Infective Endocarditis in Patients Receiving Chronic Hemodialysis: Clinical Features and Outcome

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Background and aim of the study: **Patients undergoing chronic hemodialysis are at increased risk of infective endocarditis (IE), and mortality is high in this group. The study aim was to determine clinical features and outcome of IE in patients with chronic renal failure and receiving hemodialysis.**
Methods: **Between 1987 and 2002, all consecutive patients with infective endocarditis treated at the authors' institution who were not intravenous drug abusers were selected prospectively. A comparative analysis was performed of patients undergoing hemodialysis and other patients in the series.**
Results: **A total of 241 cases of IE was diagnosed, and 14 patients (6%) were receiving hemodialysis. A lower frequency of known predisposing heart disease (14% versus 74%, p <0.01) and prosthetic valve endocarditis (0% versus 35%, p <0.05) and a higher rate of negative blood cultures (21% versus 12%, p <0.05) were detected in hemodialysis patients. Early surgery was performed in 50% of patients in both groups. The frequency of complications was similar in both groups, but early (43% versus 16%, p = 0.03) and late (22% versus 9%, p <0.05) mortality were higher in hemodialysis patients.**
Conclusion**: Patients with IE who are undergoing hemodialysis have a lower frequency of predisposing heart disease and higher rates of negative blood cultures. Although patient groups were similarly treated, early and late mortality was significantly higher among those receiving dialysis.**

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Patients undergoing chronic hemodialysis are at increased risk of infective endocarditis compared to the general population (1), and mortality is high in this group (2-6). The study aim was to determine the clinical features and outcome of infective endocarditis in patients who were not intravenous drug abusers but who required hemodialysis for chronic renal failure.

Clinical material and methods

Patients

A prospective study was conducted which involved all consecutive cases of infective endocarditis among non-intravenous drug abusers diagnosed at the authors' center between January 1987 and December 2002. This hospital is a tertiary center providing healthcare cover for the local population and the surrounding area, and has a total referral population of 1,389,000. During the study period, 241 patients with infective endocarditis were diagnosed, and 14 (6%) of these were receiving chronic hemodialysis.

Diagnosis of infective endocarditis

All patients included in the present analysis fulfilled the criteria of definite infective endocarditis. The diagnosis was made according to criteria proposed by Von Reyn et a1. (7) until 1994, and by Durack et al. (8) thereafter. When retrospectively applying the Duke criteria, none of the patients was rejected. All intravenous drug abusers were excluded from the study. Patients were screened for possible intravenous drug abuse based on personal and familial history, and in the absence of cutaneous stigma of venepuncture. All patients received antibiotic treatment according to antimicrobial susceptibility.

Surgical treatment

Surgical treatment was indicated during hospitalization, before completion of the antibiotic treatment, in the following situations: moderate to severe heart fail-

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ure; significant valve regurgitation with major ventricular volume overload; repeated major emboli (≥2); severe mechanical complications in episodes caused by virulent organisms that cannot be eradicated by antibiotic treatment alone (fungi, *Brucella*, *Coxiella*); cases of early prosthetic valve endocarditis; infective endocarditis on pacemaker leads; and in cases of persistent sepsis despite theoretically adequate antibiotic therapy. Emergency surgery was defined as surgery for patients with life-threatening conditions that could not be postponed for >24 h. Elective surgery consisted of interventions that could be delayed for a few days without risk to the patient. All survivors of the in-hospital phase were included in the prospective follow up.

Statistical analysis

Early mortality was defined as mortality within 30 days from surgery, or during the same hospitalization even if more than 30 days from surgery. Continuous variables were expressed as mean ± SD, and categorical variables as percentages. Comparisons between two categories were made using Student's *t*-test for continuous variables and chi-square or Fisher's exact test for proportional variables. Cumulative survival and event-free periods were estimated using the Kaplan-Meier actuarial method. Differences in survival at follow up were estimated using a log-rank test. A p-value <0.05 was considered to be statistically significant.

Results

The present series comprised 241 cases of infective endocarditis. All patients fulfilled the criteria of definite endocarditis, according to Durack et al. (8). Specifically, diagnosis was confirmed by, at least, two of these three criteria (typical echocardiographic findings, positive blood cultures for infective endocarditis, or pathological evidence of endocarditis) in 235 patients (97.5% of the entire series; 100% of the hemodialysis group; 97% of the remaining patients). Diagnosis was confirmed by pathology, after surgery or necropsy in 127 patients (52.7%; 50% of the study group, 53% of the remainder). Only six patients in the non-dialysis group were diagnosed with only one major clinical criterion (typical echocardiographic findings or positive blood cultures for infective endocarditis) and three or more minor criteria (predisposing heart disease, vascular phenomena, immunological phenomena, or microbiological evidence or echocardiogram consistent with a diagnosis of infective endocarditis, but not qualifying as major criteria). A total of 14 patients (6%) was receiving chronic hemodialysis. A comparison of patient characteristics for those receiving hemodialysis and other patients is listed in Table I. There were no statistically significant differences in age, gender or location of vegetation. The frequency of known predisposing heart disease was lower in the hemodialysis group than in the other patients (14% versus 74%, p <0.01).

Table I: General features in non-drug-abusing patients with infective endocarditis (IE) receiving chronic hemodialysis (CHD), compared with other patients.

Parameter	CHD (n = 14)	No CHD (n = 227)	p-value
Age (years)*	55 ± 14	48 ± 17	<0.1
Male gender (n)	6 (43)	154 (68)	<0.1
Known predisposing heart disease	2 (14)	168 (74)	<0.01
Prosthetic valve IE	0 (0)	79 (35)	<0.05
Location of vegetations			NS
Mitral	6 (43)	104 (46)	
Aortic	6 (43)	95 (42)	
Other	2 (14)	28 (12)	
Infective microorganism			NS
Staphylococcus		5 (36)	78 (34)
Streptococcus viridans	1 (7)	54 (24)	
Enterococcus		3 (21)	29 (13)
Other	2 (14)	39 (17)	
Culture-negative	3 (21)	27 (12)	<0.05
Vegetation in echocardiogram	13 (93)	204 (90)	NS
Vegetation size (mm)*	10 ± 2	10 ± 3	NS

Values are mean ± SD.
Values in parentheses are percentages.
NS: Not significant.

None of the hemodialysis patients with infective endocarditis had a prosthetic heart valve, compared to 35% of those without severe renal failure (p <0.05). Arteriovenous fistulae and grafts were used in 11 (79%) and three (21%) patients, respectively. No patient had a permanent or temporary venous dialysis catheter. The rate of negative blood cultures was different between the two groups (21% in hemodialysis patients, 12% in other patients; p <0.05). The distribution of causative microorganisms was similar in both groups, and there were no significant differences in the rate of echocardiographically detected vegetations, their size, and mobility. In one hemodialysis patient echocardiography did reveal the presence of vegetations, but the diagnosis of infective endocarditis was confirmed during surgery.

Complications

The frequency of complications during the active phase of the disease was similar in both groups (78% in hemodialysis patients, 73% in other patients). There were no significant inter-group differences with regard to peripheral embolisms, heart failure, persistent sepsis, neurological complications, abscesses or mycotic aneurysms (Table II).

Surgical requirements

Surgery during hospital admission was performed in seven hemodialysis patients (50%) and in 114 (50%) of the other patients during the active phase. In the hemodialysis group the only indication for surgery was persistent sepsis (100%), whilst among other patients the indications were heart failure (50%), persistent sepsis (27%) and other reasons (23%) (p <0.05). Surgery was performed as an emergency due to clinical instability or hemodynamic impairment in two hemodialysis patients (14%) and in 43 other patients (19%) (p = NS). Likewise, there was no significant difference between groups in terms of the elective surgery rate (36% and 31%, respectively).

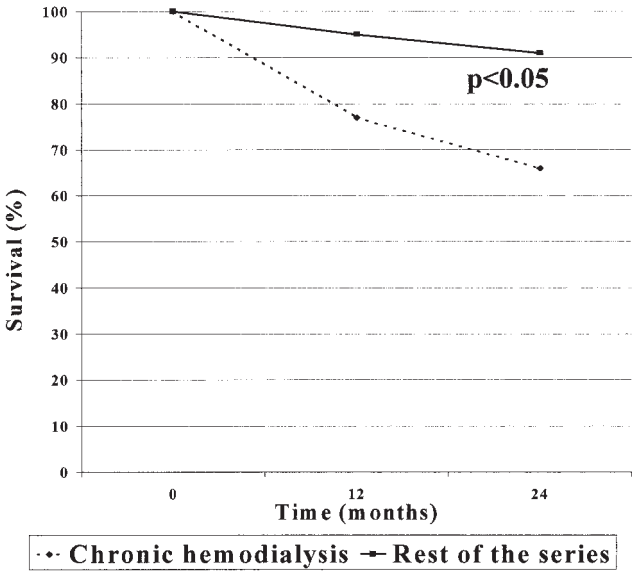

Figure 1: Late survival of patients with infective endocarditis on chronic hemodialysis and in the rest of the series (patients surviving the acute phase of the disease).

Mortality

Early mortality was significantly different between the two groups (six hemodialysis patients (43%) and 36 other patients (16%); p = 0.03). Hemodialysis patients were prospectively followed up for a mean of 21 ± 28 months, and other patients for 48 ± 47 months (p <0.01). No patients were lost during the follow up period, and there was no recurrence of infective endocarditis among hemodialysis patients. Surgery was not performed during follow up in any of the hemodialysis patients, whereas 18 other patients (8%) required surgery (p = NS). Three hemodialysis patients (21%) and 20 other patients (9%) died during the follow up period (p <0.05). Causes of death among hemodialysis patients were bronchopneumonia, colon adenocarcinoma and renal failure. Among those patients who

Table II: Cardiac and extracardiac complications in non-drug-abusing patients with infective endocarditis (IE) receiving chronic hemodialysis (CHD), compared with other patients.

Complication	CHD (n = 14)	No CHD (n = 227)	p-value
Heart failure	8 (57)	95 (42)	NS
Embolism	2 (14)	57 (25)	0.07
Central nervous system	3 (21)	39 (17)	NS
Persistent sepsis	3 (21)	39 (17)	NS
Metastatic abscesses	1 (7)	27 (12)	NS
Mycotic aneurysms	0 (0)	11 (5)	NS

Values in parentheses are percentages.
NS: Not significant.

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survived the acute phase of the disease, the probability of survival at one and two years was 77% and 66% for hemodialysis patients, compared with 95% and 91% for the other patients ($p < 0.05$; Fig. 1). Overall, late survival considering in-hospital and follow up mortality was 36% among hemodialysis patients and 75% among others ($p < 0.01$).

Discussion

The present series is the first prospective study of infective endocarditis to be conducted among hemodialysis patients who are non-intravenous drug abusers. All other studies published to date (1-6) have been retrospective in nature, and have included a similar number of cases. Although patients receiving chronic hemodialysis are at increased risk of infective endocarditis compared to the general population (1), it is difficult to assess whether the independent factor is chronic renal failure itself, as an immunosuppressant disease, or the hemodialysis procedure. Recent reports have suggested that the frequency of infective endocarditis is no higher among peritoneal dialysis patients than in the general population (1), and that the prognosis of infective endocarditis in this setting is significantly better than in hemodialysis patients (2). These facts suggest that the higher incidence and worse prognosis may be related mainly to the hemodialysis procedure. In the present series, none of the patients receiving hemodialysis was switched to peritoneal hemodialysis when infective endocarditis was diagnosed, as some investigators have suggested (2); consequently, comparative results of this strategy are not available. Some of the present results were similar to those found previously in retrospective studies, namely a low frequency of known predisposing heart disease (6), a relatively high incidence of enterococci (4), and a frequent involvement of the mitral and aortic valves (3-6). The relatively high rate of negative blood cultures among the present patients contrasted with those rates reported by others (3-5). All reported studies (2-6) showed staphylococci consistently to be the most frequent causal microorganisms, though values ranged from 40% to 80% (36% in the present patients). All recent series have shown a high mortality among hemodialysis patients that ranges from 29% to 68% during the in-hospital stay (1-6). Even if surgical treatment was more frequent in the present series than in others (2-6), and equivalent to that in patients without hemodialysis, the in-hospital mortality was high in the study group (43%).

In conclusion, in this prospective study of 241 cases of infective endocarditis in non-intravenous drug abusers, patients receiving hemodialysis had a lower frequency of predisposing heart disease and higher rates of negative blood cultures. Although both patient groups were similarly treated, early and late mortality was significantly higher among hemodialysis patients.

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