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MAJOR ARTICLE

Non-nosocomial Healthcare-Associated Infective Endocarditis: A Distinct Entity? Data From the GAMES Series (2008–2021)

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Background. Patients who acquire infective endocarditis (IE) following contact with the healthcare system, but outside the hospital, are classified as having non-nosocomial healthcare-associated IE (HCIE). Our aim was to characterize HCIE and establish whether its etiology, diagnosis, and therapeutic approach suggest it should be considered a distinct entity.

Methods. This study retrospectively analyzes data from a nationwide, multicenter, prospective cohort including consecutive cases of IE at 45 hospitals across Spain from 2008 to 2021. HCIE was defined as IE detected in patients in close contact with the healthcare system (eg, patients receiving intravenous treatment, hemodialysis, or institutionalized). The prevalence and main characteristics of HCIE were examined and compared with those of community-acquired IE (CIE) and nosocomial IE (NIE) and with literature data.

Results. IE was diagnosed in 4520 cases, of which 2854 (63%) were classified as CIE, 1209 (27%) as NIE, and 457 (10%) as HCIE. Patients with HCIE showed a high burden of comorbidities, a high presence of intravascular catheters, and a predominant staphylococcal etiology, *Staphylococcus aureus* being identified as the most frequent causative agent (35%). They also experienced more persistent bacteremia, underwent fewer surgeries, and showed a higher mortality rate than those with CIE (32.4% vs 22.6%). However, mortality in this group was similar to that recorded for NIE (32.4% vs 34.9%, respectively, $P = .40$).

Conclusions. Our data do not support considering HCIE as a distinct entity. HCIE affects a substantial number of patients, is associated with a high mortality, and shares many characteristics with NIE.

Keywords. healthcare-related infections; infective endocarditis; nosocomial infections.

The clinical and epidemiological characteristics of infective endocarditis (IE) have changed over time [1, 2]. According to place of acquisition, a distinction was traditionally made between community-acquired and nosocomial IE, with different etiological agents and prognoses in each case. The concept of healthcare-associated IE was introduced to describe IE acquired at hospital or affecting patients in close contact with the healthcare system [3–6]. However, the increasing number of invasive procedures performed outside the hospital setting, and the growing number of patients from healthcare institutions, have determined an increase over the last few decades in non-nosocomial healthcare-associated IE (HCIE) [3, 7, 8].

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While community-acquired IE (CIE) has been clearly differentiated from nosocomial IE (NIE), there is less information on HCIE. The limited evidence available has been derived from heterogeneous studies that, in most cases, are outdated and involve small sample sizes [9, 10], and consists of widely varying definitions, etiologies, and prognoses. In this scenario, it is worth considering the dimension of this problem, and whether this group of patients has etiological, therapeutic, or prognostic differences for HCIE to be considered a distinct entity.

From a public health perspective, the need to characterize this group of patients is warranted by an ever-increasing number of institutionalized patients and of invasive procedures performed outside the hospital, as well as a lack of clear indications regarding the need for prophylaxis before such procedures.

In this work, we set out to define the current reality of HCIE based on data from a large prospective cohort. Our objectives were (1) to describe the prevalence and most relevant characteristics of HCIE, (2) to analyze its differences with respect to CIE and NIE along with its value as a distinct entity, and (3) to review the available literature to compare these data with our findings.

METHODS

The GAMES (Grupo de Apoyo al Manejo de la Endocarditis Infecciosa en España [Spanish Collaboration on Endocarditis]) cohort is a nationwide, multicenter registry that from 2008 has prospectively included consecutive cases of definite IE according to modified Duke criteria [11] in 45 hospitals across Spain. The present study is an observational retrospective analysis of these prospectively obtained data. Over the period January 2008 to December 2021, 4520 definite cases of IE were diagnosed.

Data Collection

A standardized case report form was completed in each case to record the active IE episode and follow-up data, which included clinical information, including Charlson comorbidity index (CCI) [12], as well as microbiological and echocardiographic results. All patients provided informed consent to be included in the registry. All cases were assessed 1 year after inclusion in the registry to record resolution, death, or relapse.

Definitions

To simplify classification, and for the purpose of exploring its value as a distinct entity, in this work "HCIE" refers to nosohusial IE, and does not therefore include cases of nosocomial acquisition. HCIE was defined as an IE diagnosed at the time of admission or within 48 hours of admission, if a patient met any of the following criteria:

1. Received intravenous (IV) treatment at home; received wound care or skilled nursing care provided by a healthcare provider, family, or friends; or received self-administered IV medical treatment in the 30 days prior to bacteremia.
2. Visited an outpatient hospital or hemodialysis clinic or received IV chemotherapy in the 30 days prior to bacteremia.
3. Was hospitalized in an acute care facility for 2 or more days in the 90 days prior to bacteremia.
4. Lived in a nursing home or long-term care facility.

All IE cases associated with hemodialysis were classified as HCIE. NIE was defined as IE in a patient who had been hospitalized for >48 hours before the onset of signs or symptoms consistent with IE. CIE was defined as IE diagnosed within the first 48 hours of admission or according to signs or symptoms consistent with IE starting before hospital admission in a patient who did not fulfill the criteria for HCIE. While an odontogenic source was considered within the definition of CIE, in 2 patients HCIE was attributed to dental interventions of greater complexity involving total replacement of dental pieces.

Statistical Analysis

The characteristics of HCIE, CIE, and NIE were compiled and compared. Categorical variables were summarized as frequencies and percentages, and continuous variables as medians and interquartile ranges (25th–75th percentile). Categorical variables were compared using the χ^2 test (or Fisher exact test where necessary). Variables with nonnormal distribution were compared using the Mann-Whitney U test. Significance was set at $P < .05$. For a better interpretation of the results, effect sizes were calculated for each comparison. For numerical variables, Cohen d (standardized mean difference) was used, while odds ratios (ORs) are provided for categorical variables.

To identify clinical variables that were differentially associated with the presence of HCIE, a multivariate logistic regression analysis was performed through a conditional backward procedure, entering only epidemiological variables present before the IE episode and hospital admission that varied significantly between HCIE and NIE in the univariate analysis or that were considered to be of clinical relevance. Our model included sex, age, age-adjusted CCI score, native valve IE, presence of intracardiac device, previous cardiac surgery, previous IE, and presence of IV catheters. The survival curve for hemodialysis-related HCIE was constructed using the Kaplan-Meier method. All statistical tests were performed using the package IBM SPSS Statistics for Windows, version 26.

For the literature review, a search was performed of PubMed using the commands (endocarditis [MeSH Terms]) AND (healthcare [Title]), health-care [Title] AND endocarditis [Title], nonnosocomial [Title] AND endocarditis [Title], healthcare-associated [Title] AND endocarditis [Title], (healthcare[MeSH Terms]) AND (endocarditis[MeSH Terms]) and (healthcare[MeSH Terms]) AND (endocarditis[Title]) with no time restriction. Manually

Table 1. Demographic Characteristics, Predisposing Factors, and Site of Healthcare-Associated Infective Endocarditis (IE) With Respect to Community-Acquired IE and Nosocomial IE

Characteristic	CIE (n = 2854)	*P* Value (HCIE vs CIE)	HCIE (n = 457)	*P* Value (HCIE vs NIE)	NIE (n = 1209)
Age, y, median (IQR)	67 (55–76)	.90	67 (56 –76)	**<.01**	70 (61–77)
Male sex	1991 (70)	.14	303 (66.3)	.67	788 (65.1)
Comorbidities					
Age-adjusted CCI score, median (IQR)	4 (2–6)	**<.01**	6 (4–8)	**<.01**	5 (3–7)
Pulmonary disease	473 (16.5)	.40	83 (18.1)	.05	272 (22.5)
Hypertension	1494 (52.3)	**<.01**	322 (70.6)	**<.01**	726 (60.2)
Coronary heart disease	655 (22.9)	**.03**	126 (27.5)	.06	392 (32.4)
Heart failure	770 (26.9)	**<.01**	166 (36.3)	**<.01**	524 (43.3)
Diabetes	734 (25.7)	**<.01**	177 (38.7)	**.03**	399 (33.0)
HIV	70 (2.4)	.23	7 (1.5)	.20	10 (0.8)
PWID	110 (3.8)	**<.01**	6 (1.3)	**<.01**	3 (0.2)
Peripheral vascular disease	221 (7.7)	**<.01**	108 (23.6)	**<.01**	155 (12.8)
Cerebrovascular disease	336 (11.7)	.60	58 (12.7)	.47	170 (14.0)
Neoplasm	377 (13.2)	**<.01**	106 (23.2)	.19	245 (20.2)
CKD	541 (19.0)	**<.01**	289 (63.2)	**<.01**	326 (27.0)
Liver disease	290 (10.1)	.22	55 (12.0)	**.03**	104 (8.6)
Immunosuppressive therapy	91 (3.1)	**<.01**	60 (13.1)	**.03**	107 (9.0)
Cardiac history					
Native valve disease	1324 (46.4)	**.02**	184 (40.3)	**<.01**	594 (49.1)
Congenital heart disease	211 (7.4)	**<.01**	13 (2.8)	.10	56 (4.6)
Previous endocarditis	217 (7.6)	.86	34 (7.4)	.86	93 (7.6)
Previous cardiac surgery	899 (31.5)	**<.01**	106 (23.2)	**<.01**	567 (46.9)
Dental procedure	264 (9)	**<.01**	2 (0.4)		0 (0.0)
Intravascular catheter present at symptom onset	0 (0.0)		195 (42.6)	**.01**	411 (33.9)
Peripheral	0 (0.0)		36 (7.8)	**<.01**	269 (22.2)
Central short duration	0 (0.0)		24 (5.2)	.052	97 (8.0)
Central long duration	0 (0.0)		125 (27.3)	**<.01**	36 (2.9)
Intra-arterial Swan-Ganz catheter	0 (0.0)		10 (2.1)	**.01**	9 (0.7)
Days from symptom onset to diagnosis, median (IQR)	15 (10–60)	**<.01**	10 (3–21)	.18	10 (2–21)
Days from symptom onset to admission, median (IQR)	16 (10–60)	**<.01**	10 (4–21)	**.03**	10 (2–21)
IE type					
Native IE	1976 (69.2)	.53	323 (70.7)	**<.01**	550 (45.5)
Prosthetic IE	775 (27.2)	**<.01**	87 (19.0)	**<.01**	523 (43.3)
Cardiac device	168 (5.9)	**<.01**	51 (11.2)	.18	165 (13.6)
IE site					
Aortic	1563 (54.8)	**<.01**	206 (45.1)	**.02**	620 (51.3)
Mitral	1339 (46.9)	.15	198 (43.3)	**.04**	458 (37.9)
Tricuspid	155 (5.4)	**<.01**	44 (9.6)	**<.01**	67 (5.5)
Pulmonary	41 (1.6)	.9	7 (1.5)	.80	21 (1.7)
No. of patients receiving empirical treatment	403 (14.1)	.28	56 (12.2)	.24	175 (14.4)
Adequate empirical treatment for *Staphylococcus aureus*[a]	62 (88.6)	.81	19 (90.5)	.72	42 (87.5)

Data are presented as No. (%) unless otherwise indicated. Standardized differences can be found in Supplementary Table 1. Values in bold refer to results with statistically significant differences.

Abbreviations: CCI, Charlson comorbidity index; CIE, community-acquired infective endocarditis; CKD, chronic kidney disease; HCIE, healthcare-associated infective endocarditis; HIV, human immunodeficiency virus; IE, infective endocarditis; IQR, interquartile range; NIE, nosocomial infective endocarditis; PWID, people who inject drugs.

[a]Adequate empirical treatment for *S aureus* was evaluated in 139 cases (CIE, 70; HCIE, 21; NIE, 48).

selected papers of interest were also included. To the best of our knowledge, only 5 studies have analyzed HCIE in a differentiated manner [3, 9, 10, 13, 14]. Studies assessing nosohusial and nosocomial IE combined were not included in our review [4–6].

Patient Consent Statement

The case report form used was approved by the ethics committee (Comité ético de Investigación Clínica Regional de la Comunidad de Madrid CEIC-R; EC 18/07; date 11/01/2008). Written informed consent was obtained in all cases.

RESULTS

In total, 4520 episodes of definite IE were recorded in the cohort. Of these, 2854 episodes (63%) were classified as CIE, 1209 (27%) as NIE, and 457 (10%) as HCIE. The main characteristics of

these episodes of HCIE and their comparison with those of CIE and NIE are provided in Table 1 (an analysis of standardized differences can be found in Supplementary Table 1).

Characteristics of HCIE

Patients in the HCIE group were characterized by a significant number of comorbidities, a high proportion of them having hypertension, chronic kidney disease (CKD), diabetes, and heart failure. Most IE cases developed in native valves (71%). In 195 patients (43%), an intravascular catheter was present at the onset of symptoms (Table 1). The most frequent etiology was *Staphylococcus aureus* (161 episodes [35%]), 19% of which were methicillin-resistant *S aureus* (MRSA) (Table 2). Coagulase-negative staphylococci and *Enterococcus* caused 23% and 19.5% of cases, respectively. Hemodialysis was described as the source of infection in 49% of HCIE cases (Table 3).

When we considered clinical outcomes (Table 4), we found that a high proportion of patients developed heart failure, acute renal failure, and intracardiac complications (39%, 33%, and 32%, respectively). While 42% of the HCIE patients underwent cardiac surgery, 26% with an indication for surgery could not be operated on. In-hospital mortality among the HCIE patients was 32%. There were fewer deaths among those who underwent surgery compared to those who did not undergo surgery (11.1% vs 21.2%).

Analysis of Hemodialysis-Related HCIE

Of the 457 episodes of HCIE examined, almost half were recorded in patients on hemodialysis (n = 223 [49%]). These patients on hemodialysis had more comorbidities, experienced septic shock more frequently, more often could not have indicated surgery, and showed a higher mortality than patients not receiving hemodialysis (Table 5). The main etiologic agent was *S aureus* (46%). Interestingly, the percentage of those with CKD was also high in the no-hemodialysis group (28.6%). Patients who did not receive hemodialysis had a significantly lower mortality ($P < .01$) than those who did so, as may be observed in the Kaplan-Meier survival curve (Figure 1).

Comparison of HCIE With CIE and NIE

HCIE and CIE are clearly different clinical entities (Table 1). Patients with HCIE showed a higher age-adjusted CCI score, were admitted fewer days after symptom onset and diagnosis, and had a different disease etiology. In terms of the clinical course, patients with HCIE showed more persistent bacteremia, more instances of indicated surgery not performed, and a higher mortality than those with CIE, who underwent indicated surgery more frequently.

Differences were less evident between HCIE and NIE, especially in terms of etiology and prognosis (Tables 1, 2, and 4 and Supplementary Table 1). Native valves were affected more frequently in the group of participants with HCIE. In both the HCIE and NIE groups, the main etiology was staphylococcal, and there was no difference in MRSA proportions. Patients with HCIE also underwent surgery on fewer occasions, but this did not give rise to a significant difference in mortality between these 2 groups (32.4% vs 34.9%, respectively, $P = .40$). Remarkably, there were no significant differences in the proportions of patients receiving adequate empirical treatment for *S aureus* (ie, antibiotic therapy started before culture results are available) in the HCIE, CIE, and NIE groups (Table 1).

When HCIE and NIE were compared, epidemiological variables identified as significantly associated with HCIE were native valve IE (OR, 1.81) and age-adjusted CCI score (OR, 1.14) (Supplementary Table 2).

Table 2. Main Etiologies of Healthcare-Associated Infective Endocarditis (IE) With Respect to Community-Acquired IE and Nosocomial IE

Etiology	CIE (n = 2854)	*P* Value	HCIE (n = 457)	*P* Value	NIE (n = 1209)
Staphylococcus aureus	574 (20.1)	.03	161 (35.2)	.03	360 (29.8)
MRSA	58 (2.0)	<.01	30 (6.5)	.46	92 (7.6)
CoNS	332 (11.6)	<.01	105 (23.0)	<.01	405 (33.5)
Enterococcus spp	402 (14.1)	<.01	89 (19.5)	.06	188 (15.6)
Streptococcus spp	1126 (39.5)	<.01	50 (10.9)	<.01	65 (5.4)
Gram-negative bacilli	117 (4.1)	.29	14 (3.1)	.20	53 (4.4)
Anaerobes	44 (1.5)	.06	2 (0.4)	.88	6 (0.5)
Candida spp	15 (0.5)	<.01	11 (2.4)	.14	47 (3.9)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: CIE, community-acquired infective endocarditis; CoNS, coagulase-negative staphylococci; HCIE, healthcare-associated infective endocarditis; MRSA, methicillin-resistant *Staphylococcus aureus*; NIE, nosocomial infective endocarditis.

Table 3. Suspected Source of Healthcare-Associated Infective Endocarditis (n = 457)

Infection Source	No. (%)
Hemodialysis	223 (48.8)
Intravenous catheter	57 (12.5)
Colonoscopy	47 (10.3)
Urological procedure	32 (7.0)
Pacemaker implantation	32 (7.0)
Previous surgery	12 (2.6)
Dental manipulation	2 (0.4)
Other	52 (11.4)

Review of the Literature

Only 5 studies were found to have analyzed HCIE in a differential manner, excluding nosocomial acquisition [3, 9, 10, 13, 14]. Only 1 of these reports provided data for >200 patients [3]. The most frequent characteristics reported are detailed in Supplementary Table 3. Hemodialysis patients are routinely included in this group.

Table 4. Complications and Outcomes of Patients With Community-Acquired Infective Endocarditis (IE), Healthcare-Associated IE, and Nosocomial IE

Complication/Outcome	CIE (n = 2854)	*P* Value	HCIE (n = 457)	*P* Value	NIE (n = 1209)
Complications					
Intracardiac complications	1016 (35.6)	.15	147 (32.2)	.33	411 (34.0)
Vascular phenomena	287 (10.0)	.15	36 (7.8)	.13	71 (5.8)
Heart failure	1195 (41.8)	.20	177 (38.7)	.13	518 (42.8)
Persistent bacteremia	262 (9.1)	**<.01**	60 (13.1)	.05	206 (17.0)
CNS involvement	649 (22.7)	**<.01**	66 (14.4)	**.04**	228 (18.8)
Embolization	742 (25.9)	**<.01**	92 (20.1)	.92	241 (19.9)
New murmur	1064 (37.2)	.10	152 (33.2)	.07	347 (28.7)
Vegetation present	1957 (68.5)	.08	332 (72.2)	**<.01**	786 (65.0)
Acute renal failure	1000 (35.0)	.31	149 (32.6)	**<.01**	509 (42.1)
Septic shock	340 (11.9)	**.04**	70 (15.3)	.81	191 (15.8)
Sepsis	478 (16.7)	**.04**	94 (20.5)	.89	245 (20.2)
Indication for surgery	2022 (70.8)	**.03**	301 (65.9)	**<.01**	880 (72.8)
Cardiac surgery	1484 (52.0)	**<.01**	190 (41.6)	**.02**	579 (47.9)
Indicated surgery not performed	567 (19.9)	**<.01**	117 (25.6)	.93	312 (25.8)
Duration of treatment, days, median (IQR)	39 (28–45)	.53	38 (26–45)	.31	41 (23–48)
Hospital stay, days, median (IQR)	34 (21–50)	.11	36 (23–53)	**<.01**	41 (24–58)
Mortality					
In-hospital	645 (22.6)	**<.01**	148 (32.4)	.40	418 (34.9)
With surgery	274 (9.6)	.29	51 (11.1)	.60	146 (12.1)
Without surgery	371 (12.9)	**<.01**	97 (21.2)	.60	272 (22.5)
1-y mortality	779 (27.3)	**<.01**	191 (41.8)	.80	497 (41.2)
1-y recurrence[a]	35 (1.5)	.10	9 (2.9)	**.04**	9 (1.1)
Sequelae at discharge[a]	334 (15.1)	.80	45 (14.5)	.36	133 (16.8)

Data are presented as No. (%) unless otherwise indicated. Values in bold refer to results with statistically significant differences.

Abbreviations: CIE, community-acquired infective endocarditis; CNS, central nervous system; HCIE, healthcare-associated infective endocarditis; NIE, nosocomial infective endocarditis.

[a]One-year recurrence and sequelae at discharge rates were calculated using surviving patients as the denominator (CIE, 2209; HCIE, 309; NIE, 791).

Including the results of our cohort, 839 cases of HCIE have been reported to date. For these cases, the average age was 60 years and there was a high proportion of comorbidities, including hemodialysis, diabetes, and valvular heart disease. The predominance of a staphylococcal etiology coincides with most cases [3, 10, 13, 14]. Mortality figures vary widely and in some cases can be up to 50% [13, 14], with an overall mortality rate of 29.3% (246/839).

DISCUSSION

Based on current criteria, 10% of cases in our large multicenter cohort were classified as HCIE, representing one-third of all IE cases that are not community acquired. Previous studies have provided figures that vary widely [3, 9, 10, 13, 14].

We found no reason to consider HCIE as a distinct entity. In our opinion, defining a new major subclass of IE would only be justified in the case of differences in etiology, diagnosis, therapeutic approach, or prognosis. Below we provide our reasoning for this argument.

HCIE patients show a high burden of comorbidities and share many features with NIE. The few differences detected between HCIE and NIE only reflect the initial characteristics of the patients, not their clinical course.

Endovascular procedures appear to be the most common causative mechanism for both HCIE and NIE. Forty-nine percent of HCIE patients received hemodialysis and 21% had been fitted with some type of IV catheter, whose presence has been linked to the origin of HCIE in up to 40%–60% of cases [4, 13].

The presence of HCIE fails to identify a group of patients with a different etiology to NIE. In our cohort, *S aureus* was the most frequent etiological agent. In effect, staphylococci are the most frequent etiology in both HCIE and NIE. Other authors have reported similar findings (Supplementary Table 3) describing a population with a high prevalence of comorbidities, many patients on hemodialysis, and a predominantly staphylococcal etiology.

This classification should be useful to ensure the rapid and correct identification of HCIE patients. As these patients are community derived, they could easily be misclassified as CIE, with a worse prognosis and many similar characteristics to NIE. Remarkably, we observed no diagnostic delay in our HCIE series.

For IE associated with diagnostic and therapeutic procedures, empiric coverage of methicillin-resistant staphylococci, enterococci, and gram-negative pathogens is recommended [15]. According to our findings, the empirical treatment of HCIE should not differ from that of NIE. In effect, there were no significant differences in the proportions of correct empirical

Table 5. Patients With Healthcare-Associated Infective Endocarditis Receiving Versus Not Receiving Hemodialysis (n = 457)

Characteristic	No Hemodialysis (n = 234)	Hemodialysis (n = 223)	*P* Value
Age, y, median (IQR)	69 (59–78)	66 (54–74)	**<.01**
Male sex	161 (68.8)	142 (63.6)	.25
Comorbidities			
Pulmonary disease	44 (18.8)	39 (17.4)	.72
Hypertension	170 (72.6)	152 (68.1)	.29
Coronary heart disease	58 (24.7)	68 (30.5)	.17
Heart failure	74 (31.6)	92 (41.2)	**.03**
Diabetes	78 (33.3)	99 (44.4)	**.02**
Peripheral vascular disease	35 (14.9)	73 (32.7)	**<.01**
Neoplasm	72 (30.8)	34 (15.3)	**<.01**
CKD	67 (28.6)	223 (100.0)	**<.01**
Native valve disease	95 (40.6)	89 (39.9)	.88
Immunosuppressive therapy	30 (12.8)	30 (13.4)	.84
Etiology			
Staphylococcus aureus	58 (24.8)	103 (46.2)	**<.01**
MRSA	14 (5.9)	16 (7.1)	.8
CoNS	45 (19.2)	60 (26.9)	.05
Enterococcus spp	62 (26.5)	27 (12.1)	**<.01**
Streptococcus spp	40 (17.1)	10 (4.5)	**<.01**
Candida spp	5 (2.1)	6 (2.7)	.65
Gram-negative bacilli	10 (4.3)	4 (1.8)	.12
Complications			
Septic shock	24 (10.2)	46 (20.6)	**<.01**
Sepsis	33 (14.1)	61 (27.3)	**<.01**
Indication for surgery	159 (67.9)	142 (63.7)	.35
Cardiac surgery	116 (49.6)	74 (33.2)	**<.01**
Indicated surgery not performed	46 (19.7)	71 (31.8)	**<.01**
Duration of antibiotic treatment, days, median (IQR)	39 (28–44)	38 (21–46)	.61
Hospital stay, days, median (IQR)	37 (24–53)	32 (20–53)	.15
Mortality			
In-hospital death	54 (23.1)	94 (42.2)	**<.01**
1-y mortality	75 (32.0)	116 (52.0)	**<.01**
1-y recurrence[a]	7 (3.8)	2 (1.5)	.11
Sequelae at discharge[a]	33 (18.3)	12 (9.3)	**<.01**

Data are presented as No. (%) unless otherwise indicated. Values in bold refer to results with statistically significant differences.

Abbreviations: CKD, chronic kidney disease; CoNS, coagulase-negative staphylococci; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*.

[a]One-year recurrence and sequelae at discharge rates were calculated using surviving patients as the denominator (no hemodialysis, 180; hemodialysis, 129).

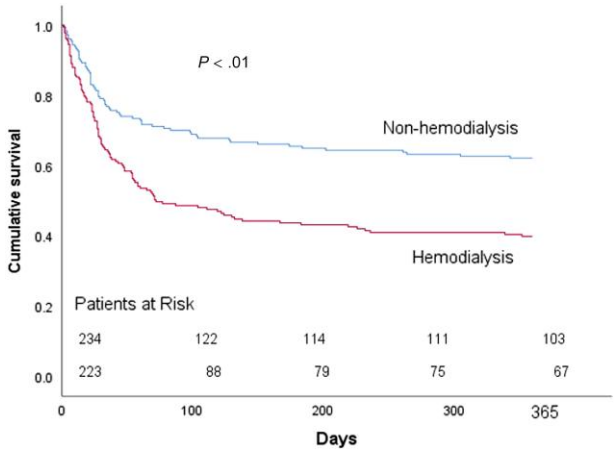

Figure 1. Survival curve of patients with healthcare-associated infective endocarditis according to hemodialysis treatment.

treatment for *S aureus* between both groups in our cohort. To our knowledge, this issue has not been previously addressed.

Patients with HCIE were found to receive surgical treatment less frequently than those with NIE. However, this was not the consequence of diagnostic delay, but rather of the high burden of comorbidities and poor baseline status of this group of patients.

A key finding of our study was the similar mortality rate detected among patients with HCIE or NIE. Other reports have indicated widely varying mortality rates of up to 58% in some cases [10, 13]. Patients with IE receiving hemodialysis have been identified as a group showing high mortality [16, 17]. Our data also reveal the importance of ruling out HCIE in patients with IV catheters or under hemodialysis, in whom the absence of prosthetic valves should not preclude the need for an echocardiogram. Infection prevention measures and catheter care precautions are essential in these patients.

Our work has several limitations. Reports describing HCIE are scarce, heterogeneous, and based on small sample sizes. Although there is a notable lack of unification of classification criteria, our definition uses the criteria described in the International Collaboration on Endocarditis–Prospective Cohort Study [3]. A significant percentage of HCIE in our series affected hemodialysis patients. This could be related to the high prevalence of CKD, catheters, or episodes caused by *S aureus* in this group. Despite this, we consider that our study has several strengths as it provides data for the largest HCIE cohort to date and includes prosthetic valve IE.

The concept of healthcare-associated infection in the case of other diseases is also under debate [18]. This classification scheme is based merely on the geographical location of the patient (eg, community, hospital, nursing homes), yet ever-changing healthcare practices such as increasing proportions of out-of-hospital invasive procedures and home treatments have blurred these boundaries.

Within the framework of this controversial topic, our aim was to make a case for a discussion that we consider necessary. While we feel that the place of IE acquisition is important, we could not find relevant differences between acquiring IE at hospital or another healthcare setting, such that this classification does not serve to identify a group of patients showing a different pathogenic mechanism or etiology, nor does it help to make an early diagnosis, or have any therapeutic or prognostic consequences.

Our argument is that the place of IE acquisition might be less relevant than other factors such as the mechanism of

acquisition. For example, if a patient acquires a bloodstream infection as a result of phlebitis due to IV treatment, for disease classification purposes, it probably matters little whether treatment was received at home, in an outpatient clinic, or at hospital. A classification system that distinguishes between community-acquired or healthcare-acquired IE, including hospital admission and all medical actions with risk factors for endovascular infection, might be more appropriate. As the invasive procedure performed (eg, endovascular catheter placement, colonoscopy) may influence the presence of a certain type of pathogen, a more directed management approach and concise prognosis could be provided according to a model based on the pathogenic mechanism of IE acquisition. Given the prognosis of this group of patients, there is a need to correctly define its characteristics. This would help guide public health strategies, for example, those directed toward identifying a need or not for prophylaxis before extrahospital interventions such as dental or endoscopic procedures.

CONCLUSIONS

HCIE affected 10% of patients in our large contemporary series. These patients had significant comorbidities and a high mortality, and the predominant disease etiology was staphylococcal. The lack of differential characteristics and prognostic factors with respect to NIE does not support its consideration as a distinct entity, and makes us question the usefulness of the current classification of IE. A pathogenic approach that analyzes individual risk factors for the acquisition of IE could help to better manage this entity.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. The manuscript was written by the authors, with D. A., E. B., and P. M. as the overall lead authors. All authors had full access to all the data in the study and had final responsibility for the decision to submit this report for publication. All authors have read and approved the final version of the manuscript.

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