Table
Clinical Characteristics and Delays

	N	%
Age, mean (SD)	64.3 (13.2)	–
Female sex	154	24.3
Diabetes mellitus	145	22.9
Hypertension	317	50.1
Hypercholesterolemia	226	35.7
Smoking habit	333	52.7
Prior percutaneous coronary intervention	61	9.6
Time symptom onset -first medical contact	76 (Q_{25} 35-Q_{75} 165)	–
Time first medical contact-activation	25 (Q_{25} 15-Q_{75} 43)	–
Time activation-arrival in the room	35 (Q_{25} 24-Q_{75} 55)	–
Time symptoms-balloon	170 (Q_{25} 120-Q_{75} 270)	–
Delay first medical contact-balloon	85 (Q_{25} 68-Q_{75} 111)	–
Delay activation-end of procedure	76 (Q_{25} 35-Q_{75} 165	–

Times are expressed in minutes.
SD, standard deviation.

in 92, and so 46 patients may have experienced a delay in reperfusion, that is, 7.2% of the overall series.

The data presented are only applicable to the network described, as the demographic characteristics, geography, hospital network, and catheterization laboratories vary for each region.[4] The fact that overlap started when the catheterization team was activated instead of when the patient arrived in the room may have increased the percentage of patients reported to have a delay. However, the end time of the procedure is not always predictable and, if the activity had been concentrated in a single center, the transfer times would have been longer for 40% of the patients in the catchment area of the second center. This may have led to overlap with patients other than those indicated, greater ambulance use with a subsequent deterioration in other areas of care, and increased mortality due to delays.[5] There may also have been an increase in the percentage of patients referred for fibrinolysis if the option of a second center were not available, while some of the 6 patients who experienced delay and who did not undergo PPCI may have received unnecessary fibrinolysis.

In summary, we believe that the design of regional networks should take potential demand into account and, once in operation, the percentage of patients who have experienced delays in the past year could be used as an indicator analyzed in annual steering committee meetings for the regional network.

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Changes in Clinical Profile, Epidemiology and Prognosis of Left-sided Native-valve Infective Endocarditis Without Predisposing Heart Conditions

Cambios en el perfil clínico, epidemiológico y pronóstico de la endocarditis infecciosa nativa izquierda sin lesión cardiaca predisponente

To the Editor,

Traditionally, infective endocarditis (IE) has been considered as a disease affecting patients with underlying heart disease (HD).[1] This profile appears to have changed in recent decades, in that EI affects both patients with degenerative valve disease and those with no apparent HD.[1–4] Various studies have shown that the proportion of patients with IE and no underlying HD has increased in our setting.[2,5,6] Although each type of IE appears to have distinct epidemiologic and prognostic characteristics,[2,5] it is not known whether the profile of non-HDIE has changed in recent years, which could have implications for prognosis. The objectives of our study were: a) to compare the characteristics of HD-associated left-sided native-valve IE (HDIE) and non-HD-associated left-sided native-valve IE (non-HDIE) diagnosed at our center between 1987 and 2013, and b) to study changes in the profile of non-HDIE during this period.

We analyzed a series of 420 consecutive patients diagnosed with IE between 1987 and 2013, of which 240 (57%) had left-sided native-valve IE. Diagnosis was made according to the Von Reyn, Duke and modified Duke criteria, depending on the time period. The management protocol did not change over this period, except for the introduction of transesophageal echocardiography during the 1990s. Each patient was classified as having either HDIE or non-HDIE, depending on the results of transthoracic and transesophageal echocardiography during the episode of IE, previous echocardiograms, medical history, and surgical and autopsy findings. The valve was considered normal when the portions of the leaflets that were unaffected by infection were normal and there was no chordal involvement or commissural fusion.[5] The active phase of the disease was defined as the first 6 weeks from symptom onset. Urgent surgery was defined as that which could not be postponed for more than 24 hours without risk to the patient's life, while elective surgery was defined as that carried out after 24 hours.

Of the 240 cases of left native-valve IE, 104 (43%) were classified as non-HDIE, and the remaining 136 (57%) were diagnosed with HDIE. The proportion of cases of non-HDIE increased significantly,

Table 1
Comparative Characteristics Between Left-sided Native-valve Endocarditis With and Without Underlying Heart Disease (n = 240)

	Non-HDIE (n = 104)	HDIE (n = 136)	*P*
Age, y	55.93 (18.73)	52.34 (18.62)	.167
Sex, male	68 (65.4)	99 (72.8)	.216
Previous endocarditis	1 (0.9)	2 (1.5)	.975
Infection site			.094
Mitral	58 (55.8)	61 (44.9)	
Aortic	46 (43.3)	753 (55.1)	
Vegetations on transthoracic echocardiography	84 (80.7)	103 (75.7)	.181
Vegetations on transesophageal echocardiography	80 (98.8)	105 (99.1)	.946
Vegetation size, mm	13.13 (4.37)	11.70 (4.23)	.025
Epidemiological characteristics			
Entry site			
Dental	5 (4.8)	17 (12.5)	.041
Respiratory	1 (0.9)	1 (0.7)	.968
Gastrointestinal	7 (6.8)	8 (5.9)	.788
Genitourinary	5 (4.8)	6 (4.4)	.935
Vascular catheter	13 (12.5)	2 (1.4)	<.001
Unknown	73 (70.2)	102 (75.0)	.869
Bacterium			
Staphylococcus aureus	21 (20.2)	24 (17.8)	.610
Staphylococcus epidermidis	8 (7.7)	13 (9.6)	.616
Streptococcus viridans	18 (17.3)	48 (35.6)	.002
Enterococci	24 (23.1)	20 (14.8)	.135
Others	14 (13.3)	11 (8.1)	.385
Unidentified	20 (14.1)	17 (12.5)	.203
Risk factors	50 (48.1)	21 (15.4)	<.001
Intravascular catheter	13 (12.5)	2 (1.4)	<.001
Renal failure	10 (9.6)	10 (7.3)	.573
Gastrointestinal disorders	17 (16.1)	5 (4.8)	.025
Immunocompromised	9 (8.6)	1 (0.7)	.040
Neoplasms	10 (9.5)	3 (2.2)	.035
Diabetes mellitus	8 (7.6)	2 (1.4)	.063
Indwelling urinary catheter	3 (2.8)	0 (0.0)	.266
Endocarditis related to healthcare	38 (36.1)	13 (9.6)	<.001
Nosocomial	10 (9.5)	1 (0.7)	.042
Nosohusial	28 (26.6)	12 (8.8)	.035
Complications, mortality, and surgery			
Development of complications	87 (83.6)	103 (76.3)	.143
Complications in the acute phase			
Heart failure/valve dysfunction	66 (63.4)	74 (54.4)	.159
Embolism	21 (20.2)	34 (25.0)	.380
Neurological	25 (24)	25 (18.4)	.285
Persistent sepsis	24 (23.1)	21 (15.4)	.133
Acute renal failure	10 (9.6)	8 (5.9)	.277
Intracardiac abscess	18 (17.5)	22 (16.2)	.790
Surgery during the active phase			
Urgent	20 (19.2)	29 (21.3)	.714
Elective	43 (41.3)	53 (39.0)	.697
Total	63 (60.5)	82 (60.3)	.985
Early mortality	32 (30.8)	30 (22.1)	.172

HDEI, heart disease-associated infective endocarditis; non-HDIE, non-heart disease-associated infective endocarditis.
Data are expressed as mean (standard deviation).

Table 2
Comparison of the Characteristics of the Subgroup of Patients With Endocarditis Without Underlying Heart Disease Between the Periods 1987 to 2000 and 2001 to 2013 (n = 104)

	1987-2000 (n = 26)	2001-2013 (n = 78)	*P*
Age, y	41.54 (21.11)	60.42 (15.22)	< .001
Sex, male	19 (73.1)	49 (62.8)	.341
Previous endocarditis	0 (0)	1 (1.3)	1
Infection site			
Mitral	16 (61.5)	42 (53.8)	.494
Aortic	10 (38.5)	36 (46.2)	.494
Vegetations on transthoracic echocardiography	22 (84.6)	62 (81.6)	1
Vegetations on transesophageal echocardiography	17 (100)	63 (98.4)	1
Vegetation size, mm	10.68 (2.93)	13.98 (4.49)	.002
Epidemiological characteristics			
Entry site			
Dental	0 (0)	5 (6.4)	.328
Respiratory	0 (0)	1 (1.4)	1
Gastrointestinal	2 (7.7)	5 (6.4)	1
Genitourinary	0 (0)	5 (6.4)	.328
Catheter	1 (3.8)	14 (17.9)	.035
Unknown	23 (88.5)	48 (61.5)	.045
Bacterium			
Staphylococcus aureus	8 (30.8)	13 (16.9)	.129
Staphylococcus epidermidis	1 (3.8)	7 (9.1)	.676
Streptococcus viridans	2 (7.7)	16 (20.8)	.230
Enterococci	7 (26.9)	16 (20.8)	.588
Others	5 (19.2)	10 (13)	.521
Negative blood culture	3 (11.5)	15 (19.5)	.551
Risk factors	7 (26.9)	43 (55.1)	.003
Intravascular catheter	1 (3.8)	12 (15.4)	.421
Renal failure	2 (7.6)	8 (10.4)	.712
Gastrointestinal disorders	3 (11.4)	14 (17.9)	.493
Immunocompromised	1 (3.8)	8 (10.4)	.523
Neoplasms	3 (11.4)	7 (9.1)	.322
Diabetes mellitus	2 (7.6)	6 (7.7)	.845
Indwelling urinary catheter	1 (3.8)	2 (2.6)	.566
Endocarditis related to healthcare	6 (23.1)	32 (41.0)	.025
Nosocomial	1 (3.8)	9 (10.5)	.679
Nosohusial	5 (19.3)	23 (29.5)	.145
Complications, mortality, and surgery			
Serious complications	17 (65.4)	70 (90.9)	.004
Type of complication			
CHF/valve dysfunction	9 (34.6)	57 (73.1)	< .001
Embolism	7 (26.9)	14 (17.9)	.324
Neurological	5 (19.2)	20 (25.6)	.508
Persistent sepsis	1 (3.8)	23 (29.5)	.007
Acute renal failure	2 (7.7)	8 (10.3)	1
Intracardiac abscess	4 (16)	14 (17.9)	1
Surgery during the active phase			
Urgent	5 (19.2)	15 (19.2)	1
Elective	4 (15.4)	39 (50)	.002
Total	9 (34.6)	54 (69.2)	.002
Early mortality	4 (15.4)	28 (35.9)	.043

CHF, chronic heart failure.
Data are expressed as mean (standard deviation).

constituting 25.7% of cases of left-sided native-vale IE from 1987 to 2000 and 56.1% from 2001 to 2013 ($P < .001$). The characteristics of both types of patients during the entire 27-year period are shown in Table 1. The rate of serious complications, premature mortality, and need for surgery were similar, whereas there were significant differences in epidemiological characteristics: patients with non-HDIE had a higher prevalence of non-cardiac risk factors and predisposing comorbidities (chronic gastrointestinal diseases, malignancies, renal failure, diabetes, immunosuppression) and healthcare-related procedures (intravascular catheters, and nosocomial and nosohusial EI), but less frequently had IE caused by *Streptococcus viridans* (Table 1). The characteristics of patients with non-HDIE from 1987 to 2000 and from 2001 to 2013 are shown in Table 2, highlighting significant changes in both the clinical and epidemiological profile between the 2 periods. In the most recent period, patients with non-HDIE were much older (almost 20 years older, on average), had larger vegetations, a tendency to have IE caused less by *Staphylococcus aureus* and more by *Streptococcus viridans*, and a higher prevalence of non-cardiac risk factors for IE, and more frequently had IE associated with health care procedures. The incidence of serious complications during the active phase of IE, especially of heart failure/valve dysfunction and persistent sepsis, was also significantly higher during the most recent period. Early mortality more than doubled in the second period (35.9% vs 15.4%; $P = .043$), as did the need for early surgery (69.2% vs 34.6%; $P = .002$) (Table 2).

Our data indicate that in our setting non-HDIE has shifted during the last 25 years toward a more serious clinical and prognostic profile (higher incidence of serious complications, need for surgery, and early mortality). This change may be because non-HDIE patients in the most recent period were much older and had a higher prevalence of severe comorbidities and non-cardiac risk factors for IE (chronic gastrointestinal and kidney diseases, immunosuppression, catheters and long-term vascular access). This type of IE now represents more than half of cases of native-valve IE,[6] which may partly explain why the clinical characteristics, morbidity and mortality of non-HDIE are increasingly similar to those of HDIE, as shown in Table 1. This change also obliges us to change our attitude toward non-HDIE, which is no longer a more "benign" disease than HDIE. Infective endocarditis without predisposing HD should be suspected in the absence of predisposing cardiac disease to allow its early diagnosis and treatment, thus helping to reduce its increasing mortality.

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Use of the New Antiplatelet Agents in Acute Coronary Syndromes: Limitations Related to Patient Characteristics

Limitaciones al uso de los nuevos antiagregantes en los síndromes coronarios agudos relacionadas con las características de los pacientes

To the Editor,

Prasugrel and ticagrelor are the drugs of choice for acute coronary syndrome, but they have a more limited profile than clopidogrel due to the risk of bleeding.[1] The percentage of patients whose clinical characteristics could limit or contraindicate the use of the new antiplatelet agents is unknown. We analyzed this percentage in a unselected cohort of consecutive patients from several Spanish centers with different forms of acute coronary syndrome.

From October 1, 2013, we studied 25 consecutive patients diagnosed with any form of acute coronary syndrome in 17 hospitals with a cardiac catheterization laboratory, 1 in each autonomous region. The only patients excluded were those taking oral anticoagulants. We studied their baseline characteristics, antiplatelet therapy, and the characteristics that could limit or contraindicate use of the new antiplatelet agents.

Prasugrel was considered as a nonindication, based on its product information sheet, as was not performing percutaneous coronary intervention, whereas active bleeding and a history of stroke and transient ischemic attack (TIA) were considered as contraindications. Age $\geq$ 75 years and weight $<$ 60 kg were considered to be limitations. According to the product information sheet, ticagrelor is contraindicated in active pathological bleeding and previous intracranial hemorrhage. On the basis of data provided by the literature, a history of TIA or nonbleeding stroke[2,3] was considered to be a limitation, as well as moderate or severe bronchopathy[4] and glomerular filtration rate $\leq$ 30 mL/h.[5]

We studied 425 patients. The baseline characteristics, treatment strategy, and antiplatelet therapy are shown in Table 1 and the conditioning factors are shown in Table 2. A total of 210 patients (49.4%) were deemed ineligible for prasugrel, 84 (19.3%) for not having undergone percutaneous coronary intervention, 139 (32.7%) for being $\geq$ 75 years, 15 (3.5%) for weighing $<$ 60 kg, and 40 (9.4%) for having a history of TIA or stroke. With ticagrelor, of 82 patients (19.3%), 42 (9.9%) could have limitations due to moderate or severe obstructive pulmonary disease, 40 (9.4%) due to stroke or TIA, and 13 (3.1%) due to glomerular