Transesophageal echocardiography was performed in all patients. In this investigation, periprosthetic leak was found in only 1 patient, vegetations were identified in 2 patients, and periannular thickening was observed in 7, but this was not diagnostic of an abscess (< 10 mm).

Due to raised clinical suspicion, 10 patients underwent ^{18}F-fluorodesoxyglucose positron-emission tomography/computed tomography (^{18}F-FDG PET/CT). In patient 2, with no findings on transesophageal echocardiography or PET, the diagnosis was confirmed on post-mortem; in patient 4, ^{18}F-FDG PET/CT was the first investigation because the patient had esophageal varices, and in patient 5 it was performed as part of the preoperative surgical planning. There was a diverse intensity of metabolic uptake among the patients, with anatomical depiction of periannular abscess in all of them (figure 1).

All 14 patients had an indication for surgery, but this was ruled out in 3 due to excessive risk. In 8 of the 11 patients who underwent surgery, a new Perceval S prosthesis was implanted after patching the aortic annulus with bovine pericardium. In all the patients who underwent surgery, the intraoperative findings correlated with those described on ^{18}F-FDG PET/CT. Furthermore, the anatomical information provided with this technique facilitated planning of the most appropriate surgical strategy.

In-hospital mortality was 14% (n = 2), and during follow-up (mean, 23 months) 5 patients died (41%), 2 of whom had previously been declined surgery.

The special design of the Perceval S prosthesis, anchoring the valve to the aortic annulus by means of the radial force of the nitinol stent alone, means that the echocardiographic presentation of endocarditis can differ from that of other valve replacements. The lack of periprosthetic leak could delay the diagnosis with transesophageal echocardiography, especially if the images of periannular involvement are not diagnostic of abscess.

Although transesophageal echocardiography is an essential tool in the diagnosis of PVE, a false negative rate of up to 10% has been described in the early stages of the disease.[4] With this type of prosthesis, it can be helpful to use other imaging techniques, such as ^{18}F-FDG PET/CT, a very useful diagnostic tool when there is suspicion of PVE, even in the early stages.[5,6] Electrocardiogram-synchronized CT has very high sensitivity for detecting periannular abscesses (> 95%), which is increased with the metabolic information from PET.[6]

In our experience, presentation of PVE on a Perceval S valve differs from that on other biological prostheses when it comes to the echocardiographic diagnosis. The use of other techniques such as ^{18}F-FDG PET/CT can facilitate an early diagnosis and better evaluation of periannular anatomical involvement. Such an approach could expedite treatment decisions and minimize the risk of severe local complications that would increase the complexity of subsequent surgery.

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CONFLICTS OF INTEREST

None.

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Impact of statins in patients with COVID-19

Impacto de las estatinas en los pacientes con COVID-19

To the Editor,

On November 11, 2020, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) had infected 9 187 237 people worldwide with an estimated mortality rate of 2.7%.[1] Initial reports hinted that a dysregulated immune system might play a key role in its lethality.[2] Patients with a prior history of cardiovascular disease (CVD) or risk factors are particularly at higher risk.[3]

Statins are common among high-risk patients and have been demonstrated to diminish the incidence of cardiovascular morbidity and mortality. Interestingly, it has previously been suggested that statins may confer a protective benefit in viral infections. In theory, statins might lessen the incidence of acute injury in coronavirus disease 2019 (COVID-19) by: *a)* decreasing L-mevalonate downstream mediators; *b)* through inhibition of protein prenylation; and *c)* upregulation of angiotensin-converting

enzyme 2 levels.[4] However, the greater use of statins in patients with a higher CVD burden might counterbalance a potential protective effect compared with nonstatin users. Our aim was to describe the characteristics and evaluate the impact of chronic statin treatment in the prognosis of patients admitted to hospital due to COVID-19.

We have performed a retrospective, observational study performed in 2 Spanish tertiary hospitals of all admitted patients between March 1 and April 30, 2020 with a definitive diagnosis of SARS-CoV-2 infection confirmed through positive reverse transcriptase polymerase chain reaction. We recorded prescribed therapy before admission and during hospital stay according to the protocols of our institutions and the discretion of the medical team. Clinical outcomes were also registered. Categorical variables are reported as absolute values and percentages. Continuous variables are expressed as mean ± standard deviation; non normally distributed variables are reported as median [interquartile range]. The effect of statins on the primary outcome (in-hospital mortality) in the overall study population was evaluated with a multivariate logistic regression model after adjustment for the main cofounding factors. All the analyses were conducted using the statistical software IBM SPSS Statistics, Version 25.0. (IBM Corp, United States). Differences were considered statistically significant when P was $< .05$. The study was approved by the local ethics committee and informed consent was waived given its retrospective and observational nature.

Out of 840 patients admitted due to COVID-19, 295 (35.1%) were under statin therapy before hospital admission and 545 (64.9%) were not. Patients treated with statins were older (73.5 ± 10.1 vs 65.7 ± 15.9; $P < .001$) and had a higher prevalence of several comorbidities including hypertension (66.9% vs 41.3%; $P < .001$), diabetes mellitus (33% vs 12.1%; $P < .001$), and prior heart disease (13.9% vs 6.4%; $P < .001$). In parallel, those under statin therapy were more often receiving antihypertensive drugs, beta-blockers, and aspirin. Time from symptom onset to admission did not differ between groups. Statin users had a more prominent inflammatory profile at admission with higher C-reactive protein (92 vs 60.3 mg/dL; $P = .002$), interleukin-6 (26.35 vs 19 pg/mL; $P = .011$), and D-dimer levels (954 vs 717; $P = .001$). Overall, patients in the statin cohort were more commonly treated with intravenous corticosteroids (66.7% vs 56.2%; $P < .026$) and anticoagulants (69.9% vs 59.7%; $P = .033$), but other empirical drugs for the treatment of COVID-19 were used in similar rates. Major in-hospital outcomes including acute respiratory failure (9.8%), intensive care admission (10.5%), and all-cause mortality (20.4%) were comparable. Main baseline characteristics according to lipid-lowering treatment at baseline are summarized in table 1.

A logistic regression model was used to study the association between chronic statin use with clinical outcomes in hospitalized COVID-19 patients. The following variables were included in the definitive model: age, sex, hypertension, dyslipidemia, diabetes,

Table 1
Baseline characteristics and outcomes of statin vs nonstatin users infected with SARS-CoV-2

Variable	Overall COVID-19 population N = 840	Statin users n = 295 (35.1%)	Nonstatin users n = 545 (64.9%)	*P*
Baseline characteristics				
Male sex	427/840 (50.8)	156/295 (52.9)	271/545 (49.7)	.382
Age, y	68.15 ± 14.73	73.47 ± 10.08	65.66 ± 15.93	< .001[d]
CKD[a]	58/837 (6.9)	21/294 (7.1)	37/543 (6.8)	.858
COPD	77/813 (9.5)	36/288 (12.5)	41/525 (7.8)	< .029[d]
Diabetes	163/839 (19.4)	97/294 (33)	66/545 (12.1)	< .001[d]
Dyslipidemia	343/836 (41)	247/292 (84.6)	96/544 (17.6)	< .001[d]
Hypertension	421/838 (50.2)	196/293 (66.9)	225/545 (41.3)	< .001[d]
Prior heart disease	73/810 (9)	39/281 (13.9)	34/529 (6.4)	< .001[d]
Treatment prior to admission				
Aspirin	128/837 (15.3)	100/295 (33.9)	28/542 (5.2)	< .001[d]
ACEi	145/836 (17.3)	78/294 (26.5)	67/542 (12.4)	< .001[d]
ARB	176/839 (21)	80/295 (27.1)	96/544 (17.6)	.001[d]
Anticoagulants	98/838 (11.7)	44/294 (15)	54/544 (9.9)	.030[d]
BB	155/839 (18.5)	88/295 (29.8)	67/544 (12.3)	< .001[d]
Laboratory findings at admission				
Hemoglobin, g/dL	13.3 [12-14.5]	13.1 [11.85-14.2]	13.4 [12.1-14.6]	.174
eGFR, mL/min/1.73 m^2[b]	82 [56-90]	73 [51-87]	85 [62-90]	.001[d]
C-reactive protein, mg/L	66 [24-123.3]	92 [35.4-150.4]	60.3 [23-111.8]	.002[d]
D-Dimer, ng/mL	760 [453-1475]	954 [534-1719]	717 [403-1301]	.001[d]
ESR, mm/h	49 [30-66]	54 [39-73]	46 [28-58]	.067
Ferritin, ng/mL	562 [287-1100]	592 [335-1100]	557 [264-1113]	.434
GOT, UI/L	35 [24-52]	32.5 [24-52]	35.5 [24-52]	.575
Interleukin-6, pg/mL	21.8 [11-42.2]	26.35 [15-50.6]	19 [9.7-37.9]	.011[d]
LDH, UI/L	297 [225-403]	316 [244-421]	291 [218-396]	.006[d]
Lymphocytes, cells/mm^3	1000 [730-1375]	960 [720-1270]	1015 [730-1460]	.184
Platelets, cells/mm^3 x 10^3	205 [161-271,5]	202 [163,5-268,5]	206 [161-272]	.914
Procalcitonine, ng/mL	0.1 [0.06-0.26]	0.1 [0.06-0.29]	0.09 [0.05-0.22]	.081
hsTTn, pg/mL	15.2 [9-37]	15.8 [11.6-18.7]	15 [9-46.5]	.948
Nonspecific COVID-19 treatment				

Table 1 *(Continued)*
Baseline characteristics and outcomes of statin vs nonstatin users infected with SARS-CoV-2

Variable	Overall COVID-19 population N = 840	Statin users n = 295 (35.1%)	Nonstatin users n = 545 (64.9%)	*P*
Aspirin	60/513 (11.7)	45/162 (27.8)	15/351 (4.3)	< .001[d]
ACEi	92/840 (11)	52/295 (17.6)	40/545 (7.3)	< .001[d]
ARB	88/839 (10.5)	40/295 (13.6)	48/544 (8.8)	.033[d]
BB	85/513 (16.6)	48/162 (29.6)	37/351 (10.5)	< .001[d]
Statins	69/832 (8.3)	60/292 (20.5)	9/540 (1.7)	< .001[d]
Anticoagulation	323/513 (63)	114/163 (69.9)	209/350 (59.7)	.026[d]
Specific COVID-19 treatment				
Azithromycin	749/798 (93.9)	271/286 (94.8)	478/512 (93.4)	.431
Hydroxychloroquine	766/801 (95.6)	276/286 (96.5)	490/515 (95.1)	.368
Betaferon	223/799 (27.9)	81/286 (28.3)	142/513 (27.7)	.846
Lopinavir/ritonavir	701/802 (87.4)	250/287 (87.1)	451/515 (87.6)	.849
Corticosteroids	293/492 (59.6)	106/159 (66.6)	187/333 (56.2)	.026
Tocilizumab	44/796 (5.5)	13/284 (4.6)	31/512 (6.1)	.382
Main in-hospital outcomes				
Length of stay, d	9 [6-14]	9 [6-15]	9 [5-13]	.549
Acute respiratory failure[c]	338/806 (41.9)	127/285 (44.6)	211/521 (40.5)	.264
Heart failure	62/804 (7.7)	22/278 (7.9)	40/526 (7.6)	.876
ICU admission	86/822 (10.5)	30/286 (10.5)	56/536 (10.4)	.985
ICU LOS, d	13 [5.5-19]	13 [8-19]	12.5 [5.5-17]	.471
Mechanical ventilation	72/738 (9.8)	23/261 (8.8)	49/477 (10.3)	.523
All-cause overall mortality	171/840 (20.4)	64/295 (21.7)	107/545 (19.6)	.479

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blockers; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; hsTTn, high-sensitivity T-troponin.
Values are expressed as mean ± standard deviation, median [interquartile range], or No. (%).
[a] Chronic kidney disease was defined as a glomerular filtration rate of < 60 mL/min or need for dialysis.
[b] Estimated with the CKD-EPI formula.
[c] Defined as pO_2 < 60 mmHg, SO_2 < 92% or need for noninvasive or mechanical ventilation.
[d] Significant *P* values.

Table 2
Predictors of 30-day mortality in the study population

	Univariate		Multivariate	
	OR (95%CI)	*P*	OR (95%CI)	*P*
Male sex	2.03 (1.42-2.91)	< .001[d]	2.22 (1.43-1.64)	< .001[d]
Age, y	1.09 (1.07-1.11)	< .001[d]	1.1 (1.08-1.12)	< .001[d]
CKD	4.44 (2.59-7.64)	< .001[d]		
COPD	2.22 (1.35-3.64)	.002[d]		
Diabetes	2.82 (1.93-4.1)	< .001[d]	2.05 (1.27-3.29)	.003[d]
Hypertension	2.86 (1.99-4.09)	< .001[d]		
Smoking[a]	1.55 (1.07-2.26)	.021[d]		
Previous heart disease	2.26 (1.35-3.78)	.002[d]		
Statins	1.13 (0.801-1.61)	.479	0.48 (0.3-0.77)	.002[d]
Aspirin	2.35 (1.55-3.55)	< .001[d]	2.21 (1.26-3.87)	.006[d]
RAAS inhibitors[b]	1.76 (1.2-2.58)	.001[d]		
Anticoagulants[c]	3.81 (2.45-5.93)	< .001[d]	1.98 (1.16-3.38)	.013[d]
Beta-blockers	2.79 (1.90-4.09)	< .001[d]		
Diuretics	2.42 (1.55-3.79)	< .001[d]		

95%CI, 95% confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; OR, odds ratio; RAAS, renin-angiotensin-aldosterone system inhibitors.
[a] Includes active and former smokers.
[b] Includes angiotensin converting enzyme inhibitors, angiotensin receptor blockers and spironolactone/eplerenone.
[c] Vitamin K antagonist and new oral anticoagulants.
[d] Significant *P* values.

chronic obstructive pulmonary disease, chronic kidney disease, history of cigarette smoking, prior heart disease, and chronic adjuvant therapies (renin-angiotensin-aldosterone system inhibitors, beta-blockers, aspirin, and anticoagulation). In this model (see table 2), chronic statin treatment (adjusted odds ratio of 0.48, 95% confidence interval, 0.3-0.77; $P = .002$) was associated with lower in-hospital mortality compared with nonstatin users. In addition, elderly patients, male patients and diabetic patients were at a higher risk of death due to COVID-19.

Statins, with their pleiotropic properties, have the potential to reduce the severity of acute lung injury and mortality. Our findings are in agreement with those of a recent retrospective study that evaluated the impact of chronic statin treatment prior to COVID-19 hospitalization, in which statin use before hospital admission was associated with a 71% reduction for developing severe COVID-19.[5] Likewise, Xiao-Jing Zhang et al.[6] observed that in-hospital statin use was also associated with improved outcomes among COVID-19 patients.

This study has several limitations. Given the study design, we cannot infer causality of statins on mortality and it should be considered hypothesis generating. Our findings may be limited by the fact that we did not evaluate patients not admitted to hospital or under the effect of some unmeasured in-hospital confounders (eg, statin maintenance and impact of concomitant treatments). However, our results suggest that statin users with COVID-19 have a greater baseline risk mainly driven by more advanced age and a high burden of cardiovascular comorbidities, which might in theory disguise a potential protective effect of statins in this particular subset of patients. There is currently no evidence from any randomized controlled trial to show whether in-hospital statins may benefit patients with COVID-19, but we would like to draw the attention of the international community to this possibility until conclusive evidence is reported (STATCO19, NCT04380402).

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CONFLICTS OF INTEREST

None conflicts of interest.

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