Dialysis-Early or Late
When to start?

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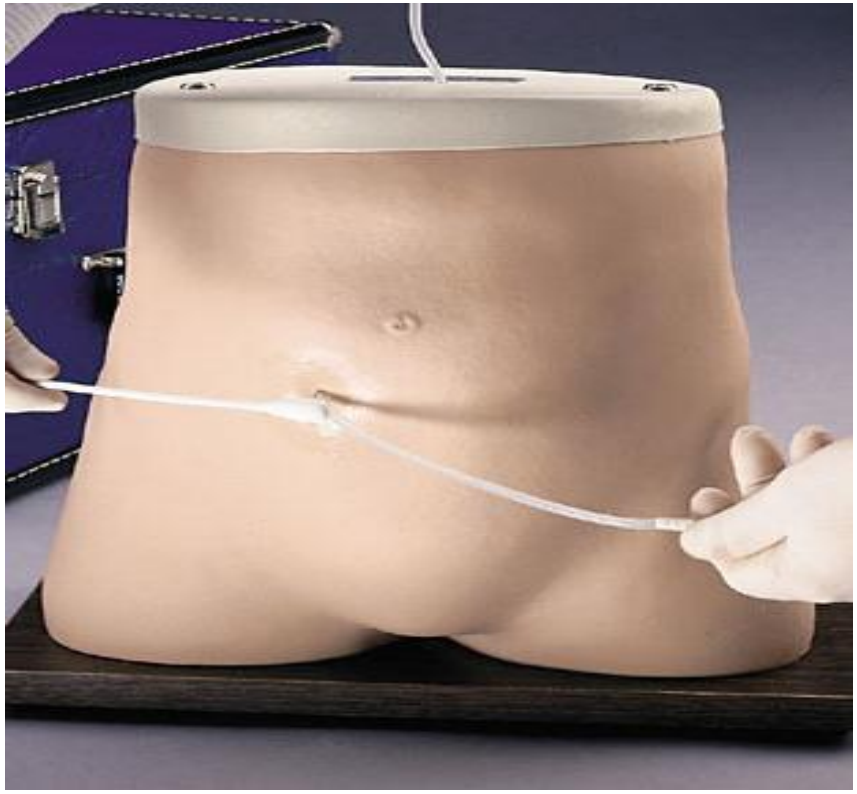
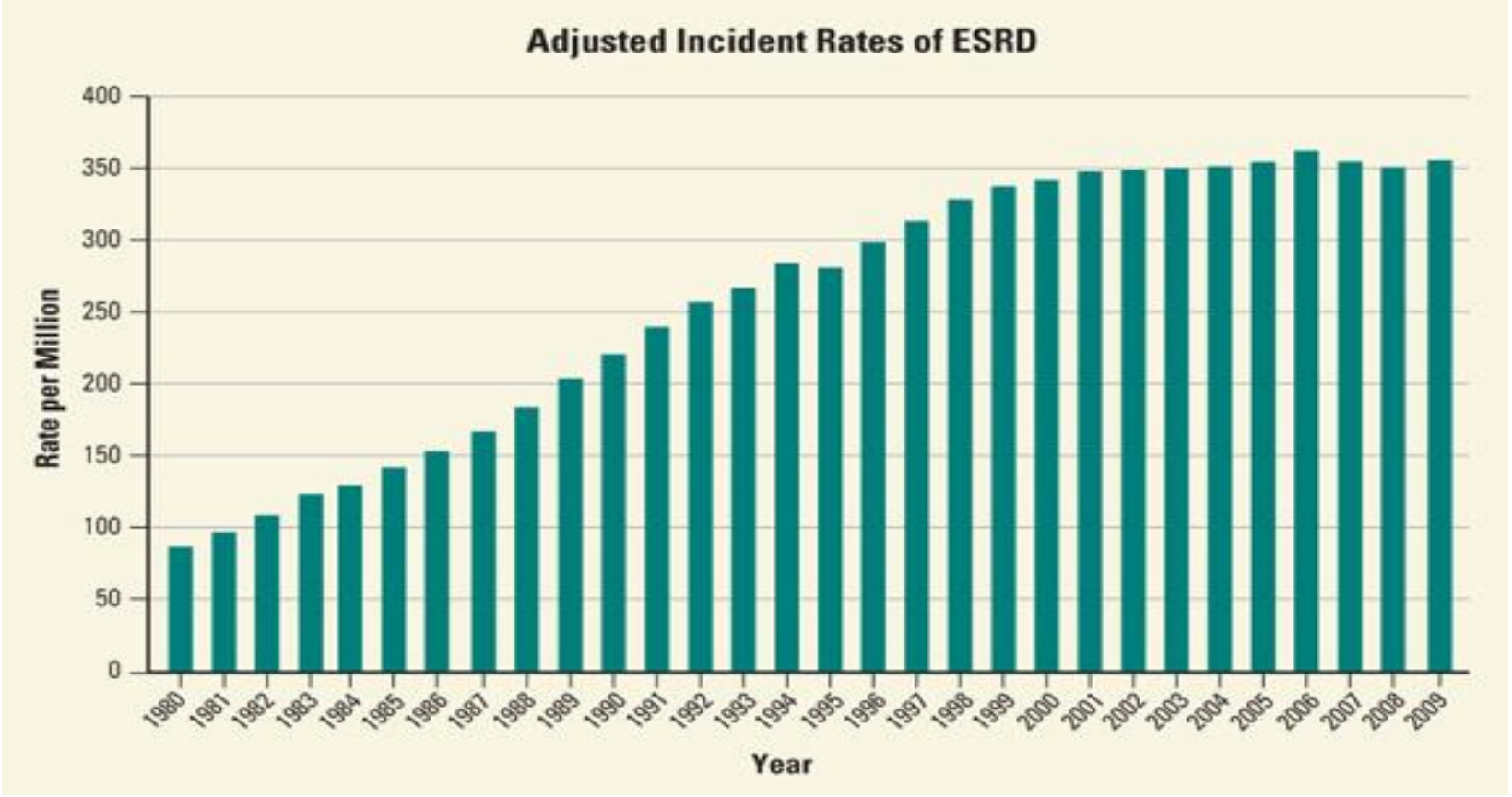
- Chronic Kidney Disease (CKD) includes patients with eGFR<60 ml/min with or without evidence of kidney damage
- End Stage Renal Disease (ESDR) is the sever form of CKD that requires renal replacement therapy (RRT).

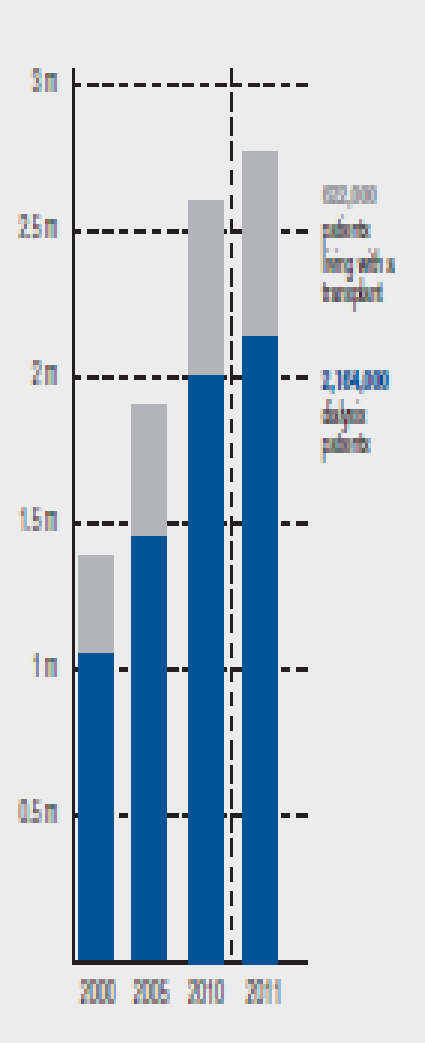
There are 3 kinds of RRT options:

- Hemodialysis (HD)
- Peritonel Dialysis (PD)
- Renal Transplantation (RT)



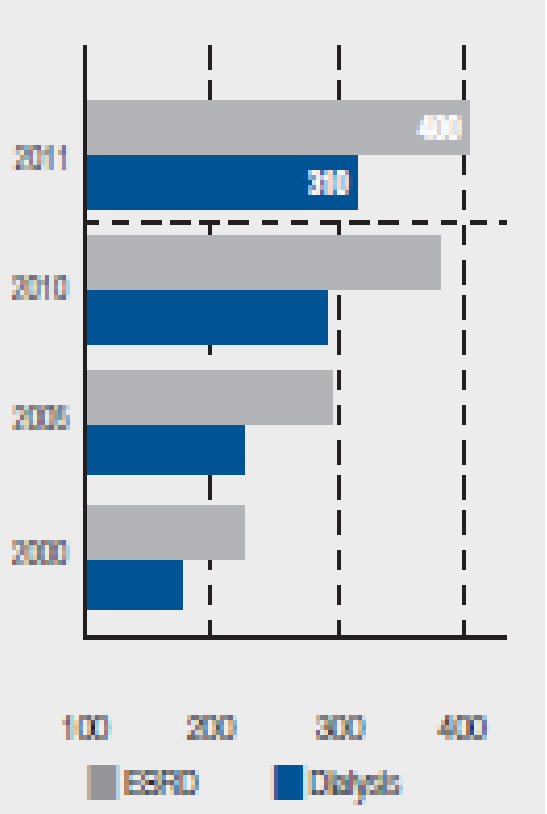
ESRD Incident Rate in US (*National Kidney and Urologic Diseases Information Clearinghouse***)**



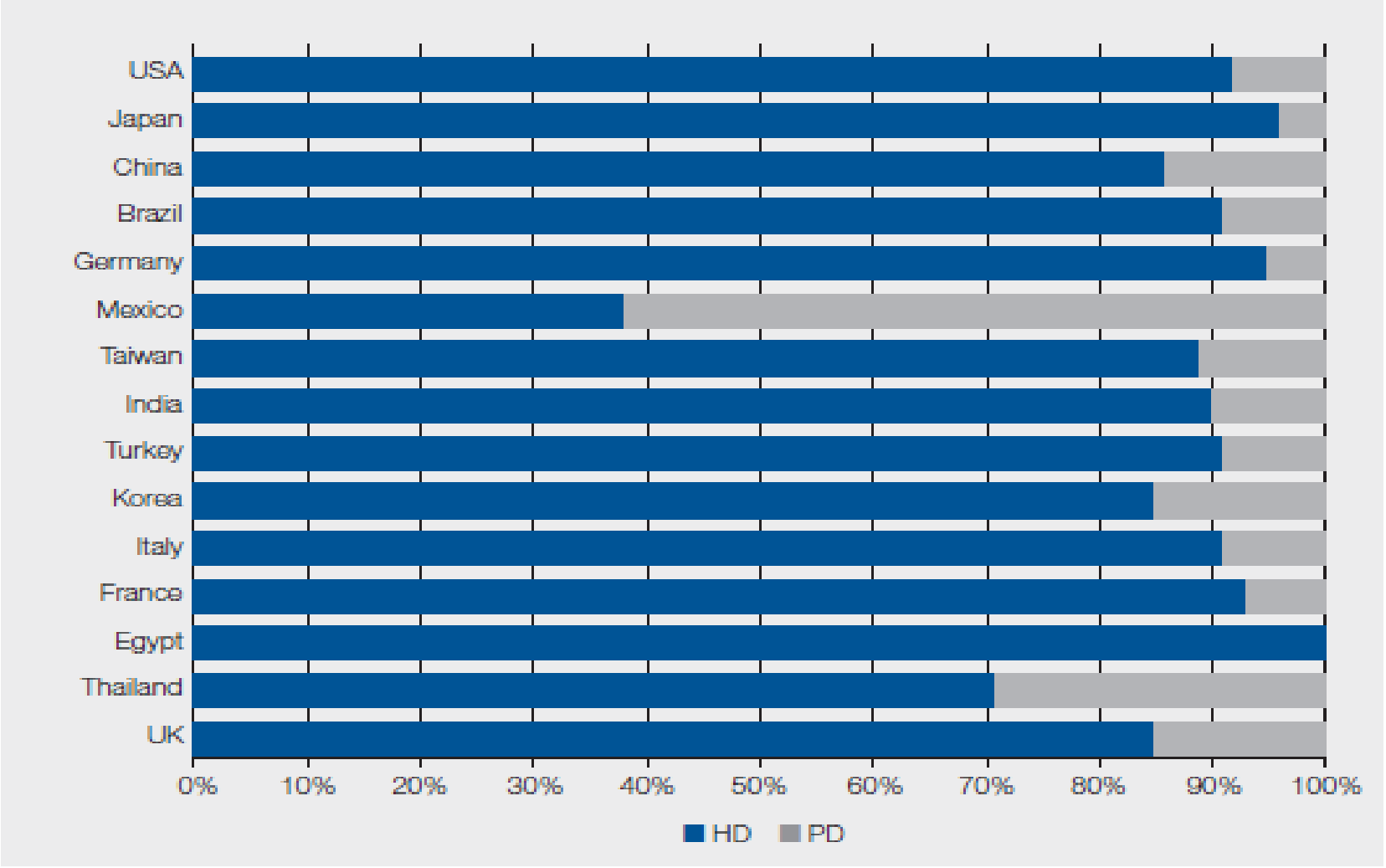


Development of ESRD patient numbers since 2000

Development of global ESRD and dialysis prevalence values since 2000 (patients per million population)



Comparison of HD and PD patient numbers in the 15 largest countries ranked by total dialysis patient population



ESRD Patients	2,786,000
thereof HD	1,929,000
thereof PD	235,000
thereof Tx	622,000
World Population	**7.0 billion**

Annual Growth Rates	
World population	1.1%
ESRD	6–7%
HD	6–7%
PD	7–8%
Tx	4–5%

The number of patients being treated for ESRD globally was estimated to be 2,786,000 at the end of 2011 and, with a 6–7% growth rate, continues to increase at a significantly higher rate than the world population.

Of these 2,786,000 ESRD patients, approximately 2,164,000 were undergoing dialysis treatment (haemodialysis (HD) or peritoneal dialysis (PD)) and around 622,000 people were living with kidney transplants (Tx).

TABLE 1. *Distribution of incident RRT patients (including pediatric patients) according to RRT type in 2013.*

	n	%
Hemodiyaliz / *Hemodialysis*	8757	82.60
Periton diyalizi / *Peritoneal dialysis*	1150	10.85
Transplantasyon / *Transplantation* *	694	6.55
Toplam / *Total*	10601	100.00

REGISTRY OF THE NEPHROLOGY, DIALYSIS AND TRANSPLANTATION IN TURKEY

TABLE 2. *Distribution of chronic HD/PD patients or patients followed with functioning graft (including pediatric patients) according to RRT type as of the end of 2013.*

	n	%
Hemodiyaliz / *Hemodialysis*	52675	78.96
Periton diyalizi / *Peritoneal dialysis*	4537	6.80
Transplantasyon / *Transplantation*	9499	14.24
Toplam / *Total*	66711	100.00

REGISTRY OF THE NEPHROLOGY, DIALYSIS AND TRANSPLANTATION IN TURKEY

Hemodialysis

- Relies on the principles of solute diffusion across a semipermeable membrane.
- According to the laws of diffusion, the larger the molecule, the slower its transfer rate.
- The moleculer weight of urea (69 Da) <creatinine's (113 Da)

- There are 3 essential components of HD.

1-The dialyzer

2-The composition and the delivery of the dialysate.

3-The blood delivery system.

- HD may be done by an access:
  - *the artery-ven fistula
  - *intravenous large-bore catheters
  - *Grafts

Residual renal function (RRF)

- The rate of RRF loss is an important consideration for the timing of dialysis initiation decision.
- Patients with low GFR may have sufficient RRF to be maintaned off dialysis for years.

The indications of emergent dialysis

- Acute renal failure

  *uremic semptoms and signs are getting worse in patient with GFR<15 ml/min/1.73 m^2
- Fluid overload which can not respond to diüretics
- Hyperkalemia which can not be controlled (K^+>6.5 mmol/L with/without ECG changes)
- Severe metabolic acidemia (pH<7.2 is persistent although $NaHCO_3$ treatment +oliguria)
- Intoxications=>salicylates, theophylline, paraquat, methanol
- Hypercalcemia
- Hyperuricemia

The History of HD

- During 1980's dialysis was initiated only when patients demonstrated clear signs of lifethreatening uremic complications.

- In 1985; Bonomini reported that earlier initiation of dialysis could convey survival benefits.

- In 1997→US National Kidney Foundation
- →Patients GFR<10.5 mL/min} start dialysis

The trend to early start of dialysis related to these 6 wisdoms

- Level of dialytic clearance of low-molecular-weight solutes (e.g., urea) is associated with a survival/morbidity benefit and is comparable to endogenous renal function
- Low albumin and nutritional issues are synonymous
- Nutrition can be improved with increased dialytic clearance of low-molecular-weight solutes (e.g., urea)
- Diabetics need to initiate dialysis earlier than nondiabetics
- At low levels of renal function: eGFR <15 ml/min/1.73 m^2
- Waiting until eGFR is <6 ml/min/ 1.73 m^2 to initiate dialysis is potentially dangerous

Level of dialytic clearance of low-molecular-weight solutes (e.g urea) is associated with a survival/morbidity benefit

- The two randomized studies showed no benefits of dialytic small molecule clerance on survival.

- *Eknoyan G, Beck GJ, Alfred K, Cheung AK, Daugirdas JT, Greene T, Kusek JW, Allon M, Bailey J, Delmez JA, Milford E, Ornt DB, Rocco MV, Schulman G, Schwab SJ, Teehan BP, Toto R: for the Hemodialysis (HEMO) Study Group: Effect of dialysis dose and membrane flux in maintenance hemodialysis. N Engl J Med 347:2010–2019,*
- *Paniagua R, Anato D, Vonesh E, Correa-Rotter R, Ramos A, Moran J, Mujais S: for the Mexican Nephrology Collaborative Study Group: Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol 13:1307–1320, 2002*

Low albumin and nutritional issues are synonymous
Nutrition can be improved with increased dialytic clearance of low-molecular-weight solutes (e.g., urea)

- The majority of international guidelines since 1997 have promoted nutritional indication for early dialysis.
* Several studies showed that serum albumin is not a reliable marker of nutrition.

- *Rocco MV, Dwyer JT, Larive B, Greene T, Cockram DB, Chumlea WC, Kusek JW, Leung J, Burrowes JD, McLeroy SL, Poole D, Uhlin L: for the HEMO Study Group: The effect of dialysis dose and membrane flux on nutritional parameters on hemodialysis patients: results of the HEMO Study. Kidney Int 65:2321–2334, 2004*
* *Cama-Axelsson T, Heimburger O, Stenvinkel P, Barany P, Lindholm B, Qureshi RA: Serum albumin as predictor of nutritional status in patients with ESRD. Clin J Am Soc Nephrol 7:1446–1453, 2012*

Diabetics need to initiate dialysis earlier than nondiabetics

- The reasons for early initiation of dialysis with diabet have been unclear.

- *Wright S, Klausner D, Bradley B, Williams ME, Steinman T, Tang H, Ragasa R, Goldfard-Rumyantzev AS: Timing of dialysis initiation and survival in ESRD. Clin J Am Soc Nephrol 5:1828–1835, 2010*
- *Mizuno T, Hayashi T, Kato R et al:Risk factors for an early dialysis in patients with diabetic nephropathy end-stage renal disease.Therapeutics and Cllin Risk Man 10:73-76,2014*

At low levels of renal function: eGFR <15 ml/min/1.73 m²

- eGFR is influenced by muscle mass and overhydration so it does not provide a good measure of uremic toxicity.
- The European Renal Best Practise advisory board have concluded that eGFR is not useful in determining need for dialysis.

- *Tattersall J, Dekker F, Heimburger O,et al:When to start dialysis:updated guidance following publications of the IDEAL study.Nephrol Dial Transplant.26:2082-2086,2011*

Harmful Effects of Dialysis

*Patients may lose approximately 10% of their endogenous renal function per month after dialysis initiation.

**After HD treatment, regional left ventricular systolic dysfunction may occur.

***It has been suggested that shorter treatment times and larger ultrafitration volumes relate to sudden death.

****Infections are another serious adverse consequence of dialysis.

*****There have been no data could showed the improvement of qualty of life according to start early dialysis.

* *Jansen MA, Hart AA, Korevaar JC, Dekker FW, Boeschoten EW,Krediet RT; NECOSAD Study Group: Predictors of the rate ofdecline of residual renal function in incident dialysis patients. Kidney Int 62(3):1046–1053, 2002*

** *Assa S, Hummel YM, Voors AA, Kuipers J, Westerhuis R, de Jong PE, Franssen CFM: Hemodialysis-induced regional left ventricular systolic dysfunction: prevalence, patient and dialysis treatment-related factors, and prognostic significance. Clin J Am Soc Nephrol 7:1615–1623, 2012*

*** *Jadoul M, Thumma J, Fuller DS, Tentori F, Li Y, Morgenstern H, Mendelssohn D, Tomo T, Ethier J, Port F, Robinson BM: Modifiable practices associated with sudden death among hemodialysis patients inthe Dialysis Outcomes and Practice Patterns Study. Clin J Am Soc Nephrol 7(5):765–774, 2012*

****Chan KE, Maddux FW, Tolkoff-Rubin N, Karumanchi SA, Thadhani R, Hakim RM: Early outcomes among those initiating chroni dialysis in the United States. Clin J Am Soc Nephrol 6:2642–2649,2011*

***** Gabbay E, Meyer KB, Griffith JL, Richardson MM, Miskulin DC: Temporal trends in the health-relate quality of life among hemodialysis patients in the United States. Clin J Am Soc Nephrol 5:261–267, 2010*

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A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis

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BACKGROUND

In clinical practice, there is considerable variation in the timing of the initiation of maintenance dialysis for patients with stage V chronic kidney disease, with a worldwide trend toward early initiation. In this study, conducted at 32 centers in Australia and New Zealand, we examined whether the timing of the initiation of maintenance dialysis influenced survival among patients with chronic kidney disease.

METHODS

We randomly assigned patients 18 years of age or older with progressive chronic kidney disease and an estimated glomerular filtration rate (GFR) between 10.0 and 15.0 ml per minute per 1.73 m^2 of body-surface area (calculated with the use of the Cockcroft–Gault equation) to planned initiation of dialysis when the estimated GFR was 10.0 to 14.0 ml per minute (early start) or when the estimated GFR was 5.0 to 7.0 ml per minute (late start). The primary outcome was death from any cause.

RESULTS

Between July 2000 and November 2008, a total of 828 adults (mean age, 60.4 years; 542 men and 286 women; 355 with diabetes) underwent randomization, with a median time to the initiation of dialysis of 1.80 months (95% confidence interval [CI], 1.60 to 2.23) in the early-start group and 7.40 months (95% CI, 6.23 to 8.27) in the late-start group. A total of 75.9% of the patients in the late-start group initiated dialysis when the estimated GFR was above the target of 7.0 ml per minute, owing to the development of symptoms. During a median follow-up period of 3.59 years, 152 of 404 patients in the early-start group (37.6%) and 155 of 424 in the late-start group (36.6%) died (hazard ratio with early initiation, 1.04; 95% CI, 0.83 to 1.30; P=0.75). There was no significant difference between the groups in the frequency of adverse events (cardiovascular events, infections, or complications of dialysis).

CONCLUSIONS

In this study, planned early initiation of dialysis in patients with stage V chronic kidney disease was not associated with an improvement in survival or clinical outcomes. (Funded by the National Health and Medical Research Council of Australia and others; Australian New Zealand Clinical Trials Registry number, 12609000266268.)

“IDEAL” Study

- The results show that with careful clinical management, dialysis may be delayed until either the GFR drops below 7.0 mL/min or more traditional clinical indicators for the initiation of dialysis are present.

Seminars in Dialysis

TRANSITION TO DIALYSIS:
CONTROVERSIES IN ITS TIMING AND MODALITY

Dialysis Initiation: What's the Rush?

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Seminars in Dialysis—Vol 26, No 6 (November–December 2013 pp. 650–657

ABSTRACT

The recent trend to early initiation of dialysis (at eGFR >10 ml/min/1.73 m^2) appears to have been based on conventional wisdoms that are not supported by evidence. Observational studies using administrative databases report worse comorbidity-adjusted dialysis survival with early dialysis initiation. Although some have concluded that the IDEAL randomized controlled trial of dialysis start provided evidence that patients become symptomatic with late dialysis start, there is no definitive support for this view. The potential harms of early start of dialysis, including the loss of residual renal function (RRF), have been well documented. The rate of RRF loss (renal function trajectory) is an important consideration for the timing of the dialysis initiation decision. Patients with low glomerular filtration dialysis for years. Delay of dialysis start until a working arterio-venous access is in place seems prudent in light of the lack of harm and possible benefit of late dialysis initiation. Prescribing frequent hemodialysis is not recommended when dialysis is initiated early. The benefits of early initiation of chronic dialysis after episodes of congestive heart failure or acute kidney injury require further study. There are no data to show that early start benefits diabetics or other patient groups. Preemptive start of dialysis in noncompliant patients may be necessary to avoid complications. The decision to initiate dialysis requires informed patient consent and a joint decision by the patient and dialysis provider. Possible talking points for obtaining informed consent are provided.

The Right Patient, the Right Treatment, the Right Access and the Right Time

Denise Keller Link and Ramesh Saxena

As the incidence of CKD increases, so will the ESRD population. Pre-ESRD care, including early referral to nephrology and patient education, enables patients and providers working together to determine which therapy modality is best suited for their individualized needs: conservative therapy, kidney transplant, hemodialysis, or peritoneal dialysis. Differentiating the therapy modality should be based on many factors and not solely based on outcome data. Acknowledging that there is no "one-size-fits-all" therapy modality allows the patient and the interdisciplinary team to ensure that the appropriate access is chosen at the appropriate time. Lastly, the timing of initiation is paramount for improving patient outcomes, including less central venous catheter placement in incident hemodialysis and more planned arteriovenous accesses, improved quality of life, less hospitalization time, and reduced costs.

Advances in Chronic Kidney Disease, Vol 21, No 4 (July), 2014: pp 360-364

CLINICAL SUMMARY

- There is no single, ideal, or best dialysis modality and access for every patient.
- Delaying the need for urgent start dialysis and medically managing for a period of time would decrease cost and allow for KDE and RRT planning.
- Determining dialysis modality should not be based solely on outcome date but on various factors related to patients' quality of life.

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Age may explain the association of an early dialysis initiation with poor survival

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Summary

Background: Some studies postulate that early dialysis initiation may increase mortality.
Aim: The aim of the present study was to assess to what extent this was due to confounding by age.
Design: Observational retrospective cohort study.
Methods: We studied all patients starting dialysis therapy between 1 January 1995 and 31 December 2009 in our center. The following variables at dialysis initiation in end-stage renal disease (ESRD) patients were analysed: estimated glomerular filtration rate (eGFR), age, gender, diabetes mellitus, serum albumin, hemoglobin, period of dialysis initiation, history of ischemic heart disease and stroke. Multivariate Cox model was used to calculate adjusted patient survival.
Results: Over the last 15 years, 428 patients initiated dialysis therapy in our reference area. Median eGFR at dialysis initiation was 8.16 ml/min. In the univariate analysis, increased eGFR, age, dialysis initiation 1995–1999/2000–2004, diabetes and history of ischemic heart disease were associated ($P<0.05$) with increased mortality in ESRD. Patients that started dialysis program with eGFR > 8.16 were older than those who did it with eGFR < 8.16 (66 vs. 61 years, $P<0.001$). The association between mortality and eGFR in the crude multivarite Cox model was lost when the model was adjusted by age. In the multivariate Cox model, dialysis initiation period, serum albumin and history of ischemic heart disease were associated with mortality.
Conclusion: History of ischemic heart disease, serum albumin and dialysis start before 2005 were risk factors for mortality in ESRD patients. Older age is usually associated with early dialysis initiation, so age adjustment is needed to perform studies aimed to calculate the effect of eGFR at dialysis initiation on survival.

Peritoneal Dialysis International, Vol. 32, pp. 595–604
doi: 10.3747/pdi.2012.00046
0896-8608/12 $3.00 + .00

ORIGINAL ARTICLES

EFFECT OF TIMING OF DIALYSIS COMMENCEMENT ON CLINICAL OUTCOMES OF PATIENTS WITH PLANNED INITIATION OF PERITONEAL DIALYSIS IN THE IDEAL TRIAL

♦ *Results:* Of the 828 IDEAL trial participants, 466 (56%) planned to commence PD and were randomized to early start (n = 233) or late start (n = 233). The median times from randomization to dialysis initiation were, respectively, 2.03 months [interquartile range (IQR):1.67 – 2.30 months] and 7.83 months (IQR: 5.83 – 8.83 months). Death occurred in 102 early-start patients and 96 late-start patients [hazard ratio: 1.04; 95% confidence interval (CI): 0.79 – 1.37]. No differences in composite cardiovascular events, composite infectious deaths, or dialysis-associated complications were observed between the groups. Peritonitis rates were 0.73 episodes (95% CI: 0.65 – 0.82 episodes) per patient–year in the early-start group and 0.69 episodes (95% CI: 0.61 – 0.78 episodes) per patient–year in the late-start group (incidence rate ratio: 1.19; 95% CI: 0.86 – 1.65; p = 0.29). The proportion of patients planning to commence PD who actually initiated dialysis with PD was higher in the early-start group (80% vs 70%, p = 0.01).

♦ *Conclusion:* Early initiation of dialysis in patients with stage 5 chronic kidney disease who planned to be treated with PD was associated with clinical outcomes comparable to those seen with late dialysis initiation. Compared with early-start patients, late-start patients who had chosen PD as their planned dialysis modality were less likely to commence on PD.

Perit Dial Int 2012; 32(6):595-604 www.PDIConnect.com
doi:10.3747/pdi.2012.00046

Early Dialysis Initiation, a Look from the Rearview Mirror to What's Ahead

Steven J. Rosansky

Clin J Am Soc Nephrol 9: 222–224, 2014. doi: 10.2215/CJN.12231213

In conclusion, the trend toward a progressively earlier start of dialysis is not supported by clinical evidence (4,8). The early-start trend is related not just to patient comorbidity issues and renal function levels but also to provider biases and practice patterns. Much more information is needed regarding dialysis initiation scenarios, including how often initiation follows an AKI episode (especially in patients with very short life expectancy), which renal failure–related symptoms triggered the start of dialysis, and the relationship between these symptoms and outcomes. Random samples of incident dialysis patients should be surveyed to document their predialysis understanding of and input into the decision to start long-term dialysis. In addition, tracking rates of discontinuation of dialysis may indicate unprepared and uninformed patients. The patterns of early, late, or no start of dialysis by urban versus rural areas and patient demographic characteristics, as well as by the size and type of dialysis practices and nephrologist characteristics, should be examined to uncover potential adverse consequences related to the dialysis start issue. Such consequences include the possible continuation of early start in less populated areas, with adverse effects on survival, and the failure to offer dialysis or wait too long to start dialysis in capitated practices that benefit from late or no dialysis start. It is hoped that future emphasis on a good death and end-of-life experience will end the trend of the past decade to early, and often unnecessary, dialysis.

Take homepoints

- There is no single criterion.
- If uremic symptoms and signs are getting worse in patient with GFR<15 mL/min/1.73 m^2 you can start dialysis
- Dialysis is usually indicated when GFR is 5-9 mL/min/1.73 m^2
- The American Society of nephrology has promoted the decision of dialysis by discussing patients, their families and dialysis providers.

Thanks....

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