

INTRODUCTION:

Why Daily Therapies?

Recent randomized, controlled studies show that traditional therapy regimens such as intermittent hemodialysis and peritoneal dialysis have limited ability to generate further improvements in patient morbidity and mortality. Daily dialysis presents great promise in enabling outcomes improvements that have eluded patients and caregivers for so long. This booklet reviews the clinical indications for daily dialysis described in the literature in order to help clinicians identify and support patients that might benefit most.

Conventional hemodialysis—administered thrice-weekly for about 4 hours—eliminates considerable amounts of uremic toxins, excess salts and water from patients with kidney failure. Nevertheless, the mortality rate for hemodialysis patients in the U.S. remains high at approximately 24.4 deaths/100 patient-years. Morbidity is also high, with the prevalence of cardiovascular complications, hypertension, anemia, amyloidosis, malnutrition, and bone disease greatly exceeds that found in the general population. Common comorbid conditions, such as diabetes and cardiovascular disease, contribute greatly to the illness and death of ESRD patients.

At least part of this morbidity can be attributed to the non-physiologic nature of the conventional thrice-weekly hemodialysis schedule.¹ Healthy kidneys work 24 hours per day, 7 days per week to rid the body of toxic compounds and maintain homeostasis of salts, water, certain proteins, and critical hormones.

In patients with ESRD, intermittent hemodialysis allows toxins, salts, and water to accumulate in the body during the interdialytic period. Some of these accumulated substances may deposit in the tissues, exacerbating tissue damage and cardiovascular disease. In addition, simply through the intermittency of the therapy, conventional hemodialysis results in large fluctuations in the levels of toxins, salts, body weight and water. This has been referred to as the “unphysiology of dialysis,” and these imbalances may be particularly hazardous in patients with underlying cardiomyopathy, cardiac arrhythmias, and coronary disease.¹

Drawbacks of the current conventional dialysis schedule have inspired clinical trials designed to determine whether more frequent renal replacement therapy can achieve better homeostasis and elimination of toxins. Only a few hundred

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patients worldwide currently receive daily hemodialysis (5 or more weekly treatments),²⁻⁸ yet reports consistently indicate that daily renal replacement therapy improves patients' overall health and well-being. Reports also indicate that patients on daily hemodialysis experience less morbidity and require fewer days of hospitalization.⁹⁻¹¹

Cardiovascular complications are responsible for about 50% of the deaths of ESRD patients. Even after controlling for effects of age, gender, race, and the presence or absence of diabetes, cardiovascular mortality in dialysis patients is 10 to 20 times higher than in the general population. Daily renal replacement therapy has been reported to improve several important risk factors for cardiovascular disease: 1) the progress of left ventricular hypertrophy can be slowed or reversed; 2) blood pressure is controlled while the need for antihypertensive medications is reduced or eliminated for many patients; 3) intertreatment fluid overload can be controlled with fewer restrictions on fluid intake; and 4) anemia improves in many patients, with some patients requiring less EPO supplementation. Taken together, these data demonstrate that daily renal therapies are associated with general improvements in cardiovascular health and risk profiles.

Daily treatment is superior to intermittent dialysis in clearing most solutes from the blood. Both kinetic models and data from patients receiving daily hemodialysis indicate that both short daily and long nocturnal treatments are more effective than conventional hemodialysis in clearing urea from the blood.¹¹⁻¹³ Beta-2 microglobulin, which precipitates in connective tissue to cause amyloidosis, is likewise removed more effectively with daily treatments. This corresponds to a reduction in the incidence of carpal tunnel syndrome in patients receiving daily renal replacement therapy. Dietary phosphate, consumed with protein-rich foods, is removed more efficiently with frequent treatments. Many patients on daily hemodialysis can consume more liberal diets, while reducing or discontinuing the use of phosphate binders.

Malnutrition, another common chronic condition in patients with renal failure and an important independent predictor of mortality, also improves with daily treatment.

Finally, a host of traditional quality of life measures – energy levels, treatment tolerance, employment/rehabilitation, skin disorders, and hospitalization – are observed to improve as patients initiate daily therapies. These benefits enhance patients' well-being and may promote greater treatment compliance, further improving patients' survival rate and quality of life.

NxStage has reviewed and summarized the body of original investigations on daily therapy published in the English language. Ninety-four (94) recent studies (published between 1996 and 2004, of which 64% are from North America, 30% from Europe, and the balance from other parts of the globe) are included in this analysis. The following sections are organized according to the eight primary clinical indications described in these published original investigations— left ventricular hypertrophy, hypertension, fluid overload, anemia, amyloidosis, hyperphosphatemia, malnutrition, and quality of life. Each section outlines the significance of the indication on patient morbidity and mortality, summarizes how daily therapy has been reported to improve patient outcomes, and tabulates the key findings for that indication from each of the published studies (in reverse chronological order) highlighting benefits in this area. We hope that this summary proves helpful in selection and support of patients who might most benefit from more frequent therapies.

