

Factors Influencing the Decision to Start Renal Replacement Therapy: Results of a Survey Among European Nephrologists

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Background: Little is known about the criteria nephrologists use in the decision of when to start renal replacement therapy (RRT) in early referred adult patients. We evaluated opinions of European nephrologists on the decision for when to start RRT.

Study Design: European web-based survey.

Predictors: Patient presentations described as uncomplicated patients, patients with unfavorable clinical and unfavorable social conditions, or patients with specific clinical, social, and logistical factors.

Setting & Participants: Nephrologists from 11 European countries.

Outcomes & Measurements: We studied opinions of European nephrologists about the influence of clinical, social, and logistical factors on decision making regarding when to start RRT, reflecting practices in place in 2009. Questions included target levels of kidney function at the start of RRT and factors accelerating or postponing RRT initiation. Using linear regression, we studied determinants of target estimated glomerular filtration rate (eGFR) at the start of RRT.

Results: We received 433 completed surveys. The median target eGFR selected to start RRT in uncomplicated patients was 10.0 (25th-75th percentile, 8.0-10.0) mL/min/1.73 m². Level of excretory kidney function was considered the most important factor in decision making regarding uncomplicated patients (selected by 54% of respondents); in patients with unfavorable clinical versus social conditions, this factor was selected by 24% versus 32%, respectively. Acute clinical factors such as life-threatening hyperkalemia refractory to medical therapy (100%) and uremic pericarditis (98%) elicited a preference for an immediate start, whereas patient preference (69%) and vascular dementia (66%) postponed the start. Higher target eGFRs were reported by respondents from high-versus low-RRT-incidence countries (10.4 [95% CI, 9.9-10.9] vs 9.1 mL/min/1.73 m²) and from for-profit versus not-for-profit centers (10.1 [95% CI, 9.5-10.7] vs 9.5 mL/min/1.73 m²).

Limitations: We were unable to calculate the exact response rate and examined opinions rather than practice for 433 nephrologists.

Conclusions: Only for uncomplicated patients did half the nephrologists consider excretory kidney function as the most important factor. Future studies should assess the weight of each factor affecting decision making. *Am J Kidney Dis.* 60(6):940-948. © 2012 by the National Kidney Foundation, Inc.

INDEX WORDS: Renal replacement therapy; dialysis start; end-stage renal disease; opinions; glomerular filtration rate (GFR).

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Patients with end-stage renal disease (ESRD) receive renal replacement therapy (RRT) to improve their survival and quality of life. The decision of when to start RRT is likely to be guided by the level and rate of decrease in residual kidney function and the clinical condition of the patient. Whereas RRT might be life-saving in certain conditions, dialysis also is unphysiologic and may have life-threatening complications. It carries a significant burden for patients and consumes substantial health care resources.¹ Many studies evaluating associations between the timing of the start of RRT and survival were limited in that they considered only serum creatinine level, which is decreased in patients with deteriorating nutritional status, as a surrogate marker of residual kidney function and an index to define “early” versus “late” starters. In addition, they were unable to assess clinical status or specific reasons to start RRT at a particular moment in time.²⁻⁵

The IDEAL (Initiating Dialysis Early and Late) trial was the first randomized controlled trial attempting to assess whether starting dialysis therapy at high (10-14 mL/min/1.73 m²) or low (5-7 mL/min/1.73 m²) estimated glomerular filtration rates (eGFRs) is more beneficial with respect to patient survival. However, 76% of patients randomly assigned to start at low eGFRs actually started at higher levels because of uremic signs and symptoms, resulting in a relatively small difference in eGFRs between the groups.⁶ The study failed to show a survival difference between those randomly assigned to start dialysis therapy with higher and lower eGFRs, possibly because of this relatively small difference, but suggested that clinical status is important in the decision making of nephrologists.⁶⁻⁸ Nevertheless, little is known about exactly which criteria nephrologists use in their decision for when to start dialysis therapy.

Better understanding of nephrologists’ decision making regarding the start of RRT would assist further studies relating residual kidney function and signs and symptoms at the start of dialysis therapy to prognosis. This ultimately would guide us to define better care for patients with ESRD. We aimed to evaluate current opinions on how clinical, social, and logistical factors influence the decision of when to start RRT in early referred adult patients by performing a survey of European nephrologists. Furthermore, we assessed whether opinions differed by nephrologists’ or facilities’ characteristics.

METHODS

Contents of the Survey

We developed a 26-item web-based survey using the online tool SurveyMonkey (SurveyMonkey.com). The survey was in English and contained multiple-choice and open-ended ques-

tions about the assessment method and target level of kidney function in relation to the start of RRT, factors bringing forward or postponing the start of RRT, factors causing a delay in the planned start, and nephrologists’ and facilities’ characteristics. The survey was administered in autumn 2010, but all respondents were asked to provide their opinions and clinical practice in place in 2009, before publication of the IDEAL trial.⁶ In addition, we asked whether opinions had changed between 2009 and the moment of survey completion.

Clarity and face validity of the survey content were tested during a pilot study of 20 nephrologists from France, Italy, the Netherlands, and the United Kingdom. Based on the feedback obtained, we added questions about reasons for delay of the planned start and whether opinions changed in the recent past. A copy of the survey is provided as Item S1 (available as online supplementary material).

Design

Through national representatives and national societies of nephrology of 11 European countries, we distributed the survey along with a cover letter by e-mail to all nephrologists in the country for whom an e-mail address was available. Four weeks later, we sent a reminder to nonresponders and those who partially completed the survey. Two weeks thereafter, another reminder was sent, together with an e-mail from the national representative stressing the importance of this survey. Survey completion was voluntary and invitations included the option to decline: those opting out were not contacted further. Responses were collected and analyzed anonymously.

Definitions

In scenarios presented to nephrologists we used the following definitions. Uncomplicated patients were defined as those without malnutrition/inflammation (wasting), fluid overload, hyperkalemia, or major comorbid conditions. Examples of unfavorable clinical conditions were defined as including malnutrition/inflammation (wasting), fluid overload, hyperkalemia, mental disorders, or major comorbid conditions. Examples of unfavorable social conditions were defined as including a lack of social support, living alone or incapable to perform exchanges themselves (peritoneal dialysis), treatment nonadherence, or language barriers.

Data Processing and Analysis

The completed surveys were downloaded and stored and subsequently analyzed using SPSS version 16.0 (SPSS Inc, www.spss.com). We applied descriptive statistics and calculated median (25th-75th percentile) values and minimum-maximum ranges for skewed data. Associations were tested using χ^2 tests, *t* tests, and Mann-Whitney *U* tests. With univariable and multivariable linear regression, we studied associations between nephrologists’ (age, sex, and residency in a low- or high-RRT-incidence country) and facility characteristics (academic vs nonacademic, private vs public, and for-profit vs not-for-profit centers) and eGFR at the start of dialysis therapy. Countries were classified as low or high incidence when the age- and sex-adjusted RRT incidence per million population (at day 91 after starting RRT) was lower or higher than the median of participating countries as extracted from the 2008 Annual Report of the ERA-EDTA (European Renal Association-European Dialysis and Transplant Association) Registry.⁹ To fulfill criteria for linear regression analysis, we log-transformed eGFR values. For easier interpretation, we added the intercept to the estimated β coefficient and consequently transformed this back to obtain median eGFRs. We adjusted the models for factors fulfilling criteria for confounding, obtaining adjusted eGFRs.¹⁰ Potential

Table 1. Characteristics of Nephrologists and Treatment Centers

	Total (N = 433)	Incidence Level of RRT in Country		P
		Low (n = 251)	High (n = 182)	
Country of residence				
Finland	—	35 (8)	—	
Italy	—	6 (1)	—	
Romania	—	18 (4)	—	
Spain	—	53 (12)	—	
The Netherlands	—	51 (12)	—	
United Kingdom	—	88 (20)	—	
Belgium ^a	—	—	37 (9)	
Croatia	—	—	17 (4)	
FYR of Macedonia	—	—	15 (3)	
Germany	—	—	69 (16)	
Greece	—	—	44 (10)	
Male sex	280 (65)	159 (63)	121 (67)	0.5
Age				0.4
≤44 y	178 (41)	107 (43)	71 (39)	
45-64 y	247 (57)	141 (56)	106 (58)	
≥65 y	8 (2)	3 (1)	5 (3)	
Years of experience				0.7
≤14 y	246 (57)	147 (59)	99 (54)	
15-34 y	171 (39)	95 (38)	76 (42)	
≥35 y	16 (4)	9 (4)	7 (4)	
Facility type				<0.001
Public vs private				
Public	350 (81)	240 (96)	110 (60)	
Private	83 (19)	11 (4)	72 (40)	
Setting				0.04
Academic	199 (46)	126 (50)	73 (40)	
Nonacademic	234 (54)	125 (50)	109 (60)	
Profit status				<0.001
For profit	100 (23)	31 (12)	69 (38)	
Not for profit	333 (77)	220 (88)	113 (62)	

Note: Percentages are column percentages. Data are presented as number (percentage).

Abbreviations: FYR, former Yugoslav Republic; RRT, renal replacement therapy.

^aDutch-speaking part (Flanders).

confounders were sex, age, country, and working in a for-profit center. A 2-sided $P < 0.05$ was considered statistically significant.

RESULTS

Survey Respondents

We obtained 433 completed surveys from nephrologists in Belgium, Croatia, Germany, Finland, Greece, Italy, FYR of Macedonia, the Netherlands, Romania, Spain, and the United Kingdom. Because we did not know how many of those receiving the survey were nephrologists and not all nephrologists are involved in decision making on when to start RRT, we were unable to determine the number of recipients eligible for participation in the survey. For reasons of data protection, it was not possible to distribute the survey in all countries ourselves. Therefore, the national societies of nephrology circulated a link to the survey. As a result, our soft-

ware could not trace how many nephrologists received or opened the survey and we were unable to assess the exact response rate. If we would assume that all recipients (excluding bounced e-mails) received the survey and were eligible respondents, response rates would range from <1% ($n = 6$ in Italy) to 44% ($n = 15$ in FYR of Macedonia). Table 1 lists characteristics of responding nephrologists. Sixty-five percent were men, and most nephrologists worked in public not-for-profit centers (71%); 13%, in private for-profit centers; 10%, in public for-profit centers; and 6%, in private not-for-profit centers. The survey reflected opinions in 2009, thus before publication of results from the IDEAL trial. Only 8% indicated that their opinions had changed at the time of the survey (autumn 2010); they reported that these changes were based on literature (46%) and their own clinical experience (14%).

Table 2. Stated Target Kidney Function as Start Time for RRT

Measure of Residual Kidney Function	No.	Median ^a	Range (min-max)
eGFR (mL/min/1.73 m ²)	382	10 [8-10]	5-20
Calculated residual GFR (mL/min)	130	10 [8-12]	5-20
Plasma urea (mmol/L)	117	33 [31-40]	11-50
Serum creatinine (μmol/L)	127	650 [530-780]	353-1,501

Note: Respondents were asked the following question: "Consider a nondiabetic, uncomplicated 60-years old male patient (weight 80 kg, height 1.80 m) in whom you confidently anticipate a further decline of renal function. On average, at what level of residual renal function do you aim to start RRT?" Conversion factor for serum creatinine in μmol/L to mg/dL, $\times 0.0113$.

Abbreviations: eGFR, estimated glomerular filtration rate; min, minimum; max, maximum; RRT, renal replacement therapy.

^aThe 25th-75th percentile is given in brackets.

Residual Kidney Function

Level of residual kidney function may be assessed using various methods. Of 433 (100%) respondents, 220 (51%) used one method: 179 respondents (41%) used a formula exclusively (eg, MDRD [Modification of Diet in Renal Disease] Study equation or Cockcroft-Gault formula), whereas 41 (9%) reported sole use of another method, such as measured 24-hour creatinine clearance ($n = 22$) or the mean of measured 24-hour creatinine and urea clearance ($n = 13$). The other 213 respondents used multiple methods. Of these, 198 (46%) used a formula plus another method, such as measured 24-hour creatinine clearance ($n = 78$), the mean of measured 24-hour creatinine and urea clearance ($n = 34$), or a combination of these 2 ($n = 23$).

Table 2 lists median values for residual kidney function at which nephrologists aimed to start RRT in uncomplicated patients; for eGFR, the median target level was 10 (25th-75th percentile, 8-10) mL/min/1.73 m², although this varied widely (Fig 1). The importance of level of excretory kidney function in the decision for when to start RRT was evaluated for: (1) uncomplicated patients, (2) patients with unfavorable clinical conditions, and (3) patients with unfavorable social conditions. For uncomplicated patients, 54% of respondents considered excretory kidney function as the most important factor in their decision to start RRT, whereas percentages were lower for patients with unfavorable clinical (24%) and social conditions (32%).

Figure 2 summarizes results regarding the perceived clinical benefit of starting RRT at GFR >10.5 mL/min/1.73 m². Most (86%) believed that starting at higher GFRs is beneficial only in the presence of symptoms, with "reduction of emergency-start dialysis" as the main reason. Some respondents stressed that patients are receiving frequent medical supervi-

sion when starting at GFR >10.5 mL/min/1.73 m², and those eligible for transplant are placed on the waiting list earlier. Reduction of emergency-start of dialysis was also the most important motive for respondents (11%) believing that starting at GFR >10.5 mL/min/1.73 m² was always beneficial.

Comparing countries with a low versus high RRT incidence, we found that respondents from high-incidence countries (18%) more often believed that starting at GFR >10.5 mL/min/1.73 m² is always beneficial compared with respondents from low-incidence countries (6%). None of the respondents from for-profit centers believed that starting at GFR >10.5 mL/min/1.73 m² was never beneficial.

Determinants of Level of eGFR at the Start of RRT

We assessed associations between nephrologists' and facilities' characteristics and the target eGFR at the start of RRT (Table 3). Adjusted target eGFRs were significantly higher for respondents from high-incidence countries than from low-incidence countries: 10.4 mL/min/1.73 m² (95% confidence interval [CI], 9.9-10.9) versus 9.1 mL/min/1.73 m². Also, female nephrologists aimed to start at higher levels (adjusted eGFR, 10.2 mL/min/1.73 m²) compared with males (adjusted eGFR, 9.4; 95% CI, 8.9-10.0 mL/min/1.73 m²), as well as nephrologists from for-profit versus not-for-profit facilities (adjusted eGFRs of 10.1 [95% CI, 9.5-10.7] vs 9.5 mL/min/1.73 m²).

Factors Accelerating the Initiation of RRT

Respondents were asked to consider a hypothetical patient with a residual kidney function at which they usually would decide to postpone treatment and to indicate how the presence of specific conditions would affect their decision. When respondents opted for either "immediate start of dialysis (with an acute access)" or "start of dialysis when a permanent access

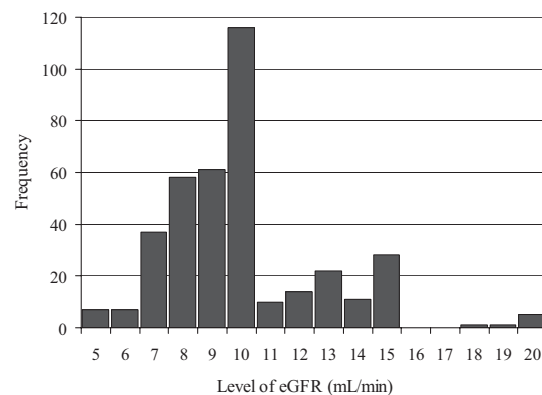


Figure 1. Level of estimated glomerular filtration rate (eGFR) at which nephrologists aimed to start renal replacement therapy in uncomplicated patients.

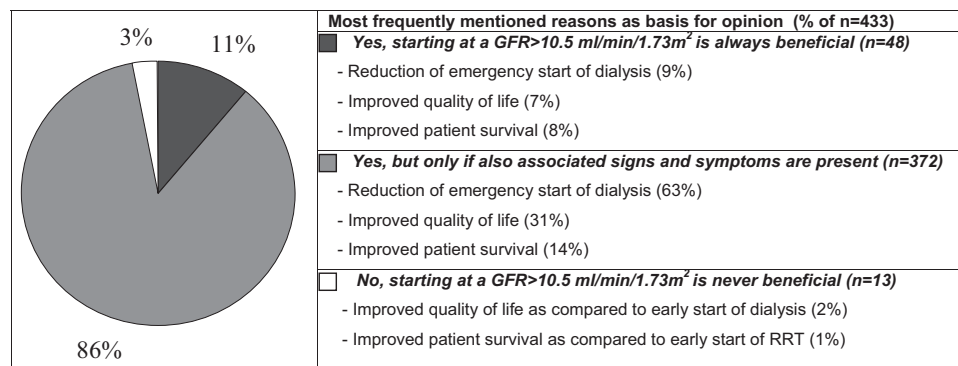


Figure 2. Attitudes toward early initiation of dialysis. Respondents were asked “In general, do you think an early start of dialysis (i.e. GFR > 10.5 mL/min/1.73 m²) is beneficial?” Abbreviations: GFR, glomerular filtration rate; RRT, renal replacement therapy.

is ready,” this indicated they were inclined to accelerate the initiation of dialysis therapy. All factors presented in the survey (Table 4) accelerated RRT initiation to some extent. In the presence of chronic conditions such as diabetes mellitus and chronic heart disease, 60% and 65% of nephrologists would start dialysis sooner. A majority considered an immediate start of dialysis therapy in the presence of more acute clinical phenomena, such as uremic symptoms (86%) and fluid overload refractory to diuretic therapy (97%). Another common reason for an earlier start of RRT (including transplant) was the availability of a matching pre-emptive transplant (kidney or kidney-pancreas) from a living donor (70%).

Compared with respondents from high-incidence countries, those from low-incidence countries less commonly indicated that they would start dialysis therapy sooner in the presence of several chronic conditions, for example, at older than 75 years (36% vs 45%; $P = 0.01$), the presence of chronic heart disease (59% vs 73%; $P < 0.001$), vascular dementia (17% vs 43%; $P < 0.001$), and cirrhosis/chronic liver disease (42% vs 60%; $P < 0.001$). There were no differences between nephrologists working in for-profit and not-for-profit centers.

Factors Postponing the Start of RRT

To evaluate the extent to which some conditions prompted nephrologists to postpone the start of RRT, respondents considered a hypothetical uncomplicated patient with a level of kidney function at which they usually would start dialysis therapy. Patient preference (69%) and vascular dementia (66%) were the most important factors in postponing the start of dialysis therapy (Table 5). Compared with respondents from high-incidence countries, those from low-incidence countries were more likely to postpone dialysis therapy in the presence of a (relative) lack of capacity in the dialysis facility (33% vs 20%; $P = 0.04$) and vascular dementia (73% vs 58%; $P = 0.001$).

Factors Delaying the Planned Start of RRT

Notwithstanding a nephrologist’s preference to start RRT at a particular moment in time, initiation may be delayed. According to 7%, RRT initiation was never delayed; 79% answered that fewer than half their patients started later than considered ideal; and for 14%, RRT initiation was delayed in at least half their patients. Common reasons for delay were patient preference (65%), lack of adequate preparation for dialysis treatment (32%), or lack of dialysis facilities (8%). Further reasons included good clinical condition (8%) and unexpected deterioration in kidney function or late referral (5%). Most (77%) reported never having a waiting list for long-term dialysis treatment at their unit, and others indicated that they often (4%) or always (3%) had a waiting list. A waiting list was present more often in not-for-profit compared with for-profit centers (26% vs 10%; $P = 0.01$), in public than in private centers (26% vs 7%; $P = 0.02$), and in low- versus high-incidence countries (30% vs 12%; $P < 0.001$).

DISCUSSION

This international survey evaluated current opinions of European nephrologists on how clinical, social, and logistical factors influence their decision to start RRT in early referred adult patients with ESRD. Only a third of all nephrologists considered level of excretory kidney function as the most important factor in their decision making; for uncomplicated patients, about half of all nephrologists selected this as the most important factor. Factors eliciting an immediate start were life-threatening hyperkalemia refractory to other therapy, uremic pericarditis, and fluid overload refractory to diuretic therapy. Patient preference and vascular dementia were reasons to postpone the start.

The most recent European guideline at the time of the survey, the European Renal Best Practice Guidelines,¹¹ states that GFR should be estimated using

Table 3. Nephrologist and Facility Characteristics and Their Associations With Target Level of eGFR at Start of Dialysis in an Uncomplicated Patient

Determinants	Median eGFR (95% CI)	Adjusted Median eGFR (95% CI)
Nephrologist characteristics		
Incidence level of country of residence ^b		
Low ^a	9.1	9.1
High ^a	10.3 (9.8-10.9)	10.4 (9.9-10.9)
Sex ^c		
Female	10.2	10.2
Male	9.3 (8.8-9.8)	9.4 (8.9-10.0)
Age ^d		
≤44 y	10.0	9.9
≥45 y	9.3 (8.9-9.8)	9.4 (9.0-9.9)
Facility characteristics^e		
Public vs private		
Public center	9.5	9.6
Private center	10.0 (9.4-10.7)	9.8 (9.1-10.6)
Setting		
Nonacademic	9.5	9.5
Academic	9.8 (9.3-10.3)	9.7 (9.2-10.2)
Profit status		
Nonprofit center	9.4	9.5
For-profit center	10.3 (9.7-11.0)	10.1 (9.5-10.7)
Excretory kidney function most important factor in decision to start RRT?^{f,g}		
In uncomplicated patients		
No	9.3	9.4
Yes	9.9 (9.4-10.4)	9.7 (9.2-10.2)
In patients with unfavorable social conditions		
No	9.5	9.5
Yes	10.0 (9.4-10.6)	9.9 (9.4-10.5)
In patients with unfavorable clinical conditions		
No	9.5	9.5
Yes	9.8 (9.3-10.4)	9.8 (9.3-10.3)
Beneficial to start RRT at GFR >10.5?^{f,h}		
No	7.6	8.2
Yes ⁱ	9.7 (8.3-11.3)	9.7 (8.3-11.2)

Note: Based on linear regression analyses. eGFRs given in mL/min/1.73 m².

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy.

^aLow-incidence countries are Finland, Italy, Romania, Spain, the Netherlands, and United Kingdom. High-incidence countries are Belgium, Croatia, Germany, Greece, and FYR of Macedonia.

^bAdjusted for sex and age.

^cAdjusted for age and country.

^dAdjusted for sex and country.

^eAdjusted for sex, age, and country.

^fAdjusted for sex, age, country, and for-profit center.

^gRespondents were asked: "Do you consider the level of excretory renal function as most important factor in the decision to start RRT?"

^hRespondents were asked: "Do you consider a start of RRT >10.5 mL/min/1.73 m² as beneficial?"

ⁱEither always or in the presence of associated symptoms.

only a technique validated in patients with advanced kidney failure. Although these guidelines mention calculating the mean of urea and creatinine clearance as the preferred method, only 15% of our respondents applied this method. Almost half the nephrologists reported using eGFR equations alone to guide the start of dialysis therapy. According to current opinions, this is problematic because the plasma creatinine concentration used in these equations is determined not only by GFR, but also by tubular secretion and creatinine generation rate. Because the latter depends on nutritional status and muscle mass, equations taking solely demographic variables into account cannot fully predict the creatinine generation rate.^{12,13} A recently updated position statement argues that eGFR equations are not appropriate to determine the need for starting RRT because they are not validated in lower ranges of GFR (<30 mL/min/1.73 m²), in other words, just before initiating dialysis therapy.¹⁴⁻¹⁶ Possibly, nephrologists do not use the recommended method because in their decision making, they consider the exact level of excretory kidney function less important than symptoms and social conditions and therefore may attribute less importance to knowing its exact value.

Most respondents (86%) believed that only in the presence of signs and symptoms is starting at GFR >10.5 mL/min/1.73 m² beneficial. Results of a survey held in 2000 showed that only 38% of respondents indicated that signs and symptoms were important reasons for starting RRT.⁷ Our survey now adds that in uncomplicated patients, level of excretory kidney function is considered the most important factor in the decision to start RRT by only half of nephrologists, a percentage decreasing further for patients with unfavorable clinical (24%) or social conditions (32%), suggesting that the importance of signs and symptoms has gained importance in comparison to level of excretory kidney function.

The target eGFR at which nephrologists aimed to start treatment in uncomplicated patients was 10.0 mL/min/1.73 m², which is slightly higher than eGFRs reported by studies using data from patient records, in which values ranged from 7.5-8.8 mL/min/1.73 m².^{4,17-19} Consistent with our finding that only 7% indicated that the planned start was never delayed, a possible explanation for these differences may be that the actual start usually is later than the planned start.

Respondents indicated that the presence of chronic clinical conditions often resulted in an earlier start of RRT, in other words, as soon as a permanent access is available. Results from Lassalle et al¹⁹ also showed higher percentages of older patients and diabetes and cardiovascular diseases in patients starting at eGFR >10 mL/min/1.73 m². Similar results were found by

Table 4. Factors Affecting Timing of Dialysis Initiation in Patients for Whom the Nephrologist Generally Would Postpone Dialysis

	Immediate Start of Dialysis (With an Acute Access)	Start of Dialysis When Permanent Access Is Ready	Not Start Dialysis (yet), Even if Access Is Available
Chronic clinical conditions			
Diabetes mellitus	39 (9)	214 (51)	168 (40)
Age >75 y	16 (4)	151 (36)	255 (60)
Chronic heart disease	75 (18)	197 (47)	150 (36)
Cirrhosis or chronic liver disease	50 (12)	158 (37)	214 (51)
Vascular dementia	10 (2)	108 (25)	312 (73)
Other low mental functional status ^a	13 (3)	210 (49)	205 (48)
Other clinical conditions			
Symptoms of uremia	372 (86)	59 (14)	2 (<1)
Fluid overload refractory to diuretic therapy	420 (97)	12 (3)	1 (<1)
Progressive deterioration in nutritional status	228 (53)	204 (47)	—
Life-threatening hyperkalaemia refractory to medical therapy	431 (100)	2 (<1)	—
Pericarditis attributed to uremia	425 (98)	6 (1)	1 (<1)
Predictive progressive decrease in GFR within the next mo	45 (11)	329 (77)	53 (12)
Social/logistical conditions			
Patient's preference to start RRT	24 (6)	305 (70)	104 (24)
Wishes of the family to start RRT	12 (3)	233 (54)	185 (43)
Nonadherence to prescribed diet and/or medication	32 (8)	252 (59)	142 (33)

Note: Respondents were asked: "Consider a patient with a level of residual renal function on which you would usually decide to still postpone dialysis: How would the following conditions affect your decision on when to start dialysis?" Values are given as number (percentage).

Abbreviation: GFR, glomerular filtration rate; RRT, renal replacement therapy.

^aFor example, Down syndrome.

Stel et al,²⁰ who reported that nephrologists tend to start earlier in the elderly and patients with diabetes, although the difference was only 0.6 mL/min/1.73 m². The higher eGFRs in the elderly and patients with chronic clinical conditions may be the result of malnu-

trition inducing lower serum creatinine levels and thus higher eGFRs.¹⁵ In line with the guidelines, acute clinical factors such as uremic symptoms and progressive deterioration in nutritional status often resulted in an immediate start, just like patient's preference and availability of a matching pre-emptive transplant from a living donor, the latter being shown previously by van Stralen et al²¹ in pediatric patients.

The start of dialysis therapy often was postponed by patient's preference and the presence of vascular dementia. However, 31% of nephrologists indicated they start dialysis therapy, or at least start preparations for dialysis therapy, despite patient preference to postpone dialysis. Vascular dementia may worsen if the patient is treated with dialysis, which may explain why the majority postpone the start of dialysis therapy.²²⁻²⁴ However, respondents stressed that the severity rather than the presence of vascular dementia has a role in their decision making.

We found several differences in opinion when examining results by nephrologists' and facilities' characteristics, for example, regarding the target eGFR in Table 3, although the clinical relevance may be questioned considering the low accuracy of eGFR in patients with ESRD. Respondents from high-incidence countries more often believed that starting at GFR >10.5 mL/min/1.73 m² is beneficial, although

Table 5. Factors Affecting Timing of Dialysis Initiation in Patients for Whom the Nephrologist Generally Would Start Dialysis

	Start of or Preparation for Dialysis	Postpone Dialysis
Patient's preference to postpone RRT	128 (31)	291 (69)
Wishes of the family to postpone RRT	243 (64)	138 (36)
Long distance to dialysis facility	293 (84)	57 (16)
(Relative) lack of capacity in dialysis facility	225 (72)	86 (28)
Vascular dementia	130 (34)	255 (66)
Other low mental functional status ^a	269 (68)	127 (32)
Nonadherence to prescribed diet and/or medication	336 (83)	71 (17)

Note: Respondents were asked: "Consider an uncomplicated patient with the level of residual renal function on which you would usually decide to start dialysis: How would the following conditions affect your decision on when to start dialysis?" Values are given as number (percentage).

Abbreviation: RRT, renal replacement therapy.

^aFor example, Down syndrome.

even in high-incidence countries, this share was only 18%. Respondents from low-incidence countries seem less inclined to start RRT sooner in patients with older age and chronic conditions (such as vascular dementia or chronic heart disease). They also more often would postpone treatment because of a relative lack of dialysis capacity and reported a waiting list for long-term dialysis treatment. Because old age and chronic heart disease are common, these observed differences may be relevant for explaining the variation in take-on rates. Nephrologists in high-incidence countries were more eager to start RRT at higher GFRs and more inclined to start in less healthy patients; the opinions thus are reflected in actual practice. Nephrologists from private and for-profit centers less often had a waiting list for long-term dialysis treatment than those from public and not-for-profit centers. We speculate that in some cases, these differences by organizational status may reflect a supply-led demand rather than the best patient interest. If a private or for-profit center has the capacity, they may start RRT earlier compared with public or not-for-profit centers. However, in these public centers, dialysis sometimes cannot be started because of a lack of capacity.²⁵ Previous studies showed a positive association between RRT incidence and the share of private for-profit HD facilities.^{26,27} Our results are in line with them and add that the higher incidence may be caused in part by applying higher target eGFRs at RRT initiation.

With this international survey including 11 European countries, we examined a wide range of current opinions of nephrologists' on their decision for when to start RRT. Since the previous survey on this matter in 2000, several debates and cohort studies were published suggesting that starting RRT at higher eGFRs may be harmful.^{2-6,8,12,14,18,19,28} Therefore, we needed an update regarding current opinions on this topic.

Limitations of this study are that we were unable to calculate the exact response rate, and with our sample size, the generalizability of our results could be questioned. We did not know how many of those receiving the survey were nephrologists and were involved in decision making for when to start RRT. Nevertheless, based on a worst case scenario, assuming that all nephrologists received the survey and were eligible for participation, we estimated a low response rate. However, surveys with a low response rate do not by definition have nonresponse bias.^{29,30} A sensitivity analysis using only countries with a response >10% provided similar results. Because we lacked information for nonresponders, we do not know whether and to what extent nonresponse bias affected our results. Another potential limitation is that respondents gave socially desirable answers because the subject ad-

ressed an extensively debated topic. We tried to minimize this by emphasizing the anonymous data collection. Additionally, nephrologists with a special interest and strong opinions may have been more eager to respond (volunteer bias). Finally, we conducted this survey several months after publication of the IDEAL trial, but respondents were asked to report their opinions prior to this publication; therefore, recall bias may have had a role.

In conclusion, our results provided insight into what is considered current best practice from nephrologists' point of view and we showed that signs and symptoms are important in decision making for when to start RRT. In the absence of those symptoms, level of excretory kidney function is considered the most important factor by only half the nephrologists. Respondents reported that they would start RRT sooner on account of chronic conditions and patient preference, but significant acceleration in RRT initiation was reported to be triggered by acute clinical factors such as hyperkalemia, uremic symptoms, and fluid overload. Whereas our survey focused on nephrologists' opinions, future research should include an additional focus on patients' perspectives. Before being able to optimize medical practice in relation to starting RRT, we first need to assess the importance of medical and shared decision making for patient prognosis.

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SUPPLEMENTARY MATERIAL

Item S1: Survey.

Note: The supplementary material accompanying this article (<http://dx.doi.org/10.1053/j.ajkd.2012.07.015>) is available at www.ajkd.org

REFERENCES

1. Ginieri-Coccosis M, Theofilou P, Synodinou C, Tomaras V, Soldatos C. Quality of life, mental health and health beliefs in

- haemodialysis and peritoneal dialysis patients: investigating differences in early and later years of current treatment. *BMC Nephrol*. 2008;9:14.
2. Hwang SJ, Yang WC, Lin MY, Mau LW, Chen HC. Impact of the clinical conditions at dialysis initiation on mortality in incident haemodialysis patients: a national cohort study in Taiwan. *Nephrol Dial Transplant*. 2010;25(8):2616-2624.
 3. Clark WF, Na Y, Rosansky SJ, et al. Association between estimated glomerular filtration rate at initiation of dialysis and mortality. *CMAJ*. 2011;183(1):47-53.
 4. Stel VS, Dekker FW, Ansell D, et al. Residual renal function at the start of dialysis and clinical outcomes. *Nephrol Dial Transplant*. 2009;24(10):3175-3182.
 5. Traynor JP, Simpson K, Geddes CC, Deighan CJ, Fox JG. Early initiation of dialysis fails to prolong survival in patients with end-stage renal failure. *J Am Soc Nephrol*. 2002;13(8):2125-2132.
 6. Cooper BA, Branley P, Bulfone L, et al. A randomized, controlled trial of early versus late initiation of dialysis. *N Engl J Med*. 2010;363(7):609-619.
 7. Ledebro I, Kessler M, van Biesen W, et al. Initiation of dialysis—opinions from an international survey: Report on the Dialysis Opinion Symposium at the ERA-EDTA Congress, 18 September 2000, Nice. *Nephrol Dial Transplant*. 2001;16(6):1132-1138.
 8. Lameire N, van Biesen W. The initiation of renal-replacement therapy—just-in-time delivery. *N Engl J Med*. 2010;363(7):678-680.
 9. ERA-EDTA Registry. ERA-EDTA Registry Annual Report. 2008. Amsterdam, The Netherlands: Academic Medical Center, Department of Medical Informatics; 2010.
 10. Jager KJ, Zoccali C, Macleod A, Dekker FW. Confounding: what it is and how to deal with it. *Kidney Int*. 2008;73(3):256-260.
 11. Kessler M; European Best Practice Guidelines Expert Group on Hemodialysis, European Renal Association. Section I. Measurement of renal function, when to refer and when to start dialysis. *Nephrol Dial Transplant*. 2002;17(suppl 7):7-15.
 12. Beddhu S, Samore MH, Roberts MS, Stoddard GJ, Pappas LM, Cheung AK. Creatinine production, nutrition, and glomerular filtration rate estimation. *J Am Soc Nephrol*. 2003;14(4):1000-1005.
 13. Fink JC, Burdick RA, Kurth SJ, et al. Significance of serum creatinine values in new end-stage renal disease patients. *Am J Kidney Dis*. 1999;34(4):694-701.
 14. Tattersall J, Dekker F, Heimbürger O, et al. When to start dialysis: updated guidance following publication of the Initiating Dialysis Early and Late (IDEAL) Study. *Nephrol Dial Transplant*. 2011;26(7):2082-2086.
 15. Grootendorst DC, Michels WM, Richardson JD, et al. The MDRD formula does not reflect GFR in ESRD patients. *Nephrol Dial Transplant*. 2011;26(6):1932-1937.
 16. Poggio ED, Wang X, Greene T, Van LF, Hall PM. Performance of the Modification of Diet in Renal Disease and Cockcroft-Gault equations in the estimation of GFR in health and in chronic kidney disease. *J Am Soc Nephrol*. 2005;16(2):459-466.
 17. Beddhu S, Samore MH, Roberts MS, et al. Impact of timing of initiation of dialysis on mortality. *J Am Soc Nephrol*. 2003;14(9):2305-2312.
 18. Kazmi WH, Gilbertson DT, Obrador GT, et al. Effect of comorbidity on the increased mortality associated with early initiation of dialysis. *Am J Kidney Dis*. 2005;46(5):887-896.
 19. Lassalle M, Labeeuw M, Frimat L, et al. Age and comorbidity may explain the paradoxical association of an early dialysis start with poor survival. *Kidney Int*. 2010;77(8):700-707.
 20. Stel VS, Tomson C, Ansell D, et al. Level of renal function in patients starting dialysis: an ERA-EDTA Registry study. *Nephrol Dial Transplant*. 2010;25(10):3315-3325.
 21. van Stralen KJ, Tizard EJ, Jager KJ, et al. Determinants of eGFR at start of renal replacement therapy in paediatric patients. *Nephrol Dial Transplant*. 2010;25(10):3325-3332.
 22. Kurella M, Chertow GM, Luan J, Yaffe K. Cognitive impairment in chronic kidney disease. *J Am Geriatr Soc*. 2004;52(11):1863-1869.
 23. Madan P, Kalra OP, Agarwal S, Tandon OP. Cognitive impairment in chronic kidney disease. *Nephrol Dial Transplant*. 2007;22(2):440-444.
 24. Rakowski DA, Caillard S, Agodoa LY, Abbott KC. Dementia as a predictor of mortality in dialysis patients. *Clin J Am Soc Nephrol*. 2006;1(5):1000-1005.
 25. Mulley AG. The need to confront variation in practice. *BMJ*. 2009;339(7728):1007-1009.
 26. Horl WH, de AF, Williams PF. Healthcare systems and end-stage renal disease (ESRD) therapies—an international review: access to ESRD treatments. *Nephrol Dial Transplant*. 1999;14(suppl 6):10-15.
 27. Caskey FJ, Kramer A, Elliott RF, et al. Global variation in renal replacement therapy for end-stage renal disease. *Nephrol Dial Transplant*. 2011;26(8):2604-2610.
 28. Rosansky SJ, Eggers P, Jackson K, Glasscock R, Clark WF. Early start of hemodialysis may be harmful. *Arch Intern Med*. 2011;171(5):396-403.
 29. Stang A, Jockel KH. Studies with low response proportions may be less biased than studies with high response proportions. *Am J Epidemiol*. 2004;159(2):204-210.
 30. Hikmet N, Chen SK. An investigation into low mail survey response rates of information technology users in health care organizations. *Int J Med Inform*. 2003;72(1-3):29-34.