

## The role of residual renal function in diabetic peritoneal dialysis patients.

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### Abstract

Peritoneal dialysis (PD) is a treatment method used in home renal replacement therapy. Recently, there has been greater focus on residual renal function (RRF) in PD patients. RRF in PD patients is clinically significant, as it contributes to survival of the treatment, as well as patient mortality rates. Not only does decreased RRF cause poor management of water removal, but also increases risk of mortality as well as PD withdrawal due to over hydration. Diabetic patients are at higher risk of mortality/comorbidities and loss of RRF than patients with other diseases. Loss of RRF is the main cause of over hydration, poor quality of life (QOL), withdrawal of PD, and high mortality rate in dialysis patients; therefore, it is clinically important to maintain RRF. Control of blood pressure, inhibition of the renin-angiotensin system, decreased proteinuria, dietary intervention, avoidance of nephrotoxins, and glucose control should be considered for maintaining RRF in dialysis patients. Additionally, sarcopenia and frailty are issues of significant importance, especially in patients with end-stage renal disease (ESRD). As metabolic acidosis can be a complication of ESRD, anemia, uremia and appetite loss are side effects; loss of appetite and inflammation are also associated with mortality.

To ensure good QOL, PD survival, and low mortality risk, it is imperative to maintain RRF. Aside from the use of icodextrin or large amounts of diuretics, tolvaptan – often used at initiation of PD in patients with overhydration – may also be beneficial in maintaining RRF. RRF that is positively maintained aids in enhancing the appetite and improving malnutrition and inflammation, both of which contribute to loss of RRF. Moreover, enhanced appetite may improve QOL and prevent the possibility of sarcopenia and frailty in PD patients. In hemodialysis patients, tolvaptan also may be useful in the preservation of RRF and decreased mortality rate, as well as improved QOL.

**Keywords:** Peritoneal dialysis, Residual renal function, Tolvaptan, Sarcopenia/frailty.

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### Introduction

Diabetes mellitus (DM) is a multifactorial progressive disease associated with systemic cardiovascular complications. Comorbid cardiovascular disease is the most important prognostic factor in DM patients with end-stage renal disease (ESRD). Peritoneal dialysis (PD) is a treatment method used home renal replacement therapy. Early discontinuation of PD is often observed in end-stage renal disease, especially in patients with diabetes mellitus, because of overhydrating due to decreased residual renal function (RRF), which in turn results in a poorer prognosis. Literature indicates that more than 30% of patients withdraw from PD treatment [1,2]. Given this, RRF is a clinically significant factor in overhydration. Moreover, frailty in elderly CKD patients, particularly dialysis patients, is associated with an impaired physical performance, disability, a poorer quality of life (QOL), and reduced survival rate. Sarcopenia is the main factor for frailty. Glycemic and blood pressure control and volume control are important factors to prevent volume

overload and subsequent cardiovascular disease and death. The maintenance of RRF, as well as appetite, may prevent overhydrating, retain PD and ensure survival rate.

### RRF in Dialysis Patients

RRF in PD patients is clinically significant as it contributes to the efficacy of dialysis, a good quality of life (QOL) and decreased risk of cardiovascular disease and mortality [3-5]. Moreover, a loss of RRF may decrease the survival rate of PD patients. Analysis of the CANUSA study revealed that every 0.5 mL/min increase in GFR was associated with a 9% lower risk of death [6] and another report showed that rapid decline in RRF was an independent factor in long term mortality risk [7]. Bad glycemic and blood pressure control are also the risk factors for a decrease in RRF. Moreover, glucose sparing is useful for preventing technical failure in PD patients.

### To Preserve Preservation of RRF

Initiating PD prior to hemodialysis (HD) as a renal replacement therapy was shown to preserve RRF [3,8].

Rapid intravascular volume depletion during HD may cause a higher risk of RRF loss than that during PD, where there is no drastic change in fluid volume, thus, preserving RRF. Additionally, both dehydration and overhydration were also reported to cause RRF loss [4,9]. In addition to volume control, ACE inhibitors and/or calcium channel blockers were also said to preserve RRF with hypertension in PD patients, but not HD patients [3,4,10]. When icodextrin-based solutions were prescribed to high-transporter PD patients, ultrafiltration volume was increased; however, that caused little impact on RRF [11]. As indicated previously, RRF was maintained when icodextrin was prescribed at PD initiation [12]. We have reported that icodextrin-based solution improves glycemic and blood pressure control and attenuates left ventricular hypertrophy. Recently, incretin-based therapy, including DPP-4 inhibitors and GLP-1 analogs, has been initiated; these drugs are useful for glycemic and blood pressure control despite renal insufficiency. We have reported that liraglutide improved glycemic and blood pressure control and attenuated atherosclerosis [13]. Moreover, an excessive glucose overload may be a risk factor for overhydration and decrease of RRF subsequent to technical failure.

Recently, tolvaptan, a vasopressin-2 receptor antagonist, has been approved for volume control in patients with heart failure. We showed the effects of tolvaptan on RRF in twelve diabetic PD patients. 15 mg/day of tolvaptan for 12 months preserved RRF in 24 PD patients with heart failure and maintained cardiac function without side effect [12]. Further, tolvaptan has been shown to improve nutrition and inflammation [14]. Moreover, we showed tolvaptan improved RRF and QOL, as indicated by SF36 in PD patients (Abstract in *Kidney Week 2016*, unpublished). Iwahori also showed the effects of tolvaptan on RRF [15]. These effects of tolvaptan may be assessed in HD patients in the future.

### **Nutritional State and Sarcopenia**

Sarcopenia may impact approximately 37% of dialysis patients [16]. Sarcopenia, cardiovascular disease, and cognitive deficits, shown in dialytic patients, cause frailty. Metabolic acidosis, common with chronic kidney disease and acidemia increase intracellular protein degradation and reduce protein synthesis and bone mineralization. Additionally, metabolic acidemia induces the rapid progression of renal failure and inflammation. In some cases, a low protein diet is recommended in order to prevent acidosis or accelerated renal failure [17]. However, low protein diets may contribute to malnutrition, and around 30% of dialysis patients are categorized as lean. Further, increased prevalence of sarcopenia is thought to be associated with attenuated renal function [18] and malnutrition remains one of the major predictors of mortality in PD patients [19]. Moreover, frailty is associated with impaired physical performance, poorer QOL and reduced survival rate [20]. Underweight diabetic patients also experienced increased risk of mortality than obese patients [21]. The effects of dialysis on protein loss

may also enhance sarcopenia [22]. There was an association between dietary protein intake and urine volume. Dietary interventions designed to enhance appetite are necessary for preserving RRF and preventing sarcopenia/frailty and to that point, it is clinically important to note that tolvaptan improved both nutrition and inflammation, by way of preserving RRF [13].

### **Conclusion**

PD patients, particularly those with DM, have a high risk of cardiovascular events, poorer QOL, sarcopenia/frailty, and death. The maintenance of RRF is important for PD, especially in diabetic patients, to prevent cardiovascular events and poorer QOL, frailty, and comorbidity/morbidity. Good RRF can be achieved by ensuring a good appetite, which in turn can help to prevent sarcopenia/frailty and decrease comorbidity/mortality risk. For this purpose, treatments for consideration should be ACE inhibitors or ARBs for hypertension, incretin-based therapy for glycemic and blood pressure control, icodextrin for dialysate and tolvaptan for diuretics. Recently, the number of elderly diabetic PD patients has increased. Preserved residual renal function to attenuate the loss of appetite and physical training are important factors for preventing sarcopenia/frailty and for a better QOL and survival rate.

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