonary vasodilator therapy of our patients could have attenuated hypoxic vasoconstriction and have favored the ventilation/perfusion balance.
   - *Protective effect of endothelin receptor antagonists (ERAs) against ARDS:* ARDS is caused by a severe inflammatory response, mediated by several proinflammatory agents and cytokines (tumoral necrosis factor, interleukins, or endothelin-1).[5] Endothelin-1 has been shown to be involved in the pathogenesis of both ARDS and PAH.[5] Previous reports suggest that ERAs might be useful in the treatment of ARDS, based on their beneficial effects in experimental preclinical studies.[5] A total of 7 patients (70%) in our cohort received ERAs when diagnosed with COVID-19, thus suggesting the possibility of a beneficial effect of chronic endothelin-1 blockade.

The clinical course of COVID-19 in our cohort of PAH patients was unexpectedly favorable. This finding could be explained by either the pathophysiological peculiarities of the disease or by a protective effect of PAH-specific treatment. PAH therapies may also have a protective effect in COVID-19, although that can only be addressed in placebo-controlled randomized controlled trials.

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Decrease in ST-segment elevation myocardial infarction admissions in Catalonia during the COVID-19 pandemic

Reducción de los ingresos por infarto agudo de miocardio con elevación del segmento ST en Cataluña durante la pandemia de COVID-19

To the Editor,

On February 2020, the coronavirus disease of 2019 (COVID-19) rapidly spread throughout Europe. Due to the lack of pharmacological treatment or vaccine, governments adopted measures called social distancing to reduce the peak intensity of the epidemic. In Spain, the government issued a decree declaring a state of alarm on 14 March, 2020.

Timely reperfusion therapy by primary percutaneous coronary intervention (pPCI) is recommended for patients with ST-segment elevation myocardial infarction (STEMI)[1] and its benefit is time-dependent, with longer delays associated with worse outcomes. A recent survey of Spanish STEMI networks reported a reduction in pPCI procedures during the COVID-19 pandemic.[2] We aimed to assess the reduction in STEMI admissions and changes in patient characteristics, delay times and early mortality during the first weeks of the COVID-19 pandemic in Catalonia.

In Catalonia, a Spanish region with 7.6 million inhabitants, acute care for patients with STEMI is organized through a regional network of 10 pPCI hospitals.

The AMI code registry collects data from all attended STEMI patients. The registry belongs to the health department of the Catalan government and its completion is compulsory and periodically audited. The database conforms to ethical and legal requirements for research purposes, and all study procedures are conducted in accordance with the ethical standards of the Helsinki Declaration.

All patients with a confirmed STEMI from 1 March to 19 April, 2020, were compared with patients attended within the same dates in 2019.

Delay times were defined according to the European Guidelines.[1] Patient delay was defined as time from symptom onset to first medical contact. System delay as time from first contact to reperfusion therapy. Ischemia time as time from symptom onset to reperfusion therapy. Delay times were stratified by site of first medical contact.

Admission rates were estimated with Poisson regression models with time (days) as a continuous variable. Categorical variables are expressed as number and percentage and were compared with the chi-square test. Continuous variables are expressed as mean ± standard deviation and were compared with the Student *t* test. Time intervals are expressed as median [interquartile range] and were compared with the Kruskal-Wallis equality-of-populations rank test. Mortality at 10 days after activation was estimated for all patients with available information about vital status (STEMI occurring between March 1 and April 10).

A total of 395 STEMI patients were admitted during the 2020 period and 524 during the same period in 2019. The mean number of daily admissions was 10.5 in 2019 and 7.9 in 2020 (incidence rate ratio, 0.75; 95% confidence interval, 0.66-0.86). In 2020, there was a significant 52% reduction in daily admissions from day 1 to day 50 (figure 1). There were few differences between the groups (table 1).

A similar reduction in STEMI admissions has already been reported in other settings.[3–5] To our knowledge, this is the first study performed in Spain using individual patient data from a regional STEMI network. We observed a 50% reduction in STEMI admissions in 50 days and only slight differences in patient characteristics and delay times compared with patients admitted during the same period in 2019. Potential causes of this decrease in STEMI admissions include avoidance of medical care due to social distancing, STEMI underdiagnosis, and competing risk