

Dialysis Adequacy (HD) Guidelines

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Dose of haemodialysis

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GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Adequacy of dialysis should be assessed on all patients at least 3-monthly, as clinically-based assessment has proven unreliable.
- Adequate dialysis should always include careful blood pressure control and ECF volume management with regular re-evaluation of ideal dry weight, salt intake and a review of the ultrafiltration rate.
- Adequacy of dialysis can be assessed in several ways. The most common acceptable methods are: formal urea-kinetic Kt/V, URR, natural log Kt/V and the Daugirdas second generation formula. A renal unit should be consistent in the method it uses. (Opinion)
- The minimum achieved spKt/V should be 1.2 (URR = 65%). To consistently achieve this in at least 80% of patients, it is recommended that the target spKt/V should be 1.4 (URR = 70%).

Background

Dialysis provides renal replacement therapy for those with end-stage kidney disease (ESKD). The process of dialysis only provides for the removal of unwanted solutes and the equilibration of desired solutes. It is also able to assist with fluid

management. Dialysis does not provide the autoregulatory or the endocrine functions of the kidney.

The provision of dialysis requires some assessment of whether the delivered dose is adequate for the patient; defining adequacy is difficult. Conventionally, urea clearance is used as a marker of dialysis adequacy although urea only represents small, readily permeable solutes. Many other molecules may also be uremic toxins but there is no data available concerning the association of these molecules with mortality, particularly in relation to dialytic removal. On the other hand, urea levels and urea removal do correlate with symptoms and wellbeing and to some extent, mortality. Other indicators of dialysis adequacy include the removal of larger solutes (e.g. creatinine, vitamin B12, β -2 microglobulin), control of the extracellular volume and blood pressure, and duration of dialysis.

The following discussion relates primarily to urea removal for 3 times per week haemodialysis. No recommendations can be made for more frequent or overnight dialysis, which is becoming more common.

Search strategy

Databases searched: MeSH terms and text words for dialysis were combined with MeSH terms and text words for creatinine clearance, dialysis adequacy and membranes. The results were then combined with the Cochrane highly sensitive search strategy for randomised controlled trials. The search was carried out in Medline (1966 – April Week 3 2003). The Cochrane Renal Group Specialised Register of randomised controlled trials was also searched for relevant trials not indexed in Medline.

Date of searches: 28 April 2003; 2 March 2004.

What is the evidence?

The clinical/bedside assessment of dialysis adequacy is unreliable (Delmez & Windus 1992; Lindsay et al 1991).

The National Cooperative Dialysis Study was an RCT which established that patients dialysed to a low average weekly blood urea level fared better than those whose dialysis was less intense and whose average urea levels were higher (Lowrie et al 1981). Gotch and Sargent (1985) then introduced the concept of Kt/V, which measures the clearance of urea during a dialysis session and normalises it to the amount of fluid in a patient's body. They showed, based on the NCDS results, that patients on thrice-weekly dialysis with a Kt/V per dialysis of less than 0.8 fared poorly, while those dialysed at a Kt/V of 0.8 or more fared better.

There was considerable controversy about the cut-off at a Kt/V of 0.8. Using cross-sectional data, Held et al (1996) showed a decline in mortality with increasing dialysis dose and suggested that raising the dialysis dose would lead to a continuing mortality improvement.

Lowrie et al (1998) examined the effect of dialysis dose on mortality using the Patient Statistical Profile system supported by Fresenius. This database includes about one fifth of the patients on dialysis in the USA. It included some 16,000 patients in 1985 and 45,000 in 1995. The data from 1991 showed that with a urea reduction ratio (URR) of 65% (equivalent to a single pool Kt/V of 1.2) as the reference point, the odds ratio of dying fell from 4.0 to 2.0 as the URR rose from less than 45% to 47%. There was a further fall in this odds ratio, from 2.0 to approximately 1.0, as the URR rose to 62% (used as the reference point). However, further increasing the URR from 62% to more than 70% had no significant effect on the risk of dying.

Over recent years in the US, the dialysis dose has increased and the average delivered URR has risen. In 1991, URR was a moderately powerful predictor of patient death, being almost as important as patient age (although not as powerful as the serum albumin). With an increase in average URR over time, URR may have become less important as a predictor of mortality (Lowrie et al 1998).

It is likely, based on the NCDS study (Gotch & Sargent 1985), that a Kt/V of less than 1.0 is associated with increased mortality in dialysis patients. It is, however, very hard to demonstrate any benefit from increasing the Kt/V beyond this point. If we accept a Kt/V of 1.0 (URR 60%) as a minimum standard, we should target a Kt/V of 1.2 (URR 65%) to ensure that this minimum is achieved (Delmez & Windus 1992).

A large US retrospective analysis (45,967 patients) published in 2002 but based on 1997–98 data, showed improving survival at higher URR values, including above 70%. This particular study also demonstrated that this improved survival held true regardless of body size or body mass index (BMI) (Port et al 2002).

A statistical correlation between URRs and protein catabolic rates can be shown (Lindsay & Spanner 1989) but the interpretation of this is difficult. Both terms are derived from pre- and post-dialysis urea measurements and there is a natural tendency for a number to show a positive correlation with itself. In an observational study of more than 12,000 patients (Owen et al 1993), it was found that when the URR increased from $58\% \pm 9\%$ to $62\% \pm 8\%$, the serum albumin decreased from $3.9 \text{ g/L} \pm 0.3\%$ to $3.7 \text{ g/L} \pm 0.3\%$ ($p < 0.001$).

The more recent HEMO study (Eknoyan et al 2002) conducted in the US, examined whether increasing the dialysis dose improved mortality (as well as examining the difference in mortality of low- and high-flux membranes, in a 2 x 2 study design). In a randomised trial, they chose to compare a URR of 65% ($\text{spKt/V} = 1.25$ or $\text{eqKt/V} = 1.05$) with a URR of 75% ($\text{spKt/V} = 1.65$ or $\text{eqKt/V} = 1.45$) and followed 1846 patients for a mean of 2.84 years. The primary outcome was death. The death rate was 16.6/100 patient years for the group as a whole; 17.1 for the low-dose group and 16.2 for the high-dose group ($p = \text{ns}$). Only in women, was there a mortality advantage (19%) for the higher dialysis dose.

Criticisms of the HEMO study include that it recruited both incident and prevalent patients, had a higher than usual proportion of women, had a high proportion of blacks and only included smaller patients (mean weight: 69 kg). Unfortunately, the HEMO study does not help to set a minimum target, as the starting point was the currently recommended Kt/V of 1.2 (URR 65%). Furthermore, while the results

suggest that a higher dose of dialysis does not offer improved survival, the criticisms of the trial suggest that this conclusion should be considered cautiously.

A recent trend has been the shift to increased frequency dialysis and/or nocturnal dialysis. The application of Kt/V and URR to these forms of dialysis is difficult and appropriate targets have not been set. The hours per week of dialysis has some influence on outcome (Kerr 2003) and Kt (without including V) has been proposed as an alternative measure of dialysis adequacy (Li et al 2000) and a recently published observational study has suggested that it is a powerful predictor of mortality (Lowrie et al 2004).

Summary of the evidence

While there are no randomised controlled trials concerning dialysis dose beyond the NCDS study and the HEMO study, full discussions of the issues surrounding dialysis dose can be found at both the NKF's K/DOQI Guidelines website (<http://www.kidney.org/professionals/doqi/index.cfm>) and the European Best Practice Guidelines website (<http://www.ndt-educational.org/guidelines.asp>).

Notes regarding measurement of the delivered dose

There are several ways to measure Kt/V, all of which give somewhat different results (Covic et al 1998). The concept of clearance is difficult to explain to patients and to some clinical staff. The URR on the other hand, is arithmetically straightforward and is an easily understood concept (Jindal et al 1987).

The URR is held to underestimate Kt/V because it does not take into account the urea removed by ultrafiltration during a dialysis session, as ultrafiltration does not alter the concentration of urea or other solutes. The whole concept of Kt/V becomes confused, since V is a moving target.

If URR underestimates the delivered dose of dialysis, this provides a safety factor that mitigates against under-treatment. The same could be said of the natural logarithm calculation of Kt/V, which also does not take into account the ultrafiltered volume.

Solute removal is perhaps a better way (than clearance) of quantifying dialysis. If the blood and dialysate flow rate is kept constant, the clearance during the first hour of a dialysis will be the same as that during the last hour. Because the blood urea concentration is at its highest at the start of dialysis, however, solute removal will be much greater during the first hour than during the fourth. URR takes this into account, but with Kt/V calculations, all clearances are equal regardless of the amount of solute removed.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative: Recommends monthly assessment of Kt/V using formal urea kinetics or the natural log approach. URR is considered

second-line but is commonly practised. A Kt/V of 1.2 (URR = 65%) is recommended as a minimum, using 1.3–1.4 as a target to achieve this.

British Renal Association: Recommends monthly measurement of dialysis dose with maintenance of URR > 65% or Kt/V > 1.2 with request made that the method used be recorded.

Canadian Society of Nephrology: Recommends Kt/V of 1.2 or URR of 65% as minimum targets for 3-times-weekly dialysis. The suggested measurement interval is at least every 6–8 weeks.

European Best Practice Guidelines: Recommends $eqKt/V \geq 1.2$ ($spKt/V \geq 1.4$) for 3 times per week dialysis.

Implementation and audit

Units should ensure that at least 80% of patients consistently achieve a URR (or equivalent) of 65%. This information is also collected by ANZDATA.

Suggestions for future research

1. The relationship between prescribed and delivered dose should be explored in an Australian setting.
2. The proportion of patients within units meeting target (URR 65%) should be audited.
3. The relationship between hours of dialysis per week and survival needs further exploration.

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