

Is Renal Function Recovery and Discontinuation of Long Term Hemodialysis Possible in Patients with Presumed End Stage Kidney Disease? The Role of Toprak's Kidney Care

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Abstract

End stage kidney disease patients who started on hemodialysis are considered to need hemodialysis forever, unless a kidney transplantation is performed. Patients with presumed end stage kidney disease that require hemodialysis over 90 days have very little chance of recovering renal function to remove from dialysis. However, according to recent studies and largescale registries, up to 8% of patients with end stage kidney disease receiving hemodialysis recover some degree of kidney function allowing discontinuation of dialysis. Toprak's Kidney Care is one of the kidney care program which allows to recover kidney functions in end stage kidney disease patients.

Keywords: Dialysis discontinuation; End stage kidney disease; Renal function recovery; Toprak's kidney care

Abbreviations: ESKD: End Stage Kidney Disease; CKD: Chronic Kidney Disease; RFR: Renal Function Recovery; AKI: Acute Kidney Injury

A relatively new definition in nephrology practice: "Renal Function Recovery" (RFR)

A consensus statement for definitions of RFR in End Stage Kidney Disease (ESKD) patients and strategies for the management of patients with RFR are not currently available. Patients with Acute Kidney Injury (AKI) have significantly higher rates of RFR [1-3]. However, RFR in Chronic Kidney Disease (CKD) patients requiring long-term dialysis is uncommon [4-7]. In normal condition, it is impossible for ESKD patients that kidney function to reach a level to discontinuation of dialysis. Although ESKD is presumed to describe an irreversible loss of kidney function, some of the patients requiring maintenance dialysis experience enough recovery of their kidney function to come off dialysis. RFR in stage 5 CKD patients is relatively a new terminology that we have encountered more recently in nephrology practice. In most studies, RFR defined as the discontinuation of dialysis after 3 months of renal replacement therapy, and the development of sufficient kidney

function allowing for complete discontinuation of dialysis [8-10]. Three months is considered to be a sufficient time for kidney regeneration, and for correcting the possible aggravating factors.

What is the incidence of RFR in ESKD patients?

Numerous case reports and registries are citing delayed RFR in dialysis dependent patients. According to recent studies and largescale registries, 0.3% to 8% of patients with ESKD receiving dialysis recover some degree of kidney function allowing the discontinuation of dialysis for a varying period of time and even permanently [3-8]. RFR could occur even after long time on hemodialysis [11-14].

Is there any criteria for cessation of dialysis secondary to RFR?

There are no standart criteria, established benchmarks or indicators for the cessation of dialysis secondary to RFR [9-13]. It is extremely dangerous and highly responsible situation to decide to stop chronic dialysis treatment in an ESKD patient because of the risk of death due to hyperpotasemia and pulmonary edema [15,16].

What should we do when we detect RFR

There are guidelines for the initiation of hemodialysis and

for the care of patients on maintenance dialysis, but little is known about the RFR in dialysis patients and there is a lack of a guideline what should we do when we detect RFR [9,17]. It is extremely important and vital decision to stop dialysis treatment in an ESKD patient because of the risk of death. This imposes a huge responsibility on nephrologist who decide to stop dialysis. My personal advice is before making the decision to remove from dialysis secondary to RFR, for safety of our patient we should hospitalize the patients in nephrology department for close monitoring. In many published cases, authors proposed a schedule for a gradual hemodialysis dose decrease in RFR patients [4,5,9,11].

What are the predictors of RFR in ESKD patients?

The possibility of renal function recovery in chronic hemodialysis patients should not be overlooked. Patient and caregiver educations, healthy lifestyle changes, well-ordered diet and exercise, giving correct medications in correct doses, improving the moral and motivation of the patient and their caregivers, fluid status regulation, preserving residual kidney function, nephroprotective alternative medicines all have potential roles in RFR [18-20]. All this factors are the components of a special kidney care which name is "Toprak's Kidney Care" [21]. Toprak's Kidney Care should be considered in RFR and dialysis discontinuation in long-term hemodialysis ESKD patients who have residual kidney function to avoid unnecessary, complicated and expensive dialysis. RFR is less likely for patients who is in older age [8,9,13], have a nonwhite race [6], long duration of ESKD [9], and who did receive over one year care from a nephrologist prior to starting dialysis [4,8]. The ESKD patients with sustained RFR had high incidence of early start of dialysis [9], unplanned emergent dialysis start in hospital [3,12], lack of prior outpatient nephrology evaluation within 1 year [4,7,22], absence of heart failure [2,4], resuming low-protein diets in dialysis [18] and lack of permanent vascular access at the time of initiation of hemodialysis [6,7], patients with preserved diuresis [7], immunosuppressive treatment in autoimmune diseases [11], heart failure patients supported by left ventricular assist device [23], starting on dialysis with low serum albumin level [9,24], preadmission high hemoglobin levels [2], and chronic liver disease [2], the dialysis modality [8], dysmetabolic disease [18], region where the patient live [3], and ethnicity such as Maori and Pacific Islanders, European descent, Polynesian, Aboriginal, Torres Straight Island descent have also role in RFR [8].

Have the underlying CKD etiologies role in RFR?

The most frequent diagnoses among patients who have RFR were acute tubular necrosis [6,7], chronic interstitial nephritis [8,12], focal segmental glomerulosclerosis [13], membranous glomerulopathy [11,25], post-infectious and rapidly progressive glomerulonephritis [13], renovascular diseases [17,26], hypertension [7,11,12,27], analgesic nephropathy [28], atheroembolism [9,13], revascularization of renal artery stenosis with percutaneous angioplasty [26], bilateral renal vein thrombosis treated with thrombectomy and thrombolysis [25], lack of kidney biopsy [13], obstructive

uropathies [8,17], HIV associated nephropathy [13], vasculitis [29,30], multiple myeloma [31], using bortezomib-based triplets in multiple myeloma, thrombotic microangiopathy [31], autoimmune diseases [5,11,29], secondary oxalosis [32], post partum renal failure [33], IgA nephropathy [34], heroin [35], typical and atypical hemolytic uremic syndrome [30,36,37], long-term eculizumab use in hemolytic uremic syndrome [37], and intravenous cyclophosphamide therapy over 3 months in antineutrophil cytoplasmic antibody-associated glomerulonephritis [29]. The lowest RFR rates in CKD patients are those who have diabetic nephropathy [8], autosomal dominant polycystic kidney disease [8,9], preexisting CKD [9], and who developed ESRD because of slowly progressive CKD [9].

Is there any time limit for the RFR?

Over 50% of patients with AKI initiated on long-term hemodialysis recover kidney function within 6 months [2,15,38]. However, the recover of kidney function time can be extended up to 7 years in hemolytic uremic syndrome patients [30].

What are the barriers front of the RFR in clinical practice?

There are too many items to collect under this title. Some of them are lack of the knowledge of RFR, defence to discontinue the dialysis even RFR occurred, false believe that ESRD patients can never discontinue the dialysis, the possibility of kidney function improvement not considering by attending nephrologists particularly when patients transfer to a new outpatient center, lack of extra effort to obtain medical records surrounding dialysis initiation, lack of optimal care for dialysis requiring AKI patients who continue to require dialysis after hospital discharge, no guidelines regarding monitoring of RFR in dialysis patients [4-8,10,13,17,22]. Many patients with CKD may develop AKI and get erroneously labeled to have reached ESKD, or ignored or was considered to be irreversible CKD and become dialysis dependent [4,9,13,22]. In addition, the continue to hemodialysis is accompanied by a reduction in residual kidney function and a progressive deterioration in kidney function secondary to dialysis related inflammation, decreased kidney perfusion due to ultrafiltration and hypotension [10,12,17]. Many patients that may have a potential for RFR missed because of wrong measurement of ideal dry weight, unnecessary fluid restriction, excessive use of diuretics, excessive ultrafiltration in hemodialysis, or dont monitoring the residual kidney function [3,12,19,20]. In patients with enough urine volumes and those who are symptomatic on dialysis might be a sign of RFR and we should be aware of possible RFR. Hypomagnesemia and vitamin D deficiency are not monitored in mostly hemodialysis patients. However, hypomagnesemia and vitamin D deficiency have role in progression to ESKD, accelerated loss of kidney function [39,40].

The serum urea and creatinine levels progressively decrease in RFR patients. This is an indication that kidney functions improve over time. Nevertheless, progressive decline in serum urea

and creatinine can also be understood as an indicator of poor nutritional status and reduced muscle mass and this is often attributed to inadequate dialysis by the nephrologists, and the patient therefore can be subjected to more aggressive dialysis [7,9,13,17]. Most of the ESRD patients who initiated dialysis do not receive any kidney care before starting dialysis [41]. As a nephrologist, we should give patient education conferences to our CKD patients, their relatives and caregivers and explain them almost all the things to eat and drink to the finest detail and what they need for a healthy life. We have done this by Toprak’s Kidney Care [21]. For 13 years, we held training conferences for patients with CKD and their caregivers in hospital every month, and shared them live on social media free of charge and open to the public (Figure 1). On March 5th 2020, we held our 133rd training conference. We also use local and national TV channels, outpatient clinic TV, and social media for the education of our patients. As a result we showed that the patients who were educated by this care have better survival outcomes, less need of renal replacement therapy, and also they have near to zero percent RFR. We have hundreds of ESRD patients with a glomerular filtration rate of below 5 ml/min and they can survive without any need of renal replacement therapy by following the Toprak’s Kidney Care.



Figure 1: Toprak’s Kidney Care education conferences for patients with chronic kidney disease and their caregivers that have been held every month in hospital since 2007.

What happens after dialysis discontinuation in ESRD patients who have RFR?

There is a high mortality rates and poor outcomes after RFR [42,43]. Only 45% of those who had RFR were alive and not on dialysis at 1-year postrecovery, and 19% died within a median period of 226 days [42]. The mean time without dialysis after RFR is about 1 year [13]. There are also cases that reports longer times [11,12]. Of the patients experiencing a recovery of kidney function, 32% had to resume kidney replacement therapy after a median recovery time of 19.7 months [14]. Therefore, some nephrologists are against stop chronic dialysis even when RFR does occur, because the period off dialysis tends to be short and is associated with increased mortality.

Conclusion

ESKD patients may recover kidney function and stop dialysis, even after a relatively long time on dialysis. The start of hemodialysis should not be a barrier to research the possibility of kidney recovery in patients who have enough urination. Appropriate diet, lifestyle changes, improving social and psychologic status, avoiding unnecessary medications, and volume regulation all may contributed to the recovery of kidney function. Toprak's Kidney Care may considered in the recovery of kidney function and dialysis discontinuation in patients who have residual kidney function to avoid unnecessary, complicated and expensive dialysis.

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