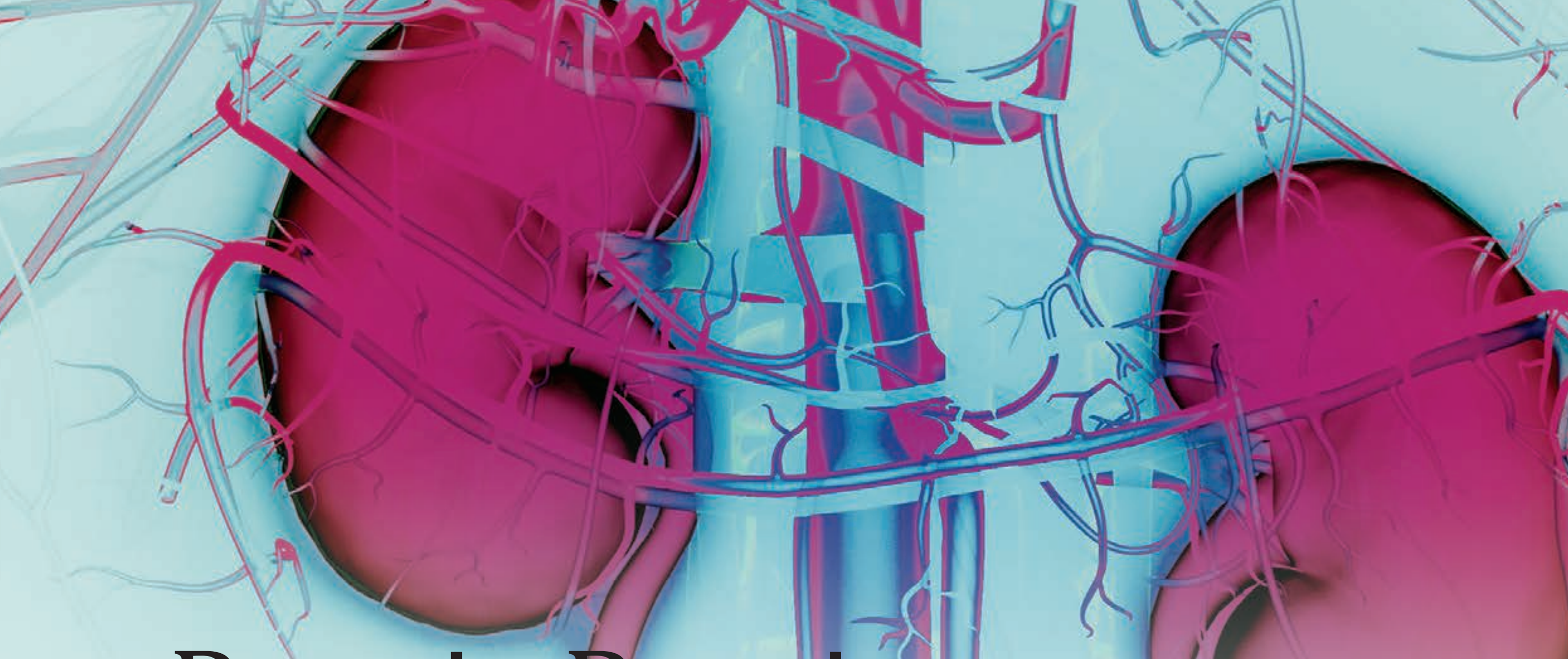

# Protein Requirements in People on Maintenance Dialysis

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Haemodialysis (HD) and peritoneal dialysis (PD) are the two forms of dialysis therapy for patients with end stage kidney disease. Dialysis is an extracorporeal treatment by which fluid and solutes – including creatinine and urea – are removed from the body. Dialysis induces inflammation, catabolism and leads to net nutritional losses, such as amino acids and protein. All these factors are likely to contribute to higher protein requirements in patients on dialysis than the general population. This article summarises the current guidelines for protein requirements in metabolically stable patients on dialysis.

## Introduction

Traditionally, patients undergoing HD go to hospitals, or satellite centres, three times a week for four hours per session – plus the time for transport and waiting times. PD is performed independently, or with assistance, at home or at work. PD can be performed several times per day every four-to-five hours – referred to as Continuous Ambulatory Peritoneal Dialysis (CAPD) – or continuously during the night, by means of a machine that makes exchanges for eight-to-10 consecutive hours – referred as Automated Peritoneal Dialysis (APD)[1] **Table 1**.

Over the past 20 years there has been increased access of hemodiafiltration (HDF), home haemodialysis (HHD), where patients are trained to self-administer HD in their own home, including nocturnal haemodialysis (NHD). There has also been a shift to present dialysis by locations as well as modalities, **Table 2**.

**Table 1: Traditional classification of dialysis treatments by modality**

| Haemodialysis (HD) | Peritoneal Dialysis (PD) |
|---|---|
| • HD in a main centre<br>• HD in a satellite unit (location is usually closer the patient's home). | • CAPD<br>• APD (peritoneal dialysis can be assisted with the help of a carer). |

**Table 2: Classification of dialysis treatments by location**

| Hospital dialysis | Home dialysis | |
|---|---|---|
| • HD/hemodiafiltration (HDF) in a main centre<br>• HD/HDF in a satellite unit | • PD:<br>- CAPD<br>- APD | • HD:<br>- Home HD (HHD)<br>- Nocturnal HD (NHD) |

## Protein requirements in maintenance dialysis

Current guidelines and protein requirements recommendations for patients on dialysis usually refer to maintenance dialysis. This is defined as a state where dialysis is provided at regular intervals in absence of infection, catabolic process, and/or acute illness. The most recent guidelines are the KDOQI 2020, which suggests – for both patients on HD and PD – a protein intake of 1.0-1.2 g/kg body weight per day is recommended to maintain a stable nutritional status.[2] There are protein recommendations for patients who are on dialysis and are metabolically stressed – such as ESPEN 2021 and Think Kidney 2021.[3, 4] Protein requirements for patients on HD and PD have not changed significantly in the past 20 years.[5] However, recommendations for HHD, NHD are lacking, and research is sparce, **Table 3**.

Dialysis is a catabolic process which influences protein metabolism and activates metabolic pathways, **Figure 1**. In addition, this catabolic state remains even after dialysis and is not corrected by simply providing more protein, indicating the need for research in this area.

## Protein requirements in haemodialysis

It is estimated that 6-12 g of amino acids are lost during each HD session.[12] Protein and amino acids losses in HD and HDF seem similar, and as a result current protein recommendation for HD have been used for patients on HDF, without distinguished nutritional guidelines.[13]

Some authors recommend a protein intake of between 1.2-1.4 g/kg body weight a day for stable patients on maintenance HD, and this can be increased to >1.5 g/kg/day in patients on HD who are hypercatabolic.[14] In addition, a transitional increase in protein intake for incremental HD has also been suggested for those patients with good residual kidney function receiving incremental dialysis.[14] However, these recommendations are based on expert options rather than patient's outcome measures.[14, 15]

Others suggest a protein intake of 1.1-1.2 g/kg/body weight/day in conjunction with an adequate energy intake.[2, 8] This is widely accepted in clinical practice as one of the main general principles of dietary counselling with patients on HD.

More than 20 years ago, Shinaberger and colleagues showed an association between normalised protein nitrogen appearance (nPNA), used to estimated protein intake, and all cause of death and cardiovascular mortality over a two-year period in a cohort of 53,933 patients on HD.[16] They showed that the best survival was associated with a nPNA between 1.0 and 1.4 g protein/kg body weight, while a nPNA less than 0.8 g or greater than 1.4 g were both associated with greater mortality.[16]

To this date, this is the reason why many guidelines refer to 1.4 g/kg/body weight being the upper limit of protein intake for a patient on maintenance HD.

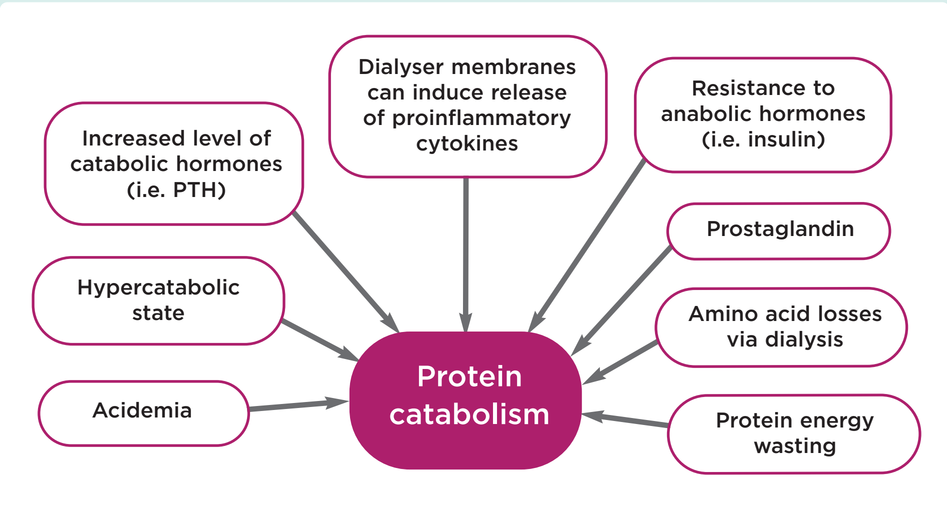
Eriguchi and colleagues showed an association between a higher protein intake and higher albumin levels and – as expected – survival was higher in patients with a high level of albumin.[17] However, these associations were based on nPNA albumin and normalised protein catabolic rate (nPCR) which were used as a surrogative to estimate protein intake and these methodologies have some limitations: such as residual kidney function, day-to-day fluctuation caused by protein intake, catabolic state and hydration status.[17]

**Table 3: Protein requirements in patients on dialysis**

(adapted from Mafrici and Armstrong-Brown 2017).[5] Values refer to g/protein/kg body weight/day (where body weight is actual body weight, unless patient is underweight or overweight, where ideal body weight should be considered instead)

| | HD (HD and HDF) | PD (CAPD and APD) | HHD | NHD |
|---|---|---|---|---|
| KDOQI 2020[2] | 1.0-1.2 g | 1.0-1.2 g | | |
| UKKA 2019[6] | 1.1-1.4 g | 1.0-1.2 g | | |
| Ash et al 2014[7] | 1.1 g | 1.0-1.2 g | | |
| RNG BDA 2013[8] | Min 1.1 g | 1.0-1.2 g | No data | No data |
| EBPG 2007[9] | 1.1-1.2 g | n/a | | |
| ESPEN 2006[10] | Min 1.2 g (1.2-1.4 g) | 1.2-1.5 g | | |
| KDOQI 2000[11] | 1.2 g | 1.2.1.3 g | | |

**Figure 1: Protein catabolism in dialysis**




## Protein requirements in patients on home haemodialysis and nocturnal haemodialysis

HHD has been reported to be associated with improved electrolyte control, reduced left ventricular hypertrophy, better quality of life and reduced mortality.[18] The Frequent Haemodialysis Network randomised study showed a 46% reduction in mortality compared with in-centre HD.[19] Studies investigating the optimal protein intake in patients on HHD are lacking. Therefore, it is difficult to make a clear statement.

There is limited evidence to recommend a specific protein intake for patients on NHD. A systematic review and meta-analysis, in 2016, showed that serum albumin levels increased significantly following the transition from HD to NHD.[20] Although Ipema and colleagues stated that the increase in serum albumin during NHD may reflect genuine improvement in nutritional status,[20] non-nutritional factors may contribute to the rise in serum albumin, e.g., improvement of inflammation. Protein intake and nPCR increase after starting NHD. This is potentially linked to an increased appetite observed in patients on NHD.[20] On average, an increase of just under 20 g of protein/day was observed. However, the studies in the systematic review had a very limited sample (total n=40). In view of the lack of evidence, close monitoring of muscle mass, protein intake and muscle strength should be put in place, and it is the opinion of the author that people on HHD and NHD should aim for the higher range of protein intake.

## Protein requirements in peritoneal dialysis

Adult patients on PD can lose between 5-15 g protein a day.[21] Protein losses are usually greater in PD because of the daily frequency, as opposed to the three times a week on HD. The continuous losses of protein via PD should be compensated with a slight increase in protein intake, although this may be difficult to achieve in the presence of malnutrition.[21] In addition, the type of peritoneal membrane transport may influence protein losses, as peritoneal protein losses are much greater in high transporters.

Additional factors may play a role in influencing protein losses, these include longer dwell times in CAPD, sodium intake and balance which may lead to extracellular water expansion, resulting in greater vascular protein permeability.[22]

Guedes provides a detailed account of the type of protein that may be lost via PD fluids.[21] For example, thyroid binding protein excretion in the PD fluid is high, despite the serum level staying within normal range, and a higher incidence of subclinical hypothyroidism has been reported in patients on PD when compared with the normal population.[21]

A recent study (2021) showed that the estimated protein intake in 50 patients on PD was between 0.6 and 1.2 g protein per kg of body weight when using a 24-hour dietary recall, and 0.7-1.0 g when using nPNA, questioning the methodology of how to best determine protein intake. Studies that are only based on PNA may underestimate overall nitrogen intake.[23]

On the other hand, a study conducted by Fein in 2015, showed that over a period of 11 years, of 57 patients on PD, those with a nPCR greater to 0.8 g/kg had a better cumulative survival than those with a nPCR less than 0.8 g/kg and that nPCR was an independent predictor of survival in patients on PD.[24] Similarly, a larger observational study conducted by Dong and colleagues, showed that in 305 patients receiving PD, those with a dietary protein intake (DPI) of <0.73 g/kg/day had worse outcomes, and it was only until a DPI of >0.94 g/kg/ day was achieved that patients experienced better outcomes and fewer complications, such as peritonitis.[25, 26]

Another important aspect is that dietary habit, including protein intake, differ between different ethnic groups. Vongsani et al showed in their study, including more than 350 patients on PD, that nPNA was much lower in south Asian patients and discussed the idea that protein requirements may indeed vary depending on ethnic group and body composition, promoting an individualised approach and more research.[27]

Overall, there is a consensus that patients on PD should aim to have 1.0-1.2 g protein/kg body weight and no less than 0.8-1.0 g protein/kg/body weight, **Table 3**.

## Monitoring protein intake in patients on dialysis

There is not a single measure, or marker, to monitor protein intake in patients on dialysis. While nPNA and nPCR may be useful, they have their own limitations and are often used in the research settings. In HD, the estimation of protein intake can be obtained by assessing the rise of urea nitrogen between two HD sessions, the urea generated during the last HD session, and 24-hour excretion of urinary urea (in presence of urine output). However, in clinical practice, these measurements are rarely conducted except for pre-HD serum urea, which is regularly measured monthly. Pre-HD serum urea, alongside a diet history, can be used as an indicator of poor protein intake in patients who are haemodynamically stable, have an adequate dialysis clearance and in absence of residual kidney function.[17, 28] However, careful interpretation of this result is needed as urea is affected by many factors (such as inflammation, severe catabolism, surgery, dialysis clearance, liver function, medication). For example, patients who are underdialysed may have a high urea level and as a result may well be uremic themselves, resulting in a reduction of appetite.[17, 28] Therefore, we cannot assume higher serum urea level to be associated with a better protein intake as this method has not been validated and there may be confounding factors. On the other hand, low serum phosphate is often used in clinical practice as a surrogate to reduce protein intake. Shinaberger and colleagues conducted a large study with a cohort of more than 30,000 patients on HD.[29] They showed a strong association between low serum phosphate, low nPNA and a significant increased risk in mortality.[29] They concluded that a low phosphate level should be used as a trigger to evaluate dietary intake in patients on HD.[29] Estimation of protein intake using food diaries and or a 24-hours food recall, in conjunction with regular anthropometric measurement, body composition measurement and muscle function, should be used inter-dependently in order to assess overall protein intake at timely intervals.

## Conclusion

**There are no RCTs that measured mortality and different levels of protein intake in patients on dialysis. Protein requirements for patients on both HD and PD have remained almost unchanged for the past two decades. We currently do not know what the optimum intake of protein is for patients on HHD and NHD.**

**Estimating protein intake is difficult and often relies on a patient recalling their consumption. A diet history and estimation of protein intake should be the minimum standard when assessing protein requirements in patients on dialysis, together with a full nutritional assessment including anthropometry measurements (including muscle mass) and measurements of muscle and function.**

**Protein requirements in patients on dialysis can be very heterogenous because they will depend on much more than the type of dialysis, Table 3. Additional factors to consider when estimating protein requirements are underlying illness, co-morbidities, polypharmacy, current protein intake, physical activity level, the dialysis itself, dialysis clearance, inflammation, catabolism, risk of frailty, sarcopenia and protein energy wasting.**

**As protein intake itself seems an independent predictor of outcome in both HD and PD, this should be closely monitored alongside appropriate renal dietetic intervention, which should ensure that a long-term protein intake less than 1.0 g protein/kg/body weight is avoided in people on maintenance dialysis.**

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