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.

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Letter to the Editor

Impact of the COVID-19 pandemic on the diagnosis, management and prognosis of infective endocarditis

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To the Editor,

On 13 March, Spain declared a state of emergency and lockdown for COVID-19. In this context, organizational changes included, among others, the prohibition of holding face-to-face clinical meetings, the cancellation of non-urgent surgeries and the redistribution of medical teams to face the emergency. The aim of this study was to evaluate the impact of the COVID-19 pandemic on the diagnosis, management and prognosis of infective endocarditis (IE) patients in Spanish referral centres. We hypothesize that during the COVID-19 pandemic, fewer IE episodes have been diagnosed, and fewer surgeries during the active phase of infection have been performed.

This multicentre retrospective observational study was conducted at 26 Spanish referral centres for IE and cardiac surgery. Investigators were asked to complete a questionnaire about the organizational changes during the COVID-19 pandemic. They were also asked to collect retrospectively from their prospective IE registry clinical and outcome data for all consecutive definite IE episodes in adult patients (≥18 years) treated during the first month after the establishment of the state of emergency in Spain (14 March to 13 April) and for those patients treated during the same period in 2019. The main outcomes were the number of definite IE episodes treated and the rate of surgeries performed when indicated [1]. Comparisons between groups (2019 vs. 2020) were performed using the chi-squared test or Fisher's exact test for qualitative variables, as appropriate, and the two-sample Wilcoxon rank-sum (Mann–Whitney U) test for continuous variables. This study was approved by the Ethics Committee of the Hospital Universitari Vall d'Hebron (PR(AG)312-2020).

Fig. 1 shows the distribution of participating hospitals and the burden of laboratory-confirmed COVID-19 episodes by region for 14 March and 13 April 2020.

Twenty-five out of 26 participating centres suffered significant organizational changes (Table S1). Notably, in 23 periodic endocarditis team meetings were cancelled. The medical staff in charge of IE patients suffered different degrees of modification in 19. Strikingly, in six centres patients were attended by professionals without experience in the management of IE. Fourteen reported fewer transfer requests and four refused patient transfer for surgery. Eighteen reported alterations in the realization of echocardiograms due to lower availability. Cardiac surgeries were cancelled in eight, mostly (7/8) non-urgent surgeries. The length of admission was intentionally reduced in 12, enhancing outpatient antibiotic therapy (10). After finishing antimicrobial therapy, fewer control blood cultures were performed in seven, and 20 centres prioritized telematic control.

Compared with 2019, there was a 34% reduction in the absolute number of definite IE episodes in 2020 (from 136 to 90 cases) (Table 1). We found no differences in the percentage of patients

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Table 1
Comparison of clinical characteristics and outcomes of 226 patients with definite infective endocarditis treated at 26 Spanish referral centres between 14 March and April 13 2019 and 2020

	2019 ($n = 136$)	2020 ($n = 90$)[a]	p
Demographics			
Age in years, median (IQR)	69.6 (60.2–79.4)	70.3 (62.5–78.2)	0.645
Male sex	88 (64.7)	59 (65.6)	0.896
Comorbidities			
Charlson comorbidity index, median (IQR)	2 (1–3)	2 (1–4)	0.635
Calendar admission			
From 14 March to 31 March	103 (75.7)	70 (77.8)	0.723
From 1 April to 13 April	33 (24.3)	20 (22.2)	
Transferred from another hospital	45 (33.1)	30 (33.3)	0.969
Transfer from 14 March to 31 March	33/45 (73.3)	29/30 (96.7)	0.009
Transfer from 1 April to 13 April	12/45 (26.7)	1/30 (3.3)	
	$n = 45$	$n = 30$	
Days from admission to transfer, median (IQR)	7 (2–11)	8 (2–12)	0.922
Type of IE			
Native valve IE	77 (56.6)	45 (50)	0.329
Prosthetic valve IE	50 (36.8)	41 (45.6)	0.187
Intracardiac electronic device	9 (6.6)	4 (4.4)	0.492
Type of acquisition			
Community acquired	94 (69.1)	62 (68.9)	0.971
Nosocomial healthcare-associated infection	30 (22.1)	17 (18.9)	0.565
Non-nosocomial healthcare-associated infection	12 (8.8)	11 (12.2)	0.408
Aetiology			
Oral streptococci	31 (22.8)	20 (22.2)	0.920
Staphylococcus aureus	29 (21.3)	11 (12.2)	0.079
MSSA	25/29 (86.2)	10/11 (90.9)	
MRSA	4/29 (13.8)	1/11 (9.1)	
Enterococci	26 (19.1)	13 (14.4)	0.363
Coagulase-negative staphylococci	21 (15.4)	18 (20)	0.375
Streptococcus gallolyticus (formerly *S. bovis*)	6 (4.4)	5 (5.6)	0.757
HACEK group	5 (3.7)	0	0.160
Non-HACEK Gram-negative bacilli	4 (2.9)	5 (5.6)	0.489
Candida albicans	0	1 (1.1)	0.398
Other[b]	13 (9.6)	9 (10)	0.913
Unknown aetiology	1 (0.7)	8 (8.9)	0.003
Performance of TEE	126 (92.7)	80 (88.9)	0.330
Local cardiac complications (some patients had >1 complication)	68 (50)	42 (46.7)	0.624
Perivalvular abscess	35 (51.5)	22 (52.4)	0.926
Valve perforation	25 (36.8)	13 (31)	0.533
Pseudoaneurysm	11 (16.2)	8 (19.1)	0.699
Fistula	7 (10.3)	3 (7.1)	0.739
Prosthetic dehiscence	6 (8.8)	6 (14.3)	0.530
Prosthetic leak	3 (4.4)	3 (7.1)	0.673
Peripheral emboli (some patients had embolisms in >1 location)	60 (44.1)	45 (50)	0.385
Central nervous system	29 (50.9)	24 (54.6)	0.714
Spleen	17 (29.8)	19 (43.2)	0.165
Osteoarticular	13 (22.8)	8 (18.2)	0.570
Kidney	6 (10.5)	6 (13.6)	0.632
Lung	6 (10.5)	0	0.034
Vessels	5 (8.8)	3 (6.8)	1
SARS-CoV-2 infection	NA	11 (12.2)	
Duration of antibiotic treatment, days, median (IQR)			
	$n = 132$	$n = 86$	
Overall ($n = 218$)[c]	42 (32–48.5)	41.5 (29–46)	0.275
	$n = 102$	$n = 67$	
Survivors ($n = 169$)[d]	43 (36–52)	42 (34–48)	0.347
	$n = 102$	$n = 61$	
Survivors excluding 6 patients who received dalbavancin (N = 163)	43 (36–52)	44 (37–48)	0.752
Use of dalbavancin as continuation treatment	0	6 (6.7)	0.004
Surgery indicated according to 2015 ESC guidelines	108 (79.4)	65 (72.2)	0.212
Indications for surgery (some patients had > 1 indication)			
Heart failure	54/108 (50)	32/65 (49.2)	0.922
Uncontrolled infection	49/108 (45.4)	35/65 (53.8)	0.280
Prevention of embolism	20/108 (18.5)	8/65 (12.3)	0.283
Intracardiac electronic device infection	9/108 (8.3)	4/65 (6.2)	0.769
Surgery performed, if indicated	85/108 (78.7)	42/65 (64.6)	0.042
Indications for surgery in not operated patients (some patients had > 1 indication)			
Heart failure	9/23 (39.1)	9/23 (39.1)	1
Uncontrolled infection	11/23 (47.8)	15/23 (65.2)	0.234
Prevention of embolism	4/23 (17.4)	1/23 (4.3)	0.346
Intracardiac electronic device infection	2/23 (8.7)	0	0.489
Reasons for no surgery, if indicated			
High-risk patient	11/23 (47.8)	12/23 (52.2)	0.768
Poor vital prognosis due to comorbidities	6/23 (26.1)	7/23 (30.4)	0.743

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Table 1 (*continued*)

	2019 ($n = 136$)	2020 ($n = 90$)[a]	p
Good outcome without surgery	4/23 (17.4)	4/23 (17.4)	1
Patient's rejection	2/23 (8.7)	0	0.489
In-hospital mortality ($n = 224$)[e]	28/136 (20.6)	18/88 (20.4)	0.981
No indication for surgery	3/28 (10.7)	1/25 (4)	0.613
Surgery indicated and performed	16/85 (18.8)	10/42 (23.8)	0.512
Surgery indicated and not performed	9/23 (39.1)	7/21 (33.3)	0.690
	N = 108	N = 70	
Length of stay in survivors, days, median (IQR) ($n = 178$)[f]	41 (30–54.5)	34 (24–45)	0.018
Hospital discharge ($n = 178$)[f]			
Home	66/108 (61.1)	33/70 (47.1)	0.067
Outpatient parenteral antimicrobial therapy	25/108 (23.2)	22/70 (31.4)	0.221
Transferred to the hospital from which the patient was referred	10/108 (9.3)	10/70 (14.3)	0.300
Transferred to a rehabilitation clinic	7/108 (6.5)	5/70 (7.1)	1
Control blood culture performed during follow-up ($n = 166$)[g]	78/99 (78.8)	41/67 (61.2)	0.014
	$n = 99$	$n = 67$	
Number of samples taken on separated days ($n = 166$)[g]	1 (1–2)	1 (0–1)	<0.001
	$n = 108$	$n = 70$	
Duration of follow-up of survivors at hospital discharge, days, median (IQR) ($n = 178$)[f]	304.5 (216.5–368)	44.5 (28–60)	<0.001
Number of patients followed-up ≥30 days ($n = 178$)[f]	104/108 (96.3)	50/70 (71.4)	<0.001
Mortality during first month of follow-up (after hospital discharge) ($n = 154$)	10/104 (9.6)	2/50 (4)	0.339
Mortality during follow-up (after hospital discharge) ($n = 178$)[f]	13/108 (12)	3/70 (4.3)	0.077
Relapse during follow-up for survivors ($n = 169$)[d]	2/102 (2)[h]	3/67 (4.5)[i]	0.386

Data are expressed as *n* (%) or median (IQR) as appropriate. IQR, interquartile range; MSSA, methicillin-sensitive *Staphylococcus aureus;* MRSA, methicillin-resistant *Staphylococcus aureus*; HACEK, *Haemophilus* spp., *Aggregatibacter* actinomycetemcomitans, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* spp.; TEE, transoesophageal echocardiogram; NA, not applicable.

[a] One patient in the series had been reported in a previous article [3].

[b] 2019: *Gemella morbillorum* in 3, *Corynebacterium striatum* in 2, *Aerococcus sanguinicola* in 1, *Bartonella henselae* 1, *Coxiela burnetii* in 1, *Finegoldia magna* in 1, *Ganulicatella adicens* in 1, *Lactococcus garviae* in 1, *Rothia dentocariosa* in 1, *Enterococcus faecalis* and Staphylococcus aureus in 1.2020: *Abiotrophia defectiva* in 2, *Cutibacterium acnes* in 2, *Aerococcus urinae* in 1, *Lactobacillus jensenii* in 1, *Paenibacillu pabuli* in 1, *Staphylococcus epidermidis* and *Staphylococcus hominis* in 1, and *Streptococcus gallolyticus* and *Streptococcus oralis* in 1.

[c] Eight patients were not included in the analysis. 2019: 2 with suppressive treatment (a native IE due to *S. oralis* with local cardiac complications not operated due to patient rejection, and an intracardiac device infection due to *E. faecalis* not operated due to high surgical risk), and 2 still on treatment due to infective endocarditis caused due to *B. henselae* and *C. burnetii*, respectively. 2020: 4 with suppressive treatment (a native IE due to *S. gordonii* with local cardiac complications not operated due to high surgical risk, a prosthetic IE due to *S. gallolyticus* with local cardiac complications not operated due to comorbidities, a prosthetic IE due to *S. epidermidis* with local cardiac complications not operated due to comorbidities, and a prosthetic IE due to *E. coli* not operated due to favourable outcome with medical treatment).

[d] Fifty-seven patients were excluded from the analysis. 2019: 30 who died during infective endocarditis antimicrobial treatment (28 during hospitalization and 2 after discharge), 2 who underwent suppressive treatment, and 2 were still on treatment for infective endocarditis caused by *B. henselae* and *C. burnetii*, respectively. 2020: 19 who died during infective endocarditis antimicrobial treatment (18 during hospitalization and 1 after discharge) and 4 who underwent suppressive treatment.

[e] Two patients from the 2020 period were not included because they had not been discharged at the time of the analysis.

[f] Forty-eight patients were excluded from the analysis. 2019: 28 patients who died during hospitalization. 2020: 18 patients who died during hospitalization and 2 patients who had finished endocarditis treatment but were still hospitalized were not included in the analysis.

[g] Sixty patients were excluded from the analysis: 2019: 28 patients who died during hospitalization, 3 patients from which it was not possible to obtain this information, 2 who underwent suppressive treatment, 2 who died after discharge during endocarditis treatment, 1 patient with *C. burnetii* endocarditis, and 1 patient with *B. henselae* endocarditis. 2020: 18 patients who died during hospitalization, 4 who underwent suppressive treatment, and 1 who died after discharge during endocarditis treatment.

[h] One relapse 151 days after antimicrobial treatment (an operated *S. epidermidis* prosthetic endocarditis) and one relapse 27 days after antimicrobial treatment (an *A. sanguinicola* native endocarditis not operated although indicated).

[i] One relapse 42 days after finishing antimicrobial treatment (an operated *P. aeruginosa* prosthetic endocarditis), one relapse 37 days after finishing antimicrobial treatment (an operated *E. faecalis* native endocarditis), and one relapse 16 days after finishing antimicrobial treatment (a prosthetic endocarditis due to *S. epidermidis* with surgical indication but not operated due to comorbidities).

transferred from other hospitals or in the transfer delay, but less patients were transferred in the first two weeks of April in 2020 compared with 2019 (3.3% vs. 26.7%, p 0.009). In the second period (2020), there was a non-significantly lower rate of infections due to *Staphylococcus aureus* (21.3% vs. 12.2%, p 0.079) and a higher percentage of episodes of unknown aetiology (0.7% vs. 8.9%, p 0.003). Interestingly, there were no differences in the percentages of community acquisition between periods in *S. aureus* episodes (15/29 (52%) in 2019 vs. 6/11 (55%) in 2020). The percentage of patients undergoing a transoesophageal echocardiogram did not differ between periods. There were no differences in the percentage of indications for surgery, but in 2020 fewer surgeries were performed when indicated (79% in 2019 vs. 65% in 2020, p 0.042). In-hospital mortality was similar in both periods (~20%), but in 2020 survivors were discharged earlier to continue treatment on an outpatient basis. During follow-up, fewer control blood cultures were performed in 2020.

In concordance with our data, a recent study carried out in Marseille and Brussels shows a 33% decrease of IE diagnosed during the first months of 2020 compared with the same period of time in 2019 [2]. Several factors could explain this decline. The strict instructions to stay at home, people's fear of infection in medical facilities, the possible confusion of IE symptoms with those of SARS-CoV-2 infection and the prescription of oral antibiotics without further examinations may have caused a decrease in the number of hospital consultations. Other possible causes could be the decrease in the number of cases transferred from other facilities in April 2020 and decrease in usual hospital activity, possibly leading to a slight decrease in nosocomial IE episodes. On the other hand, in contrast to our study, they report a higher rate of complications in 2020 and a striking in-hospital mortality rate (31% in 2019 and 61% in 2020) [2]. However, the follow-up in our study was too short to ensure that long-term mortality and relapses will not increase.

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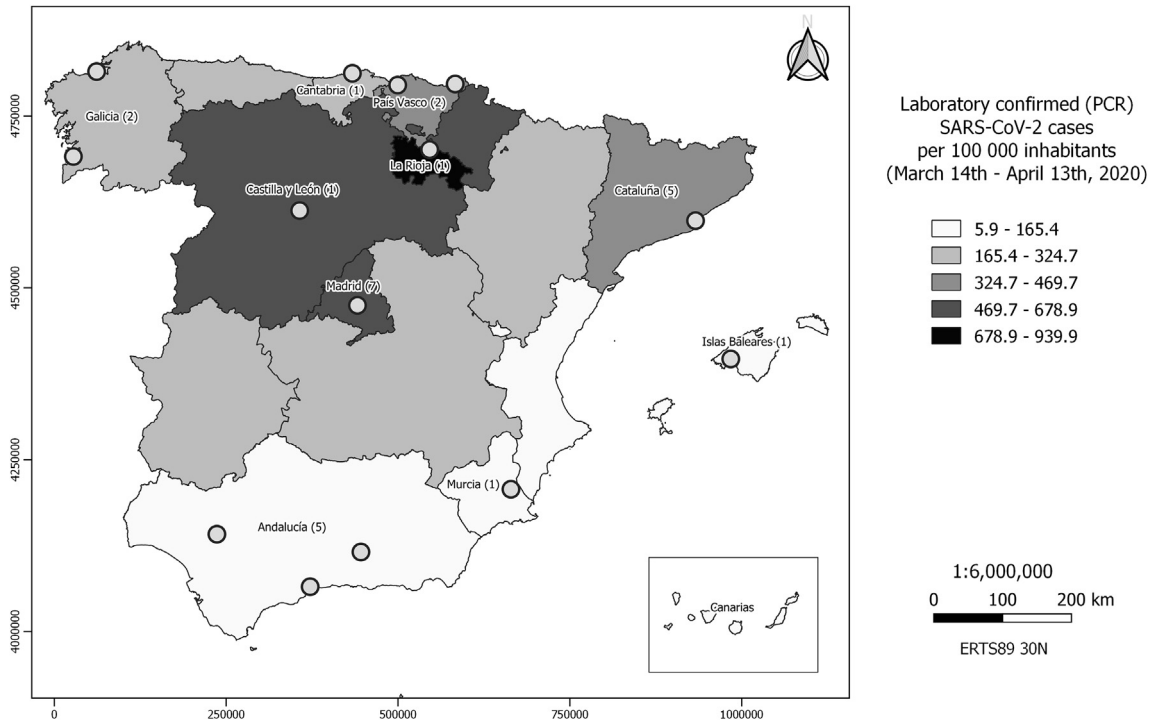

Fig. 1. Laboratory confirmed (PCR) SARS-CoV-2 cases per 100 000 inhabitants (March 14th–April 13th, 2020).

This study has several limitations. First, only referral centres for IE and cardiac surgery were included, so we cannot determine the impact of the COVID-19 pandemic in community hospitals. Second, follow-up in the 2020 period is shorter than in 2019, so long-term mortality and relapses may be underestimated, especially in non-operated patients and in those treated with outpatient antimicrobial therapy. Third, the relatively small sample size precludes any sub-analysis in regions with high and low incidences of COVID-19.

In conclusion, the COVID-19 pandemic has led to important organizational changes in the main Spanish referral centres for endocarditis. In addition, fewer definite IE cases were diagnosed and treated than in the previous year, and fewer cardiac surgeries have been performed, although these changes did not have an impact on the in-hospital mortality. Future studies should evaluate the long-term impact of these changes as well as the evolution of the epidemiology of IE in the post-COVID-19 era.

Author contributions

Writing – Original Draft: L.E. and N.F.; Writing – Review and Editing: L.E., G.C., A. A., D.S., L.V.B., N.F.; Conceptualization: L.E., N.F.; Investigation: L.E., G.C., A. A., D.S., L.V.B., N.F. and IE COVID-19 investigators; Methodology: L.E. and N.F.; Formal Analysis: L.E. and N.F.; Project Administration:: L.E. and N.F.

Transparency declaration

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2020.11.022.

Appendix B

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