

Lindner A, Charra B, Sherrard D J & Scribner B H. Accelerated atherosclerosis in prolonged maintenance hemodialysis. *N. Engl. J. Med.* 290:697-701, 1974.
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Life-table analysis of survival of the first 39 patients receiving maintenance hemodialysis in Seattle since 1960 revealed an inordinately high morbidity and mortality from arteriosclerotic cardiovascular complications. These findings indicated that accelerated atherosclerosis is a major risk to long-term survivors on maintenance hemodialysis. [The SCJ® indicates that this paper has been cited in over 395 publications since 1974.]

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August 17, 1984

"In 1974, when this study was done, long-term survival on hemodialysis had become a reality for many patients with end-stage renal disease. By that time, initial assessments of life expectancy (mostly based on unsupported data) suggested that, if a patient had remained alive on dialysis for a few years, he might survive indefinitely since major complications had not been recognized. On the other hand, we and other nephrologists had observed cases of myocardial infarction, angina pectoris, and strokes, which prompted a careful statistical analysis of our patient population. Our patients were ideal for this study since they represented a homogeneous group of fairly young adult males (mean age 37 years), with no preexistent cardiovascular disease (other than hypertension in some cases) prior to the onset of dialysis treatment.

"To our surprise, life-table analysis demonstrated an inordinately high morbidity and mortality from cardiovascular complications of atherosclerosis when compared with rates for age-matched normals or hypertensive patients without renal disease.

"The implications were serious, since they indicated an increasingly higher probability of developing (and dying from) coronary heart disease after several years of dialysis. On the other hand, this study could not elucidate the causes of this phenomenon, nor the possible role of uremia *per se* in the premature production of atherosclerotic lesions.

"One factor kept us from submitting this paper for publication for about six months after its completion. Both Scribner and I agonized about the possible psychological impact of these findings, that fear of dialysis complications might deter those with end-stage renal failure from receiving this life-saving treatment. Eventually, we came to believe that our findings would stimulate others to investigate the pathogenesis of this phenomenon and to look for specific ways of preventing it.

"We think that this publication has been so highly cited for several reasons. First, it provided the first conclusive evidence of a clinical problem that could potentially shorten survival in uremic patients on long-term hemodialysis. Second, it suggested that premature atherosclerosis in uremic patients could be a model for the study of this vascular complication in the general population. Third, it provided impetus for the subsequent performance of a number of studies of this problem in many countries. Finally, even today, the conclusions of this study continue to generate controversy. Thus, a study of over 300 patients in Alabama demonstrated complication rates almost identical to ours, yet the conclusions were not alike.¹ On the other hand, the strongest confirmation of our findings came from the life-table analysis in a population of over 50,000 patients from many European countries,² which showed annual death rates from coronary heart disease to be more than 10 times higher among uremic patients on dialysis, particularly for the younger (15-to-34-year) age group."

1. Rostand S G, Gretes J C, Kirk K A, Rutsky E A & Andreoli T E. Ischemic heart disease in patients with uremia undergoing maintenance hemodialysis. *Kidney Int.* 16:600-11, 1979.
2. Brunner F P, Brynger H, Chantler C, Donckerwolcke R A, Hathway R A, Jacobs C, Selwood N H & Wing A J. Combined report on regular dialysis and transplantation in Europe, IX, 1978. *Proc. Eur. Dial. Transpl. Assoc.* 16:2-73, 1979.