

disease progression and a decrease in the size of the endocardial lesion through antimicrobial treatment alone.

FUNDING

None declared.

AUTHORS' CONTRIBUTIONS

A. García-Olea and G. Ramírez-Escudero were the main authors. N. García, M. de la Peña, and L. Ruiz corrected different versions of the manuscript, provided critical review, and actively contributed to the selection of the audiovisual material.

CONFLICTS OF INTEREST

None declared.

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Available online 19 November 2021

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<https://doi.org/10.1016/j.rec.2021.09.012>

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Incidence and mortality of infective endocarditis caused by oral streptococci in the last three decades at a referral center in Spain



Incidencia y mortalidad de la endocarditis infecciosa causada por estreptococos orales en las últimas tres décadas en un centro de referencia en España

To the Editor,

Until 3 to 4 decades ago, infective endocarditis (IE) was considered to be a subacute disease caused by cardiac lesions infected by oral flora microorganisms (mainly *Streptococcus viridans*). This type of IE has a relatively good prognosis, bearing in mind the severity of this disease.¹ However, the clinical and epidemiological profile and prognosis of IE have changed under the impact of recent social and health care changes, such as aging

populations, increased numbers of other causal microorganisms (mainly staphylococci and enterococci), and new risk factors (eg, injectable drug use, prosthetic valves, electrical devices, or health care-related bacteremia).^{2–6} The aim of this study was to analyze the characteristics of oral streptococci IE in a Spanish tertiary hospital, as well as changes in its relative incidence, treatment, and prognosis using a large single-center series collected over the last 30 years in this setting.

We analyzed a cohort of consecutive patients diagnosed with IE and followed up in our hospital between 1990 and 2020 (n = 485) to identify cases of IE caused by oral streptococci (*S. viridans* and nutritionally variant streptococci: *Abiotrophia* and *Granulicatella*) and to compare their characteristics during 3 time periods (1990–2000, 2001–2010, and 2011–2020). The study was approved by the ethics committee of our hospital and informed consent was given by all the participants. Of the 485 cases of IE, 346 were native, 59 were early prosthetic, and 80 were late prosthetic. In total,

Table 1

Number of cases and percentage of endocarditis due to oral streptococci in the total series and by the various types of infective endocarditis during the 3 time periods analyzed

	Total 1990–2020	1990–2000	2001–2010	2011–2020	P*
Total, No.	485	138	167	180	
Oral streptococci	94 (19.4)	30 (21.7)	34 (20.3)	30 (16.7)	.045
Native IE, n	346	94	118	134	
Oral streptococci	73 (20.1)	20 (21.3)	31 (16.7)	22 (16.4)	.160
Early prosthetic IE, n	59	20	21	18	
Oral streptococci	3 (5.1)	1 (5)	0	2 (11.1)	.663
Late prosthetic IE, n	80	24	28	28	
Oral streptococci	18 (22.5)	9 (37.5)	3 (10.7)	6 (21.4)	.089

IE, infective endocarditis.

Unless otherwise indicated, data are expressed as No. (%).

* Chi-square test.

Table 2

Comparison of the characteristics of infective endocarditis caused by oral streptococci in the overall series and in the 3 time periods studied

	Total series (1990–2020) (No. = 94)	1990–2000 (n = 30)	2001–2010 (n = 34)	2011–2020 (n = 30)	P ^a
Age, y	53.3 ± 18.7	54.6 ± 18.1	53.2 ± 18.6	52.8 ± 18.9	.678
Men	66 (70.2)	22 (73.3)	22 (64.7)	22 (73.3)	.723
Site of infection					.636
Mitral	46 (48.9)	15 (50.0)	16 (47.1)	15 (50.0)	
Aortic	48 (51.1)	15 (50.0)	18 (52.9)	15 (50.0)	
Vegetations on TTE	70 (74.5)	17 (56.7)	28 (84.8)	25 (83.3)	.033
Vegetations on TEE	62 (96.9)	-	33 (97.1)	29 (96.7)	.857
Vegetation size, mm	11.7 ± 3.2	9.8 ± 2.7	11.0 ± 3.3	12.6 ± 4.1	.011
Entry point					.572
Dental	22 (24.4)	8 (26.7)	7 (20.6)	7 (23.3)	
Respiratory	0	0	0	0	
Gastrointestinal	3 (3.2)	0	1 (2.9)	2 (6.7)	
Genitourinary	2 (2.1)	0	1 (2.9)	1 (3.3)	
Vascular	0	0	0	0	
Unknown	67 (70.3)	22 (73.3)	25 (73.6)	20 (66.7)	
Underlying heart disease					.021
Rheumatic	26 (27.6)	15 (50.0)	7 (20.6)	4 (13.3)	
Congenital	21 (22.3)	7 (23.3)	6 (17.6)	8 (26.7)	
Degenerative	27 (28.7)	6 (20.0)	12 (35.4)	9 (30.0)	
Without heart disease	20 (21.4)	2 (6.7)	9 (26.4)	9 (30.0)	
Healthcare-associated IE ^b	11 (17.5)	2 (6.6)	5 (14.7)	4 (13.3)	.475
Nosocomial	3 (4.8)	1 (3.3)	1 (2.9)	1 (3.3)	
Nosohusial	8 (12.7)	1 (3.3)	4 (11.8)	3 (10.0)	
Serious complications (any complication)	66 (70.2)	20 (66.7)	21 (61.8)	25 (84.3)	.031
Heart failure	46 (48.9)	13 (43.3)	18 (52.9)	15 (50.0)	.324
Uncontrolled infection	10 (10.6)	3 (10.0)	6 (17.6)	1 (3.3)	.426
Embolism	18 (19.1)	6 (20.0)	5 (14.8)	7 (23.3)	.426
Neurologic	14 (14.9)	3 (10.0)	6 (17.6)	5 (16.7)	.512
Kidney failure	3 (3.2)	1 (3.3)	1 (2.9)	1 (3.3)	.853
Abscess	13 (13.8)	4 (13.3)	4 (11.7)	5 (16.7)	.347
Mycotic aneurysm	2 (1.8)	1 (3.3)	1 (2.9)	1 (3.3)	.853
Surgery in the active phase	51 (54.2)	16 (53.3)	18 (52.9)	17 (56.7)	.74
Urgent/emergent	11 (12.2)	6 (20.0)	3 (8.8)	2 (6.7)	.043
Elective	40 (42.0)	10 (33.3)	15 (44.1)	15 (50.0)	.043
Inhospital mortality	14 (14.9)	6 (20.0)	5 (14.7)	3 (10.0)	.045

IE, infective endocarditis; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram.

Data are expressed as No. (%) or mean ± standard deviation.

^a Analysis of variance test (ANOVA) for comparison of means for quantitative variables and chi-square test for comparison of proportions (with Yates correction in cases of low frequency) for qualitative variables.^b Not including history of visits to dentists or oral manipulation.

19.4% (n = 94) of the 485 cases were caused by oral streptococci (90 *S. viridans*, 3 *Abiotrophia*, and 1 *Granulicatella*). The most frequent causative organisms were staphylococci (37.9%), followed by enterococci (16.3%). Table 1 shows the number of patients with IE caused by oral streptococci during the 3 time periods and by the various types of IE. Oral streptococci caused 20.1% of native IE and 22.5% of late prosthetic IE, but were very rare in early prosthetic IE. A significant reduction was observed in the proportion of cases caused by these microorganisms, decreasing from 21.7% in the period 1990 to 2000 to 16.7% in the period 2011 to 2020 ($P = .045$) (table 1). Similar trends were seen regarding native and late prosthetic IE, although without reaching significance (table 1).

Table 2 shows the characteristics of oral streptococcal IE by each time period: no significant differences were observed in age, sex, entry point for bacteremia, most frequent comorbidities, endocarditis site, or relationship with health care. Significant changes were detected over time in the etiology of the underlying heart disease ($P = .021$), with a reduction in rheumatic etiology and

an increase in degenerative etiology and the absence of underlying heart disease. Vegetation size was larger during the more recent periods, although this was probably not due to greater streptococcal aggressiveness, given that the incidence of cardiac complications, persistence of infection, neurologic complications, kidney failure, embolisms, abscesses, and mycotic aneurysms were similar over the study period. All complications involved clinical symptoms, because in our protocol we did not conduct a systematic search for neurologic complications, embolisms, mycotic aneurysms, and so on, in the absence of symptoms or clinical suspicion. Of the 13 abscesses, 12 were periannular and only 1 was distant (splenic). Overall, the incidence of all serious complications, which was 70.2% during the entire period from 1990 to 2020, significantly increased between the periods 1990 to 2000 and 2011 to 2020 ($P = .031$). The rate of early surgery was similar during the 3 periods (more than 50%), although we observed a decrease in urgent/emergent surgery and a gradual increase in indications for elective surgery ($P = .04$).

Early mortality due to oral streptococcal IE significantly decreased from 16.7% in the period 1990 to 2000 to 10% in the period 2011 to 2020 (table 2), despite the increased incidence of severe complications already discussed. This inconsistency may be partly due to the higher rate of elective surgery, which prevents poor disease progression. The results of the multivariable study (stepwise logistic regression) showed an association between streptococcal etiology and a significant reduction in mortality of 26% in the total series (odds ratio = 0.74; 95% confidence interval: 0.56–0.92; $P = .043$).

In conclusion, our analysis of a large single-center series of IE spanning a long time period showed that oral streptococci, mainly *S. viridans*, continued to cause around 20% of all IE, especially native and late prosthetic endocarditis. Nevertheless, their relative incidence seems to have decreased in recent years, probably due to the increase in cases caused by other microorganisms, such as staphylococci and enterococci. Over the 3 decades analyzed, the clinical and epidemiological characteristics of IE, the incidence of serious complications, and the performance of early surgery have remained unchanged, although in-hospital mortality has recently decreased, reaching just 10% in the last decade.

FUNDING

None declared.

AUTHORS' CONTRIBUTIONS

All authors contributed equally to the concept, design, data analysis, writing, and revision of the article.

CONFLICTS OF INTEREST

None declared.

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Available online 15 November 2021

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<https://doi.org/10.1016/j.rec.2021.09.013>

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Mycotic coronary aneurysm complicated by left ventricular pseudoaneurysm after everolimus-eluting stent implantation



Aneurisma micótico coronario complicado con pseudoaneurisma ventricular izquierdo después de la implantación de stent de everolimus

To the Editor,

A 68-year-old man with a history of type 2 diabetes, dyslipidemia and hyperuricemia had been recently started on allopurinol. He was admitted to our hospital with a diagnosis of severe allopurinol-induced Stevens-Johnson syndrome and started on systemic corticotherapy with a favorable clinical response.

On day 10, the patient developed chest pain and hypotension and an electrocardiogram showed atrial fibrillation with complete heart block and inferoposterolateral ST-segment elevation. Emergent coronary angiography using the right femoral artery showed a critical stenosis in the middle segment of a dominant left circumflex artery (LCx). Percutaneous coronary intervention (PCI) with direct implantation of an everolimus-eluting stent (Xience Alpine 3.0 x 23 mm, Abbott, United States) was performed with good angiographic result. On day 11, the patient developed fever and laboratory tests showed a marked increase in C-reactive protein (400 mg/L). Empirical broad spectrum antibiotic therapy

was started. The patient was in Killip class II with a peak high-sensitivity troponin I (hs-TpI) of 14.483 ng/L. Transthoracic echocardiogram showed mild left ventricle (LV) dysfunction with inferoposterior akinesis, grade 2 functional mitral regurgitation, and small-volume pericardial effusion with no signs of vegetations. Persistent psychomotor agitation was interpreted in the context of acute disease because cerebral computed tomography (CT) was unremarkable. In the following days, the patient showed persistent fever and periods of respiratory distress requiring noninvasive ventilation. Serial hs-TpI showed a re-elevation from 2.100 to 14.483 ng/L. On day 15, antibiotic therapy was de-escalated to flucloxacillin after 2 positive cultures for methicillin-sensitive *Staphylococcus aureus*. Despite adequate antibiotic therapy, the patient maintained a fever and methicillin-sensitive *S. aureus* bacteremia. Contrast transesophageal echocardiography showed a heterogenous cavity compatible with a LCx aneurysm and a complex LV pseudoaneurysm in the posterolateral wall (figure 1). Coronary angiography showed a massive LCx aneurysm in the proximal and middle segments not limited to the area covered by the stent (figure 2 and video 1 of the supplementary data [coronary angiography showing the left circumflex artery aneurysm in multiple projections]). Cardiac CT further detailed the anatomy of the complex LV pseudoaneurysm with anterolateral and inferolateral cavities (figure 2 and video 2 of the supplementary data [cardiac computed tomography 3D reconstruction of the