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Infective Endocarditis in Chronic Hemodialysis Patients: Specificities and Therapeutic Management

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Abstract

Infective endocarditis (IE) is a frequent complication in chronic hemodialysis patients (CHD). The repeated placement and manipulation of central venous catheters, underlying valvulopathies, and immunosuppression are the main predisposing factors for these patients to develop IE. We aimed to highlight the clinical and microbiological specificities of IE in CHD patients, detail the therapeutic management in these patients and identify the risk factors for in-hospital mortality. We included 28 CHD patients in whom the diagnosis of IE was established according to modified Duke criteria. The mean age was 47 ± 17 years. Among them, 57% were hypertensive and 39% were diabetic. The average duration of hemodialysis was 3.5 ± 7 years. The vascular access was a tunnelled jugular catheter, arteriovenous fistula, and temporary catheter in 54%, 28%, and 18% of patients, respectively. Half of the patients presented with heart failure at admission. *Methicillin-sensitive Staphylococcus* is the most commonly implicated pathogen. Transthoracic echocardiography revealed vegetation in all patients. In 60% of cases, the lesion is located on the mitral valve, and in 35% it is on the tricuspid valve. Patients initially received empirical antibiotic therapy, which was adjusted according to bacteriological results. Valve surgery was indicated in 12 patients, with aortic valve replacement being the most performed procedure followed by tricuspid annuloplasty. The in-hospital mortality rate was 32%. Factors associated with mortality were severe mitral insufficiency ($p = 0.036$), heart failure ($p = 0.043$), and the presence of *Methicillin-resistant Staphylococcus* in blood cultures ($p = 0.047$). IE is a complication with high morbidity and mortality. Its increasing incidence, specificities in chronic CHD patients, and the complexity of its management require a rigorous preventive strategy. A multidisciplinary collabo-

ration between nephrologists, infectious disease specialists, cardiologists, and surgeons is crucial to optimize therapeutic management.

Keywords

Infective Endocarditis, Infectious Complications, Chronic Hemodialysis Patients

1. Introduction

Infective endocarditis (IE) is a serious cardiovascular complication with high morbidity and mortality [1]. The first case of IE in a chronic hemodialysis patient (CHD) was reported in 1966. Since then, several case series have been described in the literature [2]-[5]. Currently, it is recognized that the incidence of IE in CHD patients is high compared to the general population. Some studies report an incidence that can reach up to 6% [6]. This represents an incidence 50 folds higher than in the general population [7]. The high prevalence and constantly increasing incidence of IE among CHD patients raise questions regarding risk factors in this population. The increase in the incidence of chronic kidney disease (CKD) may contribute to the rise in the incidence of IE among CHD patients [8]-[11]. IE pathophysiology involves three critical elements: the presence of a valvular anomaly, the adherence of a microorganism to the abnormal valve and the microorganism proliferation and dissemination to distant sites [12]. Valvular calcifications due to mineral and bone disorders, bacteremia related to vascular access infections, and immune system dysregulation therefore appear to be factors exposing CHD patients to the risk of IE [5] [13] [14]. We aimed to describe the clinical profile of CHD patients with IE, detail the medical and surgical management of these patients and identify the risk factors for in-hospital mortality.

2. Materiel & Methods

2.1. Study Design

We conducted a retrospective descriptive monocentric study covering the period from January 2015 to January 2024. We included in our study all CHD patients admitted for the management of an infectious syndrome, in whom the diagnosis of IE was confirmed. This diagnosis was established according to modified Duke criteria in the presence of: 2 major criteria, 1 major criterion and 3 or more minor criteria, 5 or more minor criteria [15]. We excluded CHD patients admitted with sepsis but in whom the formal diagnosis of IE could not be established (not meeting the Duke criteria) and cases where clinical, biological or echocardiographic data were missing.

2.2. Data Collection

All data were collected retrospectively from the hemodialysis unit registry and

medical records from hospital departments (emergency department, cardiology, and nephrology).

We collected demographic data including age and sex, as well as comorbidities: diabetes, hypertension, previous valve disease, acute rheumatic fever.

We specified the initial kidney disease, dialysis modality and duration and the presence of biological hyperparathyroidism. The latter was defined according to KDIGO as an elevation of intact PTH levels 2 to 9 times the normal value, exceeding 130 - 600 pg/mL [16].

Results of transthoracic echocardiography (TTE) were collected: heart failure at admission defined as left ventricular ejection fraction (LVEF) <50%, visualization of vegetation and its location.

Admission laboratory tests were recorded: CRP, leukocytosis, anemia. Aerobic and anaerobic blood cultures were performed for all patients, and the pathogens involved in IE were noted.

Empirical antibiotic treatment was initiated for all patients at the onset of infectious symptoms. Final antibiotic therapy, maintained after bacteriological results, was noted.

Indication for valve surgery was considered in cases of acute heart failure, high embolic risk, or severe valve lesions [10]. All surgical procedures were scheduled and preceded by a hemodialysis session 24 hours before.

Complications such as valvular lesions, septic emboli and in-hospital mortality were documented.

2.3. Statistical Analysis

Data entry and statistical analysis were conducted using Jamovi 2.3.21 software. Quantitative variables were expressed as mean and standard deviation or median and interquartile range depending on their distributions. They were analyzed using the Student's t-test. Qualitative variables were expressed as frequencies and percentages and analyzed using the Chi-square test. An association was considered statistically significant for a p-value < 0.05.

3. Results

We analyzed the records of 28 CHD patients admitted to Ibn Sina University Hospital in Rabat for the management of IE. The mean age is 48 ± 17 years with a sex ratio of 1. The comorbidities observed in our patients are summarized in **Table 1**.

The median duration of hemodialysis is 1.2 [0.6 - 3.7] years. The nephropathies causing chronic renal failure in our patients are presented in **Figure 1**.

Vascular access for hemodialysis was an arteriovenous fistula (AVF), a tunnelized catheter, and a temporary catheter in 29%, 53%, and 18% of patients respectively. Physical examination of the catheters revealed pus discharge in 8 patients and tunnel infection (tunnelitis) in 6 of them. The examination showed no abnormalities in the other 6 patients with catheters. Upon clinical examination

of AVF, no inflammatory signs were observed. The other symptoms presented by the patients are summarized in Table 2.

Biological results revealed anemia in 71% and neutrophilic leukocytosis in 68% of the patients. C-reactive protein (CRP) levels were measured in all patients, with an average value of 165 ± 97 mg/L. Procalcitonin levels were measured in only 6 patients, with an average value of 6 ± 5 ng/mL.

The most commonly implicated pathogen is Staphylococcus, found in 75% of blood cultures. In 4 patients, Staphylococcus is resistant to Methicillin (Table 3).

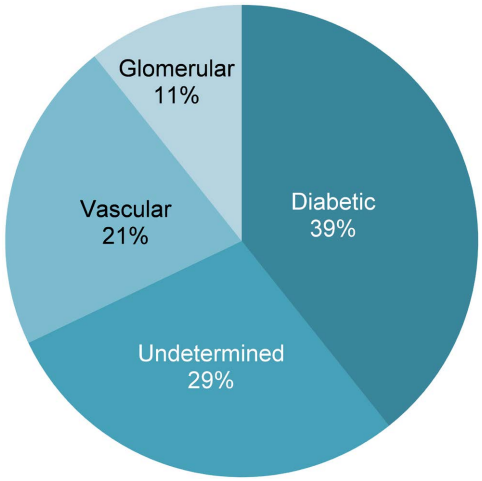

Figure 1. Nephropathies causing end-stage chronic kidney disease (CKD).

Table 1. Comorbidities observed in the included patients.

	N (%)
Diabetes	11 (39%)
Hypertension	16 (57%)
Acute rheumatic fever	0 (0%)
Previous valve disease	0 (0%)
Hyperparathyroidism	4 (14%)

Table 2. Symptoms presented by the patients upon admission.

	Effectif (N)	Pourcentage (%)
Fever (Temperature > 38˚C)	19	68%
Tachycardia	15	53%
Low blood pressure (BP < 100/60 mmHg)	7	25%
Palpitations	6	21%
Heart failure exacerbation	4	14%
Chest pain	2	7%

Table 3. Blood culture results.

	Sample size (n)	Percentage (%)
Staphylococcus Aureus	13	46.4
Methicillin-sensitive	10	
Methicillin-resistant	3	
Coagulase-negative Staphylococcus	8	28.5
Methicillin-sensitive	7	
Methicillin-resistant	1	
Negative	4	14
E. Cloacae	1	3.7
E. Faecalis	1	3.7
A. Baumanii	1	3.7

A TTE was performed, revealing vegetation in all patients. The vegetation's location is detailed in Figure 2. Half of our patients were diagnosed with heart failure with an average LVEF of 35%.

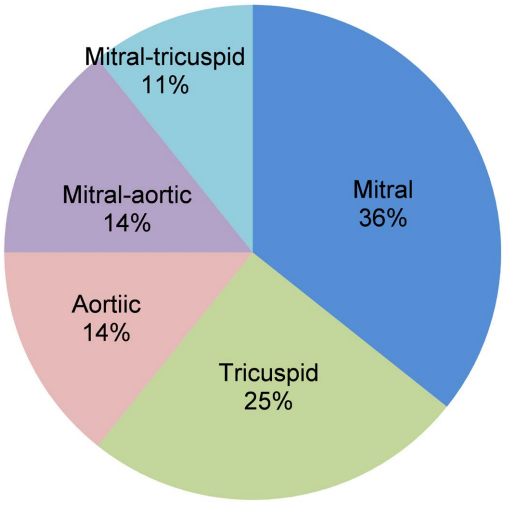

Figure 2. Valves affected during IE.

IE developed in 2 patients with pacemakers. In these 2 cases, the vascular access for hemodialysis is a catheter, and IE developed affecting the right heart.

The initial empirical antibiotic therapy and therapeutic adjustments are summarized in Table 4.

Among included patients, 12 out of 28 which is 43%, required surgical intervention in addition to antibiotic therapy. Aortic valve replacement was the most performed procedure (5 patients), followed by tricuspid annuloplasty (4 patients), and mitral valve replacement (2 patients). In 1 patient, mitral valve replacement was combined with tricuspid annuloplasty.

Among the complications identified, we found 5 local complications: 3 cases of valvular abscess, 2 cases of valvular perforation, and 13 cases of distant septic emboli. Among them, 11 were cases of pulmonary embolism and 2 of osteoarticular location. During hospitalization, 9 patients died from complications directly related to IE, thus raising the in-hospital mortality rate to 32%.

Table 4. Empirical and tailored antibiotic therapy based on the identified pathogen.

Initial treatment	Blood culture results	Adapted treatment	Evolution
Amoxicillin +/− aminoglycosides (n = 15)	***Staphylococcus M-S*** (n = 12)	Same	Death (n = 3)
	Staphylococcus M-R (n = 3)	Vancomycin	Death (n = 2)
Glycopeptides (vancomycin/teicoplanin) (n = 6)	***Staphylococcus M-S*** (n = 5)	Same (n = 5)	Death (n = 1)
	Staphylococcus M-R (n = 1)	Same	Death (n = 1)
Ceftriaxone (n = 1)	**Negative blood culture**	Teicoplanin	
glycopeptides (vancomycin/teicoplanin) (n = 6)		Same (n = 2), Amoxicillin (n = 1)	
Amoxicillin +/− aminoglycosides	***A. Baumanii*** (n = 1)	Carbapenem	Death (n = 1)
	E. Cloacae (n = 1)	Ceftriaxone	
	E. Faecalis (n = 1)	Same	Death (n = 1)

Table 5. Factors associated with in-hospital mortality.

	Percentage (%)/mean ± standard deviation	P value
Age (years)	47.8 ± 17	0.400
Sex ratio	1	0.225
Comorbidities:		
Diabetes	39%	0.657
Hypertension	57%	0.350
Hemodialysis duration (years)	3.5 ± 7	0.830
Vascular access		0.740
Symptoms:		
Tachycardia	53%	0.010
Heart failure	50%	0.043
Severe mitral insufficiency	60%	0.036
Blood cultures:		
Methicillin-resistant Staphylococcus	14%	0.047
Negative	14%	0.137
Antibiotic therapy alone	57%	0.002

In univariate analysis, factors statistically associated with higher in-hospital mortality are summarized in Table 5. The percentage of deaths is higher among patients presenting with tachycardia upon admission (p = 0.010), among patients with heart failure (0.043), and severe mitral insufficiency (0.036). The death rate also appears to be higher among patients carrying a Staphylococcus methicillin-resistant (p = 0.047) and in patients treated with antibiotics without resorting to valve surgery (p = 0.002).

In multivariate analysis, adjusted for age, sex, and duration of hemodialysis, no risk factor for in-hospital mortality could be identified (Table 6).

Table 6. Factors associated with in-hospital mortality in multivariate analysis.

Factors	P value	Odds ratio
AGE	0.816	0.988
Sex ratio	0.814	1.390
Dialysis duration	0.516	0.951
Diabetes	0.548	0.447
Staphylococcus M-R	0.979	0.950
Negative blood culture	0.998	3.08e−9
Valvular surgery	0.997	1.11e−9

4. Discussion

IE is a common complication, with prevalence reaching up to 6% among CHD patients [6]. Some studies report a prevalence 50 to 180 folds higher than in the general population. A Moroccan study reports that the prevalence has doubled over the last five years in the Oujda region. This increase is thought to be linked to the increasingly frequent use of central venous catheters, as well as the early diagnosis of IE [17].

Indeed, it is proven that bacteremia episodes due to repeated manipulations of vascular access, and immune system dysregulation make CHD patients more prone to develop IE [5] [13] [14]. A Moroccan study conducted on 31 CHD patients revealed that a bacteremia episode preceded IE in 87% of cases. In 80% of cases, the source of this infection was the hemodialysis vascular access [18]. A tunnelized hemodialysis catheter is the vascular access in half of our patients. However, no association between the type of vascular access and in-hospital mortality could be established.

Advanced age, considered a risk factor for IE in the general population, is not incriminated in the dialysis population. This is mainly due to the relatively young age of the CHD population in our context compared to countries where kidney transplantation is more accessible [18]. The mean age of patients in our series is 48 ± 17 years, confirming the young age of CHD patients with IE in our setting.

From a pathophysiological perspective, mineral and bone disorders in CHD patients are associated with an increased prevalence of degenerative valve disease and valve calcifications, which promote the development of IE [5]. In our series, biological hyperparathyroidism was found in 4 patients. However, cardiac evaluation for valvular or vascular calcifications prior to the episode of IE was not performed in our study.

The microbiological profile of IE in CHD differs from that of patients in the general population: Staphylococcus aureus is the predominant causative agent, accounting for 37% to 65% of cases [19]-[21]. In the general population, streptococci are more commonly implicated [22]. This is consistent with our findings where Staphylococcus is the identified pathogen in 75% of our patients. According to some reports, approximately half of CHD patients are nasal carriers of Staphylococcus aureus, which can lead to bacteremia, thus constituting a major risk factor for IE [23]-[25]. This underscores the importance of screening and treating nasal carriage of staphylococci in CHD patients.

Regarding the type of cardiac involvement during IE, studies report a higher frequency of right heart involvement in CHD patients, reaching up to 58% of cases [19]-[21]. It's worth noting that in the general population, right heart involvement in IE does not exceed 5% to 10% and mainly affects intravenous drug users [26]. In the Moroccan series by Bentata *et al.*, right heart involvement affecting the tricuspid valve was reported in 42% of cases [18]. In our series, tricuspid involvement was observed in 36% of cases. However, mitral involvement remains the most common and was found in half of our patients. This aligns with the findings of Pericas *et al.*, who also found predominant mitral involvement [6]. Given the significant predominance of catheters as the vascular access in our patients, we expected tricuspid involvement to be more prevalent. This underscores the complexity of IE pathophysiology and the involvement of factors favoring left heart involvement: aortic valve involvement, pre-existing mitral and/or aortic calcifications.

The treatment of IE should be initiated immediately after obtaining 3 sets of blood cultures taken 30 minutes apart. The choice of empirical treatment depends on several considerations: previous antibiotic therapies, location on a native or prosthetic valve, site of infection (community-acquired, nosocomial, or healthcare-associated) and knowledge of local epidemiology [15]. In CHD patients, IE should be considered as nosocomial.

The majority of patients received amoxicillin or glycopeptides, as empirical antibiotic therapy. This is likely related to the fact that it was initiated before the TTE confirming the diagnosis of IE and often prescribed based on the practices of each department.

Outpatient parenteral or oral antibiotic therapy should be considered once complications such as peri-valvular abscesses, acute heart failure, or septic emboli are controlled, and the patient is clinically stable [15]. Therapeutic de-escalation is recommended when indicated. The goal is to prevent the occur-

rence of bacterial resistance and antibiotic-related adverse effects.

IE can lead to valvular and para-valvular complications indicating valvular surgery. The three main surgical indications for acute IE are: heart failure, uncontrolled infection, and prevention of septic embolization [15]. However, moderate to severe renal disease has been identified as an independent predictor of nonsurgical treatment in all patients with IE [27]. Some findings indicate that cardiovascular thoracic surgeons often refrain from recommending surgery for this population, even when clear indications are present [28]. In our patients, in-hospital mortality was significantly more frequent in the non-operated group.

The rate of in-hospital mortality can reach up to 29.5% according to some series [29]. We report a higher mortality rate, estimated at 32% and statistically associated with tachycardia ($p = 0.010$), heart failure ($p = 0.043$), mitral insufficiency ($p = 0.036$), presence of Methicillin-resistant Staphylococcus ($p = 0.047$), and treatment with antibiotics without resorting to valve surgery ($p = 0.002$). This is likely due to delayed diagnosis and variability in therapeutic management across different care services.

This underscores the importance of establishing an "Endocarditis Team" within each facility, in accordance with the recommendations of the European Society of Cardiology [10]. This multidisciplinary team should be comprised of infectious disease specialists, cardiologists, surgeons, and nephrologists. The team would ensure early diagnosis and standardized therapeutic management, with early consideration of surgery when indicated especially in CHD patients for whom IE prevalence is high and its management complex.

5. Limitations

The study might be limited by the relatively small number of included patients, which can limit statistical power to detect significant associations. Selection bias could be a possibility, as the data were collected from medical records across different departments. The diagnostic criteria for IE according to the Duke criteria might have limitations as they may not capture all manifestations of the disease in hemodialysis patients.

6. Conclusion

IE represents a frequent and serious complication in CHD patients. Its incidence appears to be steadily increasing. Its specificity in HDC relies on the presence of multiple predisposing factors: frequency of underlying valvular diseases, Staphylococcus-related bacteremia linked to vascular access manipulations, immunocompromised state, and comorbidities associated with chronic renal failure. Its nosocomial nature necessitates rapid and tailored therapeutic management. Despite effective treatment, its high morbidity and mortality rates necessitate the implementation of hygiene measures and strict protocols governing the manipulation of vascular access sites.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Nucifora, G., Badano, L.P., Viale, P., Gianfagna, P., Allocca, G., Montanaro, D., *et al.* (2007) Infective Endocarditis in Chronic Haemodialysis Patients: An Increasing Clinical Challenge. *European Heart Journal*, **28**, 2307-2312. https://doi.org/10.1093/eurheartj/ehm278

[2] Schubert, C. and Moosa, M.R. (2007) Infective Endocarditis in a Hemodialysis Patient: A Dreaded Complication. *Hemodialysis International*, **11**, 379-384. https://doi.org/10.1111/j.1542-4758.2007.00204.x

[3] Pandey, R. and Sam, R. (2007) Infective Endocarditis in Hemodialysis Patients. *The International Journal of Artificial Organs*, **30**, 334-337. https://doi.org/10.1177/039139880703000409

[4] Robinson, D.L., Fowler, V.G., Sexton, D.J., Corey, R.G. and Conlon, P.J. (1997) Bacterial Endocarditis in Hemodialysis Patients. *American Journal of Kidney Diseases*, **30**, 521-524. https://doi.org/10.1016/s0272-6386(97)90311-5

[5] Bhatia, N., Agrawal, S., Garg, A., Mohananey, D., Sharma, A., Agarwal, M., *et al.* (2017) Trends and Outcomes of Infective Endocarditis in Patients on Dialysis. *Clinical Cardiology*, **40**, 423-429. https://doi.org/10.1002/clc.22688

[6] Pericàs, J.M., Llopis, J., Jiménez-Exposito, M.J., Kourany, W.M., Almirante, B., Carosi, G., *et al.* (2021) Infective Endocarditis in Patients on Chronic Hemodialysis. *Journal of the American College of Cardiology*, **77**, 1629-1640.

[7] Vieille, T., Winiszewski, H., Chirouze, C., Bertrand, X. and Fournier, D. (2019) Escherichia Coli Endocarditis in an Hemodialysis Patient. *Médecine et Maladies Infectieuses*, **49**, 478-479. https://doi.org/10.1016/j.medmal.2019.03.004

[8] Powe, N.R., Jaar, B., Furth, S.L., Hermann, J. and Briggs, W. (1999) Septicemia in Dialysis Patients: Incidence, Risk Factors, and Prognosis. *Kidney International*, **55**, 1081-1090. https://doi.org/10.1046/j.1523-1755.1999.0550031081.x

[9] Maraj, S., Jacobs, L.E., Kotler, M.N., Kung, S., Raja, R., Krishnasamy, P., *et al.* (2002) Epidemiology and Outcome of Infective Endocarditis in Hemodialysis Patients. *The American Journal of the Medical Sciences*, **324**, 254-260. https://doi.org/10.1097/00000441-200211000-00004

[10] Chaudry, M.S., Gislason, G.H., Kamper, A., Rix, M., Dahl, A., Østergaard, L., *et al.* (2018) The Impact of Hemodialysis on Mortality Risk and Cause of Death in Staphylococcus Aureus Endocarditis. *BMC Nephrology*, **19**, Article No. 216. https://doi.org/10.1186/s12882-018-1016-0

[11] Durante-Mangoni, E., Pafundi, P.C., Ravasio, V., Barbaro, F., Bassetti, M., Chinello, P., *et al.* (2016) Current Features of Infective Endocarditis in Persons on Hemodialysis: A Prevalence Study with Case Control Design from the Prospective Multicenter SEI Cohort. *Infection*, **44**, 467-474. https://doi.org/10.1007/s15010-015-0870-y

[12] MSD Manual Professional Edition (2022) Infective Endocarditis. https://www.msdmanuals.com/professional/cardiovascular-disorders/endocarditis/infective-endocarditis

[13] Hauser, A.B., Stinghen, A.E.M., Kato, S., Bucharles, S., Aita, C., Yuzawa, Y., *et al.* (2008) Characteris Tics and Causes of Immune Dysfunction Related to Uremia and Dialysis. *Peritoneal Dialysis International: Journal of the International Society for Peritoneal Dialysis*, **28**, 183-187. https://doi.org/10.1177/0896860808028035s34

[14] Chou, M., Wang, J., Wu, W., Weng, S., Ho, C., Lin, Z., *et al.* (2015) Epidemiologic Features and Long-Term Outcome of Dialysis Patients with Infective Endocarditis in Taiwan Region. *International Journal of Cardiology*, **179**, 465-469. https://doi.org/10.1016/j.ijcard.2014.11.083

[15] Delgado, V., Ajmone Marsan, N., De Waha, S., Bonaros, N., Brida, M., Burri, H., *et al.* (2023) 2023 ESC Guidelines for the Management of Endocarditis. *European Heart Journal*, **44**, 3948 4042.

[16] KDIGO (2017) Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). *Kidney International Supplements*, **7**, 1-59.

[17] Bentata, Y. (2017) Physiopathological Approach to Infective Endocarditis in Chronic Hemodialysis Patients: Left Heart versus Right Heart Involvement. *Renal Failure*, **39**, 432-439. https://doi.org/10.1080/0886022x.2017.1305410

[18] Bentata, Y., Haloui, I., Haddiya, I., Benzirar, A., El Mahi, O., Ismailli, N., *et al.* (2020) Infective Endocarditis in Hemodialysis Patients: A 10-Year Observational Single Center Study. *The Journal of Vascular Access*, **23**, 149-153. https://doi.org/10.1177/1129729820970783

[19] Nori, U.S., Manoharan, A., Thornby, J.I., Yee, J., Parasuraman, R. and Ramanathan, V. (2006) Mortality Risk Factors in Chronic Haemodialysis Patients with Infective Endocarditis. *Nephrology Dialysis Transplantation*, **21**, 2184-2190. https://doi.org/10.1093/ndt/gfl200

[20] Rekik, S., Trabelsi, I., Hentati, M., Hammami, A., Jemaa, M.B., Hachicha, J., *et al.* (2009) Infective Endocarditis in Hemodialysis Patients: Clinical Features, Echocardiographic Data and Outcome. *Clinical and Experimental Nephrology*, **13**, 350-354. https://doi.org/10.1007/s10157-009-0172-8

[21] Spies, C., Madison, J.R. and Schatz, I.J. (2004) Infective Endocarditis in Patients with End-Stage Renal Disease. *Archives of Internal Medicine*, **164**, 71-75. https://doi.org/10.1001/archinte.164.1.71

[22] Slipczuk, L., Codolosa, J.N., Davila, C.D., Romero-Corral, A., Yun, J., Pressman, G.S., *et al.* (2013) Infective Endocarditis Epidemiology over Five Decades: A Systematic Review. *PLOS ONE*, **8**, e82665. https://doi.org/10.1371/journal.pone.0082665

[23] Wertheim, H.F., Melles, D.C., Vos, M.C., Van Leeuwen, W., Van Belkum, A., Verbrugh, H.A., *et al.* (2005) The Role of Nasal Carriage in Staphylococcus Aureus Infections. *The Lancet Infectious Diseases*, **5**, 751-762. https://doi.org/10.1016/s1473-3099(05)70295-4

[24] Engemann, J.J., Friedman, J.Y., Reed, S.D., Griffiths, R.I., Szczech, L.A., Kaye, K.S., *et al.* (2005) Clinical Outcomes and Costs Due to *Staphylococcus aureus* Bacteremia among Patients Receiving Long-Term Hemodialysis. *Infection Control & Hospital Epidemiology*, **26**, 534-539. https://doi.org/10.1086/502580

[25] Troidle, L., Eisen, T., Pacelli, L. and Finkelstein, F. (2007) Complications Associated with the Development of Bacteremia with *Staphylococcus aureus*. *Hemodialysis International*, **11**, 72-75. https://doi.org/10.1111/j.1542-4758.2007.00156.x

[26] Martín-Dávila, P., Navas, E., Fortún, J., Moya, J.L., Cobo, J., Pintado, V., *et al.* (2005) Analysis of Mortality and Risk Factors Associated with Native Valve Endocarditis in Drug Users: The Importance of Vegetation Size. *American Heart Journal*, **150**, 1099-1106. https://doi.org/10.1016/j.ahj.2005.02.009

[27] Chu, V.H., Park, L.P., Athan, E., Delahaye, F., Freiberger, T., Lamas, C., *et al.* (2015) Association between Surgical Indications, Operative Risk, and Clinical Outcome in Infective Endocarditis. *Circulation*, **131**, 131-140.

https://doi.org/10.1161/circulationaha.114.012461

[28] Woller III, J.A., Walsh, V.L., Robichaux, C., Thourani, V.H. and Jacob, J.T. (2018) Predictors of Surgical Intervention in Dialysis Patients with Infective Endocarditis. *Open Forum Infectious Diseases*, **5**, ofy265. https://doi.org/10.1093/ofid/ofy265

[29] Sadeghi, M., Behdad, S. and Shahsanaei, F. (2021) Infective Endocarditis and Its Short and Long-Term Prognosis in Hemodialysis Patients: A Systematic Review and Meta-Analysis. *Current Problems in Cardiology*, **46**, Article ID: 100680. https://doi.org/10.1016/j.cpcardiol.2020.100680