IMPACT OF PATIENT CHARACTERISTICS ON PROGNOSIS OF INCIDENT DIALYSIS PATIENTS

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Disclosure of Interests

Research grants: NIH, Shire

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Consultant: Abbott Nutrition, Astra-Zeneca, Fresenius Medical Care, Keryx, Relypsa, Sanofi-aventis, ZS Pharma
Objectives

• Describe characteristics of incident ESRD patients

• Examine the effect of patient characteristics on outcomes in incident ESRD patients
transition

- [tran-zish-uh n, -sish-]
- noun 1. movement, passage, or change from one position, state, stage, subject, concept, etc., to another;
- “the transition from adolescence to adulthood.”

start

- [stahrt]
- 1. to begin or set out, as on a journey or activity.
- 2. to appear or come suddenly into action, life, view, etc.; rise or issue suddenly forth.
- 3. to spring, move, or dart suddenly from a position or place: The rabbit started from the bush.
- 4. to be among the entrants in a race or the initial participants in a game or contest.
- 5. to give a sudden, involuntary jerk, jump, or twitch, as from a shock of surprise, alarm, or pain: The sudden clap of thunder caused everyone to start.

Kalantar-Zadeh et al, NDT 2017
Very-Late-Stage Chronic Kidney Disease

- **eGFR Slope**
  - Pre-RRT lab data

- **Comorbid conditions**
  - Advanced age
  - Demographics

**Never Transition to Dialysis**

**LATE Transition to Dialysis**

**EARLY Transition to Dialysis**

**Kidney Transplantation**

- **Transplant**
  - Failing Allograft
  - Case-Mix
  - Race

- **Late Re-Start**
  - eGFR slope?
  - comorbid states?
  - Lab data?

- **Early Re-Start**
  - Dialysis Modality

**Outcomes?**

- **Loss of Residual Kidney Function**
  - Infection, dialysis access issues
  - Protein Energy Wasting
  - Anxiety, psychosocial burden

**Lower Mortality?**

**Causal Association?**

**Biologically Plausible?**

**End-of-Life Issues ↔ Dialysis Withdrawal**

Kalantar-Zadeh et al., Nephrol Dial Transplant 2017
The United States Renal Data System (USRDS) Special Study Center

Transition of Care in CKD (TC-CKD)

NIH/NIDDK

University of California Irvine School of Medicine
Harold Simmons Center for Kidney Disease Research & Epidemiology
UC Irvine Medical Center, Orange, CA; and
VA Long Beach Healthcare System, Long Beach, CA

University of Tennessee Health Sciences Center
Division of Nephrology
Clinical Outcomes and Clinical Trial Program; and
VA Memphis Healthcare System, Memphis, TN

Dept. Research, Kaiser Permanente of Southern California,
Pasadena, CA
Kalantar-Zadeh et al., Nephrol Dial Transplant 2017
Early mortality after dialysis initiation

Patterns and Predictors of Early Mortality in Incident Hemodialysis Patients: New Insights


Lilia R. Lukowsky\textsuperscript{a,b}, Leeka Kheifets\textsuperscript{b}, Onyebuchi A. Arah\textsuperscript{b,e}, Allen R. Nissenson\textsuperscript{c,d}, Kamyar Kalantar-Zadeh\textsuperscript{a,c}

Early mortality in patients starting dialysis appears to go unregistered

(Kidney Int. 2014;86:392)

Robert N. Foley\textsuperscript{1,2}, Shu-Cheng Chen\textsuperscript{1}, Craig A. Solid\textsuperscript{1}, David T. Gilbertson\textsuperscript{1} and Allan J. Collins\textsuperscript{1,2}

Worldwide, mortality risk is high soon after initiation of hemodialysis

(Kidney Int. 2014;85:158)

Bruce M. Robinson\textsuperscript{1,2}, Jinyao Zhang\textsuperscript{1}, Hal Morgenstern\textsuperscript{1,3}, Brian D. Bradbury\textsuperscript{4,5}, Leslie J. Ng\textsuperscript{4}, Keith P. McCullough\textsuperscript{1}, Brenda W. Gillespie\textsuperscript{6}, Raymond Hakim\textsuperscript{7}, Hugh Rayner\textsuperscript{8}, Joan For\textsuperscript{9}, Tadao Akizawa\textsuperscript{10}, Francesca Tentori\textsuperscript{1,7} and Ronald L. Pisoni\textsuperscript{1}
Crude Mortality Rates over First 24 Months in Incident Dialysis Patients

During the first 3 months, 10.4% of all incident ESRD Veterans died and 1.4% received a kidney transplantation.
Hospitalization Patients by Prelude and Vintage

- 12+ Month Prelude: 28730
- 12 Month Prelude: 35708
- 6 Month Vintage: 28309
- 6+ Month Vintage: 33016
- During Dialysis: 27503

KDIGO
Top 20 Reasons for Hospitalizations

N=74382
Reasons # 1-10 for Hospitalization by time period

- Acute Renal Failure
- CHF
- Hypertension
- Graft Complication
- Septicemia
- CKD
- Pneumonia
- Diabetes
- ASHD
- Fluid Disorder

Legend:
- Prelude -60 mo to <-12 mo
- Prelude-12mo to <ESRD
- During ESRD Transition
- Vintage ESRD to <6 mo
- Vintage 6 mo- to <24 mo

N=74382
Reasons # 11-20 for Hospitalization by time period

- Acute MI
- Cardiac dysrhythmias
- Rehab
- Surg Complications
- Anemia
- GI Hem
- Resp Fail
- Skin Inf
- Chest Pain
- CVD

N=74382
Patient characteristics in incident ESRD

- Important as risk factors
  - Interventions in pre-ESRD period to improve outcomes
- Important for prediction
  - Help make decisions about best course of action
Key patient characteristics

- Demographic (age, gender, race)
- Socio-economic
- Comorbidities
- Biochemical
- Treatments/interventions
- Clinical events
Trends in adjusted* ESRD incidence rate (per million/year), by age group, in the U.S. population, 1996-2014

Data Source: Reference Table A.2(2) and special analyses, USRDS ESRD Database. *Adjusted for sex and race. The standard population was the U.S. population in 2011. Abbreviation: ESRD, end-stage renal disease.
### Age at first ESRD Service in 52,172 Incident ESRD Veterans

<table>
<thead>
<tr>
<th>Age group</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>15</td>
<td>0.03</td>
</tr>
<tr>
<td>20-24</td>
<td>27</td>
<td>0.05</td>
</tr>
<tr>
<td>25-29</td>
<td>91</td>
<td>0.17</td>
</tr>
<tr>
<td>30-34</td>
<td>172</td>
<td>0.33</td>
</tr>
<tr>
<td>35-39</td>
<td>301</td>
<td>0.58</td>
</tr>
<tr>
<td>40-44</td>
<td>668</td>
<td>1.28</td>
</tr>
<tr>
<td>45-49</td>
<td>1236</td>
<td>2.37</td>
</tr>
<tr>
<td>50-54</td>
<td>2611</td>
<td>5.00</td>
</tr>
<tr>
<td>55-59</td>
<td>4718</td>
<td>9.04</td>
</tr>
<tr>
<td>60-64</td>
<td>7723</td>
<td>14.80</td>
</tr>
<tr>
<td>65-69</td>
<td>5977</td>
<td>11.46</td>
</tr>
<tr>
<td>70-74</td>
<td>6296</td>
<td>12.07</td>
</tr>
<tr>
<td>75-79</td>
<td>8479</td>
<td>16.25</td>
</tr>
<tr>
<td>80-84</td>
<td>7923</td>
<td>15.19</td>
</tr>
<tr>
<td>85-89</td>
<td>4955</td>
<td>9.50</td>
</tr>
<tr>
<td>90-94</td>
<td>946</td>
<td>1.81</td>
</tr>
<tr>
<td>95+</td>
<td>34</td>
<td>0.07</td>
</tr>
</tbody>
</table>

USRDS – TC-CKD: Data on file
Trends in adjusted* ESRD incidence rate (per million/year), by race, in the U.S. population, 1996-2014

Data Source: Reference Table A.2(2) and special analyses, USRDS ESRD Database. *Adjusted for age and sex. The standard population was the U.S. population in 2011. Abbreviations: Af Am, African American; ESRD, end-stage renal disease.
Core Demographics from TCCKD

Race in 52,095 TCCKD Patients

<table>
<thead>
<tr>
<th>Race</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Native American</td>
<td>1.05</td>
</tr>
<tr>
<td>Asian</td>
<td>1.84</td>
</tr>
<tr>
<td>Black</td>
<td>24.25</td>
</tr>
<tr>
<td>White</td>
<td>72.77</td>
</tr>
<tr>
<td>Other</td>
<td>0.09</td>
</tr>
</tbody>
</table>

USRDS – TC-CKD: Data on file
### Post-Transition Mortality: Age and Race

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Frequency</th>
<th>%</th>
<th>Age (yrs)</th>
<th>% Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 mo</td>
<td>5489</td>
<td>11</td>
<td>76±10</td>
<td>15</td>
</tr>
<tr>
<td>3-&lt;12 mo</td>
<td>8850</td>
<td>17</td>
<td>75±10</td>
<td>17</td>
</tr>
<tr>
<td>12 -&lt;24 mo</td>
<td>7358</td>
<td>14</td>
<td>73±11</td>
<td>18</td>
</tr>
<tr>
<td>&gt;=24 mo</td>
<td>12121</td>
<td>23</td>
<td>72±11</td>
<td>21</td>
</tr>
<tr>
<td>Alive after 2 years</td>
<td>18340</td>
<td>35</td>
<td>64±12</td>
<td>35</td>
</tr>
</tbody>
</table>

USRDS – TC-CKD: Data on file
Pre-existing Comorbidities

USRDS – TC-CKD: Data on file
Charlson Comorbidity Index

USRDS – TC-CKD: Data on file
Comorbidity burden at dialysis initiation and mortality: A cohort study

Alwyn T Gomez⁴, Bryce A Kiberd⁵,⁶, J Patrick Royston⁴, Talal Alfaadhel², Steven D Soroka²,³, Brenda R Hemmelgarn⁵,⁶ and Karthik K Tennankore²,³*

Table 2  Cox regression coefficients and c-index for precise and categorical CCI/ESRD-CI

<table>
<thead>
<tr>
<th>Index</th>
<th>Regression coefficient [95 % CI]</th>
<th>c-index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precise CCI</td>
<td>0.55 [0.38-0.71]</td>
<td>0.61</td>
</tr>
<tr>
<td>Categorical CCI</td>
<td>0.56 [0.39-0.72]</td>
<td>0.61</td>
</tr>
<tr>
<td>Precise ESRD-CI</td>
<td>0.52 [0.38-0.66]</td>
<td>0.63</td>
</tr>
<tr>
<td>Categorical ESRD-CI</td>
<td>0.52 [0.38-0.66]</td>
<td>0.62</td>
</tr>
</tbody>
</table>
B

LABORATORY

hemoglobin (per g/dl increase)

albumin (per 0.5 g/dl increase)

potassium (per meq/l increase)

SOCIOECONOMIC

employed (vs unemployed)

median annual income ($1000)

high school graduation rate (10%)

YEAR


Valuable information on prognosis will spur the exchange between health professionals and patients, taking into account that many individual or cultural aspects will influence the shared decision-making process, in which practitioners and patients jointly consider best clinical evidence in light of a patient’s specific health characteristics and values when choosing health care.

Although neither a clinician nor a prognostic score can predict with absolute certainty how well a patient will do or how long he/she will live, validated prognostic scores may improve the accuracy of the prognostic estimates that influence the clinical decisions and a patient-centered approach.
Prediction score for early mortality among ESRD patients transitioning to dialysis
Predicting Early Death Among Elderly Dialysis Patients: Development and Validation of a Risk Score to Assist Shared Decision Making for Dialysis Initiation

Mae Thamer, PhD, James S. Kaufman, MD, Yi Zhang, PhD, Qian Zhang, MPH, Dennis J. Cotter, MSE, and Heejung Bang, PhD

<table>
<thead>
<tr>
<th>Total Score</th>
<th>Within 3 mo</th>
<th>Within 6 mo</th>
<th>Proportion of Patients With Same Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2%</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>1</td>
<td>3%</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>2</td>
<td>7%</td>
<td>12%</td>
<td>25%</td>
</tr>
<tr>
<td>3</td>
<td>12%</td>
<td>20%</td>
<td>27%</td>
</tr>
<tr>
<td>4</td>
<td>17%</td>
<td>27%</td>
<td>19%</td>
</tr>
<tr>
<td>5</td>
<td>22%</td>
<td>35%</td>
<td>10%</td>
</tr>
<tr>
<td>6</td>
<td>28%</td>
<td>44%</td>
<td>4%</td>
</tr>
<tr>
<td>7</td>
<td>34%</td>
<td>49%</td>
<td>1%</td>
</tr>
<tr>
<td>≥8</td>
<td>39%</td>
<td>55%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

AUROC=0.69

A clinical score to predict 6-month prognosis in elderly patients starting dialysis for end-stage renal disease

Cécile Couchoud¹, Michel Labeeuw², Olivier Moranne³,⁴,⁵, Vincent Allot⁶, Vincent Esnault⁵, Luc Frimat⁷, Bénédicte Stengel³,⁴, and for the French Renal Epidemiology and Information Network (REIN) registry

Table 4. Six-month mortality rates by risk score in the training and the validation samples

<table>
<thead>
<tr>
<th>Risk score</th>
<th>Training sample</th>
<th>Validation sample</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of deaths</td>
<td>Number at risk</td>
</tr>
<tr>
<td>0 point</td>
<td>41</td>
<td>511</td>
</tr>
<tr>
<td>1 point</td>
<td>39</td>
<td>508</td>
</tr>
<tr>
<td>2 points</td>
<td>64</td>
<td>453</td>
</tr>
<tr>
<td>3–4 points</td>
<td>160</td>
<td>628</td>
</tr>
<tr>
<td>5–6 points</td>
<td>93</td>
<td>266</td>
</tr>
<tr>
<td>7–8 points</td>
<td>50</td>
<td>98</td>
</tr>
<tr>
<td>≥9 points</td>
<td>22</td>
<td>36</td>
</tr>
</tbody>
</table>

AUROC = 0.70

A Clinical Risk Prediction Tool for 6-Month Mortality After Dialysis Initiation Among Older Adults

James P. Wick, MSc, Tanvir C. Turin, PhD, MBBS, Peter D. Faris, PhD, Jennifer M. MacRae, MSc, MD, Robert G. Weaver, MSc, Marcello Tonelli, SM MD, Braden J. Manns, MSc, MD, and Brenda R. Hemmelgarn, PhD, MD

AUROC = 0.72
85,505 veterans transitioning to ESRD between Oct 2007 to Mar 2014

- 44,141 without any labs during 12M prior dialysis initiation
- 2 with no race code
- 3 with no ICD-9 codes

41,359 patients with ≥1 any lab(s) during 12M prior dialysis initiation

Patients were 68±11 years old, of which 98% were male, 29% were black, and 7% were Hispanic; 47% and 28% had diabetes and hypertension as the cause of ESRD, respectively.

Median eGFR at dialysis initiation were 12 (IQR, 8-18) mL/min/1.73m².
By using the Cox PH model, **a new prognostic score** was **developed among randomly selected 27,710 patients** based on demographics, cause of ESRD, comorbid conditions, and less-modifiable laboratory variables (i.e., WBC, Albumin, BUN, eGFR, sodium), and then **validated among the remaining 13,469 patients**.
## Summary

### Potential models with and without labs

#### Multivariable logistic regression for 6M mortality

<table>
<thead>
<tr>
<th></th>
<th>Demo +16 Comorbids</th>
<th>+eGFR</th>
<th>+eGFR +Alb</th>
<th>+eGFR +Alb +1Y Δ eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base AUC</strong></td>
<td>0.7062</td>
<td>0.7103</td>
<td>0.7147</td>
<td>0.7238</td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td>0.7062</td>
<td>0.7167</td>
<td>0.7375</td>
<td>0.7529</td>
</tr>
<tr>
<td><strong>Δ AUC</strong></td>
<td>0</td>
<td>0.006</td>
<td>0.023</td>
<td>0.029</td>
</tr>
</tbody>
</table>

*Base AUC is based on the “Demo + 16 Comorbids” model*
Calibration plots between predicted vs. observed mortality

Each group included 2,500 patients.
Dementia

- Dementia is more common in the elderly
  - Elderly patients now comprise a large proportion of the incident ESRD population
- Dementia represents a contraindication to RRT initiation
  - Decisions are often difficult in clinical practice
  - Many patients with dementia are started on RRT
- The association of dementia with outcomes in incident ESRD are unclear
Dementia in Incident ESRD

  - 1,336 (3%) patients with a dementia diagnosis
- Older age, black race and comorbid conditions (especially cerebrovascular disease) were associated with dementia

Molnar MZ et al., TC-CKD data on file
Dementia in Incident ESRD

- 8,476 patients died over the first 6 months post-transition
  - 8,080 non-demented (mortality rate 411/1000 patient-years)
  - 396 demented (mortality rate 708/1000 patient-years)
- Crude hazard ratio: 1.71 (95%CI: 1.55-1.90)

Molnar MZ et al., TC-CKD data on file
HR 1.19, 95% CI: 1.03-1.37

Number at risk:
- Dementia absent: 1328
- Dementia present: 1328

Follow-up time (months):

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>No dementia</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1190</td>
<td>1181</td>
</tr>
<tr>
<td>2</td>
<td>1074</td>
<td>1030</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Molnar MZ et al., TC-CKD data on file
Using Patient Characteristics for Prognosis: Challenges

- Do we have the most relevant end points?
  - Mortality used ubiquitously
  - Other end points may be more relevant
    - E.g. hospitalization, QOL

- Do we have the most relevant characteristics?
  - Lots of data in cohorts with limited generalizability
  - Fewer data in generalizable cohorts
Conclusions

• Early mortality is extremely high in incident ESRD patients
  – Not all “mortality” is equal!!!

• Decisions about optimal ESRD transition (e.g. HD vs. PD vs. Tx vs. palliative care) should consider multiple outcomes and patient preferences

• More research needed for development of generalizable prognostic tools