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Outcomes of infective endocarditis in patients with end-stage renal disease in Spain: a population-based study

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Abstract

Background Patients with end-stage renal disease (ESRD) have a higher risk of infective endocarditis (IE) and a worse prognosis associated with it. Our aim is to analyze the clinical characteristics and outcomes of patients with IE and ESRD in Spain, while exploring potential differences between patients undergoing dialysis and other patients with ESRD.

Methods Retrospective observational population-based study analyzing 9,008 episodes of IE recorded between 2016 and 2019, using data from the Spanish Minimum Basic DataSet. Among these, 428 patients had ESRD, including 332 who were undergoing dialysis. A multivariable and multilevel logistic regression model was constructed to assess the association between various factors and in-hospital mortality in ESRD patients.

Results Compared to patients without ESRD, those with ESRD were younger, had more comorbidities, and showed a higher prevalence of infections caused by *Staphylococcus aureus* (31.8% vs. 18.4%; $p < 0.001$) and coagulase-negative staphylococci (19.2% vs. 14%; $p = 0.006$). ESRD patients also experienced septic shock more frequently as an in-hospital complication (12.1% vs. 8.9%; $p = 0.007$). Additionally, they underwent cardiac surgery less often (12.6% vs. 19.6%; $p < 0.001$) and had significantly higher in-hospital mortality rates (33.4% vs. 26.9%; $p = 0.003$) than patients without ESRD. Among ESRD patients, those undergoing dialysis had more comorbidities and a higher proportion of *S. aureus* infections (36.1% vs. 16.7%; $p < 0.001$). The multilevel analysis revealed that neither dialysis nor cardiac surgery were independently associated with in-hospital mortality.

Conclusions Patients with ESRD and IE exhibit distinct clinical and microbiological characteristics compared to other IE patients. Additionally, they are less likely to undergo cardiac surgery and experience significantly higher in-hospital mortality rates. In ESRD patients with IE, neither dialysis treatment nor cardiac surgery were identified as independent risk factors for mortality.

Keywords Infective endocarditis, Spain, Chronic kidney disease, Dialysis, Mortality, Cardiac surgery

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Introduction

Patients with end-stage renal disease (ESRD), and especially those receiving chronic hemodialysis (HD), have a significantly higher risk of developing infective endocarditis (IE) compared to the general population [1–4]. Factors associated with this increased risk include a higher prevalence of diabetes mellitus and degenerative valve disease, immunological susceptibility, and particularly, transient bacteremia due to repeated vascular access through catheters, grafts and arteriovenous fistulas [5–9].

ESRD is not only related to a higher risk of infection, but also to a worse prognosis in IE. Several studies have shown that chronic renal failure is a risk factor for mortality in this population. This poor prognosis is multifactorial and is primarily due to immune system dysfunction, increased vascular calcification leading to cardiovascular complications, a higher prevalence of comorbidities such as diabetes, malnutrition, and chronic inflammation, and an increased frequency of more virulent microorganisms such as *Staphylococcus aureus* [1, 2, 4, 8, 10–12].

However, most data regarding the epidemiology and outcome of patients with ESRD and IE come from non-contemporary population-based studies with few clinical variables and lack of complete microbiological information, or from retrospective single-center cohorts [1–3, 11–14].

Thus, our aim was to compare the epidemiological, clinical and microbiological characteristics and outcome of IE episodes in patients with and without ESRD using the Spanish National Health Service System Database of Hospital Discharge Records (Spanish Minimum Basic Data Set, SMBD).

Methods

Study design and data source

Retrospective, population-based study, using the SMBD from January 2016 to December 2019. All patients admitted to hospitals included in the SMBD have anonymous standard data recorded. Statistics comprise age, sex, length of hospital stay, primary discharge diagnosis, up to 19 secondary diagnoses, and 20 procedures performed during hospitalization, all coded according to the International Classification of Diseases 10th Revision (ICD-10) [15].

Patient population

We identified all episodes with a primary or secondary ICD-10-CM discharge diagnosis of IE (Supplemental material -Table 1). To mitigate potential coding inaccuracies and ensure diagnostic validity, we applied strict inclusion criteria requiring microbiological confirmation for cases coded with generic IE diagnoses (I33.9, I38, I39). This approach minimizes misclassification and enhances

data specificity [16]. All episodes of IE for a single patient during the study period were included. Multiple hospitalizations that result from hospital-to-hospital transfers were considered as a single acute episode of care, which was assigned to the most complex hospital. Episodes with unknown status at discharge, age under 18 years or length of hospital stay ≤ 1 day and discharged alive to home or nursing home were excluded.

In order to identify episodes with a primary or secondary ICD-10-CM discharge diagnosis of IE in patients with ESRD, receiving or not dialysis (hemodialysis [HD] or peritoneal dialysis [PD]), the following ICD-10 codes were used: N18.6 and Z99.2. Renal transplant status was identified with the ICD-10 code Z94.0.

Infectious agents ICD-10 codes are displayed in Supplemental material - Table 2. Clinical information and evolution during hospitalization were extracted from the ICD codes reported for each episode (Supplemental material - Table 3).

Statistical analysis

Continuous variables are presented as mean and standard deviation or median and interquartile range, and categorical variables as frequencies and percentages. Student's t-test was used to compare 2 categories and ANOVA corrected by the Bonferroni test to compare 3 or more categories. Categorical variables were compared by the χ^2 test or Fisher's exact test.

A multivariable logistic regression model was developed to analyze the impact of various factors on in-hospital mortality in ESRD patients. The model was designed and adjusted to evaluate in-hospital mortality as the outcome. Risk variables included in the model were chosen based on clinical criteria. Some variables were grouped according to the Condition Categories updated yearly by the Agency for Healthcare Research and Quality [17]. Variables with p values < 0.10 were included in the multivariable logistic regression analysis. The final model was built by means of stepwise forward selection and backward elimination technique. The significance levels for selection and elimination were $p < 0.05$ and $p \geq 0.10$, respectively.

To assess the potential influence of inter-hospital differences on patient outcomes, a second model (multilevel model) incorporating a random hospital-specific intercept was developed. In-hospital mortality ratios were derived from these models, and calibration was evaluated graphically after grouping patients in deciles with respect to the predicted probabilities, and tabulating the mean predicted versus observed probabilities.

Odds ratios (OR) and 95% confidence intervals (CI) for each variable are shown. Discrimination was assessed by the area under the receiver operating characteristic curves (ROC). From the specified model, the ratios of

in-hospital mortality (risk-standardized mortality ratio -RSMR-) were calculated.

All statistical contrasts were bilateral, and differences were considered significant for $p < 0.05$. Statistical analysis was performed using STATA 17 (StataCorp, College Station, Texas, USA) and SPSS 21.0 (IBM, Armonk, New York, USA).

Results

During the study period, 9008 episodes of IE were detected and 428 (4.5%) correspond to patients with ESRD. Among the latter, 332 (77.6%) patients were receiving chronic dialysis, one with PD and the remaining 331 with HD (Fig. 1).

Comparison of IE episodes in patients with and without ESRD

Patients with ESRD were younger (mean age 66.2 [13.8] vs. 69.7 [14.7] years, $p < 0.001$), more frequently diabetic, and had more comorbidities at diagnosis (Table 1). In addition, this group had less prosthetic valve infections (17% vs. 27%; $p < 0.001$) and more cardiac implantable electronic device (CIED) infections (22% vs. 10%; $p < 0.001$).

Staphylococci infections were significantly more frequent in ESRD patients, both *S. aureus* (31.8% vs. 18.4%; $p < 0.001$) and coagulase-negative staphylococci (19.2% vs. 14.0%; $p = 0.006$). On the other hand, the incidence of *viridans* group streptococci infections was higher in non-ESRD patients (7.9% vs. 21.4%; $p < 0.001$).

Concerning clinical features, non-ESRD patients had a higher rate of stroke (3% vs. 7.2%; $p = 0.003$) and systemic embolisms (4.4% vs. 7.4%; $p = 0.022$), whereas the presence of septic shock was more frequent in ESRD patients (12.1% vs. 8.9%; $p = 0.007$). The prevalence of other complications such as congestive heart failure did not differ between both groups of patients.

Lastly, non-ESRD patients underwent cardiac surgery more frequently (19.6% vs. 12.6%; $p < 0.001$) and had significantly lower in-hospital mortality (33.4% vs. 26.9%; $p = 0.003$). Mortality remained significantly lower in non-ESRD patients when analysing separately those who underwent surgery and those who did not. During the study period, the proportion of patients who had hospital readmissions due to new IE episodes was higher in non-ESRD patients (13.4 vs. 15.7%; $p < 0.001$).

IE episodes in patients with ESRD: comparison between patients receiving and not receiving dialysis

Table 2 shows the differences between IE episodes in ESRD patients who were undergoing dialysis and those who were not.

Patients on dialysis were significantly younger (mean age 65.5 [14.2] vs. 68.7 [11] years, $p < 0.028$), and had a

higher prevalence of comorbidities and CIED infections (25.6% vs. 9.4%; $p < 0.001$).

Staphylococcus aureus was found more frequently in dialysis patients (36.1% vs. 16.7%; $p < 0.001$). Conversely, enterococci (10.5% vs. 20.8%; $p = 0.008$) were more frequent in non-dialysis patients.

Non-dialysis patients developed more frequently congestive heart failure (32.5% vs. 53.1%; $p < 0.001$).

Observed in-hospital mortality was not significantly different between dialysis and non-dialysis patients (34.3% vs. 30.2%; $p = 0.407$). The proportion of patients who underwent cardiac surgery and the duration of hospital stay did not differ between both groups either. The number of hospital readmissions for new IE episodes was comparable in both groups (13.9% vs. 11.7%; $p = 0.440$).

A comparison between transplant and non-transplant recipients is presented in Supplemental material - Table 4. Additionally, we performed a comparison of the characteristics of patients with ESRD not on dialysis, patients with ESRD undergoing dialysis, and patients with ESRD who had received a kidney transplant (Supplemental material - Table 5).

Prognostic factors associated with in-hospital mortality in patients with IE and end-stage renal disease

Table 3 shows the multilevel regression model for in-hospital mortality in ESRD patients with IE. The model had an area under the ROC curve of 0.791 (95% CI: 0.744 to 0.837). Median odds ratio (MOR) was 1.18.

Of note, neither dialysis status (OR: 0.94; 95% CI: 0.54 to 1.65), nor renal transplantation (OR: 0.97; 95% CI: 0.34 to 2.8), nor cardiac surgery (OR: 1.33; 95% CI: 0.64 to 2.75) were independent prognostic variables for in-hospital mortality in this population.

Discussion

The present study comprises the first nationwide epidemiological investigation in Spain describing the characteristics of patients with IE and ESRD, comparing patients on dialysis (HD or PD) to those not undergoing dialysis, and renal transplant recipients with those who were not.

The main findings of our work are: (1) ESRD represent 4.5% of IE episodes in Spain; (2) compared to patients without ESRD, they are younger, had more comorbidities, more cardiac implantable electronic device infections, a higher incidence of IE due to staphylococci, had more frequently septic shock, underwent cardiac surgery less frequently and had higher in-hospital mortality; and (3) in patients with ESRD, dialysis status was not an independent predictor of in-hospital mortality.

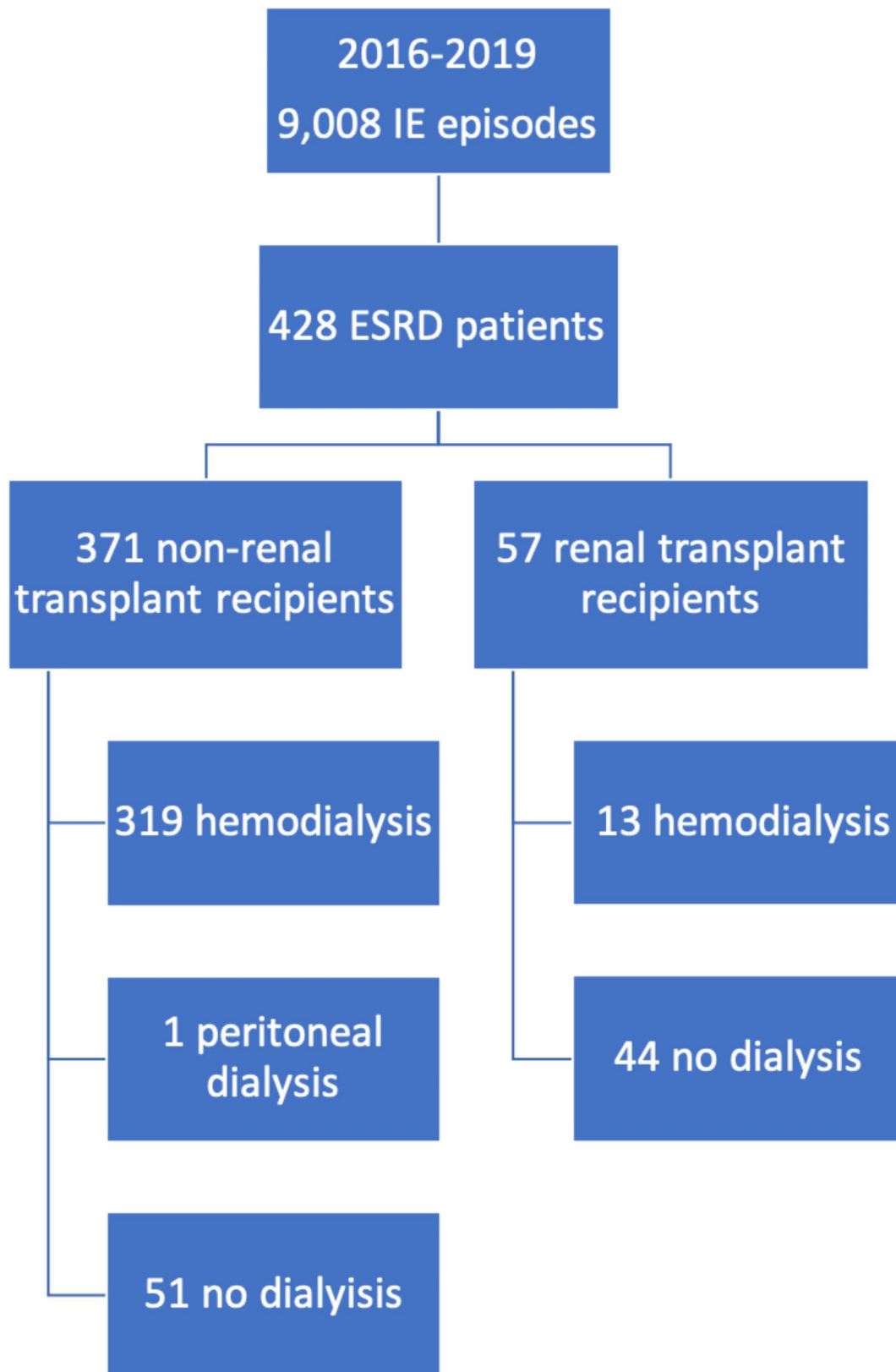


Fig. 1 Flow chart of the study population. A total of 9008 episodes of infective endocarditis (IE) were analyzed between the years 2016 and 2019, of which 428 had end-stage renal disease (ESRD). 332 ESRD patients (77.6%) were receiving dialysis, only one patient was undergoing peritoneal dialysis (PD) and the remaining episodes were in chronic hemodialysis (HD) programs. 57 ESRD patients (13.3%) were renal transplant recipients. ESRD: end-stage renal disease; IE: infective endocarditis. Figure created using PowerPoint

Table 1 Epidemiological, microbiological characteristics and outcomes of infective endocarditis episodes in patients with end-stage renal disease compared to those without end-stage renal disease

	IE no ESRD 8,580	IE ESRD 428	P
Age (years)	69.7 (14.7)	66.2 (13.8)	<0.001
Male	66.1	67.5	0.291
Charlson Index > 2	32.2	76.4	<0.001
Cancer	4.4	1.4	0.005
Diabetes mellitus	26.2	36.9	<0.001
Protein-calorie malnutrition	6.3	7	0.959
Intravenous drug use	1.6	0.2	0.030
Cardiac implantable electronic device infection	10	21.9	<0.001
Presence of prosthetic heart valve/Infection of a cardiac valve prosthesis	27.2	17	<0.001
Cardiac rheumatic disease	11.9	12.1	0.795
Valvular heart disease, including rheumatic valve disease	46.7	42.8	0.301
IE recurrences during the study period	15.7	13.4	<0.001
<i>Staphylococcus aureus</i>	18.4	31.8	<0.001
Coagulase-negative staphylococci	14	19.2	0.006
<i>Viridans</i> group streptococci	21.4	7.9	<0.001
Enterococci	15.4	12.9	0.200
<i>Streptococcus pneumoniae</i>	0.8	0.5	0.218
<i>Candida</i> spp.	1.1	1.2	0.798
Gram-negative bacilli	3.7	3.5	0.820
Anaerobes	0.1	0	0.459
Other microorganisms	17.5	15.2	0.223
Unknown infectious agent	20.7	21.3	0.657
Cardiogenic shock	3.2	2.8	0.253
Cardio-respiratory failure	18.9	17.1	0.165
Congestive heart failure	37.2	37.1	0.669
Stroke	7.2	3	0.003
Arterial embolism	7.4	4.4	0.022
Septic shock	8.9	12.1	0.007
Cardiac valve surgery	19.6	12.6	<0.001
Hospital stay (days)	26 (13–43)	23 (14–40)	<0.001
Observed in-hospital mortality (95% CI)	26.9 (26–27.9)	33.4 (29.1–38)	0.003
Observed in-hospital mortality (95% CI) in patients who underwent cardiac surgery	23.3 (21.3–25.3)	36.4 (24.6–49.5)	0.035
Observed in-hospital mortality (95% CI) in patients who did not undergo cardiac surgery	27.9 (26.8–29.0)	33.0 (28.2–38.0)	0.039

Values are n (%) or mean (standard deviation)/median (interquartile range). Bold values are significant. CI: confidence intervals; ESRD: end-stage renal disease; IE: infective endocarditis

Epidemiology

There is limited evidence on IE in patients with ESRD, as most of the data focuses only on patients with ESRD receiving dialysis. Epidemiological characteristics of IE episodes occurring in ESRD patients have been mainly described in two large retrospective population-based studies, with very disparate findings. A study in the United States [10] using the National Inpatient Sample (NIS) data (2006–2017) reported a 15.7% prevalence of ESRD among all episodes of IE. On the other hand, a registry from Scotland [18] (1990–2014) described that ESRD was present in 2.8% of IE patients, slightly lower than the 4.5% prevalence found in our study. These wide differences are probably related to diagnostic coding and case identification. The study conducted in the United

States relied on NIS data, using ICD-9 and ICD-10 codes for case identification without requiring microbiological confirmation. This approach likely led to the inclusion of a higher proportion of probable or possible IE cases compared to our study. Additionally, United States' healthcare system includes a mix of public and private hospitals, potentially leading to selection bias based on insurance coverage. On the other hand, the Scottish registry used a nationwide data-linkage approach, integrating hospitalization, mortality, and microbiology records. This approach allowed them to validate microbiological diagnoses directly, reducing the likelihood of misclassification. However, microbiological data were only available for 42% of cases, potentially introducing selection bias. Besides, using a data-linkage model could introduce

Table 2 Epidemiological, microbiological characteristics and outcomes of infective endocarditis episodes in end-stage renal disease patients, comparing patients receiving and not receiving dialysis

	IE-ESRD no dialysis 96	IE-ESRD dialysis 332	P
Age (years)	68.7 (11)	65.5 (14.2)	0.028
Male	68.8	67.2	0.771
Charlson Index > 2	71.9	77.7	<0.001
Cancer	0	1.8	0.185
Diabetes mellitus	41.7	35.5	0.273
Protein-calorie malnutrition	8.3	6.6	0.564
Intravenous drug use	0	0.3	0.590
Cardiac implantable electronic device infection	9.4	25.6	0.001
Presence of prosthetic heart valve/Infection of a cardiac valve prosthesis	22.9	15.4	0.083
Cardiac rheumatic disease	10.4	12.7	0.555
Valvular heart disease, including rheumatic valve disease	46.9	41.6	0.354
IE recurrences during the study period	11.7	13.9	0.440
<i>Staphylococcus aureus</i>	16.7	36.1	<0.001
Coagulase-negative staphylococci	24	17.8	0.175
<i>Viridans</i> group streptococci	10.4	7.2	0.309
Enterococci	20.8	10.5	0.008
<i>Streptococcus pneumoniae</i>	1	0.3	0.349
Candida spp.	0	1.5	0.226
Gram-negative bacilli	4.2	3.3	0.689
Anaerobes	0	0	0.999
Other microorganisms	21.9	13.3	0.038
Unknown infectious agent	15.6	22.9	0.125
Cardiogenic shock	2.1	3	0.627
Cardio-respiratory failure	13.5	18.1	0.299
Congestive heart failure	53.1	32.5	<0.001
Stroke	1	3.6	0.196
Arterial embolism	3.1	4.8	0.478
Septic shock	6.3	13.9	0.045
Cardiac valve surgery	16.7	12.7	0.311
Hospital stay (days)	24 (15–43)	23 (14–40)	0.933
Observed in-hospital mortality (95% CI)	30.2 (21.7–39.9)	34.3 (29.4–39.6)	0.407
Observed in-hospital mortality (95% CI) in patients who underwent cardiac surgery	31.3 (13.1–55.6)	38.1 (24.6–53.2)	0.764
Observed in-hospital mortality (95% CI) in patients who did not undergo cardiac surgery	30.0 (20.8–40.6)	33.8 (28.5–39.4)	0.523

Values are n (%) or mean (standard deviation)/median (interquartile range). Bold values are significant. CI: confidence intervals; ESRD: end-stage renal disease; IE: infective endocarditis

Table 3 Multilevel regression model. Variables independently associated with in-hospital mortality adjusted by risk in end-stage renal disease patients with infective endocarditis

	Odds ratio	95% confidence Interval	p value
Age ≥ 65 years	2.3	1.36–3.91	0.002
Cancer	10.09	1.74–58.42	0.01
Cardiogenic shock	25.71	2.93–225.57	0.003
Cardio-respiratory failure	4.14	2.3–7.46	<0.001
Stroke	4.35	1.13–16.73	0.032
Septic shock	11.44	5.14–25.45	<0.001

biases due to variability in data quality and availability across different sources. Neither of the two studies describes the percentage of patients receiving renal replacement therapy (dialysis or renal transplant), so the populations may not be comparable.

More information exists on IE features in ESRD patients undergoing dialysis. Population-based studies using national registries have consistently reported a higher incidence of IE in dialysis patients compared to the general population [2, 3, 19].

The only multicenter international prospective cohort study focused on IE and HD patients [8] described that HD patients represented 8% of IE episodes. In this study, the most common form of IE acquisition in HD patients was non-nosocomial healthcare-associated, and the main

risk factor was the presence of a vascular access catheter for dialysis.

Comorbidities and predisposing conditions

Comorbidities are more prevalent among patients with IE and ESRD [10]. In our study, most patients with ESRD (76.4%) had a Charlson index greater than 2, whereas this percentage was much lower (32.2%) in non-ESRD patients. Among ESRD patients, a high Charlson index was more common in those receiving dialysis.

ESRD patients with IE were also less frequently found to be prosthetic valve carriers, as described in the literature [10, 18]. Our findings also indicate a greater frequency of cardiac device-related IE in ESRD patients, particularly in patients receiving dialysis. As previously described [20], the presence of foreign bodies such as cardiac devices, along with a high exposure to intravascular manipulation among patients receiving dialysis and higher rates of transient bacteremia, increases the likelihood of cardiac electronic device-related infections in this population. When renal transplant recipients were compared to dialysis patients who had not undergone transplant, the transplant recipients had a higher incidence of prosthetic valve IE and a lower incidence of cardiac device-related IE. The reason for this could be that the enhanced survival benefit associated with the transplant may result in an elevated likelihood of developing degenerative valve disease, potentially needing prosthetic valve replacement [21].

Microbiology

S. aureus is the leading cause of IE in patients receiving dialysis [1, 2, 8, 9, 11, 12, 22, 23], and is still one of the most prevalent microbial etiologies of IE in the general population [24]. Consistently with previous evidence, we have found that ESRD patients had a higher frequency of staphylococcal infections, both *S. aureus* and coagulase-negative staphylococci, compared to non-ESRD episodes. Among ESRD patients, those undergoing dialysis exhibit the highest incidence of *S. aureus* infections. This is likely due to their frequent exposure to hospital environments, which raises the probability of *S. aureus* colonization, as well as the use of invasive vascular access devices, such as catheters and arteriovenous fistulas, that act as entry points for pathogens. Additionally, the ability of *S. aureus* to form biofilms on intravascular devices further contributes to infection risk in this population.

Enterococci, an increasing cause of IE in Spain [25], are another common etiology of IE in dialysis patients [8]. However, other series have reported that their incidence is lower than that in the general population [1], as found in the herein study. Interestingly, among renal transplant recipients, enterococci infections were the most frequent etiology of IE. This relationship between enterococci

infections and renal transplant status has been previously reported in the literature [26, 27]. It has been suggested that this could be related to the higher likelihood of developing pyelonephritis among renal transplant recipients, thus making urinary tract the more likely source of bacteremia.

Outcome and cardiac surgery

In our study we have been able to analyze the prevalence of different in-hospital complications, including embolisms, acute heart failure and septic shock. The incidence of embolisms was higher in non-ESRD patients, whereas septic shock was significantly more frequent in ESRD patients. Among ESRD patients, acute heart failure was more frequent in non-dialysis patients. Our findings are in line with the insights provided by the prospective ICE cohort [1, 8], in which the incidence of systemic embolisms was higher in the non-dialysis group, whereas persistent bacteremia was more frequent in dialysis patients. This higher incidence of persistent bacteremia or septic shock is probably related to the microbiological profile and the presence of vascular catheters.

Surgery rates differ significantly among studies and are considerably lower in population-based than in studies from referral centers [1, 2, 8], probably due to referral bias. In any case, all previous evidence has in common that ESRD patients are less likely to undergo cardiac surgery than non-ESRD, and our study further confirm this fact.

Patients with ESRD from our cohort were less frequently prosthetic valve carriers, but other indications for surgery, such as *S. aureus* infection, and septic shock as a sign of non-controlled infection, were more common in ESRD patients. In any case, the significantly lower surgery rates observed in ESRD and HD are likely due to the fact that the presence of ESRD itself, together with a high burden of comorbidities in this population, significantly increase surgical risk. This leads to these patients being more frequently classified as non-operable due to high surgical risk, and makes it more likely that surgery is deemed futile and ultimately avoided in these patients [5], not because they do not have a surgical indication. Unfortunately, information regarding patients who met surgical indications but were considered inoperable was not available.

Perioperative mortality of dialysis patients undergoing valvular surgery for IE varies in different studies, but the overall evidence shows that these patients had worse outcome after surgery, compared to non-HD patients. Large population-based registries reported perioperative mortality rates between 13 and 22% [13, 22, 28]. In the herein study, surgery was not found to be an independent prognostic factor for in-hospital mortality in ESRD patients. This could be explained by the prognostic benefit of

surgery being offset by the increased surgical risk in patients with ESRD. In our analysis, ESRD patients who underwent surgery exhibited a higher apparent mortality rate compared to those who did not, which contrasts with the trend observed in the general population and further supports this hypothesis. Most of the previous studies in ESRD patients did not find significant differences in mortality rates between patients who underwent cardiac surgery and those who did not [13, 28]. Only in a single-center cohort [29], dialysis patients who underwent surgery had better long-term survival compared to those who received conservative treatment. Selection bias may strongly influence the results of ours and other studies, as patients with surgical indications may not be offered surgery [28]. In addition, if septic shock is already present, surgery might not be the best option to control the infection [30].

A multicenter prospective cohort study including 2488 episodes of IE from 27 Spanish hospitals has provided further insight in this matter [31]. In this study, the mortality rate in HD patients was 41.3%, and it was higher than in non-HD patients, both in patients without indication for surgery and in those who underwent surgery. Furthermore, only half of HD-patients with a surgical indication underwent the procedure. Patients in whom surgery was indicated but were not operated had highest mortality, which was significantly higher in the HD group. Among HD patients, rates of cardiac surgery did not differ between patients who survived and those who died.

Finally, in our study, as has already been described, IE patients with ESRD had a worse prognosis than patients without ESRD. Studies from the United States reported in-hospital mortality rates around 16% in ESRD or HD patients with IE [1, 10]. However, mortality rates described in other population-based and cohort studies are up to double those reported above [4, 8, 12, 18, 22, 23, 31–33]. A main reason for these discrepancies is probably related to a high frequency of patients' early discharge to other healthcare facilities (up to 44% in the study by Khan et al.) in patients treated in the United States [25]. Readmissions due to new IE episodes have been reported to be more frequent among ESRD or HD patients [8]; in our study, readmissions were significantly higher in ESRD patients compared to the rest of IE patients.

Considering only IE episodes occurring in ESRD, our multilevel regression model identified well-known prognostic factors for in-hospital mortality such as septic shock, cardio-respiratory failure, cardiogenic shock, stroke and age [8, 12, 14, 25, 31]. However, being on dialysis treatment was not independently associated with higher in-hospital mortality in this subset of patients. This finding suggests that dialysis itself may not directly impact the prognosis in patients with ESRD, and more

robust predictors, such as septic shock or age, entail more prognostic impact in this population.

Study limitations

Our study is based on data from the SMBD, an administrative database that, while widely used for epidemiological research, is subject to potential coding inaccuracies and inter-hospital variability. Although previous validation studies support the accuracy of the SMBD, variability in coding practices across hospitals remains a limitation [34, 35]. However, the population-based and nationwide design of the study minimizes the impact of referral or selection biases. Unfortunately, due to the absence of data on non-hospitalized patients, we were unable to calculate the incidence of IE among the total population of patients with ESRD or undergoing dialysis.

We lacked relevant information such as the type of acquisition (nosocomial, community-acquired), timing of infection regarding dialysis onset or transplant intervention, the kind of vascular access for dialysis, echocardiographic findings, previous hospitalizations or indications and type of cardiac surgery. Microbiological information was absent in around 20% of cases, and we cannot discern whether these episodes were culture-negative IE or if the causative agent was not recorded. However, it is known that between 10% and 15% of patients with IE do not have microbiological isolation, and that in other population-based studies, the proportion of patients with available microbiological data barely reaches 40% [18]. Due to the nature of the SMBD database, long-term outcome such as rehospitalizations or mortality were not available either.

Subgroup analyses of clinically relevant groups were performed, in some cases with a relatively small sample size. However, we considered their inclusion valuable for descriptive purposes and hypothesis generation. Furthermore, the results are consistent with previous literature, and when assessing causal relationships and risk factors, multilevel models were used to minimize the likelihood of bias.

Additionally, surgical decision-making bias is an inherent limitation in studies based on administrative databases. Although we applied multilevel regression models to adjust for confounding variables, the influence of unmeasured factors cannot be ruled out. Future prospective studies incorporating detailed clinical data are needed to better understand the determinants of surgical decisions in ESRD patients with IE.

Finally, the lack of data from private hospitals may have resulted in an underestimation of the study population. However, in Spain, the public national healthcare system covers 96.6% of the population according to official data. Therefore, we believe that our data are likely to be representative [36].

Conclusions

Patients with ESRD who develop IE have a particular clinical and microbiological profile. ESRD patients are younger, have more comorbidities, cardiac electronic device infections are more common, and staphylococcal infections and recurrences are more frequent than in non-ESRD patients. They have significantly higher in-hospital mortality and are less likely to undergo cardiac surgery. Furthermore, within the ESRD population, dialysis treatment and cardiac surgery were not found to be independent risk factors for mortality. Further research is needed to better understand the optimal medical and surgical management of IE in patients with ESRD to improve outcomes.

Abbreviations

CIED	Cardiac implantable electronic device
ESRD	End-stage renal disease
HD	Hemodialysis
ICD	International classification of diseases
IE	Infective endocarditis
NIS	National inpatient sample
OR	Odds ratio
PD	Peritoneal dialysis
ROC	Operating characteristic curves
SMBD	Spanish minimum basic data set

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-025-10978-4>.

Supplementary Material 1

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Author contributions

CF, NP, NR, and JB conducted the data analysis and statistical analysis; DG, PZ and CO were responsible for drafting the manuscript; IV and FJE contributed to the writing process and supervised the final version of the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study adopted the ethical principles of the Helsinki Declaration regarding human experimentation (Fortaleza, Brasil, 2013). The present study was exempt from additional review by the local ethics research committee of Hospital Clínico San Carlos (Madrid, Spain) as all data were deidentified.

Consent for publication

Not applicable.

Informed consent

Informed consent was not requested because the data were anonymized from the information in the minimum data set. As specified in national and European regulations, data protection and informed consent requirements do not apply to anonymous data in which patient identification is not possible. This is explicitly stated in Regulation 2016/679 of the European Parliament and of the Council: "The principles of data protection should therefore not apply to anonymous information, namely information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable".

Competing interests

The authors declare no competing interests.

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