WHEN (AND WHEN NOT) TO START DIALYSIS

Shahid Chandna, Ken Farrington
Changing Perspectives

- **Beta blockers**
  - 1980s – Contraindicated in heart failure
  - Now – mainstay of therapy

- **HRT**
  - 1990s – must
  - Now – only if you have to

- **Early Dialysis??**
  - 1990s and 2000 – Yes
  - Now – May be
  - (Or even NOT)
Early Dialysis is Good
Says Who?

- **NKF (1997):** Start dialysis with eGFR \(~\) 10.5 (on the basis of the minimum target level of total (residual renal and dialysis) clearance for peritoneal dialysis.

- **KDOQI (2006):** RRT should be considered at
  - eGFR < 15
  - eGFR > 15 when patients have coexisting conditions or symptoms of uraemia

- **Canadian Society of Nephrology:** Start RRT
  - eGFR < 12
  - dialysis can be deferred if there is no evidence of uraemia or malnutrition

- **According to USRDS:** patients starting dialysis with GFR > 10
  - 19\% in 1996
  - 45\% in 2005
Early Dialysis is Good
Says Who?

- Bonomini et al. Kidney Int Suppl. 1978
- Bonomini et al. Nephron. 1986
- Tattersall J, Greenwood R, Farrington K.
  - Am J Nephrol. 1995
  - 63 consecutive CRF patients
  - mean follow-up period of 10 ± 4.5 months
  - 6 patients died
    - Higher age (p < 0.01)
    - Higher co-morbidity index (p < 0.05)
    - Lower mean Kt/V (p < 0.05)

- PROBLEM – LEAD TIME BIAS
retrospective analysis
USRDS
n = 896,546
99,231 (11%) patients had an early dialysis start (eGFR >15)
- White
- Male
- Higher comorbidity
- Diabetes
- Peritoneal dialysis
113,510 (12%) had a late start (eGFR ≤5)
reference group with an eGFR of >5 to 10
Cox model adjusted for potential confounding variables
Earliest start had increased risk of mortality
Late start was associated with reduced risk of mortality
CONCLUSIONS: Late initiation of dialysis is associated with a reduced risk of mortality – despite the effect of lead time bias
11,685 patients

Dialysis at a higher eGFR
- Older
- Male
- Had diabetes, cardiovascular diseases, or low body mass index and low albumin
- Peritoneal dialysis

Each 5-ml increase in eGFR
- 40% increase in crude mortality risk
- 9% increased risk after adjusting for the above covariates.

Age and patient condition strongly determine the decision to start dialysis and may explain most of the inverse association between eGFR and survival
Wilson et al: Ontario, Canada
Hemodial Int. 2007

- Retrospective cross-sectional study - n=271
- 17% started haemodialysis late (GFR<5)
  - younger (p=0.008),
  - females (p=0.013)
  - more employed (p=0.051)
  - less cardiac disease (p<0.001)
  - Less peripheral vascular disease (p=0.031),
  - Serum albumin was lower (p=0.023)
- At year 1, there was no difference in mortality
- At year 2, the earlier the dialysis, the greater the mortality rate (p=0.022)
- Adjustment for all these variables eliminated the significant association noted for the 2 year mortality in the early versus late dialysis start.
- HOWEVER - ? LEAD TIME BIAS
Population-based, prospective, observational cohort study - \( n = 901 \)

- Early-start dialysis eGFR \( \geq 7.5 \)
- Late start of dialysis eGFR <7.5
- No dialysis

- Early start - \( n = 323 \)
  - 52% died

- Late Start - \( n = 385 \)
  - 36% died

The adjusted HR for death was 0.84 [95% confidence interval (CI) 0.64, 1.10] among late versus early starters.

No dialysis - mortality increased significantly at eGFR below 7.5 mL

**Conclusion.** No survival benefit from early initiation of dialysis
81,176 non-diabetic, 20- to 64-year-old, in-centre incident haemodialysis patients with no reported comorbidity besides hypertension

piecewise proportional hazards model

Unadjusted 1-year mortality by eGFR ranged from 6.8% in the reference group (eGFR < 5.0 mL/min/1.73 m²) to 20.1% in the highest eGFR group (≥ 15 mL/min/1.73 m²).

Compared with the reference group, the HR for the HG was 1.27 (eGFR, 5.0-9.9 mL/min/1.73 m²), 1.53 (eGFR, 10.0-14.9 mL/min/1.73 m²), and 2.18 (eGFR ≥ 15.0 mL/min/1.73 m²).
IDEAL (Initiating Dialysis Early And Late) study

- Randomised Controlled Trial
- 32 centres in Australia and New Zealand
- 828 patients – GFR (C&G) 10-15 ml/min
  - mean age, 60.4 years
  - 355 (43%) with diabetes
- median follow-up period of 3.59 years
- GFR by Cockroft-Gault equation but a post hoc analysis with MDRD eGFR.

- The study protocol permitted patients who were assigned to the late-start group to commence dialysis with GFR >7 if the treating physician recommended that they do so
Planned to start dialysis with GFR 10 - 14
Mean GFR at start of dialysis 12.0 [9.0 by MDRD equation]
Median time to the initiation of dialysis: 1.8 months
75 (18.6%) started dialysis with an estimated GFR (C&G) of <10.0
HD = 188
  - Temporary dialysis catheters in 15
PD = 195
Planned to start dialysis with GFR 5 to 7
- Mean GFR at start of dialysis 9.8 [7.2 by MDRD equation]
- Median time to the initiation of dialysis: 7.4 months
- 322 (75.9%) started dialysis with GFR > 7.0 ml
- HD = 215
  - Temporary dialysis catheters in 38
- PD = 171
IDEAL Study - Results

- Mean difference in GFR 2.2 [1.8 by MDRD equation]
- A difference of 6 months between the groups in the start time for dialysis
- Early start group had
  - More PD
  - Fewer temporary dialysis catheters
A Time to Start of Dialysis

Hazard ratio, 2.09 (95% CI, 1.81–2.41)
P < 0.001

No. at Risk

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<th>Early start</th>
<th>Late start</th>
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<td>35</td>
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<tr>
<td>Late start</td>
<td>424</td>
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</table>
No significant difference in survival, cardiovascular events, infections, or dialysis complications

Mortality:
- 38% in early start group
- 37% in late start group

Hazard ratio of 1.05 (0.83 – 1.30) with early initiation
**B  Time to Death**

**No. at Risk**

<table>
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Hazard ratio, 1.04 (95% CI, 0.83–1.30)
P=0.75
With careful clinical management, dialysis may be delayed until either the GFR drops below 7.0 ml per minute or more traditional clinical indicators for the initiation of dialysis are present.
Lister Study

- Why do we need another retrospective study?
- Largest single centre study
- Not based on registry data
  - Full information available on almost all patients
  - Comorbidity from clinical record – not coding for billing purposes
- As we have full information, we excluded Acute on Chronics (who started with low GFR not by choice)
Lister Study

- 731 patients
- Age 17 – 90 (mean 58.2)
- Male 66.7%
- White 82.7%
- Diabetic 33.1%
- GFR at start of dialysis
  - 3.36 to 15.3
  - Mean – 8.03
  - Median – 7.78
- 139 (19%) started dialysis with eGFR > 10
Cox Model – Adjusted for Age, Gender, Diabetes & Other Comorbidity

GFR at Start of Dialysis

- Below Median
- Above Median

Cum Survival

'Months of Follow Up'
## Cox Proportional Hazard Model

<table>
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<td>1.429</td>
<td>1.151</td>
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<tr>
<td>Age</td>
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<td>1.038</td>
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<tr>
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<td>1.524</td>
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<tr>
<td>Female Gender</td>
<td>.681</td>
<td>.952</td>
<td>.753</td>
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Low risk patients (<65, non-diabetics, low comorbidity)

Low GFR - 148
High GFR - 118

P=0.09
Why is there a clamour for early dialysis

- Worse survival with unplanned dialysis start
- Everyone remembers patients who were known to renal services and yet had to start dialysis urgently
  - Buck et al. Leicester (NDT- 2007)
  - A retrospective survey of electronic and medical records - 2003
  - known acute (starting dialysis urgently yet known to renal services ≥ 4 months)
  - 49 of 109 (44%) - known acute

- Reasons
  - illness (21)
  - service (24)
  - patient related (17)
  - Multiple reasons (11)
Quality of Life

Does early dialysis improve QOL?


- Effect of late versus timely initiation of dialysis on the course of health-related quality of life (HRQOL)
- Part of a large Dutch prospective multicenter study (Netherlands Cooperative Study on the Adequacy of Dialysis-2)
- 90 (38%) patients started dialysis late
- All patients showed marked improvement in HRQOL during the first 6 months after the start of dialysis treatment
- Patients who started in time had significantly higher HRQOL for a number of dimensions immediately after the start of treatment
- After 12 months of dialysis treatment, these differences had disappeared

What is not mentioned is the QOL in the ‘late’ dialysed patients when they were not on dialysis
Symptoms of uraemia?

- Every Asian with fever is likely to have TB
- (Asian + Fever + Cough: MUST be TB)
- Every CKD patient with itching, nausea or tiredness MUST be uraemic
- The commonest ‘Clinical detail’ on GP blood tests request
- T.A.T.T. Tired All The Time
So why should early dialysis be associated with poor survival

- There is something else wrong with the patient which we try to treat with dialysis (even when the ‘recognised comorbidity’ is low)
- Patients with high comorbidity poorly tolerate dialysis
- Interaction between dialysis and other comorbidities.
- Dialysis is toxic
So what should we do?

- Whether early dialysis is detrimental or not – the jury is out.
- There is certainly NO EVIDENCE that early dialysis is beneficial.
- Don’t be lazy - don’t just follow the number. Assess the patient-
  - eGFR
  - Clinical condition (if tiredness is an indication for dialysis, >10% of population will be on dialysis)
  - Assess the impact of dialysis on Patient’s QOL
  - Assess the prognosis with and without dialysis