At which stage of renal failure should dialysis be started?

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Historical background

The issue of the adequate or optimal time at which renal replacement therapy (RRT) should be initiated for patients with advanced or terminal chronic renal failure (CRF) has been a matter of debate since the very first introduction of this revolutionary therapeutic concept, now close to 40 years ago, and is not yet settled. The lack of means of treatment, due mainly to economic constraints, continues to play a key role in many areas of the world for retarding (or denying) RRT for a great number of patients with CRF. However, the issue remains controversial in countries with good availability of therapeutic facilities, due either to inadequate medical management of many patients prior to the ultimate stage of renal insufficiency or to conceptual/academic conflicts between different lines of thought set forward by defendants of ‘early dialysis’ versus challengers advocating the advantages and safety of dietary restrictions for delaying to a significant extent the initiation of dialysis treatment.

Late referral

The clinical status at the start of dialysis is a major factor among those involved in the vital and functional prognosis of patients taken onto RRT [1]. Despite more intensive information provided to general practitioners and various categories of specialists pleading for an early referral of patients with even moderate renal insufficiency to competent nephrologists, it remains all too frequent that RRT is initiated either in emergency situations, such as massive fluid overload and pulmonary oedema, or uncontrollable hypertension or in patients who are severely debilitated due to malnutrition induced by anorexia and digestive symptoms in relation with a severe uraemic state. Actually, ‘Dialysis should be initiated to promote wellness and not to rescue from illness’ [2]. In many ways, a safe follow-up procedure for patients with advanced-stage uraemia can be compared with that applied for a smooth landing of an aircraft at a ‘Dialysis initiation airport’ using the navigation instruments listed in Table 1.

Table 1. Desirable clinical and biochemical profile of patients with chronic renal failure at the time of initiation of dialysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>GFR (([Cкр + Cтут]/2)) 10 ml/min/1.73 m(^2)</td>
<td>Serum calcium 2.3–2.5 mmol/l</td>
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<tr>
<td>Residual weekly (Kt/V) urea 2</td>
<td>Serum phosphate &lt; 1.6 mmol/l</td>
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<tr>
<td>Absence of fluid overload</td>
<td>Serum PTH (1–84) &gt; 60–150 ng/ml</td>
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<tr>
<td>Blood pressure &lt; 140/90 mmHg</td>
<td>Serum albumin &gt; 35 g/l</td>
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<tr>
<td>Serum bicarbonate &gt; 22 mmol/l</td>
<td>Hb concentration 10–12 g/dl</td>
</tr>
<tr>
<td>Serum potassium &lt; 5.0 mmol/l</td>
<td>MNCV* (lower limb) &gt; 40 m/sec</td>
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*Motor nerve conduction velocity.

The problem of measuring residual renal function (RRF)

Selecting the best, or perhaps only the least erroneous, indicator—altimeter—for measuring the level of RRF is of course of key importance for selecting the strategy to be applied to each individual patient. Serial measurements of serum creatinine concentration (Scr), or \(1/\text{Scr}\), or creatinine clearance (Ccr) per body surface area (BSA) are currently considered by many experts as less reliable parameters than the calculation of the residual glomerular filtration rate (GFR) according to the formula: \([\text{Cкр} + \text{urea clearance (ml/min/1.73 m}^2\)/2]. By compilation of 13 published reports grouping 115 observations, Walser and Hill found that, on average, the ‘true’ GFR was indeed about 25% lower than the measured Ccr [3]. The overestimation of the RRF based on the Ccr in patients with advanced CRF has to be stressed and the use of a less imperfect indicator is highly recommended [4]. Similarly, the accuracy of another widely used indicator of RRF, as well as of ‘adequacy of dialysis’, \(Kt/V\) urea, is also open to criticism due to the errors in evaluating the urea distribution volume (V) in clinical practice. The clinical estimation of total body water space (TBW, estimated at 55–58% of body weight) nor even the use of sophisticated formulae based on anthropometric data (e.g. Watson formula) are universally accepted as reliable compared, for example, with results obtained with Bioelectrical Impedance Techniques [5].

Recommendation and guidelines

In spite of these methodological uncertainties some groups of experts in several countries (USA, UK,
France) have elaborated evidence-based guidelines based on extensive critical review of the literature. Thus, according to the US National Kidney Foundation Dialysis Outcomes Quality Initiative (DOQI) guidelines, under appropriate conditions ‘patients should be advised to initiate some form of dialysis when the weekly renal Kt/V urea falls below 2.0’. This corresponds to a renal Ccr that ranges between 9 and 14 ml/min/1.73 m² and a residual GFR of about 10.5 ml/min/1.73 m² [6]. Also, taking into account the highly detrimental effect of malnutrition in patients with severe renal insufficiency, the DOQI guidelines also give the following advice: ‘In the absence of comorbid causes of anorexia and after unsuccessful intervention by a registered dietician, dialysis should be started in patients when normalized protein equivalent of nitrogen appearance (NPA) spontaneously falls below 0.8 g/kg/day’.

Postulate and practice

In several series of patients taken onto RRT in the early years of the present decade, the RRF expressed in terms of weekly Kt/V at the start of dialysis was actually markedly lower than the value set forward in the DOQI guidelines, ranging between 0.68, 0.72 and 1.05 in patients reviewed in the USA, Canada and the UK respectively. If one assumes an average decline of residual urea clearance of −0.333 ml/min/month, one would have to start dialysis to maintain a weekly Kt/V urea of urea 2.0 between 20 and 11 months earlier if one takes the example of patients investigated in the USA and the UK, respectively [2]. If the DOQI guidelines were implemented, of course a heavy additional burden would fall on the health-care budgets of developed countries. This looks even more unrealistic in developing countries. If the health-care fund providers are approached to accept such strategies, the proposed policy must be justified by more convincing evidence than the results of the retrospective analysis of the literature, as provided by the DOQI guidelines, or the data collected in limited clinical studies performed more than 10 years ago in Italy [7,8] and more recently in the UK [9]. An unequivocal benefit from ‘early initiation of dialysis’ (using DOQI guidelines) on the mortality and morbidity of dialysis patients remains to be demonstrated. This will require prospective, controlled, randomized trials conducted in large unselected populations of patients with CRF.

The concept of incremental dialysis

Meanwhile, the revived debate on this issue has led to the development of the concept of ‘incremental dialysis’. This concept is based on the principle that patients with advanced CRF should maintain a constant weekly global Kt/Vurea of 2.0 by adding to the RRF an adequately titrated dose of dialysis. This dose has to be increased over time according to the progress-
has not received a clear-cut response during the past two decades.

**Persisting dilemmas**

Deferred *versus* early initiation of dialysis thus currently remains a matter of controversy, diverting the nephrological community into believers and skeptics, and even opponents, of either concept. The presence of significant comorbidities has to be carefully considered in making the decision of an appropriate time for starting dialysis. The nephrologist should also not be too favourably influenced for delaying the initiation of dialysis by the improvement of the clinical status alleged by patients whose anaemia is efficiently corrected by Rh-Epo therapy.

From a practical point of view, it can be reasonably stated that timely initiation of dialysis treatment cannot be based merely on numerical data, but should be decided according to the overall clinical tolerance of each individual patient to his or her advanced stage of uraemia, the most important parameters to be considered being: adequate control of blood pressure and quality of nutritional status. Initiating dialysis at the right time for a given patient with the most appropriate technique represents a sophisticated exercise of clinical medicine, which remains, and will remain a balanced mixture of Science and Art.

**References**


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