CPE Dietary Management of Incremental Transition to Dialysis Therapy: Once-Weekly Hemodialysis Combined With Low-Protein Diet

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Initiation of thrice-weekly hemodialysis often results in a rapid loss of residual kidney function (RKF) including reduction in urine output. Preserving RKF longer is associated with better outcomes including greater survival in dialysis patients. An alternative approach aimed at preserving RKF is an incremental transition with less frequent hemodialysis sessions at the beginning with gradual increase in hemodialysis frequency over months. In addition to favorable clinical and economic implications, an incremental transition would also enhance a less stressful adaptation of the patient to dialysis therapy. The current guidelines provide only limited recommendations for incremental hemodialysis approach, whereas the potential role of nutritional management of newly transitioned hemodialysis patients is largely overlooked. We have reviewed previous reports and case studies of once-weekly hemodialysis treatment combined with low-protein, low-phosphorus, and normal-to-high-energy diet especially for nondialysis days, whereas on dialysis days, high protein can be provided. Such an adaptive dietary regimen may elicit more favorable outcomes including better preserved RKF, lower β2-microglobulin levels, improved phosphorus control, and lower doses of erythropoiesis-stimulating agents. Clinical and nutritional status and RKF should be closely monitored throughout the transition to once and then twice-weekly regimen and eventually thrice-weekly hemodialysis. Further studies are needed to verify the long-term safety and implications of this approach to dialysis transition.

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Introduction

THE TIMING OF transition to renal replacement therapy in form of maintenance hemodialysis is at the center of a long-standing debate surrounding the care of patients with advanced chronic kidney disease (CKD). Criteria suggested by the KDOQI guidelines in 2002, based on an estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2, have proved scarcely reliable, particularly because many patients in the United States initiate dialysis therapy with an eGFR >15 and as high as 25 mL/min/1.73 m^2 body surface area (BSA).[1] The IDEAL study [2] demonstrated how "earlier" initiation of dialysis (GFR 10-15 mL/min) was of no benefit compared to "later" dialysis initiation (GFR 5-7 mL/min). Moreover, during the first several months of dialysis treatment, mortality rates are exceptionally high,[3] particularly in the elderly and patients with major or multiple comorbidities.

Transition to dialysis accelerates on transition to dialysis, an accelerated loss of residual kidney function (RKF) including drop in urine output often ensues especially with conventional (thrice weekly) hemodialysis regimen.[4,5] Although it is generally believed that peritoneal dialysis preserves RKF longer than hemodialysis, a recent European study by the NECOSAD group showed similar rates of loss of RKF in both peritoneal dialysis and hemodialysis patients.[6] Evidence suggests that the rapid loss of RKF is an unfavorable prognostic factor and may contribute to the high mortality rates observed over the initial months of dialysis therapy.[7-9] Therefore, every effort should be made to preserve RKF for longer period of time.[10]

Current guidelines recommend transition to renal replacement therapy when GFR drops below 6 mL/min/1.73m^2BSA or even sooner (6-15 mL/min/1.73m^2BSA) if uremia or its complications are more severe.[10,11] Because low-protein diet is often used to slow the rate of CKD progression before transition to dialysis and to attenuate uremic complications, restricted intake of dietary protein according

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to the level of the RKF may be continued even after the transition to dialysis as an effective means of attenuating uremic symptoms or complications that may largely originate from higher dietary proteins. For this reason, we believe that a relatively low-protein intake should be the mainstay of nutritional management during the transition phase to dialysis therapy. Indeed, restricted protein intake may help delay not only initiation of dialysis but also need for more frequent hemodialysis therapy.[12,13] Indeed, evidence suggests that in patients older than 70 years with stage 5 CKD and a median RKF of 4.5 mL/min/1.73 m^2BSA, conservative management of CKD by means of diet provides a feasible alternative to dialysis therapy and may result in improved survival and lower hospitalization.[14] However, the optimal level of protein intake in patients with stage 5 CKD who are about to transition to dialysis remains to be determined.[12] In these patients, dietary protein and energy intake should be carefully monitored to avoid excessive protein catabolism and protein-energy wasting.[15]

Evidence suggests that correct implementation of the nutritional regimen with an appropriate protein and energy intake may reduce the need for a conventional dialysis in particular, in motivated patients who comply with dietary instructions. In the 80s and 90s, Mitch and Sapir,[16] Giovannetti et al.,[17] and Locatelli et al.[18] proposed a very low–protein diet (~0.3 g/kg/day) supplemented with essential amino acids and ketoacids, in combination with only once-weekly hemodialysis. The rationale behind this was to ensure an adequate metabolic control of the patients by reducing generation of uremic toxins upstream and providing some dialytic purification downstream, while preserving RKF longer by avoiding the need for ultrafiltration given that more frequent dialysis could worsen renal perfusion.

The above concept served as a forerunner of the incremental dialysis program, which then became a common practice in the setting of peritoneal dialysis, in that dialysis dose is tailored according to gradually increasing need for higher clearance.[19,20] Whereas the importance of preserving RKF and adjusting hemodialysis dose on this basis has been well recognized, this approach has rarely been practiced. Recently, Kalantar-Zadehet al.[21] proposed a twice-weekly hemodialysis schedule as a model for commencing dialysis in the presence of substantial RKF, that is, Kru > 3 mL/min. Whereas twice-weekly hemodialysis is used rarely in the United States and many other industrialized nations, in this review article we have expanded the mandate beyond a twice-weekly hemodialysis as the only possible approach to infrequent or incremental hemodialysis by proposing once-weekly hemodialysis as the initial step.[22] We have also examined data that support an alternative strategy that includes once-weekly hemodialysis combined with a low-protein low-phosphorus diet as a more promoting infrequent/incremental hemodialysis, at least in selected groups of patients.

Infrequent Hemodialysis

Twice-weekly hemodialysis, although largely overlooked in literature and poorly implemented in clinical practice in Western countries,[23] can be beneficial in the presence of a substantial RKF. This has recently been revisited by Kalantar-Zadeh et al[21,22] who proposed the concept of incremental transitioning to hemodialysis as opposed to abrupt initiation of thrice-weekly hemodialysis. This concept was first proposed by Casino[24] in 2010 who defined the choice of twice-weekly hemodialysis as a "grey area" on initiating renal replacement therapy. A recent critical review of literature by Rhee et al[25] suggested that initiation with a twice-weekly treatment schedule and a subsequent incremental increase in frequency over time may optimize patient survival.

One of the main aims of the incremental dialysis program is the preservation of RKF, as recently shown by Zhang et al.[26] Indeed, faster loss of RKF via twice-weekly or more frequent hemodialysis poses an adverse prognostic factor for both morbidity and mortality of patients[9]; however, the clinical importance of RKF has long remained underappreciated by nephrologists. Even a moderately low RKF may be good enough to increase clearance of the larger (middle) molecules including β-2 microglobulin, which common dialyzers frequently fail to remove.[8] Fortunately, most recently the potential advantages of the incremental dialysis approach on preservation of RKF appear to be more frequently acknowledged, and the heightened interest in this approach may be further facilitated by the use of highly biocompatible membranes.[7,27] However, a hemodialysis frequency of less than three sessions per week is rarely prescribed in Europe, currently only 5.2% of all patients in Europe,[23] and even less so in the United States, probably <1%,[25] despite many reported advantages including longer RKF preservation and lower patient care burden.[21] In contrast to Europe and the United States, a recent study reported that 26% of the Chinese dialysis population are treated using a twice-weekly hemodialysis schedule,[26] which may be the result of socioeconomic conditions, including less access to dialysis therapy and inadequate availability of resources.

It is important to note that available data show no significant differences in protein nitrogen appearance, an indicator of dietary protein intake, between twice- and thrice-weekly hemodialysis regimens (1.1 g/kg/day for both).[26] Conversely, data from the Chinese Dialysis Outcomes and Practice Study reported inadequate levels of estimated nPCR in both twice-weekly and thrice-weekly dialysis.[27] However, as underlined previously, this aspect may be influenced by socioeconomic status, including inadequate nutrition or inappropriate dietary restrictions among those who were assigned to less frequent hemodialysis. Most studies on twice-weekly hemodialysis have rarely reported data on dietary

prescription of such patients. It should therefore be assumed that the prescribed diet is probably similar to that recommended for thrice-weekly hemodialysis, that is, a relatively high-protein intake of 1.2 to 1.4 g/kg/day, in line of the Kidney Disease Outcomes Quality Initiative and other relevant guidelines.[28]

In our quest for most appropriate dietary regimen for twice-weekly hemodialysis patients, use of a low-protein diet on nondialysis days combined with a free to high-protein diet on the dialysis days may raise several potential concerns relate to dietary adequacy. By adopting a low-protein diet on nondialysis days, we believe that patient's nitrogen balance is maintained due to adaptation of protein turnover, given a decrease in exogenous and endogenous proteins and amino acid breakdown on nondialysis days. This adaptation can be safely implemented provided there is adequate provision of essential amino acids and energy intake, and as long as metabolic acidosis is corrected.[29] Indeed, protein catabolism may be affected by protein intake per se, in that high-protein intake may induce a higher protein catabolism and higher turnover rate, and vice versa. Indeed, a high protein–rich diet is often recommended to lose weight. However, too frequent changes in protein intake may, for example, from dialysis to nondialysis days in twice- to thrice-weekly hemodialysis patients may prevent the said adaptation of the protein metabolism to the reduced intake on nondialysis days by decreasing protein catabolism, hence leading to a higher risk of negative nitrogen balance on low-protein diet days, with potential high risk of protein-energy wasting. Nevertheless, it is

Table 1. Different Feature Recommendations Between Twice-Weekly Dialysis and CDDP

Twice-Weekly Dialysis [21]	CDDP
1) Residual kidney function 5-10 mL/min/1.73 urine output >0.5 L/	1) Residual kidney function 5-10 mL/min/1.73 and urine output >0.8-1.0 L/day
2) No signs of water retention or responsive to diuretic therapy; fluid interdialytic gain <5% of ideal dry weight	2) No signs of water retention or responsive to diuretic therapy; fluid interdialytic gain <5% of ideal dry weight
3) Limited or readily manageable cardiovascular or pulmonary symptom	3) Limited or readily manageable cardiovascular or pulmonary symptoms
4) Suitable larger body size relative to residual kidney function	4) Excluded patients with BMI >35
5) Infrequent and readily manageable hyperkalemia (>5.5 mEq/L) and/or hyperphosphatemia (P > 5.5 mg/dL)	5) Infrequent and readily manageable hyperkalemia (>5.5 mEq/L) and/or hyperphosphatemia (P > 5.5 mg/dL)
6) Good nutritional status without florid hypercatabolism	6) Good nutritional status without any signs of hypercatabolism; adherence to nutritional therapy: low-protein (0.6 g/kg/day), low-phosphorus, high energy diet
7) Lack of profound anemia (Hb > 8) and appropriate responsiveness to anemia therapy	7) Mild anemia (Hb > 9-10) and appropriate responsiveness to anemia therapy
8) Infrequent hospitalization and easily manageable comorbid conditions	8) Infrequent hospitalization and easily manageable comorbid conditions
9) Satisfactory health-related quality of life	9) Satisfactory health-related quality of life
	10) Good dialytic adequacy: eqKt/V ≥ 1.2, session duration ≥ 4 hrs
Implementation Strategies	**Implementation Strategies**
To initiate and maintain 2xW/HD, the patient should meet first criteria plus 5 of 9 of other criteria	To initiate and maintain 1xW/HD, the patient should meet all criteria
Examine these criteria every months	Checking these criteria every week; twice-monthly calculating urea nitrogen appearance
Consider transition from 2X/w to 3X/W HD regimen in case of oligoanuria, malnutrition signs, and deteriorating general health	Consider immediately transition from 1X/W to 2-3X/W HD regimen in case of oligoanuria or malnutrition signs or general health deterioration
	Free acetate dialysate, synthetic membranes

BMI, body mass index; CDDP, Combined Diet Dialysis Program.

Table 2. List of Studies Relating to Once-Weekly Hemodialysis (OWHD) Combined With Low-Protein Diet

Specific Studies	Study Design	n. Patients on OWHD Plus Diet	Age, y	GFR at Start (mL/min/1.73 sm)	Protein Prescription (g/kg/day) and Supplementation, on Nondialysis Days	Energy Intake Prescription (kcal/kg/day)
Mitch WE et al (1981)	No control group	7	45.0 ± ?	1.86 ± 0.81	0.4 plus EAA	34.3
Morelli E et al (1987)	No control group	17	48.7 ± 11.6	4.09 ± 0.9	0.3 plus EAA + KA	35
Locatelli F et al (1998)	No control group	69	62.9 ± 11.1	2.45 ± 0.94	0.4 plus EAA + KA	40
Caria S et al (2014)	No randomized control group	38	64.5 ± 13.2	7.8 ± 1.9	0.6 without external supplement	30-35

EAA, essential amino acids; GFA, glomerular filtration rate; KA, ketoanalogues; OWHD, once-weekly hemodialysis.

possible that the malnutrition associated with low-protein diet in such patients is the result of low energy intake, particularly because many CKD patients may fail to follow the prescribed energy intake due to scarce palatability of the diet or other restrictions. Table 1 shows the different features required to include patients in a once-a-week hemodialysis program plus low-protein diet compared to a twice-a-week hemodialysis program according to the suggestions by Kalantar-Zadeh and Casino.[22]

Combined Dialysis Diet Programs

Because incremental dialysis requires a more careful evaluation of clinical status and RKF, the preparation should start in the predialysis phase and before transition to dialysis therapy. Patients identified should have an RKF that has a clearance equivalent to at least two hemodialysis sessions a week to prevent complications related to water and salt retention or to uremia.

Numerous uremic toxins including protein bound toxins have a suboptimal clearance by any dialysis methods. Indeed, only a small portion (approx. 10%) of protein bound uremic toxins is eliminated by a high-flux dialysis membrane. The renal glomerulus maintains the ability to eliminate molecules with a molecular weight of approx. 60,000 Da, and once-weekly hemodialysis, although considered a bridging treatment to twice- and thrice-weekly sessions, may, combined with a low-protein diet, delay progression to thrice-weekly dialysis.

The rationale underlying use of once-weekly rather than twice-weekly hemodialysis on transition to dialysis therapy is that a combined nutritional management strategy will enhance this regimen. A reduced frequency of depurative dialysis is compensated by a reduced load of nitrogen, phosphorus, toxins, acids, and so forth as well as by preservation of RKF. To this end, once-weekly hemodialysis should be better viewed as a continuation of conservative management that is aimed at delaying the need for more frequent dialysis sessions that would more rapidly result in loss of RKF and oligoanuria. Tailored nutritional management may represent a valuable tool in reducing the need for more frequent hemodialysis, thus acting as a more gentle and gradual form of transition to thrice-weekly hemodialysis when needed.

The KDOQI 1997 guidelines for peritoneal dialysis suggested a weekly Kt/V > 2.0 as the target goal, corresponding to a GFR of 10 mL/min. The most recently recommended Kt/V values are based on patients allowed access to a free dietary regimen, usually with a high-protein content. The dialysis dose required is assessed on the basis of the uremic toxins and other molecules (i.e., phosphate, fixed acids, and so forth) generated and retained as the consequence of a high-protein diet.

If the generation of the endogenous end products of amino acids is reduced by consuming a lower protein diet, then what would be the actual function of dialysis therapy even as infrequent as once-weekly? There is no simple answer to this question, but we believe that in the presence of a mitigated catabolic state less frequent dialysis is enough due to the fact that most solutes and toxins retained are derived from dietary protein intake. In other words, depurative adequacy should correspond to the level of solute and toxin retention. To that end findings obtained in the IDEAL study confirmed a similar clinical observation and practice, namely that dialysis commenced soon after onset of uremic signs and symptoms neither endanger nor improved the patient. Hence, initiation of dialysis is not solely based on RKF, but also, more importantly, according to uremic signs and symptoms, and the latter can be affected by pharmacological and nutritional interventions.

Decisions about the dose and frequency of hemodialysis are largely dependent on the dietary habits of the patient and his/her cultural background. Therefore, in contrast to twice- and thrice-weekly hemodialysis, a stricter "Combined Diet Dialysis Program" (CDDP) should be implemented with once-weekly hemodialysis, along with more conservative dietary restrictions compared to the recommendations set forth by Kalantar-Zadeh and Casino.[22]

An appropriate clinical and metabolic balance may be achieved through restricted dietary protein intake even in the presence of a low RKF. The effect of dietary protein restriction on slowing down GFR decline is rather small,[30] whereas low-protein diet provides a significant advantage in delaying dialysis initiation by controlling uremic signs

and symptoms. Hence, appropriate nutritional therapy may contribute to reducing the need for dialysis both by delaying dialysis initiation and reducing the frequency of hemodialysis treatments. To our knowledge, very few studies have investigated the effectiveness of programs combining a low-protein diet with once-weekly hemodialysis (Table 2). In Italy, in the 1980s and 1990s, Morelli et al.[17] and Locatelli et al.[18] proposed the so-called "Integrated Dialysis Diet Program," namely a very low-protein diet in range of 0.3 to 0.4 g/kg/day supplemented with essential amino acids and/or ketoanalogues for 6 days a week, together with a once-weekly hemodialysis treatment session.[18] Both studies included patients with very low RKF: In the study by Giovanetti, eGFR was 4.1 ± 0.9 mL/min × 1.73 BSA,[17] whereas in the study by Locatelli et al,[18] RKF was 2.54 ± 0.94 mL/min. A free (unrestricted) protein diet was prescribed on the day of dialysis treatment. The free diet on dialysis day was found to exert a positive effect on psychological status, breaking the monotony from the limited food choices related to low-protein diet and consequent dietary fatigue on nondialysis days of the week.[31] In the study by Locatelli et al.,[18] dialysate composition was of paramount importance considering the very low level of RKF and the finding of several anuric patients during follow-up. To avoid fluid retention, sodium concentration in dialysate was lowered from 137 ± 3 down to 134 ± 3 mmol/L. Moreover, once-weekly dialysis schedule prevented more frequent episodes of intradialytic hypotension and thus mitigated negative impact on cardiovascular and renal flows; it is worthy of mention that the IDDP program was hindered by the development of use of acetate in dialysate, potentially resulting in low blood pressure. The rationale underlying this approach by Locatelli et al. was to balance nitrogen input and output to promote a good nutritional status. Although this dietary regimen combined with once-weekly hemodialysis produced a series of positive clinical, psychological, and economic effects, a high number of dropouts were reported largely due to difficulties in adhering to the strict dietary regimen, consequent risk of malnutrition related to reduced caloric intake, and the scarce palatability of the very low-protein diet, leading to the conclusion that this treatment was not suitable for a population-based approach but may, however, represented a viable option for use in carefully selected, strongly motivated patients.[32]

Learning from these past experiences and with the aim of improving patient adherence, Caria et al.[33] proposed a new study entitled "Combined Diet Dialysis Program." When compared with studies conducted in the 1980s and 90s,[17,18] the contemporary CDDP study introduced a less strict protein restriction (0.6/g/kg/day, compared to 0.3-0.4 g/kg/day in older studies) on nondialysis days. This moderately low-protein diet still entails a low-phosphorus content, while ensuring adequately high dietary energy intake. It is noteworthy that currently protein-free products (constituted by carbohydrates and substantially free of nitrogen, phosphorus, and potassium and low in sodium compared to regular food) are much more palatable, with a far wider range of commercially available options and recipes.[34] Unrestricted dietary protein intake on the day of dialysis was mandatory in this program to compensate for increased nitrogen demand that is caused by loss of amino acids through dialysis and tendency toward hypercatabolism [35] during the dialysis session.

In summary, the difference between the IDDP [18] and CDDP [33] programs relate to the following points: (1) The IDDP study recruited patients with a significantly lower RKF (IDDP, 2.54 versus CDDP, 7.8 ± 1.9 mL/min/1.73 m^2); therefore, the level of uremic milieu observed in patients enrolled in the study by Locatelli et al. was evidently poorer compared to the diet of 0.6 g/kg/day/provided on the CDDP regimen of Caria. (2) In view of the difference in RKF, a larger number of patients dropped out of the IDDP program due to the malnutrition-related concerns, whereas no patients dropped out of the CDDP study despite similar concerns, and dietary compliance among the patients recruited by Caria et al was enhanced due to a more varied and less vegan diet. (3) Patients adhering to the CDDP program displayed no uremia-associated symptoms, and no episodes of fluid overload of pulmonary edema were presented; no complaints of neuropathy were reported possibly due to a better RKF.

It is important to note that CDDP was only suitable for a highly selected and exceptionally motivated patients who had adhered to allow dietary sodium intake (<100-150 mEq/die). Sodium and calcium concentration in the dialysate bath were 138 mmol/L and 1.5 mmol/L, respectively, with CDDP patients displaying no sodium or fluid retention and/or hypercalcemia nor any significant parathyroid

Table 3. Schematic Differences Between the Combined Diet Dialysis Program (CDDP), the Twice-Weekly, and Three-Weekly Hemodialysis Schedules Relative Level of Impact on the Item: + Low, ++ Middle, +++ High

Properties	CDDP	Twice a Week	Thrice a Week
Nutritional support need	+++	+	+
Protein intake, g/kg/day	0.6	0.8-1.2 (?)	>1.2
Energy intake, kcal/kg/day	30-35	30-35	30-35
vascular access stress	+	++	+++
Protection of residual kidney function	+++	+/++	—
Accommodation of dialysis schedule	+/++	++/+++	+/++
Cost burden	+	++	+++

LPD, low-protein diet.

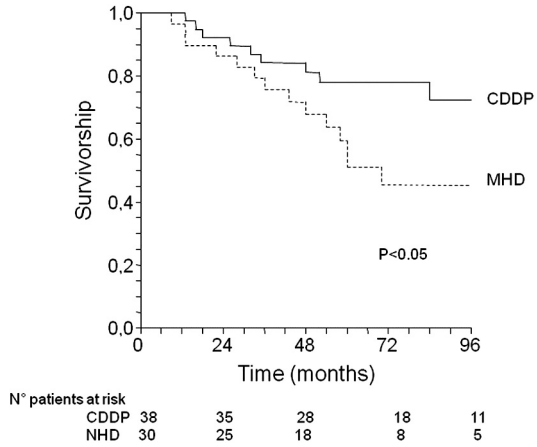

Figure 1. Survival between patients on mainstream thrice weekly hemodialysis and patients on CDDP. CDDP, Combined Diet Dialysis Program.

hormone changes. This novel CDDP approach included not only patients with less impaired RKF and good adherence to dietary prescriptions, but also benefited from recent advancements in dialysis techniques, including the highly biocompatible high-flux dialysis membranes and improved water and dialysate quality. Another advantage in Italy is that currently marketed aproteic products are more tasty and are essential components of the Mediterranean cuisine.

An extended follow-up analysis of patients enrolled in the study by Caria et al[33] provided evidence of a lower mortality in the 38 patients on CDDP compared to the 30 patients who had started dialysis three times a week by the end of the 96-month follow-up period with comparable findings at baseline for a series of prognostic factors (Table 3).[33] Figure 1 shows the overall survival of patients assigned to CDDP and of patients who started hemodialysis on a thrice-weekly schedule. However, the observed mortality rate was significantly lower for patients who chose CDDP in comparison with that of patients who started HD on a thrice-weekly schedule (Fig. 1).

Follow-up analysis demonstrated how the composite end point defined as the transition to twice- or thrice-weekly or death had been reached in 16% of patients at 12 months, 53% at 18 months, and 68% at 24 months, whereas 16% of patients were still undergoing treatment after 36 months (Fig. 2).

Other positive aspects of CDDP included reduced rate of hospitalization, lower rise in β2-microglobulin levels, better control of serum phosphorus (and less need for phosphorus binders), and better anemia management with less need for erythropoiesis-stimulating agents [33] (Fig. 3).

In these studies, careful clinical and nutritional monitoring was essential to ensure patient safety and success of the program. These results may also translate into consistent and considerable cost savings, mainly due to the reduced number of hemodialysis treatments, although possibly over a limited period of time. The cost incurred in once-weekly hemodialysis treatment is almost 2/3 lower compared to thrice-weekly treatment. Moreover, this important cost reduction is accompanied by a marked decrease in indirect costs, including lower morbidity, lower number of days in hospital, and reduced need for transportation of patients from their homes to the dialysis center.[33]

It is important to note that patients' quality of life may benefit from such a conservative dialysis program due to the fact that patients are only required to attend dialysis sessions once instead of three times a week. Similar to other programs, a crucial aspect of CDDP is patient adherence

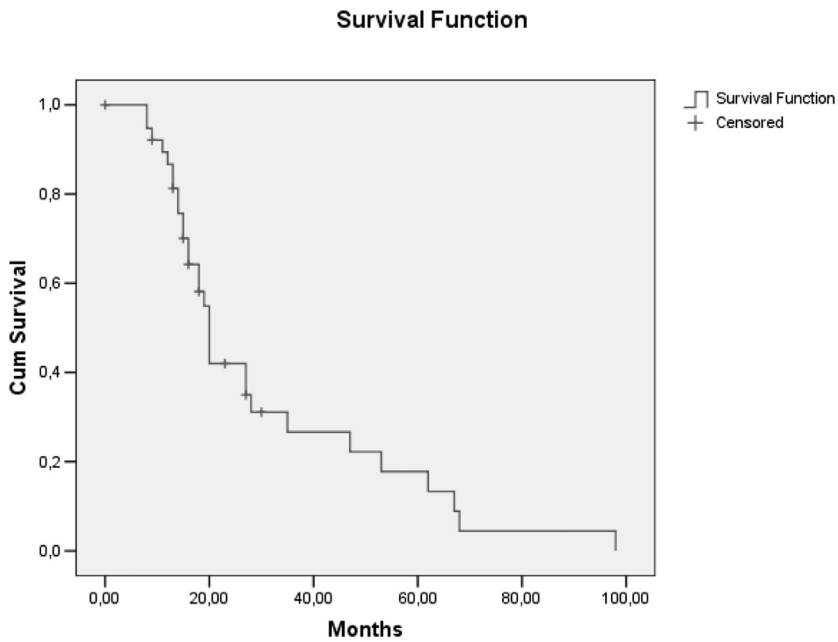

Figure 2. Cumulative survival of the CDDP treatment: the composite end point was defined as the transition to twice- or thrice-weekly dialysis or death (Caria et al.[33]). CDDP, Combined Diet Dialysis Program.

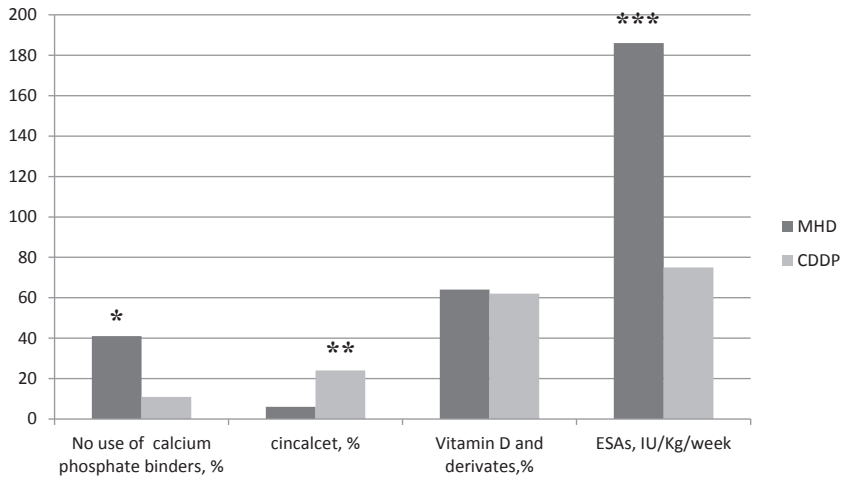

Figure 3. Prevalence of patients requiring noncalcium phosphate binders. Cinacalcet vitamin D and derivates % and ESAs requirement between CDDP group versus MHD group after 12 months/Caria et al (*) $P < .03$, (**) $P < .002$, and (***) $P < .001$. CDDP, Combined Diet Dialysis Program; ESAs, Erythopoyetin Stimulating Agents; MHD, Mainstream thrice weekly Hemodialysis.

to the dietary regimen. The most frequent reasons for dropping out of CDDP in the study by Caria et al were as follows: (1) GFR falling below 3 mL/min/1.73mq, (2) lack of dietary adherence, (3) excessive interdialytic weight gain with sodium and water retention unresponsive to diuretics, and (4) high blood pressure recurring.

As a practical application, it is strongly recommended that RKF and compliance are assessed before enrolling a patient into an incremental dialysis program based on an initial once-weekly dialysis combined with a low-protein/normal calorie diet of 0.6 g/kg/day, which is usually well accepted by most patients.

Conclusions

Initiation of dialysis treatment on transitioning from nondialysis-dependent CKD to end-stage renal disease represents an exceptionally critical phase in the clinical and psychosocial status of patients. Careful clinical, nutritional, and psychosocial assessment should be carried out during this transition. When transition starts with the abrupt onset of a thrice-weekly hemodialysis schedule, this may result in the manifestation of negative prognostic factors, including rapid loss of RKF and drop in urine output.

A lower frequency in hemodialysis schedule will lead to a slower loss of RKF. Unfortunately, protocols providing less frequent and incremental dialysis are not widely applied in many industrialized nations, where even twice-weekly hemodialysis schedules are rarely practiced, and a once-weekly hemodialysis session would likely be considered high risk or even malpractice. Similarly, in some countries, including North America, a low-protein diet is not suggested to CKD patients due to concerns over protein-energy malnutrition and wasting.

Therefore, at the current state of the art, it would seem to be an arduous task to reach a consensus on establishing an ideal GFR threshold beyond which a conventional dialysis regime should be prescribed; for this reason, we propose adopting an incremental transition featuring less frequent dialysis schedules and a low-protein diet. However, the above-discussed once-weekly hemodialysis programs associated with a moderate to severe dietary protein restriction could be implemented on the basis of level of RKF and appropriate patient motivation and adherence.

Recent studies conducted in the elderly population reveal a paradoxically higher rate of mortality following early initiation of conventional dialysis frequency, particularly during the initial months of thrice-weekly hemodialysis. It is imperative therefore that alternative measures of transition should be adopted.[35-37]

The Italian model, including once-weekly hemodialysis treatment combined with a low-protein diet throughout the remaining 6 nondialysis days, has yielded promising results, including positive short- and long-term outcomes. The less frequent hemodialysis schedule may prove to be particularly useful in the elderly, as adherence to a less restricted dietary regimen may be better accepted in this population, and a reduced burden of attending frequent hemodialysis sessions would likely result in improved patient satisfaction and lesser logistical challenges. A more gentle approach with less frequent dialysis sessions may lead to a reduction in the number of patients (particularly among the elderly) who would have refused to initiate thrice-weekly hemodialysis, deeming the schedule to be too challenging.

Further to the previously mentioned clinical and economic motives, an infrequent/incremental approach to maintenance dialysis would likely contribute to a better psychosocial and life adaptation of patients compared to the more dramatic change that use of a conventional frequent dialysis schedule would entail.

In spite of the benefits illustrated previously, even a twice-weekly hemodialysis regimen is often viewed as unfeasible in many industrialized nations, although indeed use of a similar frequency may not represent the only option for an infrequent/incremental approach to dialysis initiation. In motivated patients with better adherence to a low-

protein dietary regimen, a combination with once-weekly hemodialysis may represent a valid alternative. Careful clinical monitoring and appropriate dietary interventions are essential for the safety and optimization of infrequent hemodialysis schedules. This alternative approach is based mainly on the nutritional procedures, but the hemodialysis moment is essential to verify the patient outcome but the available experiences need to be confirmed in a larger cohort of patients and controlled trials.

Practical Application

It is strongly recommended that Renal Residual Kidney Function and compliance are assessed prior to enrolling a patient into an incremental dialysis program based on an initial once-weekly dialysis combined with a low protein/normal calorie diet of 0.6 g/Kg/day/, which is usually well accepted by most patients.

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