DOES ATHEROSCLEROSIS CAUSED BY DIALYSIS LIMIT THIS TREATMENT?

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Summary

A retrospective study of 332 dialysis patients (observation period up to 17 years) demonstrated that cardiovascular and cerebrovascular death rates due to atherosclerosis did not increase with length of time on dialysis. Data analysis showed that cardiovascular and cerebrovascular morbidity and mortality during dialysis is primarily caused by high blood pressure existing prior to commencement of dialysis and an unfavourable very low-density lipoprotein/high-density lipoprotein (VLDL/HDL) cholesterol quotient at the beginning of dialysis treatment. The treatment of the patient before acceptance onto dialysis seems therefore to be the determining factor in the prognosis on dialysis.

Introduction

Cardiovascular and cerebrovascular diseases account for 45–65 per cent of deaths in patients on maintenance dialysis [1, 2]. For dialysis patients aged over 50, the incidence of fatal ischaemic heart disease is 10 times greater than for the general population in the same age group, while for those aged 15–30 years it is 150 times greater [3]. The causes of the high incidence of cardiovascular disease in patients treated by regular haemodialysis are assumed to include hypertension, the constantly increased cardiac output, pericardial disease and carbohydrate and lipid metabolic abnormalities. As regards the latter, it has been suggested that atherosclerosis is related to the hyperlipidaemia with lowered lipoprotein lipase activity often found in dialysis patients and to the significantly reduced concentration of high-density lipoprotein (HDL) cholesterol [4, 5]. Apart from the above factors, the dialysis treatment itself, or renal insufficiency persisting over a long period, have also been suggested to accelerate atherosclerosis [2, 6]. Recent long term studies, although in small groups of patients, seems to contradict this hypothesis [7–9]. Meema et al [10] have been able to demonstrate in their patients that vascular calcification progresses more slowly in dialysis patients.
than in non-dialysed renal patients. These opposing views led us to carry out a retrospective study of our own patients, covering the prognosis, the cardiovascular and cerebrovascular mortality, and the serum lipid concentrations with particular emphasis on the long term effects of dialysis treatment.

**Patients and treatment**

We examined data on 332 patients accepted for renal replacement therapy at the Cologne University Medical Clinic and the Limited Care and Home Dialysis Centre of the Kuratorium für Heimdialyse e.V. in Cologne. The study included every patient with chronic renal failure who received dialysis at least once. The patients were divided into two groups according to length of time on dialysis: Group I with less than five years on dialysis (244 patients) and group II with more than five years (88 patients). The patients’ survival rate was calculated by the optimised mathematical method developed by Kaplan and Meier [11]. Each of the groups was analysed separately by age, sex, primary renal disease, length of treatment, and cause of death. Eighty-two per cent of patients who died underwent necropsy and the extent of their vascular disease was noted. During the period covered by the study, 68 cadaveric kidney transplants were performed on 62 of the 332 dialysis patients. Survival data for dialysis and transplantation were combined, since these two forms of therapy are not alternative but complementary modes of treatment. In addition, for 252 dialysis patients the serum lipid concentrations were determined. The data were statistically evaluated using the Student T and Wilcoxon tests.

**Results**

Of the 332 dialysis patients (147 women and 185 men), 88 (40 women and 48 men) had been treated for more than five years. The mean age of this group, 35.5 years, was about nine years lower than that of the patients dialysed for less than five years. The total treatment period for the patients treated for more than five years was 663 years, giving a mean 90.4 months per patient, of which the longest period, to the end of 1981, was 17 years. The mean treatment period for all patients in the study was 39.1 months. In both groups, chronic glomerulonephritis and chronic pyelonephritis predominated as the primary disease causing terminal renal failure. The group of patients on dialysis for more than five years (Group II) contained a remarkably low proportion of cases with vascular nephropathy. During the total period covered by the study (almost 17 years), 135 (40.7%) of the 332 patients died. The death rate for the dialysis patients treated for more than five years was 15.9 per cent, substantially lower than the 49.6 per cent recorded for the patients of Group I. Cardiovascular or cerebrovascular diseases due to atherosclerotic lesions were the cause of death in three of the 14 patients of Group II, but in 45.5 per cent of those who died after less than five years of dialysis. The cardiovascular and cerebrovascular mortality was 22.5 per cent for the patients of Group I and fell to 3.4 per cent for those on dialysis for more than five years. At the end of the period studied, 69 of the Group II patients were still on maintenance haemodialysis, while 19
had received successful kidney grafts. The survival rate for all 332 dialysis patients treated between 1965 and 1981, including transplant recipients, was 78.8 per cent during the first year, 64.4 per cent after three years and 56.4 per cent after five years (Figure 1); this compares with survival figures for the patients on dialysis for more than five years of 93 per cent after one year, 88 per cent after three years and 70 per cent after five years. Even if the 62 transplant recipients are subtracted, the shape of the curves does not substantially alter.

![Figure 1. Overall patient survival for dialysis and transplantation combined](image)

Of the 252 dialysis patients whose lipoprotein status was known, serum triglycerides exceeded 200mg/dl in 49 per cent of the patients, while in 40 per cent of the patients total serum cholesterol exceeded 250mg/dl, predominantly caused by markedly high VLDL cholesterol values. It is noteworthy that HDL cholesterol concentration was low in 61 per cent of the patients. There was a statistically significant correlation between high VLDL cholesterol and low HDL cholesterol concentrations (Figure 2). Within the group of 252 dialysis patients, a group of 35 patients, who either had already suffered myocardial infarction before commencing dialysis or showed clinical and ECG symptoms of unstable angina pectoris, was selected (IHD group). In this group the HDL cholesterol concentration (mean $31 \pm 10$SD mg/dl) was significantly lower ($p < 0.01$) than in the remainder of the 252 group (mean $39 \pm 16$SD mg/dl) (Figure 3), while for the VLDL cholesterol values the converse was true.
Figure 2. Correlation between HDL cholesterol and VLDL cholesterol concentration in 252 haemodialysis patients.

Figure 3. Contribution of HDL cholesterol concentration in 252 haemodialysis patients.
- $\bullet$ = patients with myocardial infarction or ischaemic heart disease (IHD-Group, $n = 35$);
- 0 = remainder of the 252 group; $\rightarrow$ = risk limit

171
Discussion

Our results confirm that a high proportion of dialysis and transplant deaths are caused by cardiovascular and cerebrovascular disease. However, in agreement with studies by Nicholls et al [9], Burke Jr et al [7] and Chan et al [8], it could be clearly demonstrated that the risk of atherosclerosis-related death did not increase with length of time since commencing dialysis therapy. The death rate for patients dialysed for more than five years was markedly lower than for those dialysed for less than five years. As reasons for this Chan et al [8] have suggested the partial correction of uraemic intoxication achieved by regular dialysis, the usually well controlled hypertension and the intermittent anticoagulation, which may mitigate the effects of some atherogenic factors such as hyperlipidaemia and low concentrations of high-density lipoproteins. In contrast to the findings of Levine et al [12], the present results showed that dialysis patients with unstable angina pectoris or who had suffered myocardial infarction exhibited statistically significantly lower HDL cholesterol concentration than the remainder of the dialysis patients, while the VLDL cholesterol was significantly higher. It must therefore be assumed that hyperlipoproteinaemia and the low HDL cholesterol concentration play an important role, in addition to the risk factors already mentioned, in the cardiovascular and cerebrovascular morbidity and mortality of dialysis patients.

The high early death rate from cardiovascular and cerebrovascular disease due to atherosclerosis and the lower late mortality suggest that the cardiovascular lesions had already developed before commencement of the dialysis treatment, based on the existence of uncontrolled hypertension for years in almost every case in addition to other atherogenic risk factors [9]. The prognosis for dialysis patients is therefore already predetermined in the period before regular dialysis treatment becomes necessary.

References

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Open Discussion

WIZEMANN (Geisson) This morning in the combined report there was an indication that haemodialysis patients who are treated by short methods have a higher risk of cardiovascular mortality. Do you have any data on this?

KINDLER No, we have no data on this because we perform long dialysis treatment, we dialyse our patients for three times six hours weekly. We cannot confirm the data presented this morning.

WIZEMANN So the high mortality of the patients who were treated for less than five years in your data derive from the long treatment?

KINDLER They derive from uncontrolled hypertension for years before the start of dialysis therapy.

BOMMER (Heidelberg) Have you looked in your patients for vascular calcification in organs other than the heart?

KINDLER No, we have only necropsy data. We looked at the major coronary vessels and the arteries of the cerebrum which we considered positive when the occlusion was more than 50 per cent. We did not particularly look at the calcification of the vessels. Arteriosclerosis in other parts of the body was not the cause of death. The cause of the deaths were only coronary artery disease, stroke or cerebrovascular disease.

NICHOLLS (Sheffield) Have you looked at the influence of transplantation on the short term development of thrombotic complications, in patients in the first three to six months after transplantation?

KINDLER Yes. It seems the incidence in transplantation was greater in the first three months post-transplant, but the incidence after five years is not greater than in dialysis patients. The highest incidence for death from atherosclerosis is in the first three months after transplantation.

RITZ (Heidelberg) Dr Kindler I think your observations are generally in agreement with reports in the literature and point to the paramount importance of hypertension in the genesis of vascular events. However on the basis of your findings I would hesitate to accept your statement that there is absolutely no accelerated atherogenesis in uraemia. One would have to compare age, sex and risk factors in matched dialysed patients and non dialysed patients in a prospective study.

KINDLER Yes, you are right but there is a study by Berk et al and by Rostand who found that there was no acceleration of atherosclerosis during the time on maintenance haemodialysis. If they excluded from the study all patients with risk factors such as myocardial infarction, high blood pressure or diabetes
mellitus they could then see that there was no acceleration in the remaining patients on maintenance haemodialysis.

RITZ Yes, but if you read Dr Rostand’s paper carefully you will see that the number of events observed was twice that expected in females on dialysis, I do not feel that women are to be neglected so completely.

KINDLER Yes, it was the study of Rostand, you are right, but in the study of Berk you can see that there was no acceleration on haemodialysis if you include the patients who had myocardial infarction or diabetes mellitus or who have malignant hypertension.