The Opposite View

nephron Clinical Practice

Nephron Clin Pract 2012;120:c17–c24
DOI: 10.1159/000334191

Published online: December 21, 2011

'Ideal Criteria' for Starting Chronic Hemodialysis: Numbers, Symptoms or an Alerting 'Traffic Light' System?

Mustafa Arici

Unit of Nephrology, Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

Key Words
Hemodialysis · eGFR · Starting chronic dialysis · Guidelines

Abstract
A definite criteria for starting chronic hemodialysis treatment is still lacking even after 50 years of regular hemodialysis treatment. Although none of the current guidelines have designated a certain glomerular filtration rate (GFR) level to start hemodialysis, most favor an 'earlier' start after GFR falls below 15 ml/min. Hence, since mid-1990s, more patients have initiated dialysis on higher GFR levels. Most of the observational data and one randomized trial, however, failed to find any benefit, but even harm, from an earlier start in various patient populations including the healthiest groups. This paper has reviewed the available evidence and criticized the use of only 'GFR level' in the absence of a validated method in end-stage kidney disease patients. A new patient scoring system mimicking traffic lights was proposed in which patients were placed into green, yellow or red zones for deciding the ideal time to start hemodialysis. This scoring system should include not only validated GFR criteria but also a wide set of demographic and clinical parameters.

The Question

One of the most demanding questions in nephrology practice and teaching is 'When shall this patient need hemodialysis treatment?' If the patient has some absolute (such as pericarditis, treatment-resistant fluid overload or pulmonary edema, uremic encephalopathy, significant bleeding, persistent severe nausea and vomiting) or relative (such as severe and persistent anorexia, fatigue or pruritus) indications for starting dialysis [1], the answer is rather straightforward. However, in a stable and symptom-free patient when someone (either the patient or a student) is asking the exact time dialysis will be started, there is no clear-cut answer. Patients, students and even policymakers are asking this question as 'the simplest question of nephrology', but for a clinician it is still a challenging one even after 50 years of hemodialysis treatment.

From Opinion to Guideline Recommendations

In the early times of chronic hemodialysis programs, a major focus for a physician was selection of the most suitable patient when 'faced with 10 candidates for a single place' [2]. This was a question of life or death and decision analyses involved not only medical conditions but

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Mustafa Arici
Unit of Nephrology, Department of Internal Medicine
Hacettepe University Faculty of Medicine
TR–06100 Ankara (Turkey)
Tel. +90 312 305 1710, E-Mail marici@hacettepe.edu.tr

also the personal, social and occupational factors of the patient. The limited facilities and the very high cost of treatment predicted 'the latest start' possible in 1960s and early 1970s, and the selection process was like a 'game of chance', 'since any vacancies will be filled immediately by the first suitable patients, even though their claims for therapy may subsequently prove less than those of other patients referred later' [2]. In the mid-1970s, improvements in dialysis technology, expansion of dialysis units and insurance policies increased the chance for many patients to receive regular hemodialysis [3]. This brought another question of selection, whether an 'early start to dialysis' was preferable rather than waiting until some late uremia-related indications develop [1]. In their seminal studies, Bonomini et al. [4] were the first to suggest that 'early dialysis is able to prevent the appearance and the progression of many complications of uremia'. They showed a clear survival advantage by comparing 7 cases with a residual creatinine clearance (CCr) of 15–21 ml/min (85.7% survival rate at 3–4 years) to 22 patients with a residual CCr of 0–5 ml/min (40.9% survival rate at 3–4 years) who were on almost similar dialysis schedules [4]. Over 15 years of follow-up of 82 cases with early start (mean CCr 11 ml/min) compared to those who were on rigid dietary restrictions and started dialysis late (CCr ranged from 2.1 to 4.8 ml/min), they showed significant improvement in patient survival, hospitalization time and full-time working activity as a measure of rehabilitation [5]. Later, Tattersall et al. [6] showed that urea kinetic modeling (Kt/V) was a better predictor for increased morbidity and mortality rather than conventional biochemical measures. They proposed that some patients may benefit from earlier introduction of dialysis treatment due to initial Kt/V values; however, the effect of Kt/V was not independent of age and comorbidity scores [6]. Several earlier studies highlighted the importance of time of referral in determining morbidity and mortality considering initiation of dialysis. In 1984, Ratcliffe et al. [7] showed that patients who were referred late had more complications and mortality than those referred early, despite both groups being dialyzed at a CCr of <6 ml/min. The role of nutritional status at the initiation of dialysis was another major argument for 'earlier' start. In several studies, the relation between decreased renal function and worsening nutritional status was documented and it was proposed that benefit of early initiation of dialysis may be attributed to better nutritional health [1, 8, 9]. When all earlier studies (published between 1976 and 1996) were systemically reviewed, it was found that none of them had rigorous randomization and none had eliminated age, comorbidity, referral time or starting time of follow-up biases [10]. Despite those shortcomings, the conclusion was 'offering dialysis when the CCr is 9–14 ml/min and there is clinical or biochemical evidence of malnutrition' and also 'informing the patients about the controversy regarding the timing of initiation of dialysis' [10].

The first guideline recommendations in 1997 appeared in the presence of various inconclusive observational studies, and influential expert opinions stating that 'current practice of delayed initiation of dialysis may contribute to the high mortality rate of hemodialysis patients' [1]. The 'HD Adequacy Work Group' for NKF-DOQI Clinical Practice Guidelines for Hemodialysis Adequacy [11] did not review the literature 'to define an optimal time or clinical setting for the initiation of maintenance hemodialysis', but they recognized that 'patients who are initiated on hemodialysis relatively early will have greater residual renal function that will enhance small and large solute clearance over that provided by dialysis alone'. Opinion-based guidance from NKF-DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy [12] was as follows: 'Patients should be advised to initiate some form of dialysis when the weekly renal Kt/V_{urea} falls below 2.0'. A weekly Kt/V_{urea} of 2.0 approximates a CCr of between 9 and 14 ml/min/1.73 m^2 or a glomerular filtration rate (GFR) of 10.5 ml/min/1.73 m^2 [12]. The rationale for this guidance clearly expressed that 'dialysis, or some form of renal replacement, should be strongly considered when Kt/V_{urea} falls below 2.0 and definitely implemented if a patient has unintentional weight loss, a decrease in normalized protein intake (nPNA) of <0.8 g/kg/day, or there were clinical signs or symptoms of uremia'. The Work Group has clearly acknowledged that 'the risks of early initiation are not clearly known, but the risks of late initiation are known and are unacceptable'. The rationale also admitted the 'major role of the patient in accepting the initiation of dialysis based on a certain 'laboratory value' and underlined the responsibility of care providers to make clear the rationale for initiating dialysis' [12].

Following this 'earliest' guideline, several other national and international groups proposed clinical practice recommendations about 'time to start dialysis' despite the lack of compelling evidence. Most guidelines recommended an earlier start if there were uremia-related symptoms or malnutrition: recommended estimated GFR (eGFR) levels for earlier start were <12 ml/min in the Canadian guidelines [13]; <15 ml/min in EBPG [14], and <10 ml/min in CARI [15]. The KDOQI update

Table 1. Current guideline recommendations for starting dialysis[1]

Guideline	Recommendations for 'earlier' start	Recommendations for dialysis start
US-DOQI, 1997	Advise to initiate when the weekly renal Kt/V_{urea} <2.0 (GFR <~10.5 ml/min)	Dialysis is not necessary (even if GFR <~10.5 ml/min) if body weight is stable or increased without edema or nPNA ≥0.8 g/kg/day or there is no uremic sign or symptom
Canada-CSN, 1999	Recommend dialysis when GFR <12 ml/min and uremia or PNA <0.8 g/kg/day or clinical malnutrition is present	Recommend initiation of dialysis when GFR <6 ml/min
Europe-EBPG, 2002	Institute dialysis whenever GFR <15 ml/min and there are 'symptoms or signs of uremia', 'inability to control hydration status or blood pressure' or a progressive deterioration in nutritional status	Dialysis should be started before GFR ≤6 ml/min even if optimal pre-dialysis care has been provided and there are no symptoms
Australia-CARI, 2004	Start dialysis when GFR <10 ml/min/1.73 m^2 if there is evidence of uremia. In occasional patients it may be necessary to initiate at a higher GFR	Commence dialysis when GFR <6 ml/min/1.73 m^2
US-KDOQI, 2006	When patients reach stage 5 CKD (eGFR <15 ml/min/1.73 m^2), evaluate the benefits, risks, and disadvantages of beginning dialysis. Particular clinical considerations and certain characteristic complications of kidney failure may prompt initiation of therapy at GFR >15 ml/min/1.73 m^2	NA
UK-RA Guidelines, 2009	The decision to start renal replacement therapy in patients with CKD stage 5 (eGFR <15 ml/min/1.73 m^2) should be based on a careful discussion with the patient on the risks and benefits of dialysis taking into account the patient's symptoms and signs of renal failure, nutritional status, comorbidity, functional status, and the physical, psychological and social consequences of starting dialysis in that individual	Serious consideration should be given to starting renal replacement therapy in patients with an eGFR of <6 ml/min/1.73 m^2, even if the patient is asymptomatic

[1] Adapted from KDIGO website (www.kdigo.org) with some updating and modifications.

in 2006 recommended that 'When patients reach stage 5 chronic kidney disease (CKD; eGFR <15 ml/min/1.73 m^2), nephrologists should evaluate the benefits, risks, and disadvantages of beginning kidney replacement therapy'. In this update 'prompt initiation of therapy *even* before stage 5' was also recommended in case of 'clinical considerations and certain characteristic complications' [16]. Similarly, most recent UK guidelines recommended 'a careful discussion with the patient of the risks and benefits of renal replacement therapy 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' when eGFR is <15 ml/min [17]. Almost all guidelines recommended initiation of dialysis when GFR is <6 ml/min even if there is no evidence of uremia or complications [18] (table 1).

Rise in 'Early Start' and Rise in Incidence of End-Stage Renal Disease

Although none of the guidelines directly recommended an 'earlier' start to dialysis with solid GFR criteria, there was a great difference in real practice where more patients were being initiated to dialysis on higher GFR levels since mid-1990s [19]. In the US, the percentage of patients who have initiated dialysis with an eGFR of >10 ml/min were 45% in 2005. This ratio was only 19% in 1996 [19]. This trend was similar from several other countries and regions. The Australian and New Zealand Dialysis and Transplant Registry showed that from 1992 to 2001, serum creatinine concentration at the start of end-stage renal disease (ESRD) treatment decreased from 11.3 to 8.5 mg/dl [20]. A recent analysis from ERA-EDTA registry [21] showed that median eGFR at the start of dialysis was 7.0 ml/min/1.73 m^2 in 1999 and 7.7 ml/min/1.73 m^2

in the 2003 data. In this analysis, the number of patients starting dialysis with a GFR of >10 ml/min/1.73 m^2 had doubled from 1999 to 2003. The UK Renal Registry data demonstrated that the mean eGFR at dialysis initiation has increased in a linear fashion from 6.2 to 8.4 ml/min/1.73 m^2 between 1997 and 2006 [22]. In Canada, the proportion of early starts (eGFR >10.5 ml/min/1.73 m^2) rose from 28 to 36% from 2001 to 2007 [23]. In Turkey, patients who were starting dialysis with a serum creatinine of <4.0 mg/dl increased from 8.8 to 11.0% only in 1 year's time from 2007 to 2008 [24].

All these data clearly indicate that there has been a rising trend for starting dialysis earlier in the last 15–20 years in most countries. This ultimately caused a sharp increase in the number of patients starting dialysis, i.e. the incidence of ESRD [25]. The increased incidence has been attributed to changes in patient demographics (more elderly with more comorbidities). This association, however, was critically questioned by several analyses. Hsu et al. [25] demonstrated that the incidence of ESRD has outpaced the CKD prevalence by 70% in their analysis of a US population between 1976–1980 and 1988–1994. They concluded that the ESRD epidemic may reflect larger social forces, such as patient and physician choices about the aggressiveness of providing dialysis. Another study by the same author quantified the change over time (per year) in the likelihood of receiving ESRD therapy in a cohort of 320,252 individuals from 1964 to 2000 in the US. They found an 8%/year higher risk of progressing to receive treatment for ESRD in individuals who were examined later in time even after adjustment for demographic and clinical risk factors [26]. This finding was ascribed to the hypothesis that 'an important but underappreciated contributor to the increase in number of observed cases of treated ESRD is more liberal entry into dialysis programs'. The ERA-EDTA registry data have also found that differences in the level of renal function at the start of dialysis from 1999 to 2003 between patients with and without comorbid conditions and according to age were less and much smaller than expected [21].

Tide against 'Early Start' and First Randomized Study Seeking for an 'Ideal' Start

During the last decade in parallel to the trend of 'early start', several observational studies and only 1 randomized trial have sought for the potential benefits and disadvantages of the time of initiation of dialysis. One of the earliest observational studies by Korevaar et al. [27] in 2001 found a small beneficial effect on survival (gain in survival time of 2.5 months in the first 3 years after the start of dialysis) in timely starters (with a mean GFR of 7.1 ml/min/1.73 m^2) compared to late starters (with a mean GFR of 4.9 ml/min/1.73 m^2). This gain in survival was attributed to the lead-time (initiating dialysis at an earlier stage of disease) effect [27]. In a study where lead-time bias was eliminated, Traynor et al. [28] found no significant benefit in patient survival when they compared patients with early start (estimated CCr of ≥8.3 ml/min) to late start (estimated CCr of <8.3 ml/min). This study has also eliminated the effect of late referral and studied the effects of many variables that are usually associated with increased morbidity and mortality. There was a significant inverse relationship between estimated Ccr at the start of dialysis and survival (every 1 ml/min extra renal function at the start of dialysis was associated with a 10% increased risk or hazard of death), even after morbidity and mortality variables were taken into account [28]. In a large, national random sample of the US dialysis population (n = 2,920), Beddhu et al. [29] showed that there was a 14% increased risk or hazard of death with each 5 ml/min increase in the modification of diet in renal disease (MDRD) GFR at initiation of dialysis. However, they failed to find the same relation in the subgroup of patients with measured CCr and concluded that GFR was erroneously estimated by MDRD formula [29]. In order to investigate the effect of comorbidities on 'early start' and mortality, Kazmi et al. [30] studied 3 incident US dialysis populations: (1) a general population aged 18+ years (n = 302,287); (2) older patients aged 67+ years (n = 91,083), and (3) low-risk population (n = 90,540). After adjusting for all covariates, patients who initiated dialysis therapy at a GFR of >10 ml/min/1.73 m^2 had a 42% increased risk of death compared with patients with a GFR of <5 ml/min 1.73 m^2 at initiation of dialysis therapy in the general population. The increased risk of death was attenuated (25%) but not totally eliminated in the older population with more comorbidities [30]. In a prospective cohort study from Hong Kong, Tang et al. [31] compared the 1-year mortality of patients who started peritoneal dialysis electively (n = 151, mean GFR 9.21 ml/min/1.73 m^2) with 'initial refusers' (n = 82, mean GFR 8.89 ml/min/1.73 m^2) of whom 45 (55%) developed a uremic emergency and agreed to undergo dialysis (GFR at the time of dialysis not reported). The study showed that all-cause and cardiovascular mortality was significantly higher at 1 year among initial refusers [31]. In a systemic review of the above and 4 other studies [32–35] published between 1999 and 2007, no firm conclusion was reached

Table 2. Major results of recent observational studies investigating the association between 'time to initiate dialysis' and survival

Study	Data source	n	GFR criteria	Results
Stel et al. [37], 2009	Retrospective cohort from 9 European renal registries	11,472	Higher levels of MDRD eGFR in 2003 than in 1999 (mean eGFR of 8.6 vs. 7.9 ml/min/1.73 m^2; $p < 0.001$) at dialysis start	An increase in eGFR of 1 ml/min/1.73 m^2 was associated with a higher mortality risk (HR 1.03; 95% CI 1.03–1.04) that remained similar after adjustment
Sawhney et al. [38], 2009	Retrospective cohort from British Colombian and Scotish registries	7,299	Five groups of MDRD eGFR: 0–4.9; 5–9.9; 10–14.9, and 15 ml/min/1.73 m^2, or greater	Higher starting eGFR was associated with a significant increase in the HR of death (HR per 1 ml/min/1.73 m^2 = 1.025; 95% CI 1.019–1.030; $p < 0.0001$)
Lassalle et al. [39], 2010	Prospective cohort from French REIN registry	11,685	Five groups of MDRD eGFR (≤5, 5–10, 10–15, 15–20, and >20 ml/min/1.73 m^2)	2-year crude survival decreased from 79 to 46%, with increasing eGFR from <5 to >20 ml/min/1.73 m^2
Wright et al. [40], 2010	Retrospective cohort from USRDS database	896,546	Four categories of MDRD eGFR: >15, >10–15, >5–10, and ≤5 ml/min/1.73 m^2	Those that started dialysis at an eGFR of ≤5 ml/min/1.73 m^2 had a reduced risk of mortality (HR 0.88; 95% CI 0.84–0.92; $p < 0.001$) compared with those who started dialysis at an eGFR of >5–10 ml/min/1.73 m^2
Hwang et al. [41], 2010	Retrospective cohort from Taiwan national database	23,551	Quintiles based on MDRD eGFR level (Q1 = <3.29; Q2 = 3.29–4.27; Q3 = 4.28–5.20; Q4 = 5.21–6.51; Q5 = >6.52 ml/min/1.73 m^2)	There was a 144% increase in mortality risk in the group with an eGFR in the 5th quintile compared to the reference group in the 1st quintile (HR 2.44, 95% CI 2.11–2.81)
Rosansky et al. [42], 2010	Patients enrolled from Medicare program	81,176	Four MDRD eGFR strata: 0–4.9 ml/min/1.73 m^2 (reference group); 5.0–9.9; 10.0–14.9, and 15 ml/min/1.73 m^2 or higher	Unadjusted 1-year mortality by eGFR ranged from 6.8% in the reference group (eGFR <5.0 ml/min/1.73 m^2) to 20.1% in the highest eGFR group (≥15.0 ml/min/1.73 m^2)
Evans et al. [43], 2010	Prospective, cohort from Sweden	901	Early-start dialysis (MDRD eGFR ≥7.5 ml/min/1.73 m^2) was compared to late-start dialysis (eGFR <7.5 ml/min/1.73 m^2)	The adjusted HR for death was 0.84 (95% CI 0.64–1.10) among late versus early starters
Clark et al. [44], 2010	Retrospective cohort from Canadian Organ Replacement Register	25,910	Early dialysis if the eGFR >10.5 ml/min/1.73 m^2	Unadjusted HR for mortality with early relative to late initiation was 1.48 (95% CI 1.43–1.54). The HR decreased to 1.18 (95% CI 1.13–1.23) after adjustment

and the need for a well-designed randomized trial to determine 'in which population subgroups early initiation would be more beneficial' was stressed [36].

A long-awaited randomized controlled trial appeared in 2010 in the midst of a number of observational studies involving more than 1 million patients and published during last 3 years [37–44] (summarized in table 2). The Initiating Dialysis Early and Late (IDEAL) study is a multicentered controlled trial in which 828 adult patients with progressive CKD were randomized into either an early-start group (eGFR using Cockcroft-Gault formula 10.0–14.0 ml/min, corrected for body surface area) or a late-start group (eGFR 5.0–7.0 ml/min). The primary outcome was death from any cause. After a median follow-up period of 3.59 years, there was no difference in patient survival, and the quality of life and the frequency of adverse events were similar between the 2 groups. At the time of initiation of dialysis, the mean eGFR was 12 ml/min (9.0 ml/min using MDRD) in the early-start group and 9.8 ml/min (7.2 ml/min using MDRD) in the late-start group. The study, however, suffered a significant amount of crossovers especially in the late-start group in which 75.9% of the patients started dialysis with an eGFR of >7.0 ml/min mostly due to development of uremia-related symptoms [45]. The IDEAL study has clearly documented that there is no survival difference between ear-

ly- and late-start groups and the decision to start dialysis should be based on a constellation of several clinical and laboratory parameters rather than an arbitrary eGFR value. The authors recommended that 'with careful clinical management, dialysis may be delayed until either the GFR drops below 7 ml/min or more traditional clinical indicators for the initiation of dialysis are present' [45].

The Numbers, the 'Tunnel Vision' and the Opposite View

After 50 years of hemodialysis history, the scenery for 'time to start dialysis' may be summarized as follows. Earlier observational studies from an era of 'limited dialysis facilities' showed (imprecisely) that 'being late' is detrimental. Guidelines did not point out a fixed GFR but favored an 'earlier' start after GFR falls below 15 ml/min, even before that for 'appropriate' cases. There has been a sharp increase over the last two decades in the proportion of patients starting dialysis earlier (GFR >10 ml/min) possibly due to a misinterpretation of guidelines [46] or some other ill-defined factors. The subsequent result was a vast increase in the incidence of ESRD with the cost and burden of dialysis [26]. Later observational studies, especially the most recent ones (table 2), and the only randomized trial failed to show a clear benefit from 'early start', even detrimental effects were reported in patients who started 'earlier' only due to GFR criteria.

After all, the criteria to initiate 'timely' dialysis are still unknown. A defined GFR criterion to initiate dialysis was recently and truly criticized as a 'tunnel vision' approach [47, 48]. This argument has several foundations. One is the lack of a validated GFR formula when residual renal function is very low (GFR <20 ml/min). Another point is the dependence of the formulas to serum creatinine which itself is affected by various factors such as measurement technique, muscle mass and nutritional status. It has been proposed that the use of mean urea and CCrs calculated from 24-hour urine collections may be a better predictor of true GFR compared to the MDRD formula in patients with ESRD [49]. In studies where there was measured GFR (either CCr and combined urea and CCr), no relation was found between higher GFR and mortality at the initiation of dialysis [29, 50]. The association of serum cystatin C at the time of dialysis initiation and mortality has yet to be investigated.

Another criticism is related to the association between a higher GFR at initiation of dialysis and increased mortality. It was argued that this is related to initiating dialysis in older patients with the underlying diagnosis of diabetes and several comorbidities. This hypothesis, however, has not been proved in most studies. In order to minimize confounding issues, a recent study in a 'relatively healthy dialysis cohort' (no diabetics, no elderly, no reported comorbidity) compared survival according to the MDRD eGFR. It was found that early start was still harmful especially in the healthiest subgroup (a healthier subset of patients with serum albumin levels of 3.5 g/dl or higher prior to hemodialysis initiation) of the study [42]. Higher mortality after dialysis start was attributed to the harmful effects of hemodialysis, especially on the myocardium [51] and the risk of sudden cardiac death [52]. It was, however, unclear why this increased mortality risk appears only in those who start dialysis at higher GFRs. On the contrary, this could be explained as the 'survival of the fittest' where the fittest patients will be strong enough to survive until eGFR has decreased to 5 ml/min/1.73 m^2 [48]. All these questions need to be answered with further randomized trials.

If there is no firm stance in a topic and enough controversy has piled up, it is time to formulate an opposite view [53]. My personal objections and/or proposals are as follows:

(1) Most of the recent debate has concentrated on the timing of dialysis according to a number derived from various eGFR formulae. Likewise, most guidelines formulated a GFR number, albeit with the lack of a validated method to estimate GFR in stage-5 CKD to determine the need for dialysis. The recent updated guidance from the ERBP Advisory Board still carries this discrepancy [54]. The updated guideline I.3 statements mention several GFR levels to guide the clinician, but guideline I.1.1 mentioned that there is no validated method for GFR measurement at the end stage. I think there is an urgent need to formulate an objective validated measurement method for GFR to determine the time to initiate dialysis. Guideline statements should be very cautious in writing a GFR value in the absence of a validated GFR method. The GFR number in a guideline may easily be misinterpreted in a busy clinical environment or in different healthcare settings with different resources.

(2) None of the recent studies has systematically studied the crucial role of referral time and dialysis start. The clear distinction between 'early referral with proper predialysis care and later start' and 'late referral with no predialysis care and sudden/early start together with many complications' should be made. This distinction should also be made for the settings of dialysis, i.e. a well-developed country with easy access to healthcare and educa-

tion or a developing or undeveloped country with limited healthcare facilities. The IDEAL trial in this sense has shown the value of early referral and long-term nephrology care as many patients had a 30-month median time since the first nephrology visit [45]. A systematic review, however, demonstrated that a wide range of both patient- and health system-related barriers are associated with late referral of CKD patients [55]. There is a clear need to test the 'ideal' time to initiate dialysis in more diverse populations from different healthcare settings and future global guidelines should consider this issue.

(3) Clinicians and policymakers certainly need more definite criteria for the time to start dialysis. This is crucial not only for patients' health but also for efficient use of the resources. Available evidence so far indicates that there is no 'magic number' to initiate dialysis. The IDEAL trial in this sense has shown that more than three quarters of the patients in the late-start group were unable to wait the assigned GFR criteria (eGFR 5.0–7.0 ml/min) and started dialysis earlier due to physician discretion. The most common cause of 'earlier' start was uremia [45]. Uremia, however, has no distinct criteria and lacks a validated objective measurement that may guide the clinician [54]. Moreover, the severity of uremic symptoms differ from patient to patient. To this end, I would like to propose a scoring system which labels end-stage patients into green, yellow or red zones similar to traffic lights where patients may wait for dialysis, prepare for dialysis at their own or physician's leisure, or as soon as possible, respectively. The scoring system should include a validated GFR level and a set of clinical criteria including age, gender, ethnicity, socioeconomic state, health literacy, underlying disease, referral time, major comorbidities, nutritional state, uremic symptoms, basic laboratory parameters (such as BUN, albumin, hemoglobin, potassium, phosphate, bicarbonate) and, if available, rate of renal function loss and attainment of predialysis education programs. All these items in the scoring list have been shown to affect the morbidity and mortality of CKD and dialysis patients. Such a scoring system may be validated first in a retrospective cohort of dialysis patients and then tried prospectively in a wide patient population setting.

In conclusion, deciding the 'ideal' time for initiating dialysis on a case-by-case basis with a validated scoring system may prevent unnecessary starts or delays. The use of a scoring sheet with many items may be seen as cumbersome for clinical practice, but it will lead to a vital decision for 'timely' initiation of dialysis. All scoring systems may have some outliers or 'parachuted' patients coming too late, but those are times when the art of medicine or the wisdom of doctoring should come onto the scene.

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