SUPPLEMENTARY DATA

METHODS

Variables related to infective endocarditis

The age-adjusted Charlson comorbidity index was used at admission to stratify patients according to overall comorbidity.[1] Definite infective endocarditis (IE) was defined according to modified Duke criteria[2] and, since August 2015, according to the 2015 European Society of Cardiology guidelines.[3] Healthcare-associated IE has been defined elsewhere.[4] The duration of the infection prior to the diagnosis was established as the time between the onset of symptoms and the start of targeted antibiotic treatment. Prosthetic valve IE was established when at least 1 prosthetic valve was affected. Cardiac implantable electronic device IE was defined as lead infection plus endocardial involvement. The indication for surgery was determined according to the current ESC guidelines.[3,5] The following were considered IE complications: the development of new or worsening congestive heart failure, a paravalvular complication diagnosed by echocardiography or during surgery, stroke or another symptomatic systemic embolism, and acute renal failure (defined as a baseline creatinine value x 2 or a > 50% decrease in the glomerular filtration rate).[6] Mortality during treatment was defined as death from any cause. Follow-up was defined as the period starting from the day after completing antimicrobial therapy to death or the last clinical follow-up visit for any reason. A minimum of 3 months of follow-up was required for the study in survivor patients. Relapse was established on the documentation of positive blood cultures caused by the same microorganism as the initial IE episode during follow-up.

Presumed sources of infection were evaluated by physicians with experience in infectious endocarditis and they were prospectively collected. The presumed source of IE was digestive if clinical symptoms led to the diagnosis of a gastrointestinal or hepatobiliary disease that could potentially cause a bacteremia within the 6 months prior to the diagnosis of IE. The presumed source was the genitourinary tract if the patient presented clinical symptoms of urinary tract infection with pyuria and a positive monomicrobial urinary culture or an invasive procedure of the genitourinary

tract (including cystoscopy, lithotripsy, or surgery) had been performed in the previous 6 months or the patient had repeated urinary tract infections or acute urinary tract retention during the 6 months prior to the onset of IE symptoms, without another suspected source. The presumed origin was a catheter-related bacteremia when it had been microbiologically confirmed[7] and there was no other suspected source. Other suspected origins apart from the mentioned above were specified and classified as other source and when the source was unknown it was classified as unknown source.

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Table 1 of the supplementary data

Demographic features, comorbidities, presumed source of infection, complications, surgical treatment, outcomes, and endoscopic findings of the entire cohort of patients with *Enterococcus faecalis* infective endocarditis

	All patients N= 103
Demographics	
Age, years, median [interquartile range]	76 [67-82]
Male sex	83 (81%)
Comorbidities	
Charlson comorbidity index, median [interquartile range]	5 [4-7]
Previously diagnosed colonic pathology	25 (24%)
Diabetes mellitus	31 (30%)
Chronic renal failure	25 (24%)
Neoplasm[a]	13 (13%)
Immunosuppressive therapy	10 (10%)
Transplantation	8 (8%)
Liver cirrhosis	3 (3%)
Healthcare-associated infection	51 (50%)
Presumed source of infection	
Unknown	63(61%)
Urinary	20 (19%)
Digestive	13 (13%)
Catheter-related bacteremia	5 (5%)
Others[b]	2 (2%)
Positive urine culture for E. faecalis at the same time as positive blood cultures	17/87 (20%)
Duration of symptoms, days, median [interquartile range]	24 [6-48]
Hemoglobin (g/dL)	10.5 (9.6-11.5)
Ferritin (ng/mL)[c]	273 (160-447)
Transferrin saturation (%)[d]	15 (9-21)
Type of infective endocarditis	
Native valve infective endocarditis	57 (55%)
Prosthetic valve infective endocarditis	42 (41%)
Cardiac implantable electronic device	4 (4%)
Heart valve affected	
Aortic	52 (51%)
Mitral	28 (27%)
Aortic and mitral	18 (18%)
Tricuspid	2 (2%)
Aortic, mitral, tricuspid and pulmonary	1 (1%)
Mitral and pulmonary	1 (1%)
Unknown	1 (1%)
Complications (some patients had >1 complication)	70 (68%)

Heart failure	41 (40%)
Symptomatic embolism	19 (18%)
New renal failure	19 (18%)
Paravalvular complication	16 (16%)
Stroke	13 (13%)
Surgery indicated (some patients had > 1 indication)	48 (47%)
Heart failure	31 (30%)
Uncontrolled infection	17 (17%)
Embolism prevention	11 (11%)
Cardiac implantable electronic device infection	4 (4%)
Surgery performed during the active phase of infection (if indicated)	36/48 (75%)
Duration of antimicrobial treatment (days) in all patients	42 (41-46)
Duration of antimicrobial treatment (days) in survivors	43 (42-47)
Overall mortality during treatment	14 (14%)
Follow-up in survivors after finishing antibiotic treatment (months)	8.9 (4.6-16.2)
Overall mortality at 3-months	19 (18%)
Surgery during follow-up	5 (5%)
Relapse	2 (2%)

[a] Three prostatic adenocarcinomas, 2 pancreatic adenocarcinomas, 2 melanomas, 2 urothelial carcinomas, 2 colonic adenocarcinomas, 1 hepatocellular carcinoma, and 1 rectal carcinoma.

[b] The source of infection in both cases was an infected abdominal aortic endoprosthesis.

[c] Values of ferritin available in 47 patients.

[d] Values of transferrin saturation available in 48 patients.

Table 2 of the supplementary data

Colonoscopy findings among all patients with *Enterococcus faecalis* infective endocarditis and according to the presumed source of infection

	Unknown N=63	**Urinary N=20**	**Gastro-intestinal N=8**	**Hepato-biliary N=5**	**Catheter bacteremia N=5**	**Others[a] N=2**
Colonoscopy performed	45/63	16/20	8/8	4/5	4/5	1/2
Endoscopic findings being potential portals of entry	29/45	7/16	7/8	2/4	2/4	0/1
Colorectal neoplasms	26/29	6/7	4/7	2/2	1/2	
Non-advanced colorectal adenoma	12	3	1	2	1	
Advanced colorectal adenoma	13	3	2	0	0	
Colorectal carcinoma	1	0	1	0	0	
Nonneoplastic colorectal diseases	3/29	1/7	3/7	0	1/2	
Mucosal inflammation	1	0	1	0	0	
Bleeding vascular lesion	0	0	1	0	1	
Colorectal ulcer	1	1	1	0	0	
Polyp without histopathological report	1	0	0	0	0	
Other endoscopic findings[b]						
Diverticula	9	5	2	2	0	1
Internal hemorrhoids	9	5	2	0	1	0

[a] In both cases, the presumed source of infection was an infected abdominal endovascular aortic prosthesis.

[b] Some patients had more than one endoscopic finding.

Table 3 of the supplementary data

Demographic features, comorbidities, complications, surgical treatment, and outcomes of all episodes of *Enterococcus faecalis* infective endocarditis depending on the presumed source of infection

	Unknown source N=63	**Known source N=40**	**P**
Demographics			
Age, years, median [interquartile range]	75 [66-82]	76 [67-82]	.844
Male sex	51 (81%)	32 (80%)	.905
Comorbidities			
Charlson comorbidity index, median [interquartile range]	5 [4-7]	5 [3.5-8]	.873
Previously diagnosed colonic pathology	12 (19%)	13 (33%)	.121
Diabetes mellitus	18 (29%)	13 (33%)	.672
Chronic renal failure	13 (21%)	12 (30%)	.280
Neoplasm	6 (10%)	7 (18%)	.361
Immunosuppressive therapy	4 (6%)	6 (15%)	.181
Transplantation	2 (3%)	6 (15%)	.053
Liver cirrhosis	1 (2%)	2 (5%)	.558
Healthcare-associated infection	18 (29%)	33 (83%)	< .001
Positive urine culture for E. faecalis at the same time as positive blood cultures	7/53 (13%)	10/34 (29%)	.063
Duration of symptoms, days, median [interquartile range]	21 [6-48]	27 [6-49]	.547
Hemoglobin (g/dL)	10.7 (9.8-12)	10.2 (9.1-11.3)	.057
Ferritin (ng/mL)[a]	284 (200-447)	244 (119-423)	.551
Transferrin saturation (%)[b]	18 (10-22)	13 (9-20)	.560
Type of infective endocarditis			
Native valve infective endocarditis	28 (44%)	29 (73%)	.005
Prosthetic valve infective endocarditis	33 (52%)	9 (23%)	.003
Cardiac implantable electronic device	2 (3%)	2 (5%)	.641
Heart valve affected			
Aortic	33 (52%)	19 (48%)	.629
Mitral	16 (25%)	12 (30%)	.609
Aortic and mitral	11 (18%)	7 (18%)	.996
Aortic, mitral, tricuspid and pulmonary	1 (2%)	0	1
Mitral and pulmonary	1 (2%)	0	1
Tricuspid	1 (2%)	1 (3%)	1
Unknown	0	1 (3%)	.388
Complications (some patients had >1 complication)	43 (68%)	27 (68%)	.936
Heart failure	28 (44%)	13 (33%)	.227
Paravalvular complication	12 (19%)	4 (10%)	.217
Symptomatic embolism	11 (18%)	8 (20%)	.746
Stroke	10 (16%)	3 (7.5%)	.243
New renal failure	9 (14%)	10 (25%)	.172

Surgery indicated (some patients had >1 indication)	32 (51%)	16 (40%)	.285
Heart failure	21/32 (66%)	10/16 (63%)	.369
Uncontrolled infection	11/32 (34%)	6/16 (38%)	.743
Embolism prevention	8/32 (25%)	3/16 (19%)	.522
Cardiac implantable electronic device infection	2/32 (6%)	2/16 (13%)	.641
Surgery performed during the active phase of infection (if indicated)	26/32 (81%)	10/16 (63%)	.081
Duration of antimicrobial treatment (days) in all patients	43 (41-47)	42 (41-44)	.351
Duration of antimicrobial treatment (days) in survivors	43 (42-47)	42 (42-46)	.528
Mortality during treatment			
Overall	8 (13%)	6 (15%)	.740
Surgery indicated and performed	3 (5%)	2 (5%)	.603
Surgery indicated and not performed	3 (5%)	3 (8%)	1
Without indication for surgery	2 (3%)	1 (3%)	1
Follow-up in survivors after finishing antibiotic treatment (months)	9.1 (4.6-17.5)	7.8 (4.2-12.7)	.285
3-months mortality	3/55 (6%)	2/34 (6%)	1
Surgery during follow-up	2/55 (4%)	3/34 (9%)	.374
Relapse	1/55 (2%)	1/34 (3%)	1

[a] Values of ferritin available in 25 and 22 patients, respectively.

[b] Values of transferrin saturation available in 27 and 21 patients, respectively.