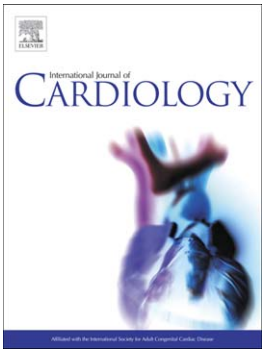

Prognostic factors of Infective Endocarditis in Patients on Hemodialysis: A Case Series from a National Multicenter Registry

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PII: S0167-5273(16)34061-X
DOI: doi:10.1016/j.ijcard.2017.04.086
Reference: IJCA 24930

To appear in: *International Journal of Cardiology*

Received date: 22 November 2016
Revised date: 6 April 2017
Accepted date: 17 April 2017

Title: Prognostic factors of Infective Endocarditis in Patients on Hemodialysis: A Case Series from a National Multicenter Registry

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Abstract

Background: Infective endocarditis (IE) is a severe complication associated with high mortality.

Objectives: To examine the clinical characteristics of IE in hemodialysis (HD) patients and to determine prognostic factors related to HD.

Methods: From January 2008 to April 2015, 2,488 consecutive patients with definite IE were included. Clinical characteristics of IE patients on HD were compared with those of IE patients who were not on HD.

Results: A total of 126 patients (63% male, median age: 66 years; IQR: 54-74 years) with IE (5.1%) were on HD. Fifty-two patients died during hospitalization (41%) and 17 additional patients (14%) died during the first year. The rate of patients who underwent surgery during hospitalization was lower in HD patients (38 patients, 30%) than in non-HD patients (1,177 patients, 50%; p <0.001). Age >70 years (OR: 4.1, 95% CI: 1.7-10), heart failure (OR: 3.3, 95% CI: 1.4-7-6), central nervous system (CNS) vascular events (OR: 6.7, 95% CI: 2.1-22) and septic shock (OR: 4.1, 95% CI: 1.4-12.1) were independently associated with fatal outcome in HD patients. Of the 38 patients who underwent surgery, 15 (39.5%) died during hospitalization.

Conclusions. HD patients with IE present a high mortality. Advanced age and complications, such as heart failure, CNS stroke or septic shock, are associated with mortality.

Keywords: Endocarditis; Hemodialysis; Age; *Staphylococcus aureus*; *Enterococcus*; Cardiac Surgical Procedure; Mortality

1. Introduction

The end-stage renal disease (ESRD) population treated with hemodialysis (HD) is constantly increasing in western countries. Infectious endocarditis (IE) is a severe complication that is found progressively more frequently in these patients [1,2]. IE has been reported in 2-6% of HD patients [3,4], which means that the incidence of IE in this group is 18 to 60 times higher than in the general population [5-7].

The high prevalence of valve dysfunction and calcification, and a certain degree of immunosuppression related to uremia, have been proposed as elements that facilitate IE among patients on HD [8-10]. However, the main risk factor for developing IE in HD patients is the recurrent episodes of bacteremia linked with indwelling intravascular catheter use or arteriovenous fistula puncture [11]. IE in HD patients has been reported to produce a very high mortality which ranges between 29-52% [2,11-21]. This adverse prognosis has been linked to increased incidence of IE due *Staphylococcus aureus* and the presence of multiple comorbidities in this special population. Despite advances in medical and surgical therapies over the last few years [16,17,20], mortality has not improved significantly.

The clinical characteristics of IE HD patients have not been well defined, and the analysis of specific prognostic risk factors in those undergoing surgery has received little attention [12,18,21]. Consequently, there is a need to improve knowledge regarding clinical characteristics, the role of surgery and prognosis in these patients.

The purpose of the present study was to outline the clinical characteristics of IE in HD compared to non-HD patients as well as to determine the prognostic factors of IE both in HD patients as a whole and in IE HD patients undergoing cardiac surgery.

2. Methods

From January 2008 to April 2015, 3,200 consecutive patients with definite or possible IE, according to the modified Duke criteria [22], were prospectively included in the "Spanish Collaboration on Endocarditis - Grupo de Apoyo al Manejo de la Endocarditis infecciosa en España (GAMES)" registry maintained by 27 Spanish hospitals. Multidisciplinary teams completed standardized case report forms with IE episode and follow-up data that included clinical, microbiological and echocardiographic sections [23,24]. Regional and local ethics committees approved the study and all patients gave their informed consent. Of the 2,488 patients with definite IE included in the GAMES series database, 126 patients (5.1%) were under chronic HD treatment at the onset of IE.

2.1. Definitions

Active IE was defined as endocarditis with at least one of the following: positive blood cultures, fever, leukocytosis, raised inflammation markers or current antibiotic treatment. Microbiological diagnosis was made by blood, valve cultures and/or by molecular techniques [25]. Transthoracic and transesophageal echocardiography were performed on patients with clinical or microbiological suspicion of IE according to international recommendations. The same protocol was implemented for the diagnosis of valve dysfunction and intracardiac complications: abscess, vegetation, pseudoaneurysm and fistula [25,26]. The EuroScore and LogEuroScore were used to assess operative risk [27]. To assess comorbidity, all the necessary variables were collected to calculate the Charlson Comorbidity Index [28]. Operative mortality was

defined as death, regardless of its cause, that occurred during the hospital admission that surgery was performed.

2.2. Patients

Data from patients with IE were analyzed, including etiology of ESRD and hemodialysis vintage, type of vascular access, clinical manifestations at IE presentation, the pathogens identified, therapy used, morbidity and mortality during hospitalization. A multidisciplinary team evaluated the indication for surgery taking into account, not only immediate surgical risk, but also the chances of long-term survival. Follow-up information was obtained via telephone or through written correspondence with each patient or their primary-care physician. The mean follow-up of IE HD patients was 3.4 years (range, 0.3 - 6.25 years).

2.3. Statistical analysis

Quantitative variables were reported as median and interquartile range (IQR); qualitative variables were reported as numbers and percentages. Continuous variables were compared using Student's t-test, and categorical variables were compared using the chi-square test or Fisher's exact test when appropriate. Adjusted odds ratios (ORs) were computed using logistic regression analysis. Stepwise logistic regression analysis was performed which included variables present at the time of admission that returned a p value <0.1 in the univariate analysis but also took into consideration the clinical significance of each variable and the number of patients that reported the event studied. A Cox regression model for 30 day-survival according to hemodialysis is

shown in figure 2. All statistical analyses were performed using SPSS software version 18 (SPSS Inc., Chicago, Illinois, USA).

3. Results

A total of 126 HD patients with definite IE were included in the study (figure 1). The median age of patients was 66 years and 62.7% (79 patients) were male. Patients had been on HD for a median period of 25 months (IQR: 5 - 61 months). The etiologies of ESRD were diabetes mellitus (40 patients, 31.7%), glomerulonephritis (18 patients, 14.2%), hypertension (16 patients, 12.7%), lupus nephritis (5 patients, 4%), polycystic disease (5 patients, 4%), myeloma/primary amyloidosis (5 patients, 4%), other causes (15 patients, 11.9%) and unknown (17.4%). The main characteristics of patients who were and were not on HD are compared in table 1. IE HD patients had diabetes, hypertension, immunosuppressive treatment, aortic valve infection and hospital-acquired IE more frequently, and prosthetic valve endocarditis, atrial fibrillation, and perivalvular abscess less frequently. IE HD patients presented higher age-adjusted Charlson comorbidity index and EuroScore, and underwent surgery to a lesser extent.

The type of HD vascular access in IE HD patients were permanent catheter (79 patients, 62.7%), arteriovenous (AV) fistula (35 patients, 27.8%), temporary catheter (10 patients, 7.9%) and AV graft (2 patients, 1.6%). Regarding microbiology, HD patients presented more cases due to *Staphylococcus aureus* and less due to streptococci (table 1). Interestingly, methicillin-resistant *S. aureus* (MRSA) was not more commonly found among HD patients (table 1). HD patients who had AV fistula

presented a higher rate of IE due to enterococci compared to patients who had a permanent catheter (table 2).

The rate of patients who underwent surgery during hospitalization was lower in HD than in non-HD patients (38 patients, 30.2% vs 1,177 patients, 49.8%; p <0.001). The indications for surgery were heart failure (15 patients), virulent microorganism (MRSA, gram-negative bacilli or *Candida*, 12 patients), severe valve regurgitation (11 patients), perivalvular abscess (5 patients), persistent sepsis (3 patients), prosthetic detachment (1 patient), and prosthetic thrombosis (1 patient). Nine patients exhibited more than one indication. Surgery consisted of aortic valve replacement with mechanical (11 patients) or bioprosthetic valve (5 patients), mitral valve replacement with mechanical (8 patients) or bioprosthetic valve (1 patient), repair of mitral (6 patients), aortic (3 patients), tricuspid (3 patients) or pulmonary (1 patient) valves and pulmonary artery homograft (1 patient). Five patients underwent surgical removal of the hemodialysis catheter and 3 patients underwent surgical removal of pacemaker wires. Eight patients (21.1%) were submitted to more than one surgical procedure.

Fifty-two patients died during hospitalization (41.3%) and 17 additional patients (13.5%) died during the first year after hospital discharge. Thirty-day mortality was higher in HD patients than in non-HD patients (p=0.003, figure 2). The leading cause of in-hospital death in HD patients was infection (15 patients, 28.9%), heart failure (10 patients, 19.2%), neurological complications (10 patients, 19.2%), and multiorgan failure (9 patients, 17.3%). During the first year after discharge the most frequent causes of death were heart dysfunction (4 patients, 23.6%), neurological disease (4

patients, 23.6%) and infectious complications (3 patients, 17.6%). Mortality was not related to IE in 2 patients who died during hospitalization (3.8%) and in 6 patients who died during the following year (35.3%, p=0.002). No differences were found in in-hospital mortality according to IE microbiology (table 3). The clinical characteristics of HD-patients according to patient outcome are shown in table 3. Age >70 years, age-adjusted Charlson comorbidity index >6, septic shock, heart failure, CNS stroke and surgery indicated but not performed, were included in the multivariate analysis. Age >70 years (OR: 4.1, 95% CI: 1.7-10), heart failure (OR: 3.3, 95% CI: 1.4-7-6), CNS vascular events (OR: 6.7, 95% CI: 2.1-22) and septic shock (OR: 4.1, 95% CI: 1.4-12.1) were independently associated with fatal outcome.

The in-hospital mortality in patients without surgical indication was 23.4% in HD patients and 11.1 % in non-HD patients (p=0.012). The mortality in patients who underwent surgical treatment was 39.5% in HD patients and 22.3 % in non-HD patients (p=0.018). In-hospital mortality was among patients with surgical indications who did not undergo surgery was 60%, and that of patients who underwent surgery was 39.5% (p=0.08). No differences in hospital stay before surgery was observed between survivors (21 days, IQR 12-33 days) and non-survivors (19 days, IQR: 9-27 days; p=0.680). The clinical characteristics related to mortality of IE patients on hemodialysis that underwent cardiac surgery are shown in table 4.

4. Discussion

The series presented here is one of the largest published to date and confirms that IE in HD patients constitutes a relevant group that is characterized by a distinct clinical and microbiological profile and high mortality. Advanced age, heart failure, CNS embolism and septic shock are associated with increased in-hospital mortality. Based on the high mortality of patients with surgical indication who did not undergo surgery, we believe that the proportion of patients submitted to surgery should be increased. This particularly applies to younger patients with a lower EuroScore and prior to the development of complications such as heart failure, septic shock or stroke.

Clinical Characteristics of IE HD patients

IE patients undergoing HD exhibited certain clinical characteristics that differ remarkably from those of non-HD IE individuals. Certain chronic diseases, such as diabetes, hypertension and peripheral arterial disease, were more common in HD patients and were related to a worse prognosis as observed in previous studies [11,12,18,21,29-32]. On the other hand, the low proportion of prosthetic valve IE in these patients may be due to repeated episodes of bacteremia being the main risk factor for IE in HD patients as well as the low number of HD patients who underwent heart valve replacement [12,21,33,34].

We found a high incidence of IE due to *S. aureus* and coagulase-negative staphylococci and a lower incidence of streptococci that, in most cases, might have been related to

the vascular origin of the bacteremia [1,8,12,29,35]. Unlike other studies, a clear majority of IE was in HD patients undergoing dialysis via a catheter [12.36]. Higher incidences of methicillin resistant *Staphylococcus aureus* have been highlighted in other studies, however this was not observed in our study despite the higher rate of hospital acquired endocarditis [11,21,29,37]. It should also be noted that patients with AV fistula presented more cases due to enterococci. A high proportion of cases due to enterococci was similarly observed in one series comprised of patients with arteriovenous fistula [12]. Other studies have observed an association between IE due to gram-negative bacilli and use of a temporary catheter [12, 38]. The particular characteristics of IE in HD patients could have an impact on the prescription of empirical treatment in this group. Based on our results, we believe that etiological peculiarities of IE in HD patients and the type of vascular access and local epidemiology are factors that should be considered when selecting antimicrobial therapy. In our study, the type of microorganism causing IE did not influence mortality, which is consonant with previous series, but may be noteworthy taking into account the higher mortality classically associated with *S. aureus* IE [15,18,36,39,40].

Outcomes of IE in HD

We found a very high in-hospital mortality among IE HD patients. Comorbidities, disturbances of hemodynamic, metabolic and immunological functions associated to ESRD and the high incidence of virulent microorganisms may partially explain the increased mortality found in these individuals [16,11,13,14,26,30,33,39,41,42,43]. Whether Duke's criteria adequately apply to HD patients with IE remains unclear

considering the lower rates of fever, the possibly lower sensitivity of echocardiography and the unfeasibility of urinalysis in this setting [16,43,44]. Our in-hospital mortality was 41.3% and the accumulated mortality during the first year was 54.8%. Although mortality was lower in other previously reported IE HD series (around 25%) [11,17,19,22,36], comparable or even higher mortality has also been described [12,13,30,33]. The heterogeneity of reported series with relevant differences regarding clinical setting, patient age and rate of chronic diseases, valve disease, congestive heart failure, septic shock, perioperative surgical complications and criteria for mortality could justify these differences in mortality [9,12,13,16,18,19,21,29,30,33,34,41,45,46]. Nevertheless our study reports a national-based cohort, which might better reflect the "real" mortality in this fragile patient population. Compared to other IE HD series, our patients showed advanced age, and all those that underwent surgery did so during the same hospital admission, therefore in the period of active IE, which might suggest greater severity of the disease [18,21]. Patient's age and the presentation of heart failure, CNS vascular events and septic shock were independently associated with fatal outcome. The most significant prognostic factor of IE in HD patients related to in-hospital mortality described in previous studies were older age [18,29], health care environment acquisition [29], active endocarditis [21], double valve endocarditis [29,31], staphylococcal etiology [18,29] methicillin-resistant *Staphylococcus aureus* [50] cardiogenic shock [21], stroke [29] and septic embolism [39]. Despite not reaching statistical significance, diabetic patients presented higher mortality than other groups (table 3). Abnormalities in neutrophil chemotaxis, adhesion and intracellular killing may be associated to the higher mortality observed in diabetes patient suffering from sepsis [47,48].

Another remarkable finding in our study is the low rate of patients who underwent surgery in comparison with the non-HD IE population. According to several studies, the rate of surgery varies from to 8%-50% in theses patients [12,16,18,19,30,33,36,39]. In our series, only half of the patients in whom surgery was indicated finally underwent this procedure. Since no randomized controlled have been performed to compare medical versus surgical treatment in these patients, certain doubts remain about whether accepted indications for valve replacement in the general population are applicable to HD patients [1]. In any case, mortality in patients with surgical indications that did not undergo surgery, which was around 60%, was remarkably high. Although the mortality in these patients is high whether or not they undergo surgery, we consider that it is essential to identify those patients who could benefit most from surgical treatment [21].

Outcome in IE HD patients who underwent surgery

Given the modest results of cardiac surgery in IE HD, the identification of factors associated with poor outcomes during surgery is highly warranted. Finally, we did not perform a multivariate analysis because of the low number of patients who underwent surgery, thereby limiting their discriminative capacity. Among the variables associated with mortality in the univariate analysis were age over 70 years and a high EuroScore [27]. Advanced age has been considered an independent predictor of mortality for IE in HD patients, both in patients who undergo surgery and in those treated medically [18,21,49]. In a previous study, Rankin et al. delineated a score that included advanced

age and several clinical characteristics, such as active endocarditis and double valve endocarditis, which may be useful to identify patients with excessive surgical risk, however, HD was not among the clinical factors which indicated surgery as having a higher risk [21]. Another study found that older age, diabetes mellitus, staphylococcal IE causative, arrhythmia and surgery during index hospitalization were independent predictors of high mortality in patients undergoing valve replacement due to IE [18].

Selecting patients who would benefit more from surgery is a delicate task that requires careful analysis by a multidisciplinary IE team, as is usually performed in our hospitals. CNS embolism has been reported as a poor prognostic factor in HD patients [17,34,41]. Some of our patients did not undergo surgery solely because they had suffered a stroke, which is associated with a poor prognosis. Therefore, in our study, CNS embolic complications emerged as important prognostic factor. In this regard, it should be noted that, according to several studies containing a small subgroup of HD patients, ischemic stroke does not seem to increase mortality in IE patients undergoing urgent surgery [50,51]. Finally, we agree with Horstkotte and Piper in that, once surgical treatment has been decided on, it would be desirable carry out this procedure as soon as possible before additional complications, such as stroke, appear [52].

Other possible matters to consider in order to reduce patient mortality may be to take advantage of thrice-weekly contacts with an HD physician for better clinical monitoring, to switch the patient from HD to peritoneal dialysis, to improve knowledge of the pharmacokinetics and pharmacodynamics of antibiotics in these patients, and to check immunoglobulin levels in appropriate cases [11,21]. In any event, establishing

accurate guidelines for selecting those patients who may benefit most from surgery is still pending. A controlled trial comparing medical versus surgical therapy would greatly assist the development of IE guidelines specifically for HD patients.

Limitations

Some limitations of the study should be noted. The first is that this was an observational study and comparisons may be biased by different patient characteristics in each group. In addition, most of the institutions participating in the GAMES registry are tertiary university hospitals that receive a substantial number of patients from other centers (most of which do not have facilities for cardiac surgery), which could represent a selection bias. Another limitation is that a possible cluster effect was not studied. However, we did not expect enough heterogeneity between centers to influence our results significantly. Furthermore, the number of HD patients who underwent surgery is low and could therefore have prevented the detection of other prognostic factors associated with mortality in those patients who did undergo cardiac surgery. As in other studies, a high proportion of IE HD patients did not undergo surgery, consequently a significant selection bias cannot be ruled out. Another limitation is that knowledge about the risk of IE according to vascular access could not be calculated because only patients with IE were included in the study.

Conclusions

This study describes the clinical profile of IE HD and identifies several factors associated to in-hospital mortality in these patients and in those who undergo surgery. According to our results, advanced age and certain IE complications are associated with higher mortality.

Funding: This study did not receive any funding.

Acknowledgements. The authors wish to thank Martin Hadley-Adams for assisting with the English language and preparation of the manuscript.

References

1. Nucifora G, Badano LP, Viale P, et al. Infective endocarditis in chronic haemodialysis patients: an increasing clinical challenge. Eur Heart J 2007; 28:2307-2312.

2. McCarthy JT, Steckelberg JM. Infective endocarditis in patients receiving long-term hemodialysis. Mayo Clin Proc 2000; 75: 1008-1014.

3. Powe NR, Jaar B, Furth SL, et al. Septicemia in dialysis patients: incidence, risk factors, and prognosis. Kidney Int 1999;55: 1081-1090.

4. Marr KA, Kong L, Fowler VG, et al. Incidence and outcome of Staphylococcus aureus bacteremia in hemodialysis patients. Kidney Int 1998;54:1684-1689.

5. Garg N, B. Kandpal B, S. Tewari S, N, et al. Characteristics of infective endocarditis in a developing country—clinical profile and outcome in 192 Indian patients, 1992–2001, Int J Cardiol 2005: 98: 253-260.

6. Abbott KC, Agodoa LY. Hospitalizations for bacterial endocarditis after initiation of chronic dialysis in the United States, Nephron 2002: 91: 203-209.

7. Hoen B, Alla F, Selton-Suty C, et al., Changing profile of infective endocarditis; results of a 1-year-survey in France, JAMA 2002; 88: 75–81.

8. Wang AY, Wang M, Woo J, et al. Cardiac valve calcification as an important predictor for all-cause mortality and cardiovascular mortality in long-term peritoneal dialysis patients: a prospective
study. J Am Soc Nephrol 2003; 14: 159-168.

9. Sharma R, Pellerin D, Gaze DC, et al. Mitral annular calcification predicts mortality and coronary artery disease in end stage renal disease. Atherosclerosis 2007; 191: 348-354.

10. Hauser AB, Stinghen AE, Kato S, et al. Characteristics and causes of immune dysfunction related to uremia and dialysis. Perit Dial Int 2008; 28(Suppl 3): S183-187.

11. Durante-Mangoni E, Pafundi PC, Ravasio V, et al. Current features of infective endocarditis in persons on hemodialysis: prevalence study with case control design from the prospective multicenter SEI cohort. Infection 2016; 44: 467-474.

12. Spies C, Madison JR, Schatz IJ. Infective endocarditis in patients with end-stage renal disease: clinical presentation and outcome. Arch Intern Med 2004; 164: 71-75.

13. Dohmen PM, Binner C, Mende M, et al. Outcome of aortic valve replacement for active infective endocarditis in patients on chronic hemodialysis. Ann Thorac Surg 2015; 99: 532-538.

14. Doulton T, Sabharwal N, Cairns HS, et al. Infective endocarditis in dialysis patients: new challenges and old. Kidney Int 2003; 64: 720-727.

15. Maraj S, Jacobs LE, Kung SC, et. Epidemiology and outcome of infective endocarditis in hemodialysis patients. Am J Med Sci 2002; 324: 254-260.

16. Kamalakannan D, Pai RM, Johnson LB, Gardin JM, Saravolatz LD. Epidemiology and clinical outcomes of infective endocarditis in hemodialysis patients. Ann Thorac Surg 2007: 83: 2081-2086.

17. Shroff GR, Herzog CA, Ma JZ, Collins AJ. Long-term survival of dialysis patients with bacterial endocarditis in the United States. Am J Kidney Dis 2004; 44: 1077-1082.

18. Leither MD, Shroff GR, Ding S, Gilbertson DT, Herzog CA. Long-term survival of dialysis patients with bacterial endocarditis undergoing valvular replacement surgery in the United States. Circulation 2013; 128: 344-351.

19. Chou MT, Wang JJ, Wu WS, et al. Epidemiologic features and long-term outcome of dialysis patients with infective endocarditis in Taiwan. Int J Cardiol 2015; 20;179: 465-469.

20. Robinson DL, Fowler VG, Sexton DJ, Corey RG, Conlon PJ. Bacterial endocarditis in hemodialysis patients. Am J Kidney Dis 1997; 30: 521-524.

21. Rankin JS, Milford-Beland S, O'Brien SM, et al. The risk of valve surgery for endocarditis in patients with dialysis-dependent renal failure. J Heart Valve Dis 2007; 16: 617-622.

22. Li JS, Sexton DJ, Mick N, Nettles R, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000; 30: 633-638.

23. Martínez-Sellés M, Muñoz P, Arnáiz A, et al. Valve surgery in active infective endocarditis: a simple score to predict in-hospital prognosis. Int J Cardiol 2014; 175: 133-137.

24. Muñoz P, Kestler M, De Alarcon A, et al. Current Epidemiology and Outcome of Infective Endocarditis: A Multicenter, Prospective, Cohort Study. Medicine (Baltimore) 2015; 94: e1816.

25. Marín M, Muñoz P, Sánchez M, et al. Group for the Management of Infective Endocarditis of the Gregorio Marañón Hospital. Molecular diagnosis of infective endocarditis by real-time broad-range polymerase chain reaction (PCR) and sequencing directly from heart valve tissue. Medicine (Baltimore) 2007; 86: 195-202.

26. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the

Nomenclature and Standards Committee of the American Society of Echocardiography. J Am Soc Echocardiogr 2002; 15: 167-184.

27. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999; 16: 9-13.

28. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987; 40: 373-383

29. Benito N, Miró JM, de Lazzari E, et al. Health care-associated native valve endocarditis: importance of non-nosocomial acquisition. Ann Intern Med 2009; 150: 586-594.

30. Yamane K, Hirose H, Bogar LJ, Cavarocchi NC, Diehl JT.Surgical treatment of infective endocarditis in patients undergoing chronic hemodialysis. J Heart Valve Dis 2012; 21 : 774-782.

31. Thourani VH, Sarin EL, Kilgo PD, et al. Short- and long-term outcomes in patients undergoing valve surgery with end-stage renal failure receiving chronic hemodialysis. J Thorac Cardiovasc Surg 2012; 144: 117-123.

32. Rahmanian PB, Adams DH, Castillo JG, Vassalotti J, Filsoufi F. early and late outcome of cardiac surgery in dialysis-dependent patients: single-center experience with 245 consecutive patients J Thorac Cardiovasc Surg 2008; 135: 915-922

33. Ruiz M, Sánchez MP, Domínguez JC, et al. Infective endocarditis in patients receiving chronic hemodialysis: clinical features and outcome. J Heart Valve Dis 2005; 14: 11-14.

34. Edwards FH, Peterson ED, Coombs LP, et al. Prediction of operative mortality after valve replacement surgery. J Am Coll Cardiol 2001; 37: 885-892.

35. Lentino JR, Baddour LM, Wray M, Wong ES, Yu VL. Staphylococcus aureus and other bacteremias in hemodialysis patients: antibiotic therapy and surgical removal of access site. Infection 2000; 28: 355-360.

36. Baroudi S, Qazi RA, Lentine KL, Bastani B. Infective endocarditis in haemodialysis patients: 16-year experience at one institution. NDT Plus 2008; 1: 253-256.

37. Kuo CB, Lin JC, Peng MY, Wang NC, Chang FY. Endocarditis: impact of methicillin-resistant Staphylococcus aureus in hemodialysis patients and community-acquired infection. J Microbiol Immunol
Infect 2007; 40: 317-324.

38. Saad TF. Bacteremia associated with tunneled, cuffed hemodialysis catheters. Am J Kidney Dis 1999; 34: 1114-24.

39. Nori US, Manoharan A, Thornby JI, Yee J, Parasuraman R, Ramanathan V. Mortality risk factors in chronic haemodialysis patients with infective endocarditis. Nephrol Dial Transplant 2006; 21: 2184-2190.

40. Hill EE, Herijgers P, Claus P, Vanderschueren S, Herregods MC, Peetermans WE. Infective endocarditis: changing epidemiology and predictors of 6-month mortality: a prospective cohort study. Eur Heart J 2007; 28: 196-203.

41. Omoto T, Aoki A, Maruta K, Masuda T. Surgical outcome in hemodialysis patients with active-phase infective endocarditis. Ann Thorac Cardiovasc Surg 2016; 22: 181-185

42. Hanslik T, Flahault A, Vaillant JN, et al. High risk of severe endocarditis in patients on chronic dialysis. Nephrol Dial Transplant 1997; 12: 1301-1302.

43. Rekik S, Trabelsi I, Hentati M, et al. Infective endocarditis in hemodialysis patients: clinical features, echocardiographic data and outcome: a 10-year descriptive analysis. Clin Exp Nephrol. 2009;13(4):350–4.

44. Tobin M, Montes M, Mookerjee BK. Endocarditis in hemodialysis patients with systemic disease. J Dial 1978; 2: 75-84.

45. Hasbun R, Vikram HR, Barakat LA, Buenconsejo J, Quagliarello VJ. Complicated left-sided native valve endocarditis in adults: risk classification for mortality. JAMA 2003; 289: 1933-1940.

46. Chang CF, Kuo BI, Chen TL, Yang WC, Lee SD, Lin CC. Infective endocarditis in maintenance hemodialysis patients: fifteen years' experience in one medical center. Nephrol 2004; 17: 228-235.

47. Trevelin SC, Carlos D, Beretta M, da Silva JS, Cunha FQ. Diabetes Mellitus and Sepsis: A Challenging Association. Shock. 2016 Oct 26. [Epub ahead of print]

48. Koh GC, Peacock SJ, van der Poll T, Wiersinga WJ. The impact of diabetes on the pathogenesis of sepsis. Eur J Clin Microbiol Infect Dis. 2012 Apr;31(4):379-88

49. Cabell CH, Pond KK, Peterson GE. The risk of stroke and death in patients with aortic and mitral valve endocarditis. Am Heart J 2001; 142 :75-80.

50. Barsic B, Dickerman S, Krajinovic V, et al. Influence of the timing of cardiac surgery on the outcome of patients with infective endocarditis and stroke. Clin Infect Dis 2013; 56: 209-217.

51. Yoshioka D, Sakaguchi T, Yamauchi T, et al. Impact of early surgical treatment on postoperative neurologic outcome for active infective endocarditis complicated by cerebral infarction. Ann Thorac Surg 2012; 94: 489-495.

52. Horstkotte D, Piper C. Chronic hemodialysis: high risk for manifestation of infective endocarditis with poor outcome. J Heart Valve Dis 2005; 14: 8-10.

APPENDIX

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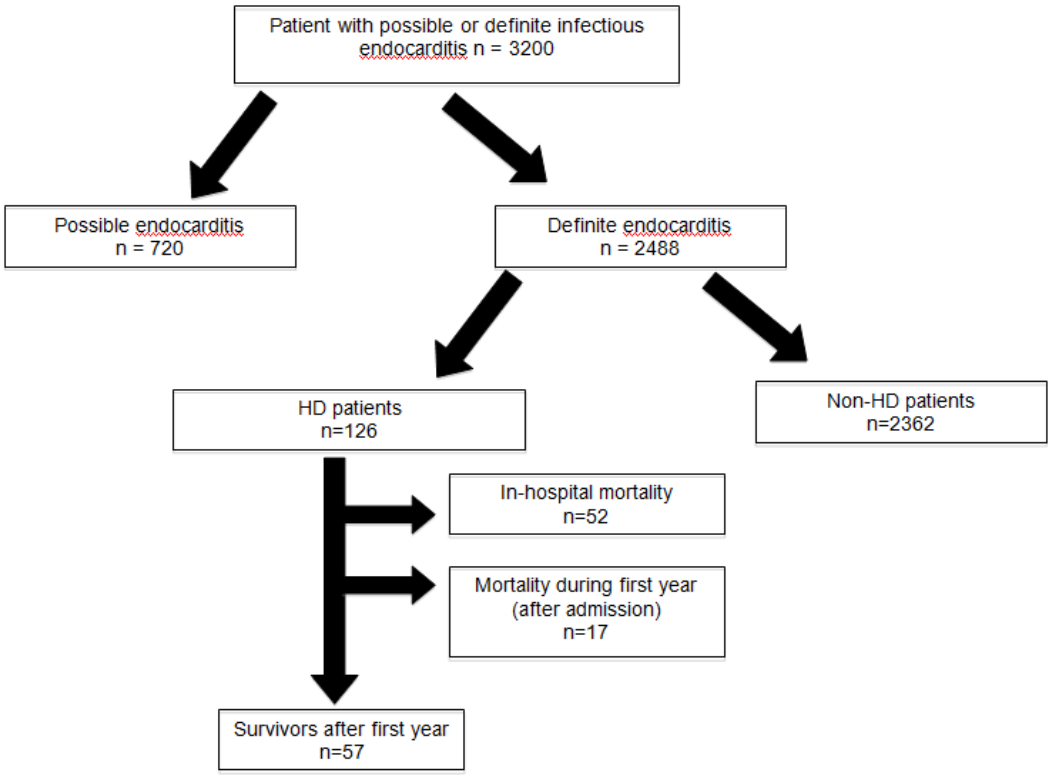

Figure 1. Flowchart showing patients studied.

Figure 2. 30-day mortality according to hemodialysis in a cohort of definite endocarditis (Cox regression model).

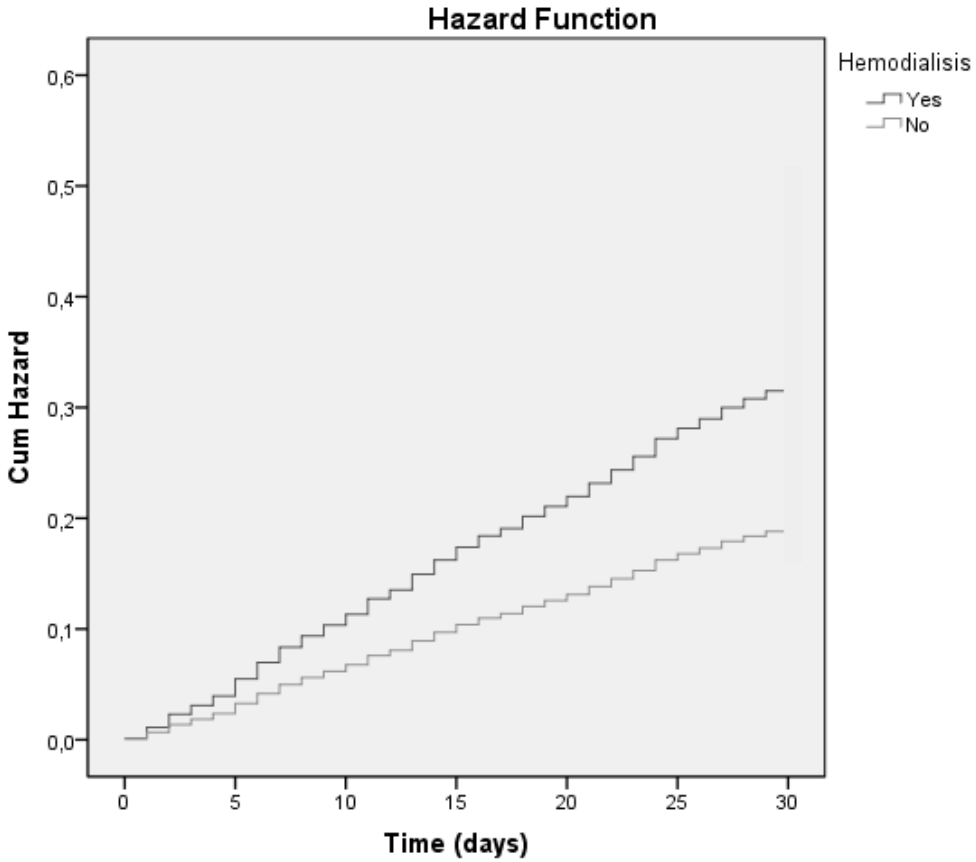

Table 1. Characteristics of patients according to hemodialysis treatment

	Hemodialysis (n=126)	Non-hemodialysis (n=2362)	P
Age (years)	66 (54 - 74)	68 (56 - 77)	0.143
Male gender	79 (62.7)	1621 (68.8)	0.153
Diabetes mellitus	56 (44.8)	625 (26.5)	<0.01
Hypertension	107 (84.9)	1251 (53.1)	<0.01
Peripheral arterial disease	43 (34.7)	227 (9.6)	<0.01
Cerebrovascular disease	19 (15.1)	298 (12.6)	0.308
Immunosuppressive treatment	21 (16.7)	125 (5.3)	<0.01
Neoplasia	12 (9.5)	364 (15.4)	0.184
Atrial fibrillation	18 (4.3)	603 (25.6)	0.017
Site of infection			0.096
Mitral	52 (41.3)	1189 (50.3)	
Aortic	57 (45.2)	1074 (45.5)	
Implanted heart device	20 (15.9)	256 (10.8)	
Prosthetic IE	11 (8.7)	728 (30.8)	
Microbiology			
Gram-positive bacteria			
Coagulase-negative staphylococci	28 (22.2)	419 (17.7)	0.202
S. aureus	55 (43.7)	540 (22.9)	<0.00

			1
MRSA	6 (4.7)	89 (3.7)	0.742
Enterococcus spp	18 (14.3)	344 (14.6)	0.931
Streptococcus spp	7 (5.6)	670 (28.4)	<0.001
Gram-negative bacilli	5 (4.0)	92 (3.9)	0.968
Anaerobic bacteria	0	26 (1.1)	0.236
Fungi			
Candida spp	3 (2.4)	37 (1.6)	0.479
Other fungi	0	10 (0.4)	0.464
Polymicrobial	2 (1.6)	48 (2.0)	0.729
Other microorganisms	2 (2.7)	72 (3.0)	0.347
Negative cultures	5 (4.0)	92 (3.9)	0.968
Fever	107 (88.4)	1980 (84.5)	0.275
Septic shock	23 (18.4)	278 (11.8)	0.086
Persistent bacteremia	16 (12.7)	275 (11.7)	0.204
CNS vascular events	19 (15.1)	490 (20.8)	0.060
Non-neurologic embolisms	32 (25.4)	537 (22.7)	0.501
Heart failure	49 (38.9)	986 (41.9)	0.470
C-reactive protein (mg/dl)	28.5 (11 - 122)	25 (9 - 91)	0.148
Echocardiographic findings			
Vegetation	8 (85.7)	1839 (77.9)	0.037
Perivalvular abscess	11 (8.7)	411 (17.4)	0.016

Valve perforation or rupture	23 (18.2)	335 (14.1)	0.255
Pseudoaneurysm	7 (5.5)	134 (5.6)	0.887
Intracardiac fistula	1 (0.8)	71 (3.0)	0.241
Surgical indication	73 (57.9)	1647 (70.1)	0.009
Surgery performed	38 (30.2)	1177 (49.8)	<0.001
Surgery indicated (but not performed)	35 (47.9)	470 (28.5)	<0.001
EuroScore (points)	12 (9 - 16)	10 (7 - 14)	<0.001
Hospital stay median (days)	42 (27 - 60)	26 (11 - 40)	<0.001
In-hospital mortality	52 (41.3)	624 (26.4)	<0.001

CNS: central nervous system. Quantitative variables are reported with median and interquartile range.

Table 2. Microorganisms identified according to type of vascular access in IE HD patients

	Arteriovenous fistula (n=35)	Catheter (n=89) [1]	P
Coagulase-negative staphylococci	7 (20.0)	20 (22.5)	0.809
S. aureus	11 (31.4)	43 (48.3)	0.106
MRSA	0	6 (6.7)	0.182
Enterococcus spp	9 (25.7)	9 (10.1)	0.027
Streptococcus spp	4 (11.4)	3 (3.4)	0.097
Other microorganisms	4 (2.9)	8 (9)	0.738
Negative cultures (no growth)	0	6 (6.7)	0.182

[1] 79 patients had permanent catheters and 10 patients temporary catheters. Two IE HD patients had arteriovenous grafts.

MRSA: methicillin-resistant *S. aureus*.

Table 3. Clinical characteristics of HD-patients according to patient outcome [1]

	Survivors (n=74)	Non-survivors (n=52)	P
Age (years)	62 (51 - 73)	71 (59 - 75)	0.036
Male gender	50 (67.6)	29 (55.8)	0.178
Diabetes mellitus	28 (37.8)	28 (53.8)	0.086
Hypertension	62 (83.8)	45 (86.5)	0.383
Peripheral arterial disease	26 (35.1)	17 (32.7)	0.793
Cerebrovascular disease	8 (10.8)	11 (21.2)	0.126
Immunosuppressive treatment	10 (13.5)	11 (21.2)	0.243
Neoplasia	6 (8.1)	6 (11.5)	0.243
Age-adjusted Charlson Comorbidity Index (points)	1 (0.75-1.25)	2 (0.5-3)	0.016
Previous IE episode	5 (6.8)	2 (3.8)	0.483
Hospital-acquired infection	28 (37.8)	20 (38.4)	0.876
Time on hemodialysis (months)	31 (4 - 73)	21 (6 - 48)	0.530
Type of vascular access			
Indwelling catheter	51 (68.9)	36 (69.2)	0.862

AV fistulae	22 (29.7)	15 (28.8)	0.920
AV graft	1 (1.4)	1 (1.9)	1
Transferred from other hospitals	17 (23.0)	11 (21.2)	0.809
Site of infection			0.451
Mitral	29 (39.2)	28 (53.8)	
Aortic	31 (41.9)	21 (40.4)	
Tricuspid	9 (12.1)	3 (5.8)	
Pulmonary	1 (1.6)	1 (1.9)	
Native valve	58 (78.4)	48 (92.3)	0.035
Prosthetic valve	8 (10.8)	3 (5.8)	0.324
Implanted heart device	13 (17.6)	7 (13.5)	0.535
Microbiology			
Gram-positive bacteria			
Coagulase-negative staphylococci	14 (18.9)	14 (26.9)	0.287
S. aureus	32 (43.2)	23 (44.2)	0.912
MRSA	3 (10)	3 (13)	0.594
Enterococcus spp	12 (16.2)	6 (11.5)	0.460
Streptococcus spp	5 (6.8)	2 (3.8)	0.483
Gram-negative bacilli	3 (4.1)	2 (3.8)	0.953
Candida spp	2 (2.7)	1 (1.9)	0.777

Polymicrobial	2 (2.7)	0	0.232
Other microorganisms	1 (1.4)	1 (1.9)	0.800
Negative cultures	3 (4.1)	3 (5.8)	0.656
Septic shock	9 (12.2)	14 (26.9)	0.041
Heart failure	22 (29.7)	27 (51.9)	0.012
Persistent bacteremia	5 (6.8)	11 (21.2)	0.017
CNS vascular events	5 (6.8)	14 (26.9)	0.017
Non-neurologic embolisms	32 (25.4)	12 (23.1)	0.501
C reactive protein (mg/dl)	31 (8 - 125)	28 (18 - 117)	0.431
Echocardiographic findings			
Vascular graft vegetations			
Perivalvular abscess	5 (6.7)	6 (11.5)	0.538
Valve perforation or rupture	13 (17.5)	10 (19.2)	0.997
Pseudoaneurysm	3 (4.0)	4 (7.7)	0.625
EuroScore (points)	11 (7 - 13)	15 (12 - 18)	<0.01
Surgical indication	37 (50)	36 (69.2)	0.010
Surgery performed	23 (31.1)	15 (28.8)	0.788
Surgery indicated (but not	14 (18.9)	21 (40.3)	0.009

performed)			
Emerging surgery	2 (8.7)	1 (6.7)	0.760

[1] Mortality during hospitalization. Quantitative variables are reported with median and interquartile range. AV: arterovenous.

Table 4. Clinical characteristics of IE patients on hemodialysis that underwent cardiac surgery (n=38)

	Survivors (n=23)	Non-survivors (n=15)	P
Age (years)	62 (54 - 69)	71 (63 - 80)	0.017
Male gender	18 (78.3)	8 (53.3)	0.106
Diabetes mellitus	8 (34.8)	8 (53.3)	0.258
Atrial fibrillation	1 (4.3)	4 (26.7)	0.047
Peripheral arterial disease	6 (26.1)	4 (28.6)	0.869
Age-adjusted Charlson Comorbidity Index (points)	5 (2-7)	6 (2-8)	0.073
Hospital-acquired infection	12 (52.2)	6 (40.0)	0.463
Transferred from other hospital	9 (39.1)	4 (26.7)	0.429
Site of infection			0.189
Aortic	15 (65.2)	6 (40.0)	
MItral	5 (21.7)	7 (46.7)	
Vegetation	80 (87.0)	14 (93.3)	0.531
Vegetation size (mm)	12 (5-8)	12 (5-7)	0.458
Septic shock	1 (4.3)	2 (13.3)	0.315
Heart failure	12 (52.2)	7 (46.7)	0.740
Persistent bacteremia	0	4 (26.7)	0.009
CNS vascular events	0	3 (20.0)	0.029

EuroScore (points)	9.9 (4.3)	20 (18.3)	<0.01
Time until surgery (days)	21 (12 - 33)	19 (9 - 27)	0.680
Mitral mechanical valve replacement	2 (8.7)	6 (40)	0.039
Aortic mechanical valve replacement	9 (39.1)	1 (6.7)	0.026

Quantitative variables are reported with median and interquartile range