

Infrequent Dialysis: A Different Strategy to Incremental Dialysis

To the Editor: With regard to your recent publication,^{1,2} I should like to highlight the nosological and methodological differences between "incremental hemodialysis" and "infrequent hemodialysis." Indeed, infrequent dialysis³ embraces the full range of therapeutic options implemented with a schedule of less than thrice-weekly hemodialysis sessions, ideally integrated by a moderately low-protein diet. Incremental dialysis^{4,5} is a strict program implemented following assessment of uremic status in a predialysis outpatient setting through a synergic nephrological and nutritional approach aimed at achieving an excellent nutritional status and preserving diuresis with a glomerular filtration rate (GFR) ranging between 5 and 10 ml/min per 1.73 m².

Total weekly GFR should be calculated on the basis not only of urea clearance, but also taking into account the mean of urea/creatinine clearance.6 An incremental dialysis program may then be set up with the assistance of a skilled logistics team in charge of monitoring patient compliance and ensuring smooth running of the program. Initially, the Combined Diet Dialysis Program⁴ comprising once-weekly dialysis associated with a low-protein diet (0.6 g protein/kg per day) and administration of essential amino acids is implemented. On dialysis days, the patient is requested to consume a meal with approximately 1.4 g protein/kg per day per 1.73 m². The Combined Diet Dialysis Program represents a dialytic "bridge" of variable duration aimed at ensuring good metabolic state and promoting quality of life. Dialysis dose is established in line with the outcome of GFR in a proportionally inverse manner. Recent studies^{4,7} have demonstrated a lower mortality for incremental dialysis than thrice-weekly dialysis, and, thanks to the contribution of phosphaturia, a neutral balance of input/output phosphoric pool compared with thrice-weekly hemodialysis patients who lose residual renal function early.⁸ Reduced contact with proinflammatory/pro-oxidative stimuli secondary to hemodialysis may enhance preservation of GFR. Residual renal function has long been underestimated⁹ in spite of the exceptional efficacy displayed in purifying protein-bound uremic toxins compared with dialysis^{10,11}; forms of indeed, other residual renal function may contribute toward establishing a phosphoric balance resulting in a reduction of cardiovascular damage and direct phosphatic lesions of the renal parenchyma.¹² Infrequent dialysis is indicated for use in patients maintaining a GFR <3 ml/min per 1.73 m², particularly smaller patients. With regard to both methods, however, the additional time spent on clinical assessment will be recouped using the Combined Diet Dialysis Program due to a two-thirds reduction in hemodialysis costs equivalent to an annual saving per patient of more than \$22,000.

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The Author Replies: We thank Dr. Bolasco for his insightful comments.¹ We agree that "incremental" hemodialysis and "infrequent"



hemodialysis can be viewed as different approaches for prescribing hemodialysis in incident patients who manifest residual renal function (RRF). Infrequent hemodialysis, with a once- or twice-weekly treatment schedule, emphasizes a complementary dietary management schema that often involves some degree of dietary protein restriction. Dietary protein restriction has been used as an adjunctive measure to delay dialysis initiation and reduce dialysis frequency in incremental treatment regimens. Decades ago, Locatelli et al.^{2,3} and Morelli et al.⁴ proposed an "Integrated Dialysis Diet Program" that focused on maintaining a predialytic blood urea nitrogen of <90mg/dl on once-weekly hemodialysis by implementing a very low protein diet in the range of 0.3 to 0.4 g/ kg per day, supplemented with essential amino acids for 6 days a week. These patients had very low levels of RRF. After 1 year, there was >50% dropout, and patients developed worrisome clinical signs, including loss of lean muscle mass and worsening uremia (e.g., decreased distal nerve conduction velocity), leading the authors to advise against broad application of this management strategy. Learning from those experiences, Caria et al.⁵ proposed a "Combined Diet Dialysis Program" that instituted a less restrictive protein diet (0.6 g/kg per day) on nondialysis days while ensuring adequate dietary energy intake and unrestricted protein intake on hemodialysis days. Adherence to this strategy was improved with no dropouts. It was noted that the Combined Diet Dialysis Program was best suited for patients with less impaired RRF, good motivation, and ability to stick with the outlined diet. Other authors have supported use of adjunctive dietary therapy to less frequent dialysis.^{6,7}

Incremental hemodialysis can really be viewed in the same manner. In our article, we emphasized the importance of formally measuring and calculating urea clearance in patients considered for an incremental schedule; however, the dietary angle is by no means trivial and should be considered. In fact, to truly gauge protein catabolism in patients with end-stage renal disease with

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Figure 1. Idealized prescription of hemodialysis (HD), taking into account urea clearance (residual kidney as well as dialyzer), volume removal needs, clinical condition, and patient's quality of life. Patients with no residual renal function may start immediately on the right side of the diagram, whereas those with substantial residual function may stay for some time on the left side.

RRF, knowing the urine urea nitrogen excretion is required. Determination of optimal protein intake when incremental or infrequent hemodialysis is prescribed is not an easy task, with protein malnutrition versus excessive protein breakdown-product accumulation in the balance.⁷

Observations that less than thrice-weekly dialysis may not confer a higher mortality risk when used in the appropriate setting are encouraging.^{8,9} Given the positive association of RRF on hemodialysis patient survival, twice-weekly therapy may provide better prolongation of RRF, especially if used in the highrisk period during the transition from advanced chronic kidney disease to end-stage renal disease. Conversely, patients with a high burden of comorbidities may require more frequent hemodialysis, even at the beginning of end-stage renal disease, and should be given the correct corresponding dialysis prescription.

At the end of the day, whether you call it "infrequent" or "incremental" hemodialysis, we are all striving to prescribe hemodialysis in the same manner as we would for any other medication: (i) to provide the correct dose, (ii) at the correct frequency, (iii) monitoring for side-effects and efficacy, and (iv) considering alternative and adjunctive treatments. Semantics aside, both approaches are meant to optimize patient clinical status and quality of life with less than the typical thrice-weekly hemodialysis schedule, when circumstances allow. Thus, prescribing hemodialysis, including its frequency, should use an individualized approach in lieu of a "one-size-fits-all" strategy (Figure 1).

^{1.} Bolasco P. Infrequent dialysis: a different strategy to incremental dialysis. *Kidney Int Rep.* 2018;3:762–763.