



Protein catabolic rate in maintenance dialysis

Authors

Robert E Cronin, MD
William L Henrich, MD,
MACP

Section Editor

Steve J Schwab, MD

Deputy Editor

Theodore W Post, MD

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INTRODUCTION — The protein catabolic rate (PCR), also called the protein equivalent of nitrogen appearance (PNA), is the parameter used in most hemodialysis units to assess dietary protein intake in patients who are in a steady state. Suppose, for example, that a patient has a desirably low predialysis BUN. This finding could represent either a well nourished patient who is adequately dialyzed, or decreased protein intake which is usually a reflection of inadequate dialysis. The PCR will distinguish between these possibilities.

The PCR is determined by measuring the interdialytic appearance of urea in body fluids plus any urea lost in the urine in patients with residual renal function. Retrospective data from a large group of dialysis patients indicates that abnormalities in a number of standard laboratory measurements related to patient nutrition (plasma concentrations of albumin, creatinine, urea nitrogen, and transferrin) are associated with increased mortality [1]; however, only PCR is of value in prospectively predicting morbidity in hemodialysis patients [2]. (See "[Assessment of nutritional status in end-stage renal disease](#)".) In the National Cooperative Dialysis Study (NCDS), for example, a PCR greater than 1 g/kg per day and a timed average urea concentration of 50 mg/dL (18 mmol/L) were associated with low morbidity [2]. The latter alone is insufficient, since it can be induced by a low protein intake.

Although PCR is often viewed as a variable that can be manipulated independently, it varies directly with the Kt/V, a measure of dialysis adequacy. (See "[Kt/V and the adequacy of hemodialysis](#)".) As examples:

- In one study of a small group of hemodialysis patients, the intensity of dialysis was increased by enhancing dialysis time, blood flow, and/or membrane surface area [3]. As the Kt/V rose from 0.82 to 1.32 over a three month period, there was a concurrent elevation in PCR from 0.81 to 1.02 g/kg per day. The rise in PCR was indicative of increased protein intake (and better nutrition) due, presumably, to improved appetite. A second group in which the dialysis regimen was unchanged had no increase in either Kt/V or PCR.
- In another report, converting 13 patients from conventional dialysis (3 x 4 hours/week) to three times per week nocturnal dialysis (3 x 8 hours/week) led to a significant increase in nPCR (1.39 g/kg per day at baseline to 2.25 g/kg per day at 12 months) [4].

The PCR is a function of protein catabolism and reflects protein intake only if the patient is in a steady state regarding nutrition. Unless there is obvious evidence of poor nutrition (eg, PCR below 0.8 g/kg per day) or underdialysis (eg, Kt/V <1,2), alterations in dialysis prescription

should be undertaken only after clear trends in these parameters are apparent. This may require several months of monitoring PCR and Kt/V to ascertain that a significant change has occurred.

Repeat measurements can overcome a potential problem in that the PCR is usually measured only once per month and may therefore not reflect day-to-day variations in intake [5]. These daily changes in dietary intake, even among clinically stable dialysis patients, may be associated with widely varying PCR values. In one study of 50 such patients, for example, three measurements from a single individual were required to obtain a PCR with an error of less than 10 percent [6].

Although a low PCR is related to increased mortality, practically all studies that have examined the relationship have used the initial or baseline level of the PCR [7]. To better assess the relationship between nPCR and mortality, a retrospective two year study evaluated the associations over time between dietary protein intake and survival among nearly 54,000 hemodialysis patients [8]. Overall, increased mortality was observed with a nPNA (eg, normalized Protein equivalent of Nitrogen Appearance, which is the same as the nPCR) of less than 0.8 or greater than 1.4 g/kg per day, while the best survival was noted with levels between 1.0 and 1.4 g/kg per day. Among patients with nPNA levels between 0.8 to 1.2 g/kg per day, an increase or decrease in protein intake during the first six months was associated with increased or decreased survival over the subsequent 18 months, respectively. Thus, reduced survival is associated with an initially low PCR and decreased protein intake over time.

CALCULATION OF PCR — The PCR is usually expressed as g/kg per day, a parameter that is also called the normalized PCR (nPCR). Less commonly, the PCR is not normalized to weight and is expressed as g/day.

Hemodialysis — The PCR in patients treated with hemodialysis is routinely calculated by various urea kinetic modeling software programs that can be purchased independently or are supplied by the manufacturers of some dialysis machines. If a computer program is not available, the following simple formulas will give a good estimate of the nPCR. In one [9]:

$$\text{nPCR, in g/kg per day} = 0.22 + \frac{(0.036 \times \text{ID rise in BUN} \times 24)}{\text{ID interval (hrs)}}$$

where the interdialytic (ID) rise in BUN (predialysis BUN minus the one to two minute postdialysis BUN from the preceding dialysis) is expressed in mg/dL. If, for example, the interdialytic rise in BUN is 50 mg/dL (18 mmol/L) and there are 44 hours from the end of one dialysis to the beginning of the next, then:

$$\text{nPCR} = 0.22 + ([0.036 \times 50 \times 24] \div 44) = 1.20 \text{ g/kg per day}$$

Another formula calculates nPCR from the Kt/V (an index of urea removal during dialysis) and the average BUN [10]:

$$\text{nPCR} = (0.0136 \times F) + 0.251$$

where F is equal to $Kt/V \times ([\text{predialysis BUN} + \text{postdialysis BUN}] \div 2)$.

Thus, if the respective values for BUN are 75 mg/dL (27 mmol/L) and 25 mg/dL (9 mmol/L)

and the Kt/V is 1.3, then:

$$nPCR = (0.0136 \times 1.3 \times 50) + 0.251 = 1.13 \text{ g/kg per day}$$

Residual renal function — Urinary nitrogen loss must be accounted for in patients with residual renal function and persistent urine output. Thus, the following term must be added to the above equation for PCR:

$$+ \frac{\text{Urinary urea nitrogen (g)} \times 150}{\text{ID interval (hrs)} \times \text{weight (kg)}}$$

where the urinary urea nitrogen is all of the urea nitrogen excreted in a urine collection obtained from the end of one dialysis to the beginning of the next (ie, in the interdialytic interval).

Peritoneal dialysis — These formulas cannot be used in patients treated with continuous peritoneal dialysis, since the BUN is relatively constant. In this setting, urea appearance is estimated from measurement of dialysate and urinary urea losses. Several equations have been used to estimate the PCR in continuous peritoneal dialysis; at present, we use the following [11,12]:

$$PCR = 6.25 \times (\text{Urea appearance} + 1.81 + [0.031 \times \text{lean body weight, kg}])$$

The last term in this formula reflects the contribution of nonurea protein metabolism. Urea appearance can be estimated from 24 hour dialysate and urine collections:

$$\text{Urea appearance, g/day} = (V_u \times C_u) + (V_d \times C_d)$$

where V and C represent volume and urea concentration in the urine (u) and dialysate (d).

The Dialysis Outcomes Quality Initiative (DOQI) guidelines for dialysis adequacy prefer the term Protein equivalent of Nitrogen Appearance (PNA) in lieu of PCR [13].

OPTIMAL PCR AND THE DIALYSIS PRESCRIPTION — A target of 1.0 to 1.2 g/kg per day or higher is recommended by both American and European hemodialysis guidelines [14,15]. This goal is often hard to achieve, however, as protein-calorie malnutrition complicates the course of more than one-third of dialysis patients. (See "[Assessment of nutritional status in end-stage renal disease](#)".)

Several factors may contribute to the development of malnutrition:

- Inability of the patient to change from a protein restricted to a protein rich diet after initiation of dialysis.
- The hemodialysis procedure is a catabolic event as 8 to 10 grams of protein are lost with each treatment; furthermore, patients may miss one or two of their normal meals on dialysis days.
- The misconception that a patient with a minimally acceptable Kt/V and a low mid-week BUN is necessarily well dialyzed. The PCR is often below the goal level in this setting, as

inadequate protein intake contributes to the low BUN.

- The delivery of less than optimal dialysis via elements of dialysis not directly associated with the Kt/V, such as the failure to adequately treat metabolic acidosis [[16,17](#)]. (See "[Treatment of metabolic acidosis in chronic kidney disease](#)".)
- The presence of other complicating clinical and social issues, including gastrointestinal disorders, inadequate understanding of dietary instructions, poor dentition, alcoholism, depression, concomitant debilitating diseases, and insufficient income (high biologic value protein-rich foods are expensive).

A small percentage of patients have a "high" PCR (above 1.2 g/kg per day). The appropriate response to this finding should be to increase the dialysis prescription (ie, increase the Kt/V) rather than to restrict dietary protein.

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