Determinants of outcome dialysis
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Link to publication

Citation for published version (APA):

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Download date: 15 Dec 2018
Chapter 1

Introduction
End-stage renal disease (ESRD) can be due to many different conditions varying from diabetes mellitus and hypertension, that also affect other organ systems, to glomerulonephritis which is limited to the kidney. Whatever its cause, ESRD will lead to death if left untreated. Forty years ago it became possible to keep ESRD patients alive. In the years to follow, dialysis and transplantation both became regular therapeutic options to take over vital parts of the patient’s renal function. However, the availability of kidneys for transplantation is highly dependent on the number of cadaver organ donors. Because of the shortage of organ donors, most ESRD patients will for at least a part of their lives be dependent on dialysis treatment.

Dialysis removes waste products and excess fluid from the blood, functions that are normally fulfilled by the kidneys. Hemodialysis is an intermittent therapy, typically performed in in-hospital dialysis units, although traditionally a small part of the patients receive hemodialysis at home or in an outpatient setting. Most patients receive 2 to 4 sessions a week with a duration of 3 to 4 hours. The patient’s blood is run through an artificial kidney. Accumulated toxic substances diffuse through a dialysis membrane to a dialysis fluid, which has similarities with blood plasma. The removal of excess fluid is achieved by a hydrostatic pressure gradient over that same membrane. In peritoneal dialysis patients a permanent catheter is inserted in the peritoneal cavity through the abdominal wall. Through that catheter dialysis fluid is periodically renewed. Toxic substances are removed from the vessels in the peritoneal membrane to the dialysis fluid in the peritoneal cavity by diffusion. Excess fluid is removed from the blood to the peritoneal cavity by an osmotic pressure gradient that is achieved by the high glucose concentrations of the dialysis fluid. Popovich and Moncrief developed the technique of continuous ambulatory peritoneal dialysis (CAPD). Approximately two liters of dialysis fluid remain in the peritoneal cavity continuously. These are exchanged by the patient four or five times a day. Not only are substances removed from the blood, there is also diffusion in the opposite direction, resulting in for example glucose uptake. In the last decade machines have been introduced that take over part of the exchanges from the patient. They are used over night, while the patient is asleep. This automated peritoneal dialysis (APD) received the name continuous cyclic peritoneal dialysis (CCPD) in case dialysis fluid is left in the abdomen during the day.

In the Netherlands, dialysis care is provided by 48 Dutch dialysis centers. Most of these centers offer both dialysis modalities. Between 1985 and 1995 the number of patients receiving dialysis almost doubled to nearly 4000 and it has been growing since. Each year more than 1300 patients start dialysis therapy. The introduction of improvements in dialysis technology could not prevent that annual mortality rates increased from 13 to 21% over those same ten years. Both developments are reflecting worldwide trends. Investigators in the US have proposed a higher acceptance rate of older and sicker patients, reduced mortality
from other conditions and a possible higher incidence of kidney disease as potential explanations. Currently, the remaining life expectancy among US dialysis patients is estimated between 20% (white women) and 40% (black men) of that of the corresponding US population of the same age.

Growing mortality rates and an interest in the determinants of outcome in dialysis have led to the initiative of the Dialysis Group Netherlands (DGN) to start the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD). The first aim of this study was to prospectively investigate the association of patient and therapy characteristics at 3 months after the start of dialysis with outcome. From the beginning it was evident that outcome was not restricted to mortality or morbidity. Also quality of life was defined as primary outcome measure, as it was recognized that not only ESRD itself but also its treatment might affect the patient perceived quality of life. Comorbidity, nutritional status and residual renal function were other specific areas of interest. The second aim of this study was to define adequate dialysis and to develop treatment guidelines applicable to the Dutch dialysis population. At that time it was suspected that most Dutch patients received a lower dialysis dose than recommended in the US, whereas patient survival seemed similar. It was also not clear if hemodialysis or peritoneal dialysis would have a survival advantage in patients without contra-indications for one of these treatment modalities.

This thesis deals with the first NECOSAD cohort of 250 new dialysis patients from 13 centers and its outcome over a maximum period of 44 months. In Chapter 2 the characteristics of these patients at 3 months after the start of dialysis (baseline) are reported. Their clinical condition, including their comorbidity, is described and put into a European perspective. In addition, associations of baseline characteristics with short-term outcome are identified (Chapter 2.1). In Chapter 2.2 details on the quality of life at baseline are provided and put into the perspective of the quality of life of a Dutch general population sample. Secondly, the relationship of quality of life with demographic, clinical and adequacy variables is identified. In Chapter 3 treatment and overall mortality are reported. The first part deals with case-mix differences among the participating centers and with dialysis treatment over time. A comparison is made with current US guidelines on the adequacy of dialysis. Mortality, hospitalization and the time course of renal function and blood pressure are described and discussed in the context of recent literature. Outcome in the elderly subgroup is reported separately and compared to the entire study population (Chapter 3.1). In the second part of this chapter the determinants of mortality and technique failure in patients who started peritoneal dialysis are presented (Chapter 3.2). The subject of Chapter 4 is nutritional status. The time course of several nutritional parameters over two years is compared between patients starting on hemodialysis or peritoneal dialysis. Subgroups with a different change in nutritional status over time on dialysis are identified. Chapter 5 deals with
the time course of quality of life over the first 18 months after the start of dialysis treatment. The two dialysis modalities are compared with respect to different dimensions of quality of life. In the general discussion, in Chapter 6, the findings are discussed in terms of determinants and outcome. Directions for future research are given.

References
