

Timing of Initiating Dialysis.

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Abstract: Timing of dialysis was earlier decided by uremic symptoms and biochemical markers. Presently, eGFR is used to decide initiation of dialysis. Debate is regarding early Vs late initiation of dialysis, however good clinical assessment along with eGFR would help in deciding when to start dialysis in particular patient.

DISCUSSION

Determining the right time to initiate long term renal replacement therapy is a challenge. For acute kidney failure indications are clearer and most nephrologists tend to go for earlier initiation (Table 1). Even for long term maintenance dialysis the trend is towards early initiation. This has been also cited the reason for rise in numbers of dialysis worldwide.

Table 1 : Indications for renal replacement therapy in patients with AKF

Indication	Characteristics	Absolute/Relative
Metabolic abnormality	BUN > 76 mg/dl (27 mmol/L)	Relative
	BUN > 100 mg/dl (35.7 mmol/L)	Absolute
	Hyperkalemia > 6 mEq/L	Relative
	Hyperkalemia > 6 mEq/L with ECG abnormalities	Absolute
	Dysnatremia	Relative
Acidosis	Hypermagnesemia > 8 mEq/L (4 mmol/L)	Relative
	Hypermagnesemia > 8 mEq/L (4 mmol/L) with anuria and absent deep tendon reflexes	Absolute
	pH > 7.15	Relative
Anuria/oliguria	pH < 7.15	Absolute
	Lactic acidosis related to metformin use	Absolute
	RIFLE class R	Relative
	RIFLE class I	Relative
Fluid overload	RIFLE class F	Relative
	Diuretic sensitive	Relative
	Diuretic resistant	Absolute

In the 1970s and 80s the term uremia was used to decide the timing of dialysis. However uremia is not a single entity but a constellation of symptoms like fatigue, lethargy, anorexia, sleep disorder, pruritus and vomiting all of which are non specific. Hence this cannot be defined as a specific entity to decide the timing of dialysis. Many of these symptoms may be due to other reasons like hepatitis, drugs being taken and dyselectrolytemia all of which may be managed by non dialytic interventions.

Another approach is determining the timing by biochemical markers like a specific value of urea or creatinine. Several factors determine the serum urea like protein intake catabolism due to infections and GI bleed all of which can be managed by measures other than dialysis. Likewise creatinine depends on muscle wears and the same value of creatinine may mean very different renal function in people with different muscle mass.

Recent trends are towards using eGFR to define the timing of initiation of dialysis and this probably is now the standard for defining the need for dialysis. The debate however is at what eGFR to start dialysis, should the nephrologist chose eGFR less than 5 ml/min or should dialysis be initiated earlier in the course of the disease.

Proponents of early initiation cite easier management of comorbid conditions, better nutritional status, better blood pressure and metabolic control and hence better outcome. It may also lead to lesser need for hospitalization and hence lower economic burden. According to the USRDS data the proportion of patients starting dialysis at

GFR of more than 10ml/min has increased from 19% in 1996 to 45% in 2005.

Many studies have supported this early initiation policy. Korevaar et al compared the survival between early (timely) or late initiation of dialysis and found that early initiation was associated with a small survival advantage of 2.5 months. In another study by Tatters et al the mean urea clearance at initiation of dialysis was lower among those who died compared to those who survived in a cohort of 63 patients. An Italian study also showed a 12 year survival of 77% in 82 patients who started dialysis early (Crcl 12.9 ml/.min.) compared to 55% in 308 patients also started late (Crcl 2.1 – 4.8 ml/min). Another study in peritoneal dialysis patients showed that each 5ml/mm increase in GFR at initiation of dialysis was associated with 5% decrease in mortality in a multivariate cox model.

However recent work by many authors show that initiation of dialysis at higher levels of GFR have had higher mortality on dialysis (Beddhu et al, Clarke et al 2010, Evans et al 2010, Rosansky 2010). Rosansky et al evaluated 81176 incident hemodialysis patients between 1996 and 2006 in United States of America and they noted that compared with reference group eGFR <5ml/min 11.73 unit there is a graded increase in mortality risk associated with higher eGFR.

Several reasons have been cited for the fact that high GFRs at initiation of dialysis may be harmful. One of the major reasons cited is that most patients initiated early were having more comorbidities. Also higher GFRs heavy mean less muscle mass and high GFRs may actually mean less creatinine production rather than higher clearances. A recent trial the IDEAL trial (Initiating Dialysis Early and Late) also showed that early initiation has no benefit. The trial compared two groups. Early initiation GFR 10-14 ml or late GFR 5-7 and found no difference in mortality between the two groups. Similarly Brunori et al showed no deference between early start of dialysis and late start. However both these studies underlined the fact that close monitoring is needed if delayed dialysis is being considered.

However clinicians despite all these studies would best make decision about the timing based not only on eGFR or serum creatinine but clinical evaluation also. As a help the guidelines of several societies and working groups (table 2) are available for reference.

Table 2

National Kidney Foundation, KDOQI 2008: when patients reach stage 5 CKD (estimated GFR <15 mL/min/1.73m²), nephrologists should evaluate the benefits, risks and disadvantages of beginning kidney replacement therapy. Particular (clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy before stage 5. (Grade B, moderately strong evidence).

Canadian Society of Nephrology 2008: No evidence currently exists upon which to recommend a GFR at which renal replacement therapy should be initiated in the absence of complications of chronic kidney disease (grade D, opinion). Patients with an estimated GFR <20mL/min/1.73 m² may require initiation of renal replacement therapy if any of the following are present: symptoms of uremia (after excluding other causes), refractory metabolic complications (hyperkalemia, acidosis), volume overload (manifesting as resistant edema or hypertension) or a decline in nutritional status (as

measured by serum albumin, lean body mass or Subjective Global Assessment) that is refractory to dietary intervention (Grade D, opinion).

Australian and New Zealand Society of Nephrology, CARI 2005: Commence dialysis when GFR falls below approximately 10 mL/min/1.73m² if there is evidence of uraemia or its complications such as malnutrition. In occasional patients it may be necessary to initiate dialysis at a higher GFR (Level III evidence). If there is no evidence of uraemia or its complications including malnutrition, commence dialysis when GFR falls below approximately 6 mL/min/1.73 m² (Level III evidence).

ERA-EDTA, 2002: Dialysis should be instituted whenever the GFR is <15 mL/min and there is one or more of the following: symptoms or signs of uraemia, inability to control hydration status or blood pressure or a progressive deterioration in nutritional status. In any case, dialysis should be started before the GFR has fallen to 6 mL/min/1.73 m², even if optimal pre dialysis care has been provided and there are no symptoms. High risk patients e.g. diabetics may benefit from an earlier start [Evidence level: C]. To ensure that dialysis is started before the GFR is <8 mL/min, clinics should aim to start at 8-10 mL/min [Evidence level:C].

United Kingdom Renal Association, 2009: We recommend that the decision to start RRT in patients with CKD stage 5 (eGFR <15 mL/min/1.73 m²) should be based on a careful discussion with the patient of the risks and benefits of RRT taking into account the patient's symptoms and signs of renal failure, nutritional status, co-morbidity, functional status, and the physical, psychological and social consequences of starting dialysis in that individual (GRADE 1D). We suggest that serious consideration should be given to starting renal replacement therapy in patients with an eGFR <6 mL/min/1.73 m², even if the patient is asymptomatic (GRADE 2C).

Guidelines from national and international expert panels have recommended the initiation of dialysis at relatively high levels of renal function, despite the lack of robust evidence in support of this approach. In 1997, the National Kidney Foundation recommended that dialysis be initiated when the estimated GFR is approximately 10.5ml per minute, on the basis of the minimum target level of total (residual renal and dialysis) clearance for peritoneal dialysis. In 2006, the National Kidney Foundation updated these guidelines to specify that the benefits, risks and disadvantages of renal replacement therapy should be considered when the estimated GFR is less than

15.0 ml per minute and also suggested that the initiation of dialysis therapy when the estimated GFR is higher than 15.0ml per minute may be warranted when patients have coexisting conditions or symptoms of uremia. The Canadian Society of Nephrology recommends the initiation of dialysis when the estimated GFR is less than 12.0 ml per minute; with a provision that dialysis can be deferred if there is no evidence of uremia or malnutrition.

However whatever may be the guidelines a good clinical assesment along with GFR would help in deciding when to start dialysis in a particular patient.

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